electronics

Article

Non-Invasive Blood Glucose Monitoring Using a Curved Goubau Line

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Received: 19 May 2019; Accepted: 9 June 2019; Published: 12 June 2019

Abstract: Non-invasive blood glucose monitoring at microwave frequencies is generally thought to be unreliable in terms of reproducibility of measurements. The failure to reproduce a blood glucose measurement from one experiment to another is in major part due to the unwanted interaction of leaky waves between the ambient environment and the blood glucose measuring device. In this work, we have overcome this problem by simply eliminating the leaky modes through the use of surface electromagnetic waves from a curved Goubau line. In the proposed methodology, a fixed volume of blood-filled skin tissue was first formed by vacuum suction and partially wound with a curved Goubau line which was coated with a 3 mm thick layer of gelatin/glycerin composite. Blood glucose levels were non-invasively determined using a network analyzer. At 4.5 GHz, a near-linear correlation exists between the measured S12 parameters and the blood glucose levels. The measured correlation was highly reproducible and consistent with the measurements obtained using the conventional invasive lancing approach. The findings of this work suggest the feasibility of non-invasive detection of left and right imbalances in the body.

Keywords: Goubau line; non-invasive blood glucose measurement; Acu-check; lancet; leaky waves; surface waves

1. Introduction

Blood glucose levels are an important bio-marker in the medical or health care industry. Almost all health problems are associated with an abnormal blood glucose level. These health problems include diabetics, candidiasis, amyloidosis, cancers, scleroderma diabeticorum, vitiligo, acanthosis nigricans and hypoglycemia. The blood glucose level, as well as the ways that it varies over time, is important information for the diabetic population, smokers wishing to quit and cancer patients. Conventional approaches to blood glucose measurement that require extraction of capillary blood through the use of a lancet are not suitable for prolonged blood glucose monitoring for two main reasons: (1) the amount of capillary blood extracted is too much for repeated measurements within a prolonged period; and (2) the wound punctured by the lancet is highly susceptible to infection.

At the time of writing, there has been a lot of negativity surrounding the idea of non-invasive blood glucose measurements. This negativity does not exist without any reason. The original idea of non-invasive blood glucose measurement involving an electromagnetic wave was based on the assumption that a change in blood glucose levels will induce a measurable change in the permittivity of the blood at high frequencies. By measuring the blood permittivity change, in theory, one can determine the blood glucose levels. However, this assumption has not factored in the uncertainties due to the following facts:

1. The blood permittivity is not a strong function of the blood glucose concentration in the blood [1]. At microwave frequencies, the real part of the blood permittivity does not change much regardless of what the blood glucose level is. A change in the blood glucose level induces a change in the imaginary part of the blood permittivity. The blood contains a variety of different substances. The blood glucose is just one of those. There is no reason to expect the relative permittivity of the blood in the body to change substantially in response to a change in the blood glucose.
2. The density of the blood underneath the skin can be different from one body part to another and from one experiment to another experiment. It is, for this obvious reason, not logical to measure the blood glucose level from the elbow area. The density of the blood underneath the skin depends on the volume. It is virtually impossible to obtain reproducible measurements if the volume of the object under test is not kept constant from experiment to experiment.
3. The blood glucose measuring device can act like an antenna at high frequencies, particularly at microwave or millimeter-wave frequencies. This antenna effect is also known as leaky wave effect. This antenna effect enables the blood glucose measuring device to release and absorb leaky electromagnetic radiations to and from the ambient environment. It can substantially dis-stabilize the measured results at microwave or millimeter wave frequencies, particularly in the presence of an electromagnetic noise source in the background.

Of all the factors that contribute to the measurement uncertainties, the leaky wave effect is the most impactful. At the time of writing, our research group has already evaluated many published methods. These methods include the traditional split ring resonator approach [2], measurement at 60 GHz [3], as well as a substrate integrated waveguide (SIW) approach [4]. These approaches rely on the nonlinear effects at the resonant frequencies where the magnitude change in the measured scattering parameters are enormously amplified in response to a very large change in blood glucose levels. Measuring the S-parameters right at the resonant frequencies is definitely a help but the energy gained or lost by the glucose measuring device at the resonant frequencies are most likely leaky modes, contributed to by the resonances of higher order modes. Depending on the environment, these ambient leaky waves can change from experiment to experiment.

On the other hand, almost all the published approaches were based on either a body part with an unknown density or volume of blood or a body part with an unknown blood volume. Most importantly, almost none of these approaches have taken the obvious effects of leaky waves into account. In all honesty, we were unable to reliably reproduce the measurements from one experiment to another with these published approaches until the measurements were conducted with the participant under test rigidly fixed in position in a completely isolated environment.

