Towards Non-Invasive Bladder Volume Sensing via Bio-Impedance Spectroscopy: Feasibility Demonstration in Ex-Vivo Bladder Models

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ABSTRACT

A bladder volume sensing method based on Bio-Impedance Spectroscopy (BIS) is presented in this paper. The 10 kHz to 0.5 MHz BIS is performed using a Vector Network Analyzer (VNA) on an ex-vivo porcine bladder. The bio-impedance response of the bladder is measured for a saline solution from 0 to 600 ml in increments of 100 ml. The measured data was further post-processed to establish a correlation between the change in bio-impedance data and the amount of change in bladder volume. The measurement was validated across five different bladders with three iterations per bladder for further assessment of data reliability. All experiments showed a decreasing pattern in bio-impedance magnitude with respect to the increase in the bladder volume, which indicates an inverse relationship between the bio-impedance magnitude and the bladder volume. In this regard, the Impedance Change Ratio (ICR) is proposed as a metric to quantitatively characterize the change in the measured impedance associated with the change in the bladder volume. The ICR showed the impedance decrease pattern for the volume increase.

KEYWORDS

Bio-Impedance Spectroscopy(BIS), Electrical Impedance Spectroscopy (EIS), Urinary Dysfunction, Neurogenic Bladder Dysfunction, Bladder Volume Sensing, Urinary Catheter, Urinary Retention

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1 INTRODUCTION

Many individuals suffer from the consequences of spinal cord injury (SCI) and congenital spinal anomalies such as spina bifida. Urinary incontinence and a loss of bladder sensation and control are common consequences observed in these patients. In 2016, more than 300,000 people are living with SCI in the USA [1]. According to the National Spinal Cord Injury statistical center, there are 40 new cases per million per year and approximately 80% of them will have some level of bladder dysfunction. The obvious limitation of mobility in these patients puts an extra burden on nursing and home care. The total cost of nursing and home care for these patients has been reported to be about 12.6 billion dollars in the US annually [2]. In SCI patients, the nerve problems that interfere with signals between the brain and the bladder result in the inability to recognize when their bladder is full and additionally empty the bladder volitionally. This sequela of SCI is termed neurogenic lower urinary tract dysfunction (NLUTD). A chronically overfull bladder with elevated pressure eventually causes detrimental effects such as hydronephrosis, vesicoureteral reflux, urinary tract infections, renal scarring, and ultimately, progression to end-stage renal disease [3, 4]. Most patients with SCI need to empty their bladder every two to four hours with a catheter, termed clean intermittent catheterization (CIC). In CIC, a catheter is inserted through the urethra into the bladder to drain urine on a defined schedule. Since urine is not produced on a regular schedule; SCI patients are recommended to routinely use a catheter every 2 to 4 hours during the daytime (4 to 6 times a day). Without timely CIC, patients will leak urine and most need to wear some form of protection, such as an adult diaper. Some patients go so far as to choose a permanent indwelling catheter, which leads to chronic infection and a higher risk of bladder cancer [5–7]. Understandably, the inflexible schedule of timely CIC negatively impacts patients' quality of life, especially considering these patients suffer from mobility difficulty which makes it difficult for them to visit the bathroom. This situation is even worse for quadriplegic patients who depend upon caregivers to perform CIC. The common problem with timed CIC is that during the bathroom visit, patients may only find a small amount of urine in the bladder or they may not get to the bathroom in time and leak urine. Since in reality, it is the bladder volume that dictates the need for bladder emptying rather than time, this research tried to replace the current time-triggered catheterization regimen with volume-triggered (demand-based) timely catheterization. In this regard, SCI patients can greatly benefit from an awareness system that frequently monitors the level of urine inside the patients' bladder and let them know when it is the right time for them to empty. Given a timely alert, patients can plan bathroom trips accordingly, improve compliance with the CIC regimen, protect their kidneys, avoid incontinence, increase social activities, and ultimately, improve their QOL.

2 PROPOSED APPROACH: BIO-IMPEDANCE SPECTROSCOPY

Our proposed method is the use of Bio-impedance Spectroscopy (BIS) for bladder volume sensing in humans. BIS has a great advantage over the other bio-impedance measurement techniques as it is based on the impedance response of tissue under test (TUT) over a wide span of frequencies, unlike other methods that rely on single frequency impedance measurement and result in a lumped value for the entire TUT impedance. It is expected that the BIS provides a more informative frequency-dependent bio-impedance profile of the TUT by searching over a wide frequency range to obtain the most suitable values in which the response is more detectable, measurable, and distinguishable.

This paper discusses the feasibility of BIS as the underlying sensing modality and is organized as follows: Section 3 discusses the existing approaches for bladder volume sensing. In Section 4, the VNA as a BIS measurement device is introduced and the errors associated with measurement are explained, followed by an explanation of the device calibration and data acquisition. Section 5 covers 2-port network fundamentals, including the s-parameters used by the VNA device. This is followed by a description of the different setup configurations for the BIS measurement using VNA and the conversion process of s-parameter data into impedance data. Section 7 of this paper is about the electrical modeling of the tissue. Section 8 shows the experimental measurement results in an ex-vivo porcine bladder model and discusses the data post-processing techniques used to establish a correlation between the impedance change with respect to the bladder volume change. This section is concluded with an assessment of the feasibility of the proposed sensing modality.

3 EXISTING APPROACHES FOR BLADDER VOLUME SENSING

Several methods have been evaluated for ambulatory bladder volume detection including ultrasound, pressure bio-sensor implant, bio-impedance measurement, and near-infrared spectroscopy (NIRS).

