Assessment of Nova Biomedical StatStrip® Glucose Meters and Test Strips in Rat Glucose Studies

Richard G Peterson[1], Robert Brockway[2]. 1. PreClinOmics, Inc., Indianapolis, IN. 2. Data Sciences International, Inc., St. Paul, MN

Introduction

Preclinical blood glucose testing methods have relied largely on human consumer market technology. The FDA accuracy requirement for consumer meters of +/-20% is not ideal for research applications. Glucose strip measurements are known to be impacted by the level of hematocrit in the blood. In research studies, the hematocrit level, size of red blood cells, and distribution of glucose in plasma vs red blood cells can vary across animal models, and the hematocrit level can further be altered based on animal condition and drug interventions. The StatStrip® Xpress™ GLU meter (Nova Biomedical) provides increased accuracy by measuring and correcting for hematocrit values and is also immune to common interferents such as ascorbic acid and acetaminophen[1,2]. The StatStrip meters have historically only been marketed for use in hospital settings, but are now available through Data Sciences International (DSI) for use in preclinical applications. The AlphaTRAK® (Abbott) meter has been used by PreClinOmics in past studies and is specifically marketed for preclinical use and has demonstrated higher accuracy in animal models than consumer meters[3]. The present study compares both systems to the model AU480® (Beckman Coulter) Chemistry System.

Materials and Methods

Normal and diabetic ZDSD rats (N=98) were used to evaluate the performance of the StatStrip and AlphaTRAK glucometers against the AU480. The StatStrip meter used is an "investigational use only" meter that has been modified by Nova Biomedical and provided by Data Sciences International to accommodate a range of 10-900mg/dL rather than the standard 10-600mg/dL for the human model.

Controls were run on each glucose meter making sure that all of the controls were in the target range. Each rat was removed from its cage and the tail cut and bled (80-100uL) into Li-Hep tubes to be run on the AU480. The rats were then passed to another person who bled them into the glucose meter strips. A third person was writing down the measured values. Two meters of each type were used and two measurements were made with each of the meter types for each time point of data collection, and whenever possible the same drop was used for all four strips. This process took three hours starting at 9:02. The two measurements were averaged for comparison across analysis methods. The tubes were kept in a cold block until post analysis started at 12:43 and continued until 14:38. Blood was well mixed before running it on duplicate samples for each meter a second time using a single pipette of blood in the same sampling sequence. The remaining blood was spun in a refrigerated centrifuge before being pipette in tubes to run on the AU480. Two sequential AU480 runs were done. Controls were run on the AU480 before and after the runs, confirming that values were within the target range.

A subsequent oral glucose tolerance test (OGTT) was performed to evaluate the performance of the StatStrip meter for blood glucose levels exceeding the standard StatStrip limit of 600mg/dL (N=12). This test was performed using very diabetic ZDSD rats in order to obtain the very high glucose levels. Sample points were taken prior to administration and at 30, 60, 90, and 120 minutes post dose.

Results

Our results will focus on the comparison of the afternoon strip measurements and the AU480 analysis results (Fig 5). The AlphaTRAK results showed a bias of -9.0% relative to the AU480 across a range of glucose from 100-600mg/dL with a zero crossing of +7.8mg/dL. The StatStrip results showed a bias of +3.6% relative to the AU480 with a zero crossing of -10.1mg/dL. The R^2 value was slightly better for the StatStrip readings at 0.993 versus 0.966 for the AlphaTRAK. The average absolute difference between the AlphaTRAK and AU480 was 15.3% for the morning and 8.1% for the afternoon measurements. The average absolute difference between the StatStrip and the AU480 was 5.4% for the morning and 4.7% for the afternoon measurements (Table 1).

We evaluated the duplicate samples for each of the initial meter measurements. Both the StatStrip and AlphaTRAK showed high correlations of R^2>0.99 (Fig 1,2)as well as average errors within about 4%. There were two instances where there was a negative bias to, and statistically significant difference between, sample two vs sample one as seen in Table 1. One instance involved the AlphaTrak meter (afternoon tube sample) and the other involved the StatStrip meter (morning fresh blood sample). The average absolute difference between the first and second readings was 3.5-4.2% for StatStrip and 2.2-3.0% for AlphaTRAK in three separate measurement groups.

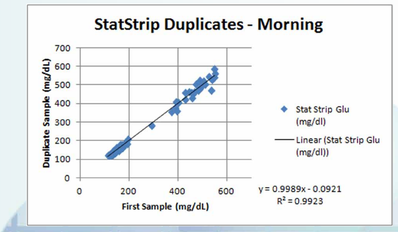

Fig. 1 – StatStrip duplicate samples

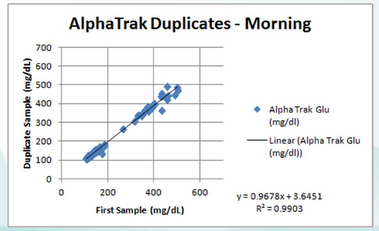

Fig. 2 – AlphaTRAK duplicate samples

Results from an initial study (same N=98) provided AU480 values that were consistently higher than both the StatStrip and AlphaTRAK values across the range of glucose evaluated. In order to investigate this further, we repeated the study as described here and included repeat StatStrip and AlphaTRAK measurements at the afternoon timepoints using the same blood sample used for AU480 analysis. The afternoon measurements registered consistently higher values with both strips than the earlier matching samples. For the AlphaTRAK samples the afternoon measurements were 12.8% higher than the morning measurements (Fig 7), and for the StatStrip the afternoon measurements were 5.0% higher than the morning measurements (Fig 6).

