Clinical Evaluation of FreeStyle™
Blood Glucose Monitoring System
Using Capillary Blood from Finger and Palm

Accuracy of the FreeStyle™ Blood Glucose Monitoring System In Situations of Rapidly Changing Glucose Levels

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Introduction

Background

The FreeStyle™ Blood Glucose Monitoring System, developed at Abbott Diabetes Care for the analysis of small volume (300 nanoliter) blood samples, is cleared by the US FDA for commercial distribution. In addition to testing on the fingers, the FreeStyle System can also be used to test blood glucose from alternate sites, specifically, the forearm, upper arm, thigh, calf, or palm (at the base of the thumb). While this ability to test on alternative, potentially less painful testing sites has been hailed as a boon to patient compliance[1], there have been concerns about the accuracy of these results. Some clinical studies to date suggest that at times of rapid glucose change, such as within two hours after a meal, exercise or taking medication, test results from some alternative sites and the finger may differ.[2,3]

Study Purpose

The purpose of this study was to evaluate FreeStyle glucose measurements from the finger and the palm (at the base of the thumb) during periods of rapidly changing glucose levels and establish whether this sampling site offers equivalent results to fingertip tests and therefore improved accuracy over other alternative test sites.

Materials and Methods

Study Subjects

The study consisted of 44 subjects, 18 to 66 years of age, with Type 1 diabetes. The study protocol was approved by a duly constituted IRB before initiating enrollment in the study. All subjects signed an informed consent form approved by the IRB. Forty-four subjects enrolled in the study at the Diabetes and Glandular Diseases Clinic in San Antonio, TX with Dr. Sherwyn Schwartz as the Principle Investigator.

Study Procedures

Subjects were given a FreeStyle Blood Glucose meter to perform all glucose tests as indicated per protocol. Subjects were to alternate the test sites between their fingers and the palm (at the base of the thumb). Subjects unfamiliar with the FreeStyle meter were trained on its use by a member of the research staff. Testing began after the subject was trained on the use of the FreeStyle meter.

Summary of Procedure

Measure glucose in finger and palm (at the base of the thumb) at 15 - 20 min intervals throughout the following:

Start intervention with patient fasting or > 2.5 hours after last meal

Measure baseline glucose values to ensure it was < 150 mg/dL before start of intervention

Give subject Glucola to raise glucose level to 300 mg/dL or 2 hours

Administer insulin to lower glucose rapidly > 2mg/dL/min

Stop when subject reached 70 mg/dL or 2 hours

Detailed Procedures

On the day of testing, subjects were instructed to eat breakfast by 7:00 am and arrive at the clinic by 9:30 am. However, in order to accommodate subject's individual schedules, subjects were also allowed to arrive at other times of the day as long as 2.5 hours or greater had passed since the last meal.

These time frames were designed to minimize the possibility that subjects would arrive to the clinic with a high blood sugar immediately following a meal.

Subjects were asked to wash their hands with soap and water and dry thoroughly prior to performing the FreeStyle glucose tests. This would eliminate the risk of potential contaminants interfering with the testing. Before study procedures were conducted, subjects completed a brief pre-study questionnaire to obtain demographic information.

Subjects were instructed to perform and record the following series of 4 FreeStyle tests:

1st test: Palm (at base of thumb) site
2nd test: Finger site
3rd test: Palm (at base of thumb) site
4th test: Finger site

The series of blood glucose tests were performed at 15-20 minute intervals until the blood glucose reached 150 mg/dL or less. If the subject's blood glucose had still not reached the criterion of ≤150 mg/dL after 2 hours, study procedures were terminated and the subject was withdrawn from the study.

When blood glucose did reach ≤150 mg/dL, the research staff administered an oral glucose challenge test. This test consisted of consuming 75 gm of Glucola or an equivalent. Glucose testing would then resume, as described above, at 15-20 minute intervals until the blood glucose reached 300 mg/dL or until the subject had been testing for 2 hours.

Upon completion of the glucose challenge test, the subject would proceed to do an insulin challenge test. This test consisted of having the subject take an insulin dose (as determined by a healthcare professional) sufficient to lower the blood glucose by at least 2 mg/dL/min. Glucose testing would then resume, as described above, at 15-20 minute intervals until the blood glucose reached 70 mg/dL or until the subject had been testing for 2 hours. At this time, the study was concluded and the subject

Table 1. Subject Demographic Data

Gender	Female: 24 (55%) Male: 20 (45%)
Age	Avg: 42.5 years Range: 18-66 years
Weight	Avg: 172 lbs. Range: 110-309 lbs.
Height	Avg: 5’7” Range: 4’10”-6’3”
Ethnicity	Caucasian: 36 (82%) Hispanic: 6: (14%) African-American: 2 (5%)
Diabetes type	All Type 1 diabetes (as required per protocol)
Duration of diabetes	Avg: 23 years Range: 2-47 years

was instructed to resume his/her normal diabetes management program.