A common method for non-invasive bladder volume sensing is the use of ultrasound which despite its ubiquity in the clinical setting, has severe limitations for ambulatory use. The fact that ultrasound devices are too bulky and expensive, and their application requires training and skill, in addition to applying a gel to improve coupling between the transducer and the skin each time the patient wants to use the device, all limit its application for clinical use. Additionally, its performance is hindered by movement and fitting to different body shapes, which results in the time and effort needed for a typical SCI patient to repeatedly set up the device and to perform the procedure being more intrusive to the patient's daily life than just performing CIC instead.

A handful of studies have attempted to measure bladder volume by measuring bladder pressure using biosensors developed and implanted onto the urinary bladder wall [8–10]. Besides the method being invasive, monitoring the pressure is not a plausible means to avoid incontinence for most patients with neurogenic bladder. In practice, this method fails to be an effective measure of bladder volume for several reasons. The main reason is that sustained pressure is detrimental to kidneys and elevated pressure in the bladder should be avoided, rather than relied upon as an alarm-generation metric. Also, pressure increase happens near the urinary leakage time for most SCI patients. In those cases, pressure-triggered alerts would not provide enough time for patients to make a bathroom trip and place a catheter.

In another non-invasive method, a group of researchers leveraged near-infrared spectroscopy (NIRS) using a single light source-detector pair to determine full versus void states of the bladder [11, 12]. Due to various noise artifacts, such as geometrical variation due to breathing and exact probe position, a reliable determination of different bladder volumes using the reported NIRS setup proved infeasible.

Another non-invasive method is based on bio-impedance measurement. As electrical impedance is found to be the signature of biological tissue, which is used in clinical investigations [13]. A handful of studies used Electrical-Impedance Tomography (EIT) to estimate the conductance distribution of the pelvic region using a device embedded inside the patient's waist belt with multiple electrodes connected [14]. This method has not been successful in practice, partly due to the unreliability of skin contacts, noisy signal acquisition, and inaccurate bladder volume estimation across diverse populations.

4 MITIGATING MEASUREMENT ERRORS IN BIS MEASUREMENT

BIS relies on a small alternating (AC) signal being injected into the TUT and the impedance response of the tissue being captured over a swept frequency. While there are many devices commercially available for performing BIS, a 2-port handheld NanoVNA-F HW3.1 device is used in this project to capture the impedance response of the bladder over a range of 10 kHz to 0.5 MHz. The reason behind this choice was due to the device being portable, low cost, and more importantly, having a high measurement accuracy thanks to the high precision calibration process. VNA is a measurement device that is used to characterize and measure the scattering parameters (S-parameters) of any arbitrary network under the small AC signal excitation, which contains both a magnitude and a phase component. The fact that the VNA device requires calibration using the provided standard calibration kit before starting the measurement removes the largest contributor to measurement uncertainty, which are systematic errors.

Systematic errors are the errors between the expected measurement result and the actual measurement which do not vary over time and account for the imperfection in the VNA hardware, measurement cables, adapters, and measurement probes error. These errors are characterized through calibration and mathematically removed during the measurement process. After successful calibration of the device, the effect of VNA port extension is de-embedded up to the tip of the probe. As a result, whatever is measured by the VNA will only be the response of the TUT attached to the VNA ports. During the calibration of the device, the known loads of short, open, and 50 Ω are attached to the VNA ports. While the expected reflection for each of the loads is known, the device is calibrated such that the systematic error between the expected and measured reflections is minimized. For the systematic transmission error calibration, both ports of the VNA are shorted together. While the injected power from port1 of the VNA is known, the device is calibrated such that the received power from port2 remains the same as the injected power from port1. By solving the matrix of equations for all transmission and reflection errors, all unknown systematic errors are characterized and removed during the future measurement process.

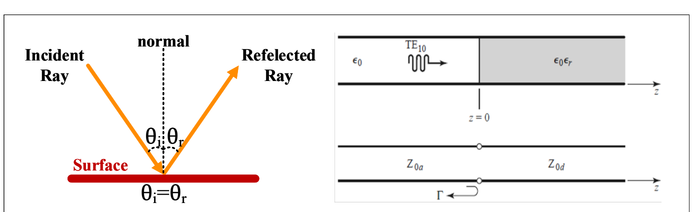


Fig. 1: Principles of reflection and transmission in Left) optics Right) electromagnetic.

5 2-PORT NETWORK PARAMETER FUNDAMENTALS

The principle behind 2-port VNA measurement is based on the 2-port network mathematical model. In this method, a 2-port network is considered a black box with properties that are specified by a 2x2 matrix of numbers. The elements of the matrix are indexed using conventional matrix notation which are frequency-dependent complex numbers. This matrix is then used to mathematically express the input and output relationships of the circuit without the need to calculate all the internal voltages and currents inside the network.

The best network model for the application is selected depending on the property of interest as well as the accuracy of the proposed model. The property of the interest can be impedance, admittance, or any other parameter. The commonly used models are referred to as Z-parameter, Y-parameter, etc. For this project, only Z, Y, and S parameters are of interest, and they are described individually below.

5.1 Z-PARAMETERS

The 2-port network model based on the Z-Parameter model, also known as the impedance parameter model, is simply the ratio of voltage over current. The unit of Z-Parameters is the Ohm (Ω). Z_{11} and Z_{21} in this model are calculated by creating an open circuit on port2 while Z_{12} and Z_{22} are calculated by creating an open circuit on port1. Hence, the Z-Parameters are also called open-circuit impedance parameters.

