# NON-INVASIVE DISCRIMNATION BETWEEN DIABETIC STATES (HBA1C<8% AND HBA1C>10%) USING PHOTOPLETHYSMOGRAPHY

SAHNIUS BT USMAN

THESIS SUBMITTED IN FULFILMENT FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

FACULTY OF ENGINEERING AND BUILT ENVIRONMENT
UNIVERSITI KEBANGSAAN MALAYSIA
BANGI

2015

# DISKRIMINASI TIDAK INVASIF ANTARA KEADAAN DIABETIK (HBA1C<8% DAN HBA1C>10%) MENGGUNAKAN FOTOPLETISMOGRAFI

SAHNIUS BT USMAN

TESIS YANG DIKEMUKAKAN UNTUK MEMPEROLEH IJAZAH
DOKTOR FALSAFAH

FAKULTI KEJURUTERAAN DAN ALAM BINA
UNIVERSITI KEBANGSAAN MALAYSIA
BANGI

2015

## ACKNOWLEDGEMENT

First and foremost I express my utmost gratitude to ALLAH, the Almighty, without whose mercy and blessing, this work would ever be possible. Next, I would like to express my sincere gratitude to my supervisors Prof. Dr. Md. Mamun Bin Ibne Reaz and Prof. Dr. Mohd Alauddin Mohd Ali for their excellent supervisions especially in giving important technical advice, invaluable guidance, many fruitful discussions and providing constant support and cooperation towards making this research progressive over the years. Additional thankful is extended to my employer, Universiti Teknologi Malaysia for allowing me to take full study leave to concentrate on the research as well as Kementerian Pengajian Tinggi (KPT) for sponsoring the study leave.

I would like to thank Universiti Kebangsaan Malaysia for sponsoring this work under Research University Grant: UKM-AP-TKP-07-2009. I am most grateful to all personnel in the Endocrine Clinic KPP2 at Pusat Perubatan Universiti Kebangsaan Malaysia for their kind contribution and cooperation.

Last but not least, this special appreciation is extended to my life-companion and beloved husband for his caring, understanding, patience, motivation, and never-ending support and encouragement. Not to forget, I also extend my exceptional appreciation towards my young and lovely children whom are the most precious in my life. They are my motivations and inspirations to continuously educate and furnish myself with sufficient knowledge and the completion of this study is part of it.

Sincerely, thank you to all!

## ABSTRACT

Diabetes mellitus is a group of metabolic diseases associated with the production and/or reaction of insulin leading to hyperglycemia. Glycated hemoglobin (HbA1c) level is generally measured for hyperglycemia. The risk of developing complications depends on both the duration of diabetes and hyperglycemia. A trend of increasing arterial stiffness has been identified in type 2 diabetes. Photoplethysmographic (PPG) pulse wave provides a 'window' into the properties of small arteries whereas stiffening of these arteries will alter the PPG waveform. In this research, the potential of PPG in discriminating between type 2 diabetic patients at risk of having HbA1c level > 10% has been investigated. To this end, PPG signals recorded from diabetic patients with different levels of HbA1c (HbA1c level < 8% and HbA1c level > 10%) were acquired from the index finger of the right arm of 101 subjects (53 subjects with HbA1c level < 8% and 48 subjects with HbA1c level > 10%) at a sampling rate of 275 Hz. The area under the curve of PPG (auc-PPG) was proposed in analyzing the PPG pulse contour. Results of t-test analysis show that auc-PPG is significantly larger in diabetic patients with HbA1c level < 8% than in those with HbA1c level > 10% (p-value <0.001). Repeated measurement of PPG using paired t-test on 30 diabetic patients with HbA1c level < 8% and 26 diabetic patients with HbA1c level > 10% (total 56 subjects) show that there is no significant difference in the mean value of auc-PPG between the first measurement and repeated measurement for both groups. Finally, a logistic regression model for estimating the risk of having HbA1c level > 10% among diabetic patients was estimated using data from 51 female diabetic patients. The model shows that the auc-PPG is an independent predictor for estimating the risk of having HbA1c level > 10% (p-value = 0.005) among female diabetic patients.

## ABSTRAK

Diabetes mellitus adalah sekumpulan penyakit metabolik yang yang dikaitkan dengan pengeluaran dan/atau tindak balas insulin yang menyebabkan hiperglisemia. Paras 'glycated hemoglobin'(HbA1c) merupakan salah satu ukuran bagi hiperglisemia. Risiko komplikasi bergantung kepada tempoh menghidap diabetes dan hiperglisemia. Suatu trend peningkatan ketegangan arteri telah dikenalpasti pada pesakit diabetes mellitus jenis 2. Gelombang denyut photoplethysmographic (PPG) menyediakan suatu 'jendela' kepada sifat-sifat arteri dan ketegangan arteri-arteri tersebut boleh mengubah bentuk gelombang PPG. Dalam kajian ini, potensi PPG dalam membezakan antara pesakit diabetes mellitus jenis 2 yang berisiko mempunyai HbA1c >10% telah dikaji. Kemudian, isyarat PPG yang direkodkan daripada pesakit diabetes dengan paras HbA1c yang berbeza (paras HbA1c < 8% dan paras HbA1c > 10%) telah diperolehi daripada jari telunjuk tangan kanan 101 orang subjek (53 orang subjek dengan paras HbA1c < 8% dan 48 orang subjek dengan paras HbA1c > 10%) pada kadar persampelan 275 Hz. Kawasan bawah lengkung PPG (auc-PPG) adalah teknik yang dicadangkan untuk membuat analisis kontur isyarat PPG. Keputusan analisis 'independent t-test' menunjukkan bahawa auc-PPG secara signifikannya lebih besar pada pesakit diabetes dengan paras HbA1c < 8% daripada mereka yang mempunyai paras HbA1c >10% (nilai $p < 0.001$). Pengukuran ulangan PPG menggunakan 'paired t-test' pada 30 orang pesakit diabetes mellitus dengan paras HbA1c < 8% dan 26 orang pesakit diabetes mellitus dengan HbA1c > 10% (berjumlah 56 orang subjek) menunjukkan bahawa tiada terdapat perbezaan yang signifikan dalam nilai min auc-PPG antara pengukuran pertama dan pengukuran ulangan untuk kedua-dua kumpulan. Akhirnya, model regresi logistik jangkaan risiko mempunyai paras HbA1c > 10% di kalangan pesakit diabetes mellitus telah dianggarkan dengan menggunakan data daripada 51 orang pesakit diabetes wanita. Model tersebut menunjukkan bahawa auc-PPG adalah suatu pembolehubah tak bersandar bagi menjangkakan risiko mempunyai paras HbA1c > 10% (nilai $p = 0.005$) di kalangan pesakit diabetes wanita.

# CONTENTS

# LIST OF TABLES

# LIST OF FIGURES

# LIST OF ABBREVIATIONS

| | |
|---|---|
| ADA | American Diabetes Association |
| AIx | Aortic augmentation index |
| AGEs | Advanced glycation end products |
| AM | Amplitude |
| ANOVA | Analysis of variance |
| ANCOVA | Analysis of covariance |
| APSS | Air pressure sensing system |
| ASCII | American Standard Code for Information Interchange |
| Auc-PPG | Area under the curve of PPG |
| Ba-PWV | Brachial-ankle pulse wave velocity |
| BL | Baseline |
| BMI | Body mass index |
| BP | Blood pressure |
| CAD | Coronary artery disease |
| cf-PWV | Carotid to femoral PWV |
| CHD | Coronary heart disease |
| CI | Confidence interval |
| CR | Coefficient of correlation |
| CRP | C-reactive protein |
| CV | Coefficient of variation |
| CVD | Cardiovascular diseases |
| ECG | Electrocardiograph/Electrocardiogram |
| FFT | Fast Fourier Transform |
| FN | False negative |
| FP | False positive |
| GCP | Good clinical practice |
| GDM | Gestational diabetes |
| GUI | Graphical user interface |
| HDL | High-density lipoprotein |
| HF | High frequency |
| HRV | Heart rate variability |

| | |
|---|---|
| hs-CRP | High-sensitivity C-reactive protein |
| ID | Identification number |
| KPP2 | Klinik Pakar Perubatan 2 |
| LDL | Low-density lipoprotein |
| LED | Light emitting diode |
| LF | Low frequency |
| M | Mean |
| NO | Nitric oxide |
| NPV | Negative predictive value |
| OA | Obliterating atherosclerosis |
| PC | Personal computer |
| PP | Pulse pressure |
| PPG | Photoplethysmography |
| PPV | Positive predictive value |
| PPUKM | Pusat Perubatan Universiti Kebangsaan Malaysia |
| PSD | Power spectral density |
| PTT | Pulse transit time |
| PWV | Pulse wave velocity |
| ROC | Receiver operating characteristic |
| ROS | Reactive oxygen species |
| SD | Standard deviation |
| SDPTG | Second derivative PPG |
| SE | Standard error |
| SEM | Standard error of mean |
| SI | Stiffness index |
| Sn | Sensitivity |
| Sp | Specificity |
| TG | Triglycerides |
| TN | True negative |
| TP | True positive |
| VLF | Very low frequency |
| WHO | World Health Organization |

