# The Use of Dexcom G4 Continuous Glucose Monitoring in Diabetes NHP Research

Poster 79-LB

CrownBio
CONNECTING SCIENCE TO PATIENTS

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## INTRODUCTION

The Continuous Glucose Monitoring (CGM) system is approved by the FDA for 24-hr real time interstitial glucose readings, every 5 min in diabetic patients. This device allows people with diabetes to observe their glucose levels and to track how quickly they increase or decrease. Non-human primates (NHPs) are a highly valuable model for diabetes research and drug discovery. In this study we use the Dexcom G4 CGM telemetric device in cynomolgus monkeys (*Macaca fascicularis)* to investigate whether this method of blood glucose monitoring can provide novel insights compared with the use of a classical glucometer. Our data show that the CGM system used in preclinical research on NHPs can provide additional important information for better characterizing diabetes as a disease, and to improve drug discovery.

## METHODS

On the day prior to sensor insertion, a small skin area on the monkey upper back was clipped and prepared, and the animal was fasted overnight following the afternoon meal. On the day of sensor insertion, the monkey was anesthetized with ketamine (10mg/kg, i.m.) and the shaved skin area was sterilized with iodine and alcohol. The sensor (**Fig. 1**) was inserted under the skin and subsequently connected to a transmitter to measure glucose levels in tissue fluid. Superglue, medical tape, and stretch bandages were used to fix the sensor/transmitter on the skin. A monkey jacket was put on to prevent device disconnection and dislocation, and the receiver and other devices were placed outside of the cage for data collection. Several calibrations with glucometer readings were conducted before data collection. The experimental plan is shown (**Table 1**). Each sensor was removed after 7-day continuous glucose monitoring.

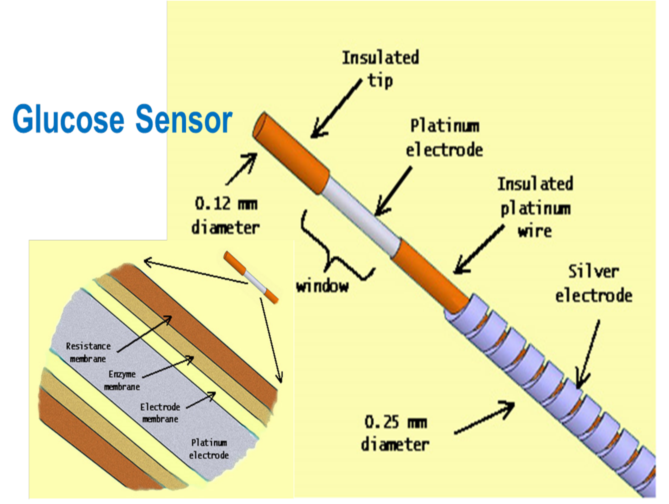


**Figure 1. Components of glucose sensor for CGM.**

Table 1. Study design for CGM basic data collection in normoglycemia and diabetes monkeys

| Group No. | Animal No. | Treatment | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 | Day 8 |
| 1 (Normal Monkey) | 1001 | • Insert sensor under ketamine 10 mg/kg • Calibrate G4 system in the evening | Collect baseline | Collect baseline | oGTT (1.75 g/kg glucose, in 35% solution) in overnight fasted monkeys in chair | Banana Test (two bananas, plus 0.8-1.7 g of sugar) in overnight fasted monkeys in cage | Collect baseline | ivGTT (0.25 g/kg glucose in 50% solution) in overnight fasted monkeys in chair | Take out sensor |
| | 1002 | | | | | | | | |
| | 1003 | | | | | | | | |
| | 1004 | | | | | | | | |
| | 1005 | | | | | | | | |
| 2 (Diabetic Monkey) | 2001 | | | | | | | | |
| | 2002 | | | | | | | | |
| | 2003 | | | | | | | | |
| | 2004 | | | | | | | | |
| | 2005 | | | | | | | | |

## RESULTS

The CGM system recorded interstitial glucose continuously up to 7 days and captured glucose level circadian oscillations (**Fig. 2**, **Fig. 3**, and **Fig. 4**) with larger fluctuations in diabetic monkeys**.** The CGM system also captured stress-induced glucose level increases (**Fig. 4**). Glucose level changes tested by glucometer and CGM during oGTTs matched well (**Fig. 5**). However, compared with the glucometer readings, an obvious delay with a smaller peak of glucose changes during ivGTT was observed by the CGM method (**Fig. 6**, left). CGM data analyses enabled the capture of daily glucose level distribution (**Fig. 6**, middle and right). CGM use in NHPs can be an informative tool for diabetes research and drug discovery.

