

# Body Metabolism Provides a Foundation for Noninvasive Blood Glucose Monitoring

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The metabolic oxidation of glucose in the human body, also known as cellular respiration, provides most of the energy necessary for cellular activities. Several authors (1–4) have suggested that the relationship between blood glucose concentration and physiological parameters relates to metabolism. Until now, this phenomenon has not been utilized to calculate blood glucose concentration (5–7). Here we describe the noninvasive measurements of glucose concentration in the blood by taking into account the body heat generated by glucose oxidation and local oxygen supply. We arrived at this concept from observing that the circadian rhythm of the human body conforms to the subtle balance seen among metabolic heat, local oxygen supply, and glucose concentration. We have developed a system that integrates both thermal and spectroscopic sensors, which simultaneously measures these related parameters and subsequently physicochemically derives the concentration of blood glucose. Our discovery shows that blood glucose concentration can be accurately and reliably measured by this novel, noninvasive technique.

## RESEARCH DESIGN AND METHODS

Our concept is based on following function equation:

[GLU] =  $F$  (heat generated, Hb, HbO<sub>2</sub>, and blood flow rate)

where [GLU] represents the concentration of glucose and  $F$  is a function of a set of metabolic parameters found in the subject's fingertip [heat generated, hemo-

globin concentration (Hb), oxyhemoglobin (HbO<sub>2</sub>), blood flow rate, and their composites]. These metabolic parameter values are, in turn, interdependent among each other.

Possibly a reverse relation, (GLU) =  $F$  (heat generated, Hb, HbO<sub>2</sub>, and blood flow rate), can be observed. This is probably the case if the observed change in temperature, in energy balance, or in the blood flow rate, respectively, is caused by the other parameters, by the change of environmental temperature (room temperature), or by metabolic disorders.

The parameters are measured by the experimental setup shown in Fig. 1A. Thermal measurements from a finger's surface are obtained from three temperature sensors. Before the measurement, moisture or wetness on the finger was carefully wiped out to avoid a negative effect.

A pyroelectric detector (D1) inside the device measures the radiation temperature of the finger. Thermistors (D2 and D3) are connected to a thin gold plate and a cylindrical material, on which the finger is placed for the contact temperature measurement. The measurement time is ~10 s. Before and after finger placement, the ambient temperatures are measured for baseline correction.

The supplied oxygen amount is estimated by using blood flow rate, Hb, and HbO<sub>2</sub>. The blood flow rate is primarily obtained by the delayed thermal conductivity being measured with the thermistor (D3). Hb and HbO<sub>2</sub> are measured by spectroscopic measurement via a modi-

fied diffuse reflection method. Wavelengths of 470, 535, 660, 810, 880, and 950 nm are produced by six light-emitting diodes (L1 to L6, respectively) and measured by three photodiodes (D4 to D6). Optical fibers lead light from the light-emitting diodes to the subject's finger. These three detectors are arranged to measure the specular (D4) and diffuse reflection (D5) on the top, just inside, and through the skin surface (D6). The concentrations of Hb and HbO<sub>2</sub> are calculated using the values of multiple components obtained by the three detectors multiplied by the six wavelengths, and the results are corrected for individual skin roughness, thickness, and chromogen. As a final step in the processing of these values, all possible regressions and stepwise elimination (8–10) are applied and a calibration function is performed.

**RESULTS** — Figure 1B shows a regression analysis involving 35 data points (29 from diabetic patients and 6 from nondiabetic volunteers) by the noninvasive method against a glucose oxidase enzymatic amperometry for whole-blood samples as the reference method. Each data point represents that the noninvasive measurement and the capillary blood collection for glucose oxidase measurement were simultaneously performed at random timing for each patient. Blood glucose concentration was measured over a range of 50 to 400 mg/dl. The coefficient of correlation ( $r$ ) was 0.96, and precision obtained was 10 mg/dl by duplicate measurements. Additionally, for healthy fasting people, repeatability of the noninvasive method was measured five times within 20 min. The mean was 100 mg/dl and the SD 6 mg/dl.

