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Experimental Based Blood Glucose Monitoring with a Noninvasive Cylindrical Biosensor

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Abstract—In this work, we have designed and fabricated a noninvasive flexible biosensor with a simple and printable structure for blood glucose monitoring. The proposed sensor has been experimentally proven to monitor blood sugar levels through frequency shifts. A cylindrical design with a coplanar waveguide (CPW) feeding technique has been proposed. A targeted frequency of 2.4 GHz with the best S_{11} at -22.623 dB and a bandwidth of 323 MHz was obtained. However, after propagating through the finger phantom, the signal is sensitive to the blood glucose levels with a significant frequency shift. The biosensor worked well at 1.55–1.88 GHz, representing a finger, without a phantom in the ISM band of 2.4 GHz. There is a bit of shifted frequency during the biosensor measurement with less than a 1.41% error. The overall size of the biosensor is 50.66 mm × 60.31 mm. The biosensor uses a flexible Dupont Pyralux substrate; thus, the index finger is easy to insert. 25 volunteers were involved in this experimental blood glucose. For this, we use an invasive device to measure the volunteers' blood glucose levels. The invasive measurement results obtained are used as a reference for the blood sugar levels of each sample. The test results using a cylindrical biosensor show a frequency shift at 7.5 MHz for every mg/dl of blood sugar levels, with a sensitivity of 0.43 1/(mg/dL). This frequency shift can be used to observe changes in the concentration of sugar levels in the blood. This flexible sensor is a good alternative biosensor for measuring blood glucose levels due to its low cost and printable structure.

1. INTRODUCTION

Diabetes is a rapidly growing global problem that affects many people. According to the International Diabetes Federation (IDF) 2021 data, the number of diabetic patients in Indonesia would reach 19.47 million in 2021, putting the country in the fifth place as the country with the highest number of diabetic patients [1]. This increases the risk of other diseases, such as heart attack, stroke, blindness, and kidney failure, and can even result in paralysis and death. Diabetes affects 537 million adults between the ages of 20 and 79. This figure is expected to rise to 643 million by 2030 and 783 million by 2045 [2]. Therefore, blood glucose monitoring is a must as an early action to prevent diabetes from getting worse. The fingerpricking process to measure blood glucose is a popular invasive method today. However, this causes pain to the patient. Another alternative is to use a painless, noninvasive method.

A healthy individual's blood glucose level should be within the normal range, or between 70 and 100 mg/dL in the fasting state and 70 and 140 mg/dL after eating. Both high blood sugar (hyperglycemia) and low blood sugar (hypoglycemia) are harmful. Hypoglycemia might result in weakness or even unconsciousness. On the other hand, hyperglycemia in the blood can potentially constitute a medical emergency or lead to diabetes-related issues [3].

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Electromagnetic wave (EM-wave) technology is the most suitable for developing noninvasive sensors. This is because of its penetration depth to biological tissue [4]. Numerous nonresonant (wide band) [5–7] and resonant (narrow band) [8, 9] techniques for evaluating EM characteristics based on microwave and millimeter waves have been developed. Resonant technologies have grown in popularity, particularly for applications requiring great speed, precision, and sensitivity. Increasing the number of sensor resonances is one way to improve the accuracy of EM parameter detection by microwave resonant sensors because a wider frequency range can be used to measure the EM parameters of the materials and obtain more detailed information about the EM properties of the sample under test (SUT) [3]. Recently, many researchers have worked on noninvasive antenna design as a sensor for blood glucose monitoring [3–25, 28, 3–32].

