Advancement in glucose monitoring & insulin Delivery

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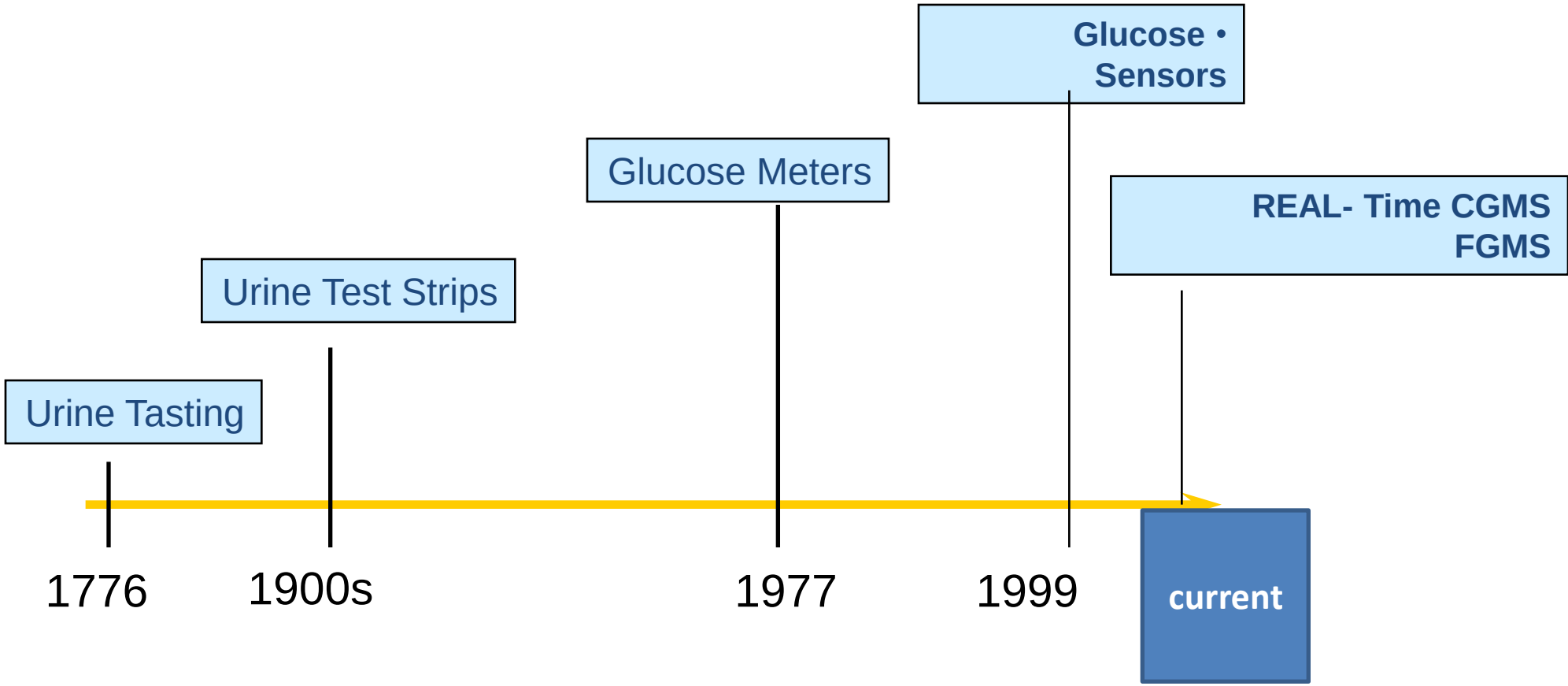
اللهم صل على محمد وآل محمد

Highlights

- Invasive & non-invasive glucose monitoring
- Insulin Injections techniques
  - Syringes/ Pens
  - I-Port advance
- Insulin Pumps
  - Evolution of insulin pumps
  - Present smart Pumps
  - Future of pumps
- Artificial Pancreas (closed Loop)

Glucose Monitoring
Invasive Vs Non - Invasive

Evolution of glucose monitoring



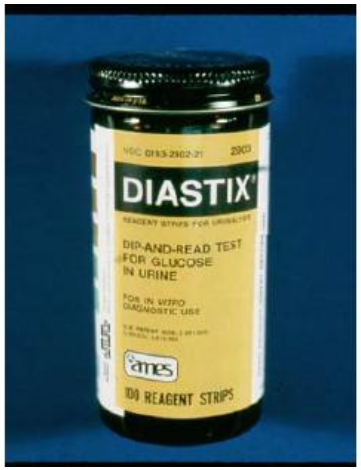
Glucose Monitoring : History

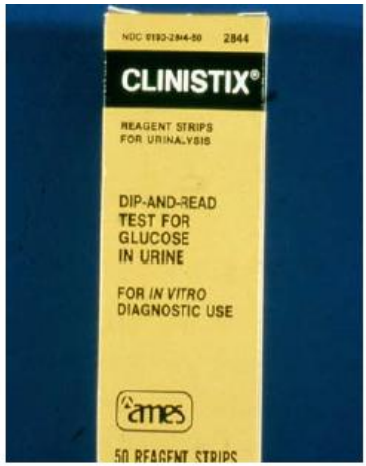
From appearance, color, sediment and often taste

Clinitest was introduced by Ames in 1945, and utilised a copper reagent tablet that contained all the reagents required for a urine glucose test.

In 1954 Glucotest/Testape roll

1960's the "dipstix"

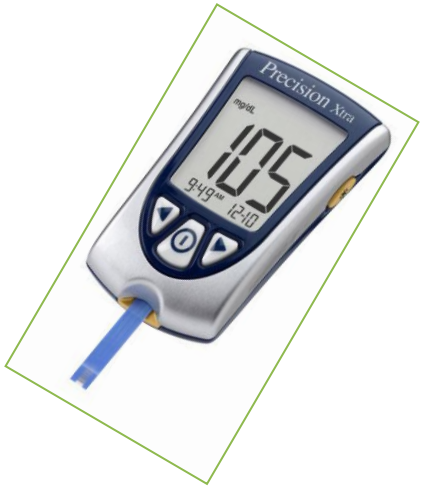




Glucose Monitoring – old time!

