For a little over a dozen years, our group has been developing, integrating, and testing various bihormonal (insulin and glucagon) bionic pancreas technologies for autonomous regulation of glycemia in people with type 1 diabetes (T1D). The technology has evolved over the years from a crude and clumsy system of interconnected pumps and sensors cobbled together around a laptop computer, to a system that runs on an iPhone, which wirelessly communicates with two infusion pumps and a sensor, and, finally, to its ultimate embodiment as a dual-chamber infusion pump, a sensor, and mathematical algorithms all housed within a single compact integrated device, which we call the iLet (in homage to the pancreatic islets of Langerhans which contain the alpha and beta cells that secrete glucagon and insulin).

The laptop version of our bionic pancreas was tested first in a diabetic swine model of T1D at Boston University (BU) between 2005 and 2009 and then in inpatient clinical trials with our collaborators at the Massachusetts General Hospital (MGH) between 2008 and 2012 in adults and adolescents with T1D. Between 2013 and 2016 we conducted outpatient clinical trials of the iPhone version of our bionic pancreas together with our clinical collaborators at MGH, Stanford, the University of North Carolina, and the University of Massachusetts. Results of these studies will be presented along with our plans for the final pivotal trials of the iLet and the pathway ahead for regulatory approval.
The long and winding road to the bionic pancreas

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The Boy Who Lived

Our Bihormonal Bionic Pancreas on the iPhone Platform
Our Bihormonal Bionic Pancreas on the iPhone Platform


Summer Camp Studies:
Summers of 2013 & 2014
Beacon Hill Study:
Q1 – Q3 2013
Bionic Pancreas Multi-Center Study:
Q2 2014 – Q2 2015


Russell et al. (2016) The Lancet Diabetes & Endocrinology

El-Khatib et al. (2016) The Lancet (appeared online ahead of print, December 19, 2016)

Clinical Results – Bihormonal Configuration

2015 Summer Camp Study: Summer 2015
32 Teens (12–20 years)
5-Day Experiments
Mean CGM: 141 ± 10 mg/dl
(Projected A1C: 6.5%)
Time < 60 mg/dl: 0.6%
Time > 180 mg/dl: 20%

Bionic Pancreas

Mean CGM: 162 ± 29 mg/dl
(Projected A1C: 7.3%)
Time < 60 mg/dl: 1.9%
Time > 180 mg/dl: 34%

Control

Mean CGM: 158 ± 27 mg/dl
(Projected A1C: 7.1%)
Time < 60 mg/dl: 2.2%
Time > 180 mg/dl: 31%

Bionic Pancreas

Mean CGM: 142 ± 12 mg/dl
(Projected A1C: 6.6%)
Time < 60 mg/dl: 1.3%
Time > 180 mg/dl: 21%

Control

2014 Summer Camp Study: Summer 2014
39 Adults (≥18 years)
11-Day Experiments
Mean CGM: 168 ± 30 mg/dl
(Projected A1C: 7.5%)
Time < 60 mg/dl: 2.8%
Time > 180 mg/dl: 36%

Control

2014 summer camp study: Summer 2014
19 Pre-Teens (6–11 years)
5-Day Experiments
Mean CGM: 142 ± 12 mg/dl
(Projected A1C: 6.6%)
Time < 60 mg/dl: 1.3%
Time > 180 mg/dl: 21%

Bionic Pancreas

Mean CGM: 137 ± 11 mg/dl
(Projected A1C: 6.4%)
Time < 60 mg/dl: 1.2%
Time > 180 mg/dl: 17%

Bionic Pancreas

Mean CGM: 130 ± 10 mg/dl
(Projected A1C: 6.1%)
Time < 60 mg/dl: 2.0%
Time > 180 mg/dl: 14%

Control
Clinical Results – Bihormonal Configuration

2013 Summer Camp Study: Summer 2013
16 Teens (12–20 years) 5-Day Experiments

2014 Summer Camp Study: Summer 2014
16 Teens (12–20 years) 5-Day Experiments

Bionic Pancreas Multi-Center Study: Q2 2014 – Q2 2015
39 Adults (≥ 18 years) 11-Day Experiments

19 Pre-Teens (6–11 years) 5-Day Experiments

TDD Insulin: 0.66 Units/kg/day
TDD Insulin: 0.62 Units/kg/day
TDD Insulin: 0.79 Units/kg/day
TDD Insulin: 0.82 Units/kg/day
TDD Insulin: 0.68 Units/kg/day
TDD Insulin: 0.68 Units/kg/day
TDD Insulin: 0.68 Units/kg/day
TDD Insulin: 0.68 Units/kg/day
TDD Glucagon: 0.51 mg/day (7 µg/kg/day)
TDD Glucagon: 0.72 mg/day (11 µg/kg/day)
TDD Glucagon: 0.36 mg/day (11 µg/kg/day)