In this work, we found that the changes in the measured S-parameters as a result of a change in the blood glucose concentration can be enormously magnified not only at the resonant frequencies, but also at the cut-off frequencies where the propagating energy turns from a surface mode to a leaky mode. To take advantage of this S-parameter magnification effect, and to minimize the effects of leaky waves, our proposed glucose measuring device was designed to absorb the leaky radiations and turn them into a dielectric loss due to the presence of blood glucose in the blood right at the cut-off frequency, where the device was about to become a leaky wave antenna. The proposed approach is based on a curved Goubau line winding an artificially fixed volume of blood-filled skin tissue [5–7]. With the help of the suction effect of a vacuum suction aspirator, the volume of the blood-filled skin tissue will remain unchanged from experiment to experiment. The Goubau line has already been applied in applications of wireless power transfer [8–13]. The use of surface electromagnetic waves associated with a curved Goubau line for blood glucose measurement is an unprecedented attempt. However, our in-vivo experimental results have proven beyond any doubt that the measured results from the proposed approach and the traditional lancing based approach have almost 100% agreement with each other.

2. Conceptual Background

Electromagnetic waves can be broadly classified into two categories: (a) surface electromagnetic waves and (b) leaky electromagnetic waves. Leaky waves propagate at a group velocity faster than the speed of light. The transverse electromagnetic nature of a leaky electromagnetic wave makes it possible to radiate in all directions, according to Poynting's theorem [14]. The process of radiations involves an exchange of electromagnetic energy between an antenna and the ambient environment. If a blood glucose measuring device acts like an antenna, then the accuracy and the stability of the measurements using this device will be negatively affected by the electromagnetic interference from the environment. On the other hand, surface electromagnetic waves propagate along the interface between two neighboring mediums at a group velocity below the speed of light, with virtually no radiation loss. Unlike leaky electromagnetic waves, surface electromagnetic waves tend to propagate with a relatively stable amplitude because they are relatively unaffected by the ambient electromagnetic interference. Therefore, there is no point of basing our blood glucose measurements on leaky electromagnetic waves. Whether an electromagnetic energy is leaky or not also depends on its frequencies. To ensure reproducibility of measurement, the blood glucose measurements should be conducted at frequencies where the group velocity of the propagating wave is less than the speed of light.

A Goubau line is a slow-wave guiding structure which, at frequencies below the cut-off frequency, primarily supports propagation of a surface electromagnetic wave at a group velocity below the speed of light (see Figure 1a). It is basically a groundless single-wire transmission line coated with a layer of dielectric material. This dielectric coating confines the evanescent electromagnetic energy on the conducting surface, which would otherwise turn the evanescent electromagnetic energy into a leaky wave. When both ends of the Goubau line are connected to a vector network analyzer for measurements of scattering parameters, we will either end up with a large magnitude of the S12 (or S21) parameter together with a small magnitude of the S22 (or S11) parameter, or the other way round. The former means that the characteristic impedance of the Goubau line is close to 50 Ω, whilst the latter means the opposite. In either scenario, the radiation efficiency of the leaky waves is low with virtually no antenna effect. The Goubau line in either of these two scenarios has vertically little or no interaction with the ambient electromagnetic interference. In the absence of any interaction with the ambient electromagnetic interference, the measured scattering parameters will be stable and reproducible.

The Goubau line, as shown in Figure 1a, is assumed to be a straight Goubau line. The radii of the dielectrically coated Goubau line and its center conductor are respectively a and b. The relative permittivity of the dielectric layer coating the center conductor is ε_r. Then the group velocity of a surface electromagnetic wave can be computed from the propagation constant using the modified version of the approximation formula proposed by Jaisson [15]:

$$k_z = k_0 \sqrt{1 + \frac{\varepsilon_r - 1}{1 + 6\varepsilon_r K_e / G}} \tag{1}$$

where

$$k_0 = \frac{2\pi f}{c} \tag{2}$$

$$K_e = 0.11593148 - 0.5\ \ln(-q) - 0.5\ln(-\ln(-q)) + \frac{0.5\ln(-\ln(-q))}{\ln(-q)} \tag{3}$$

$$q = \left(\frac{1}{\varepsilon_r} - 1\right)\frac{G}{3}(k_0 b)^2 \tag{4}$$

$$G = \left(1 - \frac{a}{b}\right)\left[6 + \left(1 - \frac{a}{b}\right)\left(5 - \frac{2a}{b}\right)\right] \tag{5}$$

The group velocity is therefore given by:

$$V_g = \frac{2\pi f}{real\{k_z\}} \tag{6}$$

In order to eliminate leaky waves, which will render the measured scattering parameters non-reproducible from one experiment to another, the frequency at which the blood glucose measurement should be conducted at should satisfy the condition given by Equation (7):

$$f < \frac{c}{5.9809\ b\ \sqrt{G\left(1 - \frac{1}{\varepsilon_r}\right)}} \tag{7}$$

where the frequency f is also known as the cut-off frequency for the fundamental transverse magnetic mode of the Goubau line.

