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First Microwave Tomography Approach Towards a Truly Noninvasive, Pain-Free and Wearable Blood Glucose Monitoring Device

Asma Bakkali¹, Clément Buisson¹, Lourdes Mounien²,
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Abstract—Despite the advancements in the field of glucose monitoring sensors, the development of noninvasive, wearable, continuous and comfortable systems is still a real challenge. New technologies are required for noninvasive, continuous and effective measurements remaining discreet, painless, comfortable to the patient and avoiding additional costs. This article presents a truly noninvasive microwave tomography prototype designed for glucose monitoring. The system is based on an array of dipole antennas placed in a circular configuration. The transmitted field data are collected using a switch matrix connected to a vector network analyzer. A heterogeneous 3-D arm model and a 3-D electromagnetic solver have been used to model the human arm and to characterize the system. Blood electromagnetic properties are affected by the glucose concentration, a promising correlation between the dielectric properties of blood and glucose level should be investigated. By simulating the antenna array on the arm phantom, the characteristics of the S -parameters were interesting at the frequencies of interest. The transmission coefficient amplitude decreases as the dielectric constant decreases from 63 to 40, and the conductivity increases from 1.5 S/m to 3.5 S/m. For each value of dielectric properties, a given transmission coefficient value can be clearly identified. Experimental measurements validated the arm phantom and confirmed the relationship between the response of the system and the dielectric properties of blood tissue. The armband sensor is designed as an inexpensive, noninvasive, and light weight device suitable for all patients with a high level of discretion. This work, under optimization for preclinical and clinical testing, demonstrates the proof of concept of an innovative microwave tomography system for noninvasive glucose monitoring. Compared to studies with a similar aim, this research may achieve distinct advances and offers promising hope in the field of noninvasive glucose sensors.

1. INTRODUCTION

Diabetes mellitus is an incurable metabolic disease affecting blood sugar levels, defined as a disorder characterized by high levels of glucose in the blood (hyperglycemia). Diabetes can be considered under three groups: type 1 diabetes (T1D), type 2 diabetes (T2D), and gestational diabetes related to pregnancy. The normal physiological level of the glucose in the blood is approximately 1.26 g/l, while in pathology it may rise to around 2 g/l, or decrease to less than 0.45 g/l [1, 2]. As the result of an increase or decrease in blood glucose levels, diabetes is a global disease, and there is no effective cure for this disease. A clinical report provided by the World Health Organization has estimated that the population with diabetes could reach approximately 366 million people in 2030 [3]. Available therapeutic approaches

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exist for this disease including the administration of insulin by traditional means and devices to monitor blood glucose levels to maintain the desired range. Various types of sensors have been developed to monitor human blood glucose level (BGL).

These devices can be classified into three categories: invasive sensors, minimally invasive sensors, and noninvasive sensors. Invasive devices are used to measure glucose from a finger prick procedure to estimate a blood sample from the fingertip on a test strip. The minimally invasive devices measure glucose concentration from interstitial fluid (ISF) through sensors inserted subcutaneously into the arm or into the abdominal wall. For most of these devices, a replacement is highly recommended to avoid any long-term side effects. Hence, truly noninvasive glucose monitoring is the most attractive approach for patients suffering from diabetes, as it provides more accurate, continuous and painless measurements, with no need to be replaced.

2. RELATED WORK

A number of noninvasive blood glucose monitoring devices have been reported in literature based on a wide range interesting technologies. Yilmaz et al., Tura et al., and Gonzales et al. provide detailed reviews focusing on glucose monitoring techniques [4–6]. There are several noninvasive glucose detection techniques based on the properties of glucose, including infrared spectroscopy, photo-acoustic spectroscopy, fluorescence spectroscopy, Raman spectroscopy, and electromagnetic sensing. Among the techniques attracting the attention of researchers is the detection of blood glucose levels by electromagnetic techniques. Over the past decade, with the development of wireless technologies, increased interest in the interaction of electromagnetic waves with biological tissues has emerged.

The multisensor proposed by *Biovotion* is one of the more developed systems [7–9]. Including two temperature sensors, one humidity sensor, an accelerometer, and optical sensors to monitor blood changes. This device is designed to be placed on the upper arm and has daily calibration and training requirements to ensure the working mode of the multi-sensor. Many future refinements should be considered. A microwave-based glucose sensor is proposed by Choi and co-workers as a noninvasive continuous sensor for blood glucose monitoring including two split ring resonators [10]. One ring interacts with the skin while the other ring is used as a reference, operating around 1.4 GHz and designed to be placed on the abdominal area. The system performance has been demonstrated by *in vivo* and *in vitro* interference tests [11].

Recently, Hanna et al. proposed a noninvasive continuous glucose sensor based on a multiband slot antenna and a multiband-reject filter. The system is designed to operate between 500 MHz and 3 GHz, and reproduces the vascular anatomy of the hand and arm. The authors reported high correlation between physical parameters of the system and blood glucose levels [12]. Another study in [13] proposed a noninvasive glucose sensor for measurement from ISF, composed of two parts: sensing tag and reader. The proposed sensor is designed to operate around the 3 GHz frequency with an accuracy of 1 mM/l and 38 kHz resonant frequency shift. However, measurements of ISF glucose level suffer from serious time delay compared to the blood glucose level. A recent study has provided a portable prototype of a microwave sensor, operating in the 2.4 GHz ISM band, to non-invasively measure glucose level variations of 70 to 120 mg/dl in blood [14]. The sensor showed frequency shifts of approximately 0.94 MHz/(mg/dl) in response to glucose level variation in blood samples. Another microwave sensor based on a conical horn with a conical conductor for noninvasive glucose monitoring is presented in [15]. The resulting relationship between the dielectric permittivity of the biological tissue phantom and the frequency dependence of the sensor parameter S_{11} is obtained at frequencies between 1.4 and 1.7 GHz. However, considering the geometry of the sensor this solution remains impractical for a continuous glucose monitoring.

For these systems, it is still necessary to have many improvements in order to set up an experimental validation platform with a possible view to commercialization. Otherwise, wide range of commercial glucose monitoring devices is available in the blood glucose monitoring market, without a truly noninvasive comfortable and continuous system. Many candidates could provide close noninvasive performance. Based on Caduff's research in 2003, the company Pendragon Medical Ltd. designed the first wristwatch *Pendra* to monitor glucose level. However, due to its poor accuracy, the device was commercialized only for a short time [16,17]. In the same context, the company Cygnus Inc.

proposed a wristwatch, named *Glucowatch G2 Biographer*, as a noninvasive glucose-monitoring device. The glucose level is detected by reverse iontophoresis technique, based on extracting the ISF through the skin [18, 19]. This device presented many limitations: must be used with a standard blood glucose meter, could cause the skin irritation, and the shift between the blood glucose level and the glucose in ISF (15–30 min). The device has finally the same fate as *Pendra* and did not survive for a long time in the market [20].

