

MEASUREMENT OF BLOOD UREA BASED IN OPTICAL SENSING BY EMPLOY IN HEMODIALYSIS TREATMENT

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Abstract. - The present paper shows the design and development the On-line measure system for blood urea concentration during dialysis treatment, using non-invasive technical by employ the optical sensing in the visible range.

Previous results obtained in Military Hospital Centre in Mexico D.F., displayed experimental evidence of a clear correlation between blood urea contents and optical absorbance in the red region obtained through the arterial line in hemodialysis machine.

Our hypothesis considers that the cause of this dependence is the volume change of the red cells with the urea concentration due to the osmotic pressure and regulation mechanisms in cellular volume. The reduction in the cells volume would lead to decrease in the proportional absorbance value.

Measurements were first performed during hemodialysis procedures in the Military Hospital Center in Mexico City, show good correlation. The most relevant interfering parameter was the water extraction along the dialysis treatment, given that changes in the blood fluid and arterial pressure (Hypotention or Hypertention), thus affecting the measurement principle.

I. INTRODUCTION

The interest to develop new mechanisms for the on-line measurement of urea in blood by indirect techniques is increasing, due to their potential use to control in the hemodialysis process. In particular, enzymatic biosensors are being incorporated to some hemodialysis systems and even to the disposable ultra filtration cartridges. Classical, off-line analytical techniques use colorimetric techniques at 550 to 590 nm after processing the blood samples with enzymatic reagents.

To reduce the cost of this measurement procedure, we propose the viability of using optical sensor for the absorption measurement way across the tube through which the blood flows. In this sense, measures preliminary carried out at a single wavelength already published [1] displayed a good correlation ($r=0.87$) with the concentration of urea for the group of patients not having other pathology than the renal disease.

However, measurements of urea dissolved in water and in physiologic serum don't show any significant absorbance in the visible range. Their absorbance peak is presented at 2.2 μm . Recent publications also propose NIR blood urea concentration measurement [2] and even flow-through measurements using FTIR in the 2.2 μm to 5.6 μm range [3]. Given that the observed optical absorption can not be a consequence of the interaction of the light with the molecule of urea, it should be due to the interaction with blood components. The hypothesis we established proposed that the change in optical absorbance was due to the change of volume of cells suspended in blood, mainly erythrocytes. This would be due to the hiper_ osmolarity induced by the urea [4].

To validate the cell shrinkage hypothesis in the laboratory using a model simpler than blood, we employed suspensions of known concentration of yeast (*Saccharomyces Cerevisiae*) in saline solution. Urea concentration was varied in the suspension samples.

Measurements of optical absorbance were performed by means of two prototypes, the first operating at a single wavelength and the second including a fiber optic spectrophotometer. Electrical impedance spectroscopy was also acquired given its ability to validate the hypothesis of cell volume change. The results of the static measurements [5] were coherent with the established hypothesis, displaying a decreasing optical absorbance (increasing photo detector voltage) with the increasing urea concentration.

The dynamic measurement principle was also determined by provoking a sudden change in urea concentration (100g/l) in a 40 g/l (wet weight) yeast cell suspension (step response). An exponential with a time constant of 60 second was obtained. This time is short enough if compared with the typical dialysis session length. [6]

After validation under static conditions, dynamic and experimental dialyzed was characterized both acquiring optical absorbance and electrical impedance spectroscopy. [7].

Clinical measurements were also performed only using optical absorbance measurement across the blood duct, given the intrinsic safety and sterility of this method. The results are presented in this communication.

II. MATERIALS AND METHODS

Measurement prototype

We arranged optical custom measurement systems based on photodiodes arrays connected to a PIC16F876 microcontroller, which implemented the acquisition and the physical interface between the optical sensors and the display and computer. The system is formed by an array of 128 photodiodes (Texas Instruments); the light source is a LED diode with a single wavelength of 620 nm. The physical construction of the system consists on a small dark chamber where the source of light (LED) and the semiconductor device used as sensor (photodiode array) are placed. They are located lengthwise regarding the probe of transparent plastic through which the liquid samples are passed. The linear disposition of photodiodes gives a better rejection of stray light conduced through the tube walls. The voltage resulting of integrating the current of each photodiode during a controlled time is used as the input signal of the 10 bit microcontroller A/D converter. The captured data are then transmitted via RS-232 to a personal computer. User's interface is developed with Visual Basic ver.6.0, performing the graphical representation of the data determination and constant of the time.