Russell et al. (2014) 371, 313–325
New England Journal of Medicine
Russell et al. (2016) 4, 233–243
The Lancet Diabetes & Endocrinology
El-Khatib et al. (2016, in press)
The Lancet
The bionic pancreas simultaneously solves the 4 greatest concerns of T1D management:

1. It reduces mean blood sugar levels in everyone to levels that would likely eradicate long-term microvascular and neurological complications if implemented at the time of diagnosis.
2. It profoundly curtails mild low blood sugar levels in everyone, and would likely eliminate severe hypoglycemia in people with T1D.
3. It automates blood sugar control for everyone, thus unburdening people with T1D from the relentless need to comply with therapy, as the bionic pancreas itself is the first technology to be entirely compliant with the patient's needs rather than the other way around.
4. It unburdens people with T1D and their families of the emotional hardship that is, for now, part of everyday life, and of the constant fear of hypoglycemia, and of the worry and dread of long-term complications.

Clinical Results – Insulin-Only Configuration

- Mean CGM: 151 ± 26 mg/dl (Projected A1C: 6.9%)
- Time < 60 mg/dl: 2.0%
- Time > 180 mg/dl: 26%

Insulin-Only Bionic Pancreas

- Mean CGM: 160 ± 9 mg/dl (Projected A1C: 7.2%)
- Time < 60 mg/dl: 0.9%
- Time > 180 mg/dl: 30%

16 Adults (≥18 years)
7-Day Experiments

*“Do you want to follow your insulin, or do you want your insulin to follow you?”*
Clinical Results – Glucagon-Only Configuration

MGH Glucagon-Only Study: 2015
22 adults with T1D (≥ 18 years)
14-Day Experiments (7 days of exposure to glucagon-only bionic pancreas)

Mean CGM: 152 ± 27 mg/dl
Projected A1C: 6.9%
Time < 60 mg/dl: 4.7%

Control
Mean CGM: 153 ± 28 mg/dl
Projected A1C: 6.9%
Time < 60 mg/dl: 1.2%

Glucagon-Only Bionic Pancreas

Clinical Results – Comparison of Insulin-Only and Bihormonal Configurations

MGH Set-Point Study: 2015–2016
16 adults (≥ 18 years)
3-Day Experiments

Mean CGM: 151 ± 26 mg/dl
Projected A1C: 6.9%
Time < 60 mg/dl: 2.0%
Time > 180 mg/dl: 26%

Control
Mean CGM: 160 ± 9 mg/dl
Projected A1C: 7.2%
Time < 60 mg/dl: 0.9%
Time > 180 mg/dl: 30%

Bionic Pancreas

Our Bihormonal Bionic Pancreas on the iPhone Platform

the iLet™
Carry your glucose metabolism in your pocket.

How to start a bionic pancreas: The iLet set-up process...
How to give an optional meal announcement
the iLet™
Carry your glucose metabolism in your pocket.

the iLet infusion set
the iLet™ and iLet infusion set

- Carrying your glucose metabolism in your pocket.

Next Steps

- **Beacon Hill Study:** February – September 2013
- **Summer Camp Study:** Summers of 2013 & 2014
- **Bionic Pancreas Multi-Center Study:** June 2014 – April 2015
- **Bionic Pancreas Insulin-Only Study:** October 2015 – January 2016
- **Bionic Pancreas Set-Point Study:** August 2014 – Dec 2016

Clinical trials using iLet platform

Clinical trials using iPhone platform

Insulin-Only Bionic Pancreas Pivotal Trial

- **Objective and primary outcome:**
  - To test the insulin-only configuration of the iLet and iLet infusion set in the final pivotal trial after completion of the Beacon Hill Study and the Summer Camp Study. The clinical data obtained for the insulin-only configuration will be necessary and sufficient for PMA approval of the device.
  - Co-primary outcomes: HbA1c and % time CGM glucose is < 60 mg/dl

Bihormonal Bionic Pancreas Pivotal Trial (tentative)

