Realization of BGM within ±10% accuracy based on innovative optical transmission absorbance system

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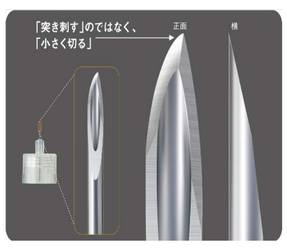
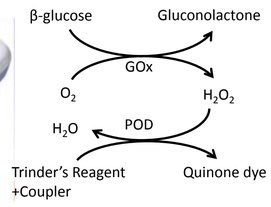
Terumo : Contributions to the diabetes treatments

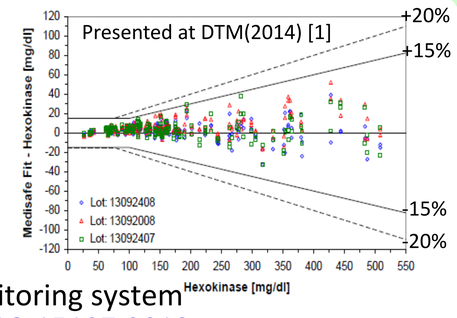


The World Thinnest Needle
Diameter of needle tip:0.18 mm

Top share in Japan



Colorimetric sensor



Blood glucose monitoring system
In compliance with ISO 15197:2013

Introduction

Concepts of our BGMs

(Conceptual image)

- High accuracy : *Within ±5%*(95% of all values)
- Short measurement time : Within 5 seconds
- Easy-to-use : Easy to handle, Calibration less
- Reasonable price

Why do you need ±5% in accuracy?

±5% accuracy enables the optimization of Diabetes treatment

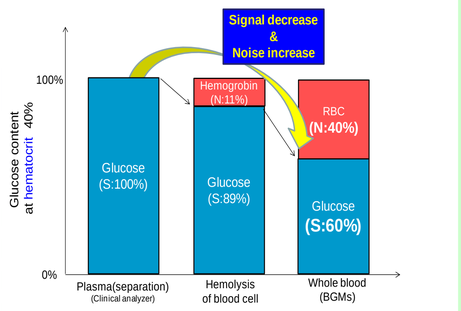
1. MDI(Multiple daily injection) [2]
- Reduce the hypoglycemia derived from BGMs errors
- Prevent the complication by lowering HbA1c under 7%

2. SAP(Sensor Augmented Pump)
- Precise sensor calibration minimize the CGM sensor errors, leads to good glycemic control

What are the technical issues to realize high accuracy BGMs?

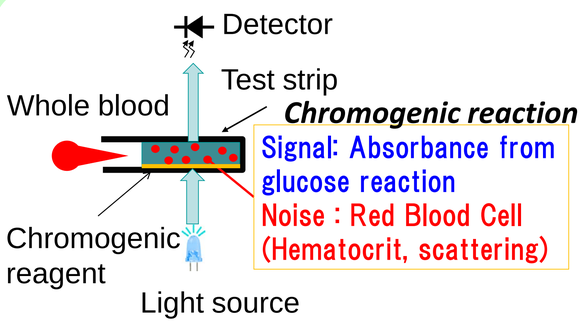
Technical issues of each samples

Sample condition	Technical issues
Plasma(separation) (Clinical analyzer)	▪ Instant & complete separation ▪ Miniaturization of system
Whole blood (BGMs)	▪ Improvement of Signal(S/N) ▪ Accurate compensation of hematocrit(Noise reduction)



Signal of each blood conditions

Principle: How to realize the accurate BGMs

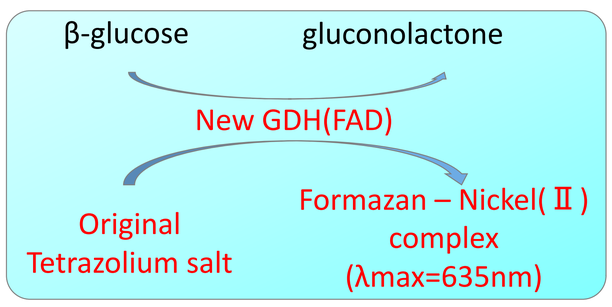


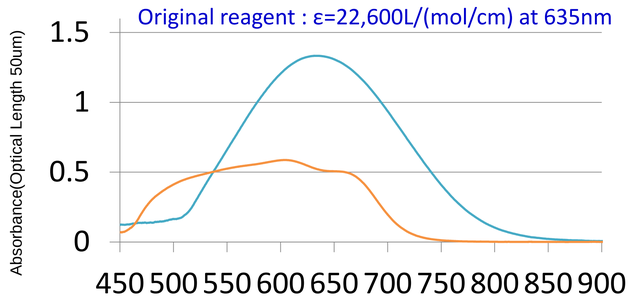
Measurement principle

Key technologies

1. To improve the Signal
   - ***>Original coloring reaction system with high-sensitive reagent***
2. To reduce the Noise
   - ***>Accurate optical measurement of RBC using multi-wavelength***

