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111



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March 22, 2016

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APPLICATION NUMBER: 62/127,328
FILING DATE: *March 03, 2015*

THE COUNTRY CODE AND NUMBER OF YOUR PRIORITY APPLICATION, TO BE USED FOR FILING ABROAD UNDER THE PARIS CONVENTION, IS *US62/127,328*



Certified by

Under Secretary of Commerce
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REFERENCES

- [1] Pocai, Alessandro, et al. "A brain-liver circuit regulates glucose homeostasis." *Cell metabolism* 1.1 (2005): 53-61.
- [2] H. R. Berthoud and T. L. Powley, "Characteristics of gastric and pancreatic responses to vagal stimulation with varied frequencies: evidence for different fiber calibers?," *Journal of the autonomic nervous system*, vol. 19, no. 1, pp. 77-84, 1987.
- [3] Inoue, Shuji, et al. "Effects of selective vagotomy on circadian rhythms of plasma glucose, insulin and food intake in control and ventromedial hypothalamic (VMH) lesioned rats." *Obesity research* 3.S5 (1995): 747S-752S.
- [4] Shimazu T. Glycogen synthetase activity in liver: regulation by the autonomic nerves. *Science* [Internet]. 1967 [cited 2014 May 2];156(3779):1256-1257

ABBREVIATIONS

BG: blood glucose
mA: milliamps
Hz: hertz
kHz: kilohertz
mg/dl: milligrams per decaliter
V: volts

ABSTRACT

A method and device for real-time modulation of systemic blood glucose levels using electrical stimulation to modulate nerve activity is described. The method uses frequencies in the range of 1 Hz-100kHz to either increase and/or decrease nerve activity in the hepatic vagus and/or the greater splanchnic nerves. The battery-powered device can measure, log systemic blood glucose levels, control an external insulin or other pumps and increase or decrease nerve activity to obtain the desired systemic blood glucose level. The device can operate in open-loop configuration where the user turns the device on or off, closed-loop configuration where the clinician or user sets the set point, or closed-loop configuration where the device optimizes a user or clinician based set point overtime and electrically stimulates to maintain the set point.

Electronic Acknowledgement Receipt

EFS ID:	21649307
Application Number:	62127328
International Application Number:	
Confirmation Number:	3074
Title of Invention:	Glucose Regulation Via Electrical Stimulation Of Nerves Innervating The Liver
First Named Inventor/Applicant Name:	Robert Butera
Customer Number:	6980
Filer:	Ryan A. Schneider.
Filer Authorized By:	
Attorney Docket Number:	GTRC6745PRV
Receipt Date:	03-MAR-2015
Filing Date:	
Time Stamp:	10:35:05
Application Type:	Provisional

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	\$130
RAM confirmation Number	11582
Deposit Account	201507
Authorized User	

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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Application Data Sheet	WebADS.pdf	107107	no	5
			faac50ede856b1187ddc2dfc13fceed00c578f5		

Warnings:

Information:

2	Provisional Cover Sheet (SB16)	ProvCoverSheet.pdf	1477511	no	3
			513ccd0504b6c0b12a5db1a61ae49b61f35bd08f		

Warnings:

Information:

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Multipart Description/PDF files in .zip description

Document Description	Start	End
Specification	1	2
Drawings-only black and white line drawings	3	3
Specification	4	4
Claims	5	5
Abstract	6	6
Specification	7	7

Warnings:

Information:

4	Fee Worksheet (SB06)	fee-info.pdf	29812	no	2
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If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

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New International Application Filed with the USPTO as a Receiving Office

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Provisional Application for Patent Cover Sheet

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c)

Inventor(s)

Inventor 1

Remove

Given Name	Middle Name	Family Name	City	State	Country
Robert		Butera	Decatur	GA	US

Inventor 2

Remove

Given Name	Middle Name	Family Name	City	State	Country
Yogi	Anil	Patel	Atlanta	GA	US

All Inventors Must Be Listed – Additional Inventor Information blocks may be generated within this form by selecting the **Add** button.