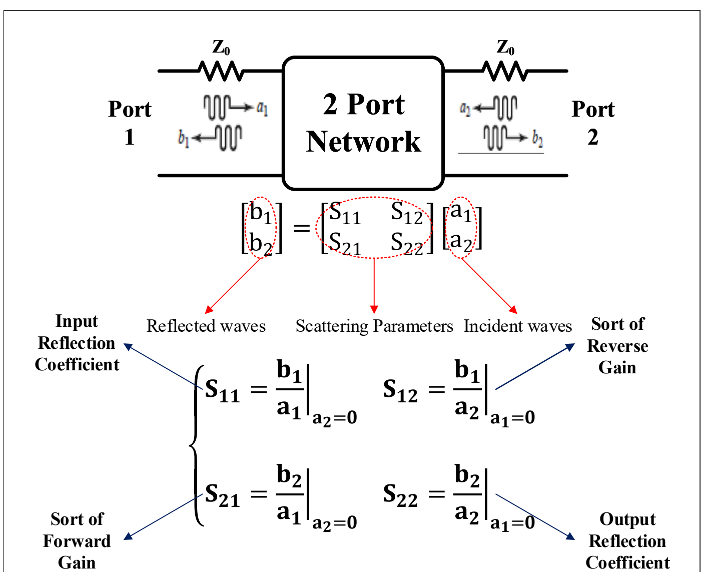
5.2 Y-PARAMETERS

Another type of 2-Port network model is based on Y-parameters, which is also called the admittance parameter model because these are simply the ratio of current over voltage. The unit of the Y-parameters is the Ohm^{-1} (Ω^{-1}). Y_{11} and Y_{21} in this model are calculated by shorting the circuit of port2 while Y_{12} and Y_{22} are calculated by shorting the circuit of port1. Hence, the Y-parameters are also called short-circuit admittance parameters. The accuracy of the models relies heavily on the accuracy of the short and open circuit conditions in the model. For example, in the Z-parameter-based network model, the open circuit condition assumes that the measurement device attached to the ports of the Device Under Test (DUT) to measure voltage does not draw any current from the network. However, because of the loading effect of the measurement device, this condition is not fully satisfied. The above-mentioned limitation of commonly used network parameters draws attention to using another type of network whose parameters are based on transmission and reflection waves. This network model is mostly used at higher frequencies where the accuracy of the model is very crucial, and this is also required for the BIS measurements in this study.

5.3 S-PARAMETERS

Figure 2 shows the network model based on scattering parameters and is denoted as the S-Parameter model. The VNA uses this type of model to characterize and measure the network parameters of the electrical 2-Port network. The motivation behind the scattering parameters is adapted from the scattering and absorption of emitted light in optics. As shown in fig. 1, when the emitted light travels from one medium to another, some of the emitted light will penetrate the boundary while some of it will be reflected from the surface, depending on the angle of radiation and the medium properties. The index of refraction in both mediums can be described using the angles of incidence and transmission through Snell's Law of refraction $n_1 sin(\theta_i) = n_2 sin(\theta_r)$. The same is true of an electromagnetic wave if it propagates from one medium to another. Depending on the dielectric properties of the materials, some of the power will be absorbed by the material, some will be reflected, and some will penetrate.

The same behavior is also observed in electronic devices when there is a mismatch between the impedance of the measurement device and the input impedance of the DUT. If an incident wave is injected from port1 of the 2-Port network and a mismatch exists between the impedance of the 2-Port network and the measurement device, some portion of the wave will reflect from port1, while the rest of the wave will enter and propagate through the network. Based on this, the scattering matrix is formed. It is the ratio of the reflected wave from a port over the incident wave to a port. S_{11} and S_{21} in this model are calculated by setting the injected signal from port2 to zero while S_{12} and S_{22} are calculated by setting the injected signal from port1 to zero. S_{11} and S_{22} are the reflection coefficients from the ports. These can be used to calculate the



$$\begin{bmatrix} b_1 \\ b_2 \end{bmatrix} = \begin{bmatrix} S_{11} & S_{12} \\ S_{21} & S_{22} \end{bmatrix} \begin{bmatrix} a_1 \\ a_2 \end{bmatrix}$$

$$S_{11} = \left.\frac{b_1}{a_1}\right|_{a_2=0} \quad S_{12} = \left.\frac{b_1}{a_2}\right|_{a_1=0}$$

$$S_{21} = \left.\frac{b_2}{a_1}\right|_{a_2=0} \quad S_{22} = \left.\frac{b_2}{a_2}\right|_{a_1=0}$$

Fig. 2: S-Parameter model of 2-port network.

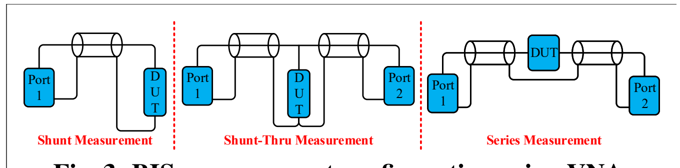


Fig. 3: BIS measurement configuration using VNA.

input and output impedance of the DUTs. S_{21} and S_{12} are sort of forward and reverse gains, which for passive elements, are forward and reverse attenuation respectively. Each element of the matrix is a frequency-dependent complex number, usually expressed in magnitude and phase. This is known as the touchstone format and is a standard in any VNA and related simulation software.

6 IMPEDANCE MEASUREMENT USING VNA

Three methods exist for accurately measuring any passive electronic components using VNA: shunt, shunt-thru, and series measurement. These measurement techniques are also applicable to the bio-impedance measurement of the bladder. The reason is that the bladder, like any biological tissue, is a lossy medium, which as discussed in Section 7 can be modeled using a capacitor and resistor. As a result, the bladder bio-impedance measurement can be treated the same way as the passive electronic components. The measurement setup and test bench are shown in figs. 3 and 4. Besides the obvious difference that the shunt measurement method relies on 1-port measurement in which the only reflection data (S_{11}) are available and the shunt-thru and series measurement are based on 2-port measurement in which the transmission data (S_{21}) are available, the major difference between these methods is related to the sensitivity of their measurement.

