Fourier Transform Infra-Red spectrophotometry observation to find appropriate wavelength for non-invasive blood glucose level measurement optical device

H Alatas¹,a, Y Suryana², S Pambudi³, T Widayanti³, R Jenie¹-⁴, R Zaheri¹, A Aridarma⁵, S K Rahayu⁵, T S Riadhie⁵, V Rahmawaty¹, N P Har¹, M Zuhri¹, T Sumaryada¹, and Irzaman¹,b

¹ Physics Department, IPB University, Babakan, Dramaga, Bogor, West Java 16680
² TIEM - BPPT, Puspiptek, South Tangerang 15314
³ LAPTIAB - BPPT, Puspiptek, South Tangerang 15314
⁴ Nutrition Department, Binawan University, Kalibata, Jakarta 13630
⁵ PT. Tesena Inovindo, Susukan, Jakarta 13750

E-mail: aalatas@apps.ipb.ac.id, birzaman@apps.ipb.ac.id

Abstract. The appropriate wavelength is essential for non-invasive blood glucose level measurement optical device. We conducted this experimental observation to find the usable wavelength candidate for non-invasive blood glucose level measurement optical device in 1000 nm to 2500 nm range. We run this observation in Prodia Bogor and Food Processing and Crops Technology Lab, Faculty of Agricultural Engineering, IPB University, July 2019. We obtained fasting, 15 mnt postprandial, and 30 mnt postprandial blood sample from 10 randomly selected non blinded healthy adult subjects between 18 to 60 years old. We measured spectrophotometric absorbance for each blood sample. We did the measurement using BUCHI NIR FLEX 500. We compared the result to blood glucose level by standard gold measurement. We also compared the Pearson correlation, and the standard deviation of all samples to then-existing wavelength source LED provided by Thorlabs. We found that the highest absorbance wavelength is at 1939 nm. Wavelength LEDs candidates that represent measuring blood glucose levels is 1200, 1300, 1450, 1750, and 1950 nm. We did not find a severe adverse effect from each participant. Researchers should confirm the trial results with in vivo human observation.

1. Introduction

Most people already aware of the general risk of conventional phlebotomy-based method, such as physical and psychological trauma, disease spread, or simple malpractice, as well as relatively high cost for daily use [1–3]. This fact fosters researchers to find generally safer methods to measure blood glucose level. Researchers have seen spectrophotometry-based methods as potent methods for blood glucose level measurement due to their potential to eliminate consumable costs [4–6]. We were previously done a review on wavelength for non-invasive blood glucose level measurement optical device using bio-assayed blood control sample. The result is promising, yet we are aware that we should verify these results with real human blood samples [7,8]. We have done this review to support our development research for non-invasive blood-glucose-level measurement device [8,9]. We have done this because the appropriate wavelength is directly related to blood-glucose-level measurement.
accuracy, sensitivity, and specificity [10,11]. We have done this experimental observation to find the usable wavelength candidate for non-invasive blood glucose level measurement optical device in 1000 nm to 2500 nm range.

2. Methods

2.1. General Methods
This article describes a quantitative experimental observation of wavelength absorbance for subject blood between 1000 to 2500 nm. We focus our observation on the change of absorbance due to the change in blood glucose level. Human Research Ethical Committee of IPB University has approved this research protocol, which we have register under ethical clearance 076/IT3.KEPMSM-IPB/SK/2018. Lembaga Pengelola Dana Pendidikan has supported this study using Riset Inovatif Produktif Invitasi, with grant number PRJ-78/LPDP/2019, 2 December 2019. This research protocol is a modification from our previous researches [7,12,13], adapted to live human blood glucose level sample in the infrared range.

2.2. Blood Sample Procurement
We have done the blood sample procurement in Prodia Office in Bogor, in July 2019. There are ten volunteers for this study which already read the research information the day prior. They also have signed informed consent before participating in this study. We did not implement randomisation nor blinding in this study. Subjects are male or female between 18 to 60 years old and did not under glucose disorder medication. We also exclude those who are pregnant or breast feeding in the duration of this observation. The Subjects underwent eight hours of fasting before blood taking procedure. We have done the blood taking procedure three times, at fasting state and 15 and 30 mins postprandial. The Subjects are taking 75 mg of pure glucose in 200 ml water solution after first blood taking session. Each blood taking procedure yields 3 ml of the blood sample, and the whole procedure yields 30 samples. Each sample is observed three times, in total yields 90 samples, which would enough for typical spectral observation study.