In Equations (1)–(7), it is assumed that the Goubau line is a straight insulated wire. It is difficult to determine the line characteristics by measuring the scattering parameters between both of the terminals of a straight Goubau line because there is a direct port-to-port coupling between these two terminals. The direct port-to-port coupling can be eliminated by measuring a curved Goubau line that has been bent by 180° as illustrated in Figure 1b. However, the curved portion of the Goubau line as shown in Figure 1b will radiate an additional amount of leaky waves in the directions as indicated by the pink arrows. This radiation loss does not depend on the cut-off frequency as given in Equation (7). Instead, it depends on the sharpness of the bend, or the radius of the bent portion of the Goubau line. In the bent portion of the Goubau line, the outer and inner radii of the curved portion of the Goubau line are respectively $R1 + (b - a)$ and $R2 - (b - a)$. This means the radiation loss due to the leaky waves at the curved Goubau line will be a function of the difference in distance between the outer edge and the inner edge of the Goubau line, which is $(R2 + (a - b) - R1 + (a - b))\pi$. According to the results of our repeated experimentation, the value of b in Equation (7) can be replaced with $b^{(R2+a-b)/(R1-a+b)}$ in order to factor in the additional radiation loss due to the bending effect at the curved Goubau line:

$$f < \frac{c}{5.9809\ b^{\frac{R2+a-b}{R1-a+b}}\ \sqrt{G\left(1 - \frac{1}{\varepsilon_r}\right)}} \tag{8}$$

The radiation loss due to the bent section of the curved Goubau line can be effectively minimized at certain frequencies by letting the curved portion of the Goubau line be partially wound over a cylindrical dielectric resonator of high permittivity, as is illustrated in Figure 1c. Because of its higher permittivity, this cylindrical dielectric resonator reduces the effective wavelength along the inner edge of the curved Goubau line, thereby reducing the overall distance difference between the outer edge and the inner edge of the curved Goubau line [7]. In the neighborhood of the cut-off frequency as given in Equation (8), whilst some of the surface electromagnetic waves in the curved portion of the Goubau line are radiating outwards as leaky waves, the cylindrical dielectric resonator is simultaneously absorbing the electromagnetic energy backward and inwards. The radiation loss in this scenario will be nullified or minimized as a result of the permittivity of the dielectric resonator. The electromagnetic energy being absorbed back to the cylindrical resonator will eventually manifest as a dielectric loss but this dielectric loss is totally independent of the ambient electromagnetic interference. On the other hand, the cylindrical dielectric resonator will also yield a series of stop bands at different resonant frequencies. These resonant frequencies can be approximately determined using the formula proposed by Siart [16]:

$$f_{m,TE} = \frac{0.5m}{b - a} \frac{c}{\sqrt{\mu_0(\varepsilon_r - \varepsilon_0)}} \tag{9a}$$

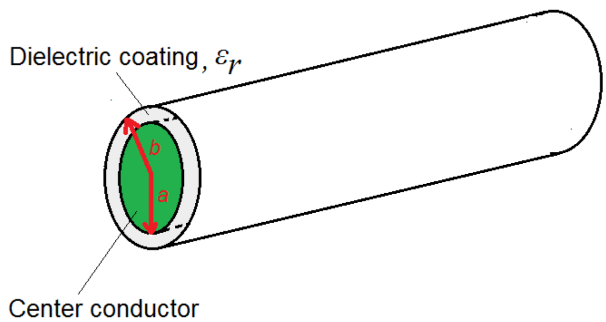
$$f_{m,TM} = \frac{0.5(m+0.5)}{b-a} \frac{c}{\sqrt{\mu_0(\varepsilon_r - \varepsilon_{0)}}} \tag{9b}$$

where m is the order of mode. $f_{m,TE}$ and $f_{m,TM}$ are respectively the cut off frequencies of the m-th transverse electric mode and the m-th transverse magnetic mode. According to Equations (9a) and (9b), a change in the blood permittivity will induce a larger increase at the resonance of a higher order mode. If this resonance occurs at the frequencies close to the cut-off frequency as given in Equation (8), the leaky modes will be absorbed and converted into a dielectric loss that is highly dependent on permittivity of the cylindrical dielectric resonator.

Reducing the radiation loss of the Goubau line through the use of a cylindrical dielectric resonator implies that, at the cut-off frequency as given Equation (9a) or (9b), the proposed glucose measuring device will be less susceptible to the ambient electromagnetic interference. The main goal of this work is to take advantage of the effects due to the presence of the cylindrical dielectric resonator to determine the blood glucose levels. If the cylindrical dielectric resonator is a cylindrical volume of skin tissue filled with blood, and if the geometry of the cylindrical dielectric resonator is fixed, then we should be able to determine the exact permittivity due to the glucose concentration in the blood. In this work, this cylindrical volume of a blood-filled skin tissue is arbitrarily formed by vacuum suction using a twisted vacuum suction aspirator (see Figure 1d).

