Glucose Monitoring

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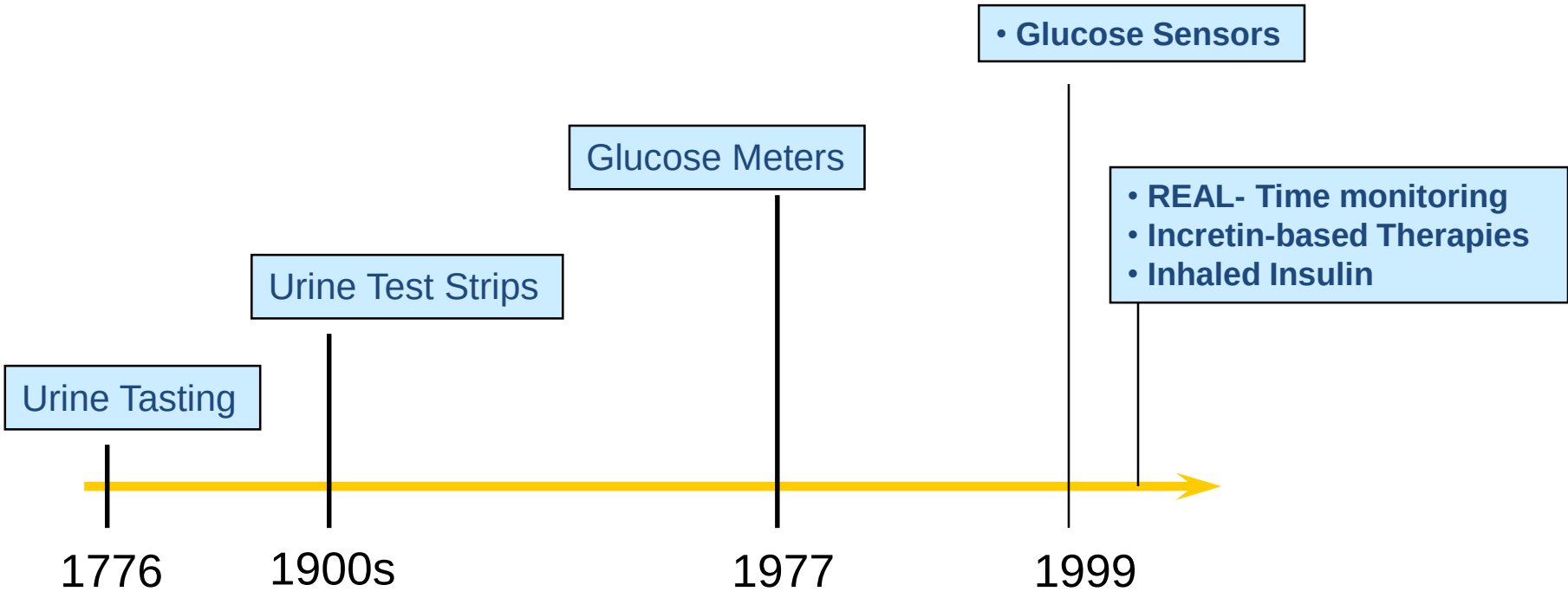
Glucose Monitoring

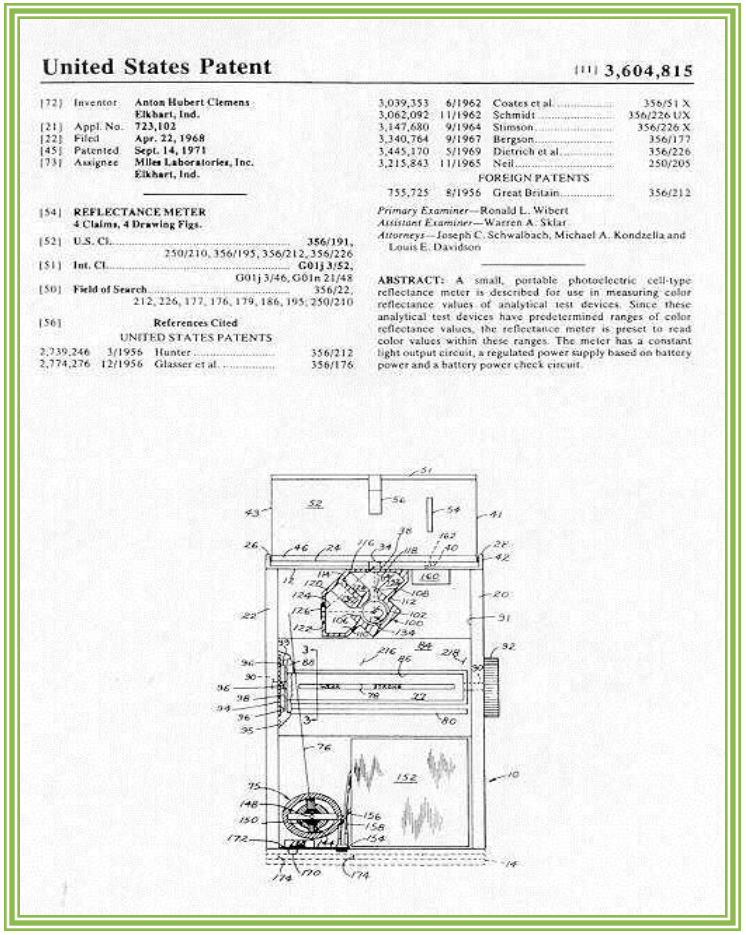
- Evolution of diabetes care.
- SMBG.
- HbA1c.
- CGMS.
- Future technology.

Evolution of Diabetes Technology



Glucose Monitoring

First Glucose Meter



United States Patent [11] **3,604,815**

[72] Inventor: **Anton Hubert Clemens**, Elkhart, Ind.
[21] Appl. No.: **723,102**
[22] Filed: **Apr. 22, 1968**
[45] Patented: **Sept. 14, 1971**
[73] Assignee: **Miles Laboratories, Inc.**, Elkhart, Ind.