## LIST OF NOMENCLATURES

| | |
|---|---|
| Hb | Deoxygenated hemoglobin |
| HbA1c | Glycated hemoglobin |
| $HbO_2$ | Oxygenated hemoglobin |
| $SpO_2$ | Blood oxygen saturation |

## LIST OF SYMBOLS

| | |
|---|---|
| $\pi$ | Probability of the outcome of interest or 'event' |
| a | Y intercept |
| B | Regression coefficient |
| ln | Natural logarithm |
| $\Delta T$ | Time delay |
| Ho | Null hypothesis |
| *p*-value | Significance level (probability of rejecting the Ho) |
| R | Correlation coefficient |
| Z | Probability distribution |

# CHAPTER I

# INTRODUCTION

## 1.1 INTRODUCTION

Diabetes mellitus also known as diabetes is defined as abnormally high blood glucose with disturbances of protein metabolism and altered fat (Iftikhar & Waqar 2011). Diabetes has been a silent killer all over the world. Hence, the primary goal of any diabetes treatment is to maintain the glucose level and the risk of developing late-stage diabetic complications. A stable blood glucose level would significantly reduce any cardiovascular disease (CVD) among diabetic patients.

There are two major types of diabetes which are Type 1 diabetes and Type 2 diabetes. The absence (Type 1) or insufficient production (Type 2) of insulin can elevate the blood glucose levels, leading to a condition known as hyperglycemia. The risk of developing complications of diabetes depends on both the duration and the severity of hyperglycemia (Fowler 2008; ADA 2002).

Hyperglycemia is the main metabolic abnormality of diabetes (Iftikhar & Waqar 2011; ADA 2010) and can be measured as glycated haemoglobin (HbA1c). HbA1c, also known as long-term glucose, shows the amount of glycation of haemoglobin, a condition where haemoglobin cell in blood had been bound to a glucose molecule. The HbA1c is measure of long-term glucose level is approximately the same for the period of six to eight weeks. The HbA1c level is given in percentage value.

The target level of HbA1c is 7% as recommended by the American Diabetes Association (ADA) in all patients with diabetes mellitus (Iftikhar & Waqar 2011). Besides, diabetic patients should be maintained their HbA1c level less than 6% without causing significant hypoglycemia (Iftikhar & Waqar 2011). Therefore, the determination of HbA1c level may assist in the initial diagnosis of diabetes and can be used to indicate the degree of long-term diabetic control among diabetic patients.

Impaired glycemic control is another possible factor, instead of aging, for increased arterial stiffness among Type 2 diabetic patients (Schram et al. 2004; Woodman & Watt 2003). Arterial stiffness reflects the rigidity of arterial wall, and other terms used to characterize the properties of the arterial wall are compliance, elasticity (or elastic modulus), distensibility and vascular impedance (Mackenzie et al. 2002). Various different techniques were applied for measuring arterial stiffness which includes pulse pressure, pulse wave velocity (PWV), ultrasound-derived indices, magnetic resonance imaging (MRI)-derived indices and waveform analysis. Technique proposed by researchers for measuring arterial stiffness using waveform analysis is photoplethysmography (PPG) (Huotari et al. 2011; Pilt et al. 2013, Qawqzeh et al. 2014). PPG is an optical non-invasive technique that detects and measures blood volume changes in the peripheral vessels at any location on skin surface (fingers, earlobes, toes, etc.) and it is often used in clinical research (Allen 2007). The blood volume pulsations, produced by heart, propagate through the arterial tree and are affected by reflected waves from the arterial branching sites (Rubins et al. 2008).The relation of PWV and PPG has been reported in previously published works (Alty et al. 2007; Padilla et al. 2006; Loukogeorgakis et al. 2002).

## 1.2 PROBLEM STATEMENT AND MOTIVATION

Previous studies have shown the relation between HbA1c level and increased risk of microvascular complications (UKPDS 33 1998; Shichiri et al. 2000), myocardial infarction, macrovascular mortality and all causes of death among Type 2 diabetes (Stratton et al. 2000; Craig et al. 2010). Selvin et al. (2005) reported that the risk of coronary heart disease (CHD) is associated with HbA1c level and thus is increased throughout the range of HbA1c level.

The ability to detect alterations in the vascular structure and function in hypertension, diabetes, and atherosclerosis such as by the assessment of vascular compliance has potential advantages for improving risk stratification (Verma & Anderson 2002). Several studies have demonstrated an increased trend in arterial stiffness for patients with Type 2 diabetes (Tamminen et al. 2002; Henry et al. 2003; Schram et al. 2004). Although previous studies reported about the cardiovascular events related to arterial stiffness for diabetic patients, these available publications did not report about the relationship of vascular condition and HbA1c level among diabetic patients. Therefore, the aim of this research is to investigate and study the relationship between vascular condition and HbA1c level.

Analysis of HbA1c usually in blood sample can be obtained by venipunture or finger prick. Such technique has the drawbacks of pain and also delay before the result is available. For this reason, it is desirable that noninvasive technique in estimation of HbA1c should be developed. The existing noninvasive PPG could be a suitable technique. Contour analysis of the PPG pulse wave is a promising method to obtain the information of vascular condition (Shi 2009). The PPG pulse wave provides a 'window' into the properties of small arteries and stiffening of the small arteries alters the magnitude and timing of reflected waves (Duprez et al. 2004).

Previously, analysis of PPG pulse contour using second derivative technique has been developed in several studies (Takazawa et al. 1993; Takazawa et al. 1998; Miyai et al. 2001; Otsuka et al. 2006; Otsuka et al. 2007). Most of these studies were focused mainly on peripheral pressure pulse that including the evaluation of ageing effect in the cardiovascular system and the screening of arteriosclerotic disease (Bortolotto et al. 2000; Takazawa et al. 1998; Takada et al. 1996; Imanaga et al. 1998). Besides artificial neural networks (Allen & Murray 1995; Salih et al. 2012), nonlinear dynamic analysis (Bhattacharya et al. 2001) and the extraction of periodic components using frequency analysis (Sherebrin & Sherebrin 1990) were also used to recognize features or patterns of pulse wave.

A study by Spigulis et al. (2002) has shown that diabetes can damp the PPG pulses and cause the dicrotic notch to become less prominent. Furthermore, Allen and Murray (2003) has reported that it is difficult to locate the dicrotic notch in subjects who are more than 50 years old as well as in some other diseases, thereby increasing the uncertainty in the timing measurements related to the reflected wave. Hence, it is meaningful to investigate the vascular condition of diabetic patients through contour analysis of PPG pulse wave without locating dicrotic notch.

The simplicity of the PPG measurements and the valuable 'global' cardiovascular information contained would make the PPG a useful clinical investigation tool (Allen 2007). Non-invasive measuring technique which is cost-effective is the reason for utilising PPG in this project. The advantages of the HbA1c level assessment among diabetic patients based on PPG signal analysis are the simplicity of the instrumentation system, manageable data size and digital signal processing techniques by computer programming that offers prospective advancement of the technique. Besides, this research is motivated by the ease in the setting-up of PPG measurement with easy application on the index finger and the measurement is operator-independence.

## 1.3 OBJECTIVES OF THE RESEARCH

The main objective of this research is to develop a non-invasive technique to discriminate between diabetic patients at risk of having HbA1c level>10% by utilizing the PPG system. Through this research, the PPG signals acquired from index finger are analyzed, and thus the area under the curve of PPG (auc-PPG) has been selected as a parameter to predict the HbA1c level of diabetic patients. The relation of the auc-PPG index and HbA1c level is investigated. This research has involved experimentation, data acquisition and data analysis on diabetic patients using PPG measurement. The specific objectives of the research are as follows:

- To determine the relationship between HbA1c and auc-PPG by statistical analysis.
- To generate the possible statistical model to estimate the risk of having HbA1c level>10%.

- To validate the PPG technique using repeated measurement.

The overall structure of the research work is shown in Figures1.1 to 1.5.