First Glucose Meter

Current various glucometers



Current Blood Glucose Meters

iBG Star meter/app (Sanofi Aventis availabl

OneTouch® Verio®S

Accu-Chek ® Aviva Expert Bolus Advisor System

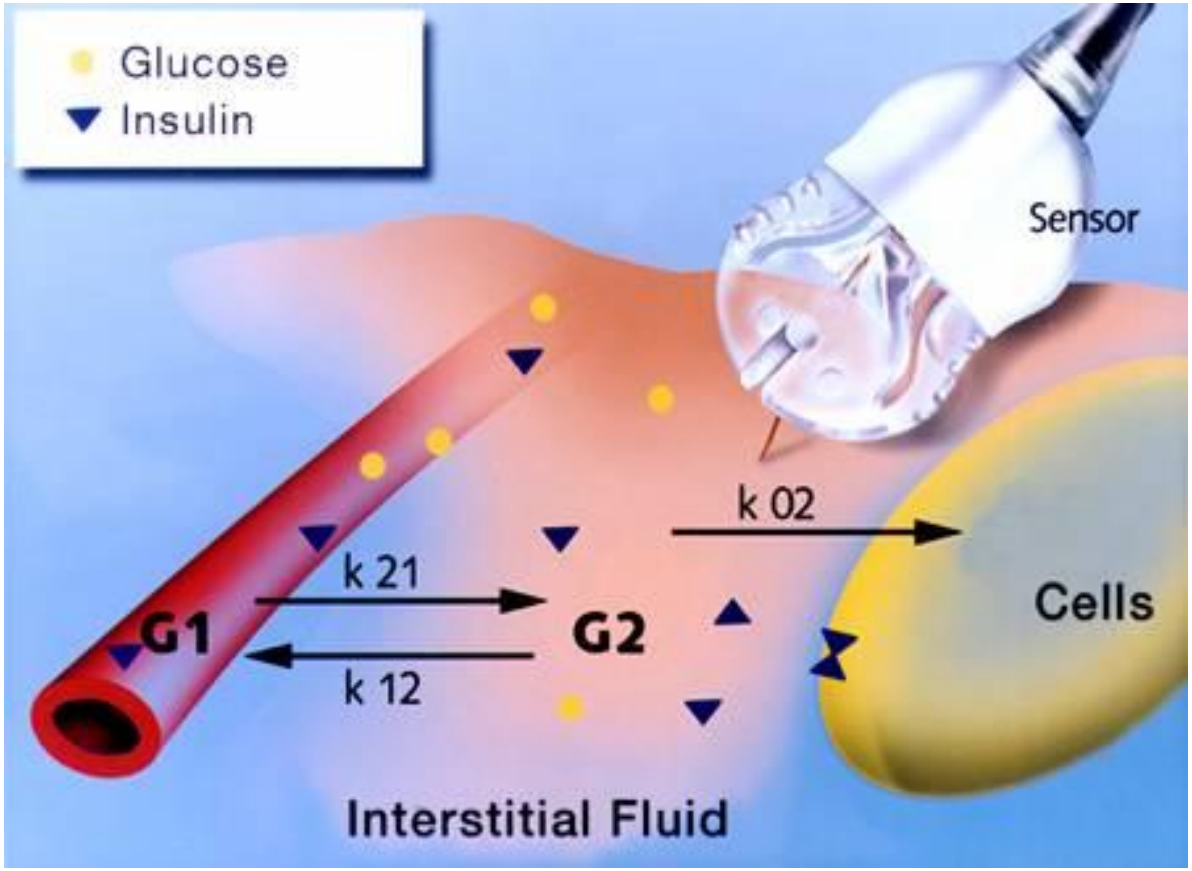
LG KP8400 cell phone (Korea, 2002);
Infopia LG Glucophone/JVAGO 5965 (US, 2008)

Freestyle InsuLinx (Abbott)

Non invasive Glucose Monitoring

- Non invasive sensors ,use a plastic needle containing a sensor inserted into the subcutaneous
- Enzymatic sensors using Glucose Oxidase are the currently used sensing systems
- Various types/ various companies
- They are replaced every 7 days and require calibration 2-3 times daily with SMBG
- FGMS (free style – Libre) by Abbott , not continuous but has advantages of 14 days sensor and no calibration, with cheapest price among all other non invasive sensors

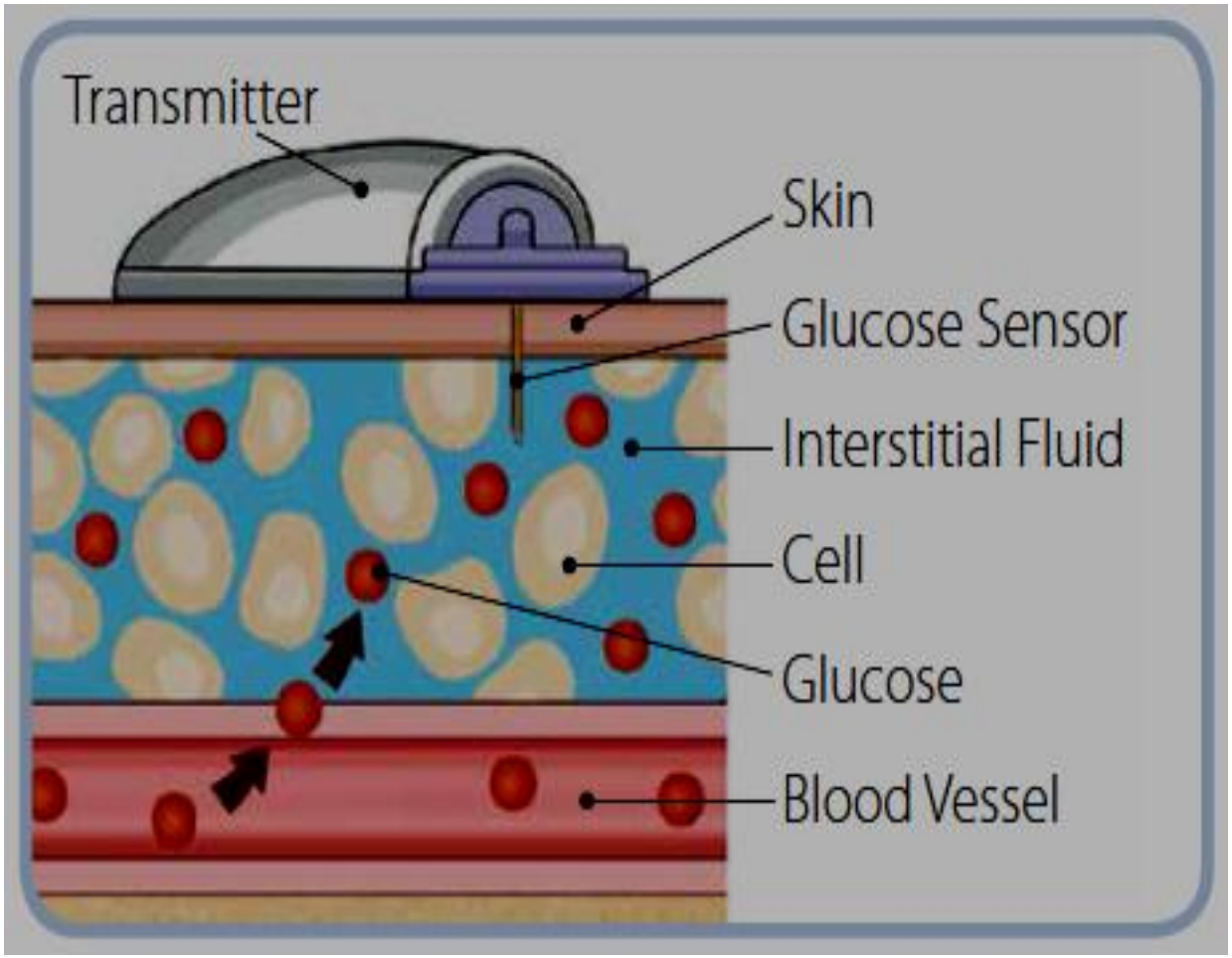
Interstitial Fluid Glucose Measurement



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

How Does CGM Work?

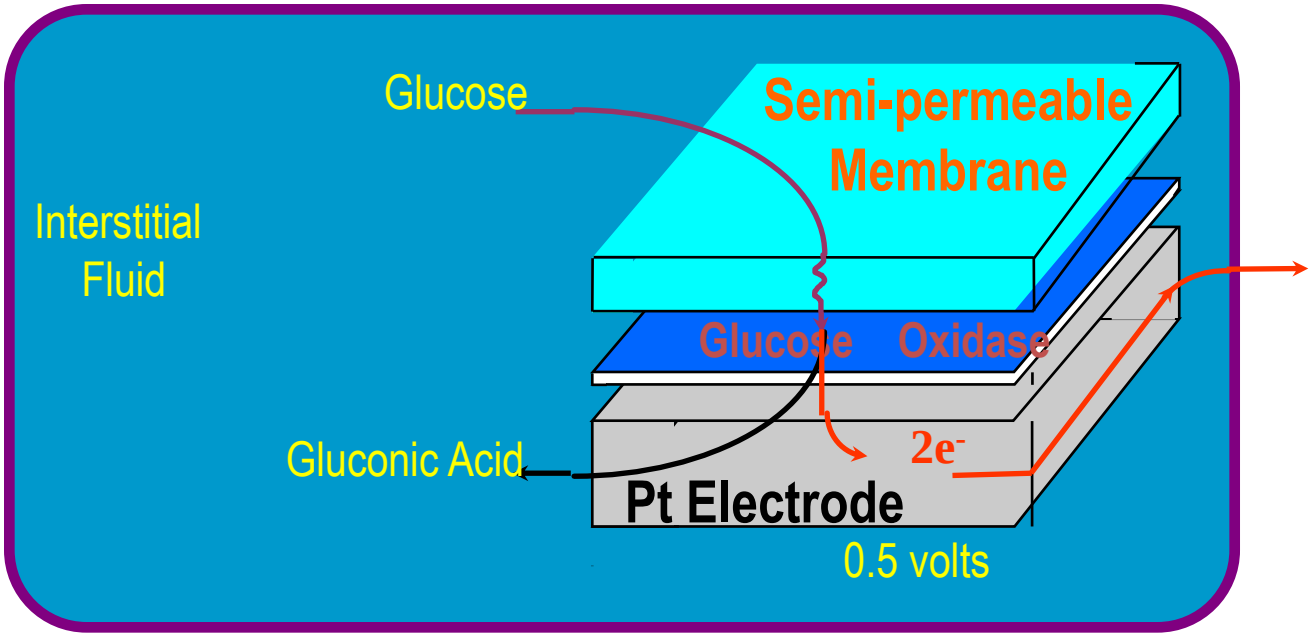
- Glucose in the **interstitial fluid** hits the sensor causing an glucose-oxidation reaction to occur



