NONINVASIVE BLOOD GLUCOSE MEASURMENT USING MODULATED ULTRASOUND AND INFRARED LIGHT

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By

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CHAPTER 7

CONCLUSION AND RECOMMENDATIONS FOR FUTURE WORK

7.1 Conclusions:

The approach of a new noninvasive innovation for blood glucose measurement will reform management of diabetes alongside expanded patient compliance, decline load on therapeutic crisis and diabetes associated complications. The requirement of accurate, noninvasive technique for blood glucose measurement in diabetic subjects for daily and long-term usages is now or never.

In this present work, we represent a modulated ultrasound and infrared light based noninvasive technique for blood glucose measurement over human subjects. Both the in-vitro and in-vivo results showed good correlation in glucose measurement. Therefore, a new technique for noninvasive blood glucose measurement using modulated ultrasound and infrared technique is developed and the observation validates the supposition of the new concept.

The finding of this present thesis work signifies towards potential and promising direction of our investigational research for noninvasive blood glucose measurement in human subjects. The important conclusions of the present investigation are as follows:

- The modulated ultrasound and infrared light-based noninvasive technique detects blood glucose levels in human subjects with clinically significant and acceptable results.
- In this present work, we demonstrated the suitability of 40 kHz frequency based ultrasound transmitter and infrared light emitting diode-based measurement at 940 nm for noninvasive glucose monitoring by evaluating our technique in in-vitro and in-vivo experiments.
- Our noninvasive technique has been proficient to detect changes in glucose levels during fasting, postprandial, random stages. This noninvasive technique also detects glucose dose induced variation in blood glucose levels in the study subjects as revealed during our clinical investigations.
- The blood glucose concentration influences light transmission phenomenon. It indicates that with increase in blood glucose levels in human subject causes minimum scattering effects, subsequently smaller optical path lengths, and this phenomenon reduces absorption characteristics, which in turn causes increased light transmission effects and vice-versa. In the FFT domain, this correlated effect

has been observed in in-vitro analysis. Subsequently, our noninvasive technique based measurements performed over human subjects also represents that the peak amplitude in FFT domain tracks the blood glucose concentration over the time.

- The phenomenon of peak amplitude variations in FFT domain with respect to actual blood glucose levels serves as the functional indicator for measuring actual blood glucose levels in study subjects. Henceforth, this typical characteristic helps us in performing calibration and preparation of look-up table for converting peak amplitude in FFT domain to its corresponding Blood Glucose Levels.
- Our overall clinical study as reported in chapter 5 of this present thesis includes investigation over 151 (male = 105; female = 46; in which normal non-diabetic healthy subjects = 84; pre-diabetic subjects = 15, diabetic subjects = 52) adult study subjects, that yields total 627 data pairs of reference (invasive) and predicted (noninvasive) blood glucose levels. Further, in paired data set of 627, the corresponding reference blood-glucose range has been 71-302 mg/dl.
- The clinical study with our developed noninvasive technique over healthy normal, pre-diabetic, and diabetic subjects for blood glucose measurement yielded promising results. Our prototype measures noninvasive blood glucose levels from 71 mg/dl to 250 mg/dl with an acceptable clinical significance. Further, our clinical study showed that Blood Pressure and Glycated Hemoglobin concentration increases with increase in blood glucose levels.
- Our noninvasive technique based system was medically safe, easy to use, and acceptable, as reflected by the overall study subject's well-tolerated compliances.
- Various statistical performance evaluation metrics including Mean Absolute Error, Percentage of Mean Relative Absolute Error, Median Absolute Error, Percentage of Median Relative Absolute Error, Root Mean Squared Error, and Standard Error of Prediction clearly revealed that our noninvasive technique is better or comparable with other prominent developing noninvasive technique based results. Further, the results are also akin with the performances of electrochemical or Micro dialysis based Continuous Glucose Monitoring system(s).

- Mean Absolute Error, Percentage of Mean Relative Absolute Error, Median Absolute Error, and Percentage of Median Relative Absolute Error values are within the permissible limits of ISO 15197-2013.
- Several statistical evaluation parameters including Clarke and Parkes Error Grid Analysis, Bland-Altman plot, Mountain plot, CUSUM test for linearity, Independent sample t-tests, and Deming regression analysis clearly revealed that our noninvasive technique based blood glucose measurements are statistically significant.

Hence, it is concluded from the present investigation that our objective of the work has been achieved, that is a new noninvasive technique using modulated ultrasound, and infrared light has been developed to measure blood glucose levels in normal, pre-diabetic, and diabetic subjects.

However, certain error induced bio-signals were observed due to multiple superfluous causes such as finger placement, finger shape and size, motion artifacts, time and machine drift issues, melanin induced skin pigmentations, variation in multiple physiological parameters (blood pressure, heart rate, skin sweating, body temperature), environmental changes, which changes blood tissue optical characteristics and induce variations in the signal acquisition processes. In future work, acquiring innovative measures is essential to reduce above-mentioned interferences.

7.2 Recommendations for future work:

The work reported in this present investigation is the development of noninvasive blood glucose measurement-technique using modulated ultrasound and infrared light. However, there are some areas, which require further exploration. Hence, the future work related recommendations are as follows:

- Developing specialized functional units to eliminate or reduce unwanted interferences.
- Large-scale experimental investigations by our newly developed technique to measure noninvasive blood glucose levels in normal, pre-diabetic, and diabetic subjects.
- Clinical evaluations for analyzing and comparing inter and intra subject's influence over NIR technique based noninvasive blood glucose estimations.

- Clinical evaluations for analyzing and comparing short-term and long-term effects of noninvasive near infrared-based blood glucose measurement in normal, pre-diabetic, and diabetic subjects.
- Large-scale calibration to prediction based clinical trials for increasing different subject based prototype specificity and sensitivity factors.
- Large-scale experimental investigations by our newly developed technique to measure noninvasive blood glucose levels in hypoglycemic (below 70 mg/dl), extreme hyperglycemic (above 300 mg/dl), and pregnant diabetic volunteers.
- Experiments with another light wavelength, ultrasound frequency to measure blood glucose in normal, pre-diabetic, and diabetic subjects.
- The present work utilizes the peak-to-peak amplitude change in FFT domain to predict the blood glucose levels in normal, pre-diabetic, and diabetic subjects. Future research may include additional time and frequency domain based parameter measurements at different ultrasound frequency and light wavelengths to validate and produce a robust calibration model.
- In general, for commercial implementation of this noninvasive technique, the clinical accuracy level of 95% or more is essential. Hence, the future research must include the application of delicate measurement probes for reducing finger positioning related interferences, different ultrasound frequency and light wavelengths, wideband ultrasonic transducers, additional signal characteristics, large-scale investigations and multiple parameter based measurement techniques to realize the same.

Our clinical study depicts that modulated ultrasound and infrared technique based measurement have good potential and are a footstep towards recognizing an ideal noninvasive blood glucose monitoring system. The accomplishment of a practicable noninvasive blood glucose monitoring system would nurture progress for artificial pancreas development; fore mostly towards insulin based closed loop delivery systems, essential for diabetic subjects. Hence, positively our technique will show its functional usage in near future for noninvasive estimations of blood glucose levels in the human subjects.