The *Glucotrack* model, based on an ear clip type sensor and a main display unit, is a CE-Mark approved device developed by Integrity Applications. This device is truly noninvasive, but only discrete readings are available, the accuracy is not sufficient, and the ear clip should be replaced every 6 months [21, 22]. The *Eversense* sensor includes a small sensor, implanted subcutaneously by a qualified doctor or healthcare professional, a removable Smart-Transmitter, and a mobile application to display glucose values [23–25]. The sensor is inserted under the skin and measures the glucose level in the ISF. Glucose levels are then calculated by the Smart-Transmitter and sent to the application. The *Eversense* sensor is designed to operate for 90 days, and the transmitter contains a reusable rechargeable battery that needs to be replaced after one year. Additional improvements are needed to increase the sensor lifetime. *Glucowise* is another noninvasive glucose sensor proposed to allow the determination of blood glucose levels in seconds. The device is placed between the thumb and forefinger or on the earlobe. The glucose level is obtained by a painless measurement technique, based on the transmission of a high-frequency signal around 65 GHz through the thickness of skin that is thin enough in selected parts of the body to allow the signal to pass through the tissue and be received by the sensor. The collected information is then sent via Bluetooth communication to a mobile device, via a pre-installed glucose reading and display application [26, 27].

FreeStyle Libre Glucose Measurement System is a continuous interstitial glucose measurement device marketed by Abbott Laboratories. It is the first system that does not require calibration. The sensor is placed on the back of the arm for a period of 14 days by an insertion performed by the patient using an applicator on the back of the arm. The subcutaneous sensor produces an electrical current, whose intensity varies according to the interstitial glucose level. The blood glucose levels in the subcutaneous interstitial environment and the capillary environment are correlated; however, there is a delay of 5 to 10 minutes between the blood glucose levels in the capillary and interstitial environment [28, 29]. Table 1 summarizes the properties of the most relevant devices listed below (With: Noninvasive (NI), Minimally-Invasive (MI), Continuous Monitoring (CGM), and Non-Continuous Monitoring (NCGM)).

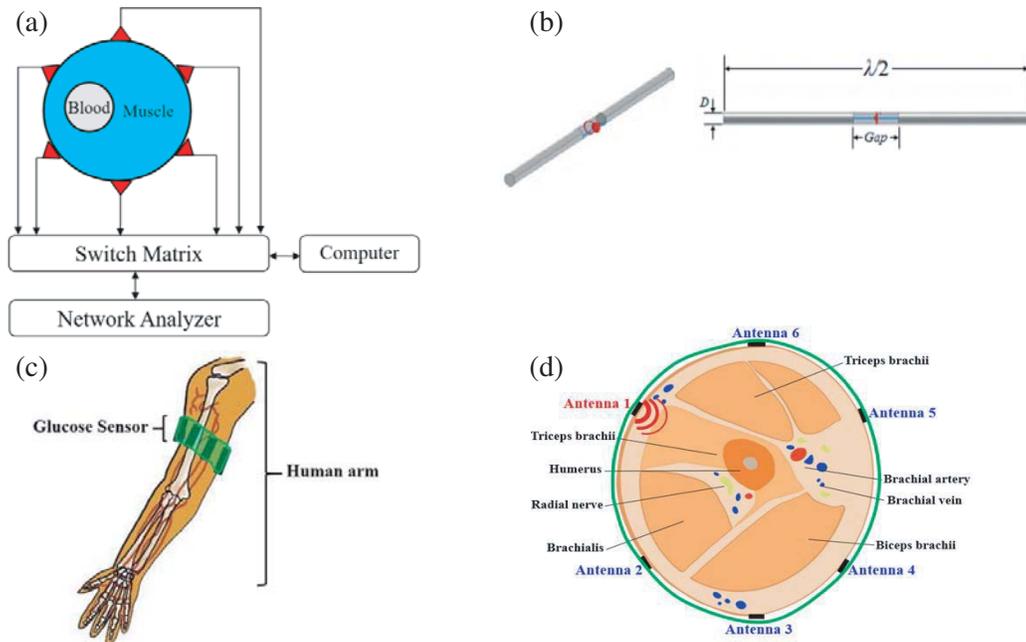
Many other research developments have been investigated in order to detect the glucose level in biological fluids such as tears [30–32], saliva [33], and sweats [34, 35]. New technologies are certainly required for noninvasive, continuous and effective measurements remaining discreet, painless, comfortable to the patient and avoiding additional costs. Blood glucose monitoring would also be of interest to people without diabetes, such as athletes and military. Continuous, wearable, noninvasive blood glucose monitoring techniques based on microwave technique have attracted lot of attention in recent years. In this paper, we propose a glucose monitoring system based on a microwave tomography approach avoiding infection risk and psychological traumas for diabetic patients. The technique applied reflection-transmission measurements based on a concept introduced for the first time.

3. PROPOSED SYSTEM DESIGN FOR NONINVASIVE CONTINUOUS GLUCOSE MONITORING

Microwave techniques are very promising for medical monitoring applications usually to discriminate between cancerous and healthy tissues [36, 37]. There are two types of microwave techniques: microwave radar and microwave tomography [38–40]. In this work, we are concerned with microwave tomography as a transmission-reflection method using numerous antennas surrounding the arm. The variation in the permittivity of the target (arm of the patient) has an impact on the response acquired from the transmitted and received fields. We introduce a first-generation prototype based on this technique in order to overcome the difficulties associated to invasive systems. A schematic diagram of the developed system is presented in Fig. 1(a). An antenna array, antenna switcher, network analyzer, and computer for control and data processing composed this system.

Table 1. Comparison table of minimally-invasive and noninvasive glucose monitoring devices currently available or close to release.