2.3. Blood Observation
We run this observation in Prodia Bogor and Food Processing and Crops Technology Lab, Faculty of Agricultural Engineering, IPB University, West Java, July 2019. We have observed each blood samples three times using Buchi NIRFlex N-500 (BÜCHI Labortechnik AG, Switzerland). We then calculated the Pearson correlation and standard deviation of all samples. We superimposed the data with the available LED from Thorlabs (Thorlabs inc., USA). We have used GNU R (The R Foundation, USA), RKward (KDE e.V., Germany), and RStudio (RStudio PBC, USA) for data analysis.

3. Result and Discussions
We have included all ten subject’s data in this data analysis. We have conducted each blood sample procurement and blood observation procedure within four hours - the whole event taking two days. We stop the procedure after we have taken and observed all sample. We did not find a severe adverse effect from each participant. We have found that there are five absorption peaks from the near-infrared test results, namely at a wavelength of 1159, 1450, 1797, 1939 and 2170 nm (Figure 1). The most significant absorption is at a wavelength of 1939 nm with a standard deviation value of 0.17296 (Figure 2). The positive correlation value is in the 1000 - 1876 nm range, which means that the absorbance and concentration of blood glucose at this wavelength have a directly proportional value, with the highest correlation value of 0.0453. The negative correlation value is shown in the range 1878 - 2500 nm with a high absorbance value against low blood glucose concentrations. This wavelength range has the highest correlation value, namely, -0.1703 (Figure 3). The wavelength at the most considerable standard deviation value makes it the best measurement for measuring blood glucose levels. The 1950 nm LED had the highest absorbance correlation values (Figure 4).
Figure 1. The absorbance of blood samples in three different subject extraction.

Figure 2. Combined view of absorbance, standard deviation, and absolute Pearson correlation of blood samples, projected to [0, 1] ratio.
The study confirms our previous observations [7,8]. This result confirms the result of Goodarzi (1500 to 1800 nm, 2050 to 2300 nm) [14], Ryckeboer (1530 to 1820 nm) [15], and Krushinitskaya (2000 to 2500 nm) [16] explicitly for reflectance-based blood glucose level measurement, due to high absorbance. On the other hand, this research also confirms the study by Abdallah (360 to 1200 nm) [17], McEwen (454 to 1200 nm) [18], Momose (700 to 1050 nm) [19], Smith (800 to 1600 nm) [20], Song (850, 950, and 1600 nm) [21], Lawand (900 to 1550 nm) [22], So (1100 to 1400 nm) [23], and Yu (1300 nm) [24] for transmittance based measurement, due to low absorbance. We take the fact that the study was only taking account of healthy Subjects as a limitation. Further verification should include those with blood glucose level disorders as well. We also plan to confirm this result using in vivo human observation.

**Conclusions**

The 1950 nm LED had the optimal absorbance correlation values at -0.17, which make it appropriate for non-invasive blood glucose level measurement. Researchers should confirm the trial results with in vivo human observation.

---

**Figure 3.** Pearson correlation of absorbance of blood samples to blood glucose level.

**Figure 4.** Combined view of absorbance, standard deviation, and absolute Pearson correlation of blood samples, projected to [0, 1] ratio.
References

[1] The State of Queensland Health 2011 Adrenal Vein Sampling

[2] Yeaw J, Lee W C, Aagren M and Christensen T 2012 Cost of self-monitoring of blood glucose in the United States among patients on an insulin regimen for diabetes J Manag Care Pharm 18 21–32

[3] Burt M G, Roberts G W, Aguilar-Loza N R and Stranks S N 2013 Brief report: comparison of continuous glucose monitoring and finger-prick blood glucose levels in hospitalized patients administered basal-bolus insulin Diabetes Technol. Ther. 15 241–245

[4] Joseph Devakumar V, Ravi T and Karthikeyan S 2019 Review on Non Invasive Glucose and Cholesterol Measurement System IOP Conf. Ser. Mater. Sci. Eng. 590 012030

[5] Villena Gonzales W, Mobashsher A and Abbosh A 2019 The Progress of Glucose Monitoring—A Review of Invasive to Minimally and Non-Invasive Techniques, Devices and Sensors Sensors 19 800

[6] Huang J, Zhang Y and Wu J 2020 Review of non-invasive continuous glucose monitoring based on impedance spectroscopy Sens. Actuators Phys. 311 112103

[7] Jenie R P, Nasiba U, Rahayu I, Nurdin N M, Husein I and Alatas H 2019 Light Wavelength for Measurement of Non-Invasive Blood Glucose Level with Optical Device Ann. Nutr. Metab. 75 187

[8] Jenie R P, Nurdin N M, Damayanthi E, Irzaman, Rimbawan, Sukandar D and Alatas H 2019 Non Invasive Optical Blood Glucose Measurement based on Discrete Fourier Transform and Fast Artificial Neural Network: Fasting Normal Glucose Participants Case Study J. Med. Devices