Figure 1: Experimental Prototype by using PIC Micro controller and connection in arterial line the Hemodialysis machine.

For the experimental Hemodialysis procedure, we using the Hemodialysis system (Figure 2) was composed by dialysis cartridge (Bellco Polysulfone NT1808H) and Hemodialysis Machine. During 210 minutes (dialysis time), the blood circulated repeatedly through the inner closed circuit, while 5 liter acid solution and bicarbonate circulated through the outer circuit, both at 300-400 ml/min. No other components were added to avoid salt interchange between circuits that had provoked conductivity changes in the blood.



Figure 2: Experimental system with both the optical absorbance probe in patients in hemodialysis treatment.

Clinical measurements (medical-protocol)

To verify the performance of the proposed method in real conditions, clinical measurements were performed over 68 hemodialysis procedures in the Military Hospital Center in Mexico City, previous authorization of the medical protocol. The optical measures (the optical chamber was placed along the arterial line) were compared with those obtained by laboratory analysis (Dade Behring equipment) was performed over blood samples and estimation the BUN (Blood Urea Nitrogen) for each patient at hemodialysis treatment. The equal forms the register the patient weights were obtained before and after the dialysis treatment.

The sensitivity between optical absorbance and urea content was calibrated by using the measurements of a young patient without any other pathology than the renal disease. Preliminary results [1] gave the best correlation for these cases.

III. RESULTS

Experimental System

The direct results obtained with the prototype display the optical transmittance in the range of 600-620 nm, corresponding to a red LED show the evolution in the urea concentration estimated during the experimental Hemodialysis procedure in a patient.

In the course of urea extraction, cells would increase in size due to the lowering of osmotic pressure thus increasing the optical absorbance of the cell suspension and decreasing the optical transmittance [5].

The exponential fitting of the transmittance time course allows the estimation and even the prediction of the dominant time constant in the cell swelling process typical values obtained range from 35 to 45 minutes.

Largely higher than the constant associated to the primary transduction mechanism (cell swelling) [5].

In the Figure 3 show the evolution of the urea concentration during Hemodialysis treatment in a patient.



Figure 3: Evolution of the urea concentration estimated from the optical transmittance during the experimental Hemodialysis procedure in a patient.

Clinical measurements

The results obtained with optical system and Laboratory (Dade Behring equipment) was coherent. In the Figure 4 we can observe that statistic factor between laboratory and prototype.

The show results indicate good correlation in average and standard deviation, the equal forms both measurement systems show wide dispersion.

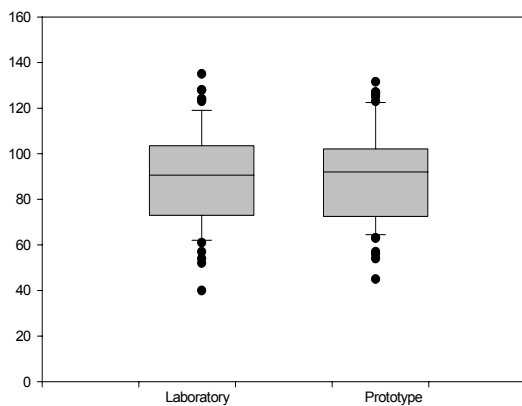


Figure 4: Results obtained by Laboratory vs. Optical. The optical system indicate good correlation, the equal forms both show wide dispersion

During the hemodialysis treatment, some patients suffered hypotention episodes and were treated by injection saline solution to compensate blood pressure.

In these cases and given the evident change in blood density, the optical transmittance shows sudden peaks (Figure 5). For the normal cases, with a quiet and monotonous urea extraction, the optical transmittance presents an exponential decay, as corresponds to a diffusion process that show in Figure 3.

