The bionic pancreas

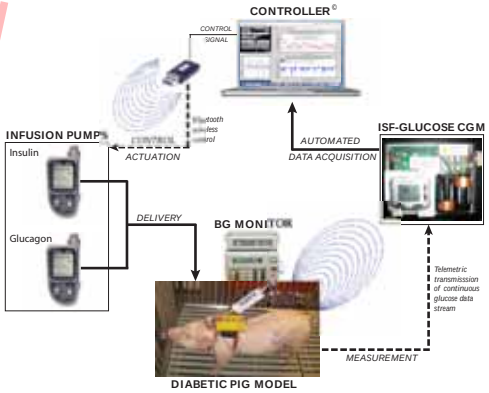
Edward Damiano, PhD

Department of Biomedical Engineering
Boston University, Boston, MA

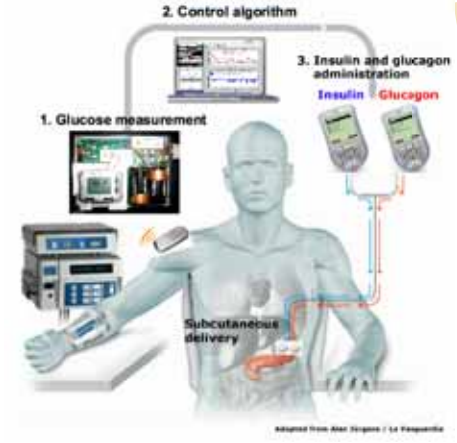
History of Preclinical and Inpatient Studies (2006–2012)

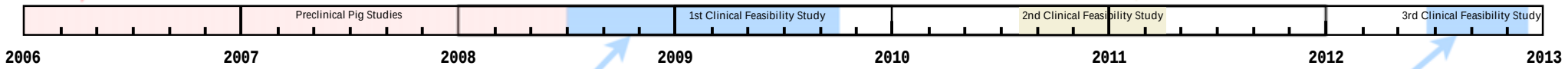
TIMELINE OF PREVIOUS PRECLINICAL AND INPATIENT STUDIES

Preclinical Pig Studies: 2006–2009

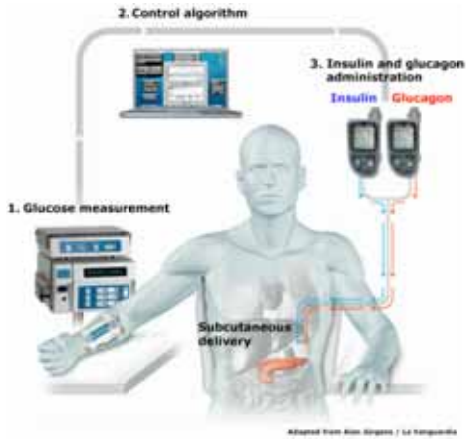


2nd Clinical Feasibility Study: 2010–2011

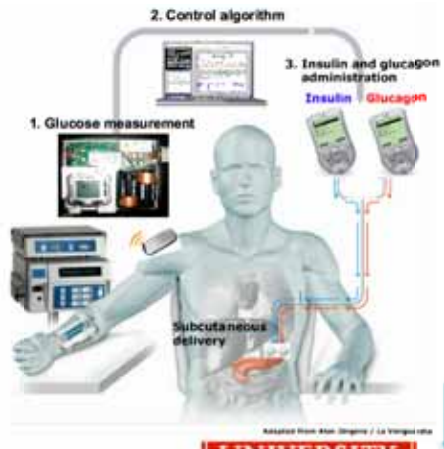




1st Clinical Feasibility Study: 2008–2009



3rd Clinical Feasibility Study: 2012



UNIVERSITY

MGH 1811

DIABETES

A Bihormonal Closed-Loop Artificial Pancreas for Type 1 Diabetes

Firas H. El-Khatib,[1]* Steven J. Russell,[2]*† David M. Nathan,[2] Robert G. Sutherlin,[2] Edward R. Damiano[1]

(Published 14 April 2010; Volume 2 Issue 27 27ra27)

Automated control of blood glucose (BG) concentration is a long-sought goal for type 1 diabetes therapy. We have developed a closed-loop control system that uses frequent measurements of BG concentration along with subcutaneous delivery of both the fast-acting insulin analog lispro and glucagon (to imitate normal physiology) as directed by a computer algorithm. The algorithm responded only to BG concentrations and incorporated a pharmacokinetic model for lispro. Eleven subjects with type 1 diabetes and no endogenous insulin secretion were studied in 27-hour experiments, which included three carbohydrate-rich meals. In six subjects, the closed-loop system achieved a mean BG concentration of 140 mg/dl, which is below the mean BG concentration target of ≤154 mg/dl recommended by the American Diabetes Association. There were no instances of treatment-requiring hypoglycemia. Five other subjects exhibited hypoglycemia that required treatment; however, these individuals had slower lispro absorption kinetics than the six subjects that did not become hypoglycemic. The time-to-peak plasma lispro concentrations of subjects that exhibited hypoglycemia ranged from 71 to 191 min (mean, 117 ± 48 min) versus 56 to 72 min (mean, 64 ± 6 min) in the group that did not become hypoglycemic (aggregate mean of 84 min versus 31 min longer than the algorithm's assumption of 33 min, *P* = 0.07). In an additional set of experiments, adjustment of the algorithm's pharmacokinetic parameters (time-to-peak plasma lispro concentration set to 65 min) prevented hypoglycemia in both groups while achieving an aggregate mean BG concentration of 164 mg/dl. These results demonstrate the feasibility of safe BG control by a bihormonal artificial endocrine pancreas.

INTRODUCTION

Achieving and maintaining near-normal blood glucose (BG) concentrations are critical for successful long-term care of patients with diabetes mellitus. The Diabetes Control and Complications Trial and its long-term follow-up demonstrated the importance of maintaining glycated hemoglobin (HbA1c), an index of the mean BG concentration, as close to the nondiabetic range as possible in individuals with type 1 diabetes (*1–3*). The internationally adopted treatment goal (*4*) of maintenance of HbA1c values at <7% (corresponding to a mean BG of ~154 mg/dl) reduces the development and progression of microvascular and cardiovascular complications by as much as 76% (*1*, *2*). Unfortunately, the therapy required to achieve this goal is extremely demanding, necessitating frequent self-monitoring of BG concentrations and multiple daily insulin injections or use of an insulin pump. Even with physiologic insulin replacement in the form of a continuous insulin delivery throughout the day combined with bolus doses of insulin at meals (basal-bolus therapy), substantial hyperglycemic excursions and episodic hypoglycemia persist in most people with type 1 diabetes (*5–7*). Hypoglycemia can result in life-threatening consequences and limits the application of intensive therapy. The development of a drug delivery device that responds to glucose concentrations and automatically "clamps" BG concentrations in the nondiabetic range, a so-called artificial endocrine pancreas, has been a long-term goal to avoid the negative consequences of type 1 diabetes.

Closed-loop BG control devices require a stream of frequent glucose concentration measurements for operation. The prospect for the development of such devices has been aided by recent improvements in minimally invasive continuous glucose monitoring (CGM) and by an improved understanding of the physiologic control of glycemia (*8–10*). In individuals without diabetes mellitus, glucose concentrations are maintained between 70 and 180 mg/dl through the interplay of insulin and glucagon secreted by the pancreatic islets (*11*). Insulin is secreted in response to elevated BG and other physiologic signals and facilitates disposal of glucose into the liver and other peripheral tissues. Glucagon counters the effects of insulin and increases glucose production by the liver, stabilizing glucose concentrations after meals and preventing hypoglycemia.

Previously reported studies testing closed-loop BG control systems using subcutaneous insulin infusion have not included a physiological counterregulatory component such as glucagon (*12–16*). Those studies with experiments lasting 24 hours or more reported repeated occurrences of hypoglycemia, which required intervention with carbohydrate administration, as required by their protocols (*17*, *18*).

On the basis of the physiological principles of endogenous BG regulation, we have developed a computer control algorithm that makes automated dosing decisions for subcutaneous insulin and glucagon administration based on regularly sampled BG concentrations measured every 5 min. This BG control algorithm has previously been tested in a porcine model of insulin-deficient diabetes (*17*, *18*). We report here our results with this bihormonal artificial endocrine pancreas in human subjects with type 1 diabetes.

[1]Department of Biomedical Engineering, Boston University, Boston, MA 02215, USA. [2]Diabetes Unit and Department of Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, MA 02114, USA.
*These authors contributed equally to this work.
†To whom correspondence should be addressed. E-mail: sjrussel@partners.org

Blood Glucose Control in Type 1 Diabetes With a Bihormonal Bionic Endocrine Pancreas

Steven J. Russell, MD, PhD[1]
Firas H. El-Khatib, PhD[1]
David M. Nathan, MD[1]
Kendra L. Magyar, MSN, NP[1]
John Jiang, BS[2]
Edward R. Damiano, PhD[2]

OBJECTIVE—To test whether safe and effective glycemic control could be achieved in type 1 diabetes using a bihormonal bionic endocrine pancreas driven by a continuous glucose monitor in experiments lasting more than two days and including six high-carbohydrate meals and exercise as challenges to glycemic control.

RESEARCH DESIGN AND METHODS—Six subjects with type 1 diabetes and no endogenous insulin secretion participated in two 51-h experiments. Blood glucose was managed with a bionic endocrine pancreas controlling subcutaneous delivery of insulin and glucagon with insulin pumps. A partial meal-priming bolus of insulin (0.035 units/kg/meal, then 0.05 units/kg/meal in repeat experiments) was administered at the beginning of each meal (on average 78 ± 12 g of carbohydrates per meal were consumed). Plasma glucose (PG) control was evaluated with a reference quality measurement on venous blood every 15 min.

RESULTS—The overall mean PG was 158 mg/dL, with 68% of PG values in the range of 70–180 mg/dL. There were no significant differences in mean PG between larger and smaller meal-priming bolus experiments. Hypoglycemia (PG <70 mg/dL) was rare, with eight incidents during 576 h of closed-loop control (0.7% of total time). During 192 h of nighttime control, mean PG was 123 mg/dL, with 93% of PG values in the range of 70–180 mg/dL and only one episode of mild hypoglycemia (minimum PG 62 mg/dL).

CONCLUSIONS—A bihormonal bionic endocrine pancreas achieved excellent glycemic control with minimal hypoglycemia over the course of two days of continuous use despite high-carbohydrate meals and exercise. A trial testing a wearable version of the system under free-living conditions is justified.

Diabetes Care 35:2148–2155, 2012

Development of a fully or semiautomated device that achieves glycemic levels demonstrated to reduce long-term complications (*1–4*) while lowering the risk for hypoglycemia (*5*) and reducing patient burden has long been a goal in the treatment of type 1 diabetes and would improve quality of life for people with type 1 diabetes. We previously demonstrated the feasibility of safe and effective bihormonal therapy with subcutaneous insulin and glucagon directed by a computer algorithm using frequently sampled venous plasma glucose (PG) in sedentary subjects over the course of 27 h (*6*). In the same study we also compared the accuracy and reliability of three commercially available continuous glucose monitors (CGMs) in each subject. Based on these results and preclinical studies in diabetic pigs, we hypothesized that glycemic control could be achieved in humans with type 1 diabetes using glucose values from one of these CGMs as the sole input to the controller. Here, we report the results of a study testing this hypothesis in experiments more than 2 days in length that included six high-carbohydrate meals and a period of exercise as challenges to glycemic control. Subcutaneous dosing of glucagon and insulin was controlled by an algorithm requiring only the subject weight for initialization.