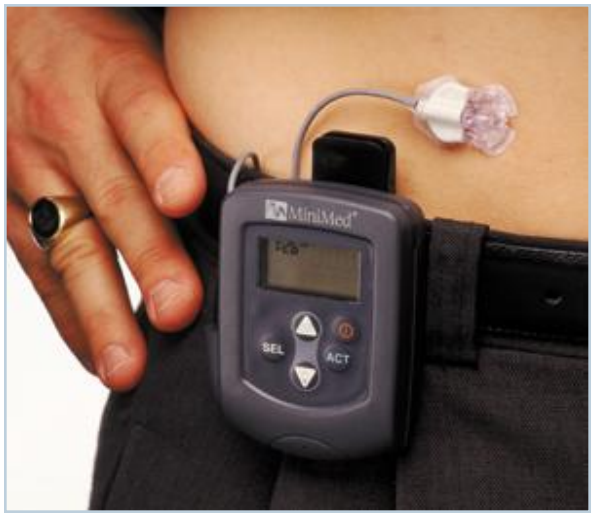
CGMS Parts

- Sensors
- Transmitters
- Receivers
- Inserters

Needle-type Subcutaneous Glucose Sensor



To Monitor



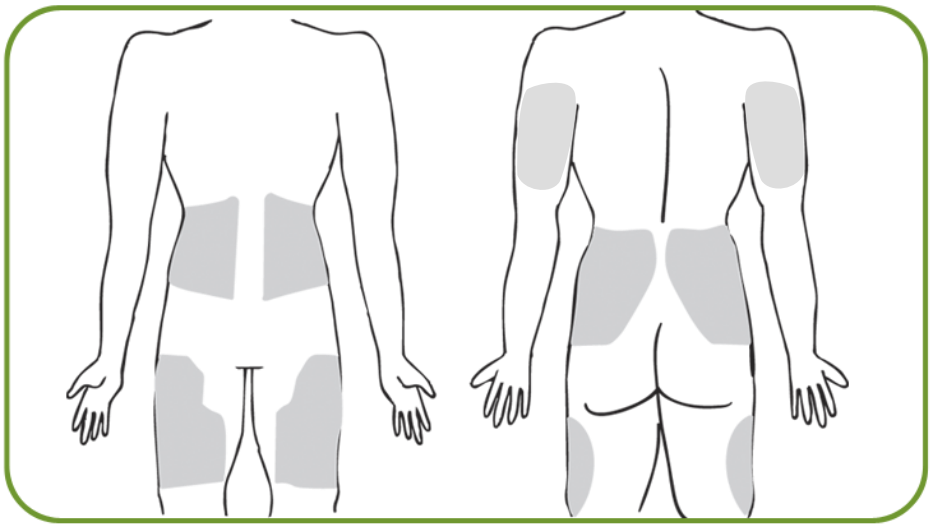
CGMS®, Medtronic

Guardian RT®, Medtronic

STS®, DexCom

Sensor Sites

- Change every 6-7 days, per manufacturer guidelines
- Adhesive wipes (Skin Tac, IV Prep) and tapes (Tegaderm, IV 3000) may be helpful to keep the sites
- For pain with insertion, try numbing with EMLA/Lidocaine cream or the Synera patch – ask MD/NP for prescription



The first Glucose Sensors

Glucowatch Biographer
FDA approval 2001 -2007
Reverse iontophoresis
Cyngnus/Animas

CGM Gold
Enzyme tipped catheter
1999

Medtronic Guardian
Real time
2004

Freestyle navigator
2008 -2011

Dexcom STS 2006

Dexcom STS 7 Continuous Glucose Monitor Sensor and Receiver. Courtesy of Dexcom.

Availability of various CGMS


home
Reports
Profile
Devices
Welcome, Bill Davis.
There is new data and reports for you.
Add a new logbook entry
07/25/2013 - 07/31/2013
Last uploaded data on 07/31/2013 20:33
Breakfast
Lunch
Dinner
Bedtime
Hypo
2
14% of your blood glucose values are below hypo limit
Target bar for all bG values
Before meal bG
2
above target
22% of your before meal blood glucose values are above target
After meal bG
3
above target
60% of your after meal blood glucose values are above target

Glucose Sensors & Blue –tooth communications

Glucose Sensors & Blue –tooth communications

- Receiver s could share blue-tooth capability built-in so no need to have a cable and phone attached to receiver
- Must have iPhone, iPod touch, or iPad with internet connection close to receiver