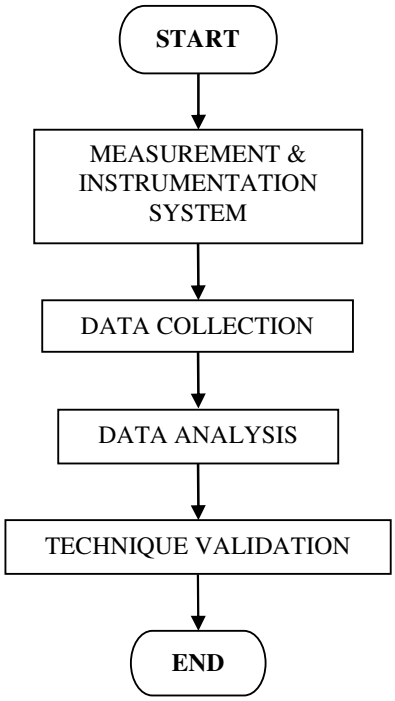


FIGURE 1.1 The structure of the research

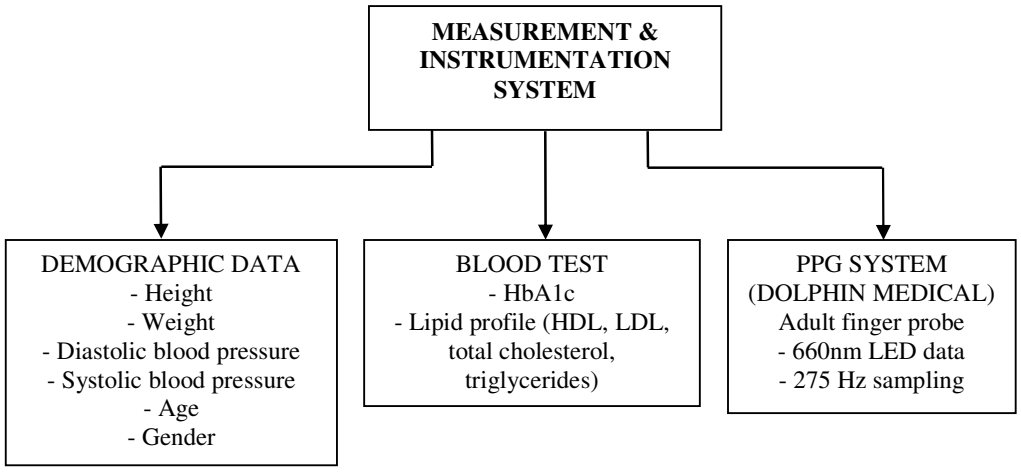


FIGURE 1.2 The structure of the measurement and instrumentation systems

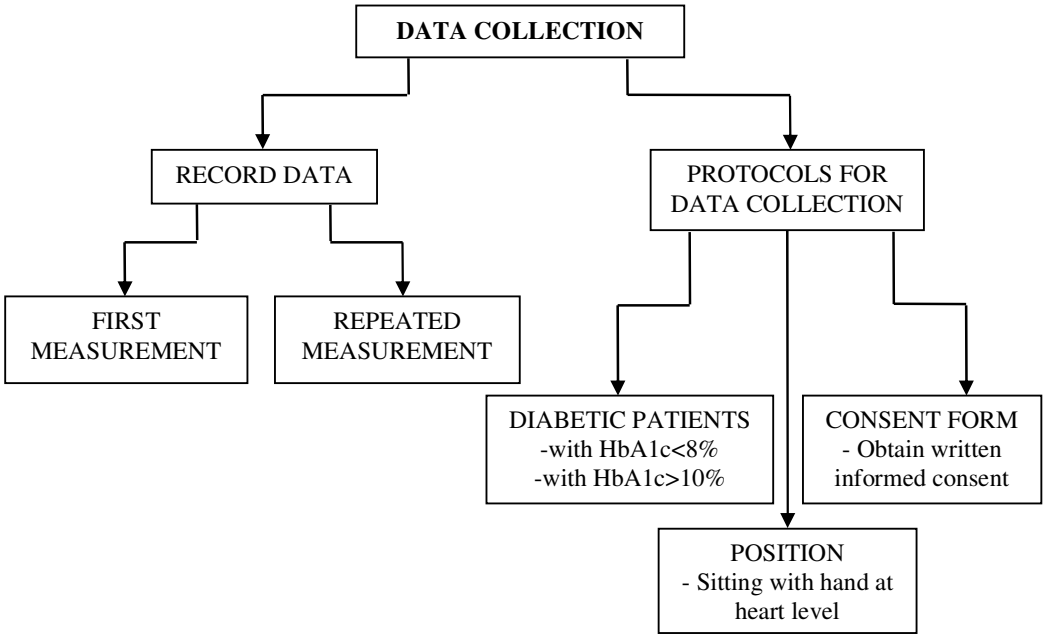


FIGURE 1.3 The structure of the data collection

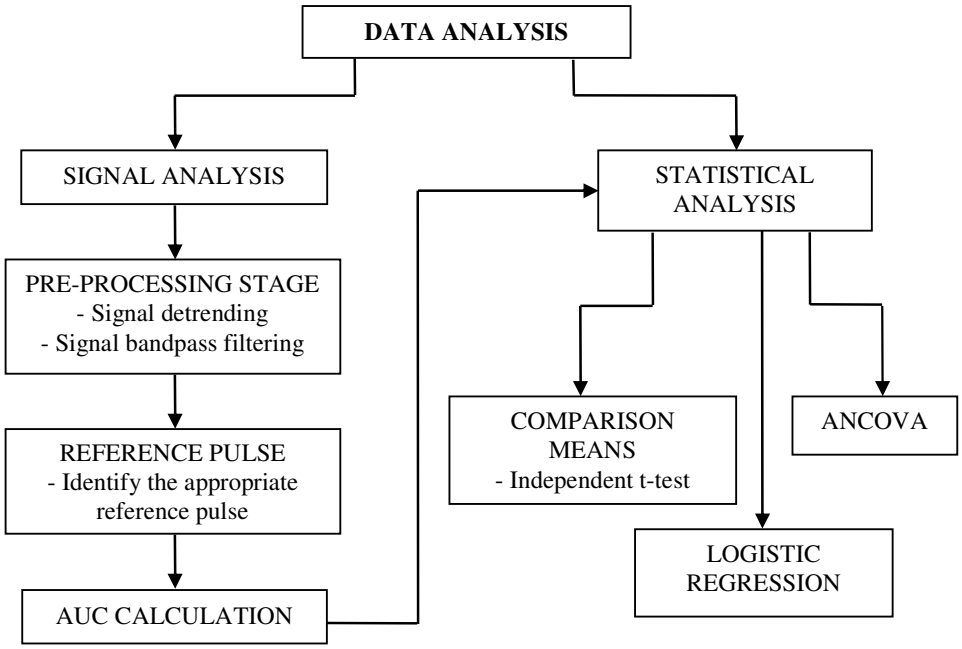


FIGURE 1.4 The structure of the data analysis

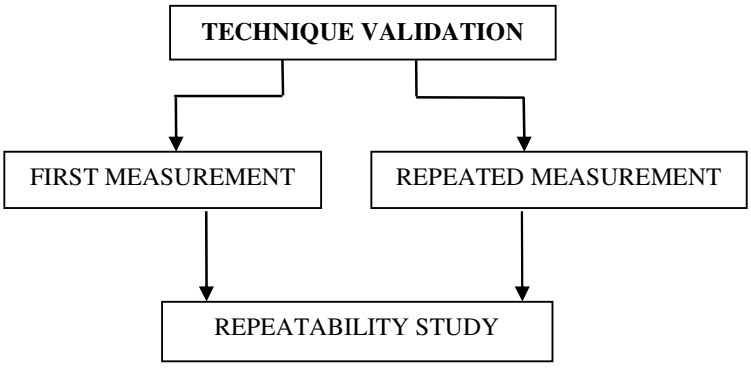


FIGURE 1.5 The structure of the technique validation

## 1.4 HYPOTHESIS OF THE RESEARCH

Well controlled diabetic patients is defined as those with Hba1c less than 7 (Iftikhar & Waqar 2011) and those with having HbA1c greater than 9 (Juarez et al. 2012; Shani et al. 2008) is categorized as poorly controlled diabetic patients. Besides, Wu et al. (1997) reported that HbA1c levels <10% were considered as indicatives of satisfactory glycemic control.

The value of HbA1c greater than 10% was chosen to make sure that only diabetic patients with very poorly controlled diabetes would be included in this study. HbA1c of less than 8% was chosen to enlarge the well-controlled group. The intermediate group was excluded from the study in advance to sharpen the differences.

The hypothesis of this research is the analysis of PPG signals of the diabetic patients with HbA1c level less than 8% and among those with HbA1c level greater than 10% will reveal significant trends, which will characterize their vascular condition based on HbA1c level.

## 1.5 ORGANIZATION OF THE THESIS

This thesis is organized to describe fundamentals of the research and activities involved in the study. The framework of this thesis dissertation is associated with the research objectives and the research structure mentioned earlier.

Chapter I begins with background information on all matters pertaining to this research as well as the motivation behind the research. The research objectives, structure of the research work, research hypothesis and the framework of the dissertation are also described in this chapter.

Chapter II begins with a comprehensive introduction regarding diabetes mellitus and reviews some literatures about the relation of diabetes and vascular condition. Subsequent to the fundamentals of PPG, descriptions of the various methods of PPG signal analysis are elaborated in this chapter. The clinical applications, advantages and limitations of the PPG technique are discussed towards the end of the chapter.

Chapter III describes the instrumentation systems utilized in this research, including their specifications for the hardware and software for PPG systems. This chapter also covers data collection, data organization and protocols for data acquisition. The primary steps involved in the data processing in preparation for further analysis for PPG are described in this chapter as well.

