

Kapalı ve Yarı-kapalı İnsulin Pompa Sistemleri

6/2021

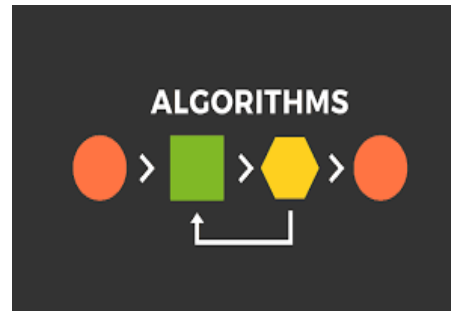
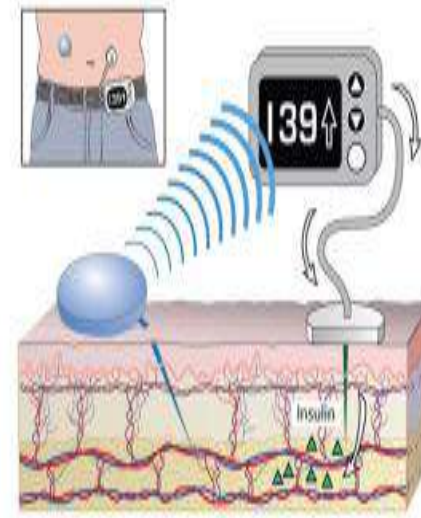
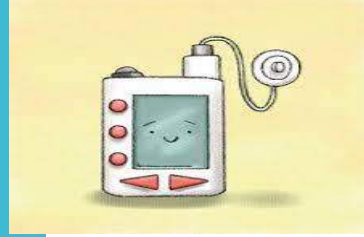
Eda Cengiz, MD, MHS, FAAP

Genel Bařlıklar

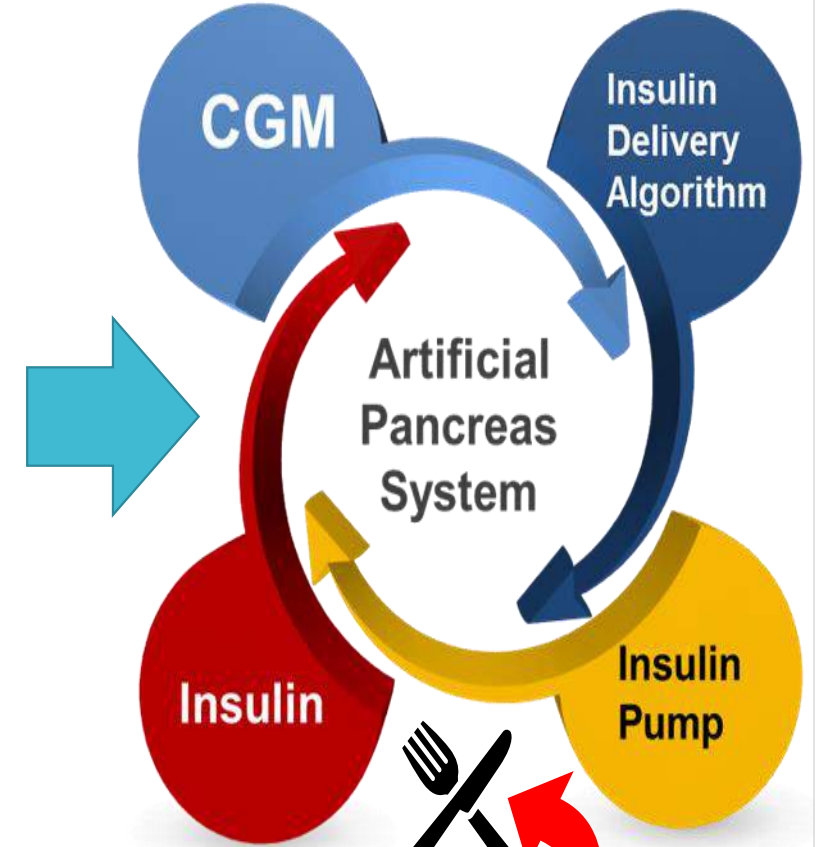
- Kapalı ve yarı kapalı İnsulin Pompa Tedavisi nedir?
- Yeni Sistem İnsulin Pompalarının Özellikleri
- Geleceğın İnsulin Tedavi Sistemleri