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

Abbott Freestyle Navigator®

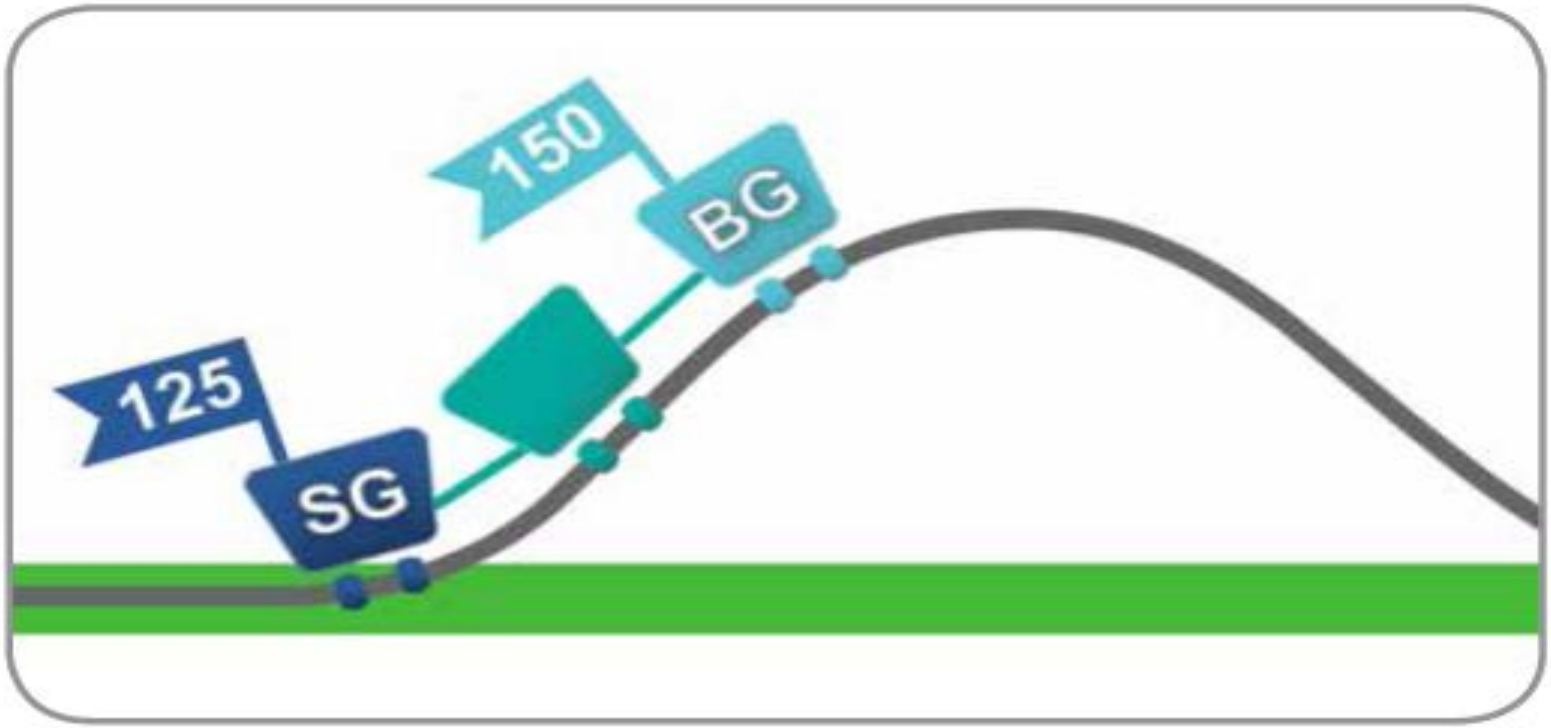
Limitations of CGMS

- 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
- **(MARD = mean average reading deviations)**
  - 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.

Limitations of CGMS

- During rapid states of change, SG and BG may differ more than 20%
- The CGM needs calibrations a minimum of twice a day (once every 12 hours)



Sensor Glucose (SG) vs. Blood Glucose(BG)

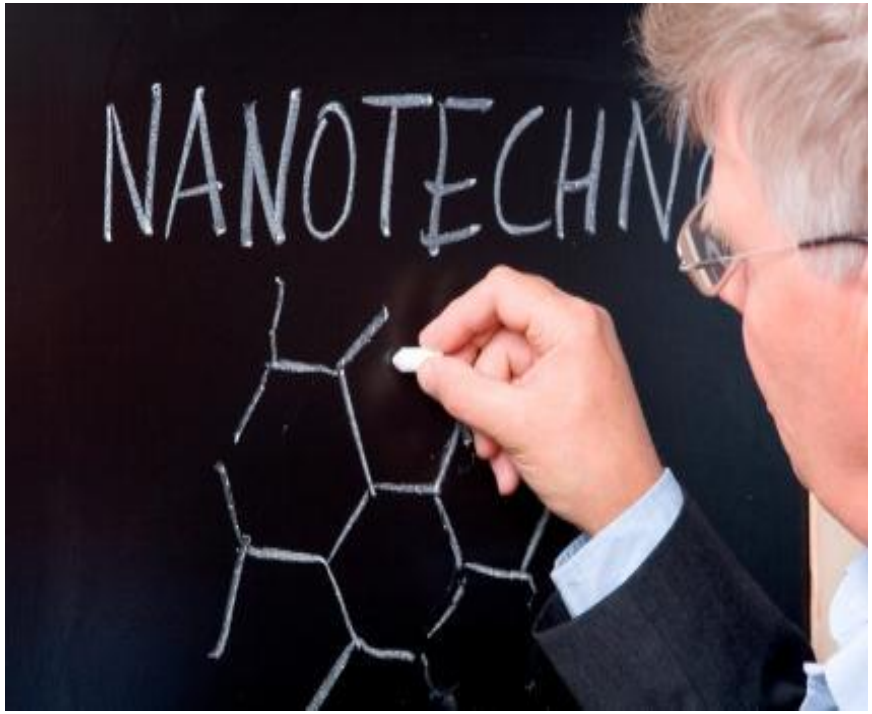
Future Non invasive glucose monitoring

Needle free transdermal sensor

GlucoTrack Ear Lobe Meter

Emerging Research on Nanomedicine & Diabetes

- *Nanos* (Greek) – one-billionth part of something
- *nanotechnology - engineering and manufacturing at the scale of a nanometer (10)* $^{-9}$
- *Nanomedicine will be available in Future sensors and future pumps*



Tears of Joy for Diabetics

21 December 2009 University of Western Ontario

The non-invasive technology uses extremely small nanoparticles embedded into the hydrogel lenses. These engineered nanoparticles react with glucose molecules found in tears, causing a chemical reaction that changes the color of the lenses.

Insulin Delivery Devices
Past /Present & Future

Insulin Delivery Devices

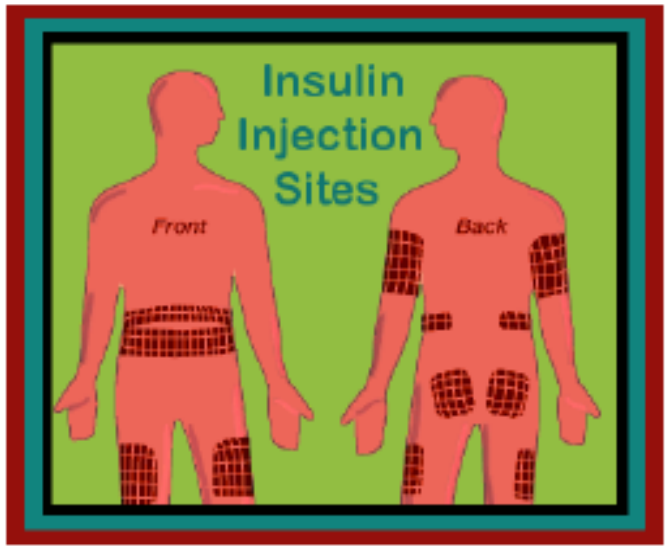
- Syringe
- Pump
- Pen Device

Insulin Syringes

- U-30
- U-50
- U-100
- **One time, one person use only!**

Where to Give Insulin: On Target!

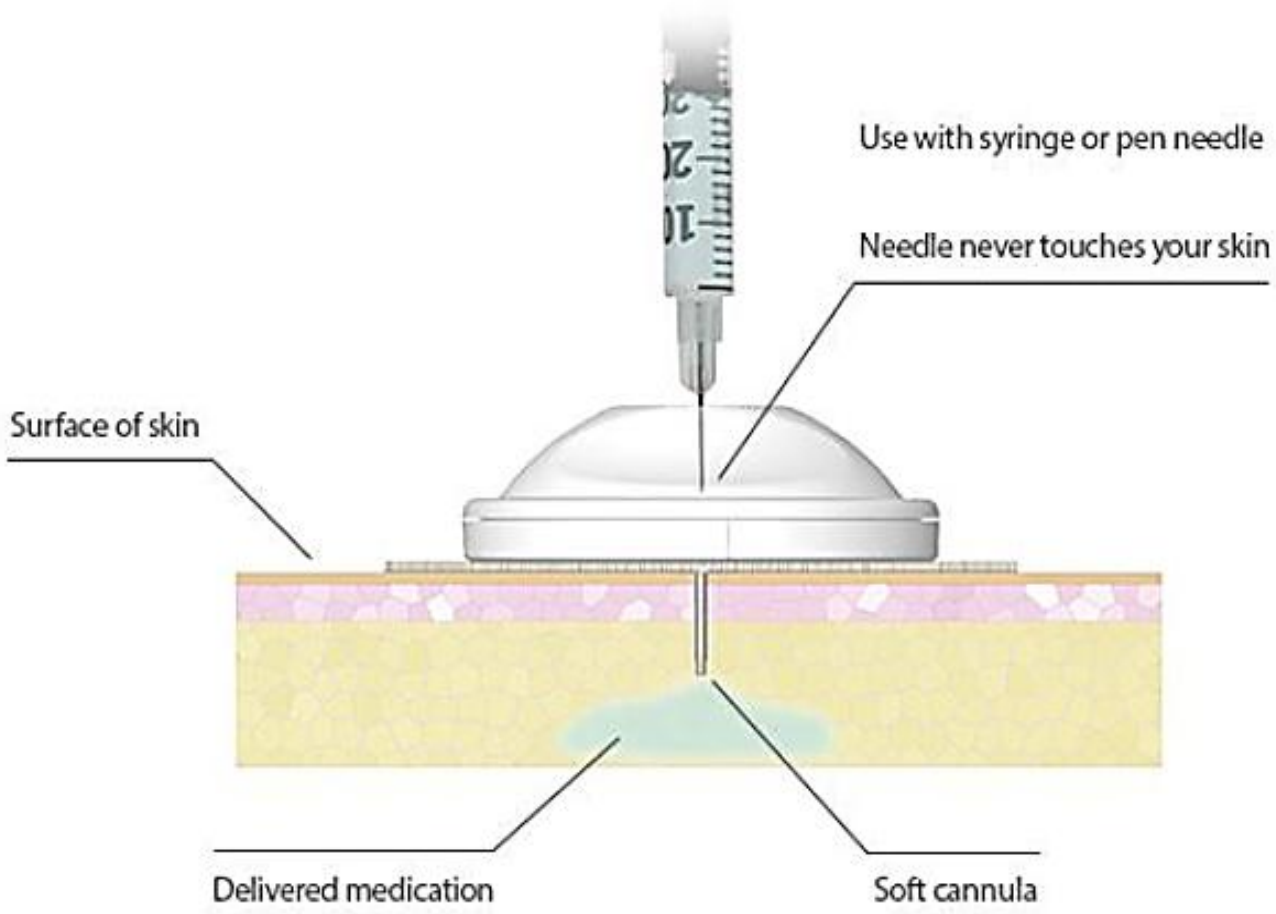
- Inject into fat layer under skin
- Rotate sites