Chapter IV covers the results and discussion of the overall research finding. This chapter begins with discussion of the results obtained from the pre-processing of raw PPG data. This is followed with the discussion on the results after comparing the mean of area under curve of PPG (auc-PPG) between the different levels of HbA1c. Then, the result of the comparison of the mean and age is discussed. The proposed method is verified by the study of the measurement repeatability. Finally, statistical modelling is identified to estimate the risk of having HbA1c level>10%.

Chapter V summarizes the research, describes some limitations of the research, recommends necessary future improvements, and proposes future research directions initiated from this study.

## REFERENCES


Abramowitz, H.B., Queral, L.A., Finn, W.R., Nora, P.F. Jr., Peterson, L.K., Bergan, J.J. & Yao, J.S. 1979. The Use of Photoplethysmography in the Assessment of Venous Insufficiency: A Comparison to Venous Pressure Measurements. *Surgery.* 86(3): 434-441.

Accetto, R., Salobir, B., Brguljan, J. & Dolenc, P. 2011. Comparison of two techniques for measuring pulse wave velocity and central blood pressure. *Artery Research.* 5: 97-100.

Allen, J. 2007. Photoplethysmography and Its Application in Clinical Physiological Measurement. *Physiological Measurement* 28: R1-R39.

Allen, J. & Murray, A. 1993. Development of a Neural Network Screening Aid for Diagnosing Lower Limb Peripheral Vascular Disease from Photoelectric Plethysmography Pulse Waveforms. *Physiol Meas.* 14(1): 13-22.

Allen, J. & Murray, A. 1995. Prospective Assessment of an Artificial Neural Network for the Detection of Peripheral Vascular Disease from Lower Limb Pulse Waveforms. *Physiological Measurement* 16: 29-38.

Allen, J. & Murray, A. 1999. Modelling the Relationship between Peripheral Blood Pressure and Blood Volume Pulses Using Linear and Neural Network System Identification Techniques. *Physiological Measurement* 20: 287-301.

Allen, J. & Murray, A. 2000a. Similarity in Bilateral Photoplethysmographic Peripheral Pulse Wave Characteristics at the Ears, Thumbs and Toes. *Physiological Measurement* 21: 369–377.

Allen, J. & Murray, A. 2000b. Variability of Photoplethysmography Peripheral Pulse Measurements at the Ears, Thumbs and Toes. *IEE Proceedings-Science Measurement Technology,* 147: 403-407.

Allen, J. & Murray, A. 2002. Age Related Changes in Peripheral Pulse Timing Characteristics at the Ears, Fingers and Toes. *Journal of Human Hypertension* 16: 711-717.

Allen, J. & Murray, A. 2003. Age-Related Changes in the Characteristics of the Photoplethysmographic Pulse Shape at Various Body Sites. *Physiological Measurement* 24: 297-307.

Allen, J., Oates, C., Lees, T. & Murray, A. 2005. Photopletysmography Detection of Lower Limb Peripheral Arterial Occlusive Disease: A Comparison of Pulse Timing, Amplitude and Shape Characteristics. *Physiological Measurement* 26: 811-821.

Alty, S.R., Jaimes, N.A., Millasseau, S.C. & Chowienczyk, P.J. 2007. Predicting Arterial Stiffness from The Digital Volume Pulse Waveform. *IEEE Transactions On Biomedical Engineering* 54(12): 2268-2275.

American Diabetes Association (ADA). 2002. Implications of the United Kingdom Prospective Diabetes Study. *Diabetes Care* 25(Suppl. 1): S28-S32.

American Diabetes Association (ADA). 2004. Nephropathy in Diabetes. *Diabetes Care* 27(Suppl. 1): S79-S83.

American Diabetes Association (ADA). 2010. Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 33(Suppl. 1): S62-S69.

Anan, F., Masaki, T., Umeno, Y., Iwao, T., Yonemochi, H., Eshima, N., Saikawa, T. Yoshimatsu, H. 2007. Correlations of high-sensitivity C-reactive protein and artherosclerosis in Japanese type 2 diabetic patients. *European Journal of Endocrinology*. 157: 311-317.

Anderson, R.R. & Parrish, J.A. 1981. The Optics of Human Skin. *J Invest Dermatol* 77(1): 13-19.

Arnett, D.K., Evans, G.W. & Riley, W.A. 1994. Arterial Stiffness: A New Cardiovascular Risk Factor? *Am J Epidemiol.*140(8): 669-682.

Aronson, D. & Rayfield, E.J. 2002. How Hyperglycemia Promotes Atherosclerosis: Molecular Mechanisms-Review. *Cardiovascular Diabetology*. 1(1): 1-10.

Asmar, R., Benetos, A., Topouchian, J., Laurent, P., Pannier, B., Brisac, A.-M., Target, R. & Levy, B.I. 1995. Assessment of Arterial Distensibility by Automatic Pulse Wave Velocity Measurement. *Hypertension* 26: 485-490.

Aso, K., Miyata, M., Kubo, T., Hashiguchi, H., Fukudome, M., Fukushige, E., Koriyama, N., Nakazaki, M., Minagoe, S. & Tei, C. 2003. Brachial-ankle Pulse Wave Velocity is Useful for Evaluation of Complication in Type 2 Diabetic Patients. *Hypertension Res* 26(10): 807-813.

Avnon, Y., Nitzan, M., Sprecher, E., Rogowski, Z. & Yarnitsky, D. 2003. Different Patterns of Parasympathetic Activation in Uni- and Bilateral Migraineurs. *Brain.* 126 (Pt 7): 1660-1670.

Avnon, Y., Nitzan, M., Sprecher, E., Rogowski, Z. & Yarnitsky, D. 2004. Autonomic Asymmetry in Migraine: Augmented Parasympathetic Activation in Left Unilateral Migraineurs. *Brain.* 127(Pt 9): 2099-2108.

Barschdorff, D. & Zhang, W. 1994. Respiratory Rhythm Detection with Photoplethysmographic Methods. *Proceeding of the 16th Annual International Conference of the IEEE*: 912-913.

Beckman, J.A., Creager, M.A. & Libby, P. 2002. Diabetes and Atherosclerosis: Epidemiology, Pathophysiology and Management. *JAMA*. 287(19): 2570-2581.

Bernardi, L., Radaelli, A., Solda, P.L., Coats, A.J., Reeder, M., Calciati, A., Garrard, C.S. & Sleight, P. 1996. Autonomic Control of Skin Microvessels: Assessment by Power Spectrum of Photoplethysmographic Waves. *Clinical Science* 90(5): 345-355.

Bhattacharya, J., Kanjilal, P.P. & Muralidhar, V. 2001. Analysis and Characterization of Photo-Plethysmographic Signal. *IEEE Trans Biomed Eng* 48(1): 5-11.

Bortolotto, L.A., Blacher, J., Kondo, T., Takazawa, K. & Safar M.E. 2000. Assessment of Vascular Aging and Atherosclerosis in Hypertensive Subjects: Second Derivative of Photoplethysmogram versus Pulse Wave Velocity. *Am J Hypertens* 13(2): 165-171.

Brooks, B. A., Molyneaux, L. M. & Yue, D. K. 2001. Augmentation of Central Arterial Pressure in Type 2 Diabetes. *Diabetic Med.* 18: 374-380.

Brumfield, A.M. & Andrew, M.E. 2005. Digital Pulse Contour Analysis: Investigating Age-Dependent Indices of Arterial Compliance. *Physiol Meas.*26(5): 599-608.

Buchs, A., Slovik, Y., Rapoport, M., Rosenfeld, C., Khanokh, B. & Nitzan, M. 2005. Right-left correlation of the sympathetically induced fluctuations of photoplethysmographic signal in diabetic and non-diabetic subjects. *Med. Biol. Eng. Comput*. 43: 252-257.

Cade, W.T. 2008. Diabetes-related microvascular and macrovascular diseases in the physical therapy setting. *Phys. Ther.* 88(11): 1322-1335.

Chan, Y.H. 2003. Biostatistics 101: Data Presentation. Singapore Medical Journal 44(6): 280-285.

Cheang, P.Y.S. & Smith, P.R. 2003. An Overview of Non-Contact Photoplethysmography. *Electronics Systems and Control Division Research - Internal Circulation of Dept of EE Engineering, Loughborough University*: 57-59.

Chellappan, K., Ali, M. A. M. & Zahedi, E. 2008. *An Age Index for Vascular System Based on Photoplethysmogram Pulse Contour Analysis. IFMBE Proceedings, 4th Kuala Lumpur International Conference on Biomedical Engineering*. 21: 125-128.

Chen, W., Kobayashi, T., Ichikawa, S., Takeuchi, Y. & Togawa, T. 2000. Continuous Estimation of Systolic Blood Pressure Using the Pulse Arrival Time and Intermittent Calibration. *Med Biol Eng Comput.* 38(5): 569-574.