The feasibility study on monopole antenna for blood glucose monitoring was reported in [4]. In [10] two mm-wave antennas operating at 37 GHz were proposed, with absorbers strategically placed around the antenna sensors. As a result, the sensing system's sensitivity to changes in glucose was increased. [11] designed a patch resonator with a two-port structure operating at 2.40–2.48 GHz, and the energy was capacitively coupled to the patch via two feeding lines. SMA connectors were used to feed the feeding lines. A sensor inspired by metamaterials was created for noninvasive blood glucose monitoring [12]. The sensor integrated three resonant cells of single split rings with a microstrip line and operated at 3–4 GHz. The authors in [13] also proposed an antenna design for noninvasive glucose concentration measurement in blood plasma, which included a complementary split-ring resonator (CSRR) loaded truncated patch and an electromagnetic band gap structure etching on the ground plane. [14] reported another CSRR antenna using a different technique. [15] investigated a small flexible ultra-wideband (UWB) monopole antenna fed by a coplanar waveguide (CPW) that operated from 4 to 10 GHz. A commercial Kapton substrate was used as antenna material. Another planar UWB antenna was developed for this system [16]. A narrowband antenna consisting of four spiral arms fed by a coaxial line through the substrate was discussed in [17]. [18] investigated a flexible slot antenna that can be integrated inside a wearable glove to allow enough electromagnetic wave penetration to monitor blood glucose variations wirelessly. [19] describes the use of spoof surface plasmon polariton (SSPP) end-fire sensor-based structures (meta-materials antennas) for measuring glucose concentrations in aqueous glucose solutions as well as on-body measurements. The textile material adopted as the dielectric substrate for the antenna sensor was developed in [20]. The authors in [3, 21] proposed planar sensors with substrate-integrated waveguide (SIW) technology for blood glucose monitoring using volunteers' fingertips. Finger placement and the influence of fingerprints affect the sensor sensitivity [21]. However, most researchers employed rigid substrates (FR4, RT/Duroid, Roger 3210, Arlon) for their antenna substrate materials [3, 4, 10–14, 16, 17, 19, 21]. A limited number of studies employed flexible/textile substrates in their antenna designs [15, 18, 20]. Microstrip line and coaxial probe are the mostly feeding techniques applied in many works of literature.

[14] summarized several microwave/RF transmission and/or reflection techniques, such as transmission lines and free-space, resonant. Method selection is influenced by the operating frequency, physical state (solid or liquid) of the material under test (MUT), losses, and volume [14]. [22] described a microstrip line (MLIN)-based glucose sensor with a T-shaped pattern for blood glucose monitoring using fingers as the object. This technology bridges the gap between transdermal and microwave/RF techniques. This is because blood glucose concentrations can change the dielectric properties of the blood [23–25]. By constructing the MLIN around the subject under sensing, such as a finger, the main field of an MLIN can be used for glucose sensing. Because of the high intensity of the main field, the sensitivity is significantly higher than that when the fringing field is used [22]. The fingertip is a common measuring site because a good amount of fresh blood is stored there [32]. Based on this idea, we propose a cylindrical biosensor with Dupont Pyralux as the flexible substrate to measure the blood glucose concentration by detecting the variation of the dielectric changes of different blood glucose concentrations. We employ CPW feeding technique to optimize the structure. This method will not harm the patient's body. It only simply inserts the finger into the sensor rather than presses onto it [31].

This paper is organized as follows. First, Section 2 presents the materials and methods used in the proposed system. Next, measurement and simulation results are discussed in Section 3. Finally, Section 4 concludes the paper.

2. MATERIALS AND METHOD

2.1. Biosensor Design Structure

The purposes of the noninvasive biosensor design are as follows. 1) A fingertip must be easily placed on the sensor sensing area. 2) It should be compact and flexible. 3) It must have easy and cost-effective fabrication. To achieve these purposes, a cylindrical biosensor with a CPW feed line is selected with Dupont Pyralux material used as a sensor to measure glucose levels in this paper. A biosensor can both transmit and receive electromagnetic waves. Figs. 1(a)–(c) presents the cylindrical biosensor with Dupont Pyralux as the substrate with the size (Table 1). Table 1 lists the biosensor with the cylindrical phantom dimension. For the housing, the thickness of the wall is 0.2 mm, and the total height is 60.31 mm with $\varepsilon_r \approx 3.5$.