The conversion formula between the measured s-parameter data and impedance data and is shown in table 1. The shunt-thru configuration has the lowest measurement error for the DUTs less than 20 Ω, while the shunt configuration is good

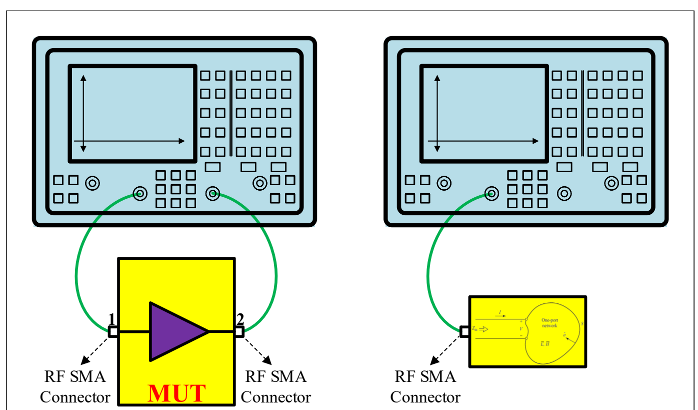


Fig. 4: 2-port and 1-port measurement test benches.

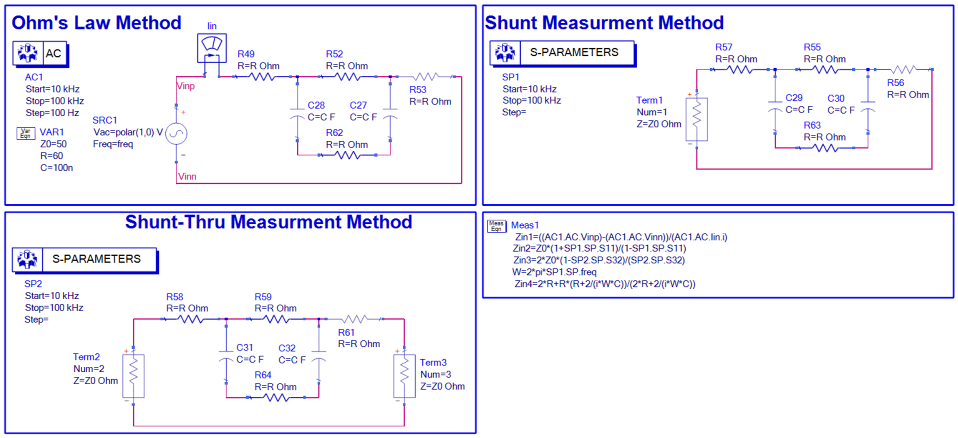


Fig. 5: Electrical impedance simulation in ADS.

to measure DUTs within the range of 20 to 80 Ω, and the series configuration is suitable for DUTs greater than 80 Ω [15]. Considering that, the DUT in this project is the bladder, which is expected to have high impedance, therefore the series configuration is the most suitable configuration for calculating the impedance data. To cross-check the conversion process, a known circuit using a lumped component is simulated in Keysight Advanced Design System (ADS) software. The test bench of this simulation is shown in fig. 5. The frequency of the simulation is swept from 10 kHz to 100 kHz and the capacitance and resistance values are selected to be 100 nF and 60 Ω, respectively. The input impedance of the circuit is calculated using the above-mentioned methods and verified against a very general method based on Ohm's law. The simulated result shown in fig. 6 indicates that all three methods are converging to the same result. The simulation result is also in line with the impedance of $Z_{in} = 2R + R||(R + 2/jc\omega)$ which is calculated theoretically.

7 ELECTRICAL MODELING OF TISSUE

Biological tissues are made up of living units called biological cells with an extracellular fluid (ECF) between them. The cells themselves are composed of a nucleus surrounded by cytoplasm and enclosed by a membrane and intracellular fluid (ICF). ECF and ICF are made of conducting materials and the cell membrane is made up of an insulating lipid bilayer. In other words, the cell membrane is sandwiched between two conductive protein layers which implies that the electrical model of the cell is a capacitor in parallel with a resistor, which corresponds to frequency-dependent electrical impedance under AC excitation.

In this direction, the impedance of tissue is found to be a combined effect of extracellular resistance (R_{ECF}), intracellular resistance (R_{ICF}), and cell membrane capacitance (C_{CM}) as shown in fig. 7. Because of nonuniform conductivity along the tissue, the values of R_{ICF}, R_{ECF}, and C_{CM} in the electrical model of tissue will be slightly different from one cell to another. Also, the relative dielectric constant and conductivity of tissue are influenced by age, gender, and other individual attributes. As such, it is difficult to accurately derive the parameters shown in fig. 7. As a result, the focus of this study is not to derive the absolute value of impedance, but rather to measure the change tendencies corresponding to urinary bladder volume.

If an alternating signal is applied to the tissue, the electrical current path within the tissue depends on R_{ECF}, R_{ICF}, C_{CM}, and the excitation signal frequency. At low frequencies, the reactance of membrane capacitance ($|X_{CM}| = 1/(C_{CM} \times \omega)$) is high compared to R_{ECF}. As a result, the AC current chooses the path of low impedance to go through, which is an extracellular path (path through R_{ECF}). On the contrary, the reactance of CM becomes low as the frequency of the signal increases, easily allowing the current to penetrate the cell membrane and pass through the cell. It can be perceived that the impedance of the cell decreases as the frequency increases.