Chen, Y., Huang, Y., Li, X., Xu, M., Bi, Y., Zhang, Y., Gu, W. & Ning, G. 2009. Association of Arterial Stiffness with Hba1c in 1,000 Type 2 Diabetic Patients with or without Hypertension. *Endocrine*. 36(2): 262-267.

Choi, B.C., Lee, H.J., Ye, S.Y., Jung, D.K., Kim, G.R., Kim, K.N. & RJeon, G. 2004. Evaluation of Arterial Compliance on Pulse Transit Time Using Photo-Plethysmography. *IECON Proceedings (Industrial Electronics Conference* 3: 3219-3222.

Choi, S.W., Shin, M.H., Yun, W.J., Kim, H.Y., Lee, Y.H., Kweon, S.S., Rhee, J.A. & Choi, J.S. 2011. Association Between Hemoglobin A1c, Carotid Atherosclerosis, Arterial Stiffness, and Peripheral Arterial Disease in Korean Type 2 Diabetic Patients. *J. Diabetes Complications*. 25(1): 7-13.

Chowienczyk, P.J., Kelly, R.P. & McCallum, H. 1999. Photoplethysmographic Assessment of Pulse Wave Reflection. Blunted Response to Endothelium-Dependent Beta2-Adrenergic Vasodilation in Type II Diabetes Mellitus. *Journal of the American College of Cardiology* 34: 2007-2014.

Chowienczyk, P.J., Watts, G.F., Cockcroft, J.R. & Ritter, J.M. 1992. Impaired Endothelium-Dependent Vasodilation of Forearm Resistance Vessels in Hypercholesterolaemia. *The Lancet* 340(8833): 1430-1432.

Cohn, J.N. 2006. Arterial Stiffness, Vascular Disease, and Risk of Cardiovascular Events. *Circulation.* 113(5): 601-603.

Cooke, E.D., Bowcock, S.A. & Smith A.T. 1985. Photoplethysmography of the Distal Pulp in the Assessment of the Vasospastic Hand. *Angiology.* 36(1): 33-40.

Couceiro, R., Carvalho, P., Paiva, R.P., Henriques, J. & Muehlsteff, J. 2014a. Detection of Motion Artifacts in Photoplethysmographic Signals based on Time and Period Domain Analysis. *Physiol. Meas.* 35: 2369-2388. http://dx.doi.org/10.1088/0967-3334/35/12/2369.

Couceiro, R., Carvalho, P., Paiva, R.P., Henriques, J., Quintal, I. & Muehlsteff, J. 2014b. Detection of Motion Artifact in Photoplethysmographic Signals: Algorithms Comparison. *IFMBE Proceedings* 42: 327-330.

Craig, J.C., Peters, J.R., Tynan, A., Evans, M., Heine, R.J., Bracco, O.L., Zagar, T. & Poole, C.D. 2010. Survival as a Function of HbA1c in People with Type 2 Diabetes: A Retrospective Cohort Study. *The Lancet* 375: 481-489.

Davis, T.M., Stratton, I.M., Fox, C.J., Holman, R.R. & Turner, R.C. 1997. U.K. Prospective Diabetes Study 22. Effect of age at diagnosis on diabetic tissue damage during the first 6 years of NIDDM. *Diabetes Care*. 20 (9): 1435-1441

Dawber, T.R., Thomas, H.E. Jr. & Mcnamara, P.M. 1973. Characteristics of the Dicrotic Notch of the Arterial Pulse Wave in Coronary Heart Disease. *Angiology* 24(4): 244-255.

Department of Statistics Malaysia. http://www.statistics.gov.my/portal/. [2 May 2013]

Deveci, E., Yesil, M., Akinci, B., Yesil, S., Postaci, N., Arikan, E. & Koseoglu, M. 2009. Evaluation of insulin resistance in normoglycemic patients with coronary artery disease. *Clin. Cardiol.* 32(1): 32-36.

Dorlas, J.C. & Nijboer, J.A. 1985. Photo-Electric Plethysmography as a Monitoring Device in Anaesthesia. Application and Interpretation. *Br J Anaesth.* 57(5): 524-530.

Drummond, G.B. & Park, G.R. 1984. Arterial Oxygen-Saturation before Intubation of the Trachea - An Assessment of Oxygenation Techniques. *Br J Anaesth.* 56(9): 987-993.

Duprez, D.A., Kaiser, D.R., Whitwam, W., Finkelstein, S., Belalcazar, A., Patterson, R., Glasser, S. & Cohn J.N. 2004. Determinants of Radial Artery Pulse Wave Analysis in Asymptomatic Individuals. *Am J Hypertens.* 17(8): 647-653.

Elwell, C. & Hebden, J. 1999. Near-Infrared Spectroscopy, Biomedical Optics Research Laboratory. http://www.medphys.ucl.ac.uk/research/borl/research/ NIR_topic s/nirs.htm (31 March 2008).

Engelgau, M.M., Narayan, K.M. & Herman, W.H. 2000. Screening for Type 2 Diabetes. *Diabetes Care*. 23(10): 1563-1580.

Erts, R., Spigulis, J., Kukulis, I. & Ozols, M. 2005. Bilateral Photoplethysmography Studies of the Leg Arterial Stenosis. *Physiological Measurement* 26: 865-874.

Fowler, M.J. 2008. Microvascular and Macrovascular Complications of Diabetes. *Clinical Diabetes* 26(2): 77-82.

Glasser, S.P., Arnett, D.K., McVeigh, G.E., Finkelstein, S.M., Bank, A.K., Morgan, D.J. & Cohn, J.N. 1998. The Importance of Arterial Compliance in Cardiovascular Drug Therapy. *J Clin Pharmacol.* 38(3): 202-212.

Gonzales, R., Manzo, A., Delgado, J., Padilla, J.M., Trenor, B. & Saiz, J. 2008. A computer based photoplethysmographic vascular analyzer through derivatives. *Computers in Cardiology*. 35: 177-180.

Gopaul, N.K., Manraj, M.D., Hébé, A., Yan, S.L.K., Johnston, A., Carrier, M.J. & Änggård, E.E. 2001. Oxidative Stress Could Precede Endothelial Dysfunction and Insulin Resistance in Indian Mauritians with Impaired Glucose Metabolism. *Diabetologica* 44: 706-712.

Gu, Y.Y., Zhang, Y. & Zhang, Y.T. 2003. A Novel Biometric Approach in Human Verification by Photoplethysmography Signals. *Proceeding of the 4th IEEE Conf on Information Technology Application in Biomedicine.* 13-14.

Hashimoto, J., Chonan, K., Aoki, Y., Nishimura, T., Ohkubo, T., Hozawa, A., Suzuki, M., Matsubara, M., Michimata, M., Araki, T. & Imai, Y. 2002. Pulse Wave Velocity and the Second Derivative of the Finger Photoplethysmogram in Treated Hypertensive Patients: Their Relationship and Associating Factors. *J Hypertens.*20(12): 2415-2422.

Heck, A.F. & Hall, V.R. 1975. An On-Line System for Measurement of Opacity Pulse Propagation Times in Atraumatic Screening of Patients for Occlusive Vascular Disease. *Med Instrum.* 9(2): 88-92.

Henry, R.M., Kostense, P.J., Spijkerman, A.M., Dekker, J.M., Nijpels, G., Heine, R.J., Kamp, O., Westerhof, N., Bouter, L.M. & Stehouwer, C.D. 2003. Arterial Stiffness Increases with Deteriorating Glucose Tolerance Status. *Circulation*. 107(16): 2089-2095.

Hertzman, A.B. 1937. Photoelectric Plethysmography of the Fingers and Toes in Man. *Proceeding of Society for Experimental Biologial Medicine,* 37: 529-542.

Hlimonenko, I., Meigas, K. & Vahisalu, R. 2003. Waveform Analysis of Peripheral Pulse Wave Detected in the Fingertip with Photoplethysmograph. *Measurement Science Review*. 3: 49-52.

Hovagim, A.R., Vitkun, S.A., Manecke, G.R. & Reiner, R. 1989. Arterial Oxygen Desaturation in Adult Dental Patients Receiving Conscious Sedation. *J Oral Maxillofac Surg.* 47(9): 936-939.

Huotari, M., Vehkaoja, A., Määttä, K. & Kostamovaara, J. 2011. Photoplethysmography and Its Detailed Pulse Waveform Analysis for Arterial Stiffness. *Journal of Sructural Mechanics*. 44(4): 345-362.

Iftikhar, A.A.S. & Waqar, A.K. 2011. Glycated Haemoglobin - A Marker and Predictor of Cardiovascular Disease. *Journal Of Pakistan Medical Association*. 61(17): 690-695.

Iketani, Y., Iketani, T., Takazawa, K. & Murata, M. 2000. Second Derivative of Photoplethysmogram in Children and Young People. *Jpn Circ J*. 64: 110-116.

Imanaga, I., Hara, H., Koyanagi, S. & Tanaka, K. 1998. Correlation Between Wave Components of the Second Derivative of Plethysmogram and Arterial Distensibility. *Jpn Heart J.* 39(6): 775-784.