[54] **REFLECTANCE METER**
4 Claims, 4 Drawing Figs.

[52] U.S. Cl. 356/191, 250/210, 356/195, 356/212, 356/226
[51] Int. Cl. G01j 3/52, G01j 3/46, G01n 21/48
[50] Field of Search 356/22, 212, 226, 177, 176, 179, 186, 195; 250/210

[56] **References Cited**
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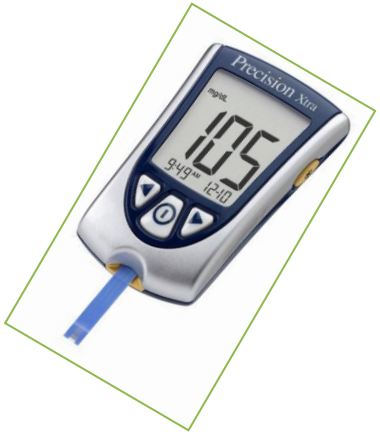
Primary Examiner—Ronald L. Wibert
Assistant Examiner—Warren A. Sklar
Attorneys—Joseph C. Schwalbach, Michael A. Kondzella and Louis E. Davidson

ABSTRACT: A small, portable photoelectric cell-type reflectance meter is described for use in measuring color reflectance values of analytical test devices. Since these analytical test devices have predetermined ranges of color reflectance values, the reflectance meter is preset to read color values within these ranges. The meter has a constant light output circuit, a regulated power supply based on battery power and a battery power check circuit.

Current glucometers



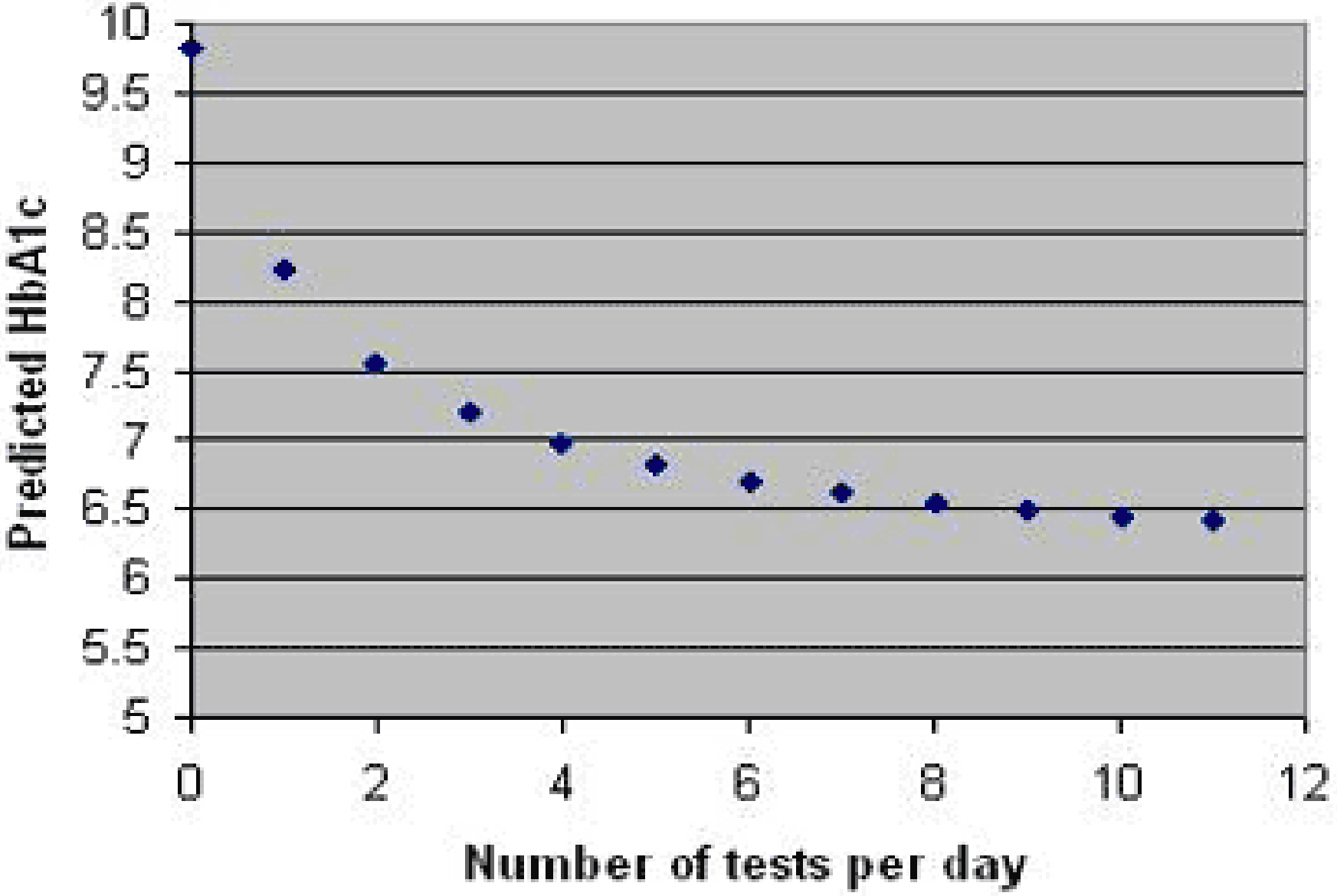
Glucose Monitoring

- Home blood glucose meters measure the glucose in whole blood, while most lab tests measure the glucose in plasma.
- Plasma glucose levels are generally 10%–15% higher than glucose measurements in whole blood.
- Most of the modern meters on the market give results as "plasma equivalent," even though they are measuring whole blood glucose.
- Sample sizes vary from 3 to 0.3 µl.
- Test times almost 5 seconds.

SMBG supplies

SMBG Use & Frequency

- Insulin-treated patients should monitor their blood glucose level varies from person to person.
- At least four times a day.
- Most commonly fasting, before meals, & before bed.
- In addition, patients using insulin can benefit by obtaining postprandial blood glucose readings to help them more accurately adjust their insulin regimen.


