NON-INVASIVE JAUNDICE MEASUREMENT USING MAGNETIC INDUCTION SPECTROSCOPY TECHNIQUE

by

JURIMAH BINTI ABD JALIL
(1531311692)

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School of Mechatronic Engineering
UNIVERSITI MALAYSIA PERLIS

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LIST OF ABBREVIATIONS

AAP	American Academy of Pediatric
AC	Alternating current
AD	Analogue device
ABS	Acrylonitrile butadiene styrene
BVR	Biliverdin reductase
CMRR	Common mode rejection ratio
CO	Carbon monoxide
DC	Direct current
HO	Heme oxygenase
IC	Integrated circuit
LED	Light-emitting diode
MIS	Magnetic induction spectroscopy
NADPH	Nicotine adenine dinucleotide phosphate
OPA	Operational amplifier
PC	Personal computer
PCB	Printed circuit board
PEP	Passive electrical properties
TSB	Total serum bilirubin
USB	Universal serial bus

LIST OF SYMBOLS

GHz	Gigahertz
MHz	Megahertz
Hz	Hertz
S/m	Siemen per meter
mg/dL	Milligram per decilitre
mole/L	Moles per litre
μmole/L	Micromoles per litre
nm	Nanometre
cm	Centimetre
mEq/L	Miliequivalent per litre
T_x	Transmitter
R_x	Receiver
NaCl	Sodium chloride
Fe^{3+}	Ferous iron
α	Alpha
β	Beta
γ	Gamma
o	Electrical conductivity
ε	Dielectric permittivity
μ	Magnetic permeability
2π	360^o
	Phase angle
π	Radian

%	Percentage
$\boldsymbol{\omega}$	$2\pi f$
$Ie^{j\omega t}$	Alternating current
ΔB	Perturbation of primary magnetic field
$B+\Delta B$	Inductive phase shift
3D	Three dimensional

Pengukuran Penyakit Kuning Secara Bukan Invasif Dengan Menggunakan Teknik Spektroskopi Induksi Magnet

ABSTRAK

Neonatal jaundis ialah warna kekuningan pada kulit dan tisu-tisu pada badan bayi yang baru lahir. Sebahagian besar bayi yang baru lahir akan mengalami jaundis pada minggu pertama kelahiran. Oleh itu, kaedah tusukan tumit telah digunakan untuk menentukan jumlah serum bilirubin (JSB) dengan mengambil sampel darah daripada tumit bayi. Walaubagaimanapun, pendekatan ini boleh menyebabkan jangkitan pada kulit dan membawa kepada keadaan yang lebih teruk. Pendekatan lain seperti meter jaundis juga mempunyai beberapa kelemahan. Hal ini disebabkan cara pengukuran meter jaundis berasaskan prinsip optik, di mana nilai penyerapan cahaya berbeza untuk setiap warna kulit. Oleh itu, kaedah Spektroskopi Induksi Magnet (SIM) diperkenalkan untuk mengatasi kelemahan kaedah sebelum ini. Kaedah SIM melaksanakan pengukuran anjakan fasa. Teknik ini mengukur sudut fasa diantara isyarat utama dan isyarat sekundar. Isyarat sekundar datang dari arus pusar yang dihasilkan oleh objek yang sedang disiasat. Oleh itu sistem 3D model SIM untuk pengukuran penyakit kuning yang terdiri daripada pemancar, penerima dan bayi jari telah direka dan disimulasi menggunakan COMSOL Multiphysics 5.0. Pemancar dan penerima telah dimodelkan menggunakan gegelung bulat (wayar tembaga) dengan diameter 1 mm dan disimulasi pada frekuensi yang berbeza di bawah rantau penyebaran beta iaitu 2 MHz, 4 MHz, 6 MHz, 8 MHz dan 10 MHz. Untuk menilai prestasi sistem SIM, lima kepekatan sampel telah disediakan dimana ia menyerupai kepekatan bilirubin (85.0 μmole/L, 170.0 μmole/L, 255,0 μmole/L, 290,0 μmole/L dan 331,5 μmole/L) dan telah diuji menggunakan litar SIM. Dalam kajian ini, dua pasang pemancar dan penerima (T_x-R_x) yang berbeza pada saiz penerima sahaja telah diuji; T_x5-R_x8 dan T_x5-R_x12. Keputusan telah menunjukkan bahawa T_x5-R_x8 mempunyai sensitiviti yang kurang untuk mengesan anjakan fasa berbanding T_x5-R_x12. Hal ini disebabkan nilai kecerunan yang lebih besar oleh T_x5-R_x12 dengan 0.0594 berbanding dengan T_x5-R_x8 iaitu 0.0584. Kajian ini telah membuktikan bahawa kekerapan yang lebih tinggi memberikan anjakan fasa yang lebih tinggi di mana sistem SIM kami mencatatkan bahawa pada 10 MHz, anjakan fasa meningkat dari 0.2758 ke 0.3004 darjah, apabila kekonduksian elektrik untuk lima sampel meningkat. Ini telah memudahkan pengiraan dari perbezaan fasa antara isyarat utama dan isyarat sekunder. Kajian ini menunjukkan bahawa sistem SIM mempunyai potensi untuk mengesan penyakit kuning pada bayi yang baru lahir melalui kaedah bukan invasif.