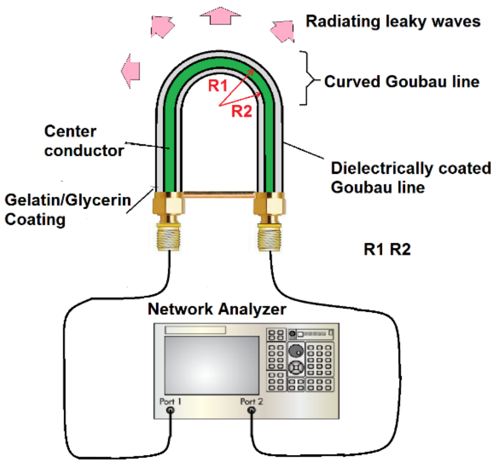
Figure 1d shows how the cylindrical volume of the blood-filled skin tissue is formed by vacuum suction. Due to the low pressure inside the vacuum suction aspirator, a large amount of blood will flow into the area of the skin where a blood glucose measurement is conducted. The proposed technique will not cause any injury to the skin or the body tissue even after several hours of use. Unlike other invasive techniques involving the use of a lancet, the proposed technique will allow the blood glucose levels to be continuously and painlessly monitored over a prolonged period. As the proposed glucose sensor releases or absorbs very little ambient electromagnetic energy, the measured scattering parameters will be highly stable. On the other hand, because the volume of the blood-filled skin tissue is very much fixed from one measurement to another, issue #2 as stated in the introduction section is very much a non-issue. In fact, the measured results have been proven to be accurate and reproducible.

The permittivity change of the blood is known to be a weak function of the glucose concentration in the blood at microwave frequencies. However, regardless of how small this blood permittivity change is, this blood permittivity change in the proposed methodology will induce an enormous change in the scattering parameters at frequencies around the cut-off frequency given by Equation (8).



(a)

Figure 1. *Cont.*



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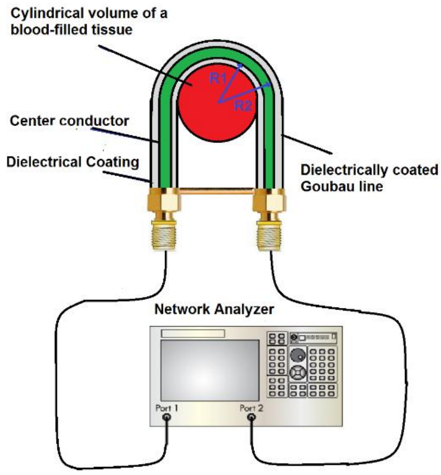
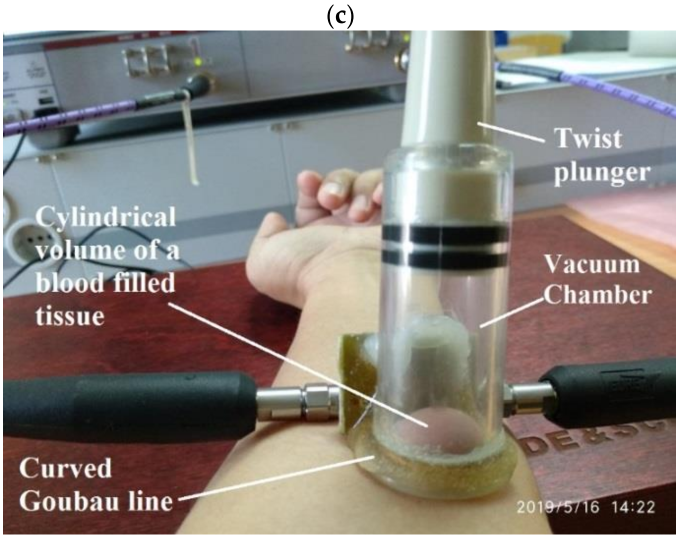


(**c**)



(**d**)

Figure 1. Concept of the proposed blood glucose measurement. (**a**) a straight dielectrically coated Goubau line; (**b**) a measurement setup for a curved Goubau line; (**c**) a measurement setup for the proposed blood glucose measurement; and (**d**) a photo showing how the cylindrical volume of a blood-filled skin tissue is formed using a vacuum suction aspirator.

3. Materials and Methods

To validate the proposed concept, we conducted a series of in-vivo blood glucose measurements in the Vietnamese German University of Vietnam as well as the Chinese Academy of Sciences in China. In each in-vivo blood glucose measurement, a participant was guided by a nurse to undergo an invasive blood glucose measurement involving the use of a lancing device known as Accu Chek Flaxclix^{TM} (Roche Diabetes Care, Inc., Indianapolis, IN, United States) at a particular time of the day. Within 15 m after this invasive blood glucose measurement, the participant was guided through a non-invasive blood glucose measurement on both left and right hands using the proposed method as illustrated in Figure 1c. The network analyzer used in this work was ZVA45B manufactured by Rohde & Schwarz R&S (in Mühldorfstraße 15, 81671 Munich Germany). During the measurements, the participants were allowed to move their body violently. Figure 2a shows the photograph of the actual setup for each non-invasive blood glucose measurement.