Jaafar, R., Zahedi, E., Ali, M.A.M., Mohamed, A.L. & Maskon, O. 2007. Photoplethysmographic Pulse Amplitude Response to Flow Mediated Dilation In *IFMBE Proceedings Biomed06*, Edited by Ibrahim, F., Osman, N.A.A., Usman, J. & Kadri, N.A. 15: 423-426.

Jaafar, R. 2008. Development of a Noninvasive Technique for Endothelial Dysfunction Assessment Using Photoplethysmography. Ph.D. Thesis. Universiti Kebangsaan Malaysia.

Jawa, A., Kcomt, J. &Fonseca, V.A. 2004. Diabetic Nephropathy and Retinopathy. *Med Clin N Am* 88: 1001-1036.

Jayasree, V.K., Sandhya, T.V. & Radhakrishnan, P. 2008. Non-invasive studies on age related parameters using a blood volume pulse sensor. *Measurement Science Review*. 8(2): 82-86.

Johansson, A. & Oberg, P.A. 1999. Estimation of Respiratory Volumes from the Photoplethysmographic Signal. Part 2: A Model Study. *Med Biol Eng Comput.* 37(1): 48-53.

Johansson, A. 2003. Neural Network for Photoplethysmographic Respiratory Rate Monitoring. *Med Biol Eng Comput.* 41(3): 242-248.

Johansson, A., Ahlstrom, C., Lanne, T. & Ask, P. 2006. Pulse Wave Transit Time for Monitoring Respiration Rate. *Medical Biological Engineering Computing* 44: 471-478.

Johnson, N., Johnson, V.A., Fisher, J., Jobbings, B., Bannister, J. & Lilford, R.J. 1991. Fetal Monitoring with Pulse Oximetry. *Br J Obstet Gynaecol.* 98(1): 36-41.

Juarez, D.T., Sentell, T., Tokumaru, S. Goo, R. Davis, J.W. & Mau M.M. 2012. Factors Associated with Poor Glycemic Control or Wide Glycemic Variability among Diabetes Patients in Hawaii, 2006-2009. *Prev Chronic Dis.* 9:1-10. http://dx.doi.org/10.5888/pcd9.120065 [5 Jan 2014]

Kamal, A.A.R., Harness, J.B., Irving, G. & Mearns, A.J. 1989. Skin Photoplethysmography: A Review. *Computer Methods and Programs in Biomedicine* 28: 257-269.

Keikhosravi, A., Aghajani, H. & Zahedi, E. 2013. Discrimination of Bilateral Finger Photoplethysmogram Responses to Reactive Hyperemia in Diabetic and Healthy Subjects using a Differential Vascular Model Framework. *Physiol. Meas.* 34: 513-525.

Kelly, R., Hayward, C., Avolio, A. & O'Rourke, M. 1989. Noninvasive Determination of Age-Related Changes in the Human Arterial Pulse. *Circulation* 80(6): 1652-1659.

Kenfack, M.A., Lador, F., Licker, M., Moia, C., Tam, E., Capelli, C., Morel, D. & Ferretti, G. 2004. Cardiac Output by Modelflow Method from Intra-Arterial and Fingertip Pulse Pressure Profiles. *Clin Sci (Lond).* 106(4): 365-369.

Khanokh, B., Slovik, Y., Landau, D. & Nitzan, M. 2004. Sympathetically Induced Spontaneous Fluctuations of the Photo-Plethysmographic Signal. *Medical & Biological Engineering & Computing* 42: 80-85.

Khanolkar, M.P., Ban, S.C. & Stephens, J.W. 2008. Review: The Diabetic Foot. *Q J Med* 101: 685-695.

Kim, J.S., Chee, Y.J., Park, J.W., Choi, J.W. & Park, K.S. 2006. A New Approach for Non-Intrusive Monitoring of Blood Pressure on a Toilet Seat. *Physiol Meas.* 27(2): 203-211.

Komatsu, K., Fukutake, T. & Hattori, T. 2003. Fingertip Photoplethysmography and Migraine. *J Neurol Sci.* 216(1): 17-21.

Kooijman, M., Poelkens, F., Rongen, G.A., Smits, P. & Hopman, M.T.E. 2007. Leg Blood Flow Measurements Using Venous Occlusion Plethysmography During Head-up Tilt. *Clinical Autonomic Research* 17: 106–111.

Kvernebo, K., Megerman, J., Hamilton, G. & Abbott, W.M. 1989. Response of Skin Photoplethysmography, Laser Doppler Flowmetry and Transcutaneous Oxygen Tensiometry to Stenosis-Induced Reductions in Limb Blood Flow. *Eur J Vasc Surg.* 3(2): 113-120.

Leech, N.L., Barret, K.C. & Morgan, G.A. 2008. *SPSS for intermediate statistics: Use and Interpretation. 3rd edition*. Taylor & Francis Group.

Lindberg, L.G., Ugnell, H. & Oberg, P.A. 1992. Monitoring of Respiratory and Heart Rates Using a Fiberoptic Sensor. *Med Biol Eng Comput.* 30(5): 533-537.

Lipsky, B.A., Weigelt, J.A., Sun, X., Johannes, R.S., Derby, K.G. & Tabak, Y.P. 2011. Developing and Validating a Risk Score for Lower-Extremity Amputation in Patients Hospitalized for a Diabetic Foot Infection. *Diabetes Care*. 34: 1695-1700.

Loukogeorgakis, S., Dawson, R., Phillips, N., Martyn, C.N. & Greenwald, S.E. 2002. Validation of a Device to Measure Arterial Pulse Wave Velocity by a Photoplethysmographic Method. *Physiol Meas* 23(3): 581-596.

Mackenzie, I.S., Wilkinson, I.B. & Cockroft, J.R. 2002. Assessment of Arterial Stiffness in Clinical Practice. *QJ Med* 95: 67-74.

Madhavan, G. 2005. Plethysmography. *Biomedical Instrumentation & Technology*. 39(5): 367- 371.

Maltz, J.S. & Budinger, T.F. 2005. Evaluation of Arterial Endothelial Function Using Transit Times of Artificially Induced Pulses. *Physiological Measurement* 26: 293-307.

McVeigh, G.E., Bratteli, C.W., Morgan, D.J., Alinder, C.M., Glasser, S.P., Finkelstein, S.M. & Cohn, J.N. 1999. Age-Related Abnormalities in Arterial Compliance Identified by Pressure Pulse Contour Analysis: Aging and Arterial Compliance. *Hypertension* 33: 1392-1398.

Mealey, B.L. 2006. Periodontal disease and diabetes: A two-way street. *JADA.* 137(10): 26S-31S.

Meierstauss, P., Bucher, H.U., Hurlimann, R., Konig, V. & Huch, R. 1990. Pulse Oximetry Used for Documenting Oxygen-Saturation and Right-to-Left Shunting Immediately After Birth. *Eur J Pediatr.* 149(12): 851-855.

Millasseau, S.C., Guigui, F.G., Kelly, R.P., Prasad, K., Cockcroft, J.R., Ritter, J.M. & Chowiencyzk, P.J. 2000. Noninasive Assessment of the Digital Volume Pulse: Comparison with the Peripheral Pressure Pulse. *Hypertension* 36: 952-956.

Millasseau, S.C., Kelly, R.P., Ritter, J.M. & Chowienczyk, P.J. 2002. Determination of Age-Related Increases in Large Artery Stiffness by Digital Pulse Contour Analysis. *Clinical Science* 103: 371-377.

Millasseau, S.C., Ritter, J.M., Takazawa, K. & Chowienczyk, P.J. 2006. Contour Analysis of the Photoplethysmographic Pulse Measured at the Finger. *J. Hypertens*. 24( 8): 1449-1456.

Miyai, N., Miyashita, K., Arita, M., Morioka, I., Kamiya, K. & Takeda, S. 2001. Noninvasive Assessment of Arterial Distensibility in Adolescents using the Second Derivative of Photoplethysmogram Waveform. *Eur J Appl Physiol.* 86(2): 119-124.

Montgomery, D.C., Runger, G.C. & Hubele, N.F. 2003. *Engineering Statistics.* John Wiley & Sons, Inc.

Murray, W.B. & Foster, P.A. 1996. The Peripheral Pulse Wave: Information Overlooked. *J Clin Monit.* 12(5): 365-377.

Murthy, V.S., Ramamoorthy, S., Srinivasan, N., Rajagopal, S. & Rao, M.M. 2001. Analysis of Photoplethysmographic Signals of Cardiovascular Patients. *Proceeding of the 23rd Annual EMBS International Conference*. 2204-2207.

Mustafa, N., Kamarudin, N.A., Ismail, A.A., Khir, A.S., Ismail, I.S., Musa, K.I. Kadir, K.A., Yaacob, N.A. Ali, O., Isa, S.H.M., Bebakar W.M.W. & Mohamud, W.N.W. 2011. Prevalence of abnormal glucose tolerance and risk factors in urban and rural Malaysia. *Diabetes Care*. 34: 1362-1364.

