DESIGN AND TESTING OF A DEVICE FOR HUMAN LIMB MULTIFREQUENCY COMPARATIVE BIOIMPEDANCE MEASUREMENT- PRELIMINARY STUDY

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Abstract

Bioimpedance is the ability of biological tissues to impede the flow of electrical current. It is often measured as a means of detecting volume and structural changes in various biological tissues. The purpose of this work was to design a twochannel portable device for measuring multifrequency bioimpedance of human limbs. The device was constructed specifically for evaluation of the bioimpedance measurement as a possible tool for aiding in diagnosis of soft-tissue structural changes in the muscles of human limbs by continuously comparing bioimpedance of one limb to the other. The proposed device is based on impedance converter AD5933. It is designed for noninvasive measurements on the human body with low amplitude alternating current at frequencies between 1 kHz and 100 kHz. The device was tested for electromagnetic compatibility, accuracy and used in laboratory measurements for detection of muscle edema on a bioimpedance model. It is capable of measuring impedance up to 100 k Ω with a relative measurement error below 1.84%.

Keywords

bioimpedance, noninvasive diagnostics, AD5933, acute compartment syndrome

Introduction

Bioimpedance measurement is most often used to record small changes in impedance depending on heart and lung function and thus provide information on changes in volumes, i.e., plethysmography [1], in the lungs, heart, and blood vessels. The second most common application of the method is to estimate body composition, which includes the percentage of fat in the body, the total volume of fluids, and the ratio of intracellular and extracellular fluids [2]. Different impedance values of different tissue types are also used by the electrical impedance tomography imaging method [3]. This method uses many electrodes, most often ranging from 16 to 64. Cross-sectional images of tissues are generated that show distribution of conductivity. The method provides a much lower contrast compared to conventional imaging methods. However, it can be used to non-invasively and continuously create images using electrodes applied to the surface of the body. With the help of these images, even small changes in tissue conductivity can be quickly captured, which can occur due to blood flow, respiration, or fluid transfer.

The main mechanism of the tissue electrical impedance changes following trauma or muscular tissue destruction is a reduction in resistance due to an increase in the volume of extracellular fluid, which is caused by tissue swelling [4]. Another significant change in impedance is a reduction in capacitive reactance, and therefore in the total phase angle, in pathological tissue conditions. This reduction can be expected with cell membrane disruption because the capacitive character of bioimpedance is caused mainly by the capacitance of cell membranes and when the cells die, the membranes are destroyed and the intracellular fluid is released into the extracellular space [5, 6].

This makes bioimpedance measurement ideal for monitoring soft tissue changes. The application of the method of measuring bioimpedance, which is closest to the goal of this work, is the method of electrical impedance myography (EIM) [7, 8], which includes a group of methods examining muscle tissue. The most common muscle disorders that EIM could diagnose include myopathy, sarcopenia, neuropathy, or amyotrophic lateral sclerosis. The aim of EIM is not the imaging of muscle tissue, but the quantitative evaluation of changes in the microscopic structures of muscle tissues resulting from neuromuscular diseases. This method has been successfully tested for edema detection in human limbs, specifically in the ankle [9] and the knee [10]. It can also provide a more robust way of monitoring muscle contraction than a standard electromyography measurement [11, 12]. And muscle bioimpedance value can also change following eccentric exercise of the muscles [13].

Concerning the measurement of soft tissue changes, the diagnosis of lymphedema [14], a chronic disorder characterized by swelling of the limbs due to insufficient function of the lymphatic system, is a frequently researched application of bioimpedance measurement as well. So far, no measurement method has been adopted as the gold standard for the diagnosis of this disease, but a possible candidate is the measurement of bioimpedance. Compartment syndrome is another condition that could be diagnosed using bioimpedance measurement, because both swelling and subsequent hypoxia are present [15], a corresponding change in impedance and phase angle can be expected. Thus, the measurement of bioimpedance appears to be a theoretically suitable method for the diagnosis of acute compartment syndrome (ACS) or other muscular injuries and diseases.