Add

Title of Invention	Glucose Regulation Via Electrical Stimulation Of Nerves Innervating The Liver
Attorney Docket Number (if applicable)	GTRC6745PRV

Correspondence Address

Direct all correspondence to (select one):

- The address corresponding to Customer Number
 Firm or Individual Name

Customer Number	06980
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The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

- No.
- Yes, the invention was made by an agency of the United States Government. The U.S. Government agency name is:
- Yes, the invention was under a contract with an agency of the United States Government. The name of the U.S. Government agency and Government contract number are:

Doc Code: **TR.PROV**

Document Description: Provisional Cover Sheet (SB16)

PTO/SB/16 (11-08)

Approved for use through 05/31/2015. OMB 0651-0032

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- Applicant asserts small entity status under 37 CFR 1.27
- Applicant certifies micro entity status under 37 CFR 1.29. Applicant must attach form PTO/SB/15A or B or equivalent.
- No

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Signature

Please see 37 CFR 1.4(d) for the form of the signature.

Signature	/Ryan A. Schneider, Reg. #45083/			Date (YYYY-MM-DD)	2015-03-03
First Name	Ryan	Last Name	Schneider	Registration Number (If appropriate)	45083

This collection of information is required by 37 CFR 1.51. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 8 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. This form can only be used when in conjunction with EFS-Web. If this form is mailed to the USPTO, it may cause delays in handling the provisional application.**

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The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that : (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

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7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
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9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	GTRC6745PRV
		Application Number	
Title of Invention	Glucose Regulation Via Electrical Stimulation Of Nerves Innervating The Liver		
<p>The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76. This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.</p>			

Secrecy Order 37 CFR 5.2

<input type="checkbox"/>	Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2(Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)
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Inventor Information:

Inventor 1						<input type="button" value="Remove"/>
Legal Name						
Prefix	Given Name	Middle Name	Family Name	Suffix		
	Robert		Butera			
Residence Information (Select One) <input checked="" type="radio"/> US Residency <input type="radio"/> Non US Residency <input type="radio"/> Active US Military Service						
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Mailing Address of Inventor:						
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City	Atlanta	State/Province	GA			
Postal Code	30332-0415	Country	i	US		
Inventor 2						<input type="button" value="Remove"/>
Legal Name						
Prefix	Given Name	Middle Name	Family Name	Suffix		
	Yogi	Anil	Patel			
Residence Information (Select One) <input checked="" type="radio"/> US Residency <input type="radio"/> Non US Residency <input type="radio"/> Active US Military Service						
City	Atlanta	State/Province	GA	Country of Residence	US	
Mailing Address of Inventor:						
Address 1	c/o Georgia Tech Research Corporation					
Address 2	10th Street, N.W.					
City	Atlanta	State/Province	GA			
Postal Code	30332-0415	Country	i	US		
All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the Add button.						<input type="button" value="Add"/>

Correspondence Information:

<p>Enter either Customer Number or complete the Correspondence Information section below. For further information see 37 CFR 1.33(a).</p>

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	GTRC6745PRV
		Application Number	
Title of Invention	Glucose Regulation Via Electrical Stimulation Of Nerves Innervating The Liver		

An Address is being provided for the correspondence information of this application.

Customer Number	6980		
Email Address	ryan.schneider@troutmansanders.com	<input type="button" value="Add Email"/>	<input type="button" value="Remove Email"/>

Application Information:

Title of the Invention	Glucose Regulation Via Electrical Stimulation Of Nerves Innervating The Liver		
Attorney Docket Number	GTRC6745PRV	Small Entity Status Claimed	<input checked="" type="checkbox"/>
Application Type	Provisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	1	Suggested Figure for Publication (if any)	

Filing By Reference

Only complete this section when filing an application by reference under 35 U.S.C. 111(c) and 37 CFR 1.57(a). Do not complete this section if application papers including a specification and any drawings are being filed. Any domestic benefit or foreign priority information must be provided in the appropriate section(s) below (i.e., "Domestic Benefit/National Stage Information" and "Foreign Priority Information").

For the purposes of a filing date under 37 CFR 1.53(b), the description and any drawings of the present application are replaced by this reference to the previously filed application, subject to conditions and requirements of 37 CFR 1.57(a).

Application number of the previously filed application	Filing date (YYYY-MM-DD)	Intellectual Property Authority or Country

Publication Information:

Request Early Publication (Fee required at time of Request 37 CFR 1.219)

Request Not to Publish. I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application **has not and will not** be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32). Either enter Customer Number or complete the Representative Name section below. If both sections are completed the customer Number will be used for the Representative Information during processing.