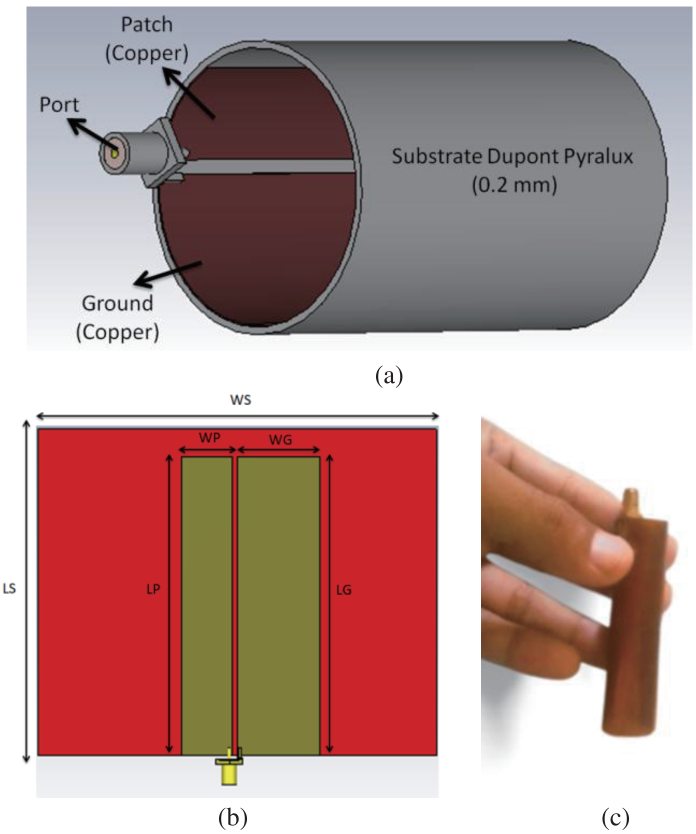

Figure 1. Configuration and prototype of the proposed biosensor: (a) 3D View; (b) biosensor geometry; (c) biosensor prototype.

Dupont Pyralux is a double-sided copper-coated polyimide laminate made in sheets and rolls with global availability that is ideal for medical and automotive applications and compatible with conventional flexible circuit fabrication processes. It has good physical, chemical, and electrical balance over a wide frequency range, with a low loss factor. Furthermore, Dupont Pyralux has a very low dimension profile (5.66×60.31 mm) but is very strong, with a tensile strength of 165 MPa at 73 F and a dielectric strength of 3500–7000 V/mil, as well as a Glass Transition Temperature rating of 280 [26]. The biosensor is fabricated using the Brother DCP-T310 printer with ink (Durabrite). The fabrication begins by entering the sensor design into Corel draw software and then printing with Dupont Pyralux substrate. The next stage is Etching, a metal dissolving process using strong acid on the unprotected part of the metal surface to make the planned design using ferric chloride ($FeCl_3$). Then connect the SMA connector using soldering tin. The final fabrication process is folding the sensor into a cylinder with insulating tape.

Table 1. Dimension of proposed cylindrical biosensor and cylindrical phantom.

Parameter	Value (mm)
WS	50.66
LS	60.31
WP	15.35
LP	38.82
WG	20.56
LG	39.32
D	20
DS	20
DF	175
DBL	52
DBO	13.8

2.2. Finger Phantom Design

The dielectric quantity in the body tissue used to analyze glucose levels changes at a specific frequency. The characteristics of these changes in several body tissues have been studied and modeled using the Cole-Cole equation [23]. In addition, variations in permittivity caused by changes in glucose concentration can impact a sensor's nearfield coupling and electromagnetic wave transmission [28].

Blood glucose level detection will be carried out on cylindrical phantom modeling as a finger will be used as a medium for testing the penetration depth of the sensor. The phantom modeling is made up of finger elements such as skin (DS), fat (DF), blood (DBL), and bone (DBO). Because it contains sufficient blood, the fingertip model is frequently used to measure invasive sugar levels. The fingertip, however, is attached to the biosensor's surface in its noninvasive measurement application. As a result, a finger model with a length of 60 mm and a diameter of 20 mm was created for this study.

To investigate the effects of blood density, a voxel-based finger phantom with varying numbers of cylinder-shaped blood slots is used. Each slot of the blood cylinder represents 30 mg/dl of blood density. It makes the blood slot easier to model the blood vessel on the finger phantom. Assuming that each blood slot is 30mg/dl, it is easier to perform a simulation to see the shift in the frequency resonance to the increase in blood sugar levels.