- **Objective and primary outcome:**
  - To test the bihormonal configuration of the iLet and iLet infusion set in the final pivotal trial after completion of the Bionic Pancreas Multi-Center Study and the Summer Camp Study. The clinical data obtained for the bihormonal configuration will be necessary and sufficient for PMA approval of the device and the NDA approval of a stable, pumpable chronic-use glucagon or glucagon analog in the iLet.
  - Co-primary outcomes: HbA1c and % time CGM glucose is < 60 mg/dl

**Insulin-Only Bionic Pancreas Bridging Study:** Mid-2017

**Bihormonal Bionic Pancreas Bridging Study:** Mid-2017

**Insulin-Only Bionic Pancreas Pivotal Trial:** Begins Late-2017/Early-2018

**Bionic Pancreas Pivotal Trial:** Begins Mid-2018

**Subjects and enrollment:**
- Type 1 diabetes for at least 1 year
- Subjects drawn from 2 therapy types: CSII or MDI (at least 1/3 from each)
- 600 subjects in 3 age bins: 4–11, 12–17, ≥ 18 yr old (at least 1/3 ≥ 50 yr)
- Staged enrollment of younger subjects – Each new age cohort is enrolled sequentially, following DSMB review of drug safety data after 30 subjects are enrolled in the age cohort.

**Overall design:**
- Two-arm study: 6-month bihormonal, 6-month usual care
- Randomized parallel design with a 2:1 randomization scheme
- 6-month bridging Study: Follows 6-month usual care usual care of iLet in entire usual care cohort

**Insulin-Only Bionic Pancreas Pivotal Trial**

- **Objective and primary outcome:**
  - To test the insulin-only configuration of the iLet and iLet infusion set in the final pivotal trial after completion of the Beacon Hill Study and the Summer Camp Study. The clinical data obtained for the insulin-only configuration will be necessary and sufficient for PMA approval of the device.
  - Co-primary outcomes: HbA1c and % time CGM glucose is < 60 mg/dl
Clinical Sites for the Bionic Pancreas Pivotal Trials

Stanford (Buckingham)
West Coast Coordinating Center:
MGH (Russell)
Northeast Coordinating Center:
Barbara Davis Center (Wadwa)
Central Coordinating Center:
West Coast Clinical Sites:
UCSD (Henry)
U of Washington (Hirsch)
CHOC (Daniels)
Nemours (Mauras)
Southeast Coordinating Center:
Southeast Clinical Sites:
Children's National Health System (Cogen/Magge)
Emory/Children's Healthcare of Atlanta (Muir)
UNC, Chapel Hill (Buse)
Northeast Clinical Sites:
Cleveland Clinic (Hatipoglu)
Henry Ford Medical Center (Kruger)
Naomi Berrie Center (Goland)
Central Clinical Sites:
U of Texas, San Antonio (Hale/Lynch)
U of Texas, Southwestern (White/Raskin)
Washington University (McGill)
Jaeb Center (Beck)
National Coordinating Center:
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The Ballard Family Charitable Foundation, 2015,
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Insulet Corporation: Smiths Medical: Robert Campbell Steve Gemmell         Kevin Schmid                           Rhall Pope   Mike Blomquist
Abbott Diabetes Care: Tim Goodnow          Marc Taub          Tim Henning          Nathan Crouther         Erwin Budiman         Jared Watkin
SweetSpot Diabetes Care: Egret Technologies:
Adam Greene Justin Schumacher                                        Liam Pender
Tandem Diabetes Care: DexCom:
Sean Saint     Bob Anacone     Kim Blickenstaff Tom Peyser     Andy Balo     Terry Gregg     Tomas Walker     Kevin Sayer
INDUSTRY FUNDING
ACADEMIC 
& CLINICAL

MGH: Human trials – Steven Russell       Courtney Flynn       Laya Ekhlaspour       Kendra Magyar       Mallory Hillard       Manasi Sinha       Mary Larkin
David Nathan
Boston University: Engineering, pre-clinical trials, human trials –
Firas El-Khatib      Raj Setty      Rob LeBourdais      Alex O'Donovan       John Jiang
Kirk Ramey      Scott Scolnick      Katherine McKeon      Niall Kavanagh
Clara Barton Center: Summer Camp Studies –
Mark Bissell          Lynn Butler          Kevin Wilcoxen          Beth Rowe
University of Massachusetts, University of North Carolina: Bionic Pancreas Multi-Center Study –
David Harlan          Celia Hartigan          John Buse
Jamie Diner         Milana Dezube
Stanford: Human trials –
Bruce Buckingham       Trang Ly       Paula Clinton       Eliana Frank
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OUR VOLUNTEERS

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