Please Select One:	<input checked="" type="radio"/> Customer Number	<input type="radio"/> US Patent Practitioner	<input type="radio"/> Limited Recognition (37 CFR 11.9)
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Application Data Sheet 37 CFR 1.76		Attorney Docket Number	GTRC6745PRV
		Application Number	
Title of Invention	Glucose Regulation Via Electrical Stimulation Of Nerves Innervating The Liver		

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, or 365(c) or indicate National Stage entry from a PCT application. Providing this information in the application data sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78.

Prior Application Status			<input type="button" value="Remove"/>
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)

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Foreign Priority Information:

This section allows for the applicant to claim priority to a foreign application. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55(d). When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX) the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(h)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

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Application Number	Country	Filing Date (YYYY-MM-DD)	Access Code (if applicable)

Additional Foreign Priority Data may be generated within this form by selecting the **Add** button.

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications

This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.

NOTE: By providing this statement under 37 CFR 1.55 or 1.78, this application, with a filing date on or after March 16, 2013, will be examined under the first inventor to file provisions of the AIA.

Authorization to Permit Access:

Authorization to Permit Access to the Instant Application by the Participating Offices

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	GTRC6745PRV
		Application Number	
Title of Invention	Glucose Regulation Via Electrical Stimulation Of Nerves Innervating The Liver		

If checked, the undersigned hereby grants the USPTO authority to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the World Intellectual Property Office (WIPO), and any other intellectual property offices in which a foreign application claiming priority to the instant patent application is filed access to the instant patent application. See 37 CFR 1.14(c) and (h). This box should not be checked if the applicant does not wish the EPO, JPO, KIPO, WIPO, or other intellectual property office in which a foreign application claiming priority to the instant patent application is filed to have access to the instant patent application.

In accordance with 37 CFR 1.14(h)(3), access will be provided to a copy of the instant patent application with respect to: 1) the instant patent application-as-filed; 2) any foreign application to which the instant patent application claims priority under 35 U.S.C. 119(a)-(d) if a copy of the foreign application that satisfies the certified copy requirement of 37 CFR 1.55 has been filed in the instant patent application; and 3) any U.S. application-as-filed from which benefit is sought in the instant patent application.

In accordance with 37 CFR 1.14(c), access may be provided to information concerning the date of filing this Authorization.

Applicant Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.			
Applicant 1			
If the applicant is the inventor (or the remaining joint inventor or inventors under 37 CFR 1.45), this section should not be completed. The information to be provided in this section is the name and address of the legal representative who is the applicant under 37 CFR 1.43; or the name and address of the assignee, person to whom the inventor is under an obligation to assign the invention, or person who otherwise shows sufficient proprietary interest in the matter who is the applicant under 37 CFR 1.46. If the applicant is an applicant under 37 CFR 1.46 (assignee, person to whom the inventor is obligated to assign, or person who otherwise shows sufficient proprietary interest) together with one or more joint inventors, then the joint inventor or inventors who are also the applicant should be identified in this section.			
<input type="button" value="Clear"/>			
<input checked="" type="radio"/> Assignee	<input type="radio"/> Legal Representative under 35 U.S.C. 117	<input type="radio"/> Joint Inventor	
<input type="radio"/> Person to whom the inventor is obligated to assign.	<input type="radio"/> Person who shows sufficient proprietary interest		
If applicant is the legal representative, indicate the authority to file the patent application, the inventor is:			
Name of the Deceased or Legally Incapacitated Inventor :			
If the Applicant is an Organization check here. <input checked="" type="checkbox"/>			
Organization Name	Georgia Tech Research Corporation		
Mailing Address Information:			
Address 1	Tenth Street, N.W.		
Address 2			
City	Atlanta	State/Province	GA
Country i	US	Postal Code	30332-0415
Phone Number		Fax Number	

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	GTRC6745PRV
		Application Number	
Title of Invention	Glucose Regulation Via Electrical Stimulation Of Nerves Innervating The Liver		
Email Address			
Additional Applicant Data may be generated within this form by selecting the Add button.			