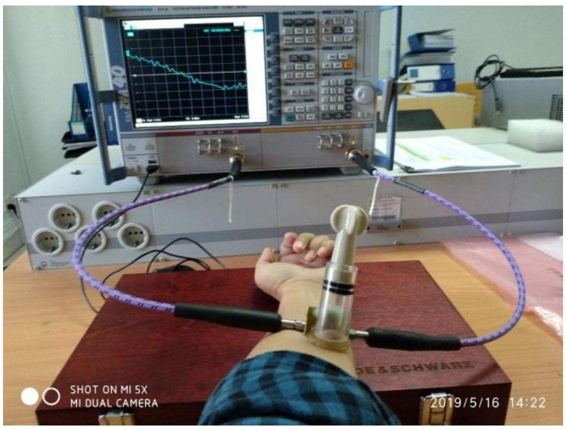
The data samples were collected over different blood glucose levels from 41 volunteers who were university staff members and school-aged students. Altogether, we managed to measure over 45 blood samples with blood glucose levels ranging from 60 mg/dl to 130 mg/dl. The measured results from the proposed non-invasive blood glucose measurements were then analyzed and compared with the results obtained using the invasive method.

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Vietnamese German University (VGU-EEIT-308).

The vacuum suction aspirator was an online shopping mall product known as a vacuum plunger, purchased from a cross-border seller in Lazada-Taobao. On the exterior wall of the vacuum suction aspirator as shown in Figure 1d, the area where the curved Goubau line was mounted was milled with a groove using a 5-axis precision CNC (Computerized Numerically Controlled) machine. The milling depth of the groove was maximized to minimize the separation between the Goubau line and the skin tissue to just 0.3 mm.

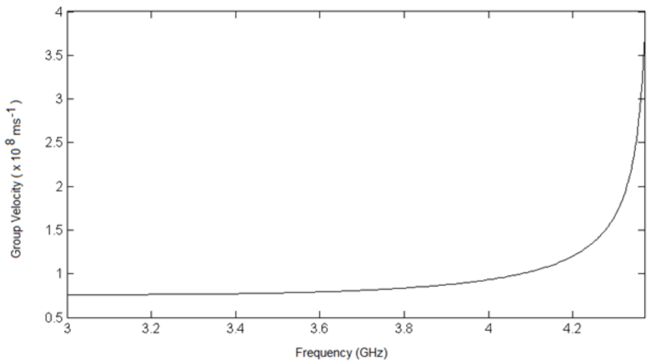
The center conductor of the curved Goubau line has a cross-sectional radius of 1mm. The dielectric material coating the Goubau line is a 3.8 mm thick layer of thermally cured gelatin/glycerin composite which has a dielectric constant of 60. Using the formula given in Equation (7), the cut-off frequency of the Goubau line was determined to be 4.36 GHz. Figure 2b shows the group velocity of the Goubau line as a function of frequency computed using the formula in Equation (6).

The diameter of the cylindrical blood-filled skin tissue is 10 mm. According to Equation (9b), there was supposed to be a transverse magnetic resonant in the neighborhood of 4.5 GHz when $m = 4$.



(**a**)

Figure 2. *Cont.*



(**b**)

Figure 2. Details of the experiment. (**a**) The photo showing the actual measurement setup for measuring the blood glucose on the left hand; and (**b**) calculated group velocity of a surface wave propagating in the curved Goubau line (of which the diameter of the central conductor is 1 mm and the thickness of the gelatin coating is 3.8 mm).

4. Results

This section presents the results of our in-vivo measurement from the data samples from the participants with a normal blood pressure from the 41 volunteers. These participants include the university staff members and school-aged students. Most of the data samples have repeated blood glucose levels. The measurements were obtained from different times of the day.

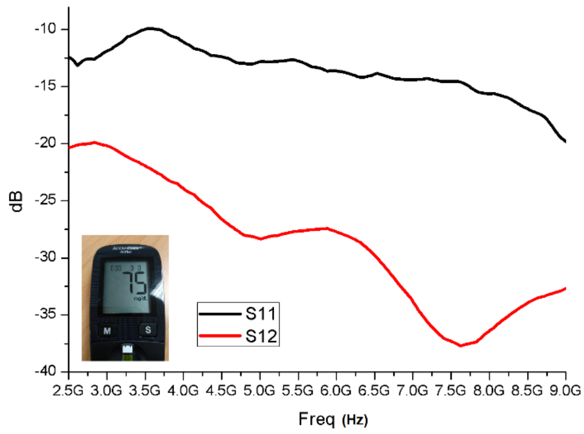
Figure 3a shows the scattering parameters as a function of frequency in the dB scale when the blood glucose level was 77 mg/dl. A similar plot was obtained for each of the other blood glucose levels. It can be observed from Figure 3a that both S11 and S12 parameters started to trend downwards at frequencies higher than 4.35 GHz. The simultaneous downtrend of S11 and S12 parameters is an indication of an increase in leaky wave radiation efficiency.

