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SCREENING FOR NEONATAL JAUNDICE USING SKIN REFLECTANCE

E. J. Hanley[1], R. K. Boyd[2] and D. P. DeWitt[3]
School of Mechanical Engineering
and
Biomedical Engineering Center
Purdue University
West Lafayette, Indiana 47907

There is a continual need to investigate new and improved medical diagnostic methods. Particularly attractive are noninvasive techniques suited for the detection and monitoring of a disease. Since characteristic features of disease conditions are often evident in the local optical properties, it is feasible that a disorder can be identified and evaluated by some measurement of the optical properties of the suspect tissue. The focus of the present study is the development of an optical method for the detection of jaundice by multispectral skin reflectance analysis. Optical diagnosis offers the advantages of being noninvasive, simple, and rapid and therefore is well suited to mass screening.

Jaundice is caused by an excessive level of bilirubin in the bloodstream resulting in diffusion of free bilirubin to the surrounding tissue where the metabolism of the invaded cells is disrupted. Severe hyperbilirubinemia (kernicterus) can cause damage to the brain or the central nervous system. It is also believed that lower level hyperbilirubinemia can cause subtle childhood learning disorders. Increased levels of serum bilirubin result in a yellowing of the skin; this subtle color change is presently the basis for clinical detection of jaundice. A positive visual diagnosis is verified by a blood test which measures the serum bilirubin concentration. The treatment regimens, phototherapy and exchange transfusion, are used to prevent bilirubin concentration from reaching excessive levels. Typically, phototherapy is initiated when serum bilirubin levels exceed 10 mg/100 ml while the exchange transfusion is warranted as the level approaches 20 mg/100 ml.

The existence of a quantitative relationship between serum bilirubin concentration and skin reflectance has previously been established [1]. In this prior study, <u>in vivo</u> reflectance spectra in the visible region were recorded for thirty full-term white infants and corresponding total serum bilirubin levels were determined. A statistical spectrocorrelation analysis was used to determine an empirical relationship between the serum bilirubin level and the skin reflectance at five wavelengths. Although this work is somewhat limited, notably due to the small, highly homogeneous sample population, the results provided conclusive evidence of a causal relationship between serum bilirubin concentration and the skin reflectance spectra.

The objective of the present research is to expand the sample population to include a larger number of infants with a wider variety of skin characteristics. In particular, the study addresses the effect of pigmentation and whether the method is suited for use on both white and black infants. It is also an aim of the study to develop a model of the infant's skin that would provide a physical basis for the relationship between serum bilirubin concentration and the skin reflectance spectra. The result of this work has been the improvement in the optical method for detection of jaundice that shows promise for clinical use.

A portable, self-contained system was developed for rapid and convenient acquisition of reflectance spectra in the clinical environment. In the apparatus, shown schematically in Figure 1, the source provides an illuminating flux which is transferred through one branch of a bifurcated, fiber-optic bundle to the target, the surface of the skin. Reflected flux is transmitted through the second branch of the fiber optic to a spectroradiometer where the radiation is separated into spectral components (400-800 nm) and measured using a silicon photodiode detector. The spectral information is recorded on magnetic tape for later computer analysis. The experimental procedure involves alternately observing the infant's skin and that of a standard material, barium sulfate. A single skin observation consists of eight spectral scans which are averaged, compared to the reference observation and ultimately converted to absolute spectral reflectance. Concurrent to each skin reflectance measurement, a blood sample was taken and the serum bilirubin was determined (Jendrassik method).

Clinical observations were made on infant subjects in the nurseries and neonatal intensive care units of Wishard Hospital and Riley Hospital, Indianapolis, Indiana. The primary sample population is comprised of 103 full-term infants whose serum bilirubin levels are under 15 mg/100 ml and are otherwise healthy. Measurements were performed on consecutive days for a number of these infants such that a total of 221 observations are included in this data set. Additional data was obtained for three full-term infants during phototherapy; for a single infant during the course of an exchange transfusion and for 23 premature infants. Table 1 summarizes the sample populations for which observations were obtained, classifies the populations according to race and sex, and lists the total number of observations per group.

For proper interpretation of skin reflectance information, a physical model describing the optical behavior of the skin was developed [2]. Based upon

1. Graduate Research Assistant; 2. Analyst and Training Specialist, Laboratory for Applications of Remote Sensing (LARS); 3. Professor of Mechanical Engineering

Table 1. Summary of Infant Populations and Clinical Observations

Infant Subjects	Black		White		Total
	Female	Male	Female	Male	Observations
Full-Term Healthy	18	27	24	34	221
Full-Term, Phototherapy	1	-	-	2	14
Exchange Transfusion	-	-	1	-	12
Premature	3	3	8	9	64

the characteristic absorption and scattering mechanisms of human skin, an optical parameter, $\overline{\xi}$ is derived which isolates the skin absorption due to bilirubin. This parameter is a function of the reflectance at three wavelengths according to the expression

$$\overline{\xi} = \overline{\xi}(460,510,420) = \frac{\xi_{460}-\xi_{510}}{\xi_{420}}$$

where $\xi_i = \rho_i/2 + 1/2\rho_i - 1$ and ρ_i are the spectral reflectance values. Based upon the analysis to include the effects of hemoglobin and skin melanin (pigment) content, the model predicts that this optical parameter will be linear with serum bilirubin concentration BL(mg/100 ml), that is

$$BL = A + B \cdot \overline{\xi}$$

The skin model provides a physical basis for the optical detection of jaundice and provides the means of translating the reflectance measure to a meaningful physiologic parameter.