Two studies dealing with the use of bioimpedance measurement for detection of acute compartment syndrome were published by Tonkovic et al. and their results indicated the possible use of this method [16, 17]. The study was done on 29 patients with a confirmed diagnosis of ACS of one lower limb. Bioimpedance and intramuscular pressure (IMP) were measured on both lower limbs and the values were compared between the injured and uninjured limbs. Patients with ACS showed a large difference between the limbs in both (IMP) and impedance values. On average, the damaged limb had 18 mmHg higher IMP and 346 Ω lower impedance. The control group with healthy limbs had this difference on average of only 1.2 mmHg and 29.9 Ω .

According to mentioned research papers, bioimpedance could be a suitable method for detecting edema and structural changes in muscle compartments. The device was constructed specifically for evaluation of the bioimpedance measurement as a possible tool for aiding in diagnosis of soft-tissue structural changes in the muscles of human limbs. The hypothesis of using such a device is that when measuring the bioimpedance of both limbs at the same time, with placement on the contralateral muscle compartments of the limbs, it should be possible to detect a change in bioimpedance due to local structural changes. These changes include edema or muscular damage due to exercise, trauma, or muscular disease. A shortcoming of this approach is that it cannot be expected that the patient will always have only one limb damaged, which may make it impossible to use the device in certain cases.

The remaining chapters of this work deal with designing a device for testing this hypothesis and testing and evaluating the proposed device.

Device design

The core of the device is an integrated impedance converter AD5933 (Analog Devices, Massachusetts, USA). It is capable of measuring impedance and phase angle at frequencies from 1 kHz to 100 kHz. The measurement along this frequency range is performed through a frequency sweep with an adjustable settling duration at each frequency and an adjustable number of frequencies of each sweep. The proposed device uses two AD5933 chips for simultaneous measurement of both limbs. Each chip needs an analog frontend circuit for improving accuracy and ensuring compliance with medical device regulations.



Fig. 1: Block diagram of the proposed device. The AD5933 ICs are connected to the patient through an analog frontend monitoring circuit and the results are sent to Arduino Nano.

The block diagram of the proposed device can be found in Fig. 1. The measurement circuit incorporating the AD5933 chip will be connected to a selected compartment either on the lower or upper limb and the other circuit will be connected to the contralateral compartment (for example left and right leg, both on the same compartment of the calf). Standard adhesive ECG electrodes will be used for the measurements.

The measured values are processed by an Arduino Nano, which is responsible for controlling the device, initiating bioimpedance measurement, saving and displaying data. The data is stored on a microSD card along with time stamps generated by a real-time clock module. The device also features an LCD capable of displaying currently measured data. Specifications of the proposed device can be found in Table 1.

Table 1: Electrical characteristics of the batterypowered portable device for two-channel bioimpedance measurement.

Parameter	Value		
Impedance Range	$10 \ \Omega - 100 \ k\Omega$		
Frequency Range	1–100 kHz		
Supply Voltage	7–12 V		
Operating Voltage	5 V		
Current	30 mA—Standby mode		
Consumption	80 mA—Measurement mode		
Measurement	580 mV_{pp}		
Voltage			
Measurement	max. 242 µA _{pp}		
Current			

The AD5933 generates a sine-wave measurement signal with a DC offset. Both the amplitude of the signal and the DC offset are dependent upon the chosen range. The DC offset is removed in the frontend circuit with a first-order high pass filter because it cannot be applied to the patient. It could cause polarization of the electrodes during the measurement and distort the values of the measured impedance as well as increase the total current through the patient. The AD5933 measures the real and imaginary components of the impedance via the Discrete Fourier transform (DFT) algorithm, and the exact value of impedance and phase angle is then calculated in the Arduino. To compute the correct value of impedance, the amplification of the frontend circuit needs to be considered. For determining the phase angle, it is necessary to always subtract the system phase from any given result, which is the phase shift caused by the measurement circuit itself.

The safety of the patient is of the utmost importance when constructing medical devices and for this reason, the maximum value of current through the patient is limited by current-limiting resistors and is safely below the limit value set by the IEC 60601-1 standard.

When measuring bioimpedance in the frequency range from 50 kHz to 100 kHz, the electrode-skin interface shows about 2 to 10 times higher value of impedance than human soft tissue [18]. When using only 2 electrodes, it is impossible to measure the exact impedance value of the tissue, because the impedances

of the two interfaces between the electrodes and the skin are always added to the measured values. However, a bipolar electrode connection shows smaller dependence on the correct placement of the electrodes and it is not necessary to obtain the exact value of the impedance, but rather to compare the impedances of the two limbs against each other [19]. The device can be used in either of these two measurement modes.