Predicted HbA1c
10
9.5
9
8.5
8
7.5
7
6.5
6
5.5
5
0
2
4
6
8
10
12
Number of tests per day

Common Errors in SMBG

- Using expired test strips.
- Wrong test strips code.
- Exposing test strips to humidity (leaving bottle open).
- Exposing test strips or glucometer to high temperature (e.g. Leaving in a car).
- Re-using lancets.
- Inaccurate meter – test annually compared to lab value.

Common Errors in SMBG

- Too small sample size.
- American Vs Canadian units.
- Low battery.
- Waiting too long before adding blood.
- Not washing hands before taking sample.
- Using rubbing alcohol to wash hands.

Fingertip Testing vs Alternate Site Testing

- Alternate site testing (eg, forearm or thigh) has the advantage of convenience for patients and tends to be less painful than fingertip testing; a disadvantage is that readings may be less accurate if blood glucose levels are rapidly fluctuating (potential lag time); eg, immediately after a meal[a,b]
- For fingertip testing: using firm pressure at the side of the finger is preferable

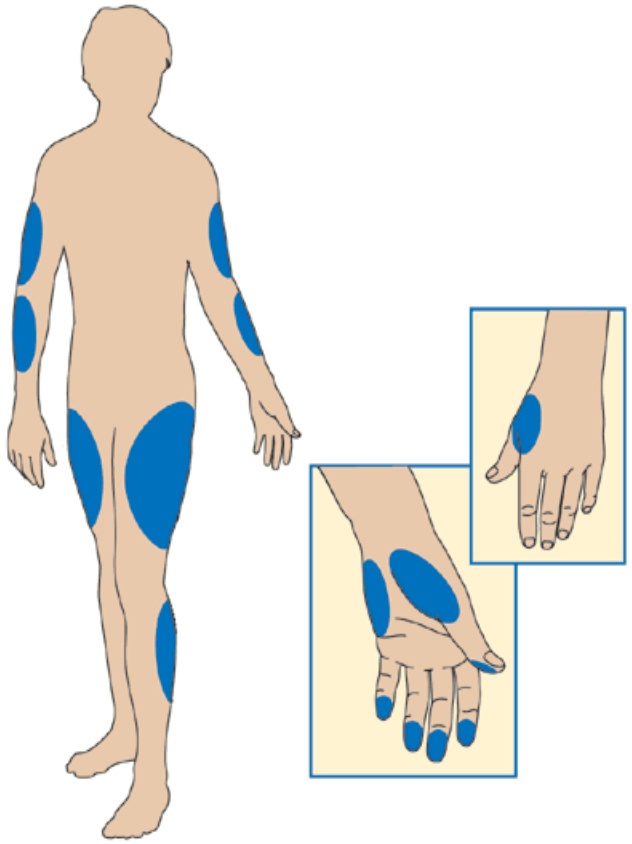
a. Saudek CD, et al. *JAMA*. 2006;295:688-1697.
b. Schrot, RJ, et al. *Clin Diabetes*. 2007;25:43-49.

Glucometers: Alternate Site Testing

Certain meters allow for testing from "alternative sites" (upper arm, forearm, base of thumb, thigh)

- Limitation: blood in tip of finger shows changes in glucose levels faster than blood in other parts of body

** Inappropriate for glucose concentrations after a meal, insulin or exercise, when these values may be changing rapidly



Limitations to SMBG

- Discomfort with the measurement.
- Motivational/behavioral issues, particularly in the adolescent subgroup.
- In many countries, the cost of SMBG monitoring is very expensive relative to the cost of living.
- Complete dependence of parents on their children to do it in our population.

Meter Downloads and Data Management Systems

14-DAY SUMMARY

Patient:
Age/Gender: 24 / Female
Date Range: 4/14/2005 - 4/27/2005
Report Date: 4/27/2005 9:09 AM
Units: mg/dL (Plasma)
Doctor: ALI A. RIZVI, M.D.

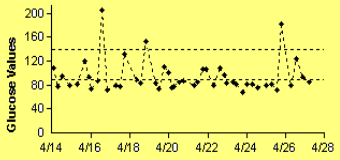
Date	Breakfast					Lunch					Dinner					Night		
	Bef.	Aft.	Meds	Carb	Ex	Bef.	Aft.	Meds	Carb	Ex	Bef.	Aft.	Meds	Carb	Ex	Gluc	Meds	Carb
4/27/2005	86																	
4/26/2005	79					*123*						93						
4/25/2005	87					72					*182*							
4/24/2005	87					76										80		
4/23/2005	86					82					68					87		
4/22/2005	79					108					96					83		
4/21/2005	79					86					107					106		
4/20/2005	78					86					87					75		
4/19/2005	83					74					110					101		
4/18/2005	90					84					*152*							
4/17/2005	80					78					*132*							
4/16/2005	87					*206*					77							
4/15/2005	82					*120*					92					73		
4/14/2005	78					94					80					109		
Average	82	0				99	0				107	93				89		
In Target	7%	0%				15%	0%				36%	100%				38%		
SD	4	0				36	0				35	0				14		
#Results	14	0				13	0				11	1				8		

Results shown in bold italics are out of range.