Acik ve Kapalı İnsulin Pompa Tedavisi

Acık Sistem (Open Loop)



Kapalı Sistem (Closed Loop)



Yarı-kapalı Sistem (hibrid)

Akıllı İnsulin Pompaları ve Teknolojik Interoperabilite



- ACE Pump
- “alternate controller-enabled”
- iCGM
- “integrated continuous glucose monitor”
- iAGC
 - “interoperable automated glycemic controller”

FDA’ın Tandem Insulin Pompası ile farklı sensorler arasında iletişim izni ve onayını kabul etmesi ile gelişen diyabet teknolojisi.

Yapay Pankreas: Closed-loop Systems (Artificial Pancreas, Bionic Pancreas)



Medtronic 670G

Large RCT of Control-To-Range Algorithm
 (NHLI UKA UK 308485)

Design:
 ✓ 50/50 participants in 6-month RCT comparing Closed-Loop vs. SAP
 ✓ Age 15 to 75+
 ✓ Inclusion of all different insulin pumps
 ✓ HbA1c < 10.5% at screening

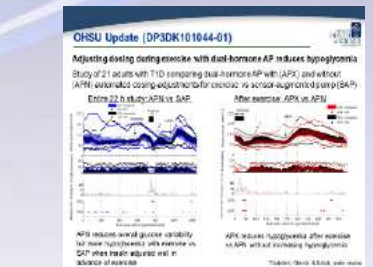
Outcomes:
 ✓ HbA1c
 ✓ Incidence of Hypoglycemia

Objectives:
 ✓ Establish closed-loop control as a viable treatment for type 1 diabetes
 ✓ Generate safety and efficacy data satisfying requirements by regulatory agencies
 ✓ Demonstrate clinical effectiveness to facilitate reimbursement

DiAs – Type Zero



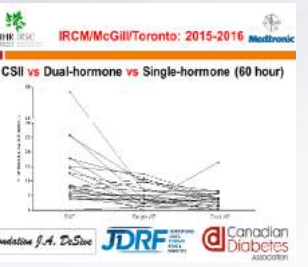
iLet-
BetaBionics



OHSU



Diabeloop (DBLG1)-France



CLASS

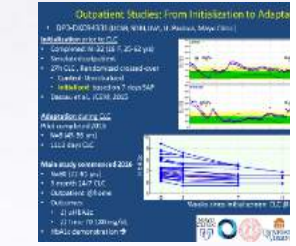
Optimization of the Artificial Pancreas Meal Response

BCH/Harvard Med.

In Progress

- 1) FC dosing algorithm now runs on an ultra-low-power microcontroller chip. Power consumption testing under way.
- 2) New investigational device in work for Animal (T1D) Model study.
 - Ultra-low-power, 1000s of mAh battery
 - Sensor, insulin pump, insulin, and glucose meter
 - Fully integrated system
 - Fully integrated system
 - Fully integrated system
- 3) T1D (animal) subcutaneous model study.
 - Outcome: reduction in hypoglycemia and time in range
 - HbA1c
 - Time in range
 - Time in range

DSC



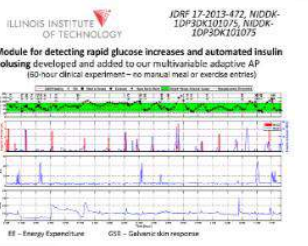
ZMPC



Camdiab FX



Medtronic 770G, 780G



IMAPP



BigFoot

#OpenAPS:

Taking the DIY artificial pancreas from (n=1) to (n=1) many by:

- Focusing on safety
- Limiting dosing ability in hardware and software
- Using same dosing calculations a person would use
- Responding (or not) to unexpected data
- Tolerating communication failures
- Falling back safely to standard device operation

@DanaMLewis

#OpenAPS



Omnipod 5

Hybrid Closed-Loop Algorithm

TANDEM
 DEXCOM
 typezero

Tandem-Type Zero

Lilly
 Menarini
 Roche



Kapalı, Yarı- Kapalı İnsulin Pompa Sistemleri



**Medtronic
Minimed**



**Tandem
tSlim
Control IQ**



Omnipod 5

The iLet™
Carry your glucose metabolism in your pocket.



**iLet
Beta
Bionics**



**Tidepool
Loop**



**Lilly-
Ypsomed**



MEDTRONIC MINIMED INSULIN POMPA SİSTEMLERİ

Akıllı İnsulin Pompa Donemine Geçiş

1st Sensor Augmented
 MiniMed™ Paradigm™ REAL-Time Pump (2006)

1st Threshold Suspend
 MiniMed™ Paradigm™ Veo™* Pump (2009)

1st Predictive Suspend
 MiniMed™ 640G System* (2015)

1st Hybrid Closed Loop
 MiniMed™ 670G System (2017)

Bluetooth®-enabled pump
 Peds (2-6 yr) indication

Advanced Hybrid Closed Loop**
 Auto correction boluses

Personalized Closed Loop,[^]**
 Automatic meal control

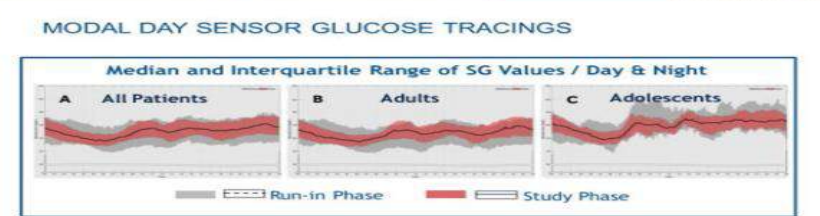
İlk FDA Onayı Alan Yapay Pankreas Sistemi: Medtronic 670G Hybrid Closed-loop (HCL)

HCL System
 Insulin only System
 1st FDA Approved HCL for ≥14yo with T1D

Study Population
 Pediatric & Adult

Study & Outcomes
 -2 week run-in; 3 month, non-randomized study HCL vs. SAP
 -One week hotel, rest of time AT HOME
 -124 subjects, 10 centers

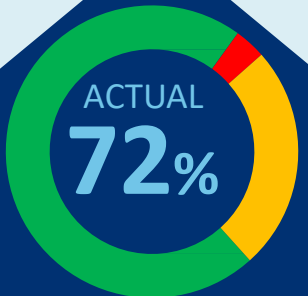
Bergenstal RM, et al. JAMA. Published online September 15, 2016 ; Garg SK, et al. DTT 2017



- Adult Group:**
 - Hypoglycemia reduction
- Adolescent Group:**
 - Hyperglycemia reduction
 - **0.5% reduction in A1c, bringing subjects from a low initial A1c of 7.4% to 6.9%**

* System has CE Mark; System not approved in the US
 ** Investigational program not approved by the FDA; not commercially available
[^] Breakthrough Devices Program. www.FDA.gov. Accessed April 23, 2019.