There are 8 blood slots in this finger phantom with a total of 240 mg/dl, as presented in Fig. 2. This is based on a predetermined blood glucose setting; diabetes is diagnosed at a blood sugar of greater than or equal to 200 mg/dl [27].

From the literature [3, 4, 10–21], the diagnostic method using a noninvasive antenna is through reflection coefficient, input impedance, and resonance frequency. Two diagnostic methods, reflection

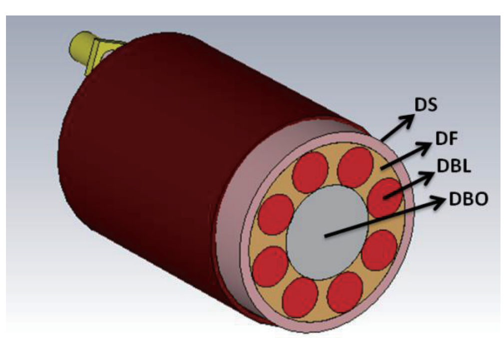

Figure 2. Finger phantom design.

coefficient and resonance frequency, are used in this paper. The cylindrical sensor works well at a frequency of 2.4 GHz without phantom and shifts to 1.5–1.8 GHz with phantom at different blood glucose concentrations.

2.3. Experimental Setup

Figure 3 shows an illustration of the experimental setup. The SMA connector was connected to Port 1 of a pocket vector network analyzer (VNA). The measurements were conducted $20x$ for each volunteer so that the real test for all samples was 500 times. The results were averaged for further analyses. 25 volunteers were involved in this research.

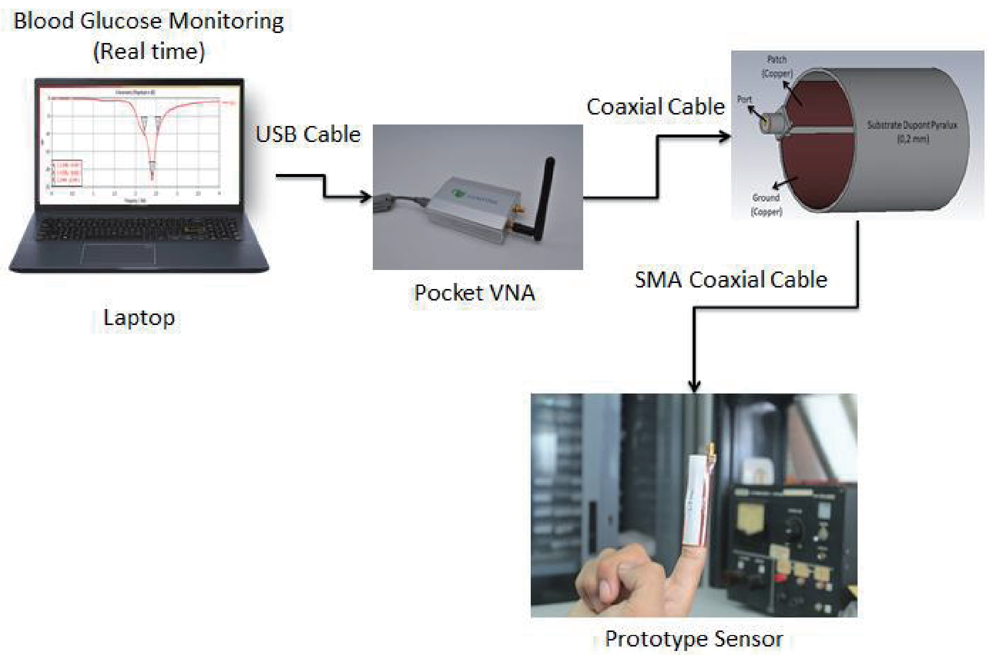

Figure 3. Experimental setup.

The process begins with measuring blood sugar levels from 25 volunteers using an Invasive Device. The measurement results obtained are used as a reference for the blood sugar levels of each sample. The sensor requirements for biological measurement applications differ from those for free space sensors in a number of ways. The inhomogeneity of the sensor environment and significant variation depending on the humidity of the patient's skin and the measurement point are the most difficult [28, 30].