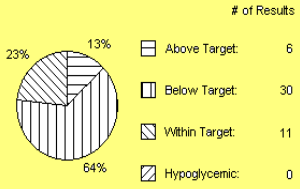
Statistics

Glucose Average:	94	Target Type:	Personal
% Within Target:	23	Before Meal Target:	90 - 110
# of Glucose Readings:	47	After Meal Target:	90 - 140
# of Hypo. Readings:	0	Hypoglycemic:	67
Standard Deviation:	27	Avg. Readings/Day:	3.36

Glucose Trend



Overall Totals



DATA

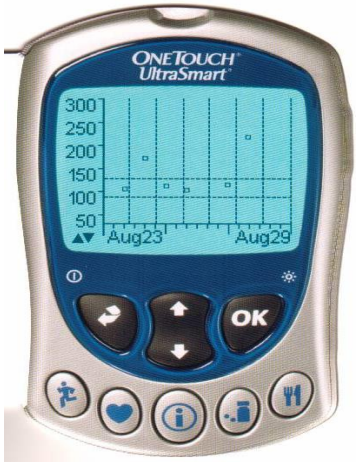
Patient:
Age/Gender: 62 / Male
Date Range: 3/8/2005 - 3/21/2005

Date	Time	Slot	Result Type	Value
3/21/2005	6:49 AM	Before Breakfast	Glucose	*129*
3/21/2005	5:43 AM	Before Breakfast	Glucose	*192*
3/21/2005	3:21 AM	Night	Glucose	*173*
3/20/2005	2:59 PM	After Lunch	Glucose	109
3/20/2005	9:27 AM	After Breakfast	Glucose	*209*
3/20/2005	5:01 AM	Before Breakfast	Glucose	*276*
3/19/2005	8:58 AM	Before Breakfast	Glucose	*375*
3/19/2005	4:54 AM	Night	Glucose	*229*
3/18/2005	2:38 PM	After Lunch	Glucose	109
3/18/2005	9:05 AM	After Breakfast	Glucose	98
3/18/2005	4:04 AM	Night	Glucose	117
3/17/2005	3:08 PM	After Lunch	Glucose	*201*
3/17/2005	3:22 AM	Night	Glucose	*189*
3/16/2005	2:54 PM	After Lunch	Glucose	94
3/16/2005	10:53 AM	After Breakfast	Glucose	*66 **
3/16/2005	6:40 AM	Before Breakfast	Glucose	*200*
3/16/2005	5:39 AM	Before Breakfast	Glucose	*295*
3/16/2005	3:50 AM	Night	Glucose	*197*
3/15/2005	3:06 PM	After Lunch	Glucose	*178*
3/15/2005	8:59 AM	Before Breakfast	Glucose	*207*
3/15/2005	5:46 AM	Before Breakfast	Glucose	*173*
3/14/2005	9:16 PM	After Dinner	Glucose	*149*
3/14/2005	3:59 PM	After Lunch	Glucose	*257*
3/14/2005	10:06 AM	After Breakfast	Glucose	*307*
3/14/2005	6:43 AM	Before Breakfast	Glucose	*241*
3/14/2005	5:50 AM	Before Breakfast	Glucose	*256*
3/14/2005	3:55 AM	Night	Glucose	118
3/13/2005	6:07 PM	Before Dinner	Glucose	109
3/13/2005	4:13 PM	After Lunch	Glucose	*78*
3/13/2005	11:44 AM	Before Lunch	Glucose	*153*

ONETOUCH® things everything®

OneTouch DMS

Date	Breakfast					Lunch					Dinner					Night			Comments
	Bef.	Aft.	Meds	Carb	Other	Bef.	Aft.	Meds	Carb	Other	Bef.	Aft.	Meds	Carb	Other	Gluc	Meds	Carb	
1/11/2005							225									*60**			
1/10/2005		*294*					*182*					91				*165*			
1/9/2005	*301*					*121*	*200*												
1/8/2005	*128*	*238*																	
1/6/2005	*176*						*58**					112							
1/6/2005	*81*																		
1/5/2005	*157*	*87*																	
1/4/2005	*275*	*187*					*67**												
1/3/2005							*170*												
1/2/2005	*245*																		
1/1/2005	*199*	*213*																	
2/31/2004	*224*																		
2/30/2004	*153*																		
Average	194	204				121	150				0	102				113			
In Target	0%	0%				0%	0%				0%	100%				0%			
SD	68	76				0	71				0	15				74			
#Results	10	5				1	6				0	2				2			



Meters with Built-in Data Analysis

Graph by Time of Day

HbA1c

History of Hemoglobin A_1c

1978 – Assays commercially available.

1988 – ADA recommends routine testing.

Currently > 30 glycohemoglobin assay methods are available:

- immunoassays
- ion-exchange HPLC
- boronate affinity HPLC

A1C Goals for Children

young age group < 6 yr. = < 8 – 8.5 %

6 – 11 yr. = <7.5%

12 – 20 yr. = <7.0%

A1c Derived Average Glucose (ADAG) Study and eAG

Translating the A1c assay into estimated average glucose

Diabetes Care, August 2008

- Increased accuracy of HbA1c in reflecting the true average glycemia
- Results reported as A1c-derived average glucose (in mmol and mg/dl) or "estimated average glucose", eAG

A1C	eAG	
%	mg/dl	mmol/l
6	126	7.0
6.5	140	7.8
7	154	8.6
7.5	169	9.4
8	183	10.2
8.5	197	11.0
9	212	11.8
9.5	226	12.6
10	240	13.4

Non – invasive glucose monitoring

Glucowatch

Results are affected by sweating, hair with almost 20 minutes lag as well sensors have to be changed every 20 minutes, with high costs.