Assignee Information including Non-Applicant Assignee Information:

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Assignee 1				
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If the Assignee or Non-Applicant Assignee is an Organization check here <input type="checkbox"/>				
Prefix	Given Name	Middle Name	Family Name	Suffix
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Address 2				
City		State/Province	OT	
Country i		Postal Code		
Phone Number		Fax Number		
Email Address				
Additional Assignee or Non-Applicant Assignee Data may be generated within this form by selecting the Add button.				

Signature:

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications					
Signature	/Ryan A. Schneider, Reg. #45083/				
First Name	Ryan	Last Name	Schneider	Registration Number	45083
Additional Signature may be generated within this form by selecting the Add button.					

GLUCOSE REGULATION VIA ELECTRICAL STIMULATION OF NERVES INNERVATING THE LIVER

FIELD OF INVENTION

This invention relates to the regulation of systemic blood glucose via electrical stimulation of peripheral nerves.

BACKGROUND OF INVENTION

The liver is implicated in a variety of functions that contribute to homeostasis of systemic blood glucose levels. The hepatic branch of the vagus nerve is a sub-population of axons from the vagus nerve that innervate the liver along with the greater splanchnic nerves [1]. Chemical and anatomical manipulation of the hepatic vagus has shown a change in systemic blood glucose levels over a range of time periods after manipulation [2]. Manipulation is typically in the form of a nerve transection (cutting the nerve) so the nerves are no longer connected to the liver or via electrical stimulation (periodic perturbations) of the nerve. Electrical stimulation of the hepatic branch of the vagus using low frequencies (up to 30 Hz) have shown higher systemic blood glucose levels within minutes of turning on the stimulation [2] and vagotomy (cutting of the cervical vagus) studies have shown a decrease in systemic blood glucose levels hours after cutting the nerve [2,3]. However, cutting of these nerves is permanent and not typically viable for clinical applications. The invention claimed in this disclosure relates to a device that increases or decreases neural activity in the hepatic vagus and/or greater splanchnic nerves to increase or decrease systemic blood glucose levels. The increase and/or decrease in nerve activity is due to a choice of appropriate frequencies and amplitudes that can either excite the nerve or inhibit indigenous electrical activity, effectively inhibiting the nerve. The device can also be used in a closed-loop manner utilizing measurements of systemic blood glucose levels and appropriately controlling stimulation to achieve a desired blood glucose level.

The novelty of this application is the use of electrical stimulation to inhibit nerve activity to cause a decrease in measured blood glucose levels, which has never been shown before. We know of no published paper or patent that illustrates the use of coordinated electrical nerve stimulation to effectively manipulate the liver to both increase **and decrease** blood glucose levels.

SUMMARY OF INVENTION

The present invention is an implantable device that interfaces with the hepatic vagus and/or greater splanchnic nerve and electrically stimulates to excite or inhibit nerve activity, leading to an increase or decrease of systemic blood glucose levels.

Nerve activity is increased or decreased in the target nerves by electrically stimulating the nerves. Turning the electrical stimulation on or off to either increase or decrease (depending on stimulus parameters) nerve activity will cause either an increase or decrease in systemic blood glucose levels. Electrical stimulation can be used to excite or inhibit either nerve to maintain blood glucose levels at a desirable level via manipulation of liver function.

Figure 1 depicts one such possible combination where the hepatic vagus nerve was electrically stimulated to excite nerve activity (blue curve) and the greater splanchnic nerve was electrically stimulated to inhibit neural activity (green curve). Measured blood glucose levels increased when the hepatic vagus was electrically stimulated to excite activity and the measured blood glucose levels decreased when the greater splanchnic was electrically stimulated to inhibit neural activity (Fig. 1).

When combined with a means of glucose measurement, a control algorithm can be used to control which nerve to electrically stimulate and whether or not to excite or inhibit that nerve. This algorithm would attempt to ensure that blood glucose levels are maintained at a desired set point, which may be set by a clinician or a user.

The present invention provides a method through which the systemic blood glucose levels can be manipulated directly by altering liver uptake and release of glucose through electrical stimulation to excite or inhibit either hepatic vagus and/or the greater splanchnic nerve activity.