Testing and Evaluation

To ensure the device is ready for evaluation in the clinical setting, a series of tests was designed. These include accuracy evaluation, electromagnetic compatibility, and laboratory experiments.

The values of bioimpedance measured on patients can be expected to be below 50 k Ω , so to verify the accuracy of impedance measurements of the proposed device, high-precision resistors ranging from 50 Ω to 50 k Ω were measured with both channels of the device.

The accuracy of the device was also tested by measuring the complex impedance of an RC bioimpedance model. A Cole-Cole model was chosen, i.e., a resistor modeling the resistance of an extracellular fluid R_e connected in parallel with a capacitor C_m and resistor R_i . The R_i represents the resistance of the intracellular fluid and the capacitor models the capacity of the cell membranes and is characterized by its frequency-dependent capacitance X_c . The values used are shown in Fig. 2.

Many models have been proposed for characterizing the behavior of living tissue bioimpedance. Biological tissues are composed of cells and the cell membranes can be thought of as a dielectric between two plates of a capacitor. These plates are composed of intracellular and extracellular fluids. Bioimpedance models range from simple RC single-dispersion models to multiscaled models with constant phase elements for multiple dispersions over a wider frequency range [6, 20]. The model used in this work is a simple singledispersion RC model because it was used only for gauging the accuracy of impedance measurement of a circuit with a capacitive character.

The following equation was used to determine the real component of the impedance values of the model:

$$R = \frac{R_i R_e * (R_i + R_e) + R_e X_c^2}{(R_e + R_i)^2 - X_c^2}.$$
 (1)

To determine the reactance i.e., the imaginary component of the impedance, the following equation was used:

$$X = \frac{X_c R_i R_e - R_e X_c^* (R_i + R_e)}{(R_e + R_i)^2 - X_c^2}.$$
 (2)

The results of the impedance measured by both channels of the device were compared to the values of the model determined by calculations and a precise impedance analyzer ISX-3 (Sciospec Scientific Instruments, Bennewitz, Germany) in bipolar measurement mode. The measurements were performed for 8 frequencies between 10 and 90 kHz.



Fig. 2: Values of the Cole-Cole bioimpedance model components.



Fig. 3: Lab experiment: Top—Measurement setup with one channel of the device connected to a turkey leg in tetrapolar configuration; Middle—Injecting saline to increase IMP; Bottom—IMP measurement in the meat with intramuscular pressure monitor.

A laboratory experiment on a piece of commercial meat (turkey leg) was conducted as a preliminary test of the hypothesis, that muscular tissue edema would change bioimpedance values. The setup of the experiment is shown in Fig. 3. The turkey legs were kept at room temperature with constant bioimpedance monitoring with one-channel tetrapolar configuration. The meat was injected with saline solution during measurement to artificially increase IMP. The pressure was then measured with Stryker Compartment Pressure Monitor (C2Dx, Michigan, USA).

Results

The results of the accuracy tests show that the device can measure resistances in the defined range with absolute deviation of phase angle under 1°. The relative deviation of impedance in the tested range was under 1.84% for the right channel and less than 1.08% for the left channel. The values are summarized in Table 2.

Table 2: Results of the accuracy tests on resistors for both channels showing the values of precision resistors and the values measured by both channels of the device both impedance and phase angle

device, boin impedance and phase angle.					
	Impedance	Phase	Impedance	Phase	
Resistor	right	angle	left	angle	
value	channel	right	channel	left	
(Ω)	(Ω)	channel	(Ω)	channel	
		(°)		(°)	
50	50.92	0.77	49.91	-0.04	
100	101.62	0.51	99.64	0.51	
200	203.59	0.61	199.37	0.37	
500	506.30	0.71	500.15	0.49	
1000	1015.32	0.64	1004.67	0.53	
2000	2024.23	0.57	2004.18	0.60	
5000	5045.24	0.53	4994.09	0.50	
10000	10100.02	0.32	9989.66	0.31	
20000	20115.21	-0.02	19897.35	0.01	
50000	50107.00	-1.02	49458.33	-0.87	

The differences between the calculated values and the reference bioimpedance analyzer on the RC model can be explained by non-ideal components and their deviations from the declared values. Impedance values are plotted in Fig. 4 and the phase angle is shown in Fig. 5.