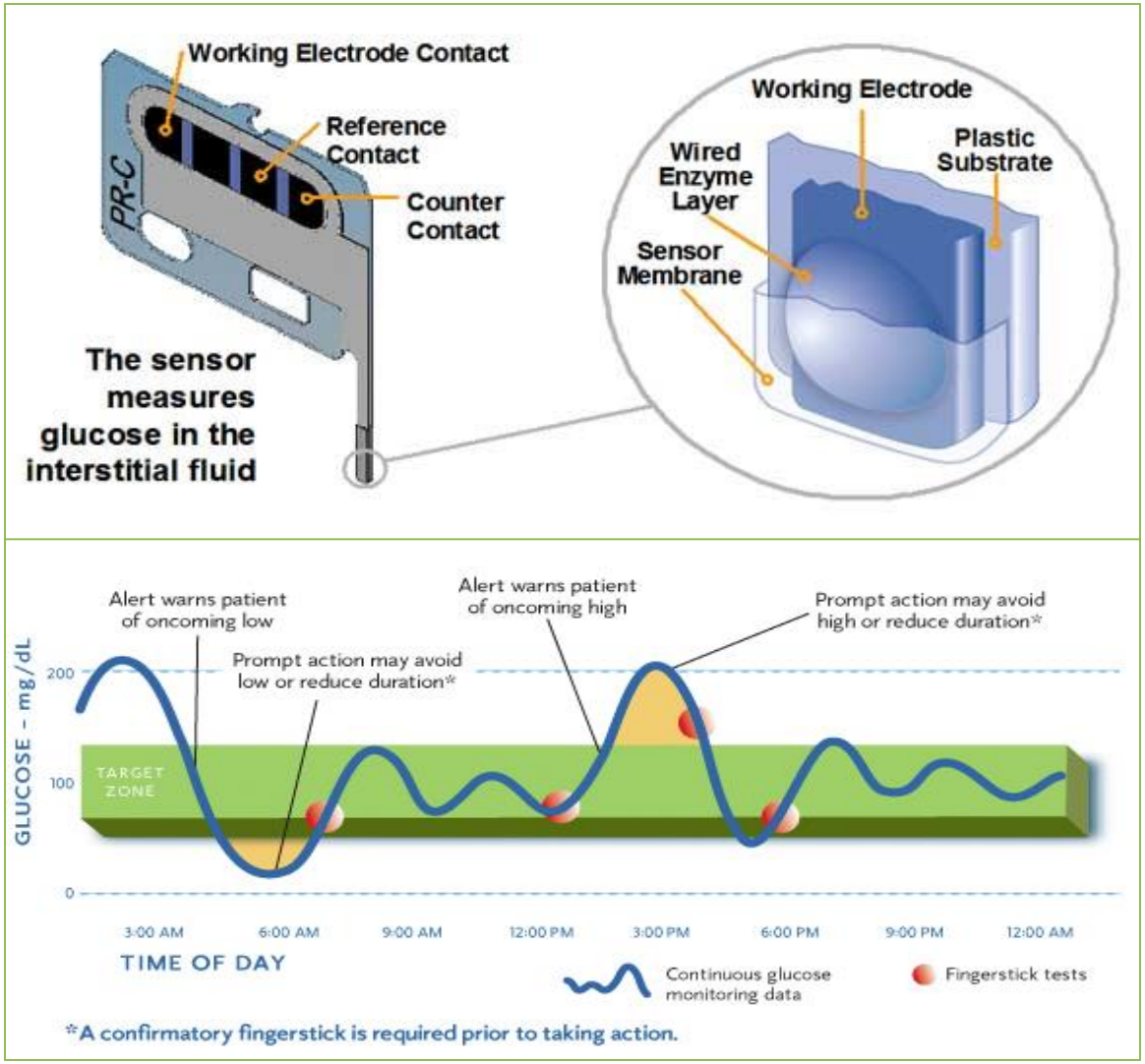
GlucoWatch Biographer®, Cygnus

- Iontophorèse inverse
- Etalonnage 1/j
- Durée: **12**h
- 97% corrélation BG
- **20 min** délai réponse

CGMS

Continuous Glucose Monitoring System

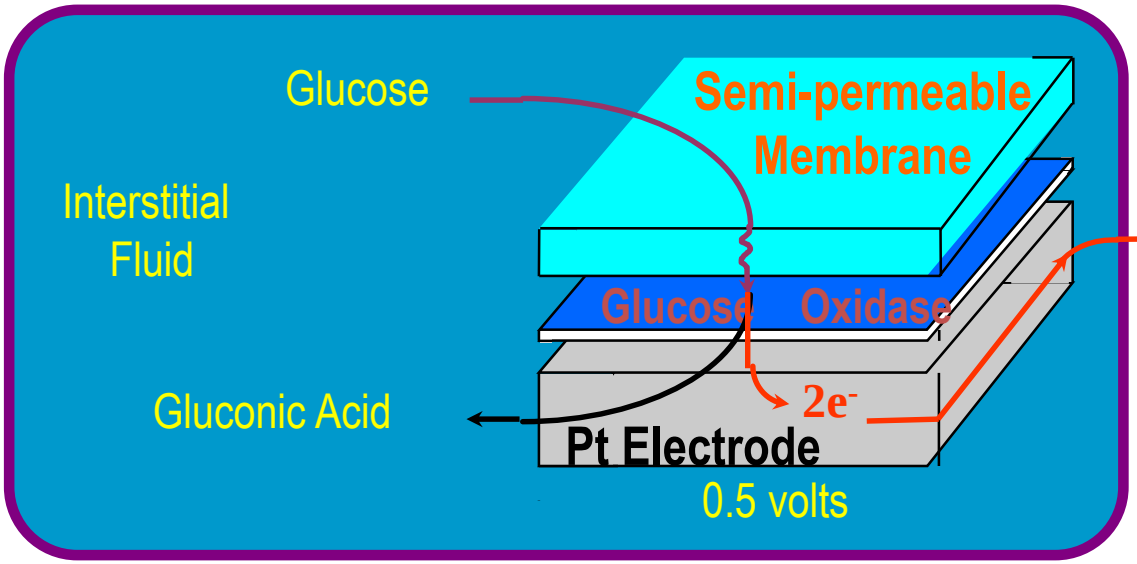
- test glucose in the IF every few minutes for up to 7 days
- alarm system warns if glucose rapidly changes
- real time results

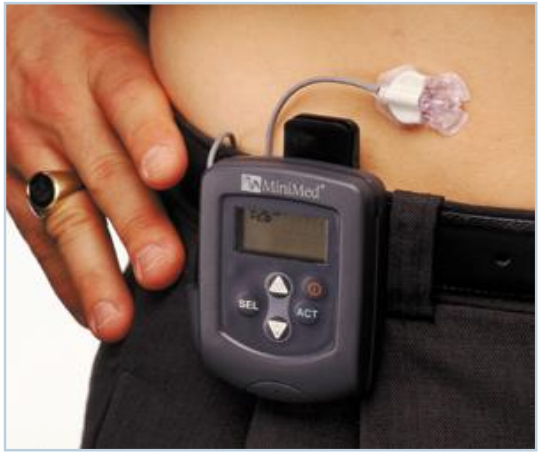


Continuos Glucose Monitoring in the Clinical Setting: How to perform it?