MOVING INTO THE FUTURE WITH ALGORITHMS AND SYSTEMS THAT MATTER




ACTUAL
72%

MINIMED™ 770G HYBRID CLOSED LOOP SYSTEM^{1,2}




Designed to:


-  Stay up to date with upgradable pump software
-  Provide discretion with smartphone display



MINIMED™ 780G ADVANCED HYBRID CLOSED LOOP³




Designed to:

-  Deliver 100% of correction to meet target
-  Deliver a correction every 5 mins, as needed
-  Allow setpoint of 100 or 120 mg/dL



PERSONALIZED CLOSED LOOP⁴

Designed to:

-  Provide optional carb counting
-  Adapt to behavior and physiology
-  Improve connectivity through Smartphone control

NEXT BIG STEP IN CLOSED LOOP

FDA BREAKTHROUGH DESIGNATION

 Time above 180 mg/dL
 Time in Range of 70-180mg/dL
 Time below 70 mg/dL

¹ Time in Range of 72% obtained from Bergenstal RM, et al. *JAMA*. 2016;316(13):1407-1408.

² Investigational. Not approved by the FDA for any use and not commercially available in the US.

³ Investigational. Not approved by the FDA for any use and not commercially available in the US. Data based on feasibility studies.

⁴ In development. Not approved by the FDA for any use and not available for research or commercial use in the US. Data based on simulation modeling.

ADVANCED HYBRID CLOSED LOOP SYSTEM

GOAL: ACHIEVE MAXIMUM TIR WITH MINIMAL EFFORT

Currently in Pivotal Trial

Design Goals

Control highs w/automated correction boluses

Adjustable target glucose of as low as 100 mg/dL

Fewer fingersticks with Day 1 calibrations only*

Extended wear infusion set

MiniMed™ 780G System



Unsurpassed glycemic control:
TIR Goal >80%

Investigational program not approved by the FDA; not commercially available

*Day 1 calibrations only

PERSONALIZED CLOSED LOOP SYSTEM

SIMPLIFYING THERAPY MANAGEMENT

**With FDA Breakthrough Designation

Algorithm

Fizyolojiye adapte olarak çalışan sistem

Otomatik yemek insulin dozu düzenlemesi
“Automated Meal Handling”
Reduced Carb counting

100% Auto Mode Capable
TIR goal of >85%



Design Goals

Comfort
Personalization
Meaningful outcomes

Sensor & Key Features

50% daha küçük ve atılabilen sensor (CGM)

10 saniyede sensor takabilme özelliği

Akıllı telefon ile kontrol edilebilir

Control IQ-Tandem Tslim

-Control-IQ kullanan çocuklar **67% time in range (TIR)**, SAP(kontrol) kullanan çocuklar 55%.

-Gece kontrol IQ **80% TIR**, 54% (kontrol)

-Control IQ ile **6 saat daha uzun sureli TIR**

-Control IQ gercek hayat kullanim (n=1659):