RESEARCH DESIGN AND METHODS

Subjects

The protocol was approved by the Massachusetts General Hospital (MGH) and Boston University Human Research Committees, and all participants gave written informed consent. At baseline, subjects were required to be 18 years of age or older, have had type 1 diabetes for at least 1 year, and be treated with an insulin pump. In addition, glycated hemoglobin A_{1c} (HbA_{1c}) had to be ≤9.0%, BMI had to be 20–35 kg/m^2, daily insulin requirement was ≤1 units/kg/day, and a peak stimulated C-peptide level had to be ≤0.1 nmol/L after a mixed meal tolerance test. Other criteria are detailed in the Supplementary Data.

Closed-loop glucose control system

Insulin and glucagon were administered under closed-loop control (Supplementary Fig. 1) using control algorithms similar to those previously described (*6*). The only input signal was data from the Freestyle Navigator (Abbott Diabetes Care), an interstitial fluid CGM approved by the U.S. Food and Drug Administration (FDA). Insulin dosing was controlled by a customized model predictive control algorithm incorporating a pharmacokinetic model for insulin lispro that assumed a t_{max} of 65 min. Glucagon dosing was controlled by a customized proportional derivative algorithm. Insulin lispro and glucagon (Eli Lilly) were administered subcutaneously by OmniPod pump systems (Insulet). With the exception of a weight-based partial meal-priming bolus, delivered at the

From the [1]Diabetes Unit and Department of Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts; and the [2]Department of Biomedical Engineering, Boston University, Boston, Massachusetts.
Corresponding author: Edward R. Damiano, edamiano@bu.edu.
Received 12 January 2012 and accepted 12 June 2012.
DOI: 10.2337/dc12-0071. Clinical trial reg. no. NCT01161862, clinicaltrials.gov.
This article contains Supplementary Data online at http://care.diabetesjournals.org/lookup/suppl/doi:10.2337/dc12-0071/-/DC1.
S.J.R. and F.H.K. share equal responsibility for this work.

See accompanying commentary, p. 2111.

Autonomous and Continuous Adaptation of a Bihormonal Bionic Pancreas in Adults and Adolescents With Type 1 Diabetes

Firas H. El-Khatib,* Steven J. Russell,* Kendra L. Magyar, Manasi Sinha, Katherine McKeon, David M. Nathan, and Edward R. Damiano

Department of Biomedical Engineering (F.H.E.-K., K.M., E.R.D.), Boston University, Boston, Massachusetts 02215; and Diabetes Unit and Department of Medicine (S.J.R., K.L.M., M.S., D.M.N.), Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts 02114

Context: A challenge for automated glycemic control in type 1 diabetes (T1D) is the large variation in insulin needs between individuals and within individuals at different times in their lives.

Objectives: The objectives of the study was to test the ability of a third-generation bihormonal bionic pancreas algorithm, initialized with only subject weight; to adapt automatically to the different insulin needs of adults and adolescents; and to evaluate the impact of optional, automatically adaptive meal-priming boluses.

Design: This was a randomized controlled trial.

Setting: The study was conducted at an inpatient clinical research center.

Patients: Twelve adults and 12 adolescents with T1D participated in the study.

Interventions: Subjects in each age group were randomized to automated glycemic control for 48 hours with or without automatically adaptive meal-priming boluses.

Main Outcome Measures: Mean plasma glucose (PG), time with PG less than 60 mg/dL, and insulin total daily dose were measured.

Results: The 48-hour mean PG values with and without adaptive meal-priming boluses were 132 ± 9 vs 146 ± 9 mg/dL (*P* = .03) in adults and 162 ± 6 vs 175 ± 9 mg/dL (*P* = .01) in adolescents. Adaptive meal-priming boluses improved mean PG without increasing time spent with PG less than 60 mg/dL: 1.4% vs 2.3% (*P* = .6) in adults and 0.1% vs 0.1% (*P* = 1.0) in adolescents. Large increases in adaptive meal-priming boluses and shifts in the timing and size of automatic insulin doses occurred in adolescents. Much less adaptation occurred in adults. There was nearly a 4-fold variation in the total daily insulin dose across all cohorts (0.36–1.41 U/kg · d).

Conclusions: A single control algorithm, initialized only with subject weight, can quickly adapt to regulate glycemia in patients with TID and highly variable insulin requirements. (*J Clin Endocrinol Metab* 99: 1701–1711, 2014)

The Diabetes Control and Complications Trial and its long-term follow-up showed that maintaining mean blood glucose (BG) concentration close to the nondiabetic range prevents development of and slows progression of both microvascular and macrovascular complications in individuals with type 1 diabetes (T1D) (1–3). However, the therapy required to maintain near-normal BG values is extremely demanding for patients, requiring frequent BG

ISSN Print 0021-972X ISSN Online 1945-7197
Printed in U.S.A.

Received November 19, 2013. Accepted January 24, 2014.
First Published Online January 31, 2014

* F.H.E.K. and S.J.R. contributed equally to this work.

Abbreviations: AMB, adaptive meal-priming bolus; AUC, area under the curve; BG, blood glucose; CGM, continuous glucose monitoring; CGMG, CGM glucose; HbA1c, glycosylated hemoglobin; MARD, mean absolute relative difference; NMB, no meal-priming bolus; PG, plasma glucose; T1D, type 1 diabetes; t_{max}, peak time.

Journal of Diabetes Science and Technology
Volume 1, Issue 2, March 2007

ORIGINAL ARTICLES

Adaptive Closed-Loop Control Provides Blood-Glucose Regulation Using Dual Subcutaneous Insulin and Glucagon Infusion in Diabetic Swine

Firas H. El-Khatib, Ph.D., John Jiang, B.S., and Edward R. Damiano, Ph.D.

Abstract

Background:
In order to stave off deleterious complications of the disease, the ultimate task for people with diabetes is to maintain their blood glucose in euglycemic range. Despite technological advancements, conventional open-loop therapy often results in prolonged hyperglycemia and episodic hypoglycemia, in addition to necessitating carbohydrate counting, frequent glucose monitoring, and drug administration. The logical conclusion in the evolution of exogenous insulin therapy is to develop an automated closed-loop control system.

Methods:
Eleven closed-loop control experiments were conducted in four anesthetized diabetic pigs, with carbohydrate loads simulated by intravenous glucose administration through ear-vein catheters. Type 1 diabetes-like pathology was induced using intravenous administration of cytotoxin streptozotocin. The augmented model-predictive control algorithm accounts for the accumulation of subcutaneous insulin, which is critical in avoiding excessive insulin dosing.

Results:
Control results consistently showed successful blood-glucose regulation to euglycemic range within 80–120 minutes after intravenous glucose loads, with no incidence of hypoglycemia. This is consistent with a negative oral glucose tolerance test for diabetes and is the optimal postprandial regulation that can be achieved with subcutaneous insulin administration. Results also demonstrated the potency of subcutaneous glucagon in staving off episodic hypoglycemia and revealed efficacy of the control algorithm in coping with a twofold variation in subject weights, while simultaneously overlooking erratic blood-glucose fluctuations.

Conclusions:
Using an automated adaptive glucose-control system, we show successful blood-glucose regulation *in vivo* and establish, definitively, the plausibility and practicality of closed-loop blood-glucose control using subcutaneous insulin and glucagon infusion in type 1 diabetes. The control system strikes an intricate balance between tight blood-glucose control and optimal drug consumption, while simultaneously maintaining emphasis on simplicity and reliability.

J Diabetes Sci Technol 2007; 2:181-192

Author Affiliation: Department of Biomedical Engineering, Boston University, Boston, Massachusetts

Abbreviations: (BG) blood glucose, (GPC) generalized predictive control, (IV) intravenous, (STZ) streptozotocin, (SC) subcutaneous

Keywords: counterregulatory hormone, hyperglycemia, hypoglycemia, infusion pump, *in vivo*, predictive control, swine

Corresponding Author: Edward R. Damiano, Ph.D., Associate Professor, Department of Biomedical Engineering, Boston University, 44 Cummington Street, Boston, MA 02215; email address edamiano@bu.edu

Journal of Diabetes Science and Technology
Volume 3, Issue 4, July 2009

ORIGINAL ARTICLES

A Feasibility Study of Bihormonal Closed-Loop Blood Glucose Control Using Dual Subcutaneous Infusion of Insulin and Glucagon in Ambulatory Diabetic Swine

Firas H. El-Khatib, Ph.D, John Jiang, B.S., and Edward R. Damiano, Ph.D.

Abstract

Background:
We sought to test the feasibility and efficacy of bihormonal closed-loop blood glucose (BG) control that utilizes subcutaneous (SC) infusion of insulin and glucagon, a model-predictive control algorithm for determining insulin dosing, and a proportional-derivative control algorithm for determining glucagon dosing.

Methods:
Thirteen closed-loop experiments (~7–27 h in length) were conducted in six ambulatory diabetic pigs weighing 26–50 kg. In all experiments, venous BG was sampled through a central line in the vena cava. Efficacy was evaluated in terms of the controller's ability to regulate BG in response to large meal disturbances (~5 g of carbohydrate per kilogram of body mass per meal) based only on regular frequent venous BG sampling and requiring only the subject's weight for initialization.

Results:
Closed-loop results demonstrated successful BG regulation to normoglycemic range, with average insulin-to-carbohydrate ratios between ~1:20 and 1:40 U/g. The total insulin bolus doses averaged ~6 U for a meal containing ~6 g per kilogram body mass. Mean BG values in two 24 h experiments were ~142 and ~155 mg/dl, with the total daily dose (TDD) of insulin being ~0.8–1.0 U per kilogram of body mass and the TDD of glucagon being ~0.02–0.05 mg. Results also affirmed the efficacy of SC doses of glucagon in staving off episodic hypoglycemia.

Conclusions:
We demonstrate the feasibility of bihormonal closed-loop BG regulation using a control system that employs SC infusion of insulin and glucagon as governed by an algorithm that reacts only to BG without any feed-forward information regarding carbohydrate consumption or physical activity. As such, this study can reasonably be regarded as the first practical implementation of an artificial endocrine pancreas that has a hormonally derived counterregulatory capability.

J Diabetes Sci Technol 2009;3(4):789-803

Author Affiliation: Department of Biomedical Engineering, Boston University, Boston, Massachusetts

Abbreviations: (A1C) hemoglobin A1c, (BG) blood glucose, (CGM) continuous glucose monitoring, (FDA) Food and Drug Administration, (GPC) generalized predictive control, (ISF) interstitial fluid, (IV) intravenous, (SC) subcutaneous, (STZ) streptozotocin, (TDD) total daily dose

Keywords: counterregulatory hormone, hyperglycemia, hypoglycemia, infusion pump, *in vivo*, pig, predictive control

Corresponding Author: Edward R. Damiano, Ph.D., Department of Biomedical Engineering, Boston University. 44 Cummington St., Boston, MA 02215, email address edamiano@bu.edu

Components of Our Outpatient Bihormonal Bionic Pancreas

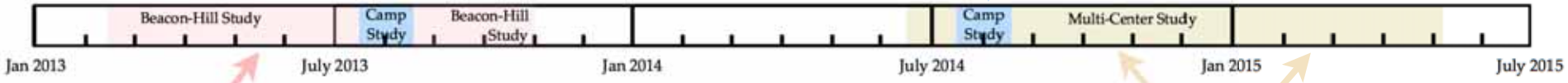
Our standalone, wearable iPhone-driven system for automated blood-glucose regulation in T1D

BOSTON UNIVERSITY MGH 1811

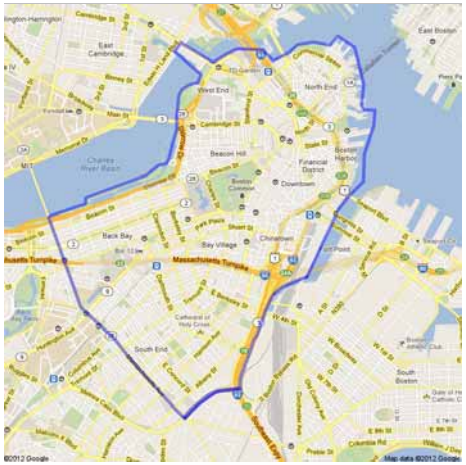
Bionic Pancreas Out-Patient Studies (2013–2015)