Device	Technology	Target	Type	Status	Ref.
Multisensor (Biovotion)	Dielectric spectroscopy	Upper arm	NI NCGM	Proof of concept	[7–9]
Choi et al.	Microwave technology	Abdominal area	NI CGM	Proof of concept	[10, 11]
Hanna et al.	Electromagnetic sensing	Hand	NI NCGM	Proof of concept	[12]
Pendra Watch (Pendragon Medical Ltd.)	Impedance spectroscopy	Arm wrist	MI CGM	Dropped	[16, 17]
GlucoWatch (Cygnus Inc.)	Reverse iontophoresis	Arm wrist	MI NCGM	Dropped	[18–20]
GlucoTrack (Integrity Applications)	Combination of: • Ultrasound • Thermal • Electromagnetic sensing	Ear lobe	NI NCGM	Available	[21, 22]
Eversense [®] (Senseonics)	Fluorescence	Upper arm	MI CGM	Available	[23–25]
GlucoWise (MediWise)	mm-Wave Transmission spectroscopy	Hand	NI NCGM	Under development	[26, 27]
FreeStyle Libre (Abbot)	Enzymatic detection/microneedles	Arm or Abdominal area	MI CGM	Available	[28, 29]

**Figure 1.** (a) A simplified schematic view illustrating the setup measurement. (b) The dipole antenna used in our system, with $D = 1$ mm and $\lambda/2 = 30$ mm. (c) Placement of the antenna array on the upper arm. (d) Detailed illustration of the proposed system configuration.

The antenna array is a 6-element dipole surrounding the arm. The dipole antenna is the basic antenna used to transmit the microwave signal through the arm in order to receive it by the same type of antenna. The dipole array is designed specifically for this application thanks to its potential advantages. The dipole antenna, simple and inexpensive, is promising as a potential element used in an array of antennas placed in a circular configuration for glucose monitoring application. Two metal sheets separated by a feeding gap, as shown in Fig. 1(b), represent each antenna. They are mounted on a Polylactic Acid (PLA) plastic support with a relative dielectric constant of 2.7 and a loss tangent of 0.01 at 2.45 GHz [41]. Antennas are equally spaced following a circular form of diameter of 80 mm (as an average diameter of a human arm) around the arm phantom with angular separation of 60° in order to reduce coupling problems if this angle is reduced. By using a reflector plan around the antenna array, the penetration of the propagated electromagnetic waves from the antennas inside the arm is improved. The prototype is manufactured based on a 6-element antenna array, which will be integrated into an armband as shown in Fig. 1(c). The antennas will be located in contact with the skin when the armband is worn. The connectors of the antenna array lead out from the armband. They are connected to a switch device used to allow independently driving the 6 antennas placed around the arm phantom. The wave propagates through the tissues of the arm, scattering at each interface of different types of tissues as presented in Fig. 1(d). The resulting wave is collected at each of the 5 receiving antennas in turn using the switch matrix ZTVX-8-12-S from Mini-Circuits [42]. The process is repeated until all possibilities have been exploited. The antenna array was initially designed to operate in a frequency band including 2.4–2.5 GHz ISM band in order to detect the blood glucose level (as measurements of interstitial fluid glucose level suffer from serious time delay compared to the blood glucose level). The dielectric properties of the arm principal tissues at 2.45 GHz, as reported in literature [43, 44], are summarized in Table 2.

Table 2. Dielectric properties of the different layers of the arm at 2.45 GHz [43, 44].

Tissues	Permittivity	Conductivity (S/m)
Skin	38	1.46
Fat	10.8	2.68
Humerus	11.4	0.39
Artery	58.3	2.54
Vein	58.3	2.54
Muscle	52.7	1.74

4. SYSTEM VALIDATION BY NUMERICAL SIMULATIONS

Due to the electrical characteristics of the biological tissues, the body-antennas (antennas in contact with biological tissues) present different behaviors compared with antennas in free space. This impact must be considered in the design of the system in order to provide the real behavior of the antenna array placed near the arm under test. The several biological layers in the arm with different dielectric constants and conductivities lead to a complex RF interaction between the monitoring system and the target.

Computer Simulation Technology (CST[®]) Microwave Studio Software is used to create arm phantoms and obtain results from the proposed tomography microwave system as shown in Fig. 2. Although the main objective of this work is to validate a continuous, noninvasive self-monitoring glucose sensor under the most realistic conditions, in this study, we have designed a simplified arm model based on two main tissues to represent muscle and blood layers. The inhomogeneous arm model, defined by the electrical parameters of the layers around 2.5 GHz, and the antenna array placed in contact with this model are simulated in order to perform a realistic scenario. The immediate layer in contact with the

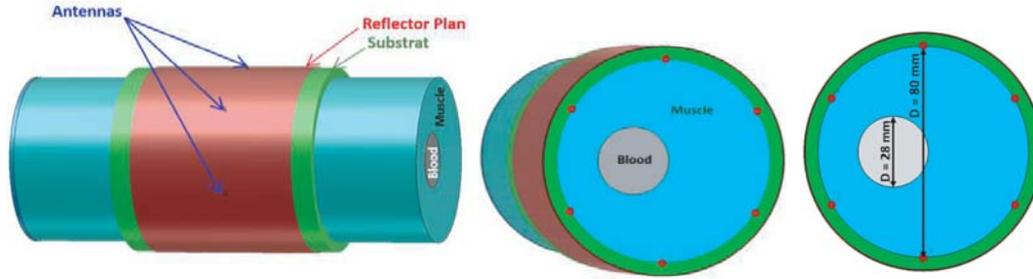


Figure 2. First simplified 3 D-model of glucose monitoring system using an antenna array constructed in CST[®].

antenna array corresponds to the muscle. The next layer, which represents the blood, is the main layer that will determine the response of the sensor. The substrate is the PLA material used as a coupling medium to ensure matching between the antenna array and the arm phantom in order to increase the field penetration with an optimized thickness equal to 5 mm. The reflector plan, used to improve the penetration of the electromagnetic field inside the arm phantom, is placed in contact with substrate and around the arm phantom.

Simulation results of the proposed system, carried out in the frequency range 1–5 GHz, are presented in Fig. 3(a). In this Figure, the relative permittivity and conductivity of the blood layer have been changed to represent the three cases of hypoglycemia, normal glucose level, and hyperglycemia, while the muscle layer keeps the same dielectric properties. The values of the dielectric properties used in the simulations are provided as indicative values in order to demonstrate the ability of the system on detecting possible changes in the dielectric properties of the blood. The dielectric constant decreases in case of hyperglycemia and increases in case of hypoglycemia, while the conductivity increases/decreases respectively (Table 3).

Table 3. Dielectric properties of three cases for simulated setup.

