OPTICALLY BASED NONINVASIVE GLUCOMETER DEMONSTRATES CLINICAL TREND ACCURACY DURABILITY 24 HOURS AFTER CALIBRATION

Combs A.[1], Rawson B.[2], Keating J.[3], Burrell R.A.[3], Schurman M.[3], Lock J.P.[4]

[1]Management, Grove Instruments Inc., Worcester, MA, USA
[2]Clinical, Grove Instruments Inc., Worcester, MA, USA
[3]Engineering, Grove Instruments Inc., Worcester, MA, USA
[4]Diabetes Center of Excellence, University of Massachusetts Medical School, Worcester, USA

ABSTRACT: Self-monitoring of blood glucose (SMBG) is critical for individuals with diabetes to achieve the glycemic control required to avoid the disease's dreaded complications. A noninvasive (painless, bloodless) technology that could encourage patients' interest in SMBG has long been sought. We report on the progress toward such an instrument as developed by Grove Instruments, Inc. (Worcester, MA) and the results of a clinical trial demonstrating the durability of a calibration scheme in ambulatory adult patients with diabetes.

Methods: 10 adult volunteers with diabetes (6 males, 4 females, ages 29-72, 2 T1D, 8 T2D, 6 using insulin, 8 Caucasians, 2 non-whites) spent 5 hour sessions in Grove's clinical laboratory on 2 consecutive days. Patients presented fasting and were fed a standard glucose meal (Glucola®).
Noninvasive glucose determinations (Grove Instruments "D-Plat Prototype" Instrument, Optical Bridge® technology) were made every 10 minutes (35 seconds on the earlobe), and invasive blood glucose determinations made every 20 minutes (Hemocue™) for the entire 5 hours.

Using the data from Day 1 a calibration model for the device was developed using partial least squares for each patient. On the second day the identical protocol was followed. On Day 2 the noninvasive glucose determinations were all predictions made by the device based on the previous day's calibration model. Investigators were blinded both days to all noninvasive testing results including device performance, signal quality and clinical results. These data, 579 data pairs, were analyzed for accuracy (MARD), Pearson correlation, and statistical significance and plotted on the Clarke Error Grid. Because the Grove device measures the glucose signal from the blood compartment, a second analysis was carried out on second day predictions based on perfusion quality as measured by a green LED (525 nm) absorbance and water movement (Grove proprietary method) during a measurement.

Results: All 10 patients completed both full 5 hour sessions of the protocol. Of the 620 data pairs obtained in blinded fashion, 63 noninvasive determinations could not be analyzed due to laser instability in one light source. No patients or data pairs were excluded from the subsequent glucose prediction analysis. The range of blood glucose values in the data set was 63 – 363 mg/dL. For the entire data set (579 data pairs) Day 2, prediction only, MARD was 19.7%, Pearson (r) = 0.593, Clarke A space = 68.7%, A+B = 96.6%, $p < 8 \times 10^{-44}$. 6 patients were

found to have threshold or better perfusion quality. For these 6 the results for Day 2, prediction only, MARD was 13.4%, Pearson (r) = 0.699, Clarke A space = 80.1%, A+B = 98.9%, $p < 1 \times 10^{-41}$. A further *post hoc* analysis revealed that a durable calibration model can be successfully constructed using as few as 4 paired data points at the fasting, high, and 2 intermediate blood values after a standard glucose challenge.

Conclusions: Grove Instruments' noninvasive glucometer is capable of producing trend accuracy results (comparable to all marketed Continuous Glucose Meters) 24 hours after a calibration model is built. These results suggest that the Grove device can be further developed into a noninvasive glucose monitor with an acceptable calibration requirement. Studies are being undertaken to reduce the calibration requirements and to determine the durability of single day calibrations over long periods of time.