Fig. 4: Impedance in the frequency spectrum between 10 and 90 kHz showing the calculated values, ScioSpec analyzer and values from both channels of the proposed device.

The measured impedance results of the proposed device differ only slightly compared to the values from the impedance analyzer. The average absolute deviation between them was 7.49 Ω for the right channel and only 1.48 Ω for the left channel.



Fig. 5: Phase angle in the frequency spectrum between 10 and 90 kHz showing the calculated values, ScioSpec analyzer and values from both channels of the proposed device.

The phase angle results in Fig. 5 show an absolute deviation from the values measured by the analyzer of 2.85° for the right channel and 2.73° for the left. The difference between the left and right channel was negligible, which is important, concerning the purpose of the device is to compare the impedances of the two compartments measured simultaneously by both channels of the proposed device.



Fig. 6: Measurement 1 impedance plot showing that each saline injection decreased impedance of the measured tissue.

The impedance results of the first laboratory experiment on turkey leg are shown in Fig. 6. The moments of saline injections are highlighted by a red asterisk. Each injection decreased the measured impedance significantly. Green asterisk shows when the IMP measurements were made. A slight change in impedance can be observed during IMP measurement when the needle is inserted between the measurement electrodes. This change however quickly returns to baseline.

In the second measurement there is a certain tendency of both impedance and phase angle values to return to baseline after each saline injection, which was caused by leakage of the saline from the turkey leg because the skin did not cover the whole leg to prevent the liquid from escaping. The impedance is plotted in Fig. 7 and phase angle in Fig. 8.



Fig. 7: Measurement 2 impedance plot showing similar behavior as measurement 1 and each injection lower impedance.



Fig. 8: Measurement 2 phase angle values were also affected with each saline injection.

It can be seen from the results of the preliminary laboratory experiments that injecting saline, which models edema of the tissues, can in fact decrease both impedance and phase angle of the measured tissues.

The device was also tested for electromagnetic compatibility, and it was found, that no significant

interference is caused by it. It is also resistant to electrostatic discharges applied with air discharge method up to 10 kV with only the LCD panel being susceptible. The LCD however is not an essential part, and its malfunction does not interfere with the basic functions of the device, which are collecting and saving data of the measured impedances.

Discussion

The proposed device was designed specifically for simultaneously measuring contralateral muscle compartments in human limbs to monitor soft tissue changes like edema, cell damage and more.

The accuracy testing showed that both channels of the device are capable of measuring impedance of resistors in the range between 50 Ω to 50 k Ω with relative measurement error below 1.84%. The impedance converter AD5933 has also been used in many studies focused on creating a low-cost impedance measurement device, with uses ranging from bioimpedance of the human body [21, 22] and/or plants [23] to the impedance of technical objects for monitoring of corrosion [24, 25]. The available studies vary in the analog circuits used for interfacing the AD5933 to the device under test. But most of the studies show similar levels of accuracy using this integrated circuit. Hoja et al. used two AD5933 ICs to measure single impedance, using one for measuring the voltage and one for measuring current flowing through the circuit in tetrapolar configuration with the result of relative error in impedance modulus of $\pm 1.6\%$ [24]. Schwarzenberger et al. achieved 2% relative error when measuring cell cultures [26]. The AD5933 was also used as an implantable bioimpedance monitor with Zigbee enabled and the authors reached a relative error of measurement of 2.5%. And the same accuracy was reached by Margo et al. when designing a system for tetrapolar measurement for physiological samples [27].

The accuracy of the proposed solution is comparable to the devices based on the same impedance converter integrated circuit designed by other authors for various bioimpedance measurements. Another part of this work was testing the hypothesis that increased extracellular fluid would be detectable with the proposed device. This was verified with a laboratory experiment using injected saline solution and measuring intramuscular pressure. In all cases the increase in fluid lead also to an increase in IMP and decrease in impedance.

The device is capable of monitoring impedance of soft tissues and could therefore be used for monitoring developing edemas, for example in patients at risk of acute compartment syndrome onset. A bioimpedance measuring device that would be used would however need to be able to communicate wirelessly and notify or alarm when the values of bioimpedance would start to decrease. Future directions for this device should be clinical testing whether this method could be useful to improve diagnostic accuracy in such conditions as ACS. For this reason, the device was evaluated by the ethical committee of the University Hospital of Ostrava, Czech Republic and it was allowed for longterm measurements and data collection in patients suffering lower limb fractures, which are at risk of developing acute compartment syndrome.