Nakajima, K., Tamura, T. & Miike, H. 1996. Monitoring of Heart and Respiratory Rates by Photoplethysmography Using a Digital Filtering Technique. *Medical Engineering & Physics* 18(5): 365-372.

Naschitz, J.E., Bezobchuk, S., Mussafia-Priselac, R., Sundick, S., Dreyfuss, D., Khorshidi, I., Karidis, A., Manor, H., Nagar, M., Peck, E.R., Peck, S., Storch, S., Rosner, I. & Gaitini, L. 2004. Pulse Transit Time by R-Wave-Gated Infrared Photoplethysmography: Review of the Literature and Personal Experience. *J Clin Monit Comput.* 18(5-6): 333-342.

Nasimi, S.G., Harness, J.B., Marjanovic, D.Z., Knight, T. & Mearns, A.J. 1992. Periodic Posture Stimulation of the Baroreceptors and the Local Vasomotor Reflexes. *J Biomed Eng.*14(4): 307-312.

Nasimi, S.G., Mearns, A.J., Harness, J.B. & Heath, I. 1991. Quantitative Measurement of Sympathetic Neuropathy in Patients with Diabetes Mellitus. *J Biomed Eng.* 13(3): 203-208.

Njoum, H. & Kyriacou, P.A. 2013. Investigation of finger reflectance photoplethysmography in volunteers undergoing a local sympathethic stimulation. *Journal of Physics: Conference Series* 450: 1-6.

Nilsson, L., Johansson, A. & Kalman, S. 2000. Monitoring of Respiratory Rate in Postoperative Care Using a New Photoplethysmographic Technique. *J Clin Monit Comput.* 16(4): 309-315.

Nitzan, M., Babchenko, A. & Khonokh, B. 1999. Very Low Frequency Variability in Arterial Blood Pressure and Blood Volume Pulse. *Medical and Biological Engineering and Computing* 37: 54-58.

Nitzan, M., Babchenko, A., Khanokh, B. & Landau, D. 1998. The Variability of the Photoplethysmographic Signal a Potential Method for the Evaluation of the Autonomic Nervous System. *Physiological Measurement.* 19: 93-102.

Nitzan, M., Khanokh, B. & Slovik, Y. 2002. The Difference in Pulse Transit Time to the Toe and Finger Measured by Photoplethysmography. *Physiological Measurement.* 23: 85-93.

Nketia, P. & Reisman, S. 1997. The relationship between thermoregulatory and haemodynamic responses of the skin to relaxation and stress. *Proceedings of the IEEE 1997 23rd Northeast Bioengineering Conference*. 27-28.

Oliva, I. & Roztoĉil, K. 1983. Toe pulse wave analysis in obliterating atherosclerosis. *Angiology*. 34: 610-619.

Orimo, H., Ito, H., Suzuki, T., Araki, A., Hosoi, T. & Sawabe, M. 2006. Reviewing the definition of “elderly”. *Geriatr Gerontol Int*. 6: 149-158.

O'Rourke, M.F & Hashimoto, J. 2007. Mechanical factors in Arterial Aging : A Clinical Perspective. *Journal of the American College of Cardiology* 50(1): 1-13.

Osmundson, P.J., O'Fallon, W.M., Clements, I.P., Kazmier, F.J., Zimmerman, B.R. & Palumbo, P.J. 1985. Reproducibility of Noninvasive Tests of Peripheral Occlusive Arterial Disease. *J Vasc Surg.* 2(5): 678-683.

Otsuka, T., Kawada, T., Katsumata, M. & Ibuki, C. 2006. Utility of second derivative of the finger photoplethysmogram for the estimation of the risk of coronary heart disease in the general population. *Circulation Journal*. 70: 304-310.

Otsuka, T., Kawada, T., Katsumata, M., Ibuki, C. & Kusama, Y. 2007. Independent determinants of second derivative of the finger photoplethysmogram among various cardiovascular risk factors in middle-aged men. *Hypertens Res*. 30: 1211-1218.

Padilla, J.M., Berjano, E.J., Sáiz, J., Fácila, L., Díaz, P. & Mercé, S. 2006. Assessment Of Relationship Between Blood Pressure, Pulse Wave Velocity And Digital Volume Pulse. *Computers In Cardiology* 33: 893-896.

Peňaz, J. 1973. Photoelectric Measurement of Blood Pressure, Volume, and Flow in the Finger. *Digest 10th Int Conf Med Biol Eng*. Dresden, Germany. 104.

Peskin, B.S. & Rowen, R.J. 2010. Breakthrough in Clinical cardiology: In-office assessment with pulse wave velocity (PWV) and digital pulse analysis (DPA). *Townsend Letter.* 80-86.

Pilt, K., Ferenets, R., Meigas, K., Lindberg, L.G., Temitski, K. & Viigimaa, M. 2013. New photoplethysmographic signal analysis algorithm for arterial stiffness estimation. *The Scientific World Journal.* 1-9. http://dx.doi.org/10.1155/2013/169035. [5 Jan 2014]

Qawqzeh, Y.K., Ali, M.A.M., Reaz, M. & Maskon, O. 2010. Photoplethysmography Analysis of Artery Properties in Patients Presenting with Established Erectile Dysfunction. *Proceedings of the 2010 2nd International Conference on Electronic Computer Technology*. 165-168.

Qawqzeh, Y.K., Reaz, M B. I., Maskon, O., Chellappan, K. & Ali, M. A.M. 2011a. Photoplethysmogram Reflection Index and Aging. *Proc. SPIE 8285, International Conference on Graphic and Image Processing (ICGIP 2011).* 82852: R1-R6. http://dx.doi.org/10.1117/12.913587

Qawqzeh, Y.K., Reaz, M.B.I., Maskon, O., Chellappan, K., Islam, M.T., & Ali, M.A.M. 2011b. The Investigation of the Effect of Aging Through Photoplethysmogram Signal Analysis of Erectile Dysfunction Subjects. *Proceedings of the 10th WSEAS international conference on Telecommunications and informatics and microelectronics, nanoelectronics, optoelectronics, and WSEAS international conference on Signal processing*. 53-58

Qawqzeh, Y., Reaz, M.B.I., & Ali, M.A.M. 2012. The Analysis of PPG Morphology: Investigating the Effects of Aging on Arterial Compliance. *Measurement Science Review*. 12(6): 266-271.

Qawqzeh, Y., Reaz, M.B.I., & Ali, M.A.M. 2013. Determination of the Presence of Early Sub-clinical Atherosclerosis in Erectile Dysfunction Patients by Measuring CIMT. *Advances in Control Engineering (ACE-2013).* 239-242.

Qawqzeh, Y., Reaz, M.B.I., & Ali, M.A.M. 2014. Sub-clinical Prediction of High-risk of Atherosclerosis by Measuring CIMT. *International Journal of Conceptions on Computing and Information* Technology. 2(2): 5-8.

Reisner, A., Shaltis, P.A., McCombie, D. & Asada, H.H. 2008. Utility of the photoplethysmogram in circulatory monitoring. *Anesthesiology*. 108(5): 950-958.

Roberts, V.C. 1982. Photoplethysmography—Fundamental Aspects of the Optical Properties of Blood in Motion. *Trans Inst Meas Control* 4(2): 101-106.

Roebuck J. When does old age begin?: the evolution of the English definition. 1979. *Journal of Social History*. 12(3): 416-428.

Rubins, U., Grabovskis, A., Grube, J. & Kukulis, I. 2008. Photoplethysmography Analysis of Artery Properties in Patients with Cardiovascular Diseases. *IFMBE Proceedings*. 20: 319-322.

Sackett, D.L., Rosenberg, W.M., Gray, J.A., Haynes, R.B. & Richardson, W.S. 1996. Evidence Based Medicine: What It Is and What It Isn't. *BMJ* 312(7023): 71-72.

Salih, F., Hameed, L., Kamil, A. & Bolz, A. 2012a. Arterial stiffness detection depending on neural network classification of the multi-input parameters. *World Academy of Science, engineering and Technology*. 70: 1204-1207.

Salih, F.M., Abdallah, O., Qananwah, Q. & Bolz, A. 2012b. Normalized Area Under Catacrotic Phase of the Photoplethysmogram Pulse for Estimating Vascular Aging. *Proceedings of the IASTED International Conference Biomedical Engineering*, 166-170.

Saville, B.P. 1998. Physical Testing of Textiles. Boca Raton, CRC Press.

Schram, M.T., Henry, R.M., Van Dijk, R.A., Kostense, P.J., Dekker, J.M., Nijpels, G., Heine, R.J., Bouter, L.M., Westerhof, N. & Stehouwer, C.D. 2004. Increased Central Artery Stiffness in Impaired Glucose Metabolism and Type 2 Diabetes. *Hypertension*. 43(2): 176-181.

