Conference contribution :
Choi, H., Luzio, S., Beutler, J. & Porch, A. (2018). *Microwave Noninvasive Blood Glucose Monitoring Sensor: Penetration Depth and Sensitivity Analysis.*(pp. 52-54). Philadelphia, PA, USA: 2018 IEEE International Microwave Biomedical Conference (IMBioC).
http://dx.doi.org/10.1109/IMBIOC.2018.8428850

Microwave Noninvasive Blood Glucose Monitoring Sensor: Penetration Depth and Sensitivity Analysis

Heungjae Choi[1], Steve Luzio[2], Jan Beutler[3], and Adrian Porch[1]
[1] School of Engineering, Cardiff University, CF24 3AA Wales, United Kingdom
[2] College of Medicine, Swansea University, SA2 8PP Wales, United Kingdom
[3] University of Luxembourg, L-4365 Luxembourg

***Abstract*— Previously reported clinical performances of microwave noninvasive blood glucose monitoring sensor look promising. It is clear that dielectric properties are changing when the food intake takes place, but the exact physiological mechanism is not clear. In an attempt to figure out the physiological mechanism of microwave noninvasive blood glucose monitoring sensor, this paper presents a series of studies to find out a) the penetration depth of the microwave resonator-based sensor and b) the effect of permittivity variation of human tissues on the microwave resonator parameters.**

***Index Terms*—Diabetes, microwave sensors, permittivity measurement, penetration depth, resonators, sensitivity.**

I. Introduction

Diabetes is affecting 7% of the world's population and the number is ever increasing according to the changes in dietary habits and lifestyles [1]. There is no known cure for diabetes yet, therefore frequent monitoring and tight control of blood glucose level is the alternative solution to reduce the risk of further complications due to diabetes. Finger-prick test with a glucose meter is a simple but accurate, and most widely used method. However the maintenance costs for lancets, needles, and test-strips are not negligible, not to mention the pain and the risk of infection. Continuous glucose monitors (CGMs) based on tiny flexible subcutaneous needles have recently been gaining popularity [2]. One of the merits is that they provide history and continuous trends of glucose levels. However, these devices measure interstitial fluid glucose concentration, which is a time-delayed version of blood glucose concentration found in blood plasma. Therefore finger-prick test must always accompany CGMs to confirm actual blood glucose concentration.

Microwave sensors have been widely used in the precise dielectric characterization of organic and inorganic materials in minimally invasive or noninvasive ways, especially for biomedical applications [3]. Noninvasive glucose monitoring sensors have been actively researched across the whole electromagnetic wave spectrum including RF, microwave, mm-wave and terahertz frequencies [4]-[6], including the promising human clinical trial results by the authors [7][8].

It is clear that microwave sensors are able to monitor subtle change in dielectric properties in human tissues. However, it is not obvious specifically *what* causes the change in dielectric properties, and *where* in the tissue layer this change happens. Therefore this paper presents a series of studies to find out a) the penetration depth of the microwave resonator-based sensor and b) the effect of permittivity variation of tissues on the microwave resonator parameters.

II. Penetration Depth Analysis

As mentioned in the previous section, at first, it is necessary to understand the penetration depth of the microwave sensor. This study is based on the split-ring resonator sensor operating around 1.4 GHz proposed in [7][8] with the human tissue model designed in COMSOL Multiphysics v4.4.

A. Simulation Model and Parameter Setup

Fig. 1 shows the multilayer tissue model around abdominal area where the microwave sensor is attached. The thickness of skin, fat, muscle layers is 3 mm, 7 mm, and 35 mm, respectively. Electric conductivity, relative permittivity, and loss tangent of human tissue layers at the frequency of operation were obtained from the literature [9]. Adhesive tape is not included in the model. The input power to the coupling port of the resonator is 0 dBm. E-field profile is obtained along the axis of penetration (see side view in Fig. 1) at three different location of a split-ring resonator, at the gap (point A), at the center of the ring, and at the opposite side of the gap (point C) where magnetic field (H-field) component is strongest.