During the measurements, the measured scattering parameters were very much unchanged at frequencies below 4.5 GHz even though the participants moved their bodies. The measured scattering parameters remained stable even when the nearby metal objects were moved. However, when the participants moved their bodies, the instability in terms of measured scattering parameters started to become obvious at frequencies higher than 4.6 GHz.

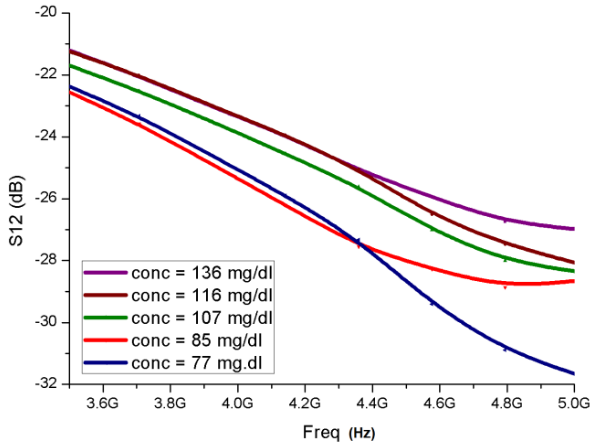
Figure 3c shows that there is a positive correlation between the blood glucose levels and the S12 parameters. This near-linear correlation was obtained by extracting the data of Figure 3b right at 4.57 GHz. The linearity of this correlation was almost completely lost at frequencies higher than 4.8 GHz.

During the non-invasive blood glucose measurement, we also observed an imbalance between the left and right hands on two participants. The measured differences in scattering parameters were small and, in terms of percentage, the differences were within 3%. We repeated the measurements several times but the observed phenomena remained.

We also used the same experimental setup to conduct a series of similar in-vivo measurements at frequencies very close to 60 GHz. The measured S21 or S12 parameters were between −65 dB and −80 dB. However, the measured scattering parameters at around 60 GHz were found to be unstable and non-reproducible from one experiment to another.



(**a**)



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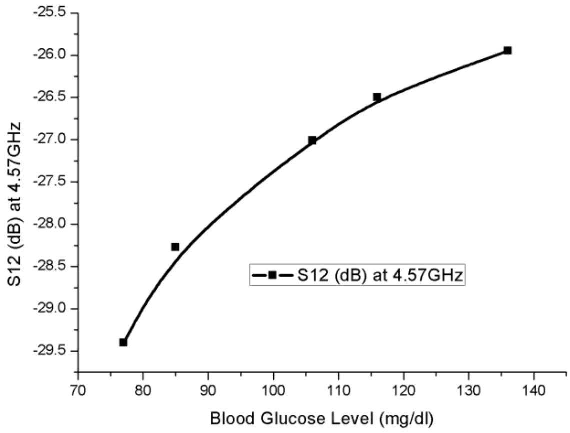

(**c**)

Figure 3. Measured results. (**a**) The measured S11 and S12 parameters against frequency when the blood glucose level was 75 mg/dl; (**b**) the measured S12 parameters as a function of frequency for different blood glucose levels (as denoted as "conc" in the graph). It is important to note that the blood glucose levels in this graph were obtained using the traditional lancing method within 15 m before the measurement of the S-parameters was conducted; (**c**) a graph showing the near-linear relationship between the blood glucose levels and the S12 parameters right at 4.57 GHz.

5. Discussion

The results of this investigation have proven beyond any doubt that the non-invasive blood glucose measurement using the proposed approach was reliable only when the interference from ambient leaky waves was significantly suppressed. The equations as given in Section 2 predicted the existence of the fundamental cut-off frequency at around 4.35 GHz, whilst the measured results reveal that the measurements started to be erratic and unstable at frequencies higher than 4.6 GHz, particularly at the time when the participant moved his/her body. It is possible that, at around 4.57 GHz, the cylindrical volume of the blood-filled skin tissue absorbed most of the leaky waves that would otherwise be lost to the surrounding. At 4.8 GHz, the effects of leaky waves of the blood glucose monitoring device completely took over those of the surface electromagnetic waves. At frequencies between 4.35 and 4.6 GHz, the measured scattering parameters were not only stable but also reproducible from experiment to experiment.

The effects of leaky waves were clearly counter-productive as far as non-invasive blood glucose measurements are concerned. The proposed blood glucose sensor as illustrated in Figure 1d was designed to minimize all forms of leaky waves. However, at each of the SMA terminals, the discontinuity between the coaxial line and the Goubau line did encourage excitation of higher order modes, which were mostly leaky in nature. In order for the measurement errors to be further minimized, there should be a smooth tapered transition between the coaxial cable and the Goubau line. We expect to implement this improvement in the next stage of the project.