- Common sites: abdomen, thigh buttocks, upper arms

Value summary

The value of i-Port Advance® in patients requiring daily subcutaneous injections



No needle remains under the skin

i-Port Advance®

Number of skin punctures required in thirty days using i-Port Advance versus standard injection*[1]

Month **without i-Port Advance**

S	M	T	W	TH	F	S
4	8	12	16	20	24	28
32	36	40	44	48	52	56
60	64	68	72	76	80	84
88	92	96	100	104	108	112
116	120					

120 skin punctures

Month **with i-Port Advance**

S	M	T	W	TH	F	S
1			2			3
		4			5	
	6			7		
8			9			10

10 skin punctures

*Assuming four injections per day

1. i-Port Advance. i-Port injection port mitigates problems identified by injection impact report. Medtronic MiniMed, Inc. 2014

Clinical Benefit of I-Port Advance

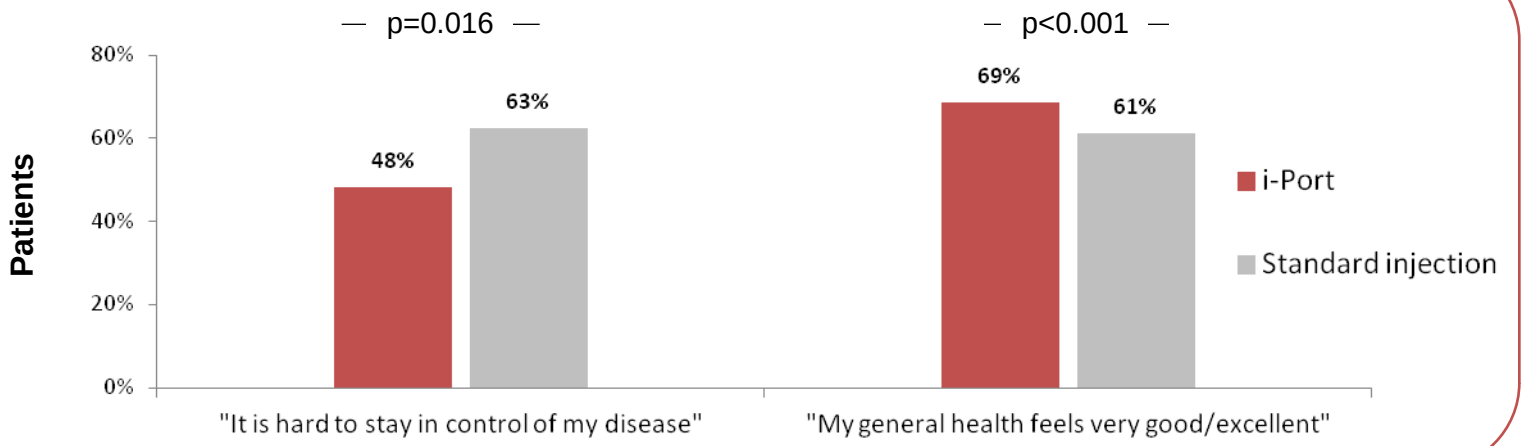
69% of patients felt **i-Port was useful and helped manage their condition**

68% of patients **forgot they were wearing i-Port**

71% of patients thought **using i-Port was not difficult**

- Using i-Port significantly improved patient-reported disease control and general health versus standard injection*[1]:

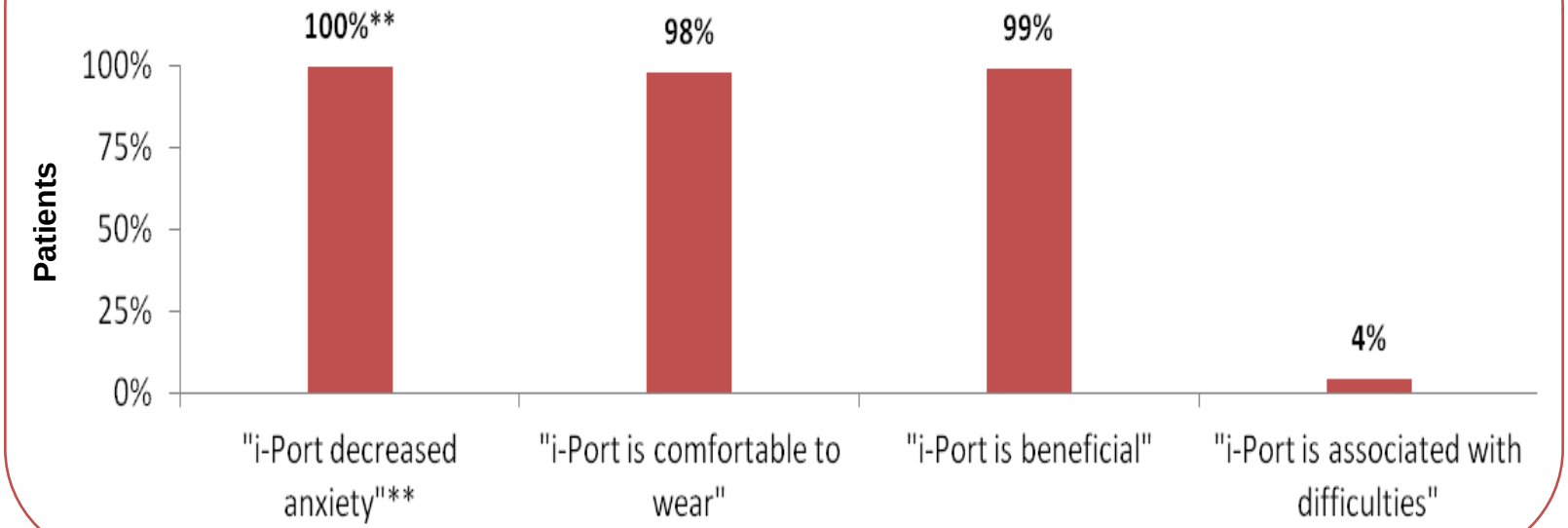
User experience with i-Port versus standard injection[1]