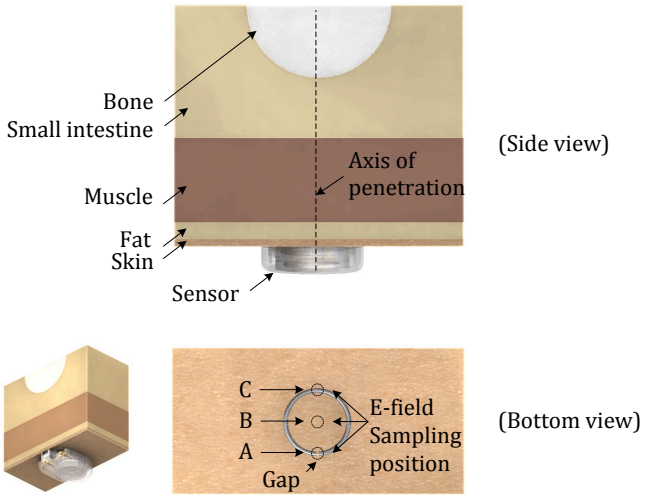


Fig. 1. Multilayer tissue model around abdominal area where the microwave sensor is attached. In the bottom view, only the split-ring resonator is shown to illustrate where the electric field intensity is monitored (point A, B, and C).

B. Penetration Depth Analysis

Attenuation profile of the normalized E-field in log-scale along the axis of penetration at three different points A, B, and C is shown in Fig. 1. The distance from 0 to 10 mm is inside the sensor device. The ring resonator is placed about 2 mm away from the skin. When there is a split-ring resonator, intuitively we expect that E-field is strongest at the gap of the ring (A) and weakest at the opposite side of the ring (C). As expected, the E-field is strongest at the gap of the ring (square), to be ~1.5 kV/m. However, the slope of attenuation is much higher at point A than B and C inside the sensor through PTFE. At the sensor/skin boundary, the incident E-field intensity is almost identical at point A and C, to be ~9 V/m. Also, through skin and fat layer, the slope of attenuation at point A is much higher, therefore at the fat/muscle boundary the incident E-field intensity is the lowest, both of which are counter-intuitive to what we expect from a split-ring resonator. This could help explain the position-dependent performance variation of the proposed sensor [8]. If we draw a reference line at the field intensity of 1 V/m, the penetration depth at point A, B, and C can be estimated as 8 mm, 18 mm, and 20 mm. If we assume that 1 V/m reference line is valid threshold, this means the sensitivity is better at the opposite side of the ring than at the gap. This will be further investigated in the next section.

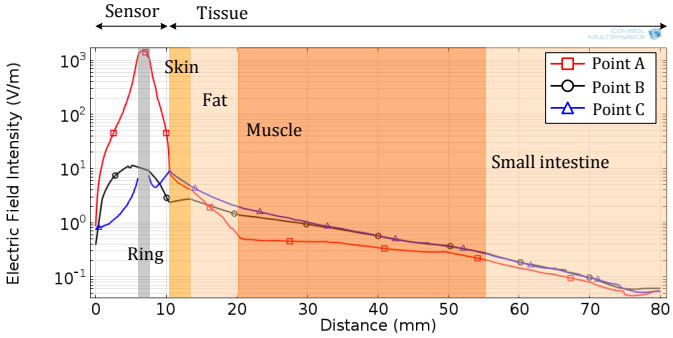


Fig. 2. Electric field intensity profile along the axis of penetration at point A, B, and C of the split-ring resonator (see Bottom view in Fig. 1).

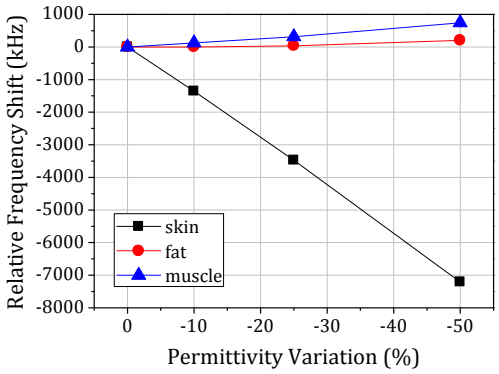
III. Effect of Permittivity Variation at Tissue Layers

To be able to understand *what* causes the change in dielectric properties and *where* in the tissue layers the change happens, two parametric case studies have been carried out. In Study 1, we investigated the change in microwave resonator response as a result of the variation in relative permittivity (ε_r) of one layer at a time. From our previous studies, the amount of expected resonant frequency shift and change in 3 dB bandwidth due to varying blood glucose concentration in humans is less than 1 MHz [7][8]. In dielectric characterization of aqueous glucose solution by the authors, there was about 10% change in real and imaginary permittivity when the glucose concentration was varied between 0 to 500 mmol/L [10].