Non-Invasive Jaundice Measurement Using Magnetic Induction Spectroscopy Technique

ABSTRACT

Neonatal jaundice is a yellowing of the skin and other tissues of newborn infants. The vast majority of newborn infants suffers from jaundice during their first week of life. Therefore, the heel puncture technique is used to determine the total serum bilirubin (TSB) by taking blood sample from the baby's heel. This approach, however, may cause skin infection and lead to more damage. Other approach such as jaundice meters may possess some vulnerability due to the fact that the device implements optical based measurement, in which the value of light absorption varies for every skin colour. Thus, Magnetic Induction spectroscopy (MIS) technique is introduced to overcome the weaknesses of the previous approaches. MIS method implements phase shift measurements. This technique is capable of measuring phase angle between primary signal and the secondary signal. The secondary signal comes from eddy current generated by the object under investigation. A 3D model of MIS system for jaundice measurement consisted of transmitter, receiver and baby finger was designed and simulated using COMSOL Multiphysics 5.0.The transmitter and receiver were modelled using circular coil (copper wire) with 1 mm diameter and simulated at different operating frequencies under beta dispersion region which are 2 MHz, 4 MHz, 6 MHz, 8 MHz and 10 MHz. To experimentally evaluate the performance of the MIS system, five sample solution to mimic bilirubin concentrations (85.0 μmole/L, 170.0 μmole/L, 255.0 μmole/L, 290.0 μmole/L and 331.5 μmole/L) were tested using MIS circuit. In this research, two pairs of transmitter and receiver (T_x-R_x) which only differ at receiver size were tested; T_x5-R_x8 and T_x5-R_x12. The results have shown that T_x5-R_x8 has less sensitivity to detect phase shift compared to T_x5-R_x12. This is due to the greater gradient value of T_x5-R_x12 with 0.0594 relative to T_x5-R_x8 which is 0.0584. Through this research study, it is proven that higher frequency gives higher phase shift where our MIS system recorded that at 10 MHz, phase shift increased from 0.2758 to 0.3004 degree when the electrical conductivity of five samples solution increased. This contributes to an easy calculation of phase difference between primary field and the secondary field. This study shows that MIS system has the potential to detect jaundice in newborn infants through non-invasive method.

CHAPTER 1

INTRODUCTION

1.1 Research Background

Neonatal jaundice or neonatal hyperbilirubinemia is the yellowing of the skin and other tissues of a newborn infant body. The vast majority of newborn infants suffer from jaundice during the first week of life, and are required to be monitored frequently in order to identify the infants who might develop severe hyperbilirubinemia. Neonatal jaundice is a medical condition that normally occurs to among 60% to 70% of newborn infants as a result of an imbalance between production and elimination of bilirubin during the breakdown of red blood cells. This phenomena occurs because of the immaturity of newborn's liver which is not able to metabolize bilirubin effectively and prepare it for excretion through the urine (Yang et al., 2013). Then, the excessive bilirubin in the blood stream diffuses into the surrounding tissue and leads to the yellowing of the skin – the elevated bilirubin levels may have harmful effects on the babies themselves (Alla, Huddle, Clark, & Beyette, 2010). Newborn infants who have extremely high level of bilirubin may be exposed to Kernicterus, which will cause a permanent brain damage to the baby. Besides that, newborn infants might be subjected to physical abnormalities, severe retardation and also blindness.