As pointed out in Sections 1 and 2, the change in S-parameters due to a change in the blood glucose concentration can be magnified right at the cut-off frequency, which was 4.35 GHz in the proposed glucose measuring device. In Figure 3b, it can be seen that, at 3.5 GHz, a blood glucose level change from 75 mg/dl to 136 mg/dl produced an overall magnitude change of 1.42 dB in the S12 parameter. This magnitude change in the S12 parameters gradually increased as the frequency went higher. When the frequency was at or higher than 4.35 GHz, the magnitude of the S12 parameter for each concentration of blood glucose became noticeably observable. At frequencies in the neighborhood of 4.57 GHz, the same change in the blood glucose level resulted in an overall magnitude change of 4 dB in the S12 parameter. This amplified magnitude change in the S12 parameter was due in major part to the blood glucose levels when the propagating energy was changed from the transverse fundamental magnetic mode into the higher order transverse electromagnetic modes at the cut off frequency (i.e., 4.35 GHz). In this device, which is fundamentally different from other published counterparts [3,17–20], the majority of the energy from these higher order transverse electromagnetic modes was absorbed back as dielectric losses by the cylindrical volume of blood filled skin tissue, which, according to Equation (9a), also resonated at around the cut-off frequency.

One of the potential contributing factors to the uncertainties in the non-invasive blood glucose measurement was the accuracy of the calibration of a vector network analyzer. We were mindful of this issue. In this work, the TRL (Thru, Reflect, Line) calibration we used was based on the ZV-Z229 CALIBRATION KIT 2.92 mm from Rohde & Schwarz R&S (in Mühldorfstraße 15, 81671 Munich Germany). So far, we have not encountered any problem with the calibration. The measured S-parameters were consistently reproducible with little loss of accuracy from one experiment to another even though the calibration was re-done again and again.

During the non-invasive blood glucose measurement, the S12 parameters for 85 mg/dl and 77 mg/dl also overlapped at frequencies below 4.35 GHz. This was due to the fact that the participants' blood pressures were not 100% stable during the time when they were going through the non-invasive blood glucose measurements.

During our non-invasive blood glucose measurement, we observed an imbalance in terms of the measured scattering parameters in two individuals. This imbalance did not appear to be removable even after several attempts. The amount of blood flowing into the skin area where the proposed sensor was applied was dependent upon the combined effect of the individual's blood pressure and the air pressure inside the vacuum suction aspirator. If there is any difference in terms of the measured

S12 parameters between the left and right hands, then this imbalance was most likely due to the issue of blood circulation in their bodies. This imbalance cannot be detected using the conventional invasive Acuu-chek lancing approach. Although our observation is inconclusive at this stage, there is an implication that the proposed methodology can be further applied in detecting a left and right imbalance in the human body.

The results of this investigation have clearly proven beyond any doubt that the proposed methodology can be used to conduct in-vivo measurements with accurate and reproducible results. At the time of this writing, there has been a widespread misconception in the scientific community that non-invasive blood glucose monitoring is not possible. The findings of this work have demystified this misconception not only in terms of accuracy but also in terms of reproducibility and reliability.

6. Conclusions

This paper has presented an approach for non-invasive blood glucose monitoring at microwave frequencies based on surface electromagnetic waves. According to the results of our investigation, failure to obtain a reproducible blood glucose measurement was mainly due to the leaky wave interaction between the blood glucose measuring device and the ambient environment. This problem has been overcome through the use of surface electromagnetic waves propagating along a curved Goubau line. In the proposed methodology, a fixed volume of blood-filled skin tissue was created by vacuum suction and partially wounded with the said curved Goubau line. Non-invasive blood glucose measurements were conducted by measuring the S12 or S21 parameters between two terminals of the curved Goubau line using a network analyzer. At 4.5 GHz, there is a near-linear correlation between the measured S12 parameters and the blood glucose levels. The measured results at 4.5 GHz were both reproducible and consistent with the measurement obtained using the conventional invasive lancing approach. Implicated in the findings of this work is the feasibility of non-invasive detection of a left and right imbalance in the body.

Author Contributions: L.W.Y.L. has the original idea. L.W.Y.L. and A.K. participated in organizing the in-vivo and ex-vivo experiments using the proposed methodology. All other authors had a varying degree of intellectual contribution to this work. All authors helped in improving the article.

Funding: This research is internally funded by the authors' universities. This research received no external funding.