Cases	Permittivity	Conductivity (S/m)
Test 1 (Hypoglycemia)	63	1.5
Test 2 (Normal Glucose)	58	2.5
Test 3 (Hyperglycemia)	40	3.5

The transmission coefficients S_{ij} are obtained from each of the 5 receiving antennas while the excitation is performed with one antenna (S_{ij} corresponds to the S parameter when antenna i is receiving, and antenna j is transmitting). Here the variation of the blood dielectric properties can be continuously observed by using the transmission coefficients as detection parameters. The sensor indicates transmission coefficients S_{12} , S_{45} , S_{41} around -35 dB at approximately 2.5 GHz. After simulation of the blood layer with a normal glucose level, as shown in green, it was exchanged with the blood layers with higher and lower levels in turn, and the system response is compared. From Fig. 3(a) we can conclude that the transmission coefficient amplitude decreases as the dielectric constant decreases from 63 to 40, and the conductivity increases from 1.5 S/m to 3.5 S/m. The results show that for each value of dielectric properties, a given transmission coefficient value can be clearly identified. A relationship between the response of the system (S -Parameters) and the dielectric properties of blood tissue is demonstrated. Therefore, the proposed system is suitable for detecting different glucose concentration ranges in order to provide information about a hypoglycemic or hyperglycemic cases.

From the obtained results, we also notice that the transmission between antennas presents considerable losses. The wavelength of electromagnetic waves is considerably reduced in tissues due

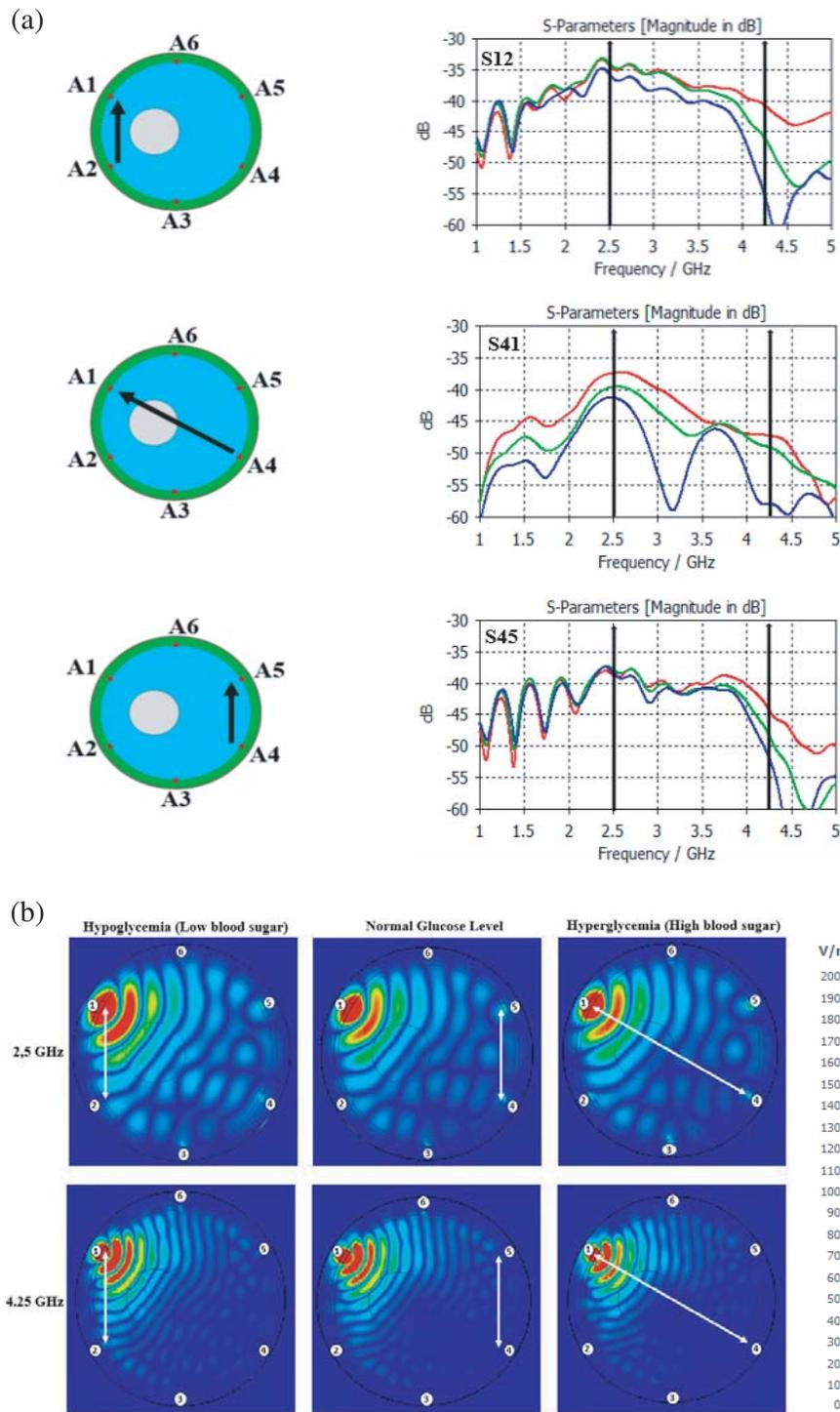


Figure 3. (a) Simulated sensor response versus the variation of the dielectric properties of the blood layer. Hypoglycemia (red curve), normal glucose level (green curve), and hyperglycemia (blue curve). (b) Electromagnetic simulation of the antenna array placed on the arm phantom-Electric field distribution for different glucose level at 2.5 GHz and 4.25 GHz.

to the high dielectric constant of biological tissues. Here, the EM field present in the substrate concentrated between the muscle layer and the reflector plan is shown in Fig. 3(b) at 2.5 GHz and 4.25 GHz, respectively. This plan placed around the system plays an important role in the orientation of the field inside the arm phantom. It could be seen that the EM field is lower as the glucose level increases.

Any variation in the dielectric properties of the blood sample is expected to result in a response change of the system. The simulations include very interesting results achieved for glucose level monitoring. These results are a useful starting point in the implementation of a noninvasive monitoring system. The next section presents the first experimental proof-of-concept of glucose prototype device.

5. EXPERIMENTAL VALIDATION OF THE MICROWAVE TOMOGRAPHY APPROACH FOR VARIATION GLUCOSE DETECTION

Different types of mimicking materials have been reported in the literature to evaluate biomedical devices, imaging techniques or specific absorption rates (SARs). Mimicking biological tissues can be presented in liquid, solid or semi-solid form [45–47]. In this work, a liquid form is proposed to test the microwave tomography system. In previously reported studies, the addition of ethanol to water decreases the dielectric constant and increases conductivity [47]. Based on these results, the human blood layer can be mimicked using a simple mixture of water and ethanol while SATIMO body fluid [49] is used to mimic the human muscle layer in the 2.4–2.5 GHz ISM band. First, water and ethanol solutions were prepared precisely using a micropipette device in the laboratory with the following ethanol concentrations: 20%, 30%, and 40%.