TIMELINE OF BIONIC PANCREAS OUTPATIENT STUDIES (2013–2015)

Summer Camp Studies: Summers of 2013 & 2014



Beacon Hill Study: First Half 2013, Fall 2013

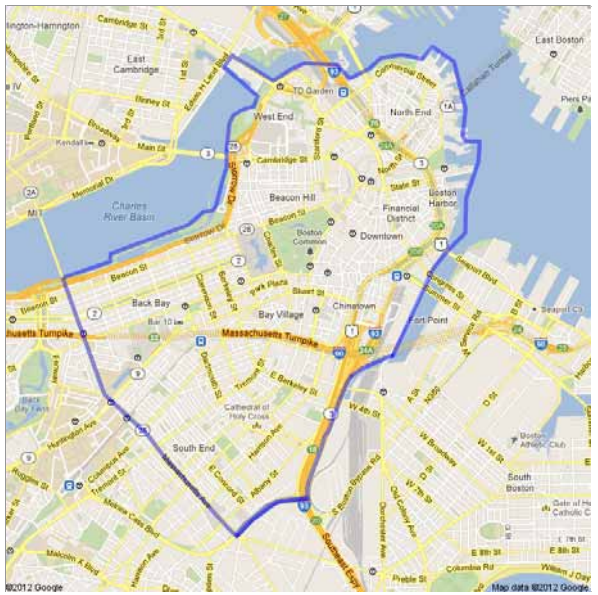


Bionic Pancreas Multi-Center Study: Spring 2014 – Q2 2015

THE BEACON HILL STUDY

- 5-day experiments in adults with T1D
  - Randomized cross-over design (5 days on bionic pancreas, 5 days usual care)
  - Free run of Boston peninsula east of Mass Ave (three square mile area)
  - Point of care capillary BG checks during day, 1:1 nursing
  - Sleep in hotel with venous BG monitoring at night, 1:2 nursing
  - 20 adult subjects 21 years and older (100 bionic pancreas days)

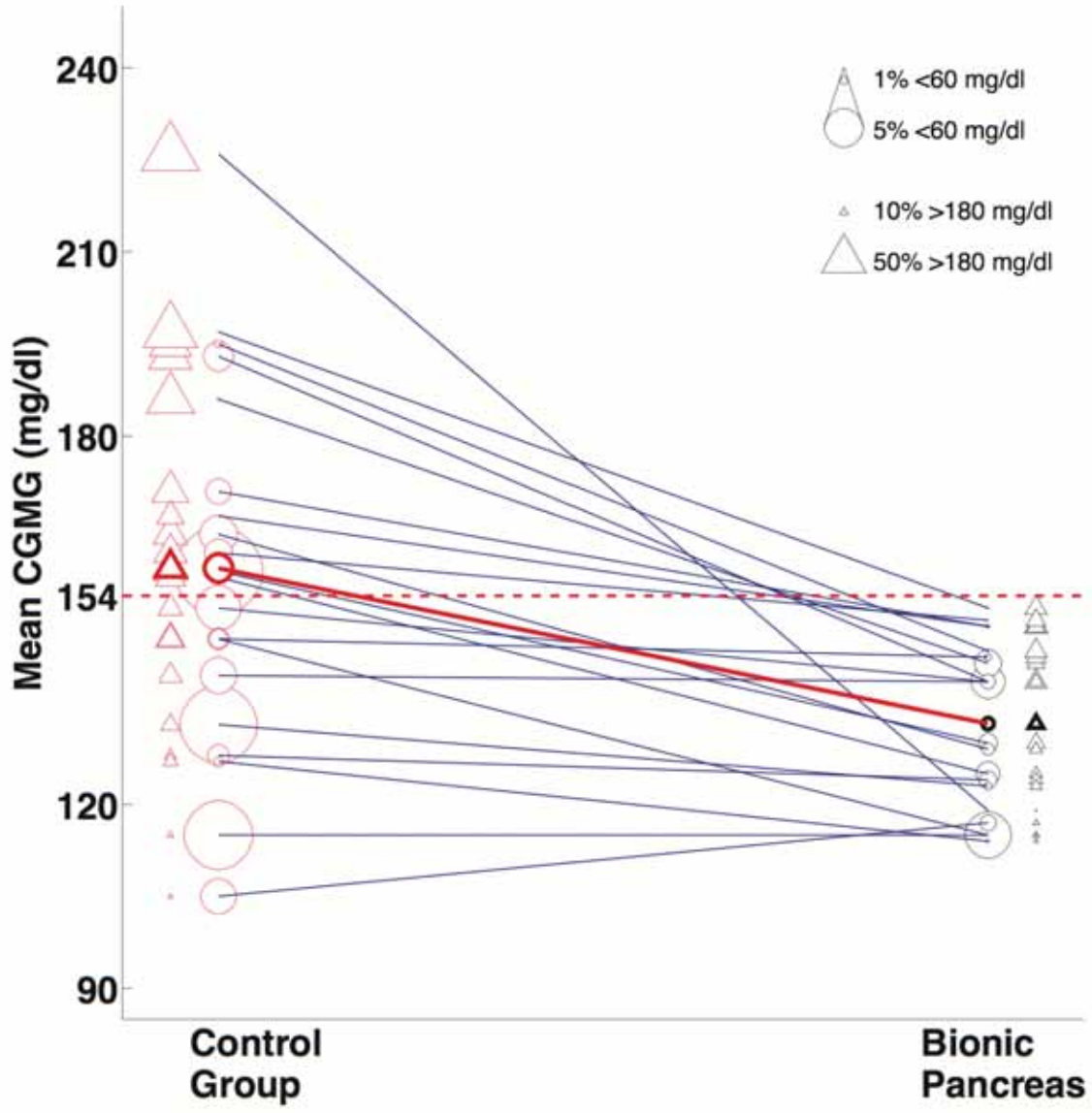
First Half 2013, Fall 2013



BOSTON UNIVERSITY

MGH 1811

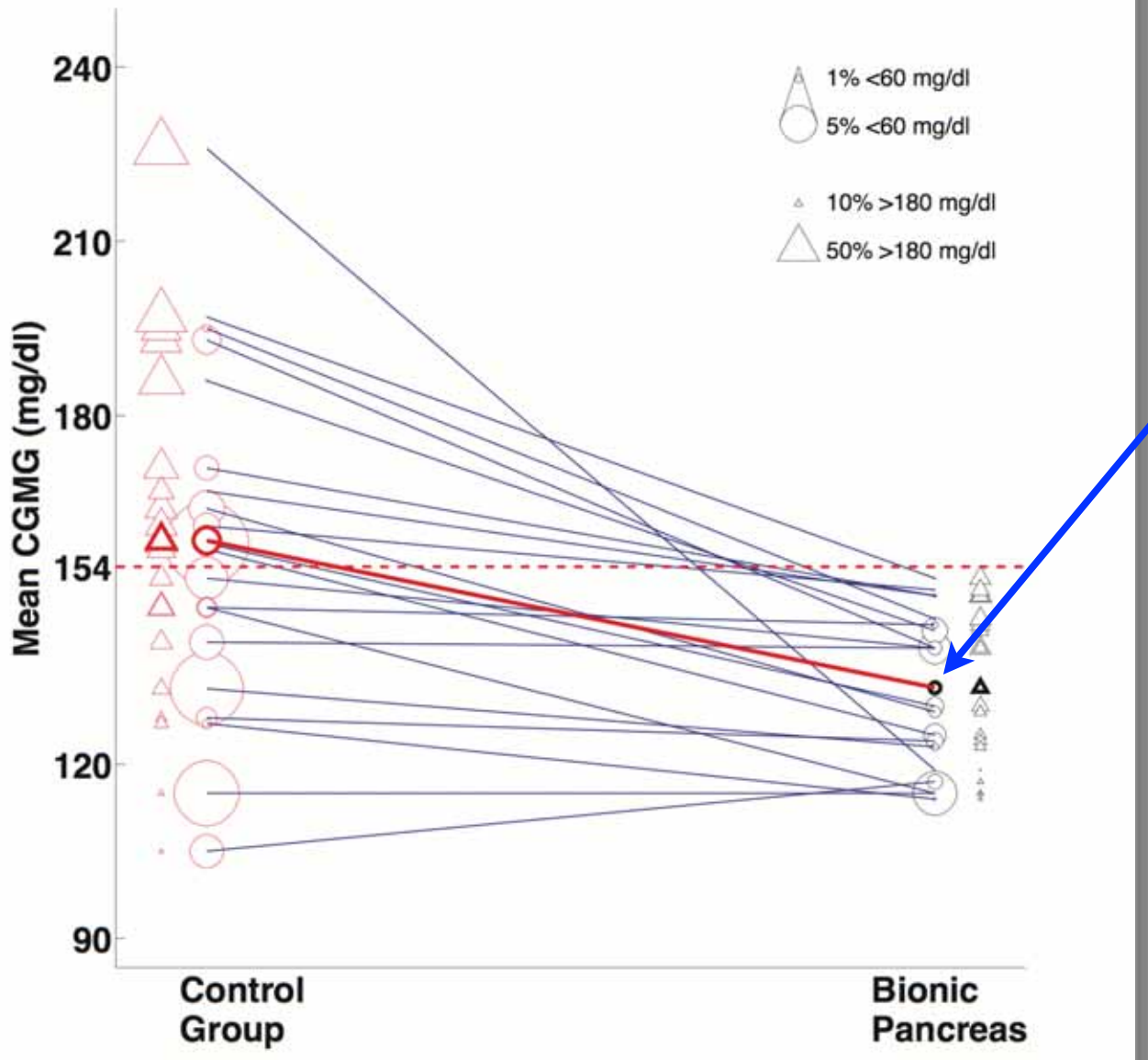
Summary Results from Beacon Hill Study (Days 2–5)



BOSTON UNIVERSITY

MGH 1811

Summary Results from Beacon Hill Study (Days 2–5)



On Bionic Pancreas

Mean CGM: 133 mg/dl
(Projected A1C: 6.2%)

