Development of Urine Glucose Level Monitor for Home Healthcare Using Near Infrared Spectroscopy

Shinobu Tanaka *Member, IEEE*, Mitsuhiro Ogawa *Member, IEEE*, Tao Gu and Ken-ichi Yamakoshi, *Member, IEEE*

***Abstract*— We have been developing a urine glucose level monitoring technique using near infrared spectroscopy in conjunction with the chemometric method aiming for the use of home health care. In this study, validity of the calibration models were assessed using urine samples from nine healthy male subjects. For the individual measurement, reasonable accuracy was obtained in predicting urine glucose level for each subject (mean value of standard error of prediction; 25.8 mg/dl, S.D.; 10.8 mg/dl), however, the accuracy decreased (around 60 mg/dl) when the calibration models were generated using data from multiple subjects. One of the causative factors seemed to be urine urea concentration level which may vary within very wide range (0-2000 mg/dl) under physiological condition, and therefore, it was suggested that any idea, e.g., classification of data by urea level, would be required for improving the accuracy.**

I. Introduction

ALTHOUGH there are several drawbacks of urine glucose test compared to blood testing [1], daily monitoring of urine glucose level has still been widely used as a rough indicator of high blood glucose levels [2]. For this purpose, there are several kinds of commercially available items such as test strips [3], a pen-shaped enzyme sensor [4] and a sensor system installed in a toilet [5]. Among these, the third one would be an ideal type for long-term home health care, however, there are several drawbacks [5] such as a limited sensor life (4 months or 700 measurements), cumbersome maintenances and a high cost. To overcome these practical drawbacks, we have developed a new technique for measuring urine glucose concentration using near infrared spectroscopy. In the previous paper, we reported some results of preliminary experiments for assessing feasibility of this method [6]. In this study, we increased the number of urine sample and evaluated the effect interfering substance, *i.e.* urine urea, on the accuracy in measuring urine glucose level. We also carried out a preliminary study for predicting urine protein concentration together with glucose using mixed solution of glucose, albumin and urea.

Manuscript received July 5, 2008. This work was partly supported by the Grant-in-Aid for Scientific Research (B), Japan Society for the Promotion of the Science, and by the Knowledge-based Cluster Creation Project (Ishikawa High-tech Sensing Cluster Creation Project), Ministry of Education, Culture, Sports, Science and Technology.

S. Tanaka, M. Ogawa, T. Gu and K. Yamakoshi are with the Graduate School of Natural Science and Technology, Kanazawa University, Kanazawa, 920-1192 Japan (Phone; +81-76-234-4763 & Fax: +81-76-234-4738; e-mail: shinobu@ kenroku.kanazawa-u.ac.jp).

II. Materials and Methods

For measuring urine glucose level, FTIR spectroscopy in conjunction with the chemometric method of partial least squares (PLS) was adopted and the accuracy in measuring urine glucose level was assessed by the experiments described below.

A. Calibration and Validation using Urine sample

Calibration and validation studies were conducted using urine samples obtained from nine young healthy adults. Total volume of about 400 ml of first morning urine specimens were collected from each subject. In order to obtain urine samples with various glucose concentration level (0-600 mg/dl), appropriate amount of glucose was added. Altogether 126 samples were prepared for each subject and the glucose concentration of the samples (measured Glu conc.) was determined using an automatic analyzer (DRI-CHEM 7000; Fujifilm Medical Co. Ltd., Japan). Near infrared spectra of each sample were collected over the spectral range of 1100-1830 nm using a FTIR spectrophotometer (Spectrum One NTS; Perkin Elmer Co. Ltd., USA). Using these data, PLS calibration models were generated by the PLS Toolbox 3.5 of MATLAB (Eigenvector Inc., USA). The leave-one-out cross validation method was applied to obtain the Standard Error of Calibration (SEC) for assessing the validity of the model. The glucose concentration was predicted using this model, and the accuracy of the model was assessed by the values of the Standard Error of Prediction (SEP) and the correlation coefficient (r).116 samples were used for obtaining PLS calibration model and 10 samples were used for the accuracy assessment.

B. Experiments using mixed solution of glucose, albumin and urea.

To investigate applicability of the above mentioned method for predicting urine protein level together with glucose, preliminary experiments described below were carried out.

As shown in Table 1, all together one thousand kinds of mixed solution of glucose, albumin (bovine serum albumin: BSA) and urea were prepared. Urea was chosen as a most dominant interference substance. The concentration ranges of glucose and albumin were chosen from those of a commercially available test strip, and that of urea was chosen to cover physiological range. Near infrared spectra of each sample were collected in the same way, and albumin concentration were predicted using the same method mentioned above.