The dielectric properties measurements were performed on the frequency range: 1 GHz–3 GHz using the EpsiMu[®] Kit Tool, [48, 50], and Anritsu MS2036C Vector Network Analyzer (Fig. 4(a)). EpsiMu[®] dielectric measurements tool (Fig. 4(b)) consists of a coaxial cell based on the reflection-transmission technique.

From the data represented in Fig. 4(c), we can confirm that both real and imaginary parts of permittivity are influenced by the ethanol concentration. This information is considered as input data for the proposed microwave tomography system. The dielectric constant of water-ethanol 30% is equal to 58 around 2 GHz which is in a very good agreement with human blood dielectric constant for a patient with no diabetes. The glucose detection approach explored in this study is based on a concept of microwave tomography technique, which can allow the identification of the target properties by evaluating the reflected and transmitted signals collected by antennas. The first preliminary tests of the proposed system have been performed using the configuration previously described (Fig. 5(a)). The dimensions of the device are the same as the simulated model. The shape arm model is fabricated from 3D-printed structures and the previous water solutions with different ethanol concentrations. The dipole antenna array placed around the arm phantom is connected to the switch matrix device using standard SMA connectors. The switch matrix is automatically controlled by the computer and connected to the input/output of the network analyzer in order to select all the pair antenna combinations. After preparation, the phantoms are placed in circular Polylactic Acid plastic forms to approximate the shape and multi-layer structure of the arm, as shown in the Fig. 5(b). We start by filling the muscle phantom with SATIMO Body liquid [49] into the outer layer, which is 2 mm thick and 80 mm in diameter (Average of diameter human arm). We use an additional cylindrical shape (diameter = 28 mm) in the phantom, filled by a mixture of water and 30% of ethanol into the phantom to mimic human blood, having a permittivity higher than normal value or lower, to reproduce the two cases of hyperglycemia or hypoglycemia diabetes, respectively.

All the measurements were performed in a closed experimental room with normal temperature. The S -parameters of the reflection and transmitted signals are obtained in a frequency range of 1 to 5 GHz using the switch matrix and the VNA to collect all the possible antenna pairs. The six antennas can serve as both transmitters and receivers, creating a 6×6 matrix. The S -parameters S_{12} , S_{45} , and S_{41} are plotted in Fig. 6. The VNA measurements of the collected S -parameters from the proposed noninvasive glucose sensor were recorded instantly (5s between each measurement). The obtained results indicate the amplitude shift of transmission parameter responses according to the dielectric properties changes in the under test sample especially in the frequency range 2.5 GHz–5 GHz. During the simulations, the

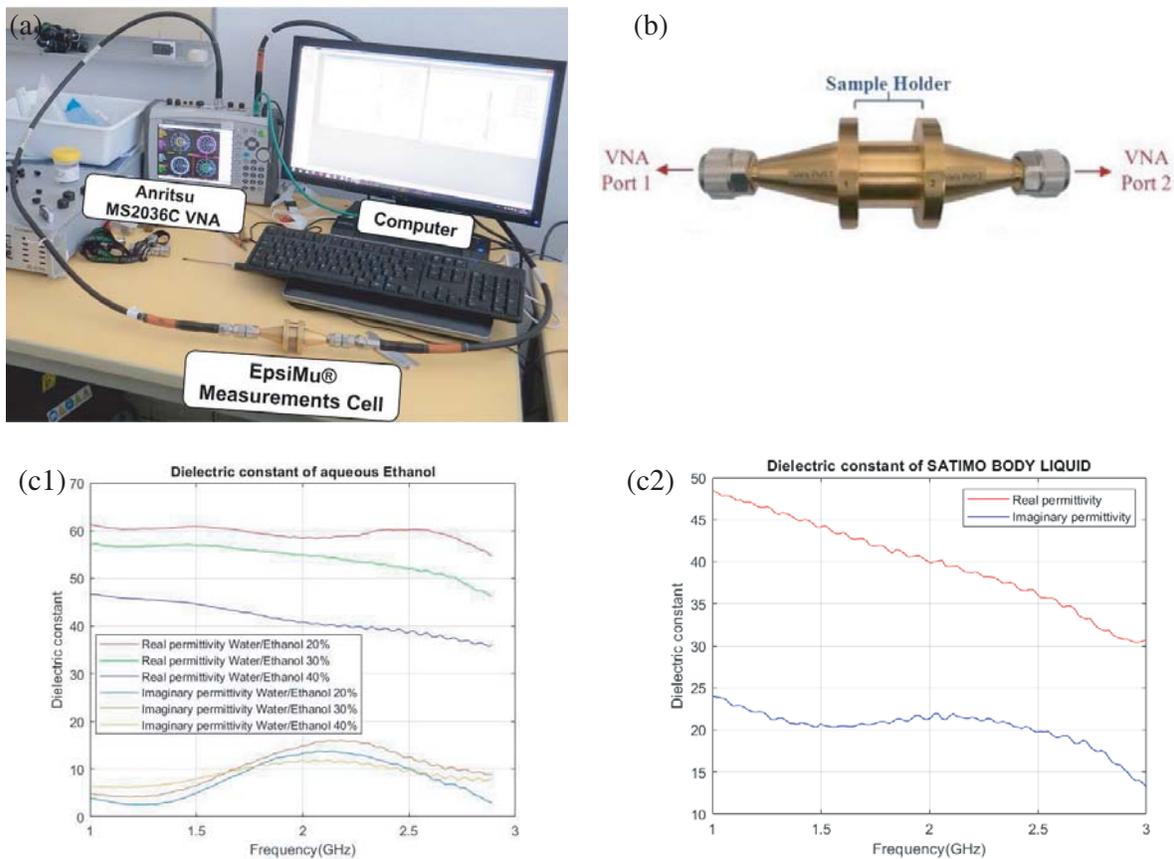


Figure 4. (a) Dielectric property measurements setup using EpsiMu[®] Tool [48, 50], and Anritsu MS2036C Vector Network Analyzer. (b) Photograph of the coaxial cell for the dielectric measurements. EpsiMu[®] toolbox consists of a coaxial cell based on the two-port transmission line technique and a related software to monitor a calibrated Vector Network Analyzer. (c1) Comparison between the measured dielectric properties of the mimicking mixtures of human blood (Water-Ethanol). (c2) Measured dielectric properties of the SATIMO Body Liquid, mimicking tissue of muscle, in 1–3 GHz band.