Time < 60 mg/dl: 1.5%
Time > 180 mg/dl: 16%

BOSTON UNIVERSITY
MGH 1811

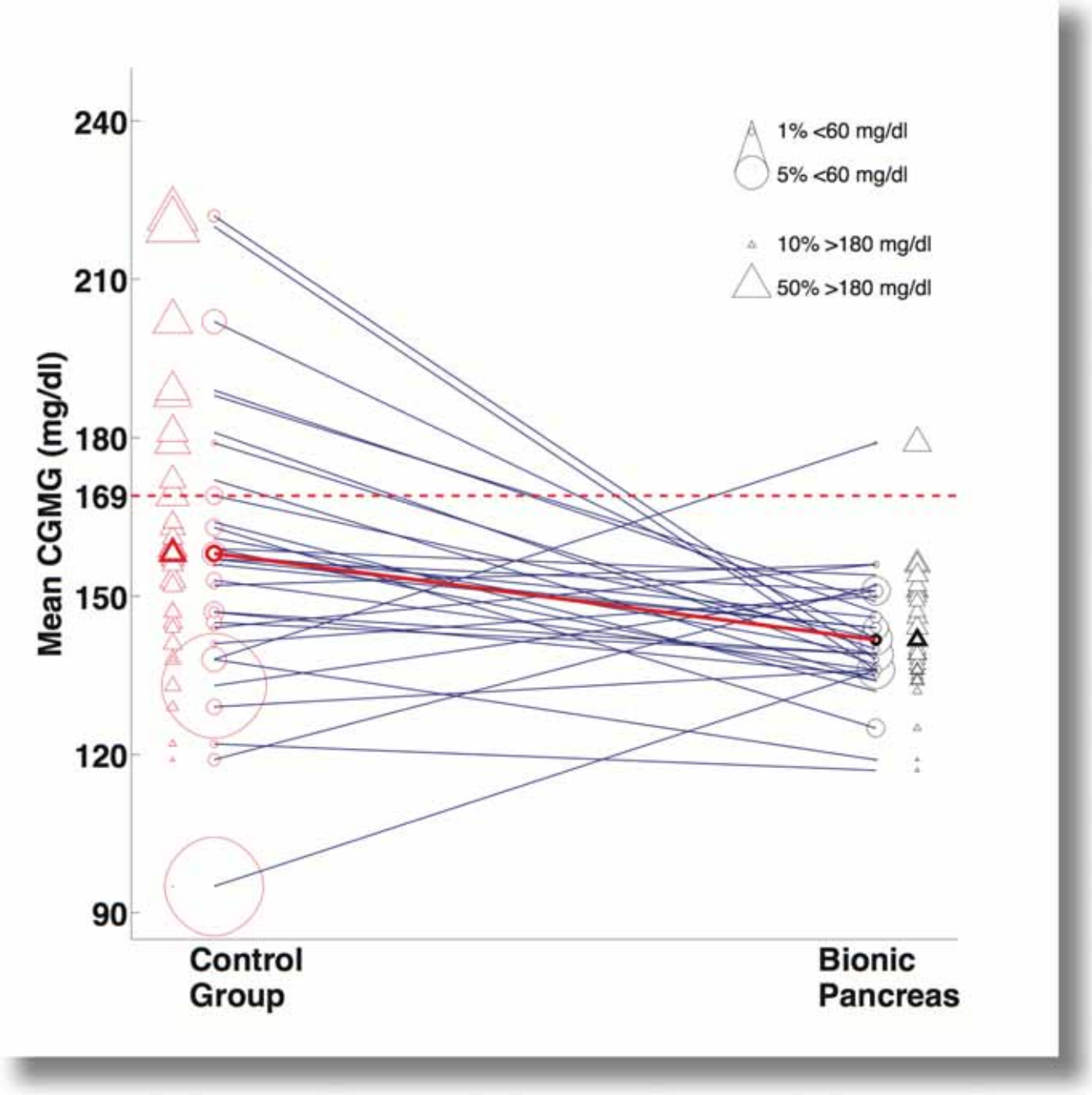
2013 SUMMER CAMP STUDY

- 5-day experiments in adolescents with T1D
  - Randomized cross-over design (5 days on bionic pancreas, 5 days on insulin pump therapy)
  - Integrated camp experience at Camp Joslin (boys) and Clara Barton Camp (girls)
  - Point of care capillary BG checks during day and night
  - Study staff and camp staff provide 24-hour coverage; round-the-clock telemetry to monitor glycemia
  - 16 boys, 16 girls (12–20 years old) with T1D (160 bionic pancreas days)

Summer 2013

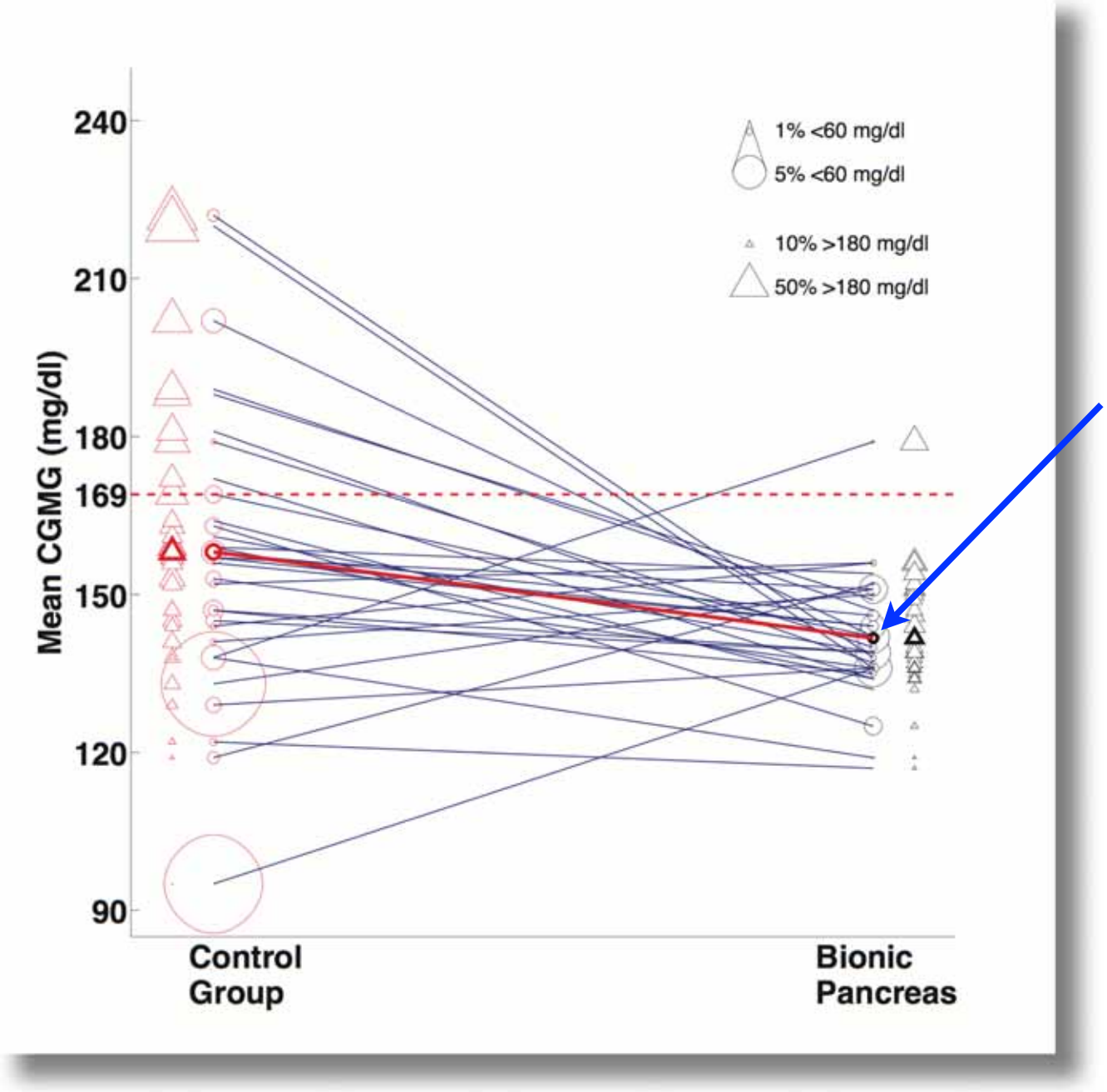
BOSTON UNIVERSITY MGH 1811

Summary Results from 2013 Summer Camp Study (Days 2–5)



BOSTON UNIVERSITY

Summary Results from 2013 Summer Camp Study (Days 2–5)



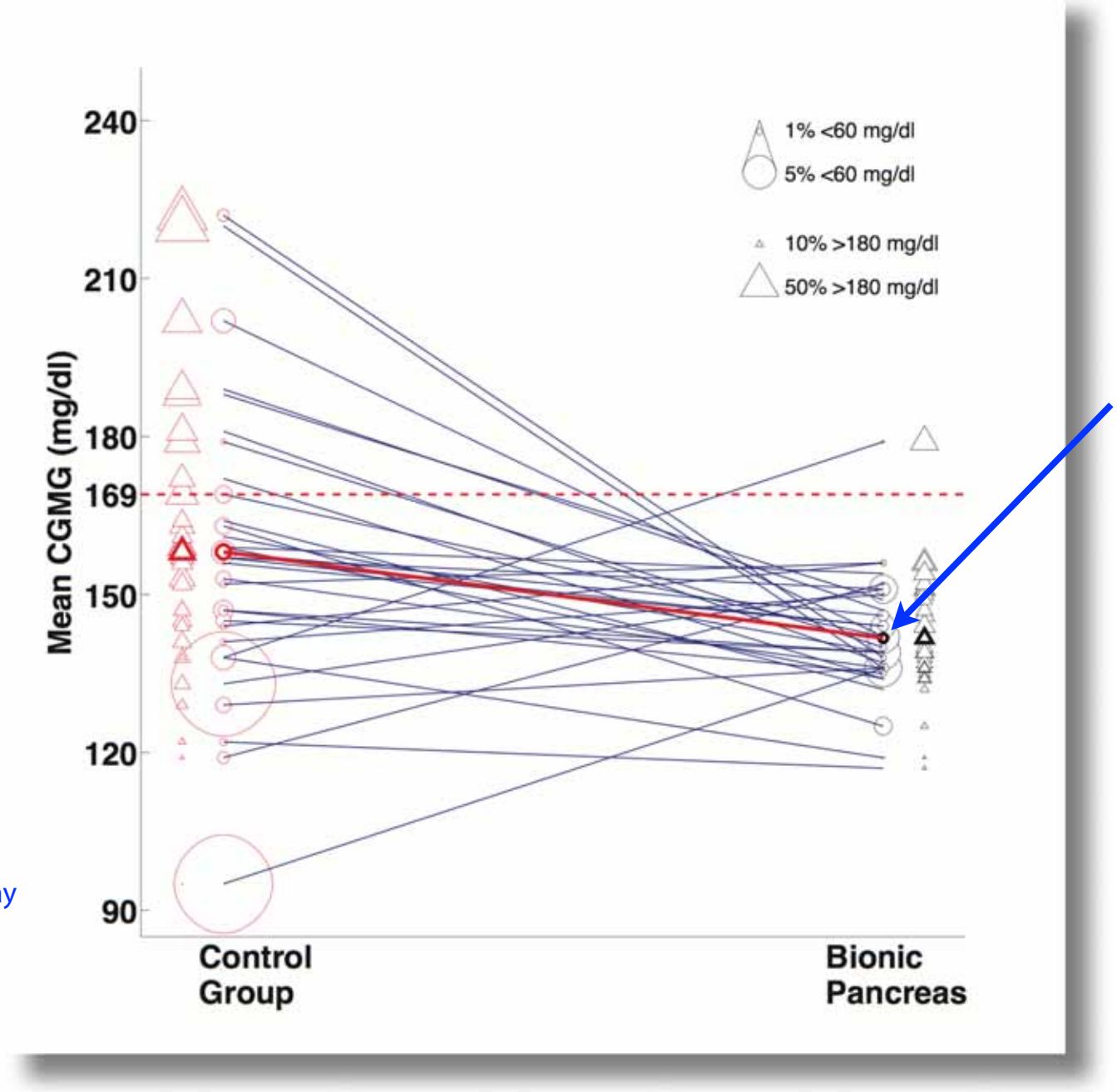
On Bionic Pancreas

Mean CGM: 142 mg/dl
(Projected A1C: 6.6%)

Time < 60 mg/dl: 1.3%
Time > 180 mg/dl: 21%

BOSTON UNIVERSITY

Summary Results from 2013 Summer Camp Study (Days 2–5)



TDD insulin:

0.79 Unit/kg/day

On Bionic Pancreas

Mean CGM: 142 mg/dl
(Projected A1C: 6.6%)

Time < 60 mg/dl: 1.3%
Time > 180 mg/dl: 21%

TDD insulin:

0.82 Unit/kg/day

BOSTON UNIVERSITY

ORIGINAL ARTICLE

Outpatient Glycemic Control with a Bionic Pancreas in Type 1 Diabetes

Steven J. Russell, M.D., Ph.D., Firas H. El-Khatib, Ph.D., Manasi Sinha, M.D., M.P.H., Kendra L. Magyar, M.S.N., N.P., Katherine McKeon, M.Eng., Laura G. Goergen, B.S.N., R.N., Courtney Balliro, B.S.N, R.N., Mallory A. Hillard, B.S., David M. Nathan, M.D., and Edward R. Damiano, Ph.D.