The sample population is divided into two groups according to race to reduce the hereditary related effect of variation in melanin pigmentation. A composite summary for the spectral reflectance of the 221 observations is shown in Fig. 2 where the results have been averaged for three ranges of serum bilirubin concentration. A depression in the spectra is observed, as anticipated, in the 460 nm region for higher bilirubin levels. There is considerable variation between infant spectra and in this form, the spectra is not useful for diagnostic purposes. For each of the two groups, the optical parameter $\overline{\xi}(460,510,420)$ has been calculated from the spectra and is presented in Fig. 3 and 4 for the healthy, full-term, black and white infant groups, respectively. A linear relationship is observed between the optical parameter, $\overline{\xi}$, and the serum bilirubin level as shown by the solid line. The dashed lines in these figures signify the limits of an uncertaintity interval of ± 2 mg/100 ml which represents the minimal acceptible uncertainty for clinical use. The correlation of the bilirubin value predicted from the triple-wavelength function and the actual serum bilirubin value show a correlation coefficient (R) of 0.86 for the black group and 0.78 for the white group. Much of the variation observed in the data may be explained by uncertainty in the serum bilirubin determination (± 1.5 mg/100 ml) in addition to skin reflectance measurement error.

Clinical observations on infants during the course of phototherapy and exchange transfusion treatments demonstrate that the skin reflectance may not be an accurate index of the serum bilirubin level. However, results indicate that skin reflectance may provide information toward a more basic understanding of these treatment modalities which are presently not well understood. Furthermore, the optical measurement appears useful for evaluation of the effectiveness and progress of these treatment regimens. Representative reflectance spectra data for the premature infants is consistent with results of the full-term group and demonstrate that the optical parameter, $\overline{\xi}$, is a valid indicator under a wide variety of physical conditions.

The results of this study indicate that the multi-spectral skin reflectance analysis method can be useful for the clinical detection and management of jaundice. More detailed information on the absorbing and scattering mechanisms of the skin is needed if an improved relationship between skin reflectance and serum bilirubin level is to be developed. However, our present understanding is sufficient to account for skin characteristics such as pigmentation, and as such, we need no longer rely on just empirical correlations. Refinements in the method for estimating bilirubin level are certainly possible, however, the method is presently close to the acceptable limits for clinical methods now used in nurseries. In addition to the obvious advantages of the optical method over the blood test, this new method may be a better indicator of risk due to jaundice. The reflectance method is sensitive to the bilirubin absorbed by the tissue while the blood test provides a measure of bilirubin concentration (free or bound to albumin) in the blood stream.

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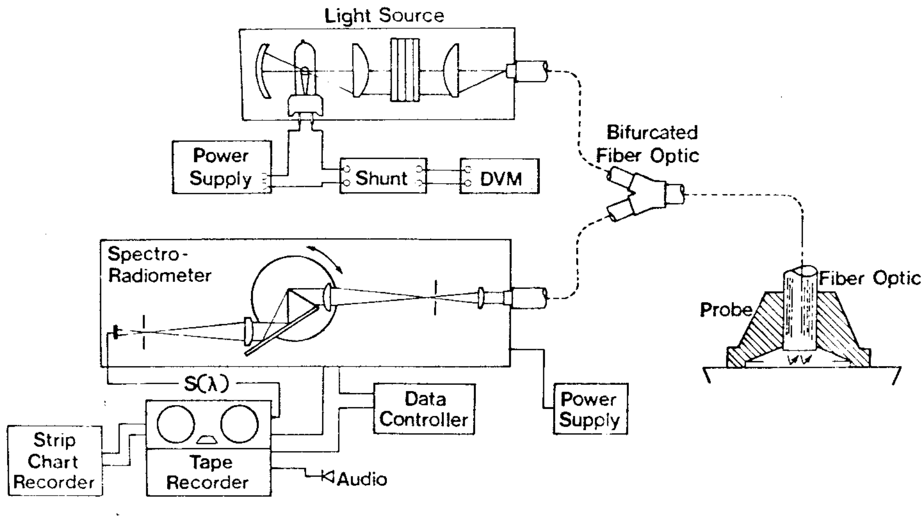

Figure 1. Schematic of the skin reflectance measurement system.