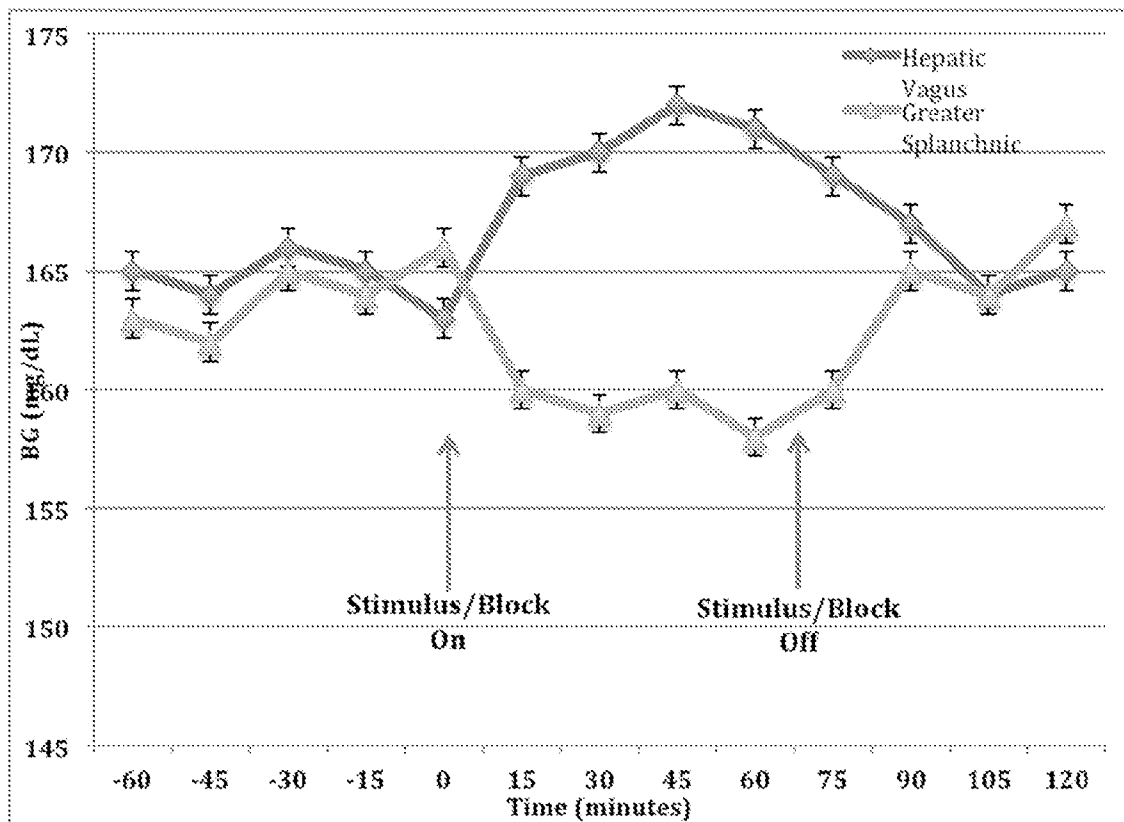


Figure 1: One possible combination of electrical stimulation to excite or inhibit nerve activity in the hepatic vagus and/or the greater splanchnic. This data is from a trial where the hepatic vagus was electrically stimulated to excite nerve activity and the greater splanchnic was electrically stimulated to inhibit nerve activity. Average blood glucose levels before, during, and after electrical stimulation to excite the hepatic vagus or inhibit via kilohertz high frequency alternating current (KHFAC) stimulation of the greater splanchnic. Electrical stimulation in both cases was achieved using a tripolar cuff electrode. Hepatic vagus nerve was stimulated with cathode first, biphasic stimulation pulses in voltage mode of 5 V at 10 Hz, 50% duty cycle. Greater splanchnic nerve was electrically stimulated to inhibit nerve activity using a charge-balanced periodic waveform in current mode of 1 mA at 50 kHz. Blood glucose measurements were made every 15 minutes using over the counter blood glucose strips. Three measurements were made at every time point and the average values being recorded and plotted. Each triangle or diamond represents an average of these three measurements with their standard error shown.

the device. The device provides a programmable interface for a user or clinician to program the set point. The unit measures systemic blood glucose levels and provides the user with readout of the levels. The device can then electrically stimulate to increase or decrease activity of the hepatic vagus and/or greater splanchnic nerve using electrical stimulation to increase or decrease systemic blood glucose levels. The device consists of a battery-powered stimulation unit [101] with programmable logic [102], cuff electrodes [103] attached to the hepatic vagus and/or greater splanchnic nerve, a systemic blood glucose sensor to [104], a display device viewing measurements [105], and a programming unit to program the stimulation device [106].