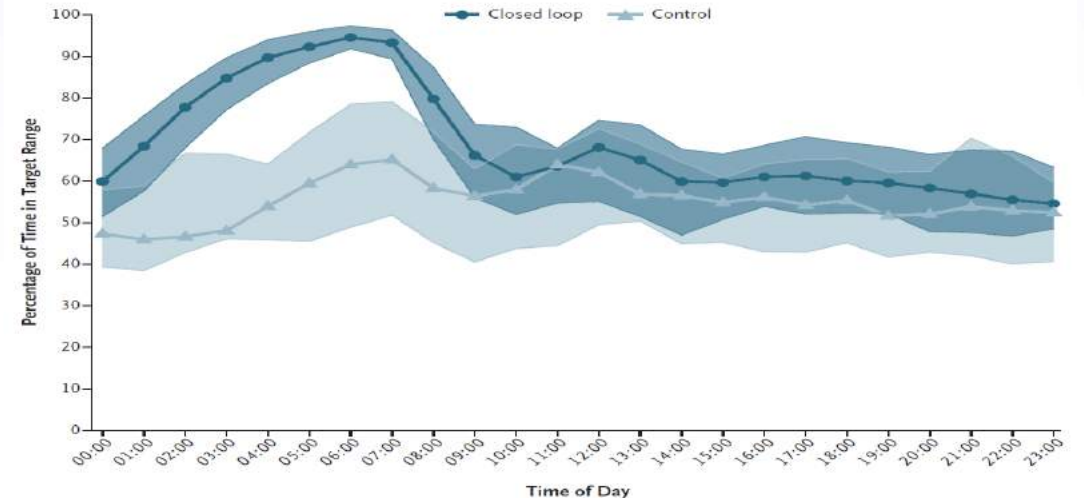
Hb A1c 7.2% den 6.9% geriledi

Yapay pankreas kullanimi :96%



A Randomized Trial of Closed-Loop Control in Children with Type 1 Diabetes

Marc D. Breton, Ph.D., Lauren G. Kanapka, M.Sc., Roy W. Beck, M.D., Ph.D., Laya Ekhlaspour, M.D., Gregory P. Forlenza, M.D., Eda Cengiz, M.D., Melissa Schoelwer, M.D., Katrina J. Ruedy, M.S.P.H., Emily Jost, M.P.H., R.D., C.D.E., Lori Carria, M.S., Emma Emory, R.N., Liana J. Hsu, B.S., Mary Oliveri, C.C.R.C., Craig C. Kollman, Ph.D., Betsy B. Dokken, Ph.D., Stuart A. Weinzimer, M.D., Mark D. DeBoer, M.D., Bruce A. Buckingham, M.D., Daniel Cherňavsky, M.D., and R. Paul Wadwa, M.D., for the iDCL Trial Research Group*



Tandem tslim Control IQ

- Dokunmatik, renkli ekran
- Akilli telefon app, bilgisayar programi
- Upgrade internetten yapilabiliyor
- Pil sarj edilebilir



180	 Delivers	Delivers an automatic correction bolus if sensor glucose is predicted to be above 180 mg/dL.
160	 Increases	Increases basal insulin delivery if sensor glucose is predicted to be above 160 mg/dL.
112.5	 Maintains	Maintains active Personal Profile settings
70	 Decreases	Decreases basal insulin delivery if sensor glucose is predicted to be below 112.5 mg/dL.
70 mg/dL	 Stops	Stops basal insulin delivery if sensor glucose is predicted to be below 70 mg/dL.

Omnipod 5



- Patch pump
 - Infuzyon seti olmadan direkt cilt altına insulin infuzyonu
 - Insulin algoritması pompa (pod) içinde
 - Android telefon app ile insulin dozu ayarlamak mümkün (telefon yakında olmasa bile)
 - -Hedef kan şekeri 110-150 arası değiştirebiliyor



MiniMed® 670G



MiniMed® 770G



MiniMed® 780G



Control IQ



Omnipod 5

Pompa	Minimed	Minimed	Tslim X2	Omnipod
CGM	Guardian 3	Guardian 3	Dexcom G6	Dexcom G6
Sistemi Baslatma	3-6 gun insulin data	3-6 gun insulin data	Diyabetli kisinin kilosu (kg)	Son pod degisimindeki total gunluk insulin dozu
Otomatik sistemden cikis	Safe basal: 1.max/min delivery 2.loss of CGM connection or system concerns regarding CGM accuracy	Time to exit (similar to safe basal) Lasts 4 hours before exit to manual mode Fingerstick BG to prevent exit to manual mode	Gecis donemi olmadan otodan manuel sisteme geciyor	Automated limited: static basal without SG dependent adjustment Activates AL if no CGM data >+20min Or Min/max delivery constraints