In most hospitals or medical centers, a traditional invasive technique, which is heel puncture, is employed to determine the total serum bilirubin (TSB). Nevertheless, the accuracy of the traditional invasive technique is relatively poor, which is ± 0.03mg/dL. Additionally, this traditional method can precipitate trauma to newborn infants and parents due to the pain experienced by the babies (E. Ho, Lee, Chow, & Chung, 2006). This trauma is caused by the determination of total serum bilirubin (TSB) by using heel puncture that might be painful to newborn infants as blood sample is drawn through the heel area (Riskin, Tamir, Kugelman, Hemo, & Bader, 2008). This technique holds some limitations; it is occasionally dangerous due to the risk of infection to infants, besides time-consuming. Thus, the non-invasive technique is considered much safer in handling this kind of condition. Having known these issues, non-invasive assessment technique should be aggressively explored.

In this research study, magnetic induction spectroscopy (MIS) technique will be applied by using multiwavelength to the non-invasive device. The concept is first designed and simulated using COMSOL Multiphysics software – the prototype of the device is designed by using microcontroller unit as part of it. The system consists of two essential parts which are the transmitter and receiver. The system in the device is a single channel measurement which applies physics of magnetic induction phenomena. The system is then simulated by using COMSOL Multiphysics software.

This research focuses on the application of magnetic sensors by utilizing magnetic induction principle in the measurement of the signal based on the phase shift technique (Wei & Soleimani, 2012). The principle of the system begins when electromagnetic fields are generated through the transmitter, then propagated through the tissues of the baby's finger and procured by the receiver on the opposite side. The increasing phase shift value of the received signal, due to the existence of bilirubin underneath the skin, will determine the jaundice level of newborn infants.

In the current market, there are jaundice meters which implement the non-invasive technique and the system based on the optical technique (Alla et al., 2011). Unfortunately, these devices require the optical sensor to make contact with tissue for optimum accuracy as it is sensitive to light exposure, which may contribute errors in the measurement. In this case, the babies' skin colour may cause different readings because of the different absorption light value. Due to this issue, the measurement mechanism, that can produce an accurate result regardless of light exposure and skin colour, should be probed. Hence, the magnetic induction principle with the phase shift measurement scheme could be the best alternative.

The phase shift measurement technique has been employed in many low conductivity applications, such as the low conductivity solution and the biological tissues (Gursoy & Scharfetter, 2010; Zakaria et al., 2012). This technique, which utilizes the frequency of several megahertz (MHz), is capable of measuring phase angle between primary signal and secondary signal where the secondary signal comes from the eddy current that is generated by object that is put under investigation (Watson, Wee, Griffiths, & Williams, 2011; Wolff, Farias, Ramos, & Nogueira, 2012). The differences in the phase angle are related to the electrical properties of the material itself, where in these low conductivity material cases, the value is eminently paltry and almost cannot be clarified through magnitude base measurement technique. However, through the phase shift scheme, the changes have been proven to be successfully measured (Ahmad Mustafa, Ahmed, Ali, Yit, & Zainal Abidin, 2009).

Additionally, an increasing recognition has been given to biological properties studies with an electromagnetic field, which is associated with the interaction between biological tissues and the electromagnetic field. For instance, it can be used to monitor vital activities in the human body, such as breathing and cardiac activities (Mahdavi & Ferrer, 2012). Therefore, the electromagnetic field concept is reliable to apply in jaundice detection as it is practical in assisting neonatal nurses in checking bilirubin level without having to bear any blood sample via baby's heel.