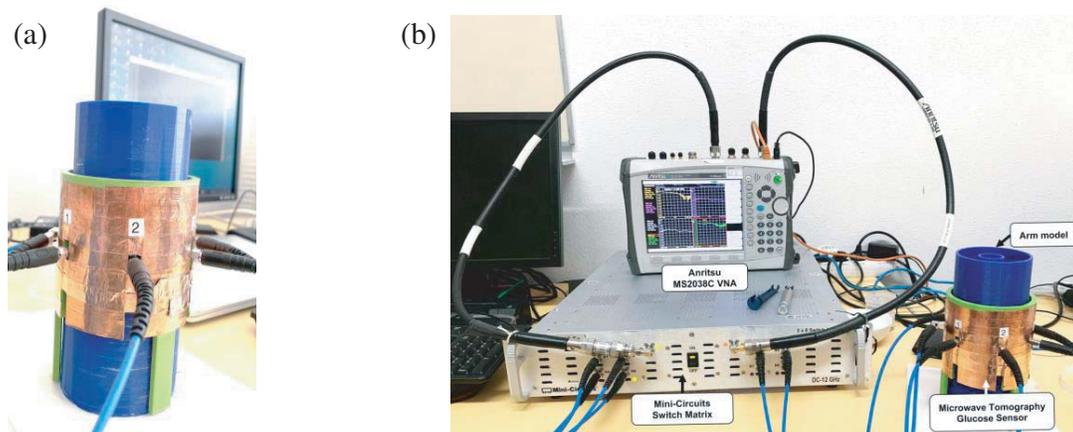


Figure 5. (a) Photograph of microwave tomography prototype for blood glucose measurements using our simplified arm model. (b) Photograph of the experimental measurement setup performed to test the first microwave tomography prototype for blood glucose measurements.

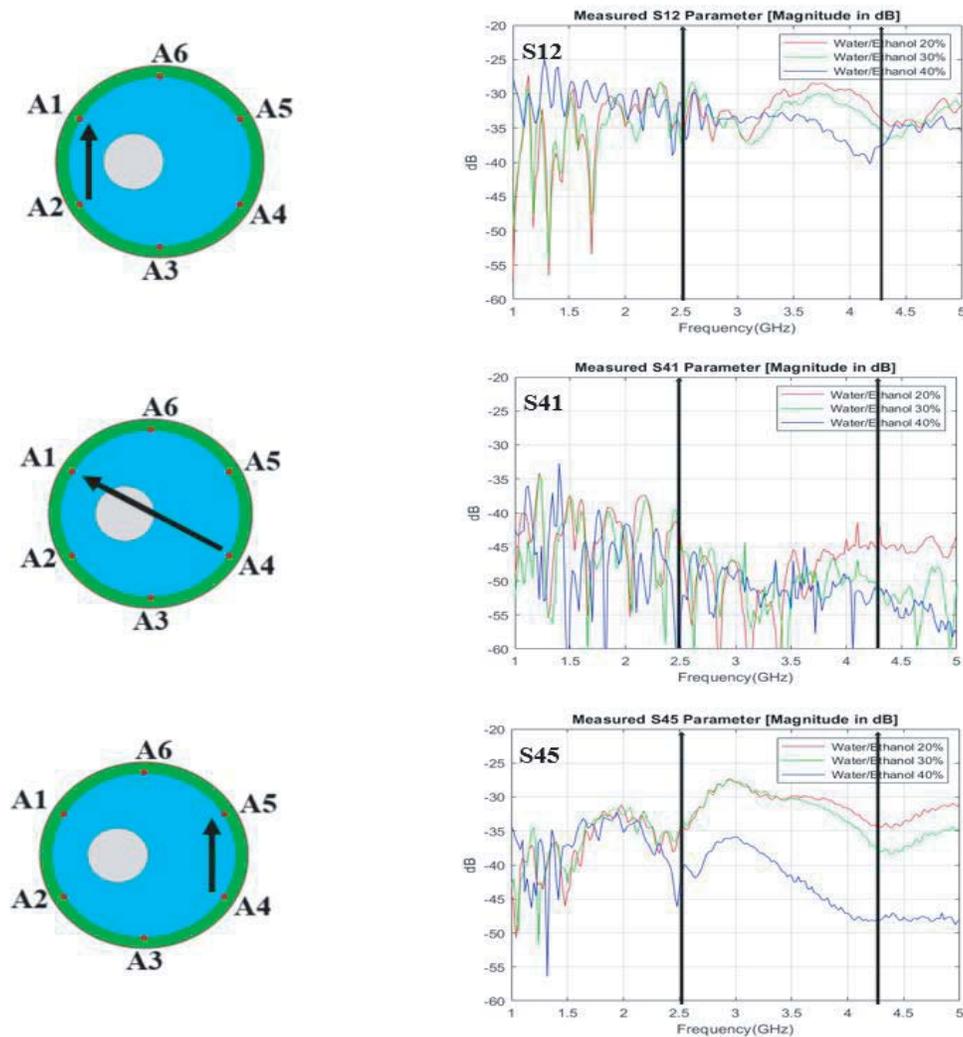


Figure 6. Experimental results of samples with different Ethanol concentrations in DI water. Hypoglycemia (red curve), normal glucose level (green curve), and hyperglycemia (blue curve).

size and shape of the phantoms were considered ideal and homogeneous. However, many parameters such as temperature and the condition of the phantom may not be the same for the measurements, introducing measurement errors.

The experimental results are generally matched with the previous simulations, since the variation in the ethanol concentration induces a transmission coefficient shift. Although the values for dielectric properties are provided as indicative values, it presents an overview of the performance of the system concerning the ability of the system to eventually detect changes in glucose levels. The proposed approach can have a great potential for measuring changes in the dielectric properties of blood.

Since changes in glucose levels can significantly affect the composition of the blood tissue, these changes are usually the result of shifts in the amplitude of the transmitted signals inside the antenna array. The experimental results further confirm the performance of the proposed sensor as noninvasive, wearable, calibration-free, and continuous blood glucose monitoring device. This work demonstrates that the proposed microwave tomography technique could be capable of determining blood glucose level without the need for invasive blood sampling.