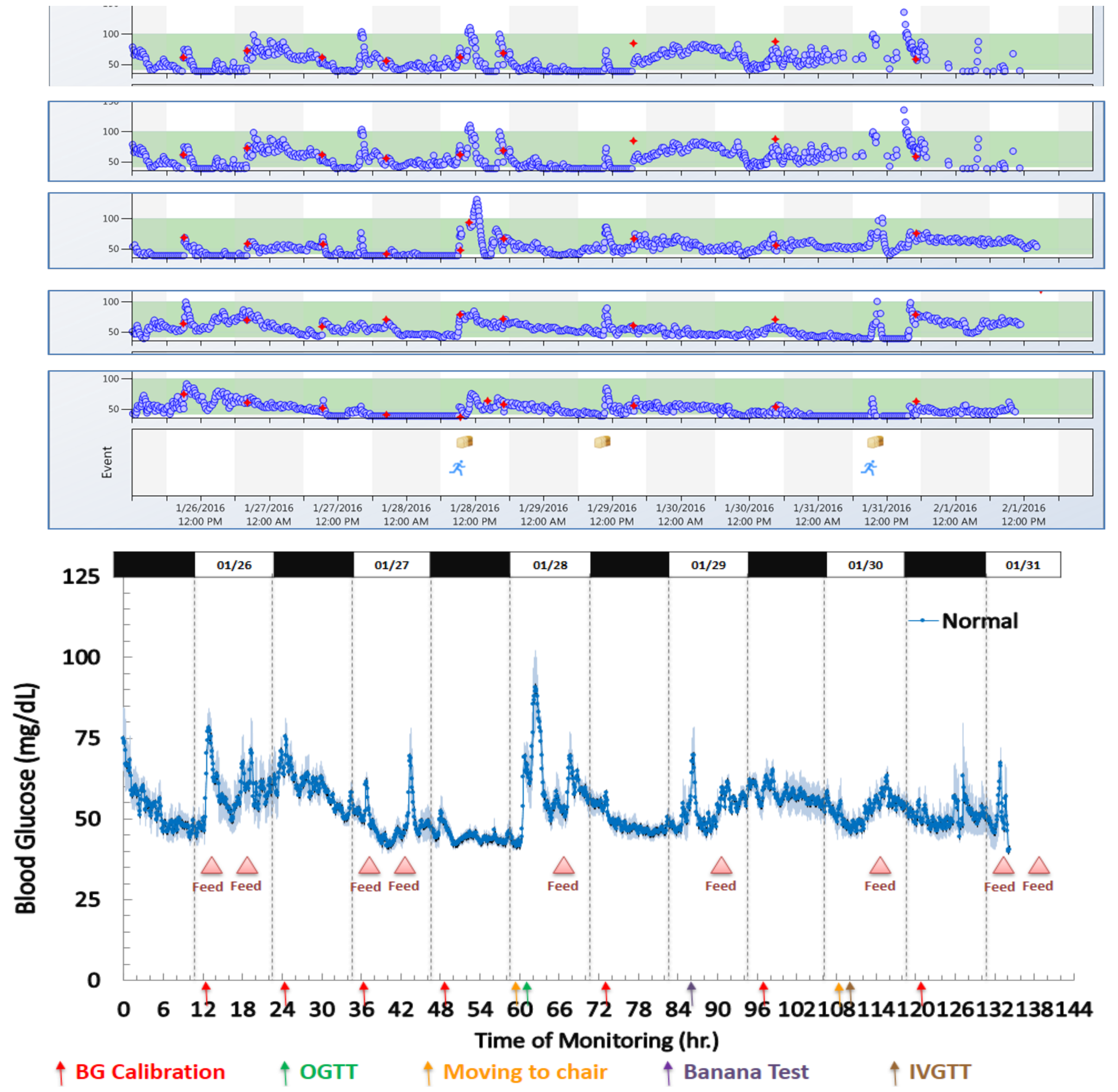


**Figure 2. Glucose levels in normal NHPs (n=5), individual readings (upper) and mean (lower).**

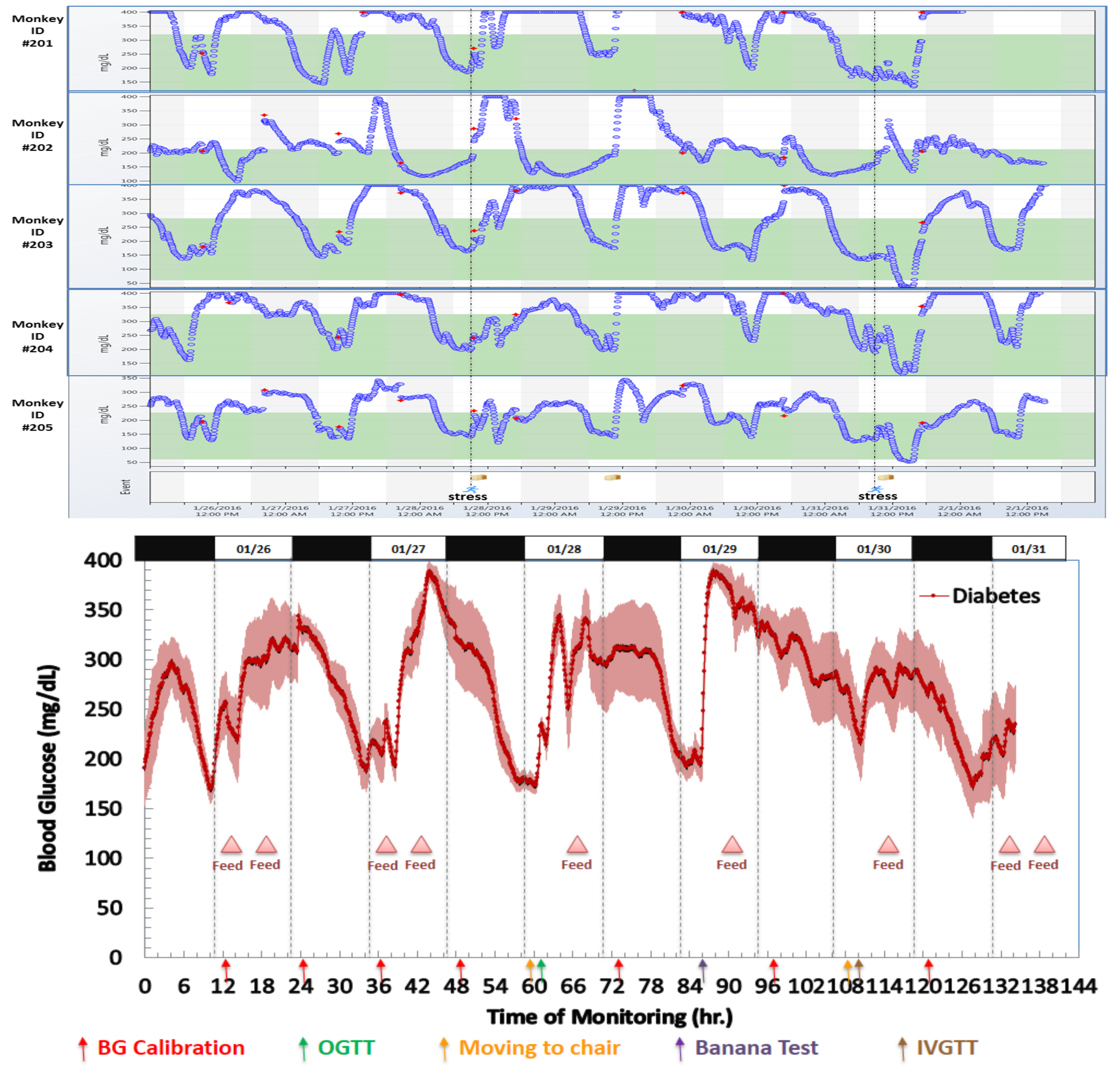


**Figure 3. Glucose levels in diabetic NHPs (n=5), individual readings (upper) and mean (lower).