3. RESULT AND DISCUSSIONS

Figure 4 shows the cylindrical biosensor's simulated and measured S_{11} using Dupont Pyralux. From the results, the simulated bandwidth is 323 MHz in the frequency range of 2.210 GHz to 2.533 GHz, while in the frequency range of 2.264 GHz to 2.541 GHz, the measured bandwidth is 277 MHz. The error of 1.41% is obtained during the sensor measurement and calculated using Eq. (1).

$$Error\,(f) = \left|\frac{fm - fs}{fs}\right| \times 100(\%) \tag{1}$$

where f is the error obtained in the measurement, and fm and fs are for the measurement and simulation resonant frequency, respectively.

The signal is sensitive to blood glucose levels after passing through the finger phantom with a significant frequency shift. The simulated S_{11} of a cylindrical biosensor tested with the finger

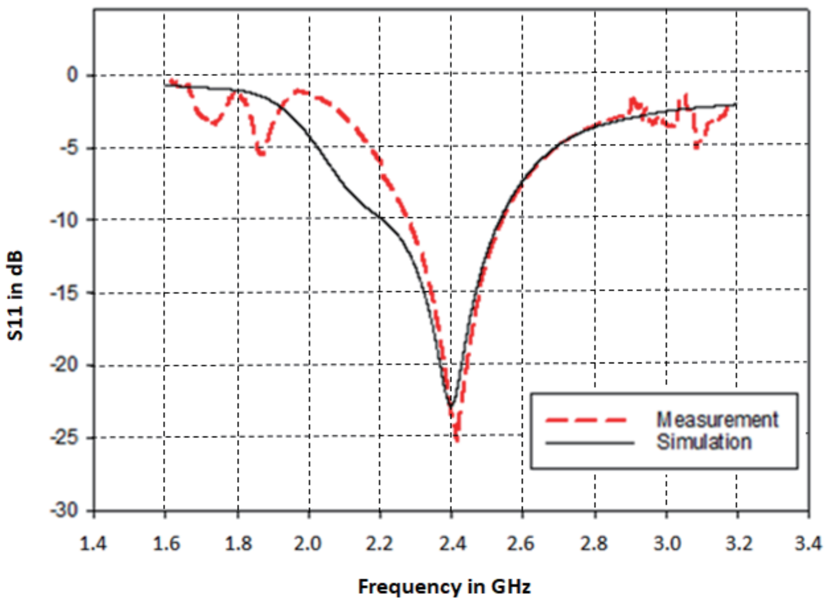

Figure 4. Measured and simulated S-parameters of the proposed biosensor.

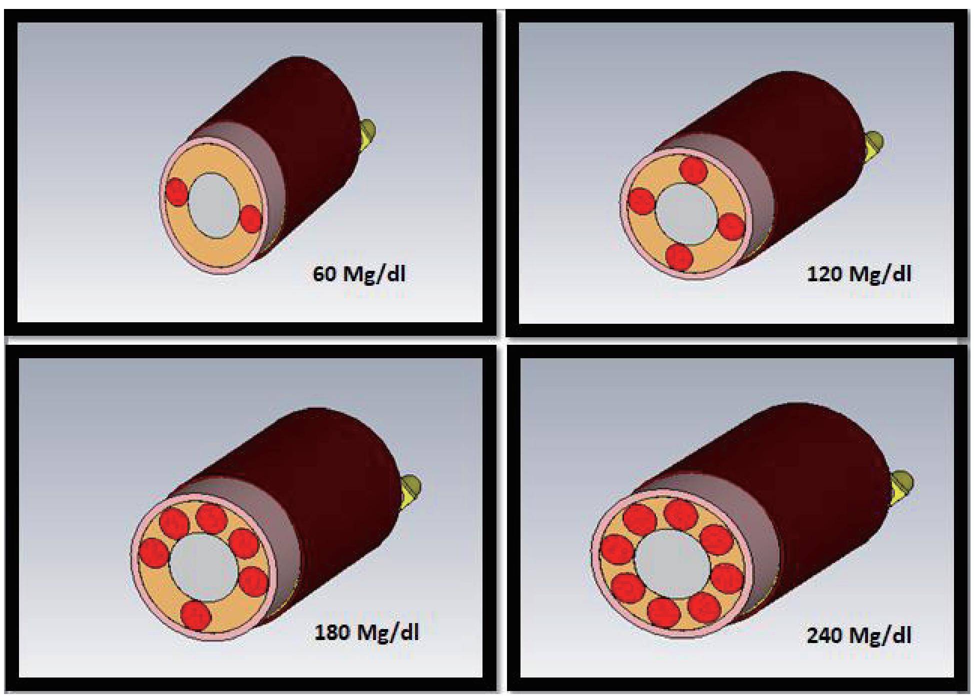

Figure 5. Cylindrical biosensor with finger phantom.