MiniMed® 670G



MiniMed® 770G



MiniMed® 780G



Otomatik sistem cikis	90 dk safe basal sonrası otomatik sistemden cikis	4 saat safe basal sonrası otomatik sistemden çıkış	CGM bağlantısı yoksa 20dk sonra otomatik sistemden çıkıyor	Sınırlı otomatik sistemde bir kaç saat kalıp manuele geçiyor
Hedef CGM değeri	120	100 Ya da 120	112.5-160 Uyku: 112.5-120 Egzersiziz: 140-160	110,120, 130,140,150mg/dl Hipoglisemi koruma: hedefi 150 ye değiştirip, insulini de azaltıyor (1-72hr)
Yuksek kan şekeri düzeltme Otomatik	150 —	120 KS>120	110 + Uyku modunda yok	
Insulin zamani	degistirilebilir	degistirilebilir	5saat (sabit)	degistirilebilir

open source do-it-yourself (DIY) Loop code base

#OpenAPS:



Taking the DIY, artificial pancreas from (n=1) to (n=1)*many by:



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@DanaMLewis

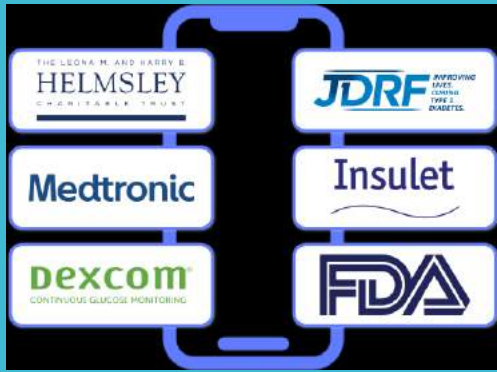
Reference design, code, documentation at OpenAPS.org

Open APS -Kendi Yapay Pankreasini Kendin Yap Sistemi





Tidepool-Loop



- ACE Pump
 - “alternate controller-enabled”
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 - “interoperable automated glycemic controller”
- #WeAreNotWaiting