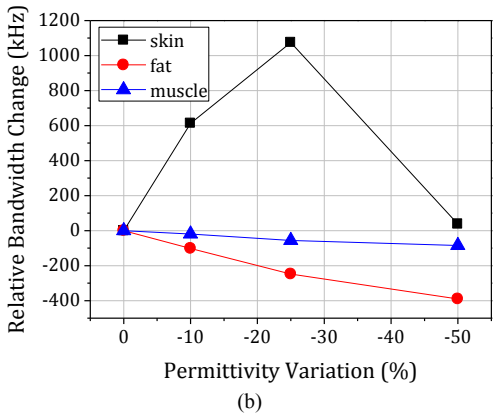
In Study 2 additional layer of blood with thickness of 0.5 mm is added and the position (depth) of this blood layer is moved from skin/fat boundary to fat/muscle boundary to muscle/small intestine boundary and the effect on the resonator parameter is analyzed. At each position, relative permittivity is varied while other layers remain constant. Relative permittivity is varied by 0, 10, 25, and 50% in both studies to clearly observe the trend, although 25% and 50% may seem to be excessive considering realistic permittivity change according to blood glucose fluctuation within clinical range. Eigen frequency analysis is used in the same model shown in Fig. 1 to obtain resonant frequency and 3 dB bandwidth.

A. Study 1: Change in ε_r at Each Layer

In Fig. 1 (a), when ε_r of skin layer is reduced by 0, 10, 25, and 50% while other layers do not change, resonant frequency is increased by 1.3, 3.4, and 7.2 MHz, respectively. This causes huge changes in resonant frequency and bandwidth as the skin is closest to the sensor. Fat layer does not affect the resonance much, as we know that there is no blood within the fat tissue. Muscle shows more contribution to the frequency shift than fat tissue. This also confirms that the penetration depth estimation from the previous section is valid, in other words, the sensor is able to monitor the change in muscle layers (assuming other layers remain constant).



(a)



(b)

Fig. 3. Effect of percentage permittivity variation at each layer.

B. Study 2: Change in ε_r at a Thin Blood Layer Placed Between Two Layers

As explained, additional layer of blood (0.5 mm) is added at skin/fat boundary, fat/muscle boundary, and muscle/small intestine boundary, respectively, to more realistically estimate the origin of the changes in resonator parameters that we observed on our sensor on the skin. When the thin blood layer is placed at skin/fat boundary (square in Fig. 4), this emulates cutaneous vascular plexus located between epidermis and adipose tissues. When the blood layer is placed at fat/muscle boundary, this emulates major arteries and veins deep inside (circle in Fig. 4). Due to the penetration depth, no effect on resonant frequency is observed due to the change at the blood layer beyond muscle layer (triangle in Fig. 4).