III. Results and Discussion

A. Calibration and Validation using Urine sample

In Table 2, the results of calibration and validation studies using urine sample were summarized together with the urine urea concentration measured in a clinical laboratory. As shown here, quite good linear relationship (mean r_c; 0.993, mean r_v; 0.942) and the low value of SEC (mean; 8.4 mg/dl) and SEP (mean; 25.8 mg/dl) were obtained, indicating validity of the PLS model obtained in each subject. Fig. 1 shows the result of the validity study of the calibration model generated using three subjects with different urine urea level (sub. C, G and I). As shown in this figure, the accuracy, in term of linearity and SEP, is comparable to the results of individual calibration models. However, it should be noted that in the two subjects with high urea concentration level (sub.F and H), the values of r_v and SEP were worse (see Table 2), and if we use these data for generating a calibration model, we could not obtain a good result (see Fig. 2). The reason for the lower accuracy in these two subjects may be related to the urea concentration level. To clarify this problem, we need to increase the number of subjects with various concentration level of urine urea.

B. Experiments using mixed solution of glucose, albumin and urea.

Fig. 3 is the result of the accuracy assessment of glucose concentration prediction using mixed solution. As the concentration range was expanded to 2000 mg/dl, the SEP between predicted and measured glucose concentration became worse than the results using urine sample (see Fig. 1 and Fig. 2). However, this value (60.4 mg/dl) is comparable to the value reported by Pezzaniti et al [7] (4.3 mmol/l = 77.4 mg/dl).

Fig. 4 shows the result of albumin concentration prediction. Improvement of accuracy would be required especially in the low concentration range (<100 mg/dl), however, the value of SEP (18.4 mg/dl) is also comparable to the reported value (0.18 g/L) of ref [7] suggesting the availability of our method for predicting protein concentration in urine sample.

Improvement in accuracy of the present method will be achieved by increasing the number of urine samples for the PLS calibration.

The problems to be solved for the home healthcare use will be (i) reduction of the number of the wavelength for spectral collection, (ii) shift of the present complicated optical system to the convenient LED-photo diode multi-array sensor system, and (iii) development of a urine sampling system which could be installed in a toilet.

Table 1 Concentration levels of glucose, albumin and urea in the mixed solutions

	concentration (mg/dl)									
glucose	5	10	20	30	50	100	120	500	1000	2000
albumin	5	10	15	20	30	40	50	80	100	300
urea	500	650	800	950	1100	1250	1400	1600	2000	2800

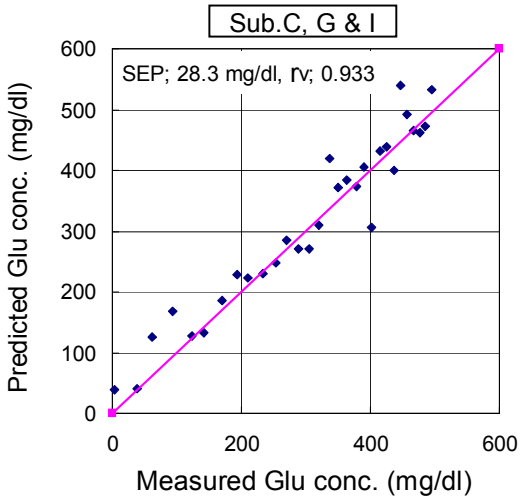

Fig. 1 NIRS predicted vs. measured values for glucose model validation using urine samples from sub. C, G and I.

IV. Conclusion

A technique for measuring urine glucose concentration

Table 2 Summary of calibration and model validation results using PLS regression for glucose

subject	Calibration		Validation		Urea
	SEC (mg/dl)	r_c	SEP (mg/dl)	r_v	Conc. (mg/dl)
A	7.6	0.996	22.2	0.967	370
B	6.5	0.992	23.4	0.960	463
C	7.2	0.996	20.9	0.978	622
D	9.0	0.994	24.3	0.966	951
E	3.1	0.999	23.7	0.964	970
F	15.9	0.981	48.4	0.787	1085
G	8.5	0.993	13.9	0.985	1110
H	10.8	0.990	38.1	0.889	1330
I	7.4	0.995	17.0	0.985	1340
mean	8.4	0.993	25.8	0.942	916
s.d.	3.5	0.005	10.8	0.065	356