ABSTRACT

BACKGROUND

The safety and effectiveness of automated glycemic management have not been tested in multiday studies under unrestricted outpatient conditions.

METHODS

In two random-order, crossover studies with similar but distinct designs, we compared glycemic control with a wearable, bihormonal, automated, "bionic" pancreas (bionic-pancreas period) with glycemic control with an insulin pump (control period) for 5 days in 20 adults and 32 adolescents with type 1 diabetes mellitus. The automatically adaptive algorithm of the bionic pancreas received data from a continuous glucose monitor to control subcutaneous delivery of insulin and glucagon.

RESULTS

Among the adults, the mean plasma glucose level over the 5-day bionic-pancreas period was 138 mg per deciliter (7.7 mmol per liter), and the mean percentage of time with a low glucose level (<70 mg per deciliter [3.9 mmol per liter]) was 4.8%. After 1 day of automatic adaptation by the bionic pancreas, the mean (±SD) glucose level on continuous monitoring was lower than the mean level during the control period (133±13 vs. 159±30 mg per deciliter [7.4±0.7 vs. 8.8±1.7 mmol per liter], P<0.001) and the percentage of time with a low glucose reading was lower (4.1% vs. 7.3%, P=0.01). Among the adolescents, the mean plasma glucose level was also lower during the bionic-pancreas period than during the control period (138±18 vs. 157±27 mg per deciliter [7.7±1.0 vs. 8.7±1.5 mmol per liter], P=0.004), but the percentage of time with a low plasma glucose reading was similar during the two periods (6.1% and 7.6%, respectively; P=0.23). The mean frequency of interventions for hypoglycemia among the adolescents was lower during the bionic-pancreas period than during the control period (one per 1.6 days vs. one per 0.8 days, P<0.001).

CONCLUSIONS

As compared with an insulin pump, a wearable, automated, bihormonal, bionic pancreas improved mean glycemic levels, with less frequent hypoglycemic episodes, among both adults and adolescents with type 1 diabetes mellitus. (Funded by the National Institute of Diabetes and Digestive and Kidney Diseases and others; ClinicalTrials.gov numbers, NCT01762059 and NCT01833988.)

From the Diabetes Unit and Department of Medicine, Massachusetts General Hospital and Harvard Medical School (S.J.R., M.S., K.L.M, L.G.G., C.B., M.A.H., D.M.N.), and the Department of Biomedical Engineering, Boston University (F.H.E.-K., K.M., E.R.D.) — both in Boston. Address reprint requests to Dr. Damiano at the Department of Biomedical Engineering, Boston University, Boston, MA 02215, or at edamiano@bu.edu.

Drs. Russell and El-Khatib contributed equally to this article.

This article was published on June 15, 2014, at NEJM.org.

DOI: 10.1056/NEJMoa1314474

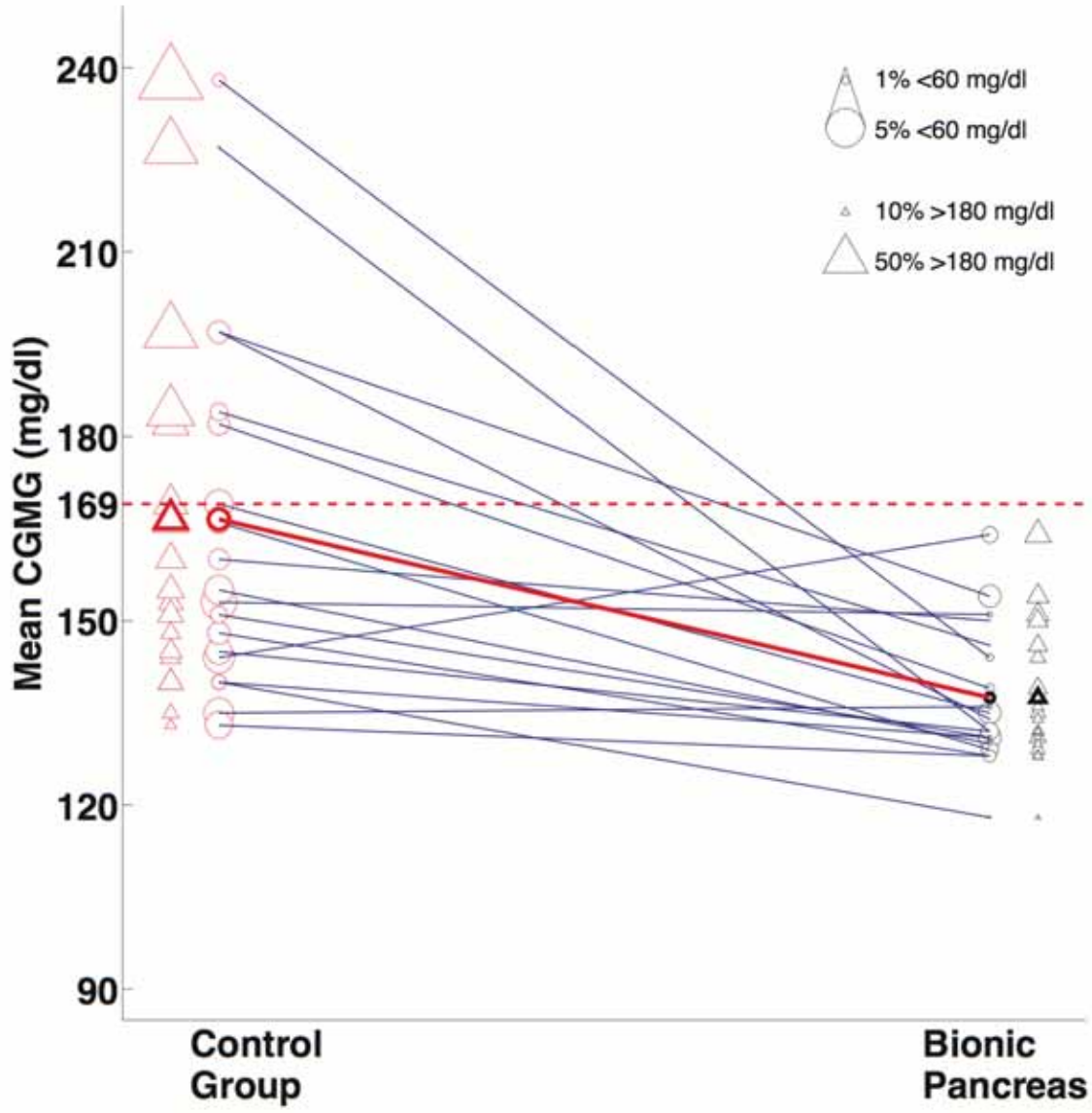
2014 SUMMER CAMP STUDY

- 5-day experiments in pre-adolescents with T1D
  - Randomized cross-over design (5 days on bionic pancreas, 5 days on insulin pump therapy)
  - Integrated camp experience at Camp Joslin (boys) and Clara Barton Camp (girls)
  - Point of care capillary BG checks during day and night
  - Study staff and camp staff provide 24-hour coverage; round-the-clock telemetry to monitor wireless connectivity of pumps and CGM
  - 6 boys, 13 girls (6–11 years old) with T1D (120 bionic pancreas days)

Summer 2014

BOSTON UNIVERSITY MGH 1811

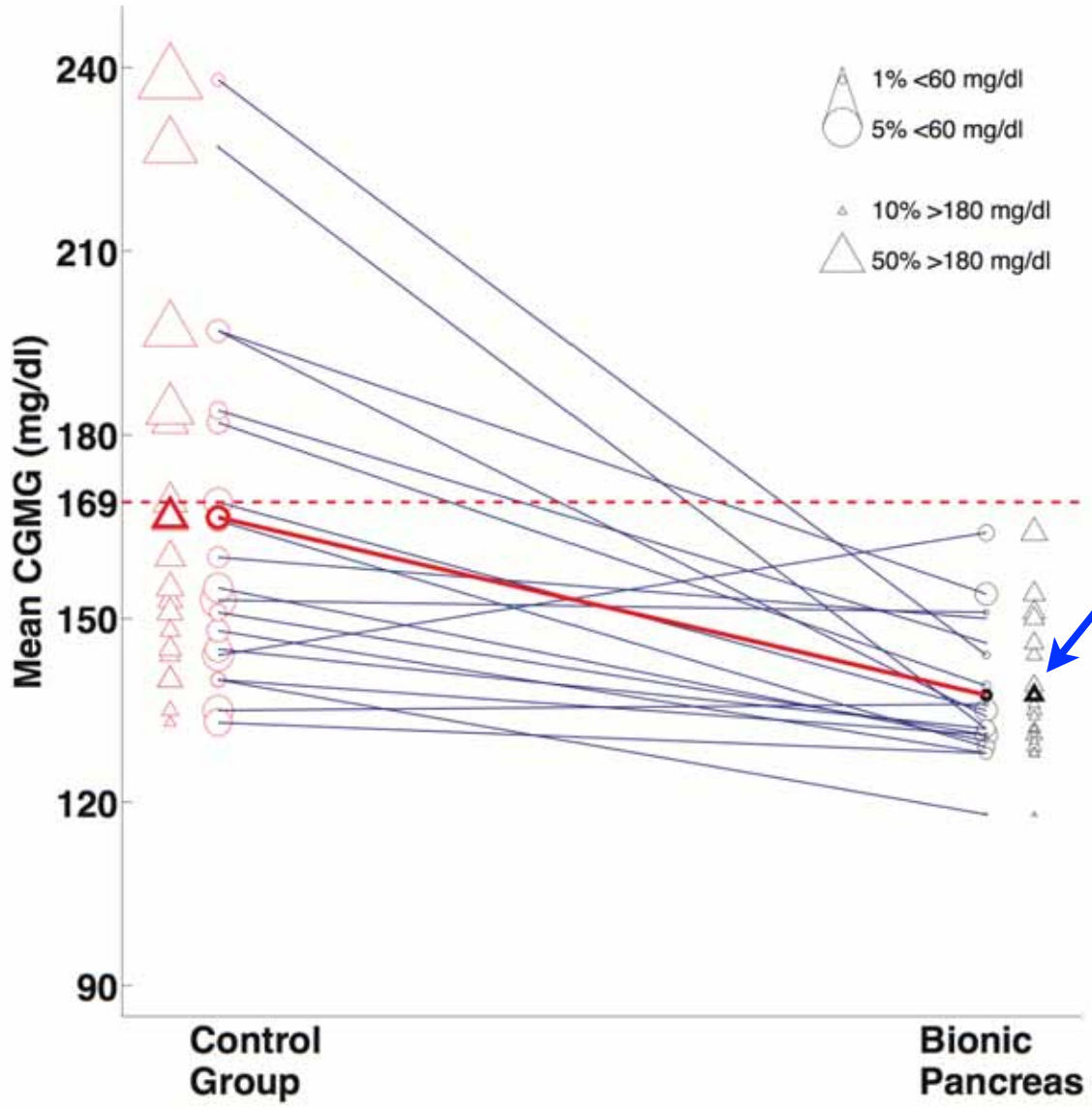
Summary Results from 2014 Summer Camp Study (Days 2–5)



BOSTON UNIVERSITY

MGH 1811

Summary Results from 2014 Summer Camp Study (Days 2–5)