Selvin, E., Coresh, J., Golde, S.H., Brancati, F.L., Folsom, A.R. & Steffes, M.W. 2005. Glycemic Control and Coronary Heart Disease Risk in Persons with and without Diabetes. *Arch Intern Med* 165: 1910-1916.

Shani, M., Taylor, T.R., Vinker, S., Lustman, A. Erez, R., Elhayany, A. & Lahad, A. 2008. Characteristics of Diabetics with Poor Glycemic Control Who Achieve Good Control. *J Am Board Fam Med* 21(6): 490-496. http://dx.doi.org/10.3122/jabfm.2008.06.070267

Shariati, N.H., Zahedi, E. & Jajai, H.M. 2008. Classification of Vascular Function in Upper Limb Using Bilateral Photoplethysmographic Signals. *Physiological Measurement* 29(3): 365–374.

Shaw, J.E., Sicree, R.A. & Zimmet, P.Z. 2010. Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Research and Clinical Practice*. 87: 4-14.

Sherebrin, M.H. & Sherebrin R.Z. 1990. Frequency Analysis of the Peripheral Pulse Wave Detected in the Finger with a Photoplethysmograph. *IEEE Trans Biomed Eng* 37(3): 313-317.

Shi, P. 2009. Photoplethysmography in noninvasive cardiovascular assessment. Ph.D.Thesis. Loughborough University

Shichiri, M., Kishikawa, H., Ohkubo, Y. & Wake, N. 2000. Long-Term Results of the Kumamoto Study on Optimal Diabetes Control in Type 2 Diabetic Patients. *Diabetes Care* 23(Suppl. 2): B21-B29.

Short, L., Hecker, R.B., Middaugh, R.E. & Menk, E.J. 1989. A Comparison of Pulse Oximeters During Helicopter Flight. *J Emerg Med.* 7(6): 639-643.

Spigulis, J. 2005. Optical Non-Invasive Monitoring of Skin Blood Pulsations. *Applied Optics* 44(10): 1850-1857.

Spigulis, J., Erts, R. & Ozols, M. 2003. A portable two-channel PPG cardiovascular sensor device. *Proceedings SPIE*. 5138: 65-71.

Spigulis, J., Kukulis, I., Fridenberga, E. & Venckus, G. 2002. Potential of Advanced Photoplethysmography Sensing for Non-Invasive Diagnostics and Early Screening. *Proceeding SPIE*. 38-43.

Spigulis, J., Venckus, G. & Ozols, M. 2000. Optical Sensing for Early Cardiovascular Diagnostics. *Proceeding SPIE,* 3911: 27-31.

Spigulis, J., Venckus, G. & Ozols, M. 2004. Optical Multi-Channel Monitoring of Skin Blood Pulsations for Cardiovascular Assessment. *Proceeding SPIE (Advanced Biomedical and Clinical Diagnostic Systems - BIOS'04),* 5318: 133-139.

Stevens, J. 2002. *Applied multivariate statistics for the social sciences. 4th edition*. Lawrence Erlbaum Associates, Inc.

Stratton, I.M., Adler, A.I., Neil, H.A.W., Matthews, D.R., Manley, S.E., Cull, C.A., Hadden, D., Turner, R.C. & Holman, R.R. 2000. Association of Glycaemia with Macrovascular and Microvascular Complications of Type 2 Diabetes (UKPDS 35): Prospective Observational Study. *BMJ*. 321(7258): 405-412.

Takada, H., Washino, K., Harrell, J.S. & Iwata, H. 1996. Acceleration Plethysmography to Evaluate Aging Effect in Cardiovascular System. Using New Criteria of Four Wave Patterns. *Med Prog Technol.*21(4): 205-210.

Takazawa, K., Fujita, M., Yabe, K., Sakai, T., Kobayashi, T., Maeda, K., Yamashita, Y., Hase, M. & Ibukiyama, C. 1993. Clinical Usefulness of the Second Derivative of a Plethysmogram (Acceleration Plethysmogram). *J Cardiol.* 23(suppl 37): 207-217.

Takazawa, K., Tanaka, N., Fujita, M., Matsuoka, O., Saiki, T., Aikawa, M., Tamura, S. & Ibukiyama, C. 1998. Assessment of Vasoactive Agents and Vascular Aging by the Second Derivative of Photoplethysmogram Waveform. *Hypertension* 32: 365-370.

Tamminen, M., Westerbacka, J., Vehkavaara, S. & Yki-Järvinen, H. 2002. Insulin-Induced Decreases in Aortic Wave Reflection and Central Systolic Pressure are Impaired in Type 2 Diabetes. *Diabetes Care*. 25(12): 2314-2319.

Taylor, B.N. & Kuyatt, C.E. 1993. Guidelines for Evaluating and Expressing the Uncertainty of Nist Measurement Results. NIST Technical Note 1297, prepared under the auspices of the NIST Ad Hoc Committee on Uncertainty Statements (U.S. Government Printing Office, Washington, DC).

Trang, H., Boureghda, S. & Leske, V. 2004. Sleep Desaturation: Comparison of Two Oximeters. *Pediatric Pulmonology.* 37(1): 76-80.

UK Prospective Diabetes Study (UKPDS) Group. 1998. Intensive Blood-Glucose Control with Sulphonylureas or Insulin Compared with Conventional Treatment and Risk of Complications in Patients with Type 2 Diabetes (UKPDS 33). *The Lancet* 352: 837-853.

Verma, S. & Anderson, T.J. 2002. Fundamentals of Endothelial Function for the Clinical Cardiologist. *Circulation* 105: 546-549.

Webster, J.G. 1997. *Design of Pulse Oximeters.* Bristol: Institute of Physics Publishing Ltd.

Wei, C., Sheng, L., Lihua, G., Yuquan, C. & Min. P. 2011. Study on Conditioning and Feature Extraction Algorithm of Photoplethysmography Signal for Physiological Parameters Detection. *4th International Congress on Image and Signal Processing*. 2194-2197.

Wild, S., Roglic, G., Green, A., Sicree, R. & King, H. 2004. Global Prevalence of Diabetes: Estimates for the year 2000 and projections for 2030. *Diabetes Care*. 27: 1047-1053.

Wilkinson, I.B., Hall, I.R., MacCallum, H., Mackenzie, I.S., McEniery, C.N., Arend, B.J.V.d., Shu, Y.E., Mac-Kay, L.S., Webb, D.J. & Cockcroft, J.R. 2002. Pulse-Walve Analysis Clinical Evaluation of a Noninvasive, Widely Applicable Method for Assessing Endothelial Function. *Arteriosclerosis Thrombosis Vascular Biology* 22: 147-152.

Woodman, R.J. & Watts, G.F. 2003. Measurement and Application of Arterial Stiffness in Clinical Research: Focus on New Methodologies and Diabetes Mellitus. *Med. Sci. Monit.*9(5): RA81-RA89.

World Health Organization (WHO). 1999. Definition, Diagnosis and Classification of Diabetes Mellitus and Its Complications. Part 1: Diagnosis and Classification of Diabetes Mellitus. Geneva.

World Health Organization (WHO). 2006. Definition and Diagnosis of Diabetes Mellitus and Intermediate Hyperglycemia. Geneva.

World Health Organization (WHO). 2009. Global Health Risks. Mortality and Burden of Disease Attributable to Selected Major Risks. Geneva.

World Health Organization (WHO). 2011. Global Status Report on Noncommunicable Diseases 2010. Geneva.

World Health Organization (WHO). 2012. Global Data on Visual Impairments 2010. Geneva.

Wu, M.S., Yu, C.C., Yang, C.W., Wu, C.H., Haung, J.Y., Hong, J.J., Chiang, C.Y.F., Huang, C.C. & Leu, M.L. 1997. Poor Pre-Dialysis Glycaemic Control is a Predictor of Mortality in Type II Diabetic Patients on Maintenance Haemodialysis. *Nephrol. Dial. Transplant* 12: 2105-2110.

Wu, H.T., Lee, C.H., Liu, A.B., Chung, W.S., Tang, C.J., Sun, C.K. & Yip, H.K. 2011. Arterial Stiffness Using Radial Arterial Waveforms Measured at the Wrist as an Indicator of Diabetic Control in the Elderly. *IEEE Trans Biomed Eng*. 58(2): 243-252.

Zahedi, E. & Mohd Ali, M.A. 2004. Parametric Differential Approach for Modeling the Upper Limb Human Vasculature. *Proceedings of the 26th Annual International Conference of the IEEE EMBS*. 742-745.

Zahedi, E., Chellappan, K., Ali, M.A.M. & Singh, H. 2007. Analysis of the Effect of Ageing on Rising Edge Characteristics of the Photoplethysmogram Using a Modified Windkessel Model. *Cardiovascular Engineering* 7: 172–181.

Zahedi, E., Jaafar, R. & Ali, M.A.M. 2008. Finger Photoplethysmogram Pulse Amplitude Changes Induced by Flow Mediated Dilation. *Physiological Measurement* 29: 625-637.