- Monitoring of SC interstitial glucose is the current way to approach blood glucose.
- Enzymatic sensors using Glucose Oxidase are the currently used sensing systems.
- All are at least minimally-invasive.
- They allow retrospective ('Holter-style') or 'On-line' monitoring.
- Obtained data are blood glucose estimations according to sensor signal calibration.

Needle-type Subcutaneous Glucose Sensor





CGMS®, Medtronic

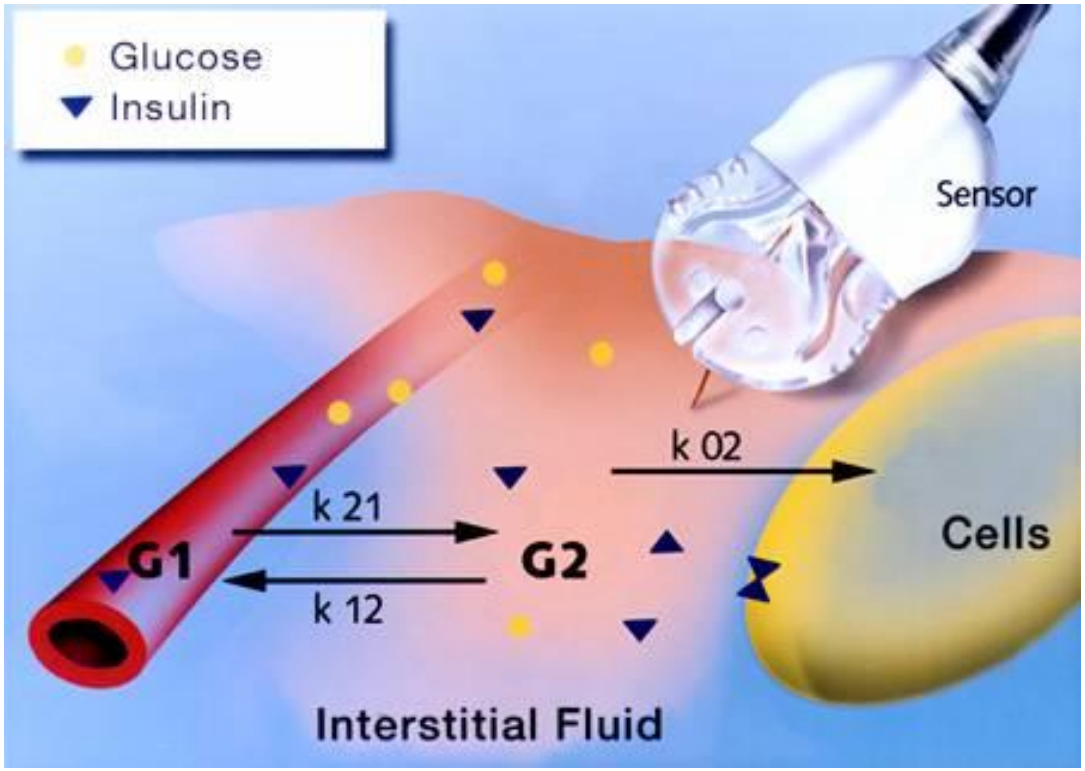
Guardian RT®, Medtronic

STS®, DexCom

Sensor

- A tiny, sterile, flexible electrode inserted just under the skin
- The sensor measures glucose values every 10th second, up to 5-7 days