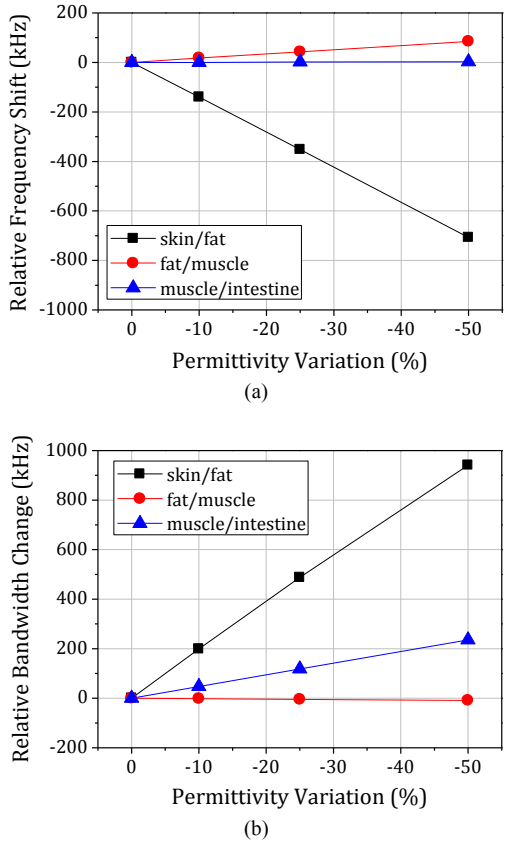


Fig. 4. Effect of percentage permittivity variation at each layer with a blood layer placed at the boundary.

IV. Conclusion

If we assume that 10% permittivity variation takes place in human tissue due to fluctuation in glucose concentration, especially in a thin layer of blood as in Study 2 while other tissue layers remain constant, the microwave interaction with blood plasma in cutaneous vascular plexus layer seems like a promising explanation. Further experimental verification and consultation with clinician and medical experts will follow up as future work.

Acknowledgment

This work was supported by the Wellcome Trust [WT096848MA]; Cardiff Partnership Fund through Cardiff University; Part-funded by the European Regional Development Fund through the Welsh Government.

References

[1] International Diabetes Federation. *IDF Diabetes Atlas, 7 ed.* Brussels, Belgium: International Diabetes Federation, 2015.

[2] H. Choi, "Recent developments in minimally and truly non-invasive blood glucose monitoring techniques," *SENSORS, 2017 IEEE*, Glasgow, United Kingdom, 29 Oct. – 1 Nov. 2017.

[3] M. Hofmann, G. Fischer, R. Weigel, and D. Kissinger, "Microwave-based noninvasive concentration measurements for biomedical applications," *IEEE Trans. Microw. Theory Techn.*, vol. 61, pp. 2195-2204, May 2013.

[4] K. Zarkogianni, E. Litsa, K. Mitsis, P. W, C. D. Kaddi, C. Cheng, M. D. Wang, and K. S. Nikita., "A review of emerging technologies for the management of diabetes mellitus," *IEEE Trans. Biomedical Engineering*, vol. 62, no. 12, pp. 2735-2749, Dec. 2015.

[5] A. Caduff, E. Hirt, Y. Feldman, Z. Ali, and L. Heinemann, "First human experiments with a novel non-invasive, non-optical continuous glucose monitoring system," *Biosensors and Bioelectronics*, vol. 19, no. 3, pp. 209-217, Nov. 2003.

[6] P. H. Siegel, *et al*, "Millimeter-wave non-invasive monitoring of glucose in anesthetized rats," *in 39th Int. Conf. Infrared, Millimeter, and Terahertz waves (IRMMW-THz)*, Tucson, AZ, Sept. 14-19, 2014, pp. 1-2.

[7] H. Choi, J. Naylon, S. Luzio, J. Beutler, J. Birchall, C. Martin, and A. Porch, "Design and in vitro interference test of microwave noninvasive blood glucose monitoring sensor," *IEEE Trans. Microw. Theory Techn.*, vol. 63, no. 10, pp. 3016-3025, Oct. 2015.

[8] H. Choi, S. Luzio, J. Beutler, and A. Porch, "Microwave noninvasive blood glucose monitoring sensor: human clinical trial results," *Microw. Symp. (IMS), 2017 IEEE MTT-S Int'l*, Honolulu, HI, USA.4-9 June 2017.

[9] S. Gabriel, R. W. Lau, and C. Gabriel, "The dielectric properties of biological tissues: II. Measurements in frequency range 10 Hz to 20 GHz," *Phys. Med. Biol.*, vol. 41, no. 11, pp. 2251-2269, Nov. 1996.

[10] H. Choi, S. Luzio, and A. Porch, "Dielectric properties of aqueous glucose solutions using microwave cavity and coaxial probe," *2nd Australian Microwave Symposium 2016*, Adelaide, Australia, Feb. 2016.