phantom is presented in Fig. 6. The simulated results obtained a change in frequency according to the addition of phantom blood slots, as shown in Fig. 5. As illustrated in Fig. 6, combining two simulated phantom blood slots provides a frequency of 1.552 GHz with a bandwidth of 86.3 MHz. In comparison, a combination of 4 phantom blood slots gets a frequency of 1.663 GHz with a bandwidth of 91.2 MHz. A combination of 6 blood slots shows a change in S_{11} at a frequency of 1.772 GHz with a bandwidth of 94.5 MHz. Last, a combination of 8 phantom blood slots results from 1.879 GHz, a

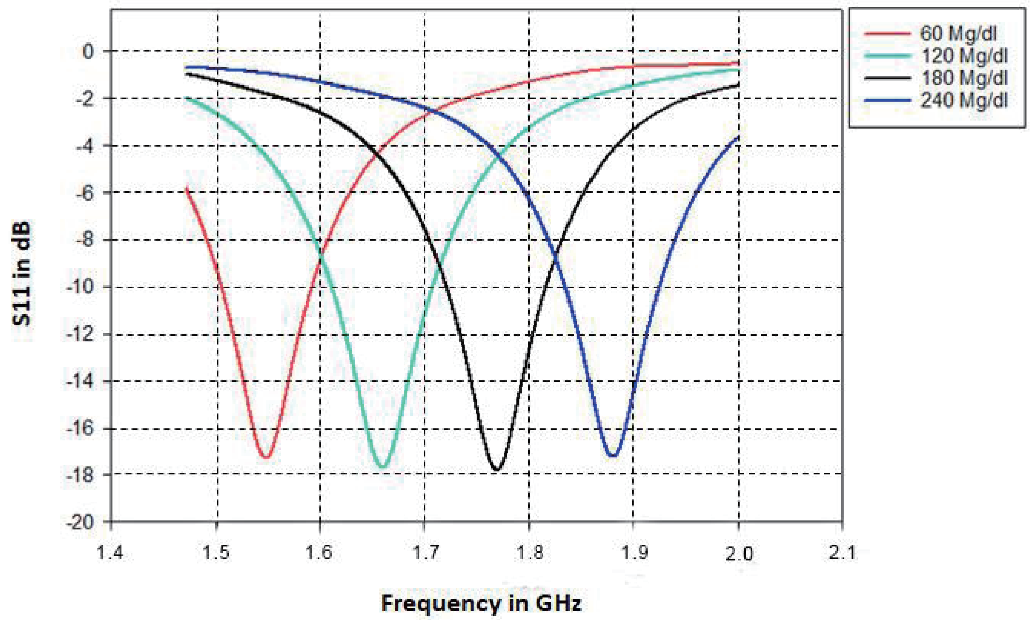

Figure 6. Simulated S_{11} of a cylindrical biosensor tested with finger phantom.

bandwidth of 89.4 MHz. By examining the results obtained for different concentrations of blood glucose, it can be found that the resonant frequency of the proposed sensor shifts for every increase in glucose concentration.

On the other hand, low frequencies have more penetration inside the tissues than higher frequencies due to the inherent conductivity of biological tissues. Therefore, when the finger is in contact with the sensing area, EM waves penetrate the fingertip and disturb the EM fields. Furthermore, noticeable changes are induced in the sensor transmission response because of the change in the effective permittivity at the sensing area [3].

Table 2. Comparative study of different types of flexible sensors.