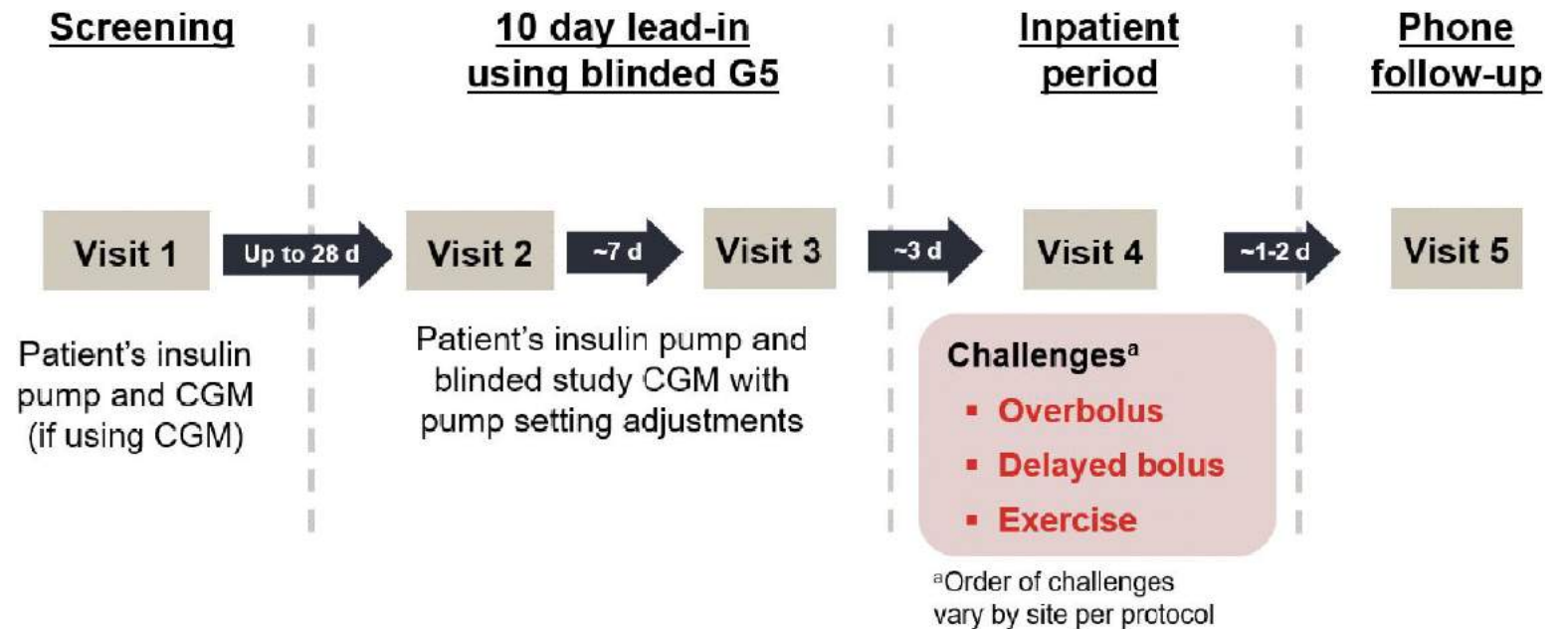
Projects / Tidepool Loop / Loop Sprint

Loop Sprint 9

8 days remaining | Complete sprint

NEW 6	IN PROGRESS 7	BLOCKED 3	IN CODE REVIEW 4	IN DESIGN REVIEW 2	WAITING FOR TEST 5	IN TEST 1	WAITING FOR APPROVAL 4
<ul style="list-style-type: none"> Insulin Delivery Table header calculation (LOOP-966) Review and create an initial test using the scenarios in loop (Test automation of Loop) (LOOP-959) Resolve ownership and collaboration of stores and managers in Loop (LOOP-969) Review loop risks and plan UI testing priorities from that (LOOP-978) Rename 'Override Presets' to 'Custom Presets' (LOOP-918) Refine interaction between Pre-Meal mode and overrides (LOOP-914) 	<ul style="list-style-type: none"> Implement TidepoolKit authentication & UI (Tidepool Kit) (LOOP-9) Implement TidepoolKit base networking (Tidepool Kit) (LOOP-1) Sensor Pair Flow Implementation (Dexcom SDK and Experience L...) (LOOP-952) Transmitter Pair Flow Implementation (Dexcom SDK and Experience L...) (LOOP-953) unintentional reset of Dexcom alert (DEXCOM ALERTING) (LOOP-941) Updated Copy for Dexcom Notifications (DEXCOM ALERTING) (LOOP-976) Automated Loop UI Smoke Test is Running as Part of Build Process (Test automation of Loop) (LOOP-938) 	<ul style="list-style-type: none"> Pairing & pod replacement screens (DASH SDK Integration) (LOOP-34) Settings Page Design Implementation (DASH SDK Integration) (LOOP-355) Setting page UI refresh (DASH SDK Integration) (LOOP-940) 	<ul style="list-style-type: none"> Device Comms Logging (DASH SDK Integration) (LOOP-354) Notifications Subviews Implementation (Dexcom SDK and Experience L...) (LOOP-933) Dexcom Settings Subviews Implementation (Dexcom SDK and Experience L...) (LOOP-934) Create API Smoke Test that can be run on a schedule from the perspective of an API client (LOOP-939) 	<ul style="list-style-type: none"> Bolus confirmation on Apple Watch (LOOP-913) Unify carb entry + bolus flow (LOOP-949) 	<ul style="list-style-type: none"> Do not display stale BG data. (LOOP-927) DIY Sync (LOOP-903) Fault Handling: Notifications (DASH SDK Integration) (LOOP-352) Remote Overrides (LOOP-926) Crash when attempting to deactivate pod that fails to pair. (DASH SDK Integration) (LOOP-943) 	<ul style="list-style-type: none"> Resolve CoreData migration issue with CachedInsulinDeliveryObject programmedTempBasalRate field (Tidepool Service) (LOOP-948) 	<ul style="list-style-type: none"> Refactor RemoteDataService to pull data from sources rather than have sources push data to (Tidepool Service) (LOOP-19) Implement Nightscout remote data synchronization (Tidepool Service) (LOOP-345) Transmitter EOL (3/2/10 remaining sessions) (DEXCOM ALERTING) (LOOP-955) Design updates to new carb entry screen, for small screen support (LOOP-975)