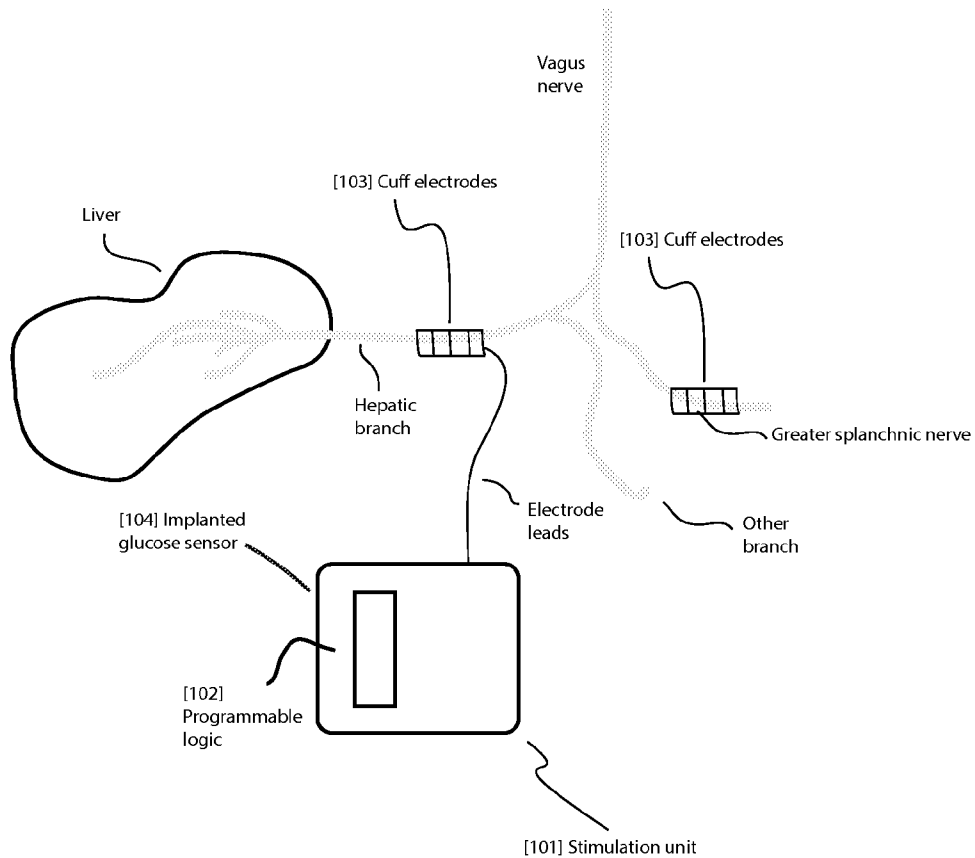


Figure 4. One possible combination for control of blood glucose levels through electrical stimulation of hepatic or greater splanchnic nerves. Closed-loop device with autonomous control for setting systemic blood glucose levels. The device is configured to a set point by the user or clinician. The device measures systemic blood glucose levels and automatically adjusts the electrical stimulation to either increase and/or decrease nerve activity in the hepatic vagus and/or greater splanchnic nerves to maintain the set point. The device can automatically adjust the set point for desired systemic blood glucose and automatically adjust the stimulation to increase and/or decrease nerve activity in either nerve. The device consists of a battery-powered stimulation unit [101] with programmable logic [102], cuff electrodes [103] attached to the hepatic vagus and/or greater splanchnic nerves, and a systemic blood glucose sensor [104].

DESCRIPTION OF PREFERRED EMBODIMENTS

Electrical stimulation of the hepatic vagus and/or greater splanchnic nerves allows for drug-free modulation of systemic blood glucose levels. Here we consider three embodiments that use either an open-loop or closed-loop configuration.

The scenario in Figure 2 is an open-loop configuration that has an implanted stimulator connected to the hepatic branch of the vagus and the greater splanchnic nerve. The stimulator also measures the systemic blood glucose levels and shows them on a display/control unit that is carried on the person. The display/control unit provides the user with measurement information along with the option to turn the electrical stimulation on or off to excite or inhibit nerve activity in either (or both) nerves, and thus increase or decrease systemic blood glucose.