Acknowledgments: The authors would like to acknowledge the help from the nurse at Vietnamese German University, Nguyễn Thị Hoa.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Karacolak, T.; Moreland, E.C.; Topsakal, E. Cole-cole model for glucose-dependent dielectric properties of blood plasma for continuous glucose monitoring. *Microw. Opt. Technol. Lett.* **2013**, *55*, 1160–1164. [CrossRef]
2. Choi, H.; Nylon, J.; Luzio, S.; Beutler, J.; Porch, A. Design of continuous non-invasive blood glucose monitoring sensor based on a microwave split ring resonator. In Proceedings of the 2014 IEEE MTT-S International Microwave Workshop Series on RF and Wireless Technologies for Biomedical and Healthcare Applications (IMWS-Bio2014), London, UK, 8–10 December 2014.
3. Cano-Garcia, H.; Gouzouasis, I.; Sotiriou, I.; Saha, S.; Palikaras, G.; Kosmas, P.; Kallos, E. Reflection and transmission measurements using 60 GHz patch antennas in the presence of animal tissue for non-invasive glucose sensing. In Proceedings of the 2016 10th European Conference on Antennas and Propagation (EuCAP), Davos, Switzerland, 10–15 April 2016.
4. Xie, K.; Liu, L.W.; Zhang, Q.; Cheng, Q. Monitoring blood glucose fluctuation using SIW cavity with a coupling slot. In Proceedings of the 2017 Sixth Asia-Pacific Conference on Antennas and Propagation (APCAP), Xi'an, China, 16–19 October 2017.
5. Goubau, G. Surface Waves and Their Application to Transmission Lines. *J. Appl. Phys.* **1950**, *21*, 1119. [CrossRef]
6. Goubau, G.J.E. Surface Wave Transmission Line. U.S. Patent 2,685,068, 27 July 1954.

7. Chiron, B.P. Surface Wave Transmission Line Element. U.S. Patent 2,807,786, 21 May 1953.
8. Liu, L.W.Y.; Zhang, Q.; Chen, Y. Harvesting Atmospheric Ions Using Surface Electromagnetic Technology. *Adv. Technol. Innov.* **2017**, *2*, 99–104.
9. Liu, L.W.Y.; Ge, S.; Zhang, Q.; Chen, Y. Capturing surface electromagnetic energy into a dc through single-conductor transmission line at microwave frequencies. *Prog. Electromagn. Res. M* **2017**, *54*, 29–36. [CrossRef]
10. Liu, L.W.; Zhang, Q.; Chen, Y.; Teeti, M.A.; Das, R. Wireless Energy Harvesting by Direct Voltage Multiplication on Lateral Waves from a Suspended Dielectric Layer. *IEEE Access* **2017**, *5*, 21873–21884. [CrossRef]
11. Liu, L.W.; Kandwal, A.; Eremenko, Z.E.; Zhang, Q. Open-ended voltage multipliers for wireless transmission of electric power. *J. Microw. Power Electromagn. Energy* **2017**, *51*, 187–204. [CrossRef]
12. Liu, L.W.; Zhang, Q.; Chen, Y. Avramenko Diode Circuit Topology for Microwave Energy Harvesting in Goubau Line and Wireless. *IEEE Access* **2018**, *6*, 18883–18893. [CrossRef]
13. Louis, W.L.; Abhishek, K.; Hongjian, S.; Qingsha, S.C. Wireless Power Transfer using An RF Plasma. *IEEE Access* **2018**, *6*, 73905–73915.
14. Poynting, J.H. On the Transfer of Energy in the Electromagnetic Field. *Proc. R. Soc. Lond.* **1883**, *36*, 186–187. [CrossRef]
15. Jaisson, D. Simple formula for the wave number of the Goubau line. *J. Electromagn.* **2014**, *34*, 85–91. [CrossRef]
16. Siart, U.; Adrian, S.; Eibert, T. Properties of axial surface waves along dielectrically coated conducting cylinders. *Adv. Radio Sci.* **2012**, *10*, 79–84. [CrossRef]
17. Saha, S.; Cano-Garcia, H.; Sotiriou, I.; Lipscombe, O.; Gouzouasis, I.; Koutsoupidou, M.; Palikaras, G.; MacKenzie, R.; Reeve, T.; Kosmas, P.; et al. A Glucose Sensing System Based on Transmission Measurements at Millimetre Waves using Micro strip Patch Antennas. *Sci. Rep.* **2017**, *7*, 6855. [CrossRef] [PubMed]
18. Shaker, G.; Smith, K.; Omer, A.E.; Liu, S.; Csech, C.; Wadhwa, U.; Safavi-Naeini, S.; Hughson, R. Non-Invasive Monitoring of Glucose Level Changes Utilizing a mm-Wave Radar System. *Int. J. Mob. Hum. Comput. Interact.* **2018**, *10*, 10–29. [CrossRef]
19. Shaker, G.; Liu, S.; Wadhwa, U. Non-invasive glucose monitoring utilizing electromagnetic waves. In Proceedings of the ACM 19th International Conference on Human-Computer Interaction with Mobile Devices and Services, Vienna, Austria, 4–7 September 2017.
20. Torii, T.; Chiba, H.; Tanabe, T.; Oyama, Y. Measurements of glucose concentration in aqueous solutions using reflected THz radiation for applications to a novel sub-THz radiation non-invasive blood sugar measurement method. *Digit. Health* **2017**, *3*, 2055207617729534. [CrossRef] [PubMed]