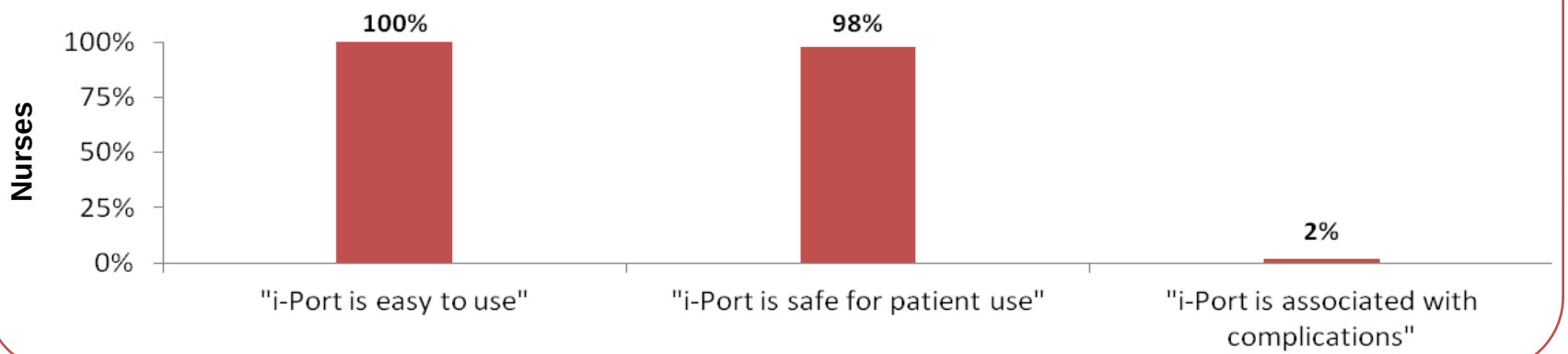
*Multicenter, randomized, prospective, controlled, open-label, two-period crossover study investigating the function of i-Port versus standard injections in 74 patients with diabetes

1. Blevins T, Shwartz SL, Bode B et al. A study assessing an injection port for administration of insulin. *Diabetes Spectr.* 2008;21(3):197–202

Patient experience with i-Port Advance[1]



Nurse experience with i-Port Advance[1]



*Prospective study conducted in an inpatient setting, in which patients requiring multiple subcutaneous injections of insulin were offered i-Port Advance;

**39 of 100 patients reported needle anxiety prior to using i-Port Advance – of these, 39/39 (100%) stated that i-Port Advance reduced anxiety

1. Riley D, Raup G. Impact of a subcutaneous injection device on improving patient care. *Nurs Manage.* 2010;41(6):49–50

Significantly lower perception of pain

when using injection ports versus standard injections, as reported by patients, their parents and their provider*[1]

Lower anxiety

in parents of children using injection ports versus standard injections*[1]

Improved QoL

as reported by the parents of children using injection ports versus standard injections**[2]

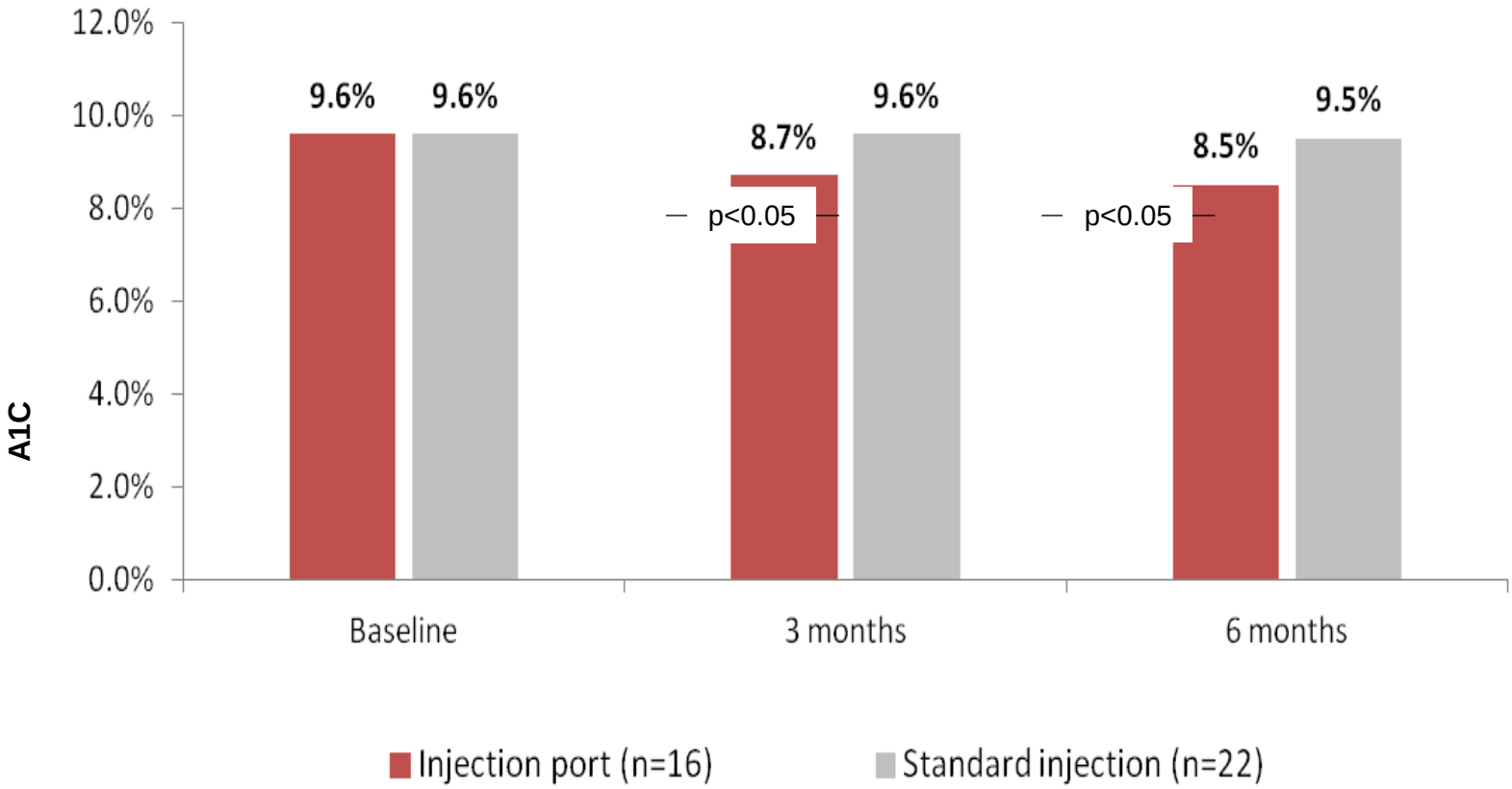
*Open label, randomized, controlled trial of 41 young patients (aged 3–15 years) with diabetes, investigating patient anxiety and pain when using an injection port versus standard injection to deliver insulin

**Study of 40 young patients (aged 1–5 years) with diabetes, investigating glycemic control and QoL when using an injection port versus standard injection to deliver insulin

HCP=healthcare professional; QoL=quality of life

1. Hanas R, Adolfsson P, Elfvin-Åkesson K et al. Indwelling catheters used from the onset of diabetes decrease injection pain and pre-injection anxiety. *J Pediatr.* 2002;140(3):315–320; 2. Rabbone I, Bobbio A, Di Gianni V, Sacchetti C, Cerutti F. Intensive insulin therapy in preschool-aged diabetic children: from multiple daily injections to continuous subcutaneous insulin infusion through indwelling catheters. *J Endocrinol Invest.* 2008;31(3):193–195

A1C control with injection port versus standard injections*[1]



*Randomized controlled trial of 66 young patients with diabetes, investigating A1C control when using an injection port versus standard injection ± alarm to administer insulin