To minimize risk to the subjects, vital signs were monitored every 15 minutes during the glucose and insulin challenges. Signs or symptoms of hyper- or hypoglycemia were also monitored during the challenges. If any signs or symptoms became apparent, the challenge was discontinued and the appropriate medical treatment was administered.

The possible risks to subjects participating in this study were those associated with the transient states of hypoglycemia and hyperglycemia. Other possible risks to the subjects included bruising at the lancing site and/or discomfort from the lancing procedure itself. The presence of such adverse events as a result of participation in the study was monitored and recorded by the research staff.

Results and Discussion

Table 1 summarizes the subject demographic information obtained from a pre-study questionnaire.

Incidence of Adverse Events

No hypo- or hyperglycemia events were reported. Bruising of the palm (at the base of the thumb) following the study was observed in 28 of the 44 enrolled subjects (64%). No other adverse events were reported for the palm (at the base of the thumb) test sites. No bruising or other adverse events were noted at the finger test sites.

Since two palm (at the base of the thumb) tests were repeated every 15-20 minutes, this implicated that subjects performed a total of 6-8 FreeStyle tests on the palm (at the base of the thumb) every hour. Given that most subjects took 4-6 hours to complete the study, this would imply that approximately 24-48 tests were done on both palm (at the base of the thumb) areas during the course of the study. This explains the incidence of bruising on the palm (at the base of the thumb) observed in a large percentage of the subjects.

It is likely that adverse events were not observed at the finger sites because the fingers are where most diabetic patients are accustomed to testing their blood sugars. Over time, a diabetic patient's fingertips normally become calloused as a result of repeated lancet sticks required for blood sugar tests. Consequently, this test site is much more tolerant to repeated lancet sticks than the palm (at the base of the thumb) site would be.

Palm vs. Finger FreeStyle Glucose Data

Three subjects did not complete the study because their blood glucose values did not reach the criterion of ≤150 mg/dL required to begin the glucose challenge. Consequently, only 41 out of 44 subjects completed all study procedures, including the glucose and insulin challenges.

The object of the study was to rapidly bring the subject from a low or normal glucose concentration to a high glucose concentration by intake of carbohydrate, and then reduce the glucose back to a low or normal concentration by subcutaneous insulin injection or by infusion from an insulin pump. In this manner any physiological lag in the measurements could be observed.

The two finger tests and the two palm (at the base of the thumb) tests taken at each time point were averaged in order to reduce noise, and to make any pattern more easily discernable. The rates of change were determined from the measurements taken on the finger. The rates were calculated by averaging the two FreeStyle tests at each time point and dividing the difference in glucose by the difference in time in minutes.

The distribution of rates is graphed in **Figure 1**. As shown in the figure, 47.3% of the measured rates were greater than ± 2 mg/dL/min. Calculated rates less than +/- 1 mg/dL/min were observed when the blood glucose peaked and began to decrease. Representative results of glucose values versus time are shown in **Figure 2**. Despite very high rates of change which were achieved in this study, there were no clinically or statistically significant differences between blood glucose values in fingertip or palm (at the base of the thumb) capillary blood. It is clear from inspection of the graphs that there is little or no difference between finger and palm (at the base of the thumb) measurements for most of the subjects. Where there are apparent differences, there is no consistent pattern to the differences. A statistical analysis was performed in order to make a complete assessment of the data set.Analysis by two sample test was conducted to determine if the glucose measurement taken on the palm (at the base of the thumb) were statistically different than the glucose (at the base of the thumb) measurements taken on the finger.

Taking the data set as a whole, there is no statistical difference between the finger tests and the palm (at the base of the thumb) tests. A statistical test was also performed for each subject individually. There was no statistical difference for any of the subjects.

Conclusions

There is no clinically or statistically significant difference between blood glucose measurements performed on the palm (at the base of the thumb) and those performed on the finger even during times of very rapid glucose change when using the FreeStyle glucose monitoring system. For the purpose of blood glucose measurements these sites can be considered physiologically equivalent. As a result of this study, new labeling for FreeStyle test strips was submitted to Food and Drug Administration. This was accepted. The FreeStyle system uses an extremely small sample of blood and is technically very different from other glucose monitoring systems. This conclusion is only applicable to the FreeStyle system and is not to be extrapolated to other BGM systems.