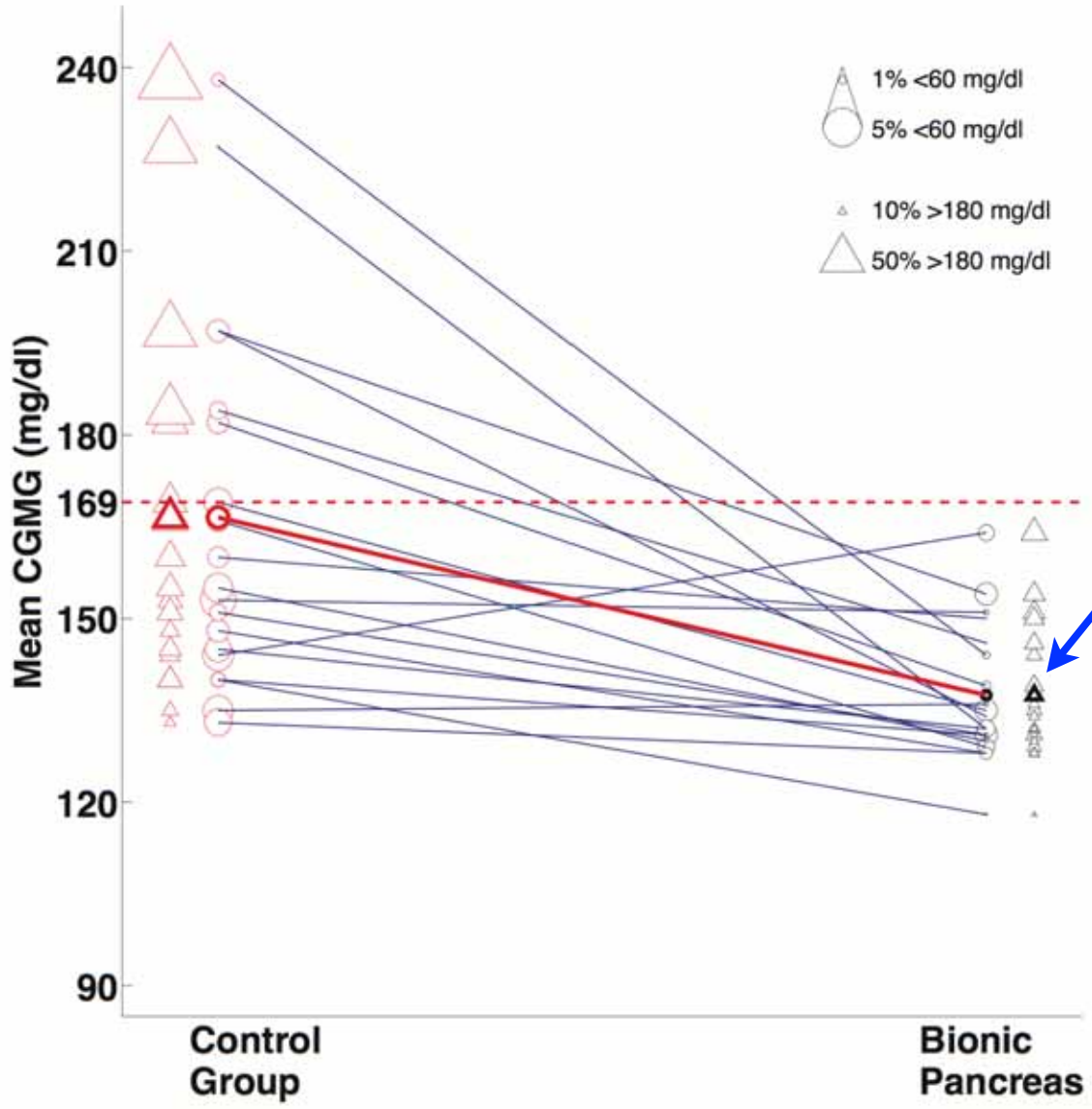
On Bionic Pancreas

Mean CGM: 137 mg/dl
(Projected A1C: 6.4%)

Time < 60 mg/dl: 1.2%
Time > 180 mg/dl: 17%

BOSTON UNIVERSITY
MGH 1811

Summary Results from 2014 Summer Camp Study (Days 2–5)



TDD insulin:

0.68 Unit/kg/day

On Bionic Pancreas

Mean CGM: 137 mg/dl
(Projected A1C: 6.4%)

Time < 60 mg/dl: 1.2%
Time > 180 mg/dl: 17%

TDD insulin:

0.66 Unit/kg/day

BOSTON UNIVERSITY MGH 1811

BOSTON UNIVERSITY MGH 1811	**Adults** (Beacon Hill)	**Teens** (2013 Summer Camp)	**Pre-Teens** (2014 Summer Camp)
Day and Night	Mean CGM: 133 mg/dl (Projected HbA1c: 6.2%) 1.5% of time < 60 mg/dl	Mean CGM: 142 mg/dl (Projected HbA1c: 6.6%) 1.3% of time < 60 mg/dl	Mean CGM: 137 mg/dl (Projected HbA1c: 6.4%) 1.2% of time < 60 mg/dl
Nighttime Only	Mean CGM: 126 mg/dl 0.4% of time < 60 mg/dl	Mean CGM: 124 mg/dl 1.0% of time < 60 mg/dl	Mean CGM: 122 mg/dl 0.6% of time < 60 mg/dl

THE BIONIC PANCREAS MULTI-CENTER STUDY

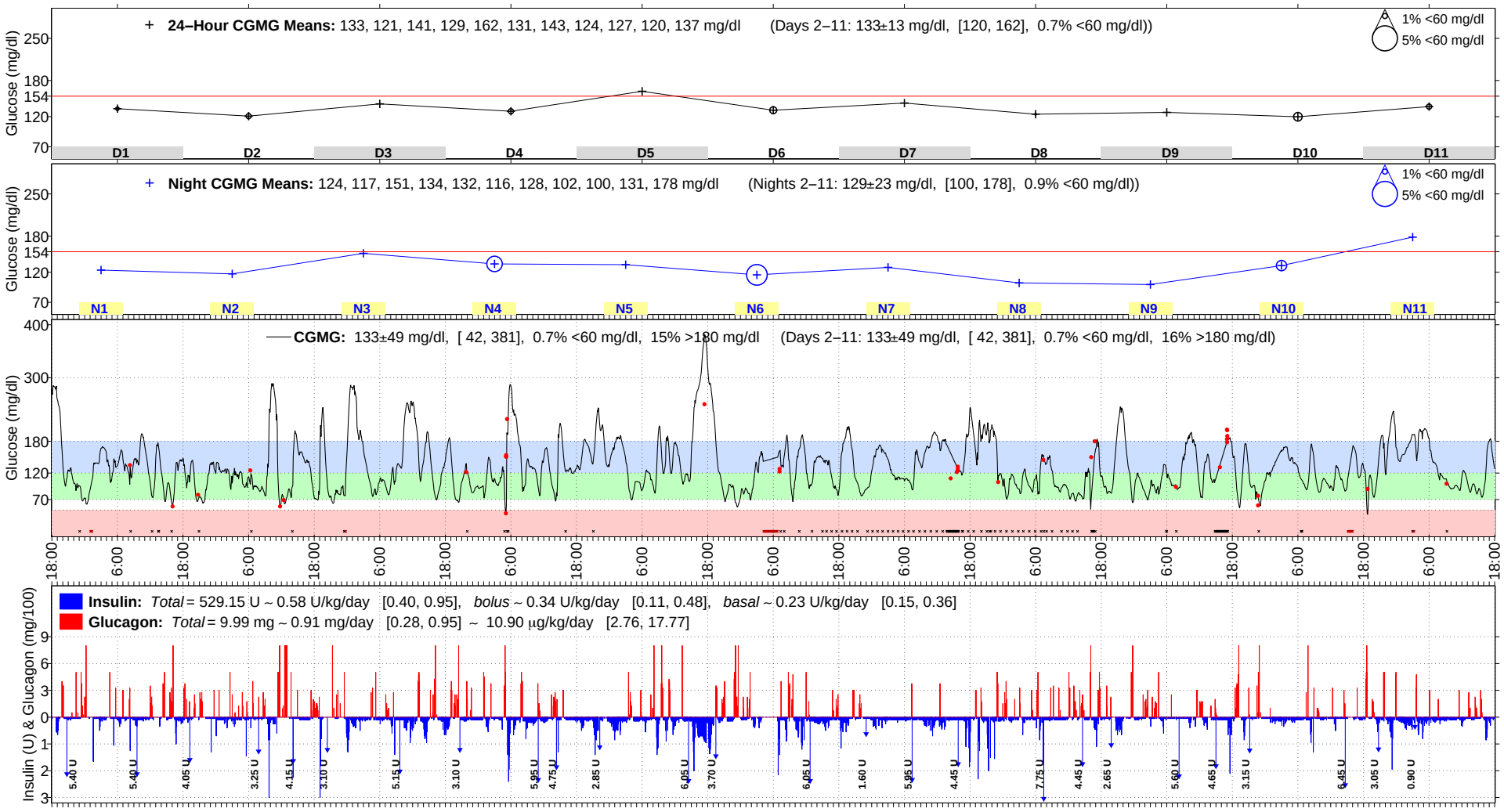
- 11-day experiments in adults with T1D – Multi-Center Study
  - Randomized cross-over design (11 days on bionic pancreas, 11 days on usual care)
  - Home use study: People with T1D engaged in usual daily work and leisure routine
  - Must live within 30 minutes, stay within 60 minutes of study base
  - Sleep at home (with a designated contact), technical & medical support on call
  - Telemetry to monitor wireless connectivity of pumps and CGM, and if the CGM reads < 50 mg/dl
  - 40 adult subjects 18 years and older (440 bionic pancreas days)

Q2 2014 – Q1 2015

BOSTON UNIVERSITY MGH

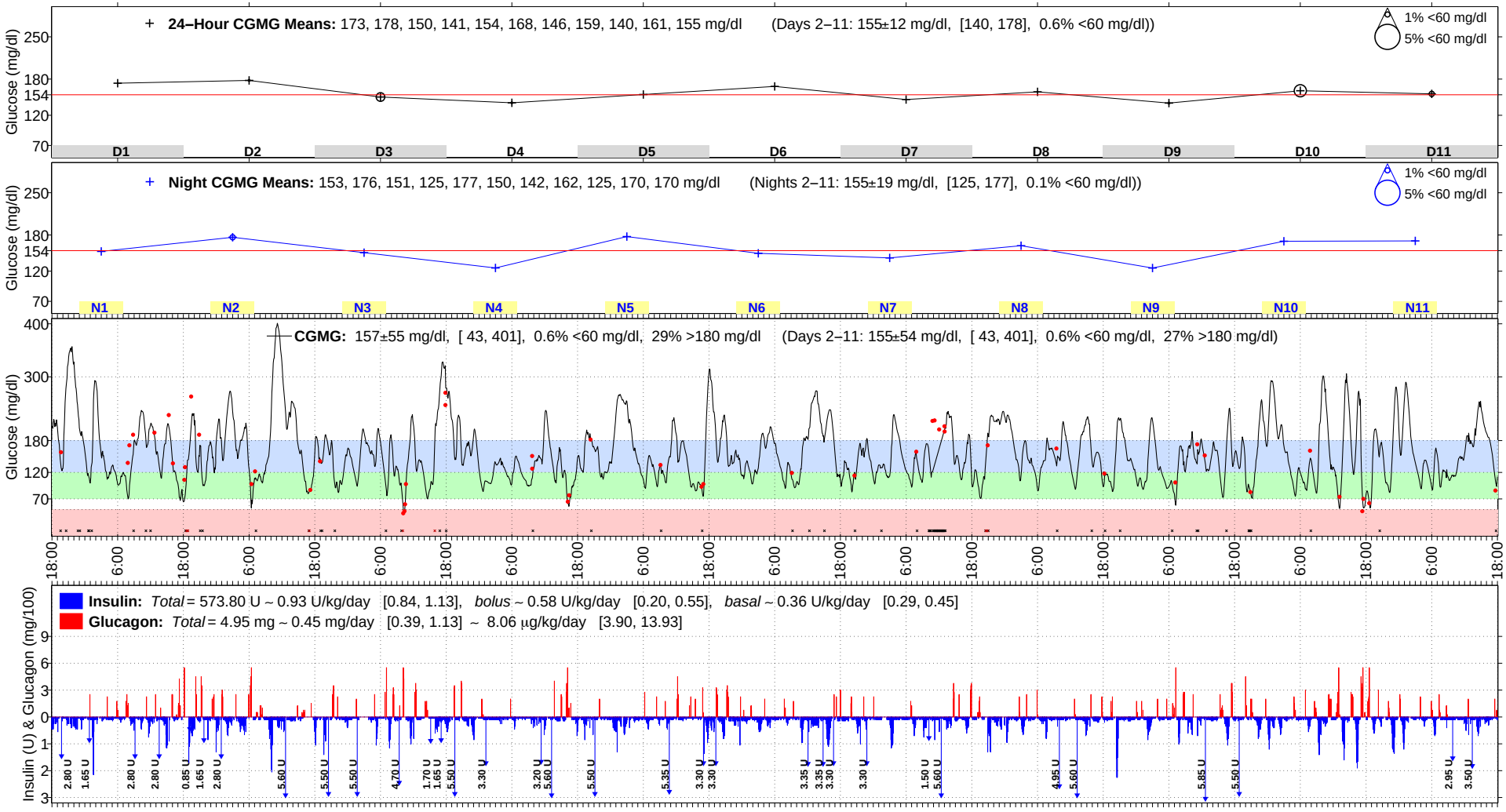
Preliminary Results from the Bionic Pancreas Multi-Center Study