[9] Jenie R P, Iskandar, J, Kurniawan A, Rustami E, Syafutra H, Nurdin N M, Handoyo T, Prabowo J, Febryarto R, Rahayu M S K, Damayanthi E, Rimbawan, Sukandar D, Suryana Y, Irzaman and Alatas H 2017 Proposed Application of Fast Fourier Transform in Near Infra Red Based Non Invasive Blood Glucose Monitoring System IOP Conference Series: Earth and Environmental Science vol 58, ed S Y.W (Institute of Physics Publishing)

[10] van Hooijdonk R T, Winters T, Fischer J C, van Dongen-Lases E C, Krinsley J S, Preiser J-C and Schultz M J 2014 Accuracy and limitations of continuous glucose monitoring using spectroscopy in critically ill patients Ann. Intensive Care 4 8

[11] Wojciechowski P, Rys P, Lipowska A, Gaweska M and Malecki M T 2011 Efficacy and safety comparison of continuous glucose monitoring and self-monitoring of blood glucose in type 1 diabetes Pol Arch Med Wewn 121 333–43

[12] Jenie R P, Nasiba U, Rahayu I, Nurdin N M, Husein I and Alatas H 2019 Review on Wavelength For Non-Invasive Blood Haemoglobin Level Measurement Optical Device Proceedings of The 2nd International Conference on Science, Mathematics, Environment and Education (ICoSMEE) The 2nd International Conference on Science, Mathematics, Environment and Education (ICoSMEE) (Universitas Sebelas Maret, Surakarta, Solo: AIP Conference Proceedings)

[13] Nasiba U, Jenie R P, Irzaman and Alatas H 2019 Determination of Wavelength Candidates for Non-Invasive Hemoglobin Measuring Devices and Energy Spectrum Analysis Proceeding of International Conference on Science, Mathematics, Environment and Education International Conference on Science, Mathematics, Environment and Education (Universitas Negeri Surakarta Sebelas Maret) p 7

[14] Goodarzi M, Sharma S, Ramon H and Saeys W 2015 Multivariate calibration of NIR spectroscopic sensors for continuous glucose monitoring TrAC Trends Anal. Chem. 67 147–58

[15] Ryckeboer E, Bockstaele R and Baets R 2013 Absorption spectroscopy of glucose based on a silicon photonics evanescent sensor IEEE photonics conference

[16] Krushinitskaya O 2012 Osmotic sensor for blood glucose monitoring applications (Vestfold University College)
[17] Abdallah O, Bolz A, Hansmann J, Walles H and Hirth T 2012 Design of a Compact Multi-Sensor System for Non-Invasive Glucose Monitoring Using Optical Spectroscopy International Conference on Electronics, Biomedical Engineering and its Applications (ICEBEA 2012)

[18] McEwen M P and Reynolds K J 2014 Noninvasive monitoring with strongly absorbed light Opt. Appl. 44

[19] Momose A, Ikehata A, Uwadaira Y and Miura M 2016 Comparative Study on Self-Monitoring of Blood Glucose and Non-invasive Blood Glucose Sensor Using Short-wavelength Near-infrared Spectroscopy in Glycemic Index Determination Nippon Shokuhin Kagaku Kagaku Kaishi 63 538–44

[20] Smith J L 2011 The Pursuit of Noninvasive Glucose: “Hunting the Deceitful Turkey” Last Accessed May 2

[21] Song K, Ha U, Park S and Yoo H-J 2014 An Impedance and Multi-wavelength Near-infrared Spectroscopy IC for Non-invasive Blood Glucose Estimation Symp. VLSI Circuits Dig. Tech. Pap. 2

[22] Lawand K, Parihar M and Patil S N 2015 Infrared Led Based Non Invasive Blood Glucometer History 44 95–99

[23] So C F, Chung J W, Siu M S and Wong T K 2011 Improved stability of blood glucose measurement in humans using near infrared spectroscopy J. Spectrosc. 25 137–145

[24] Yu X, Liu R, Yu H, Wang J, Wang J and Xu K 2016 Research on the best measurement situation between optical probe and tissue surfaces in non-invasive detection Rev. Sci. Instrum. 87 114303

Acknowledgement
Lembaga Pengelola Dana Pendidikan has supported this study using Riset Inovatif Produktif Invitasi with grant number PRJ-78/LPDP/2019, 2 December 2019. We would like to thank Konsorsium Penelitian Kadar Biomarker Darah Non-Invasive between IPB University, Agency of Assessment and Application of Technology, and PT Tesena Inovindo, for their continued support to our research. We declare no competing interest.