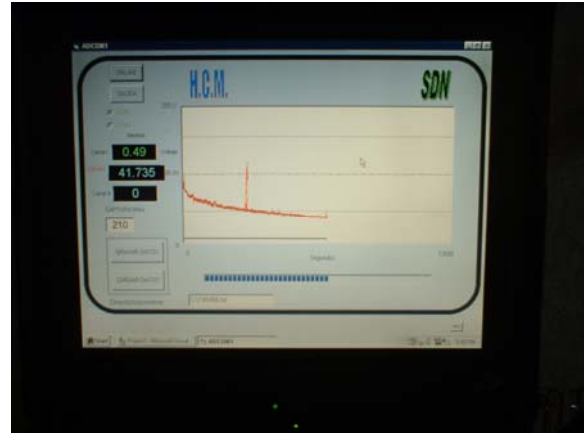


Figure 5 Show typical hypotention episodes and were treated by injection of saline solution to compensate blood pressure.

Experimental results showing the relationship between urea estimation from optical transmittance and blood urea concentration by Laboratory procedure in the totality the patients subject a Hemodialysis treatment.

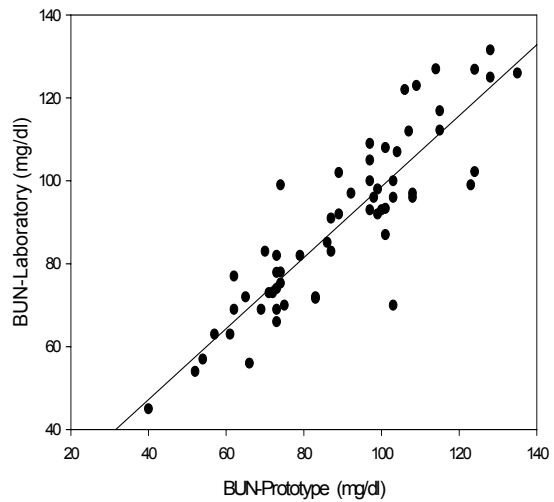


Figure 6 shows the correlation between the laboratory analysis (BUN) and the prototype results (pre-dialysis $R^2= 0.7$).

We determined that the error in the measurement of the urea decrement estimation between pre and post analyses is kept below 18 % if the water extraction has been lower than 2.5 %. Relative error in the estimation of extracted blood urea related with water extraction (weight loss) in Hemodialysis patients.

IV. DISCUSSION AND CONCLUSIONS

The results obtained in the hemodialysis blood circuit confirm the preliminary results optical absorbance in the visible range decreases when urea concentration increases.

Given that dissolved urea only presents absorbance peaks in the IR, we should infer that the absorbance change is due to urea induced changes in cell through the mechanisms of regulation of the cellular volume.

Measurements with the prototype show absorbance changes in a wide peak that corresponds to the bulk color a single wavelength measurement at 620 nm allow obtaining a monotonic quasi-linear relationship between transmittance and urea concentration. In the case of the blood, the center of absorbance peak will change, but it will be obviously placed around the red color, given that the main population of blood cells subject to volume shrinkage will be erythrocytes.

Measurements confirm the proposed hypothesis. During the urea extraction both optical measurements showed behavior consistent with the cell volume increase.

The dynamic behavior of the described mechanism shows a dominant time constant of the minute order. This means that the measurement system based on this phenomenon is potentially useful for monitoring and controlling the urea exchange in the dialysis process, that can take several hours and whose critical phase can last some tenths of minutes.

The statistical results between laboratory analysis and prototype show a direct dependence between both techniques. Considering all measures in patients, the dispersion is elevated in both cases. This dispersion lowers if we consider homogeneous patient groups. Independently of the accuracy of the urea estimation, this method provides a way for estimation and early prediction of urea extraction dynamics, through the exponential fitting of the estimator time course. This parameter can help to adjust the settings of the hemodialysis machine and even be used as a control loop input.

Finally we conclude that there is scientific evidence of a correlation between the urea concentration and optical absorbance at 620nm. Due to it is low cost, simplicity and the null interference with the dialysis system (intrinsically safety) it possible to consider its clinical use as a complementary method to monitor the dialysis performance.

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