Tab. 1: Impedance calculation using VNA

Configuration	DUT Impedance (Z_{DUT})	Sensitivity (dZ/dS)
Shunt	$Z_0(1 + S_{11})/(1 - S_{11})$	$2Z_0/(1 - S_{11})^2$
Shunt-Tru	$Z_0(S_{21})/2(1 - S_{21})$	$Z_0/2(1 - S_{21})^2$
Series	$2Z_0(1 - S_{21})/S_{21}$	$-2Z_0/{S_{21}}^2$

8 EXPERIMENTAL RESULTS

8.1 Measurement Setup

The BIS of 10 kHz to 0.5 MHz is conducted on an ex-vivo porcine bladder using a handheld NanoVNA-F HW3.1 device. For reliable skin connection, the 50Ω surface mount (SMD) miniature IPEX U.FL connectors are used to connect the tip of the probe to the bladder. The measurement was validated

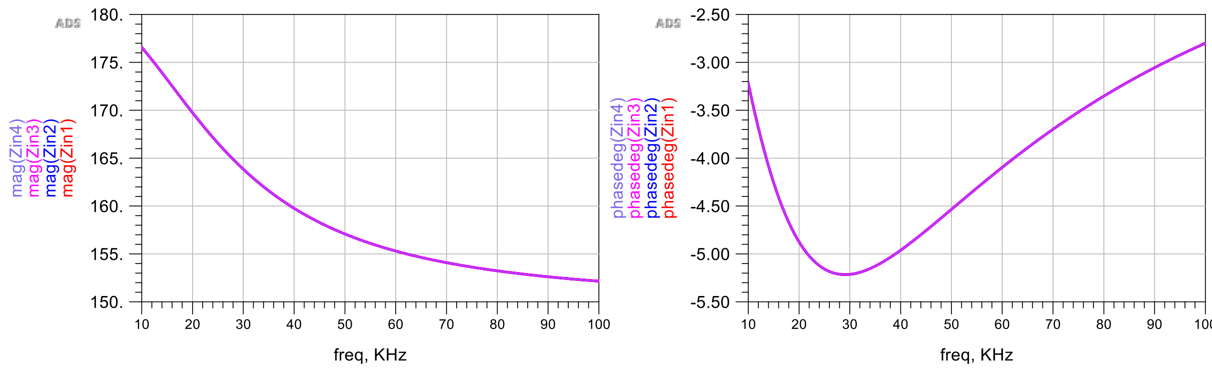


Fig. 6: Plot of input impedance versus frequency Left) magnitude Right) phase.

across five different bladders with three iterations per bladder for further assessment of data reliability. The bladder was filled with 0.9 % saline solution in 100 ml increments up to its maximum capacity of 600 ml. 0.9% saline solution was chosen as a filling liquid because of its electrical properties bearing resemblance to human urine. The connectors were attached to the bottom of the bladder wall with 1cm spacing which is shown in fig. 8. The other side of the connector was connected to a coaxial cable and extended to reach the VNA which performs BIS. The VNA was also connected to the computer for data acquisition of the Bladder Under Test (BUT) response.

The SOLT calibration technique was used for VNA calibration and to remove systematic measurement errors. Because the number of sweep points on the device was limited to 301, the frequency range of 10 kHz to 0.5 MHz for BIS was divided into smaller frequency spans to achieve higher accuracy

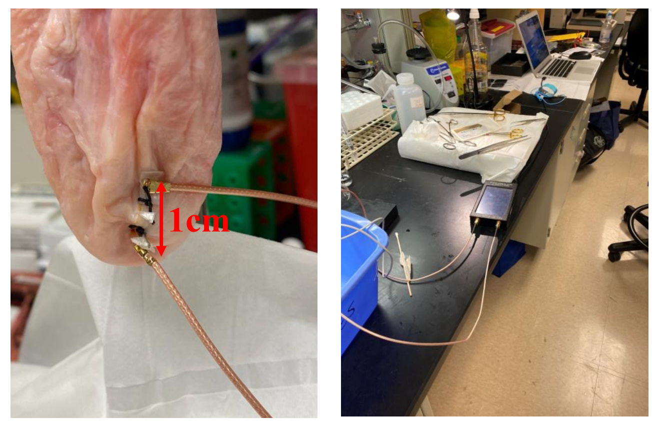


Fig. 8: Ex-vivo measurement test bench for invasive estimation of bladder volume based on BIS using VNA.