**

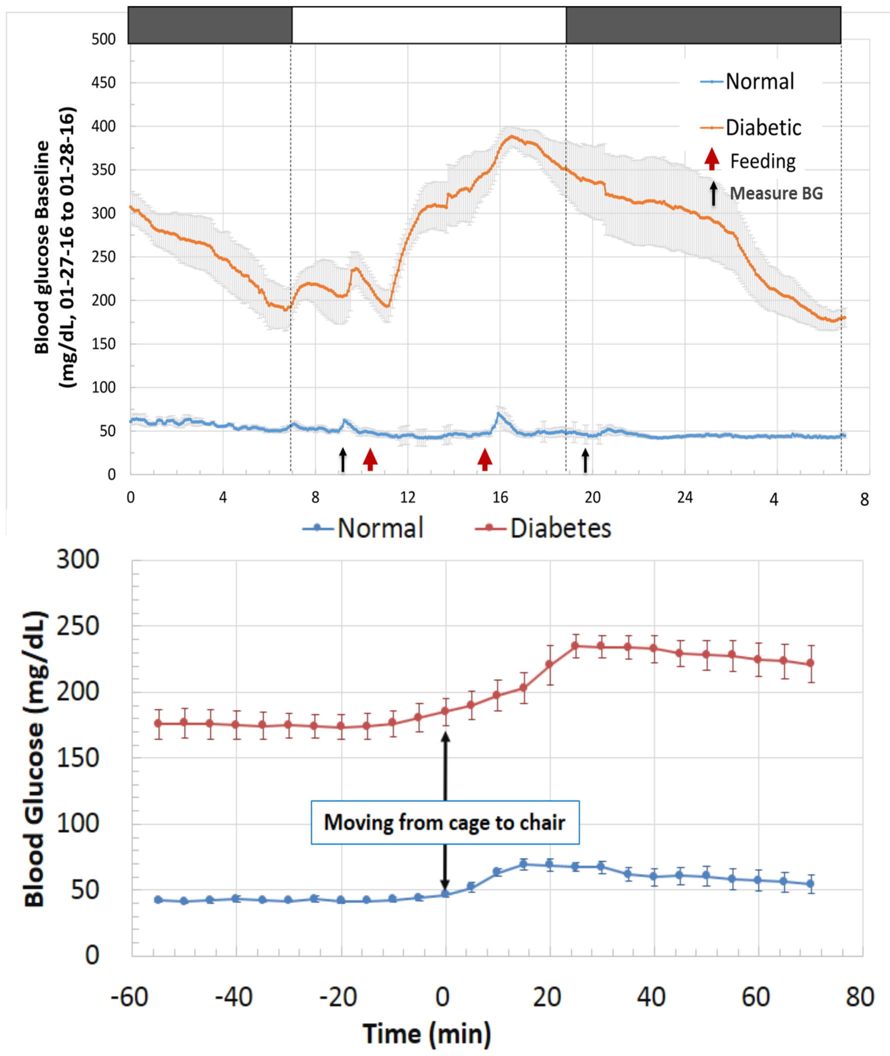


**Figure 4. Typical circadian (upper) and stress-related (lower) changes of body glucose levels in normoglycemic and diabetic monkeys.**

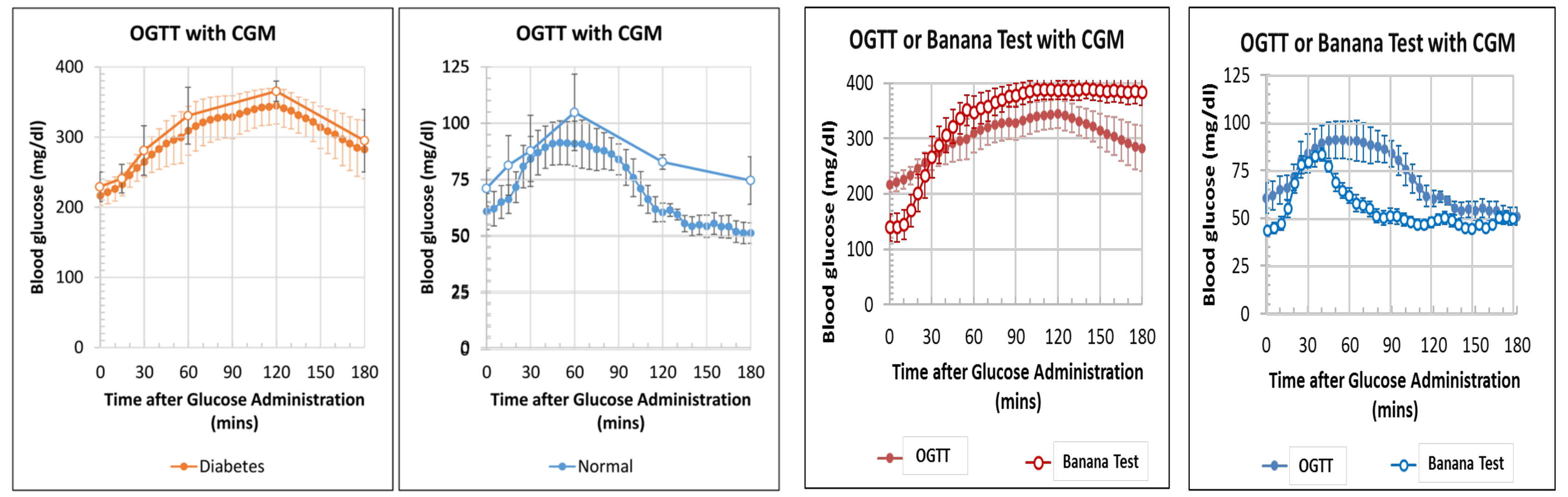


**Figure 5. Body glucose changes during oGTTs recorded with CGM (●) and glucometer (○) in diabetic (red lines) and normal (blue lines) monkeys (left 2 panels). Body glucose changes during glucose (●) and banana (○) oGTTs recorded with CGM in diabetic (red lines) and normal (blue lines) monkeys (right 2 panels).**