Conclusion

Bioimpedance measurement is a simple way of monitoring the structural changes in soft tissues that has potential in aiding the diagnosis of several conditions, most notably acute compartment syndrome. The proposed device for evaluation of the onset of soft tissue structural changes in the limbs based on the measurement of bioimpedance was constructed and tested. Basic accuracy and safety tests were performed and based on these results the device is ready to be used to test the suitability of the bilateral bioimpedance measurement method in a clinical setting for monitoring of structural changes in muscles of the limbs. Testing the method of measuring bioimpedance in patients in a clinical setting can provide important data for considering this method as a viable tool in diagnosing the onset of ACS and other soft tissue structural changes noninvasively in the future. The proposed device showed comparable accuracy to other similar devices described in the literature.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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References

- Piuzzi E, Pisa S, Pittella E, Podestà L, Sangiovanni S. Low-cost and portable impedance plethysmography system for the simultaneous detection of respiratory and heart activities. IEEE Sensors Journal. 2018 Dec 19;19(7):2735–46. DOI: 10.1109/JSEN.2018.2887303
- [2] Campa F, Toselli S, Mazzilli M, Gobbo LA, Coratella G. Assessment of body composition in athletes: A narrative review of available methods with special reference to quantitative and qualitative bioimpedance analysis. Nutrients. 2021 May 12; 13(5):1620. DOI: <u>10.3390/nu13051620</u>
- [3] Adler A, Boyle A. Electrical impedance tomography: Tissue properties to image measures. IEEE Transactions on Biomedical Engineering. 2017 Jul 17;64(11):2494–504. DOI: <u>10.1109/TBME.2017.2728323</u>
- Kassanos P. Bioimpedance Sensors: A Tutorial. IEEE Sensors Journal. 2021 Sep 3;21(20):22190–219.
 DOI: <u>10.1109/JSEN.2021.3110283</u>
- [5] Bera TK. Bioelectrical Impedance Methods for Noninvasive Health Monitoring: A Review. Journal of Medical Engineering. 2014 Jun 17;2014:381251. DOI: <u>10.1155/2014/381251</u>
- [6] Naranjo-Hernández D, Reina-Tosina J, Min M. Fundamentals, Recent Advances, and Future Challenges in Bioimpedance Devices for Healthcare Applications. Journal of Sensors. 2019 Jul 15;2019:9210258. DOI: <u>10.1155/2019/9210258</u>
- [7] Rutkove SB. Electrical impedance myography: Background, current state, and future directions. Muscle & Nerve. 2009 Sep 18;40(6):936–46. DOI: <u>10.1002/mus.21362</u>
- [8] Li L, Shin H, Li X, Li S, Zhou P. Localized Electrical Impedance Myography of the Biceps Brachii Muscle during Different Levels of Isometric Contraction and Fatigue. Sensors. 2016 Apr 22;16(4):581. DOI: <u>10.3390/s16040581</u>
- [9] Mabrouk S, Hersek S, Jeong HK, Whittingslow D, Ganti VG, Wolkoff P, et al. Robust longitudinal ankle edema assessment using wearable bioimpedance spectroscopy. IEEE Transactions on Biomedical Engineering. 2019 Jul 10;67(4):1019–29. DOI: <u>10.1109/TBME.2019.2927807</u>
- [10] Hersek S, Töreyin H, Inan OT. A robust system for longitudinal knee joint edema and blood flow assessment based on vector bioimpedance measurements. IEEE Transactions on Biomedical Circuits and Systems. 2015 Dec 24;10(3):545–55. DOI: <u>10.1109/TBCAS.2015.2487300</u>
- [11] Kusche R, Ryschka M. Combining bioimpedance and EMG measurements for reliable muscle contraction detection. IEEE Sensors Journal. 2019 Aug 19;19(23):11687–96. DOI: 10.1109/JSEN.2019.2936171
- [12] Kusche R, Ryschka M. Multi-Frequency Impedance Myography: The PhaseX Effect. IEEE Sensors Journal. 2020 Sep 9;21(3):3791–8. DOI: <u>10.1109/JSEN.2020.3022899</u>
- [13] Freeborn TJ, Regard G, Fu B. Localized bicep tissue bioimpedance alterations following eccentric exercise in healthy young adults. IEEE Access. 2020 Jan 29;8:23100–9. DOI: <u>10.1109/ACCESS.2020.2970314</u>
- [14] Ward L. Is BIS ready for prime time as the gold standard measure? Journal of Lymphoedema. 2009 Oct 1;4(2): 52–6.
- [15] Schmidt AH. Acute compartment syndrome. Injury-International Journal of the Care of the Injured. 2017 Apr 24; 48:S22–5. DOI: <u>10.1016/j.injury.2017.04.024</u>
- [16] Tonkovic S, Voloder D. Compartmental syndrome diagnostics using custom designed bioimpedance analyzer. In: MELECON '98. 9th Mediterranean Electrotechnical Conference. Proceedings (Cat. No.98CH36056); 1998 May 18–20; Tel-Aviv, Israel. IEEE; 1998. p. 1480–4. DOI: <u>10.1109/MELCON.1998.699486</u>