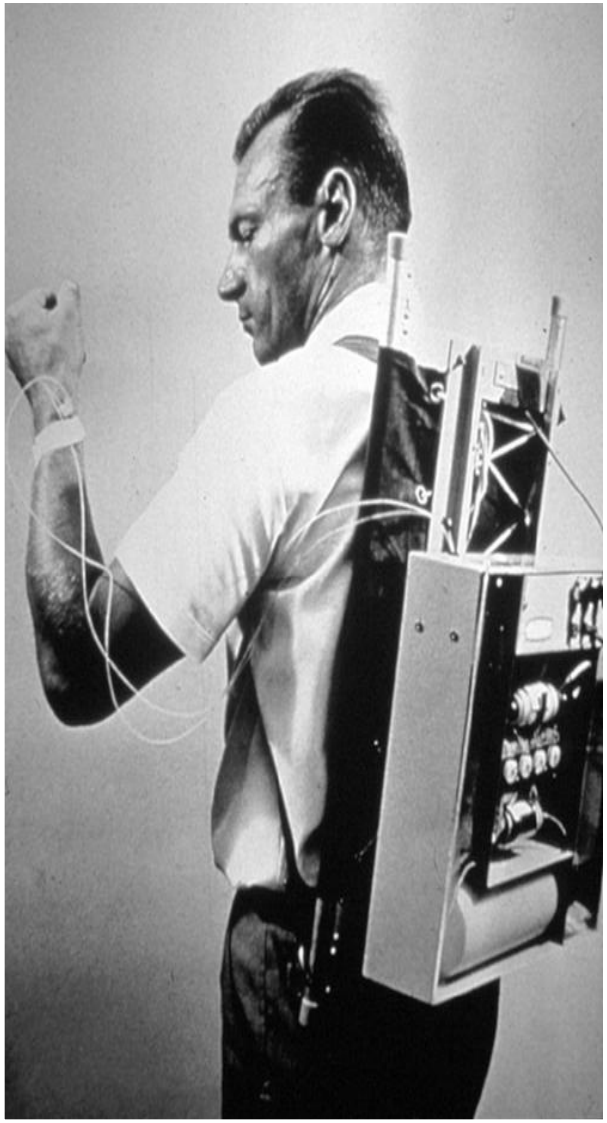
A1C=glycated hemoglobin

1. Burdick P, Cooper S, Horner B, Cobry E, McFann K, Chase HP. Use of a subcutaneous injection port to improve glycemic control in children with type 1 diabetes. *Pediatr Diabetes.* 2009;10:116–119

EVOLUTION OF INSULIN PUMP THERAPY

- The idea of continuous insulin delivery first emerged in the early 1960s when Dr Arnold Kadish from Los Angeles fashioned a device that would permit such insulin delivery
- This device was the size of an army backpack making it impractical for everyday use
- First pump employed continuous intravenous insulin delivery, and then by the more practical means of continuous subcutaneous insulin infusion (CSII)

Insulin Pump Therapy: Past



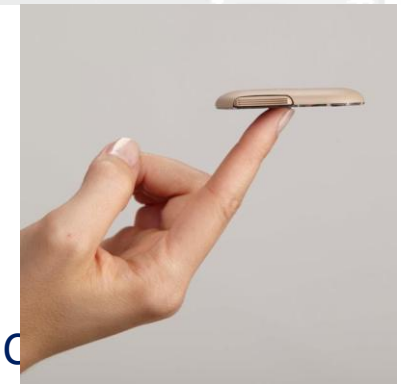
Insulin Pump Therapy: Present

Benefits of Insulin Pump Therapy

- Improved glycemic control
- Less frequent / severe hypoglycemia
- Enhanced quality of life
- Improved patient satisfaction
- Ease of management
- Reduced glucose toxicity, which may also result in improved β-cell function

Patch Pumps

Cellnovo
France & UK



C
(FDA approved in Jan. 2010)
Launch in 2016
200 units of insulin
Bolus only pump 1-2 units of Insulin / 0.5-5 unit boluses

Medingo Solo Roche
(FDA approved in July 2009)

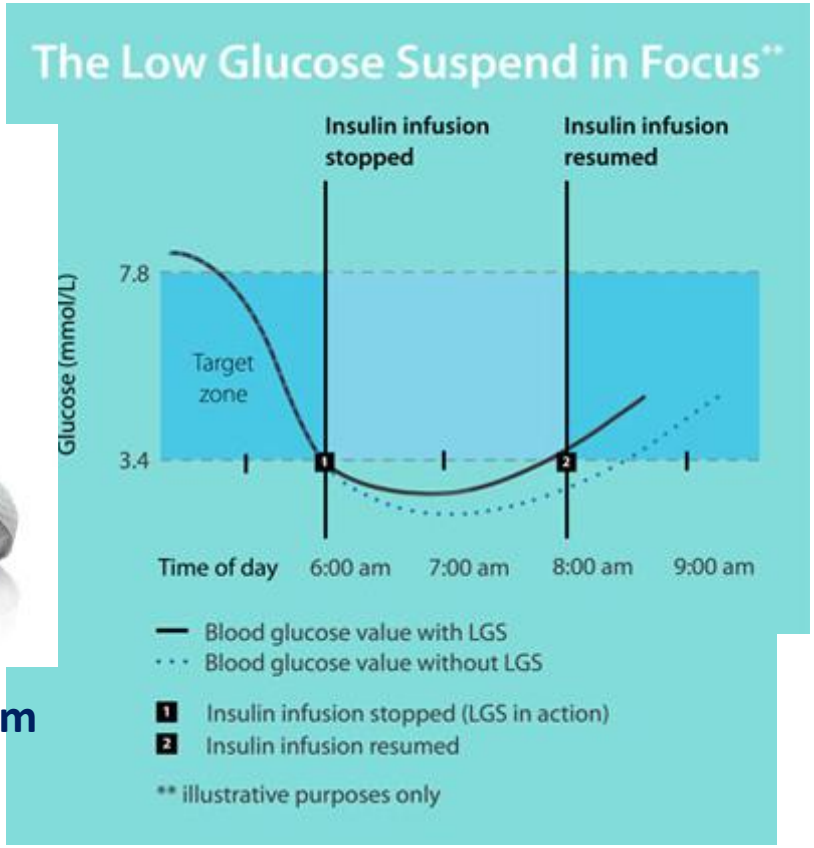
Valeritas V-Go
(FDA approved in Dec. 2010)
Preset basal rate to deliver 20, 30, or 40
Bolus dosing in 2 Unit increments up to 36 Units

Wearable Pumps

Relatively large

Sensor Augmented Insulin Pumps (SAP)

Medtronic MiniMed 530G system



Animas Vibe system

‘SMARTGUARD™ TECHNOLOGY PROVIDES ADVANCED PROTECTION AGAINST HYPOGLYCEMIA (AUTO SUSPENSION & AUTO-RESUME OF INSULIN)

Bionic Pancreas – the iLet
Dual Chamber pump (Glucagon and Insulin Reservoir)