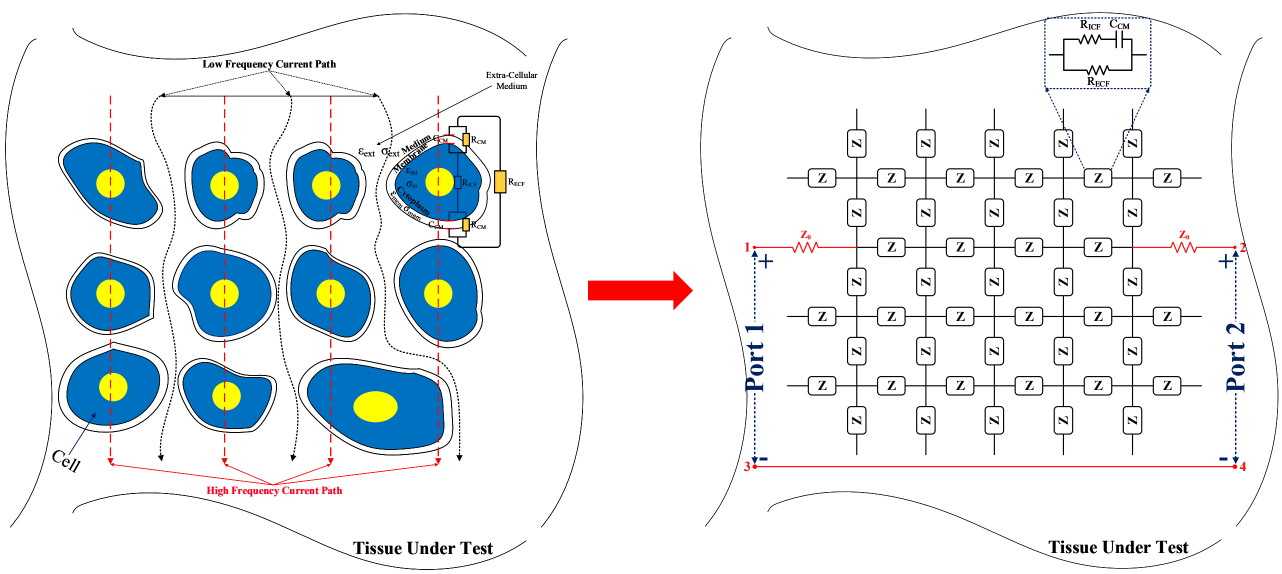
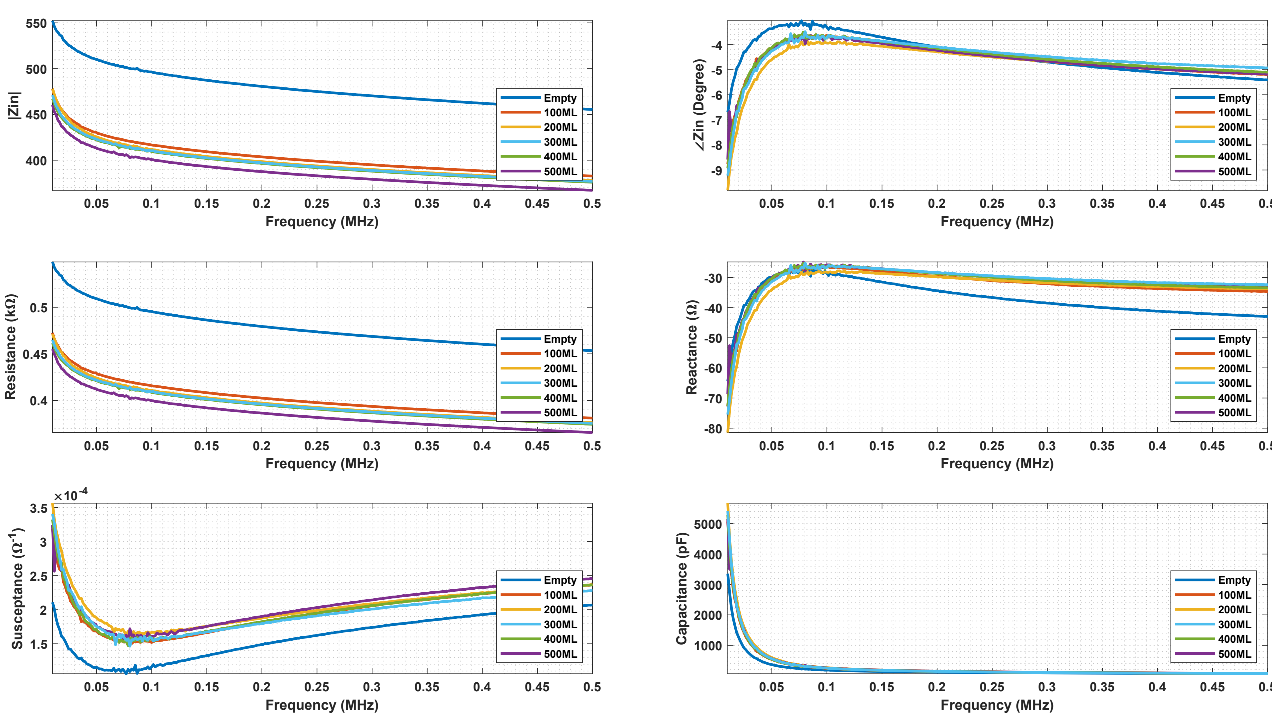


Fig. 7: Electrical modeling of TUT



(f)

Fig. 9: a) Bio-impedance magnitude b) Bio-impedance phase c) Bio-resistance d) Bio-reactance e) Bio-susceptance f) Bio-capacitance response of bladder from 10 kHz to 0.5 MHz for solution filling from 0 to 600 ml in the increments of 100 ml.

for broadband calibration and measurement. The collected s-parameter data were stored in the computer and used to calculate the bio-impedance of BUT using the formula of table 1.

