Comparison of Continuous Glucose Monitoring Systems in Type 1 Rat Model

Paul Haefner1, Kimberly Holliday-White1, Dr. Mark Clements2.

Introduction
There are currently few options to provide continuous glucose monitoring (CGM) for preclinical research. Available alternatives consist of a handful of clinical interstitial CGM systems which are not tailored to serve the preclinical market. This study compares the performance of one of those systems (Pro: Medtronic MiniMed, Northridge, CA) to that of a fully implantable, direct blood monitoring, prototype (Data Sciences International, St. Paul, MN) utilizing a custom configured glucose sensor (Nova Biomedical, Waltham, MA).

Materials and Methods
Ten weight-matched Sprague Dawley rats were implanted with the Data Sciences prototypes at 8 weeks of age. The prototype’s glucose sensor was positioned in the rat’s abdominal aorta and the transmitter electronics located in the intra-peritoneal cavity. One week later, the interstitial sensors were carefully placed in the dorsal skin near the scapulae and the rats were dosed with streptozotocin (65 mg/kg). Continuous glucose readings were collected by both systems throughout their useful lifetimes. The interstitial system provided a new glucose reading every 5 minutes while the prototype system provided a new value roughly every 3 milliseconds. Additionally, the prototype transmitters provided temperature and activity information. Daily glucose measurements (twice daily during the duration of the interstitial sensor) and approximately weekly glucose tolerance tests (GTTs; dextrose, 1-2.6 g/kg, ip; insulin, 0.5-1.0 unit/kg, im) were measured with an extended range (10 to 900 mg/dl), non-clinical version of the StatStrip Xpress point of care glucometer (Nova Biomedical, Waltham, MA).

Results
Diabetes was induced in 8 of 10 animals. Two of 10 interstitial sensors failed to perform correctly; one of two failed because it poked through the skin. Two of 10 prototype sensors failed to perform correctly due to improper placement during implantation. One sensor was placed in the abdominal cavity and the other was placed in the vena cava. The interstitial sensors exhibited an average useful lifetime of 5.6 days while the prototype sensors averaged 24.9 days (figure 2). Interstitial glucose readings were, on average, delayed 9.5 minutes from those of the prototype devices (figure 3). Figures 4 and 5 show the absolute relative errors for sensors. All prototype readings and 4/5 interstitial readings above 100% error occurred below 100 mg/dl. One of 5 interstitial readings above 100% error occurred between 100 and 200 mg/dl.

Error Grid Analysis
Figures 6 and 7 show results from the error grid analysis with 98.5% (DSI sensor) and 90.8% (MDT sensor) of points in zones A and B.

Discussion
Generally the DSI prototypes produced cleaner data than the MDT system (figure 8). The DSI prototypes also exhibited a longer useful life though a few factors shortened their performance. Two of 10 sensors were implanted incorrectly, 2 of 10 sensors stopped functioning when the electronics got wet due to a housing leak, 1 of 10 sensors pulled out of the vessel (“old” Vetbond was used at implant), 1 of 10 sensors physically broke and 1 of 10 sensors exhibited an unexplained rapid degradation of sensitivity.

Conclusions
The prototype devices produced high resolution glucose measurements for a longer duration than the interstitial sensors tested. Additionally, the prototype devices directly measure blood glucose and provide both temperature and activity information. These devices, with improved housing design, sensor form factor and surgical techniques, provide a promising alternative to clinical interstitial systems for preclinical continuous glucose monitoring in a free roaming type 1 rat model.

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