http://sites.bu.edu/bionicpancreas/about-us/the-bionic-pancreas-ilet/

Insulin

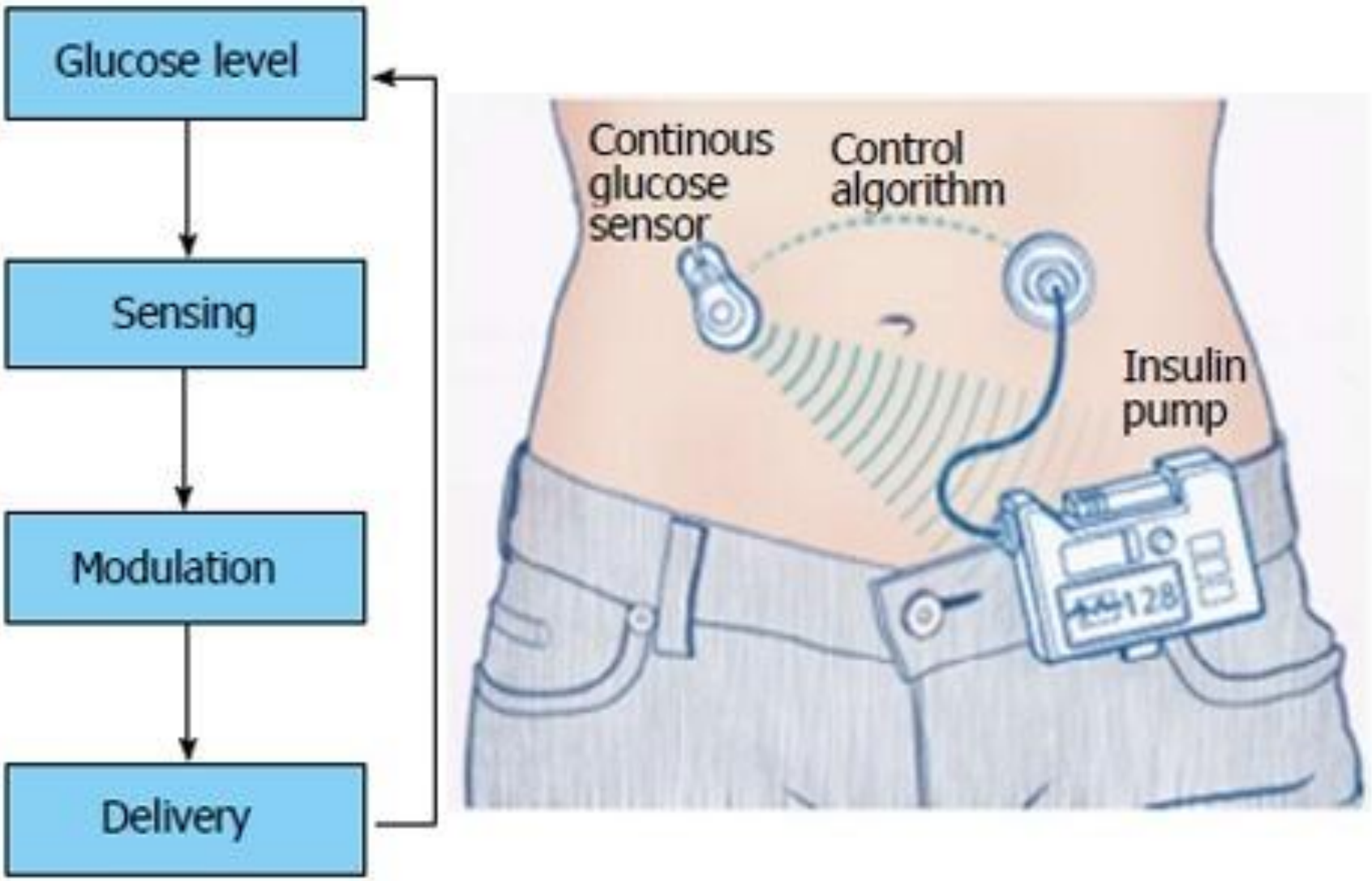
Glucagon

Ilet –"Bionic Pancreas"

The artificial pancreas (AP)

- known as closed-loop control of blood glucose in diabetes, is a system combining of:

  - glucose sensor
  - smart" control algorithms
  - insulin infusion device


Glucose level
Sensing
Modulation
Delivery
Continous glucose sensor
Control algorithm
Insulin pump

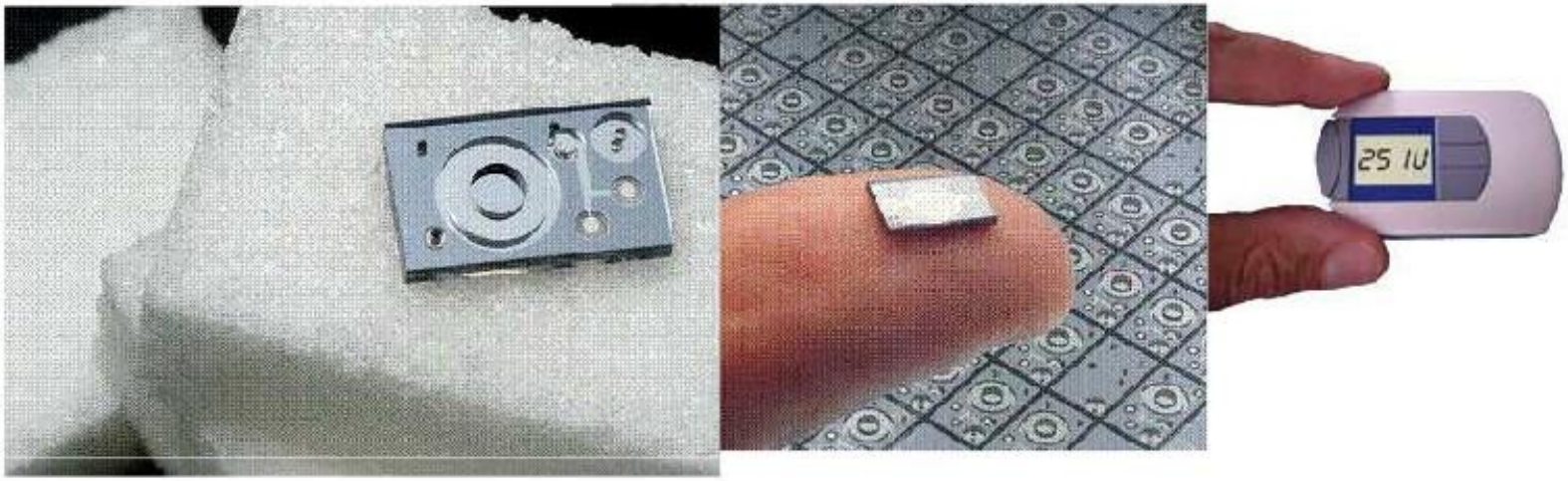
Breaking News: FDA Approves the MiniMed 670G System, World's First Hybrid Closed Loop System

September 28, 2016

Medtronic's 670G

- "hybrid-closed loop" system with Enlite 3 CGM sensor
- Software automatically increases/decreases insulin delivery to target a blood glucose of 120 mg/dl
- Give bolus for meals
- Notify - exercise

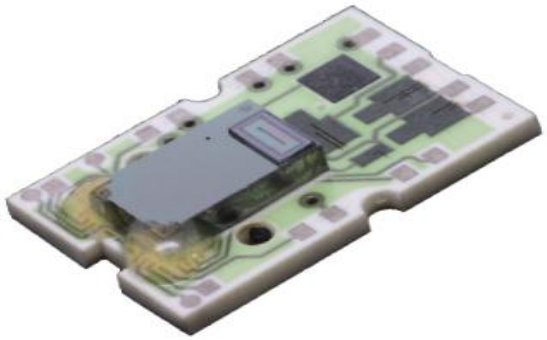
Micro-pump



Debiotech has been developing small pumps from Micro-Electro-Mechanical Systems or MEMS technology. These devices are made from silicon (not silicone!) and easily mass-produced to keep cost low.

Silicon is harmless, but it is not clear how insulin may interact with silicon surfaces.

JewelPUMP™



Nanopump™

Debiotech Jewel
Micro-chip
7 day wear
500 IU of insulin
Clinical trials in France
(FDA application filed 2014?)

Ultrafast insulin which are absorbed more quickly than the currently available rapid acting insulin which have a peak at about 60 minutes

It theoretically coordinate with meals better, and allow faster recovery from hyperglycemia if the insulin infusion is suspended.

They are in development by Biodel Halozyme, and Novo Nordisk

Conclusions

- Non – invasive glucose monitoring is helping all patients to monitor their glucose variability continuously and adjusting their insulin doses much better than SMBG
- SmartGuard™ Technology provides advanced protection against Hypoglycemia (Auto Suspension & auto-resume of insulin)
- FDA has Approved MiniMed 670G System, World's First Hybrid Closed Loop System in September 28, 2016 with strong hope that, further artificial pump technology will be advancing gradually to help all people with type 1 diabetes


Thanks