- [17] Tonkovic S, Tonkovic I, Kovacic D. Bioelectric impedance analysis of lower leg ischaemic muscles. In: Proceedings of the 22nd Annual International Conference of the IEEE Engineering in Medicine and Biology Society; 2000 Jul 23-28; Chicago, IL, USA. IEEE; 2000. p. 757–60. DOI: <u>10.1109/IEMBS.2000.900859</u>
- [18] Taji B, Chan AD, Shirmohammadi S. Effect of pressure on skin-electrode impedance in wearable biomedical measurement devices. IEEE Transactions on Instrumentation and Measurement. 2018 Aug;67(8):1900–12. DOI: <u>10.1109/TIM.2018.2806950</u>
- [19] Grimnes S, Martinsen ØG. Sources of error in tetrapolar impedance measurements on biomaterials and other ionic conductors. Journal of Physics D: Applied Physics. 2006 Dec 15;40(1):9. DOI: <u>10.1088/0022-3727/40/1/S02</u>
- [20] Chang BY. Conversion of a constant phase element to an equivalent capacitor. Journal of Electrochemical Science and Technology. 2020 Jun 4;11(3):318–21. DOI: <u>10.33961/jecst.2020.00815</u>
- [21] Zhang G, Huo X, Wu C, Zhang C, Duan Z. A bioelectrical impedance phase angle measuring system for assessment of nutritional status. Bio-Medical Materials and Engineering. 2014;24(6):3657–64. DOI: <u>10.3233/BME-141193</u>
- [22] Rossi S, Pessione M, Radicioni V, Baglione G, Vatteroni M, Dario P, et al. A low power bioimpedance module for wearable systems. Sensors and Actuators A: Physical. 2015 May 12; 232:359–67. DOI: <u>10.1016/j.sna.2015.05.004</u>
- [23] Bera TK, Bera S, Kar K, Mondal S. Studying the variations of complex electrical bio-impedance of plant tissues during boiling. Procedia Technology. 2016 Apr 7;23:248–55. DOI: <u>10.1016/j.protcy.2016.03.024</u>
- [24] Hoja J, Lentka G. Interface circuit for impedance sensors using two specialized single-chip microsystems. Sensors and Actuators A: Physical. 2010 Aug 2;163(1):191–7. DOI: <u>10.1016/j.sna.2010.08.002</u>
- [25] Hoja J, Lentka G. A family of new generation miniaturized impedance analyzers for technical object diagnostics. Metrology and measurement systems. 2013;20(1):43–52. DOI: <u>10.2478/mms-2013-0004</u>
- [26] Schwarzenberger T, Wolf P, Brischwein M, Kleinhans R, Demmel F, Lechner A, et al. Impedance sensor technology for cell-based assays in the framework of a high-content screening system. Physiological Measurement. 2011 Jun 7;32(7):977–93. DOI: <u>10.1088/0967-3334/32/7/S18</u>
- [27] Margo C, Katrib J, Nadi M, Rouane A. A four-electrode low frequency impedance spectroscopy measurement system using the AD5933 measurement chip. Physiological Measurement. 2013 Mar 13;34(4):391–405.
 DOI: <u>10.1088/0967-3334/34/4/391</u>

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