Bionic Pancreas at Home and at Work – Subject MGH 01



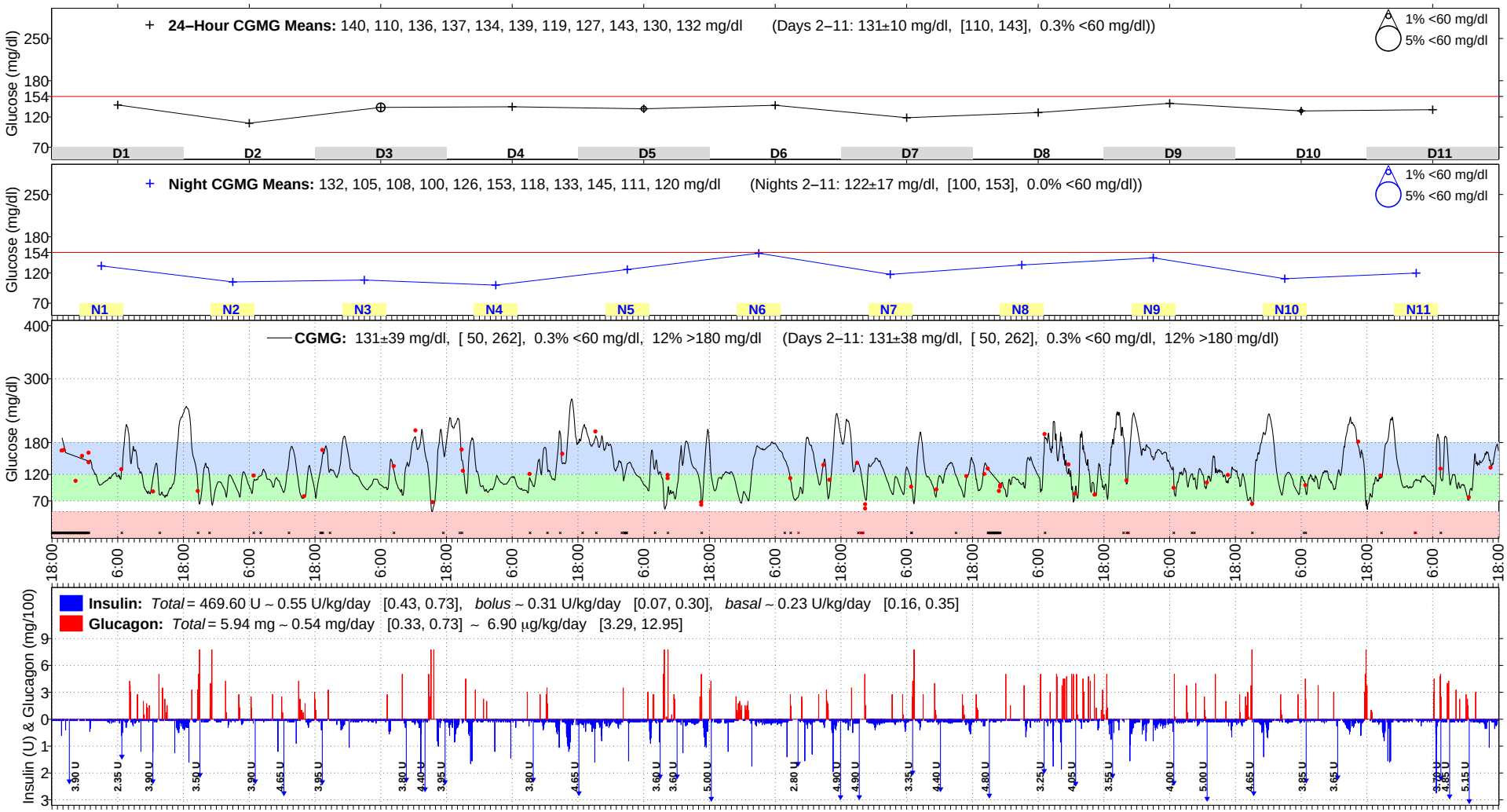
Preliminary Results from the Bionic Pancreas Multi-Center Study

Bionic Pancreas at Home and at Work – Subject MGH 02



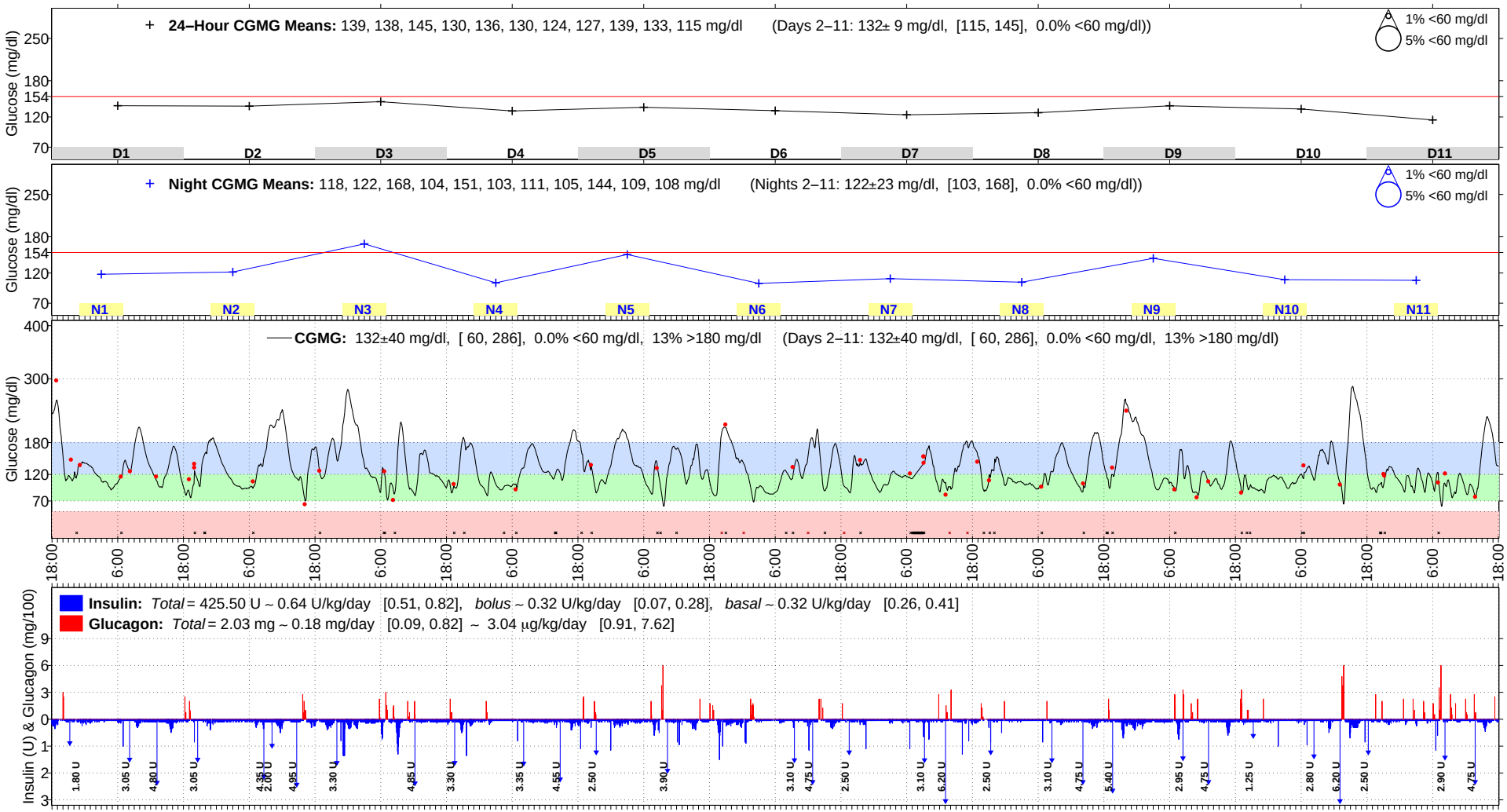
Preliminary Results from the Bionic Pancreas Multi-Center Study