Characteristic	Proposed cylindrical sensor	Flexible polyester antenna [15]	Wearable antenna [20]	MLIN [22]
Size (mm)	50.66×60.31	19.2×17.8	4×4	11×20
Thickness (mm)	0.02	3	0.01	1.5
Band/F (GHz)	Single/2.4	Dual/5.76 and 10.1	Single/2.4	Dual/0.95 and 2.99
Substrate	Pyralux $\varepsilon_r = 3.5$	flexible polyester $\varepsilon_r = 2.8$	Denim Material $\varepsilon_r = 1.6$	NaCl $\varepsilon_r = 4.4$
Tensile Strength (MPA)	High 165	High 860		
Flexural strength (p.s.i)	High 50000	High 11117		
Deformability	Low	Low	Low	Low
Thermal Stability	High	low	High	High
Fabrication Complexity	Simple/Printable	Complex/ Non-printable	Complex/ Non-printable	Complex/ Non-printable

Given the applications envisioned in this paper, this paper compares various flexible antennas reported in [15, 20, 22]. Compactness (size and thickness), electrical properties, and robustness are all compared in the study. The term "robustness" refers to the mechanical properties of flexible/conformal electronic devices such as tensile strength, flexural strength, deformability, and thermal stability. This comparative study takes into account the fabrication complexity criteria as well. Table 2 demonstrates that the proposed sensor provides extremely robust and flexible designs. This sensor is also printable and offers low-cost, roll-to-roll production.

Table 3. Experiment results with invasive and noninvasive devices.

No	Blood Glucose (mg/dl) (Invasive)	NonInvasive (proposed sensor)			
		Blood Glucose (mg/dl)	$\bar{f}$ (GHz)	S_{11} (dB)	Bandwidth (MHz)
1	73	73	1.5343	−26.32	93.61
2	86	86	1.6045	−26.05	98.65
3	90	90	1.6301	−26.12	95.65
4	103	103	1.7031	−26.04	96.72
5	112	112	1.7478	−25.71	98.32
6	129	129	1.7857	−25.92	100.1
7	151	151	1.832	−26.34	97.29
8	163	163	1.8605	−26.71	99.54
9	190	190	1.8921	−25.92	96.48
10	213	213	1.9712	−25.90	97.54

Table 3 represents the 10 experimental results of the blood glucose test for volunteers. The test is performed for invasive and noninvasive devices. For a noninvasive device, measurements were made using a VNA operating at 1–4 GHz. Before testing with a cylindrical sensor, calibrate the VNA with a frequency setting of 1–4 GHz, then insert a finger on the sensor and measure it using VNA. Fig. 7 shows the experimental blood glucose detection using the cylindrical sensor. The test results using a cylinder sensor show that the S_{11} values range from −25.62 dB to −26.32 dB, while the bandwidth obtained ranges from 92.47 MHz to 100.1 MHz. Therefore, the testing for blood sugar levels of 73 mg/dl–98 mg/dl or belonging to the non-diabetic category, carried out with a cylindrical sensor, will display results at a frequency of 1.5343 GHz–1.6712 GHz, for 100 mg/dl–123 mg/dl, or pre-diabetes category will display test results in the frequency range 1.7031 GHz–1.7857 GHz, and 129 mg/dl–213 mg/dl or diabetes category the test results obtained at a frequency of 1.7857 GHz–1.9712 GHz.

The tests using a cylindrical sensor showed a significant change, where an increase in blood sugar levels made a frequency shift towards a larger one. The test results using a cylindrical sensor obtained a frequency shift of 7.5 MHz for every mg/dl blood sugar level. Glucose is present in blood vessels and interstitial fluid (ISF). The change in glucose levels in these two parts and their interaction with the EM waves that penetrate the skin shifts the resonance frequency of the sensor and leads us to controling the blood glucose levels of the user [3]. The frequency shift distribution can be seen in Fig. 8.

The stability sensing of the sensor indicates sensitivity. Sensitivity is used to determine the accuracy of the sensors that is expressed with Eq. (2) [3].

$$S = \frac{\text{FDR}}{f_{FL}} \times 100\,(1/(\text{mg/dL})) \tag{2}$$

where FDR is the frequency detection resolution (7.5 MHz/(mg/dL)) and is f_{FL} for freeload resonance frequency of the sensor (2.4 GHz). Thus, the sensitivity of the proposed sensor is 0.43 1/(mg/dL).