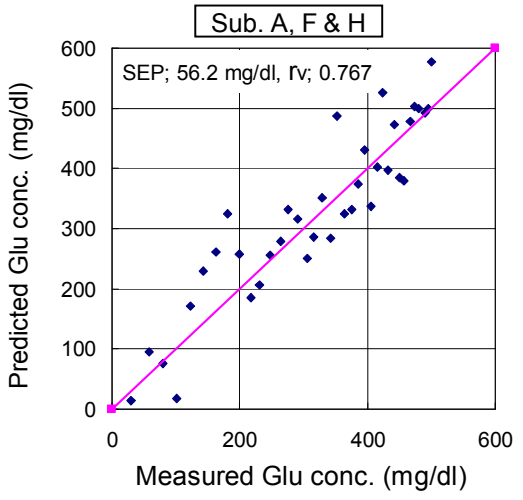

Fig. 2 NIRS predicted vs. measured values for glucose model validation using urine samples from sub. A, F and H.

using NIRS in conjunction with PLS was evaluated through the experiments using urine samples and mixed solution of glucose, albumin and urea. From the results obtained, it was suggested that the urine urea concentration level may affect the accuracy in predicting urine glucose level. Also suggested was the possibility of simultaneous prediction of urine protein level by the same technique using NIRS and PLS.

REFERENCES

[1] U.S. FDA, "Diabetes Information, Glucose Meters & Diabetes Management, Urine Glucose" Available: http://www.fda.gov/ diabetes/glucose.html#20

[2] International Diabetes Federation, "The role of urine glucose monitoring in diabetes," Available: http://www.idf.org/home/index.cfm?node=1383.

[3] P. Voswinckel, "A marvel of colors, and ingredients: The story of urine test strips," *Kidney International*, vol. 46, pp. S3-S7, (1994).

[4] T. Matsumoto, A. Ohashi, N. Ito, H. Fujiwara, T. Matsumoto, "A long-term lifetime amperometric glucose sensor with a perfluorocarbon polymer coating," *Biosensors & Bioelectronics*, vol. 16, pp. 271-276, (2001)

[5] Y. Takeuchi, "Urine sugar level checker 'WELL-YOU' and home health checker,"(in Japanese) *FED Review*, vol. 3, no. 7, pp. 1-11, Mar. (2004).

[6] S. Tanaka, K. Motoi, M. Nogawa, T. Yamakoshi and K. Yamakoshi: Feasibility study of a Urine Glucose Level Monitor for Home Healthcare using near infrared spectroscopy, Proceedings of the 28th Annual Conference of the IEEE Engineering in Medicine and Biology Society, New York, CD-ROM (2006.8)

[7] J. L. Pezzaniti, T-W. Jeng, L. McDowell and G. M. Oosta, "Preliminary investigation of near-infrared spectroscopic measurements of urea, creatinine, glucose, protein, and ketone in urine," *Clinical Biochemistry*, vol. 34, pp. 239-246, (2001).

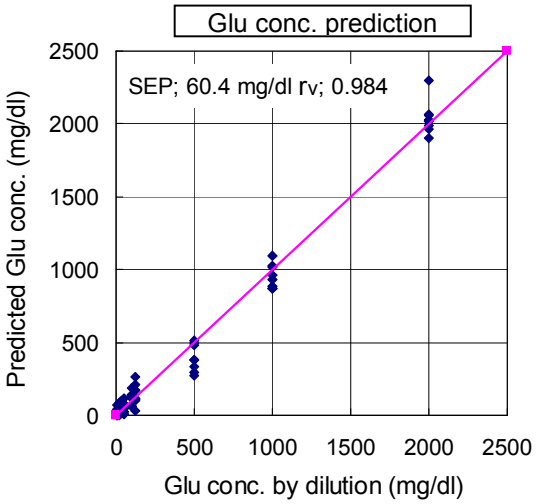

Fig. 3 NIRS predicted vs. measured values for glucose model validation using mixed solution.

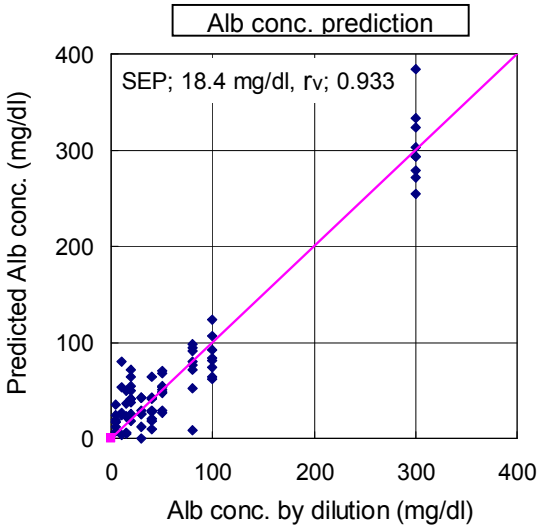

Fig. 4 NIRS predicted vs. measured values for albumin model validation using mixed solution.