Original coloring reaction system with high-sensitive reagent

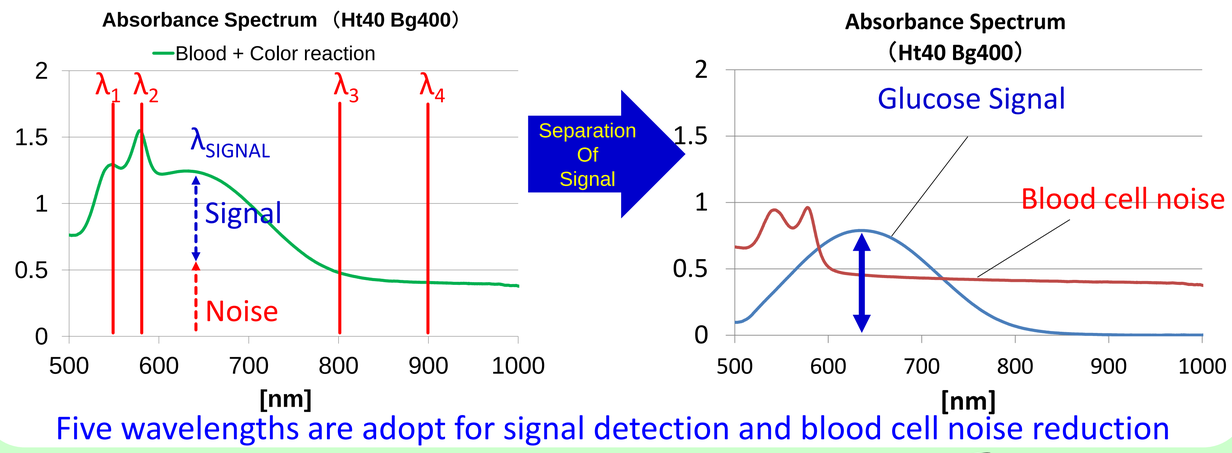




Glucose measuring principle
- High- absorptivity : To obtain large signal
- Low Km & High-solubility : High reaction rate to achieve end-point measurement
- λmax>600nm: To separate signal and blood colors

Absorbance spectrum (glucose 300mg/dL)
- 2.3 times larger chromogenic signal was achieved than WST-4(commercially available Water-soluble tetrazolium salts from Dojindo) at 635nm

Accurate optical measurement of RBC using multi-wavelength

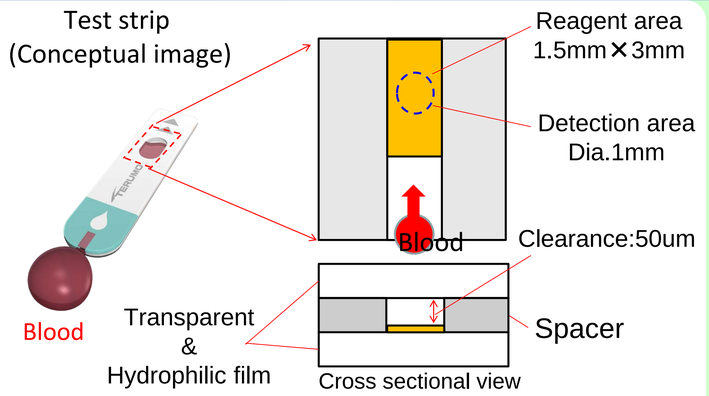


Five wavelengths are adopt for signal detection and blood cell noise reduction

Experimental method

System Accuracy

New BGMs was evaluated with in-house blood samples (Individual 3 persons per blood glucose levels), adjusted to six blood glucose levels (0mg/dL, 50mg/dL, 100mg/dL, 400mg/dL, 800mg/dL, 1200mg/dL) with various hematocrit (Hct20%, Hct40%, Hct60%).