The scenario in Figure 3 is a closed-loop configuration that can be programmed by the user or the clinician to a desired set point. The stimulator is implanted and the cuff electrodes are connected to the hepatic branch of the vagus and/or the greater splanchnic nerve. The stimulator has a logic controller inside of it that can be configured to turn on or off when the systemic blood glucose measurement falls below or above a programmed set point, which can be programmed by the user or clinician.

The scenario in Figure 4 is a closed-loop configuration that only requires initial programming by a user or clinician to set the set point. The stimulator is implanted and the cuff electrodes are connected to the hepatic branch of the vagus and/or the greater splanchnic nerve. The stimulator is set to an initial set point by the clinician based off of blood glucose measurements made prior to implantation by the clinician. The algorithm then uses this set point as a starting point and may calibrate the set point overtime based upon the user's metabolic changes.

These scenarios are not the sole possible embodiments. For example, it is possible for the device (such as in Fig 2) to be used in conjunction with existing therapies to reduce the load on a subject with diminished pancreatic function. For example, it could enhance the efficacy of oral therapies used for subjects with type II diabetes.

WHAT IS CLAIMED IS

1. A device and method for increasing or decreasing systemic blood glucose by exciting and/or inhibiting activity in the hepatic vagus and/or the greater splanchnic nerves via electrical stimulation. The device can either excite and/or inhibit activity in the hepatic branch of the vagus and/or and the greater splanchnic nerves depending upon the stimulation waveform and parameters used for the electrical stimulation.
2. By appropriate choice of stimulus frequency and amplitude, selective activity on the hepatic vagus and splanchnic nerves can be blocked while leaving other propagating activity on the nerve unmolested, minimizing unwanted effects of said stimulation.
3. The electrical stimulation can operate in an open-loop configuration that can be controlled by the user with a control unit that is worn or carried on the person.
4. The electrical stimulation can operate in a closed-loop configuration by setting the baseline systemic blood glucose levels to a set point by the user or the clinician. By regular measurements of blood glucose, the stimulator can alter its parameters to maintain that set point.
5. Various waveforms can be used for electrical stimulation to increase and/or decrease hepatic vagus and/or and the greater splanchnic nerve activity and can be in the range of 1 Hz to 100 kHz.
6. The electrical stimulation for either increasing or decreasing the nerve activity can be current mode and/or voltage mode stimulation, with amplitudes from .1mA to 10 mAs in current mode and up to 10V in voltage mode.
7. The duration of the stimulation is not limited and may be as short as a few seconds or as long as a few days.
8. The device connects to the hepatic branch of the vagus and/or and the greater splanchnic nerve using nerve cuff electrodes of varying geometries, materials, configurations, number of contacts, and electrical characteristics.
9. The user control and display unit can show the real-time measurements in systemic blood glucose along with trends in blood glucose.
10. The user control and display unit can be wireless.
11. The stimulation unit, cuff electrode, and glucose sensor can all be implanted into the user.
12. The device can be autonomous and function on its own with minimal programming from the user or clinician, allowing for optimization of the set point.
13. The device can log all details of the device function, including but not limited to, blood glucose measurements, stimulation times and parameters.