	% Error	% Absolute Error	R-square	Slope	Offset	H(o) p-value
Morning AlphaTrak sample 1 vs 2	-1.0%	3.0%	0.99	0.968	3.65	0.008
Afternoon AlphaTrak sample 1 vs 2	-0.4%	2.8%	0.985	0.99	1.43	0.287
Morning AlphaTrak vs Afternoon AU480	-14.9%	15.3%	0.984	0.805	8.75	NA
Afternoon AlphaTrak vs Afternoon AU480	-5.1%	8.1%	0.966	0.91	7.72	NA
Morning StatStrip Sample 1 vs 2	-0.1%	3.5%	0.992	0.999	-0.09	0.393
Afternoon StatStrip Sample 1 vs 2	-1.7%	4.2%	0.991	0.969	2.58	<0.001
Morning StatStrip vs Afternoon AU480	-5.0%	5.4%	0.994	0.982	6.21	NA
Afternoon StatStrip vs Afternoon AU480	-1.7%	4.7%	0.993	1.036	10.1	NA
Afternoon AU480 sample 1 vs 2	1.1%	1.5%	0.999	1.014	0.52	<0.001
OGTT AlphaTrak vs AU480 (Tail)	-8.80%	10.60%	0.946	0.946	-14.149	NA

Table 1 – Key Study Statistics

The OGTT test drove glucose values to nearly 800mg/dL (total N=60) and this data was added to the dataset. The StatStrip meter performed well with R^2 = 0.99, slope = 0.94 and offset = +4.9. The difference in slope and offset from our other study results seems to indicate a small non-linearity at glucose ranges beyond 600mg/dL.

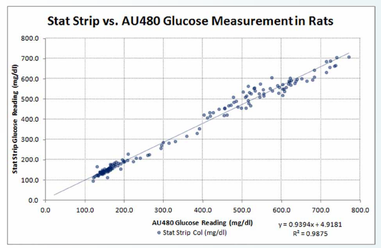

Fig. 3 – OGTT StatStrip vs AU480

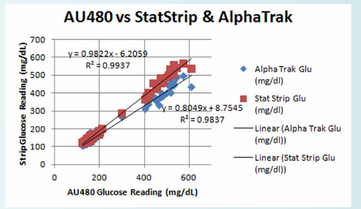

Fig. 4 – Strip measurements at time of sample

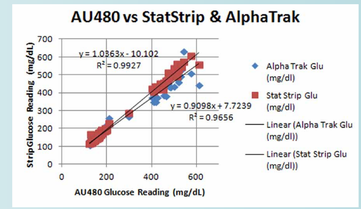

Fig. 5 – Strip measurements at AU480 analysis

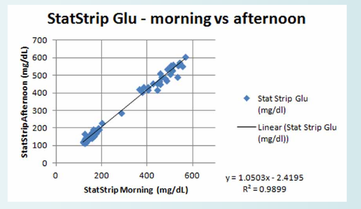

Fig. 6 – StatStrip morning/afternoon measurement

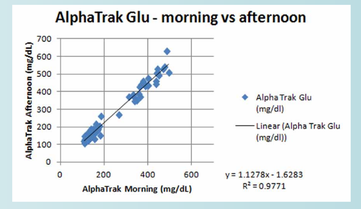

Fig. 7 – AlphaTRAK morning/afternoon measurement

Discussion

We don't have an explanation for the statistically significant differences between two sequential samples seen on one dataset each for StatStrip, AlphaTrak, and AU480. We used the same lot of strips, so we don't suspect a variation between strip lots. It is possible that there were differences between the duplicate meters of each type, but this didn't show up consistently. While the differences were not huge (-1.7% to +1.0 bias), the statistical significance of the differences is puzzling.

Further investigation is needed to determine whether the higher afternoon values were a result of the plasma glucose level changing, the hematocrit value changing, or some other unknown influence on the measurement system(s). The difference in magnitude of the change between the AlphaTRAK and StatStrip might also be explained by these further studies.

Summary/Conclusion

Both meters provided very good correlations with the AU480 across the range of study conditions. The StatStrip system provided more accurate data than the AlphaTRAK system and data nearly equivalent to the AU480 clinical analyzer over the range of glucose studied. Importantly the StatStrip introduced less bias to the measurements relative to the AU480. PreClinOmics has elected to standardize on the StatStrip to take advantage of the improved accuracy for preclinical research studies. The ability to perform up to 900mg/dL will provide significant benefit for research studies involving glucose challenges.

We found that timing of analysis relative to the blood sampling had a significant impact on the values obtained, and that it is important to analyze the same blood sample at the same time in order to correctly compare analysis methods. Follow up studies will be considered to further assess the impact of timing of analysis relative to blood sampling and factors contributing to error/bias.

References

1. Lyon ME, et. al., Interference studies with two hospital-grade and two home-grade glucose meters. Diabetes Technol Ther. 2009 Oct; 11(10):641-7.
2. Vanavan S, et. al., Performance of a new interference-resistant glucose meter. Clin Biochem. 2010 Jan; 43(1-2):186-92.
3. Zini E, et. al., Evaluation of a new portable glucose meter designed for the use in cats. Schweiz Arch Tierheilkd. 2009 Sep; 151(9):448-51.