Fluorescence-based Implantable Glucose Sensor with Smartphone Interface

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Background: A fluorescence-based implantable glucose sensor has been developed. The small cylindrical sensor, which is approximately 3 mm in diameter and 14 mm long, has been designed to be inserted subcutaneously. A portion of the outer shell of the sensor includes a polymer hydrogel containing a proprietary indicator molecule that becomes fluorescent when it binds glucose. The sensor includes a miniature fluorometer, with a tiny LED for excitation and multiple photodiodes for detection of the fluoresced signal. It also includes a highly accurate temperature sensor for compensation of the detected fluorescence. The glucose sensor has been designed to remain inserted for at least six months.

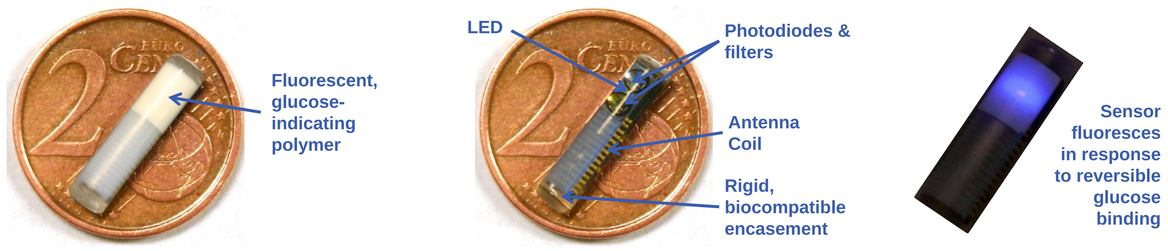

Figure 1. Sensor is a miniature fluorometer that detects the fluorescence of an indicator molecule that becomes fluorescent when it binds glucose

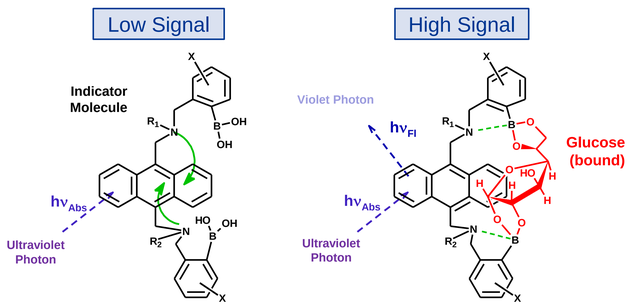

Figure 2. Indicator molecule fluoresces only when glucose is reversibly bound

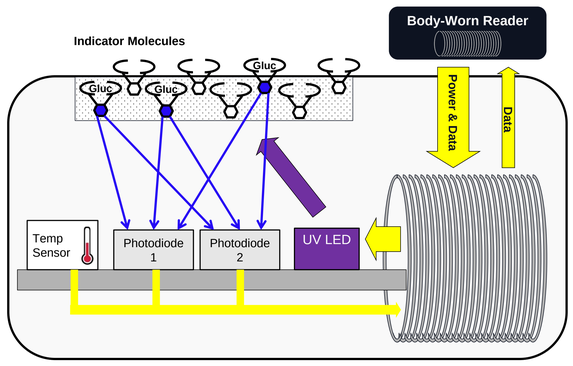

Figure 3. Sensor demonstrates greater fluorescence in presence of increased glucose concentration

The sensor is RF-powered, and an external body-worn reader is required to provide power to the sensor via a wireless inductive link. The reader also communicates with the sensor via a digital wireless inductive link to send commands to the sensor and to receive data from the sensor. The reader processes the sensed data to determine the sensor glucose value as well as the rate of change, and it is capable of storing up to 6 months of data. The reader includes a beeper and a vibration motor that are used to alert the patient, for example, when glucose passes a threshold value. The reader also includes a Bluetooth Low Energy link for communication with a smartphone as well as a USB port for charging and data exchange.

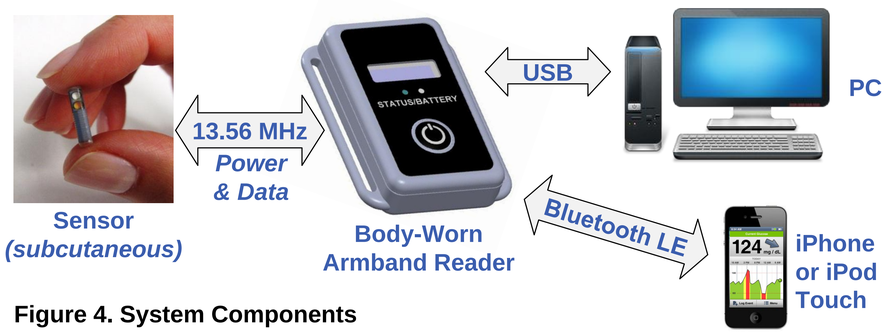

Figure 4. System Components

Figure 5. Subject wearing Armband Reader

Apps for the latest models of iPhone and iPod Touch have been developed. The smartphone operates essentially as a user interface device for the reader, displaying data and providing user input, but it is not used to process sensor data or store data long-term. The smartphone app may be used to view sensor glucose data displayed graphically. The smartphone app also allows the user to enter data on daily events, for example, meals, insulin bolus administration, and exercise. All information entered by a patient is immediately transmitted to the reader.