DESCRIPTION OF THE DRAWINGS

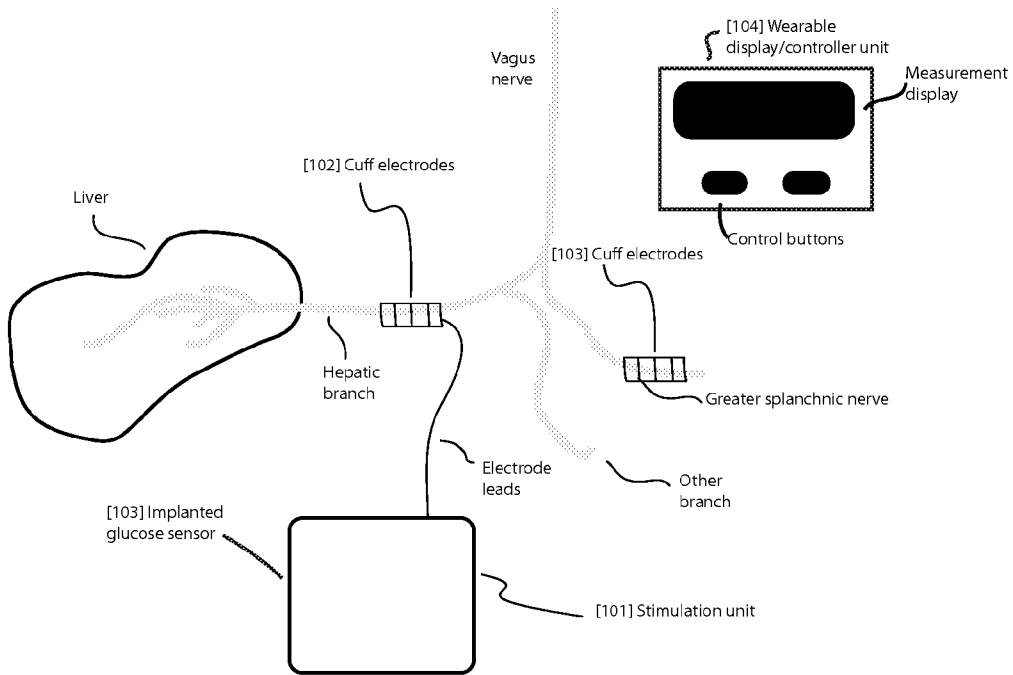


Figure 2. One possible combination for control of blood glucose levels through electrical stimulation of hepatic or greater splanchnic nerves. Open-loop device with user control. Device allows the user to change the set point for the blood glucose level and/or turn the electrical stimulation on or off for either nerve. The device consists of a stimulation unit [101], cuff electrodes [102] attached to the hepatic vagus and/or greater splanchnic nerves, a glucose sensor [103], and a display/controller unit for turning the stimulation on and off [104].

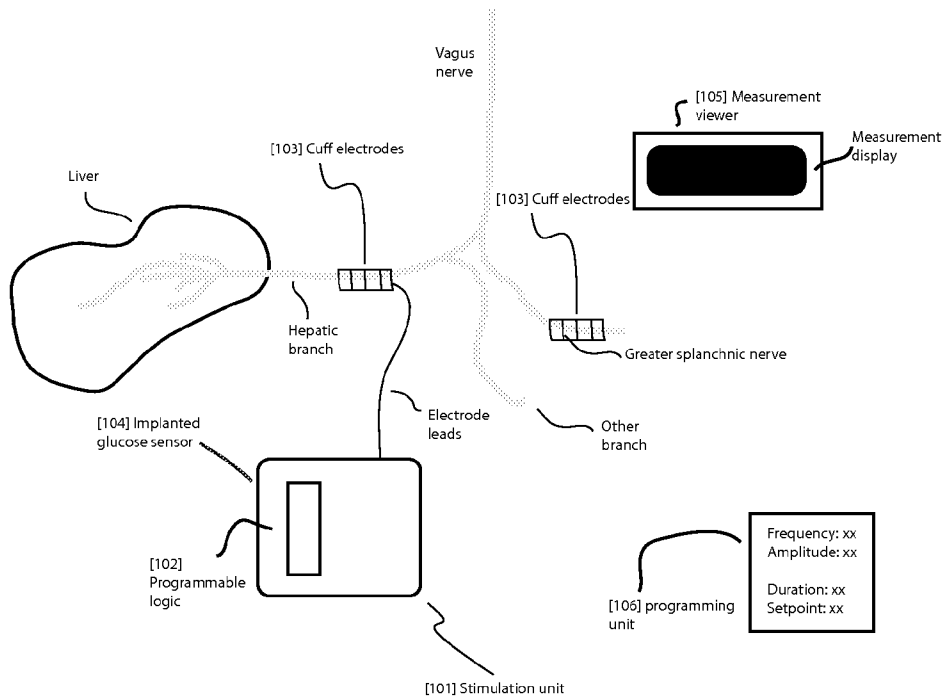


Figure 3. One possible combination for control of blood glucose levels through electrical stimulation of hepatic or greater splanchnic nerves. Closed-loop device with programmable interface for user or clinician to set the set point of