6. CONCLUSION

This paper presents a new glucose monitoring system able to provide a truly noninvasive, calibration-free, wearable, and continuous blood glucose measure. The device is based on a microwave tomography approach as a highly sensitive, noninvasive, and safe glucose monitoring technique. The antenna array contained in this system is the main component responsible for transmitting and receiving signals to and from the arm of the patient. The system consists especially of 6-element antenna sensors to gather the transmitted and reflected signals from the arm model. This work presents, for the first time, an initial experimental validation of a specific microwave tomography prototype for diabetes detection. The key aim was to identify the changes in the S -parameter response of the antenna array, resulting from changes in the dielectric properties of biological tissues. We have demonstrated, by simulating the antenna array and confirmed with the first test measurements on the arm phantom, that the characteristics of the transmission coefficients are acceptable at the frequencies of interest. A relationship between the response of the system and the dielectric properties of blood tissue is clearly established.

Future improvements will be aimed at performing wider experimental tests including complex phantoms, with the integration of the system into a wearable armband. The armband sensor will allow an intimate contact with patient skin, and it is suitable for all types of patients as it will be very easy to wear. The sensor can be able to effectively detect glucose concentrations for hypoglycemia and hyperglycemia diabetes patients. The version discussed here is an early prototype for the intended application of wearable continuous BG monitoring; however, further integration of the necessary electronics is anticipated. The proposed system is very promising leading to potential applications of noninvasive measurements of different substances in blood such as lactate, cholesterol, alcohol, or drugs. The variation in the biological target leads to the change in the blood permittivity and S -parameters of the antenna array providing detection of blood anomalies. Certainly, the proposed system is very efficient for various blood property monitoring applications. In brief, the results presented in this paper demonstrate an interesting approach for sensors of physiological parameters, offering a significant advancement compared to the existing noninvasive sensor technologies.

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CONTRIBUTIONS OF THE AUTHORS

All authors contributed to the development of the content and the interpretation of the literature collected; all reviewed and approved the article.

REFERENCES

1. American Diabetes Association, "Diagnosis and classification of diabetes mellitus," *Diabetes Care*, Vol. 37, S81–S90, 2014.
2. Tan, S. Y., J. L. M. Wong, Y. J. Sim, et al., "Type 1 and 2 diabetes mellitus: A review on current treatment approach and gene therapy as potential intervention," *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, Vol. 13, No. 1, 364–372, 2019.
3. Wild, S., G. Roglic, A. Green, et al., "Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030," *Diabetes Care*, Vol. 27, 1047–1053, 2004.
4. Yilmaz, T., R. Foster, and Y. Hao, "Radio-frequency and microwave techniques for non-invasive measurement of blood glucose levels," *Diagnostics*, Vol. 9, 1–6, 2019.
5. Tura, A., A. Maran, and G. Pacini, "Non-invasive glucose monitoring: Assessment of technologies and devices according to quantitative criteria," *Diabetes Research and Clinical Practice*, Vol. 77, No. 1, 16–40, 2007.

6. Gonzales, W. V., A. T. Mobashsher, and A. Abbosh, "The progress of glucose monitoring — A review of invasive to minimally and non-invasive techniques, devices and sensors," *Sensors*, Vol. 4, 15–19, 2019.
7. Caduff, A., M. Zanon, P. Zakharov, et al., "First experiences with a wearable multisensor in an outpatient glucose monitoring study, Part I: The users' view," *Journal of Diabetes Science and Technology*, Vol. 12, 562–568, 2018.
8. Zanon, M., M. Mueller, P. Zakharov, et al., "First experiences with a wearable multisensor device in a noninvasive continuous glucose monitoring study at home, Part II: The investigators' view," *Journal of Diabetes Science and Technology*, Vol. 12, No. 3, 554–561, 2018.
9. Caduff, A., M. S. Talary, M. Mueller, F. Dewarrat, J. Klisic, M. Donath, L. Heinemann, and W. A. Stahel, "Non-invasive glucose monitoring in patients with Type 1 diabetes: A multisensor system combining sensors for dielectric and optical characterisation of skin," *Biosens Bioelectron*, Vol. 24, No. 9, 2778–84, May 15, 2009.
10. Choi, H., S. Luzio, J. Beutler, et al., "Microwave noninvasive blood glucose monitoring sensor: Human clinical trial results," *IEEE MTT-S International Microwave Symposium (IMS)*, 876–879, 2017.
11. Choi, H., J. Naylon, S. Luzio, et al., "Design and in vitro interference test of microwave noninvasive blood glucose monitoring sensor," *IEEE Transactions on Microwave Theory and Techniques*, Vol. 63, No. 10, 3016–3025, 2015.
12. Hanna, J., M. Bteich, Y. Tawk, et al., "Noninvasive, wearable, and tunable electromagnetic multisensing system for continuous glucose monitoring, mimicking vasculature anatomy," *Science Advances*, Vol. 6, No. 24, eaba5320, 2020.
13. Baghelani, M., Z. Abbasi, M. Daneshmand, et al., "Non-invasive continuous-time glucose monitoring system using a chipless printable sensor based on split ring microwave resonators," *Sci. Rep.*, Vol. 10, 12980, 2020.
14. Omer, A. E., G. Shaker, S. Safavi-Naeini, et al., "Low-cost portable microwave sensor for non-invasive monitoring of blood glucose level: Novel design utilizing a four-cell CSRR hexagonal configuration," *Sci. Rep.*, Vol. 10, 15200, 2020.
15. Zapasnoy, A. S., V. P. Belichenko, V. P. Yakubov, et al., "Application of broadband microwave near-field sensors for glucose monitoring in biological media," *Appl. Sci.*, Vol. 11, No. 4, 1470, 2021.
16. Weinzimer, S. A., "PENDRA: The once and future noninvasive continuous glucose monitoring device," *Diabetes Technology & Therapeutics*, Vol. 6, No. 4, 442–444, 2004.
17. Wentholt, I. M. E., J. B. L. Hoekstra, A. Zwart, et al., "Pendra goes Dutch: Lessons for the CE mark in Europe," *Diabetologia*, Vol. 48, 1055–1058, 2005.
18. Tierney, M. J., A. T. Janet, O. P. Russell, et al., "The GlucoWatch[®] biographer: A frequent automatic and noninvasive glucose monitor," *Annals of Medicine*, Vol. 32, 632–641, 2000.
19. Gandrud, L. M., H. U. Paguntalan, M. M. Van Wyhe, et al., "Use of the Cygnus GlucoWatch biographer at a diabetes camp," *Pediatrics*, Vol. 113, 108–111, 2004.
20. Diabetes Research in Children Network (DirecNet) Study Group, "Accuracy of the GlucoWatch G2 Biographer and the continuous glucose monitoring system during hypoglycemia: Experience of the diabetes research in children network," *Diabetes Care*, Vol. 27, No. 3, 722–726, 2004.
21. Pfützner, A., S. Strobl, D. Sachsenheimer, et al., "Evaluation of the non-invasive glucose monitoring device GlucoTrack[®] in patients with Type 2 diabetes and subjects with prediabetes," *J. Diabetes Treat.*, Vol. 4, No. 02, 2019.
22. Bahartan, K., K. Horman, A. Gal, et al., "Assessing the performance of a noninvasive glucose monitor in people with Type 2 diabetes with different demographic profiles," *Journal of Diabetes Research*, 1–8, 2017.
23. Christiansen, M. P., L. J. Klaff, R. Brazg, et al., "A prospective multicenter evaluation of the accuracy of a novel implanted continuous glucose sensor: PRECISE II," *Diabetes Technology & Therapeutics*, Vol. 20, No. 3, 197–206, 2018.