Figure 6. Smartphone app displays sensor glucose and issues an alert when a threshold is exceeded

Figure 7. Smartphone app allows entry of daily events such as meals (carbs), health events, etc.

Materials and Methods: Reader prototypes were developed in support of pilot clinical studies, designed for use with a sensor inserted subcutaneously in either the wrist or the upper arm. The readers were programmed to read the inserted glucose sensor every 2 minutes. In 3 pilot studies, 12 subjects were inserted with 1 or 2 sensors each. **Cohort 1** included 4 subjects, each inserted with 2 sensors, one in each upper arm (8 sensors total). Following the study with Cohort 1, a slight improvement was made to the sensor to improve long-term stability. **Cohort 2** included 4 subjects, each inserted with 1 improved sensor in the upper arm and 1 improved sensor in the contralateral wrist (8 sensors total). **Cohort 3** included 4 subjects, each inserted with 1 improved sensor in the upper arm (to confirm the results seen with the sensors inserted in the upper arms of Cohort 2).

Results: The pilot clinical study results are shown in the tables and figure below.

Conclusion: Clinical data from three 28-day pilot studies of an implantable fluorescence-based glucose sensor have demonstrated the feasibility of the sensor.

Purpose	• Evaluate *in vivo* stability • Evaluate sensor improvement • Evaluate upper arm vs. wrist
Sensors	8 sensors (Cohort 1) 12 improved sensors (Cohorts 2A, 2B, 3)
Insertion Site	• Wrist (Cohort 2A) • Upper Arm (Cohorts 1, 2B, 3)
Population	• Age 22 – 65 years, male and female • Type 1 Diabetic or Type II insulin dep. • HbA1c < 10%; BMI < 35 kg / m^2
Insertion Period	29 days
Clinic Visits	• Six clinic visits of 8+ hours each • Days 3, 6, 12, 18, 24, & 29 post-implant
Reference Standard	Blood glucose measured with YSI analyzer

Table 1. Synopsis of Study Protocol

Patient ID (Upper Arm)	MARD (%)	MAD (mg/dL)
D57LU	9.2	11.7
D59LU	15.4	26.5
D58LU	29.6	16.9
D57RU	11.0	13.0
D56LU	12.8	14.3
D59RU	11.1	6.5
D58RU	16.5	12.3
D56RU	8.4	9.1
Combined	**14.1**	**14.1**

Table 2. Clinical Results for Cohort 1 (sensors in upper arm)

Patient ID (Wrist)	MARD (%)	MAD (mg/dL)
D60LL	17.9	19.3
D61RL	17.2	18.8
D62LL	13.8	17.4
D63LL	18.5	19.8
Combined (SE)	**16.8 (0.5)**	**19.0 (1.3)**

Table 3. Clinical Results for Cohort 2A (improved sensors in wrist)

Patient ID (Upper Arm)	MARD (%)	MAD (mg/dL)
D60RU	11.0	11.2
D61LU	10.7	12.8
D62RU	15.8	7.0
D63RU	12.2	19.0
Combined (SE)	**12.4 (0.4)**	**12.4 (1.1)**

Table 4. Clinical Results for Cohort 2B (improved sensors in upper arm)

Patient ID (Upper Arm)	MARD (%)	MAD (mg/dL)
D64LU	11.9	10.0
D65LU	12.2	30.1
D66LU	13.6	9.5
D67LU	11.2	7.2
Combined (SE)	**12.2 (0.7)**	**12.2 (0.5)**

Table 5. Clinical Results for Cohort 3 (improved sensors in upper arm)

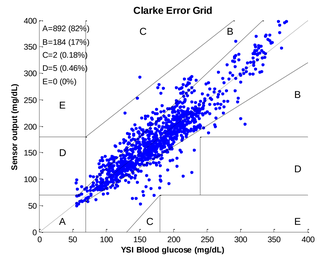

Figure 8. Clarke Error Grid for Cohort 3 (improved sensors in upper arm)