1.2 Problem Statement

In Malaysia, the common technique practised by neonatal nurses in pursuance of jaundice assessment for newborn infants is through the conventional method by acquiring blood samples from the baby's heel. Blood sample is taken from newborn infants for bilirubin level analysis. Unfortunately, this method causes trauma and distress to both babies and parents. Besides that, it also exposes the newborn infants to infection as a result of the small cut on the skin (Hakimi, Hassan, Anwar, Zakaria, & Ashraf, 2016) . On the other hand, the neonatal nurses also applied non-invasive device such as jaundice meter for jaundice assessment in newborn infants (Hakimi et al., 2016). However, jaundice meters which are available in the market may possess some vulnerability due to the fact that the device implements the optical based measurement – in which the value of light absorption varies for every skin colour (Gupta, Kumar, & Khera, 2016). Thus, an assessment tool, which relatively has better measurement mechanism compared to the optical based measurement, should be explored without taking skin colour of the babies and light exposure environment into account. The magnetic induction spectroscopy technique fulfills and suits this requirement as the skin colour does not affect the accuracy of the measurement.

1.3 Objectives

The objectives of this research are:

i. To design and simulate the sensor for jaundice measurement system.
ii. To identify a suitable frequency for measuring sample solutions.
iii. To study the relationship of phase shift and concentration of sample solution

1.4 Research Scope

The scope of this research is related to the magnetic induction technique and frequency used throughout the research which is below 10MHz. The main software that used for simulation is COMSOL Multiphysics version 5.0. This project focuses on single-channel transmitter (T_x) and receiver (R_x). During simulation, this study is focuses on the nail, skin, fat, muscle, bone, and hemolysed blood as biological tissue to be simulated. As for the experimental part of the sample solution, electrolyte solution and iodine solution, will act as blood containing bilirubin. The sample solution mimics bilirubin concentration in the blood of newborn suffering from jaundice. The concentration of sample solution starts at the lowest concentration (85.0 μmole/L) to the highest concentration (331.5 μmole/L).

1.5 Outline of Thesis

Chapter 1 begins with an overview of jaundice and background study regarding the research. This chapter explains about problem statements, the objectives of the research and also the scope of the experiment.

Chapter 2 discusses the literature review and background study of the research. In this chapter, a detailed explanation on jaundice, bilirubin production and current method, which is used by neonatal nurses to detect jaundice level, will be presented. Besides that, the important sub-topics about this chapter are included in the study as well as past experiment that has been done by previous researchers.

Chapter 3 revolves around the methodology of this research which starts with the study of the non-invasive measurement. This chapter explains the method that has been applied throughout the research to conduct the simulation and experiment. The simulation tool which is operated throughout the research study is discussed in this chapter. The discussion includes experiment steps and how the experiment is carried out. Furthermore, a detailed explanation on the molarity formula, that is used to calculate the concentration of iodine solution and electrolytes solution which acts as measured sample, is also presented in this chapter.

Chapter 4 contains result and discussion. The result obtained will be presented in tables and graphs, and discussed correspondingly. From the result and discussion, the characteristics of sensor coils will be selected and recommended.

Chapter 5 is the conclusion chapter which will summarize and conclude the research study as well as cover on future works.

1.6 Summary

In this chapter, neonatal jaundice, which caused the yellow colour to appear on the baby's skin, has been discussed in the introduction section. The technique that is applied in the measurement has also been pointed out through this chapter. Furthermore, we have also discussed the overall research problem briefly.

The objectives of this research have been listed out and the scope selection has been elaborated explicitly in the research scope. In the next chapter, the literature review done for this research will be presented and a comprehensive study of the theoretical part of this research will be displayed. All topics will be separated into different sections for cursive insight.

CHAPTER 2

LITERATURE REVIEW

2.1 Jaundice

2.1.1 Neonatal Jaundice

Neonatal jaundice is a yellow discolouration of a baby's skin, mucous membrane, sclera and inner lining of the human tissues as shown in Fig. 2.1 (Houlihan, Armstrong, & Newsome, 2011). Yellow discolouration of the baby's skin is caused by the delay in conjugation and increased bilirubin level in the blood (Abdul Saleem, Junaid, Mohammadi, Jebran, & Indikar, 2013). Neonatal jaundice is the most common clinical problem among newborns which it can affect them shortly after birth. The condition of neonatal jaundice is mostly benign (Alireza & Firoozabadi, 2012; Stillova et al., 2007). Neonatal jaundice occurs when the bilirubin level in the baby's blood is rising. Based on the previous researchers, jaundice is a common condition in new-born affecting over 50-60% of all babies. Approximately 50% of term infant and 80% of preterm infants developed jaundice in the first week of life (Ahmed Sadik et al., 2015; Prasad & Singh, 2013). Untreated jaundice will cause brain damage. Also, high level of bilirubin may be toxic to the development of the central nervous system and it also may cause neurological impairment even to the newborn infants (Adama, Corwin, Pakula, Harley, & Weinblatt, 1994; R. Agarwal, Aggarwal, Deorari, & Paul, 2002). Thus, premature infants and newborn infants with jaundice symptoms should be treated quickly by the neonatal nurses and to be monitored before the bilirubin level in the baby's blood reaches to a dangerous level.