Interstitial Fluid Measurement

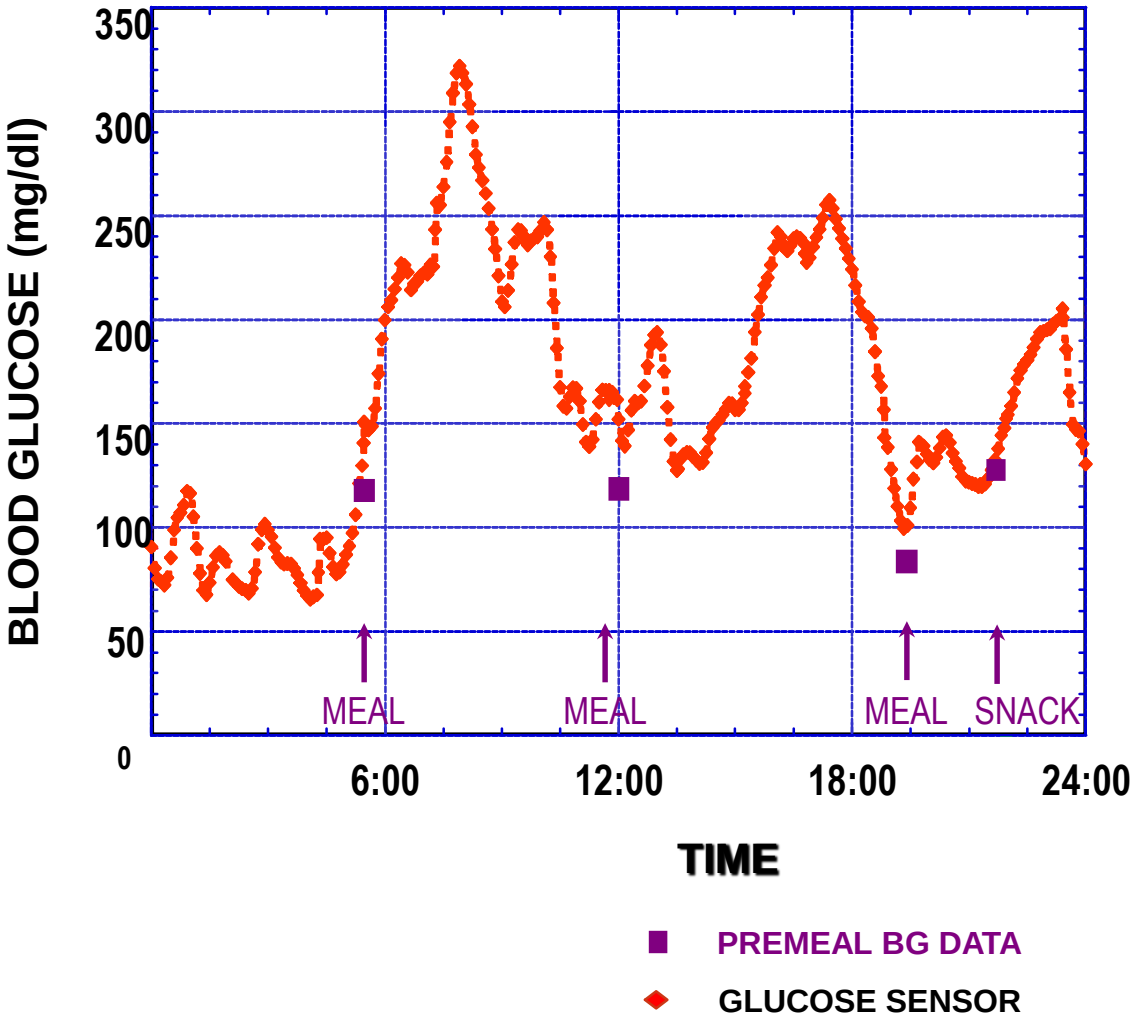


Interstitial fluid glucose (G2) is almost always comparable with blood glucose (G1)

CGMS

- Minimally invasive sensors use a catheter or a small plastic chip containing a sensor inserted into the subcutaneous space to measure the interstitial glucose.
- They are replaced every 3-7 days and require calibration 2-3 times daily with SMBG.

It's hard being good all the time!




1:46P
24 Hour
128
SHIFT
ESC
ACT
Medtronic

Abbott Freestyle Navigator®

Trends better than just points

Insight

Not clue what to do!!

Dexcom sensors

Trend Graphs
Shows the effect of diet, exercise, medication and lifestlye on glucose levels.

Alarms
Protect patients by warning of low and high glucose levels.

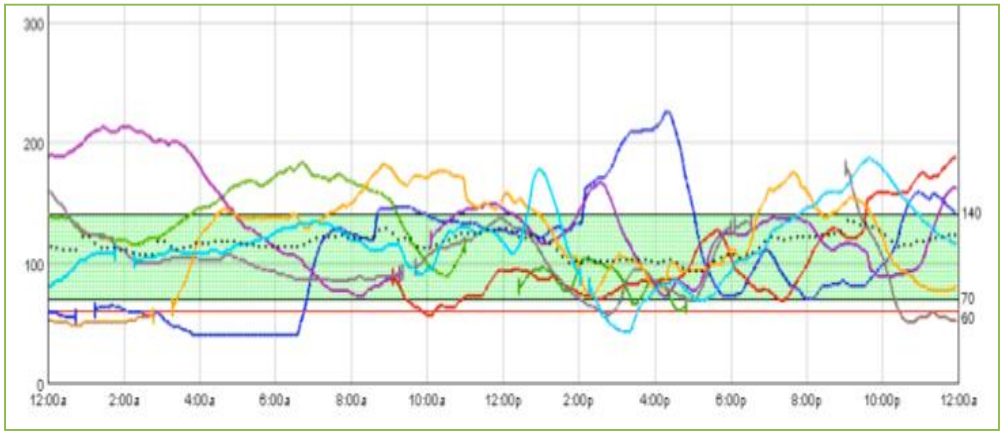
Continuous Readings
Help patients take action sooner
Up to 288 glucose readings per day, every 5 minutes, 24 hours a day

Glucose Sensor
Up to 3-day of continuous use.

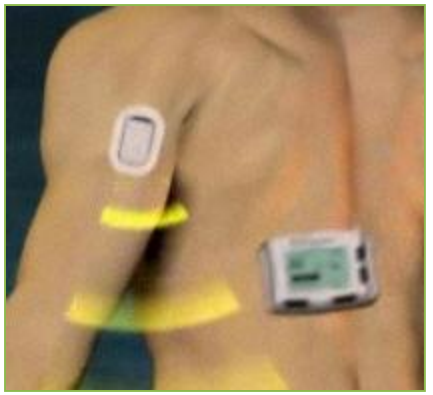
Trend Arrows
Point up or down to show the direction and rate of change in glucose levels

Wireless Transmitter
Small, discreet and waterproof

Glucose Monitoring - CGMS



- By analyzing the trends, the patient or the physician can adjust insulin.
- Leads to better glycemic control.



Reports from the web-based *CareLink™ Personal Software*

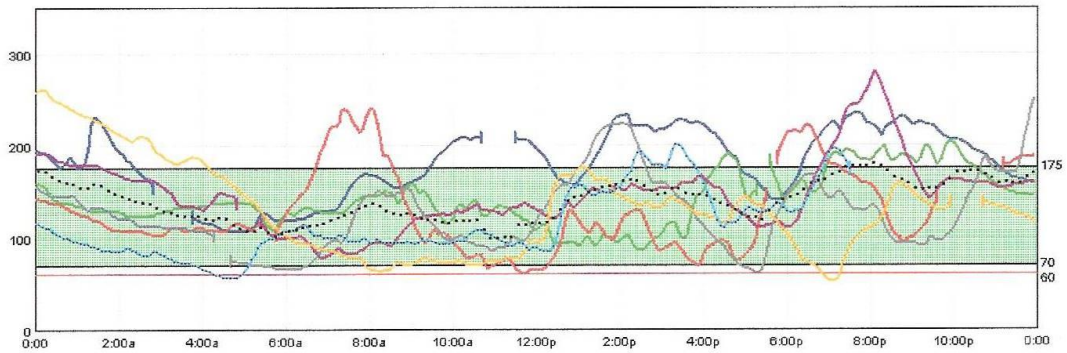
Jul 24 - Jul 30, 2007
(7 days)

HbA1c:7.0% (10/17/06)

Pump: Paradigm 722 #197074
Sensor: In use

Sensor Data (mg/dL)

7/24/07 7/25/07 7/26/07 7/27/07 7/28/07 7/29/07 7/30/07 Avg.