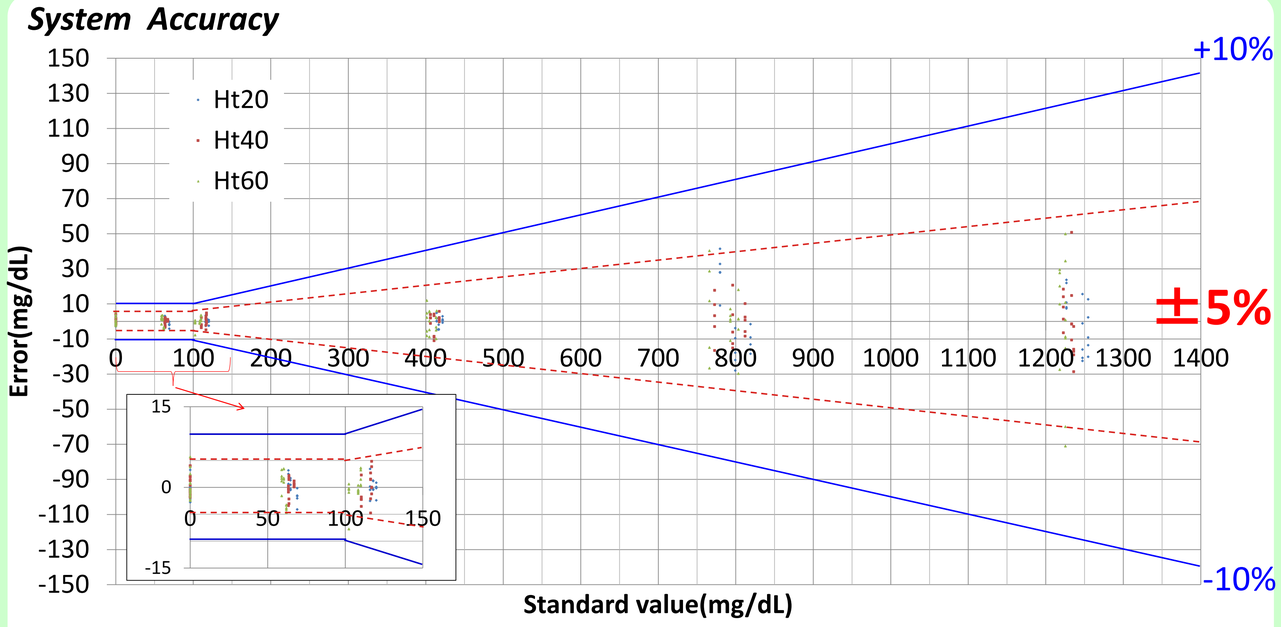
Interfering Substances

Interfering substances was evaluated with six common substances (acetaminophen, uric acid, bilirubin, galactose, maltose and ascorbic acid).
Each interfering substances was added to 7% albumin solution(As a substitute for plasma) adjusted to 3.4mM and the bias was measured. (Maltose was evaluated with 10000mg/dL)

Test strip structure

Results

System Accuracy



Measurement results of N=270

Difference range	Within ±5% (±5mg at bg0-50)		Within ±10% (±10mg at bg0-50)	
Percent (and number)	**98.1%**	(265/270)	**100%**	(270/270)

Blood glucose level

BG mg/dL	Within ±5% (±5mg at bg0-50)		Within ±10% (±10mg at bg0-50)	
bg0	97.8%	(44/45)	100%	(45/45)
bg50	100%	(45/45)	100%	(45/45)
bg100	97.8%	(44/45)	100%	(45/45)
bg400	100%	(45/45)	100%	(45/45)
bg800	95.6%	(43/45)	100%	(45/45)
bg1200	97.8%	(44/45)	100%	(45/45)

Hematocrit level

Hematocrit %	Within ±5% (±5mg at bg0-50)	
Ht20	98.9%	(89/90)
Ht40	100%	(90/90)
Ht60	95.6%	(86/90)

More than 95% of data was in ±5% at low glucose level and hematocrit (Ht20, Ht40)

Accuracy of Hematocrit measurement

Accuracy of **hematocrit measurement was ±1.5 as 2SD**.
⇒**Applicable for measuring components using whole blood.**

Interfering Substances

Our new system are unaffected by common interfering substances with FDA concentrations (shown as <±1).

Interfering substances	Interfering substance at 3.4mM (mg/dL)	Bias at 3.4mM (mg/dL)	FDA recommendations (mg/dL)	Bias at FDA (mg/dL)
Acetaminophen	51	-2	20	**<±1**
Ascorbic acid	60	94	3	**5**
Uric Acid	57	2	24	**<±1**
Bilirubin	199	6	50	**<±1**
Galactose	61	3	15	**<±1**
Maltose	10000 (FDA)	-1	10000	**<±1**

Conclusion & future works

- We have developed a novel BGMs based on an innovative optical transmission absorbance system, and achieved accuracy within ±10%
- We will try clinical evaluation in compliance with FDA requirement
- We are acceptable to cooperate with R&D, Clinical research

Achieved and target specification

Specification	Achieved(Now)	Target
Accuracy	Within ±10%	Within ±5%
Measurement range [mg/dL]	0 to 1200	0 to1200
Hematocrit renge [mg/dL]	0 to 60	0 to 70
Measurement time [seconds]	Within 10	Within 5

References

1] Freckmann G. et al. "Analytical and User Performance Evaluation of a Blood Glucose Monitoring System following ISO 15197 :2013.",Poster Session; 6th November 2014; Diabetes Technology Meeting 2014

[2] BP Kovatchev et al. "Impact of Blood Glucose Self-Monitoring Errors on Glucose Variability, Risk for Hypoglycemia, and Average Glucose Control in Type 1 Diabetes: An In Silico Study", Journal of diabetes science and technology 4 (3), 562-570