Bionic Pancreas at Home and at Work – Subject MGH 03

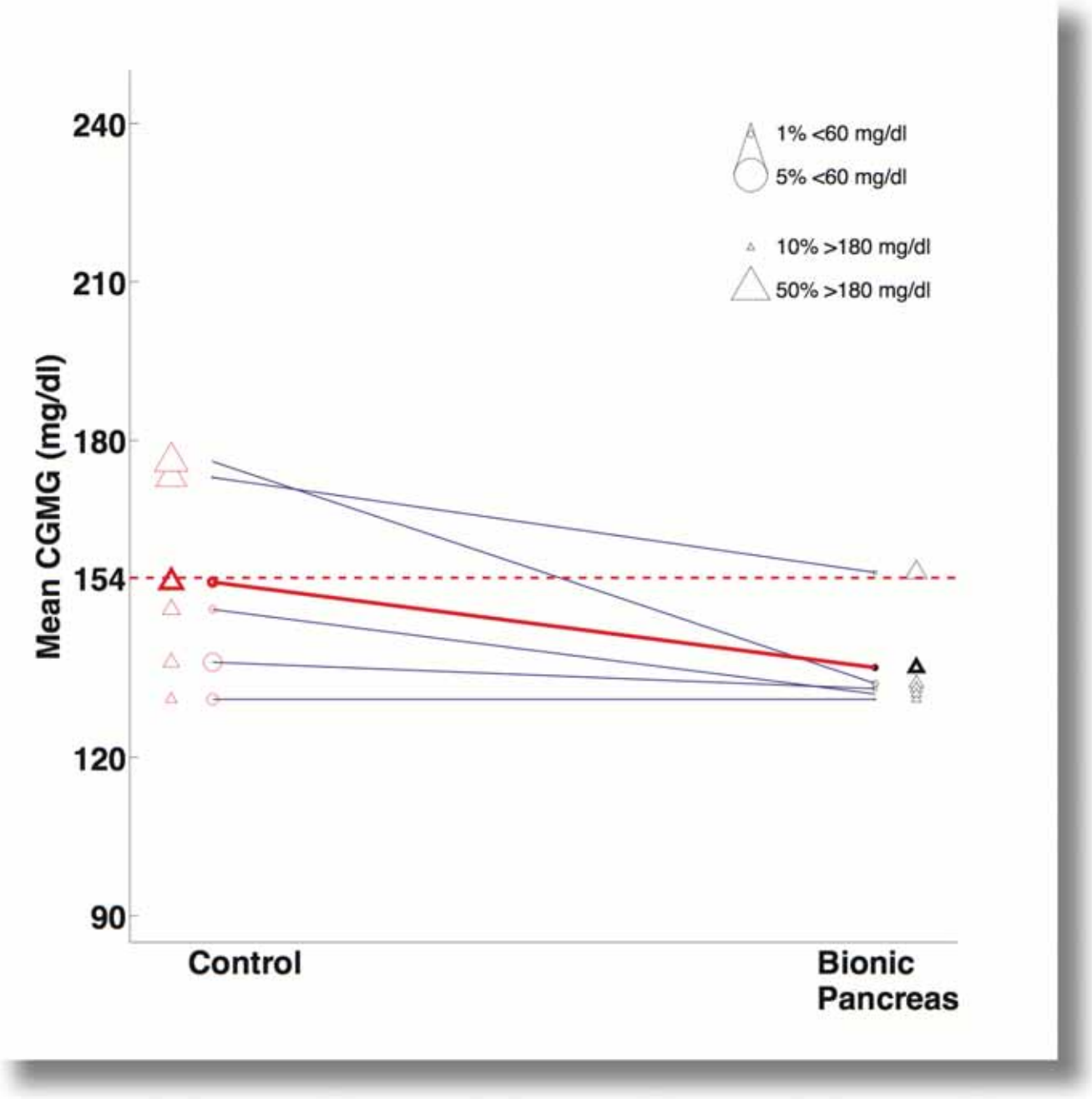


Preliminary Results from the Bionic Pancreas Multi-Center Study

Bionic Pancreas at Home and at Work – Subject MGH 04

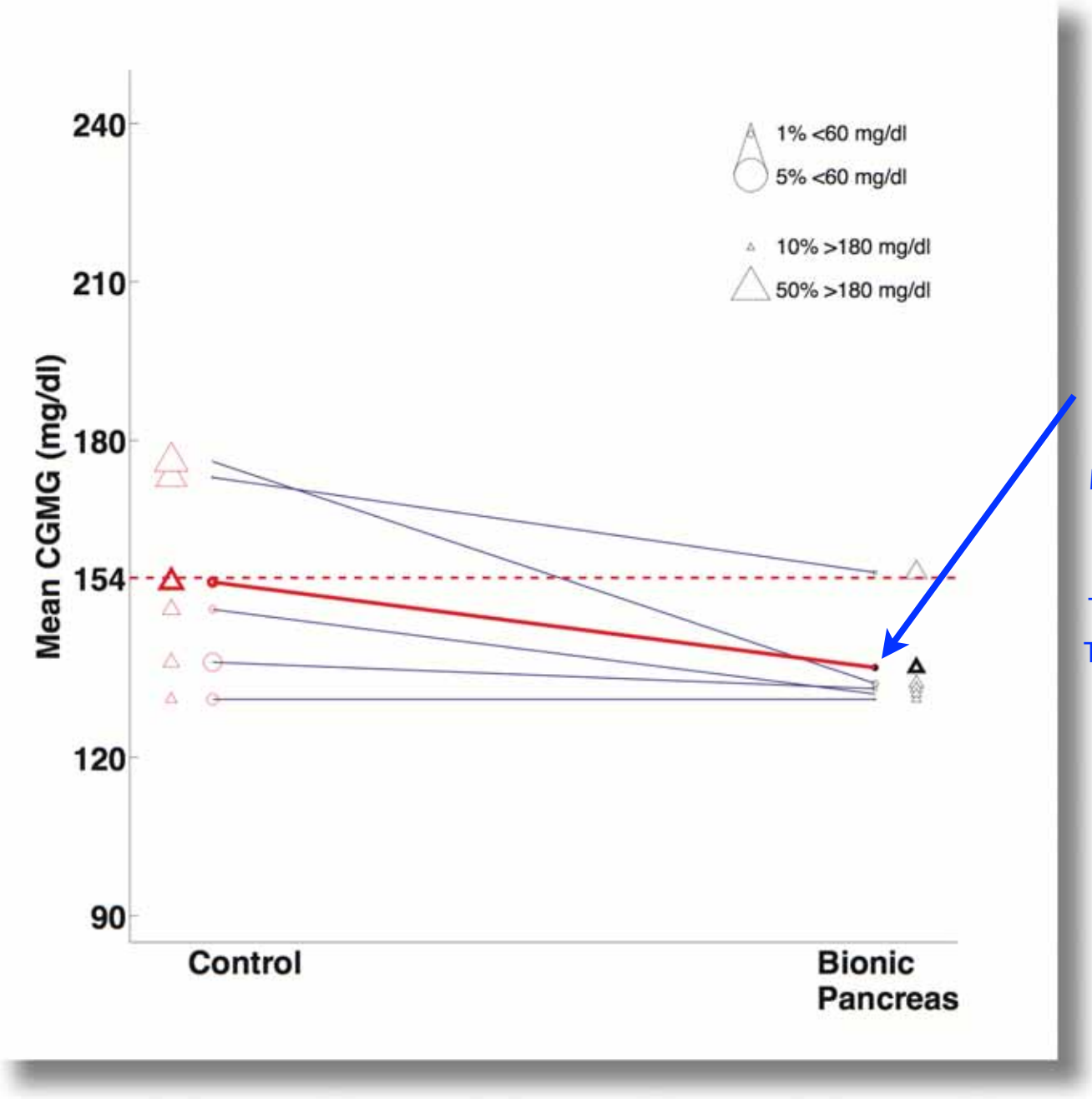


Preliminary Results from Multi-Center Study (Days 2–11)



BOSTON UNIVERSITY

Preliminary Results from Multi-Center Study (Days 2–11)



On Bionic Pancreas

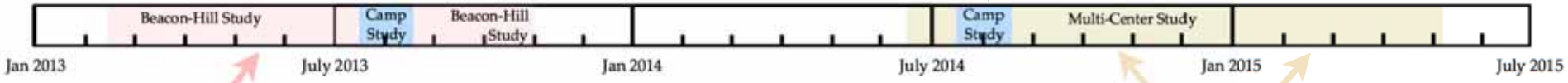
Mean CGM: 137 mg/dl
(Projected A1C: 6.4%)

Time < 60 mg/dl: 0.5%
Time > 180 mg/dl: 17%

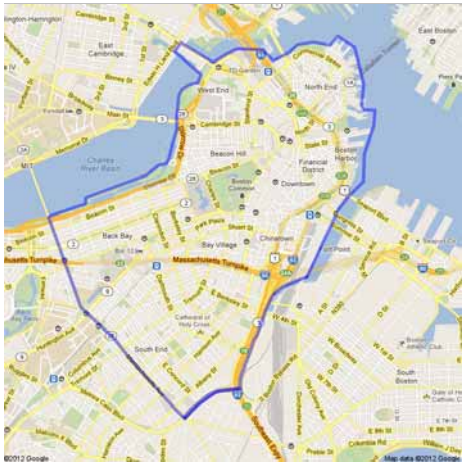
BOSTON UNIVERSITY

TIMELINE OF BIONIC PANCREAS OUTPATIENT STUDIES (2013–2015)

Summer Camp Studies: Summers of 2013 & 2014



Beacon Hill Study: First Half 2013, Fall 2013



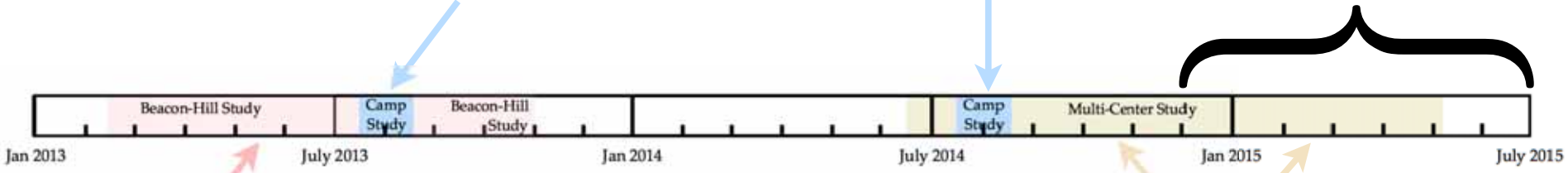
Bionic Pancreas Multi-Center Study: Spring 2014 – Q2 2015

TIMELINE OF BIONIC PANCREAS OUTPATIENT STUDIES (2013–2015)

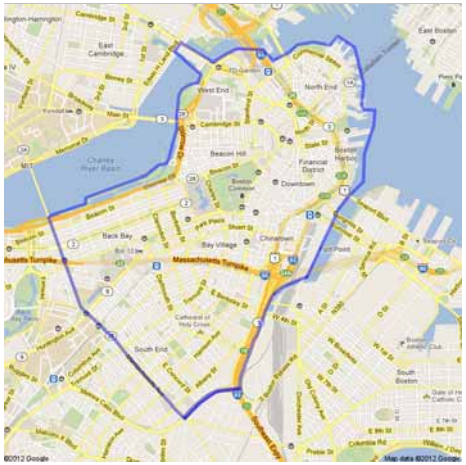
Summer Camp Studies: Summers of 2013 & 2014

2015 Studies Under Development

- **Bionic Pancreas Set Point Study**
- **Alcohol Tolerance Clamp Study**
- **Pediatric Bionic Pancreas Study**



Beacon Hill Study: First Half 2013, Fall 2013



Bionic Pancreas Multi-Center Study: Spring 2014 – Q2 2015

ACKNOWLEDGEMENTS

Our Volunteers

BU: Human trials and pre-clinical trials in diabetic pigs:

Firas El-Khatib Raj Setty Katherine McKeon John Jiang Niall Kavanagh

MGH: Human trials:

Steven Russell, Manasi Sinha, Kendra Magyar, Kerry Grennan, Courtney Flynn, Laura Goergen,

Kari Lynch, Caroline Macharia, Caitlin Morris, Mallory Hillard, Laurel Macey, Mary Larkin, David Nathan

UMass and Clara Barton Center: Summer Camp

Mark Bissell Lynn Butler Kevin Wilcoxen Beth Rowe Mary Lee

Tandem Diabetes Care: ***DexCom:***

Sean Saint Bob Anacone Kim Blickenstaff Tom Peyser Andy Balo Terry Gregg

SweetSpot Diabetes Care: ***Egret Technologies:***

Adam Greene Justin Schumacher Liam Pender

Abbott Diabetes Care:

Tim Goodnow Marc Taub Tim Henning Nathan Crouther Erwin Budiman

Insulet Corporation: ***Smiths Medical:***

Robert Campbell Steve Gemmell Kevin Schmid Rhall Pope Mike Blomquist

Research support provided by:

NIH (NIDDK R01 DK085633, NIDDK R01 DK097657, NIDDK DP3 DK101084, MGH Clinical Research Center), 2009–present
The Leona M. & Harry B. Helmsley Charitable Trust, 2009–2011, 2013–present
The Claire Friedlander Family Foundation, 2014
The Frederick Banting Foundation, 2012–2013
JDRF (Postdoctoral Fellowship & Clinical Investigations Research Grant), 2006–2011
The Wallace H. Coulter Foundation (Translational Partners Grant), 2006–2008

BOSTON UNIVERSITY

bionicpancreas.org OR artificialpancreas.org