Lilly - Ypsomed Loop System



Ypsomed insulin pumpasi+Dexcom G5

iLet Beta Bionics -insulin -insulin+glucagon



- Insulin ve coklu hormone sistem (insulin+glucagon)
- Insulin rezervuar yerine kartus sistemi





Bigfoot Unity Bigfoot Loop

Pens or Pumps? YES.



Bigfoot Inject

For individuals who wish to control insulin delivery through self-administration of insulin injections



Bigfoot Loop

For individuals who wish to automate management of diabetes through a fully integrated pump system

Geleceğin Kapalı ve Yarı kapalı Sistemleri

- Insulin + hormon kombinasyonlar
- Yemek yendigini tahmin eden sensor, algoritmalar
- Nanoteknoloji patch pompalar ve CGM
- Akilli insulinler

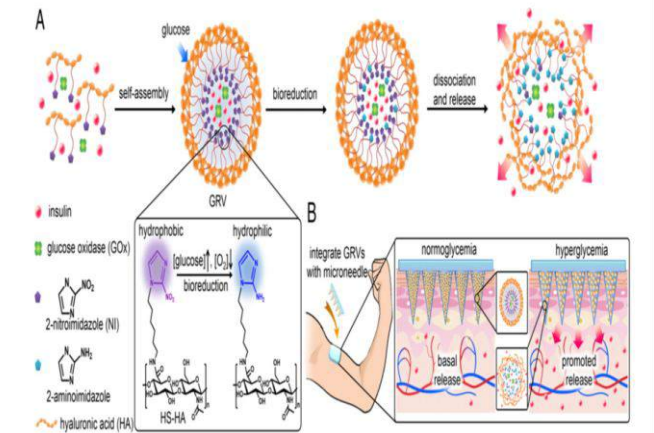
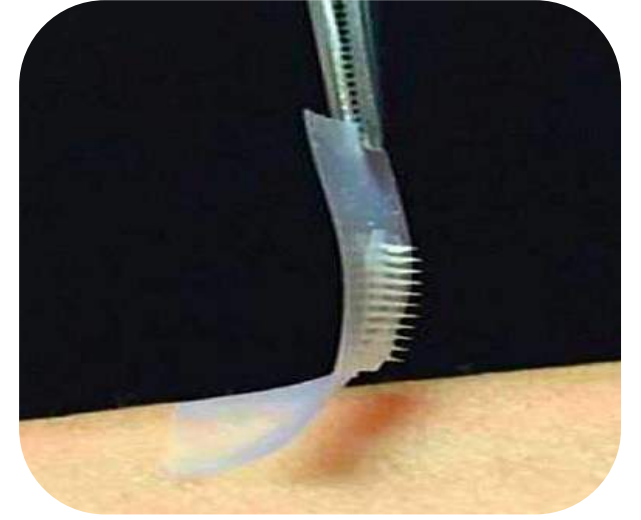
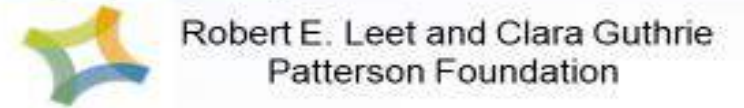


Fig. 1. Schematic of the glucose-responsive insulin delivery system using hypoxia-sensitive vesicle-loading MN-array patches. (A) Formation and mechanism of GRVs composed of HS-HA. (B) Schematic of the GRV-containing MN-array patch (smart insulin patch) for in vivo insulin delivery triggered by a hyperglycemic state to release more insulin.

1. Tai, Biomacromolecules 2014
2. Bakh et al., 2017 Nature Chemistry



Tesekkurler