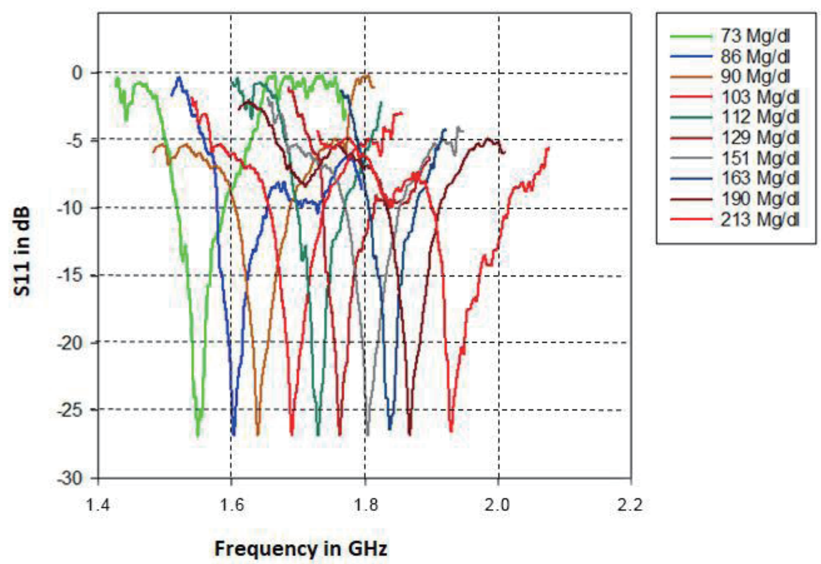

Figure 7. Result of blood sugar levels tested by the cylindrical biosensor.

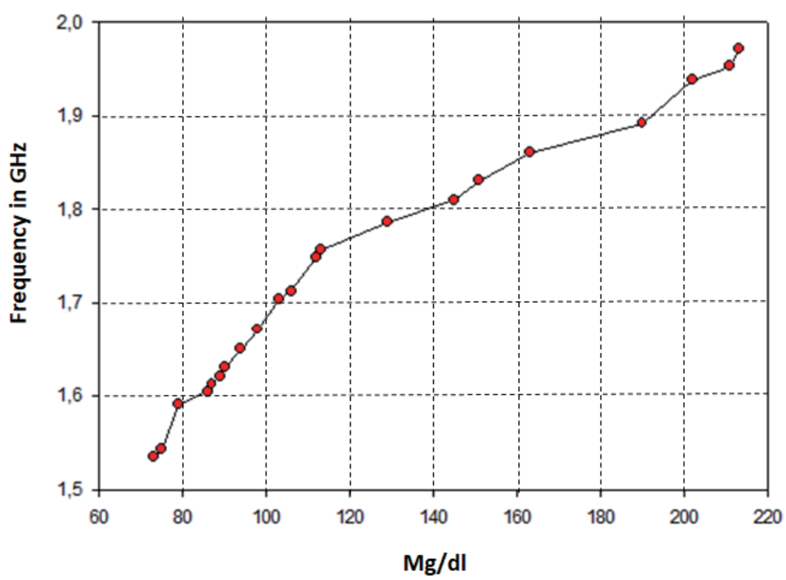

Figure 8. Blood glucose level versus frequency.

4. CONCLUSION

In this paper, a cylindrical biosensor with CPW feeding technique was designed to work at a targeted frequency of 2.4 GHz with the best S_{11} at -22.623 dB and a bandwidth of 323 MHz. Comparatively, the prototype's measurement findings yield an S_{11} value of -25.02 dB at 2.411 GHz with a bandwidth of 277 MHz and an error of less than 1.41%. Changes in frequency occur when detection is carried out using a finger phantom ranging from 1.55 GHz to 1.88 GHz for each slot test. Blood glucose values between 73 and 213 mg/dL have been determined for 25 individuals. In addition, the proposed noninvasive blood glucose sensor's measured findings were analyzed and compared to the invasive approach. The proposed flexible biosensor may be a promising option for application in a glucose monitoring system based on the obtained results and comparisons with similar studies due to its simple design, robustness, ease of integration, simplicity of fabrication, and low cost.

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