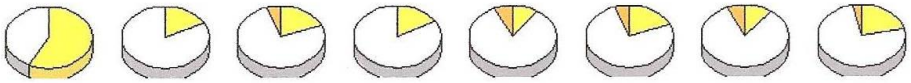


	Tue Jul 24	Wed Jul 25	Thu Jul 26	Fri Jul 27	Sat Jul 28	Sun Jul 29	Mon Jul 30	Average / Total
# Sensor Values	269	285	265	282	284	280	235	1,900
High SG (mg/dL)	234	204	240	280	250	260	202	280
Low SG (mg/dL)	106	86	60	78	60	52	56	52
Average SG (mg/dL)	181	140	127	146	126	131	114	138
Standard Dev.	37	29	45	38	40	51	36	44
MAD %	4.4	29.3	38.9	6.3	13.9	12.1	4.3	11.7
# Valid Calibrations	4	2	4	2	3	3	2	21

Excursion Summary

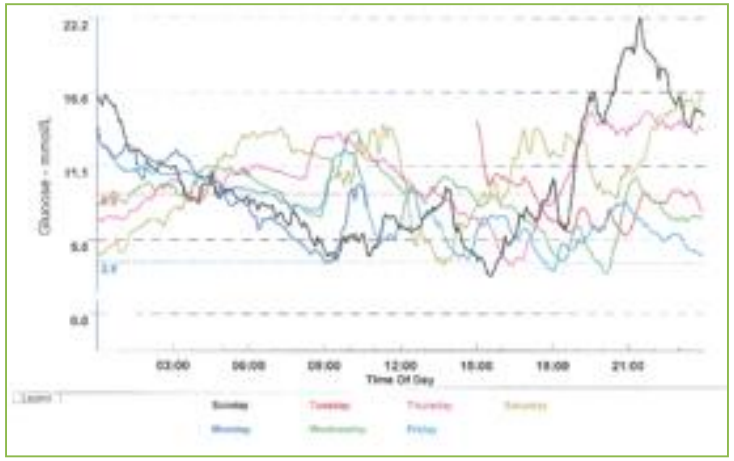
	Tue Jul 24	Wed Jul 25	Thu Jul 26	Fri Jul 27	Sat Jul 28	Sun Jul 29	Mon Jul 30	Average / Total
# Excursions	4	2	1	1	3	2	3	16
# High Excursions	4	2	1	1	3	1	2	14
# Hypo Excursions	0	0	0	0	0	1	1	2
AUC Above Limit	18.7	2.3	5.6	5.6	3.1	7.2	1.3	6.3
AUC Below Limit	0.0	0.0	0.3	0.0	0.3	0.5	0.6	0.2

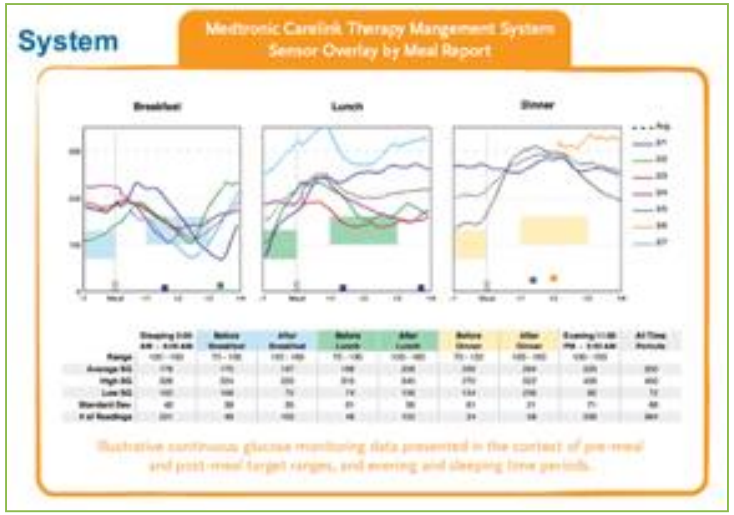
Duration Distribution (hh:mm)



Above 175	12:55	58%	4:10	18%	4:15	19%	3:55	17%	2:20	10%	4:20	19%	2:00	10%	33:55	21%
Within (70 - 175)	9:30	42%	19:35	82%	16:40	76%	19:35	83%	19:40	83%	17:40	75%	16:20	84%	119:00	76%
Below 70	0:00	0%	0:00	0%	1:10	5%	0:00	0%	1:40	7%	1:20	6%	1:15	6%	5:25	3%

Benefits of CGMS





- Increased security from alarms & alerts.
- Immediate feedback - look and learn.
- BG trend provides more information than static readings.
- Control & safety.

Limitations of CGMS*

- Interference with glucose readings by sensor can occur with certain substances
  - i.e.gluthatione, ascorbic acid, uric acid, salicylates
- Lag-time for up to 15 minutes when glucose changes rapidly.
- Overall percentage of error – near 15%.
  - Guardian Real-Time – 17%
  - Dexcom - 11-16%
  - Navigator 12-14%

* E. Cenzic, MD and William tamboriane, MD. *A Tale of Two Compartments: Interstitial Versus Blood Glucose Monitoring.* DIABETES TECHNOLOGY & THERAPEUTICS. Volume 11, September 2009.

Summary

- Home blood glucose meters measure the glucose in whole blood, while most lab tests measure the glucose in plasma.
- Plasma glucose levels are generally 10%–15% higher than glucose measurements in whole blood.
- Most of the modern meters on the market give results as "plasma equivalent," even though they are measuring whole blood glucose.
- Monitoring of SC interstitial glucose is the current way to approach blood glucose.
- In near future, Non-invasive glucose monitoring via implanted nanosensors will be available.

Thanks شكرا" لكم