24. Deiss, D., A. Szadkowska, D. Gordon, et al., "Clinical practice recommendations on the routine use of everSense, the first long-term implantable continuous glucose monitoring system," *Diabetes Technology & Therapeutics*, Vol. 21, No. 5, 254–264, 2019.
25. Oppel, E., S. Kamann, L. Heinemann, et al., "The implanted glucose monitoring system everSense: An alternative for diabetes patients with isobornyl acrylate allergy," *Contact Dermatitis*, Vol. 82, No. 2, 101–104, 2019.
26. Saha, S., H. Cano-Garcia, I. Sotiriou, et al., "A glucose sensing system based on transmission measurements at millimetre waves using microstrip patch antennas," *Sci. Rep.*, Vol. 7, No. 1, 6855, 2017.
27. Gouzouasis, I., H. Cano-Garcia, I. Sotiriou, et al., "Detection of varying glucose concentrations in water solutions using a prototype biomedical device for millimeter-wave non-invasive glucose sensing," *EuCAP*, 2016, DOI:10.1109/EuCAP.2016.7481921.
28. The Free Style Libre System, <https://www.freestylelibre.fr/libre/>.
29. Fokkert, M. J., P. R. Van Dijk, M. A. Edens, et al., "Performance of the FreeStyle Libre Flash glucose monitoring system in patients with Type 1 and 2 diabetes mellitus," *BMJ Open Diabetes Research and Care*, Vol. 5, No. 1, e000320, 2017.
30. Badugu, R., E. A. Reece, and J. R. Lakowicz, "Glucose-sensitive silicone hydrogel contact lens toward tear glucose monitoring," *J. Biomed. Opt.*, Vol. 23, No. 5, 1–9, 2018.
31. Park, J., J. Kim, S. Y. Kim, et al., "Soft, smart contact lenses with integrations of wireless circuits, glucose sensors, and displays," *Science Advances*, Vol. 4, No. 1, eaap9841, 2018.
32. Zhang, J. and W. G. Hodge, "Contact lens integrated with a biosensor for the detection of glucose and other components in tears," U.S. Patent US8385998B2, 2009.
33. Zhang, W., Y. Du, M. L. Wang, "Noninvasive glucose monitoring using saliva nano-biosensor," *Sensing and Bio-Sensing Research*, Vol. 4, 23–29, 2015.
34. Zhao, J., Y. Lin, J. Wu, et al., "A fully integrated and self-Powered smartwatch for continuous sweat glucose monitoring," *American Chemical Society*, Vol. 4, No. 7, 1925–1933, 2019.
35. Lee, H., C. Song, Y. S. Hong, et al., "Wearable/disposable sweat-based glucose monitoring device with multistage transdermal drug delivery module," *Science Advances*, Vol. 3, No. 3, e1601314, 2017.
36. Kuwahara, Y., "Microwave imaging for early breast cancer detection," *New Perspectives in Breast Imaging*, IntechOpen, 2017.
37. Nikolova, N. K., "Microwave imaging for breast cancer," *IEEE Microwave Magazine*, Vol. 12, 78–94, 2011.
38. Wang, Z., et al., "Medical applications of microwave imaging," *The Scientific World Journal*, Vol. 2014, Article ID 147016, 2014.
39. Misilmani, H. M. E., T. Naous, A. S. K. Khatib, et al., "A survey on antenna designs for breast cancer detection using microwave imaging," *IEEE Access*, Vol. 8, 102570–102594, 2020.
40. Klemm, M., J. A. Leendertz, D. Gibbins, et al., "Microwave radar-based breast cancer detection: Imaging in inhomogeneous breast phantoms," *IEEE Antennas and Wireless Propagation Letters*, Vol. 8, 1349–1352, 2009.
41. Dichtl, C., et al., "Dielectric properties of 3D printed polylactic acid," *Advances in Materials Science and Engineering*, 1–10, 2017.
42. Mini-Circuits Datasheet, https://www.minicircuits.com/pdfs/ZTVX-n-12_Series.pdf.
43. Gabriel, S., R. W. Lau, and C. Gabriel, "The dielectric properties of biological tissue II: Measurements in the frequency range 10 Hz to 20 GHz," *Physics in Medicine and Biology*, Vol. 41, No. 11, 2251–2269, 1996.
44. The Foundation for Research on Information Technologies in Society (IT²S), "Dielectric properties of human tissues," <https://itis.swiss/virtual-population/tissue-properties/database/dielectric-properties>.

45. Lazebnik, M., E. L. Madsen, G. R. Frank, et al., "Tissue-mimicking phantom materials for narrowband and ultrawideband microwave applications," *Phys. Med. Biol.*, Vol. 50, No. 18, 4245–4258, 2005.
46. Yilmaz, T., T. Karacolak, and E. Topsakalet, "Characterization of muscle and fat mimicking gels at MICS and ISM bands (402 MHz 405 MHz) and (2.40–2.48 GHz)," *XXIX General Assembly of the International Union of Radio Science*, 2008.
47. Mashal, A. and F. Gao, "Hagness SC: Heterogeneous anthropomorphic phantoms with realistic dielectric properties for microwave breast imaging experiments," *Microw. Opt. Technol. Lett.*, Vol. 53, No. 8, 1896–1902, 2011.
48. Antunes Neves AL, "Application au domaine biomédical des moyens de caractérisation électromagnétique de matériaux dans le spectre des micro-ondes," Thesis, 2017.
49. Microwave Vision Group, "Liquids products reference: HAC accessories," <https://www.mvg-world.com/fr/products/sar/sar-accessories/liquids>.
50. Electromagnetic measuring device EpsiMu[®], <https://www.epsimu.com>.