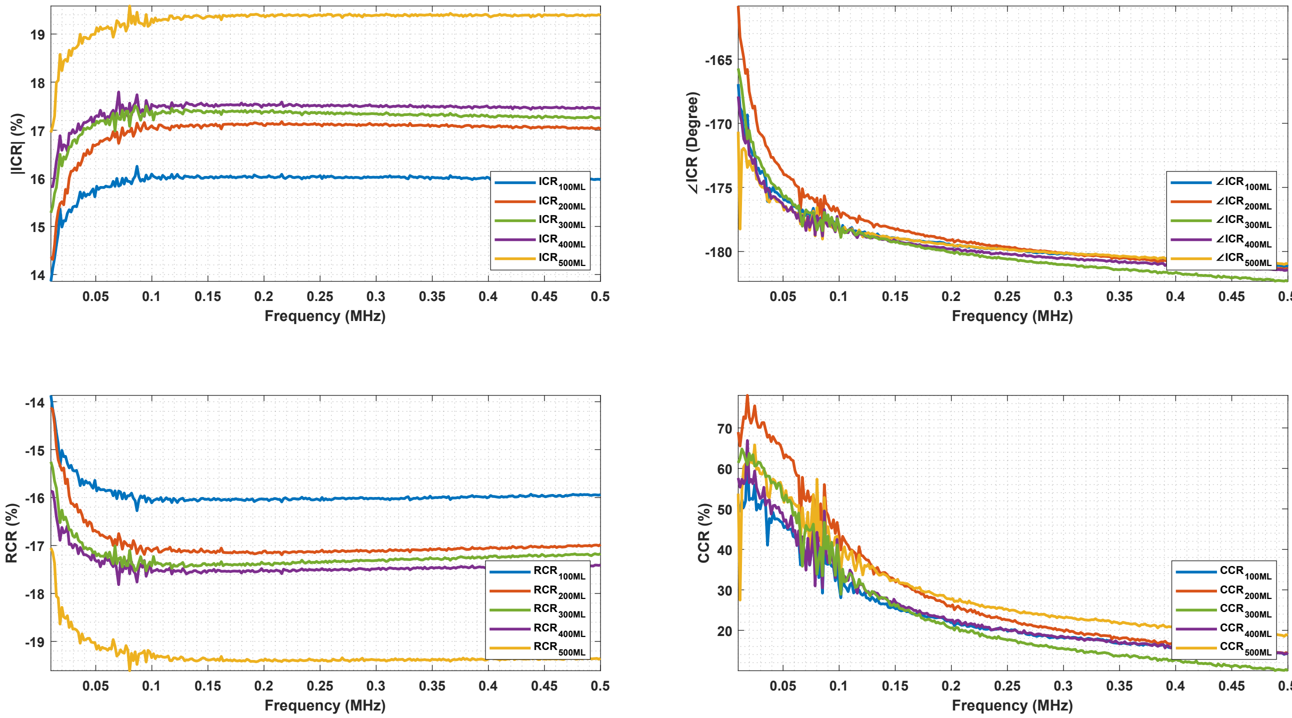
8.2 Results

The magnitude of the measured bladder bio-impedance response from 10 kHz to 0.5 MHz is shown in fig. 9a which was acquired for saline solution fillings ranging from 0 to 600 ml in increments of 100 ml. As seen in Figure 9a, the magnitude of the bio-impedance response of the bladder tends to decrease as the frequency increases. Also, it is seen that the bio-impedance magnitude tends to decrease with the increase of bladder volume which indicates an inverse relationship between the bio-impedance magnitude and the bladder volume which is aligned with the studies of [16].

The measured bio-impedance data were further used to calculate bio-resistance ($R(f) = \Re\{Z(f)\}$) and bio-reactance ($X(f) = \Im\{Z(f)\}$) which respectively are the real and imaginary parts of bio-impedance. From electrical modeling of tissue in section 7, it was expected that the capacitance in the model would result in the bio-impedance phase and bio-reactance holding negative values and the bio-resistance and bio-susceptance holding positive values. Bio-susceptance is the imaginary part of bio-admittance ($B(f) = \Im\{Y(f)\}$) which is further used to calculate the capacitance of the BUT by dividing it by the angular frequency. ($C(f) = B(f)/(2\pi f)$).

Figure 9b and fig. 9d show the bio-impedance phase and bio-reactance of BUT, respectively. As expected, the phase and reactance of the bio-impedance response always stay negative, indicating the bladder system has a capacitive response and is in line with the electrical modeling of tissue in section 7. Furthermore, bio-resistance, bio-susceptance, and bio-capacitance plots of the measured BUT as shown in fig. 9c, fig. 9e and fig. 9f all show positive values, as expected.

The focus of this study is not to derive the absolute value of impedance, but rather to measure the change tendencies corresponding to urinary bladder volume. To quantitatively characterize the bio-impedance change observed with respect to the change in bladder volume, three metrics are defined. The first metric is defined as the Impedance Change Ratio (ICR) which is the difference between the last measured impedance and the reference measured impedance (Z_{ref}) divided by the reference impedance, expressed as a percentage. The reference measured impedance (Z_{ref}) is the impedance of the BUT each time the bladder is emptied. The mathematical expression for the ICR calculation is shown in eq. (1) where ICR is a



(d)

Fig. 10: a) Impedance change ratio magnitude b) Impedance change ratio phase c) Resistance change ratio d) Capacitance change ratio response of bladder from 10 kHz to 0.5 MHz for solution filling from 0 to 600 ml in the increments of 100 ml.

frequency-dependent complex vector that has both magnitude and phase values.

$$ICR(f) = \frac{Z(f) - Z_{ref}(f)}{Z_{ref}(f)} \times 100\% \tag{1}$$

Figure 10a and fig. 10b respectively show the magnitude and phase plots of ICR. Since the bio-impedance decreases with the increase in bladder volume, it was expected that the ICR magnitude increases as the bladder volume increases.

In the same way, the second and third metrics can be defined as Resistance Change Ratio (RCR) and Capacitance Change Ratio (CCR), respectively which are unlike the ICR takes on the real values. Figure 10c and fig. 10d shows RCR and CCR plots. As is seen the RCR holds negative values. The reason is that the resistance of BUT tends to decrease with the increase in bladder volume which results in the difference between the last measured data being negative.

The reliability of the measurement was verified across five different bladders as well as a three-time iteration on each bladder. The correlation between the bio-impedance data and the bladder volume was observed in all the experiments. The major difference between them was related to the measured reference values (Empty state). However, as mentioned earlier, the objective of the project was not about finding absolute values for bladder impedance but rather a correlation between the bio-impedance change with respect to the bladder volume change. As a result, the consistent correlation between the defined metrics was relied upon to draw a conclusion. The ICR and RCR in all experiments showed a correlation between the bio-impedance measured data and the bladder volume.

8.3 Discussion

Like any other bladder volume sensing method, the proposed BIS measurement in a human subject is expected to have other contributors to the measured bio-impedance data other than the contributor of interest, the amount of urine inside the bladder. As a result, using the proposed method for the human subject in the future requires a thorough study of the other contributors to the BIS measurement. In addition, there are several limitations that need to be explored before expecting a fully functional system, some of which are discussed below.

(A) The Skin Contact Location

The optimum location for the skin contacts, the spacing between the contacts, and the number of contacts are yet to be explored and have to be determined before expecting a reliable measurement from the proposed method. It is expected that in some locations, the sensitivity of the measured BIS data will be high for the urine volume changes compared to the other locations.

(B) Input Power Level
It is expected that for a certain input power level the sensitivity of ICR with respect to the bladder volume changes to be high compared to others because the input power affects which tissue depth is most strongly measured. Furthermore, the input power level needs to be low enough to ensure patient safety. Based on these two parameters, the optimal input power level can be found.