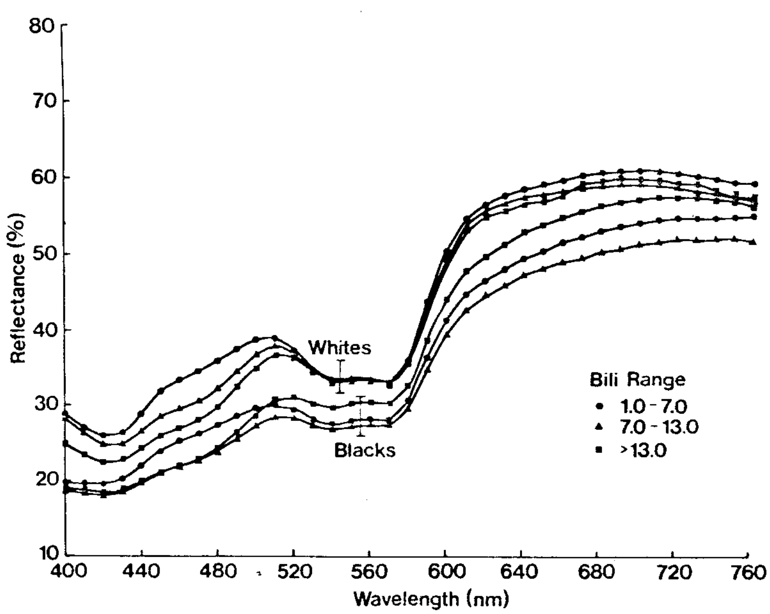

Figure 2. Averaged reflectance spectra for three ranges of serum bilirubin concentration based upon white and black, healthy, full-term infants.

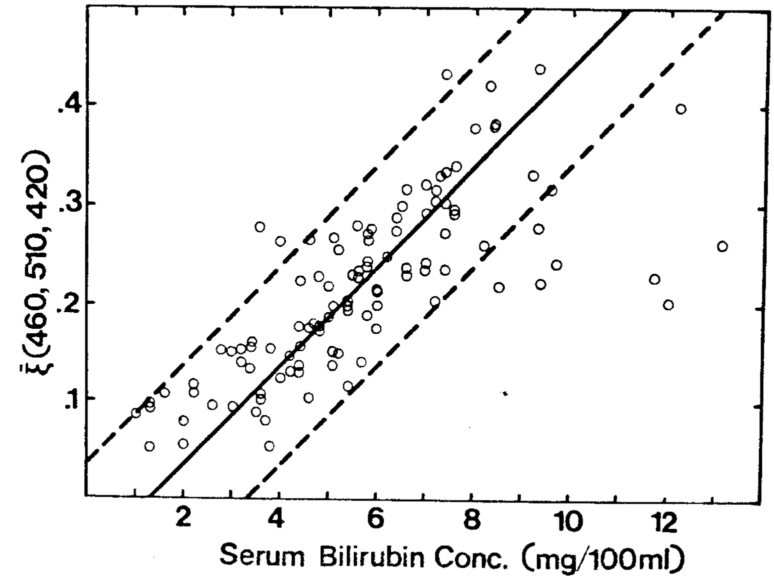

Figure 3. Optical parameter, $\bar{\xi}$, as a function of serum bilirubin concentration for normal, full-term white infants.

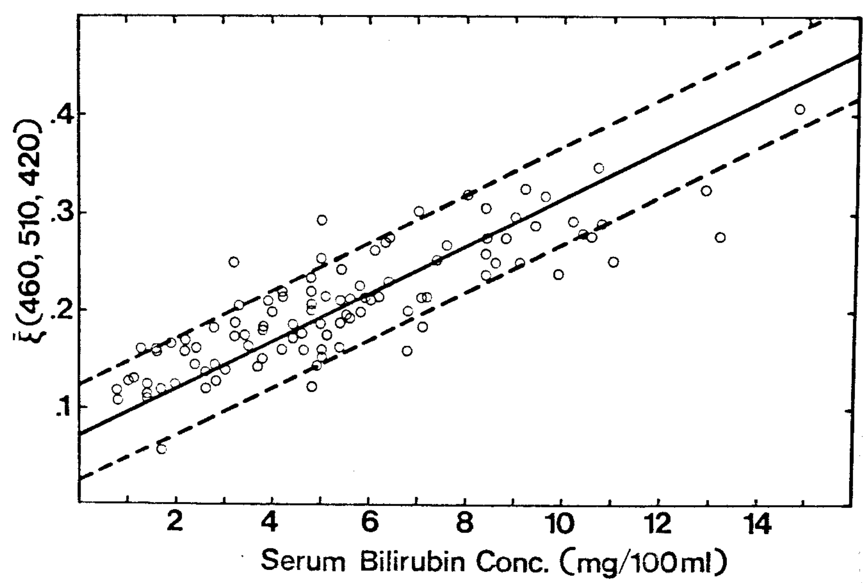

Figure 4. Optical parameter, $\bar{\xi}$, as a function of serum bilirubin concentration for normal, full-term black infants.