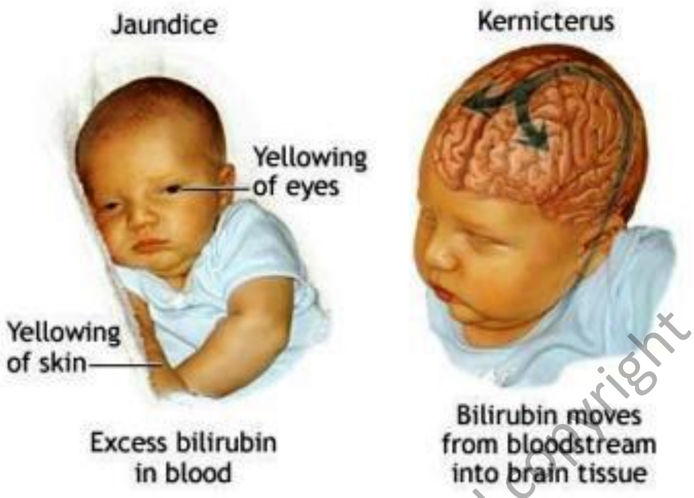

Figure 2.1 : Jaundice in Newborn Infants (Hakimi et al., 2016)

2.1.2 Types of Jaundice

Neonatal jaundice is also known as a neonatal hyperbilirubinemia which is divided into two types of hyperbilirubinemia; unconjugated hyperbilirubinemia and conjugated hyperbilirubinemia. Unconjugated hyperbilirubinemia occurs when there is an over production of the bilirubin in the blood. Besides that, it is also resulting from an immature hepatic enzyme glucoronosyl transferase. The enzyme is responsible for glucuronidation of bilirubin. This kind of hyperbilirubinemia is fat soluble. Thus, bilirubin will be absorbed by the intestinal epithelium and phospholipid membrane such as the skin and sclera. Then, it will turn these membranes to a yellow colour and might be toxic to the cell (Houlihan et al., 2011).

In addition, untreated unconjugated hyperbilirubinemia can lead to kernitures problem to the newborn infants, thus it develops secondary binding of bilirubin in specific areas of the brain such as the basal ganglia, causing severe movement disorder which is called choreothetosis. Choreothetosis can lead to deafness and mental retardation to newborn infants (Gilmore & Garvey, 2013; Imhoff, 2013; Patanwala, Richardson, Gilmore, & Garvey, 2016). On the other hand, conjugated hyperbilirubinemia is a water soluble and not reabsorbed by the epithelial cells. Conjugated hyperbilirubinemia is caused by the neonatal hepatitis syndrome, duct paucity syndrome and biliary atresia. This hyperbilirubinaemia appears at any time after birth (Gilmore & Garvey, 2013; Patanwala et al., 2016). The level of bilirubin in the conjugated hyperbilirubinemia is normally measured more than 25 μmole/litre (Ives, 2011).

2.1.3 Formation of Bilirubin

Approximately, 75% of bilirubin is originated from the degradation of the hemoglobin which is released from the red blood cells. The rest of the 25% of bilirubin comes from catabolism of other hemoproteins such as catalase, peroxides, cytochromes and myoglobin (Bland, 1996). Production of bilirubin is related to two essential mechanisms which are intravascular and extravascular as shown in Fig. 2.2. Intravascular is a production inside the blood vessel while extravascular is the production outside the blood vessels in the reticuloendothelial system or in tissue macrophages (Fialova & Vejrazka, 2013). Approximately more than 90% of hemoglobin (under normal condition) is degraded in the extravascular mechanism