New Freestyle Product Labeling

Important Note: If you are testing for hypoglycemia (low blood glucose) or if you suffer from hypoglycemia unawareness, we recommend that you test on your fingers or palm (at the base of the thumb).[4]

References

1. Ary DV etal, Patient perspectives on factors contributing to non adherence to diabetes regimes. *Diabetes Care* 1986. vol. 9 p 168 - 172
2. Jungheim K, Koschinsky T. Glucose monitoring on the arm. *Diabetes Care* 2002, vol 25, p 956-960.
3. Ellison JM et al Rapid changes in post prandial glucose produce concentration differences between finger, forearm and thigh sampling sites. *Diabetes Care* 2002, vol 25 p. 961 - 964.
4. FreeStyle Blood Glucose Test Strips – instructions for use P/N ART03979 Rev A

Figure 1. Distribution of rates of glucose change.

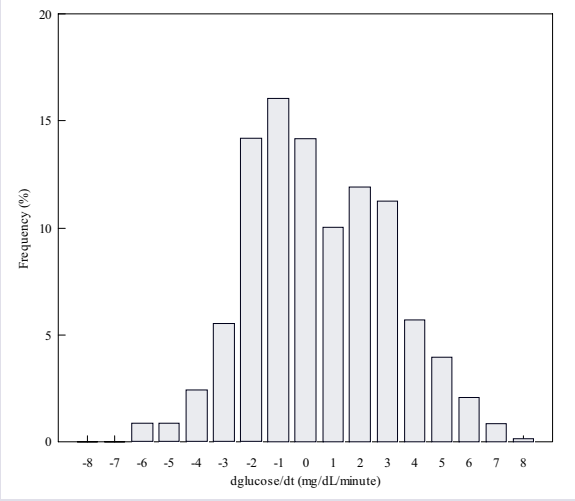
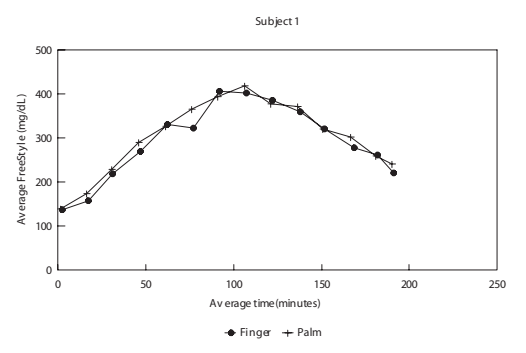
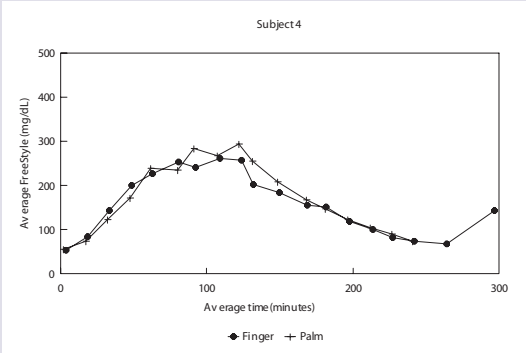
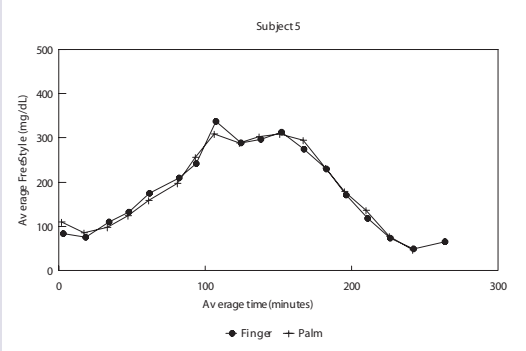
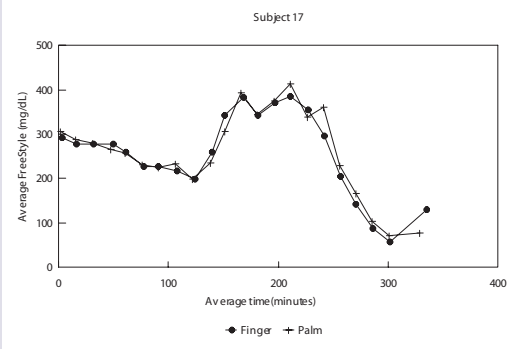


Figure 2. Graphs of glucose versus time for a sampling of subjects









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