**CONCLUSIONS** — We have shown that the physiological parameters of glucose oxidative metabolism can be measured by various modalities and that blood glucose concentration can be accurately and reliably physicochemically derived. Therefore, it is possible to repro-

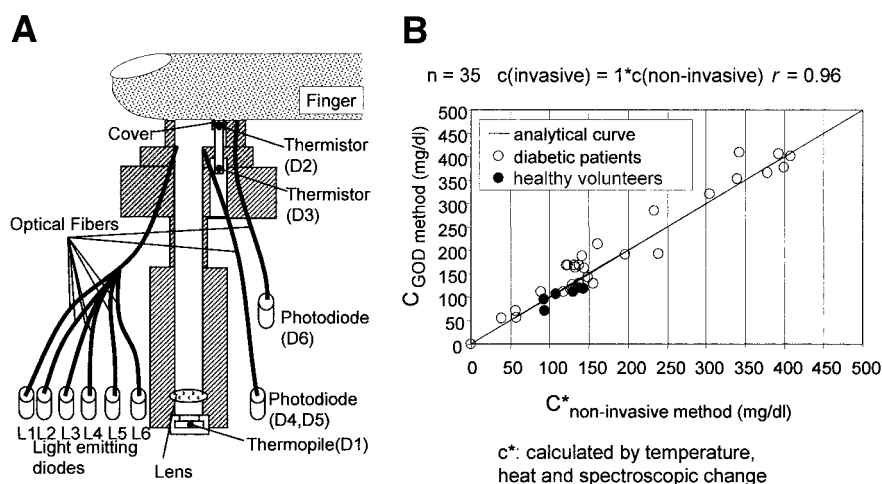
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**Figure 1**—A: The experimental setup. B: Regression analysis involving 35 data points (29 from diabetic patients and 6 from healthy volunteers) by the noninvasive method against a glucose oxidase (GOD) enzymatic amperometry for whole-blood samples as the reference method. n = number of measurements. c, blood glucose concentration; r, coefficient of correlation.

ducibly measure glucose concentration by this novel, noninvasive manner. Studies are ongoing to further evaluate the clinical utility of this innovative, noninvasive, glucose measurement method, which could provide important public health benefits for the increasing diabetic population.

**References**

1. Seaman GVF, Engel R, Swank RL, Hissen W: Circadian periodicity in some physicochemical parameters of circulating blood. *Nature* 207:833–835, 1965
2. Hillson RM, Hockaday TDR: Facial and sublingual temperature changes following intravenous glucose injection in dia-

betes. *Diabete Metab (Paris)* 8:15–19, 1982

3. Cho OK, Holzgreve B, inventors: Process and device for detecting the exchange of heat between the human body and the invented device and its correlation to the glucose concentration in human blood. U.S. patent 5 924 996, 1999
4. Cho OK, Holzgreve B, inventors: Process and device for non-invasive determination of glucose concentration in parts of the human body. U.S. patent 5 795 305, 1998
5. Waynant RW, Chenault VM: Overview of non-invasive fluid glucose measurement using optical techniques to maintain glucose control in diabetes mellitus. *IEEE Lasers Electro-optics Soc Newsletter*, 1998, p. 3–6
6. Khalil OS: Spectroscopic and clinical aspects of noninvasive glucose measurements. *Clin Chem* 45:165–177, 1999
7. Klonoff DC: Noninvasive blood glucose monitoring. *Diabetes Care* 20:433–437, 1997
8. Seber GAF: *Linear Regression Analysis*. New York, John Wiley & Sons, 1977
9. Hocking RR: The analysis and selection of variables in linear regression. In *Biometrics*. 32:1–49, 1976
10. Walls R, Weeks D: A note on the variance of a predicted response in regression. *Am Stat* 23:24–26, 1969