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Principal Investigator	Michael Rickels, MD., MS
Study Title:	Effect of Hybrid Closed-Loop Insulin Delivery on Glucose Counterregulation in Long Standing Type 1 Diabetes: A Proof of Concept, Mechanistic, Single-Arm Clinical Trial

Purpose:
This study aims to determine whether hypoglycemia avoidance achieved through the use of a hybrid closed-loop insulin delivery system can improve glucose counterregulation in type 1 diabetic patients with hypoglycemia unawareness.

We are measuring glucose counterregulatory responses using hyperinsulinemic hypoglycemic clamps at baseline before intervention, after 6 months of intervention and after 18 months of intervention to assess the durability of any benefit from the avoidance of hypoglycemia, especially nocturnal hypoglycemia, with continued standard use of sensor augmented pump therapy (SAP) with low glucose suspend (LGS).

The demonstration of improved physiologic defense against hypoglycemia is critical to understanding whether protection from hypoglycemia may persist when the glucose sensor is not in use or functioning appropriately.

Brief Description
This study is expected to continue for approximately 1 more year. We expect to enroll 15-18 participants in this study and have 5 remaining open slots available. The University of Pennsylvania is the only site performing this research.

Participant involvement will last approximately 22 months (10-13 visits). This includes a Screening phase that will last 4 weeks and an Intervention phase that will last 18 months.

In order to assess hypoglycemia and confirm nocturnal patterns; participants will complete several questionnaires (Clarke Survey, Hypo Score, Hypoglycemia Awareness Questionnaire) as well as wear a wGT3X-BT Actigraph Monitor watch or ActiWatch2 at several time points throughout the study. At baseline, if not already on a sensor, participants will wear a blinded iPro®2 Professional Continuous Glucose Monitor for 7 days.

Participants who have met all inclusion criteria will receive the Medtronic 670G system and ongoing supplies from the study team or may also join the study if they are using or about to start using the Tandem TslimX2 system. We will work with each individual and their insurance to assess the best-cost option for participation. (i.e. upgrade eligibility and costs, ongoing supply delivery etc.)

Please see attached schedule of events for details of each study visit.

Eligibility
MAIN INCLUSION CRITERIA
- Male and female subjects age 25 to 70 years
- Type 1 diabetes onset < 40 years of age
- Insulin-dependent for > 10 years
- Involvement in intensive diabetes management as defined:
a) under the direction of an endocrinologist, diabetologist, or diabetes specialist
b) 2-3 clinical evaluation during the previous 12-18 months
c) by the administration of three or more insulin injections each day or insulin pump therapy
d) self-monitors glucose values no less than a mean of three times each day averaged over each week
- Hypoglycemia unawareness
- Documented >5% time spent in hypoglycemic range (glucose < 60mg/dl)
- At least one episode of hypoglycemia during the 7 days must occur overnight
MAIN EXCLUSION CRITERIA
- Body mass index (BMI) > 38 kg/m2.
- Insulin requirement of > 1.0 IU/kg/day

or Medtronic 670G systems

Compensation (if applicable)
For each of the visits where an overnight metabolic test was completed, participants will receive $150.00. They will also receive $50.00 for the completion of the remaining 10 visits, whether completed via phone or in the clinic. There will be no compensation for any extra training visits a participant might require besides the initially scheduled visits.

Participants will be paid in an ongoing manner as each visit is completed. The study coordinator will provide a visa gift card to each participant at the screening visit and will load it throughout the study within 4 hours of visit completion.

In addition, at each visit (including any overnights), parking tickets will be stamped. If transportation was public, participants will be compensated at the end of the study for their travel.

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