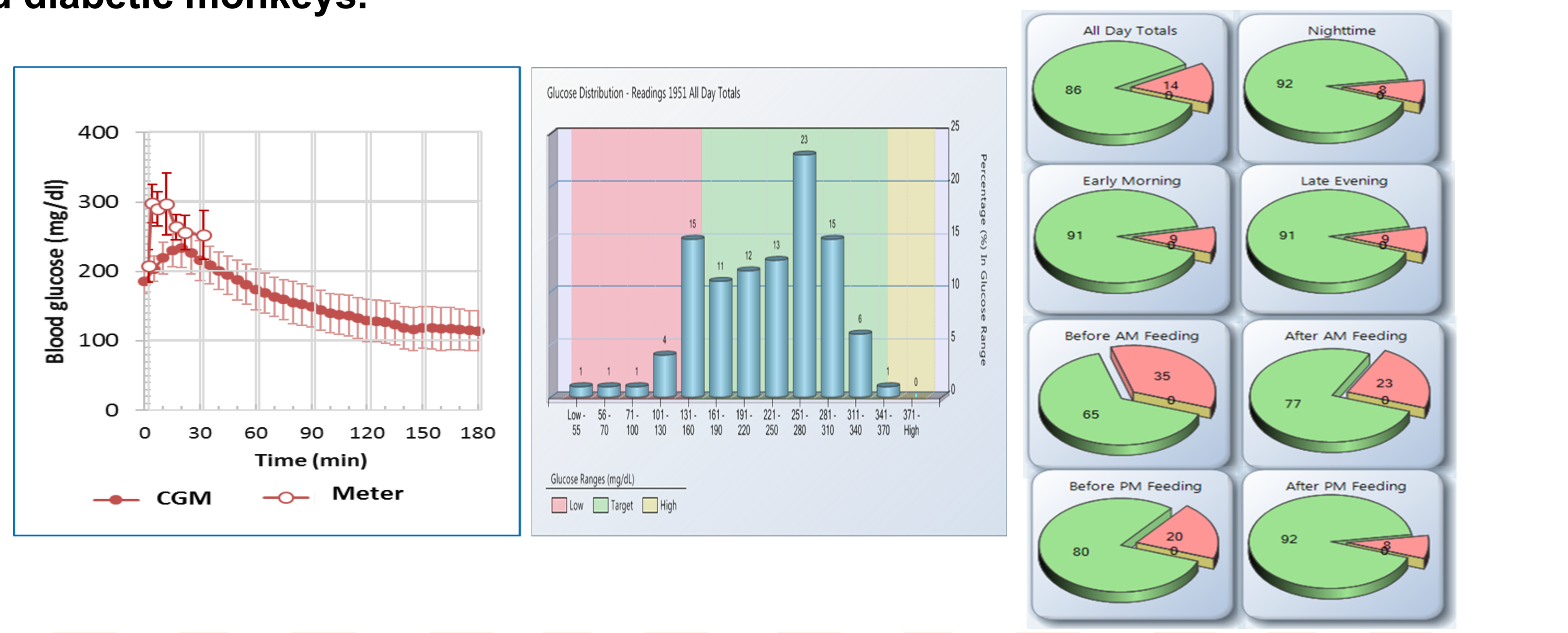


**Fig. 6. Glucose changes recorded by glucometer (○) or CGM (●) during ivGTT (left) and distribution during a day (middle and right).**

## SUMMARY

**The CGM device is a useful tool for NHP diabetes research, allowing the gathering of important data once considered impossible to collect.**

**Advantages:**

- **Collect unique information such as a 24hr body glucose profile in euglycemic and hyperglycemic models.**
- **Record baseline data in diabetic monkeys subjected to the desired protocol, to identify stressors which lead to glucose variability, and adjust protocols to minimize stress (such as use of the "banana test").**

**Limitations:**

- **Detectable glucose range of device is 40 to 400mg/dl. Any measurement close to either end of the range can be less accurate.**
- **Delayed response to fast glucose change of CGM can result in missing the "peak" during ivGTT.**