(C) Baseline Variation
The measured BIS data for the patient may start at different baselines (bladder empty state) or have a different change in frequency response from one bladder filling cycle to the next. One reason for this variation is a difference in urine conductivity, which is dependent on the patient's diet, among other factors. One way to overcome this challenge would be to have the user or caregiver in the loop to notify the system of bladder catheterization, so the device is made aware of the baseline for the subsequent empty state of the bladder.

Besides what is discussed above, the errors in the measured BIS data can be divided into 2 categories: systematic errors and random errors. An error is considered systematic if it changes in a pattern. For example, this could happen with BIS measurements if, just before the measurements were to be made, something always or often caused the measured BIS data to go up. Since the behavioral pattern of this error is deterministic, the error can be canceled out by subtracting it from the measurement result. The actual system can remove systematic errors by utilizing multiple sensing electrodes to take advantage of differential sensing, as shown in fig. 11. Random errors in the data can be addressed by capturing the pattern of the patient's bladder voiding and the amount of urine after voiding. Given enough measurement data, the bladder volume estimation algorithm supported by reinforcement learning is expected to cancel out the effect of random error on the measured data which will be addressed in our future work after the complete system is built up.

8.4 Comparison with Alternative Sensing Modalities

Table 2 compares the overall accuracy, cost, ease of use, and the current development stage of different sensing methods used in wearable bladder monitoring. The accuracy of ultrasonic devices is moderate to high; however, it requires a coupling gel to improve coupling between the transducer and the skin which in turn impacts its cost and ease of use. The NIRS devices on the other hand are easy and inexpensive to use; however, their accuracy is less compared to the ultrasonic devices. The bio-implantable sensors are more accurate than other sensing modalities. However, research in this area is still in its infancy. The advantage of the proposed BIS sensing modality compared to the state of the art is the device's portability, low cost, and ease of use which does not require professional assistance and more importantly, has high measurement accuracy thanks to the advance and high precision calibration process.

9 FUTURE WORK

The proposed method has the potential of extending its use as a non-invasive, small, wearable device with multiple sensing electrodes which can be worn by SCI patients. Figure 11 shows a conceptual high-level illustration for urine volume detection in the human bladder. The sensing electrodes can be placed in the lower abdomen (pelvic area) of a patient and the device can sit on top of the electrodes which are embedded inside the patient's waist belt and powered by a battery. The complex bio-impedance can then be measured over time within the BIS frequency range. The measured impedance data can further be post-process to establish a correlation between impedance change with respect to bladder volume change. The device can frequently trigger measurements to strike a balance between sensing bio-impedance and battery life. The reinforcement-learning techniques can be used to incrementally improve estimation accuracy as the patients use the device, and can automatically personalize the prediction algorithm to better serve the SCI patient's specific situation.

A patient alert mechanism can be implemented in several possible ways. Examples include on the device (e.g., a discreet ringtone or vibration) for device self-sufficiency; shown on the patient's smart devices (e.g., a smartwatch); implemented by a dedicated uninterruptible alarm (e.g., a vibrating wristband that can be turned off only by the device as the bladder volume reduces: mimicking the natural feeling of urge-to-urinate which is relieved only as the bladder is being

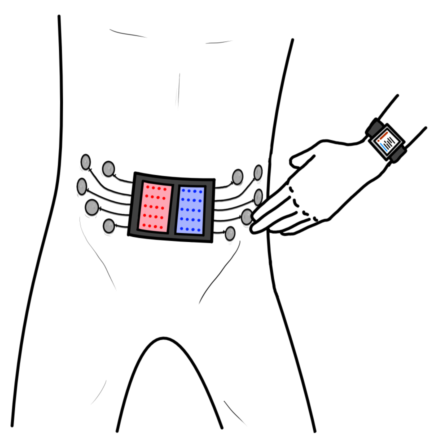


Fig. 11: High-level illustration of non-invasive bladder volume sensor.

Tab. 2: Comparative assessment of leading approaches to bladder volume sensing.

Sensing Modality	Accuracy	Cost	Ease of Use	Development Stage	Non-Invasive	Ref.
Ultrasound	Moderate to High	Medium	Moderate	Production	yes	[17]
Near Infrared Spectroscopy	Low	Low	Easy	Experimental	yes	[11, 12, 18]
Implantable Capacitive Sensors	High	High	Difficult	Prototype	no	[19]
Bio-Impedance Spectroscopy	Moderate to High	Low	Easy	Experimental	yes	This work

emptied); or sent to patient's caregivers. The best strategy would depend on the patient's preferences and circumstances.

The proposed method is meant to alert the patient and their caregiver about the bladder volume who in turn, will be in a position to close the loop by making a trip to the bathroom and emptying the bladder via catheterization. Inaccuracy in bladder volume sensing will degrade the control objective. Specifically, underestimating the bladder volume may lead to trips to the bathroom before the bladder is sufficiently filled, which is inconvenient for the user and will reduce the practical utility of the system. Overestimating the bladder volume may lead to delayed emptying of the bladder, which runs the risk of renal health issues in the long term or incontinence. Given the integration of human operators in the loop and the possible space of control actions (ignoring the alert or emptying the bladder), the resulting CPS system will not realistically face control issues such as stability. It is expected that human operators will develop an understanding of the sensing accuracy, and can adjust their control actions to balance out any predictable sensor inaccuracy to still gain value from the technology.

10 CONCLUSION

The feasibility of BIS as a sensing modality was investigated through an ex-vivo measurement. The s-parameter data was acquired using the VNA device and used to obtain the bio-impedance data. The bio-impedance data was further used to establish a correlation between the change in bio-impedance data and the change in bladder volume. The bio-impedance magnitude showed a decreasing pattern with respect to the increase in the bladder volume, which indicates an inverse relationship between the bio-impedance magnitude and the bladder volume. In this regard, ICR, RCR, and CCR are proposed as metrics to quantitatively characterize this relationship. The ex-vivo measurement showed promising results for bladder volume sensing using BIS.

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