GlucoTrack™

A Unique Method for Non Invasive Glucose Monitoring

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Background:

Non-invasive (NI) glucose measurement, by definition, does not measure glucose levels in blood, but a physiological phenomenon (PP) that is reflected by a change in tissue parameters that are correlated with blood glucose concentration. Since glucose represents the most variable solute in blood (Fig. 1), it is responsible for the majority of the changes in the tissue parameters. Measurement of such parameters can therefore reflect blood glucose levels.

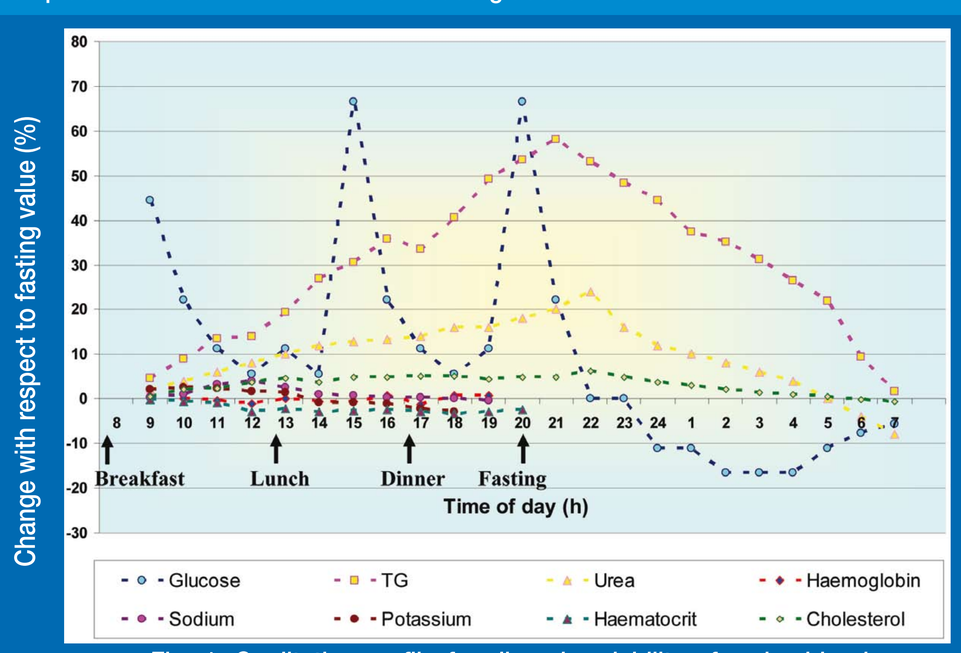

Fig. 1: Qualitative profile for diurnal variability of major blood components (Healthy individuals) [1, 2, 3, 4, 5]

A NI device is a combination of appropriate sensor(s) that measure the specific PP using tissue parameters, with sufficient resolution for glucose determination and an integrated interpretation of these parameters into prospective glucose values.

The actual glucose value derived from such correlations is, however, different than the absolute (capillary) glucose level, since factors other than glucose, which represent the noise factor in the system, influence tissue parameters as well, causing inaccuracies in the reading. The mechanism of the influence of glucose and other blood solutes on the measured parameters in different tissue compartments (e.g. interstitium, blood, cells) needs to be well understood and the measuring techniques should be chosen appropriately.

Innovative Approach:

A possible, unique way to minimize the impact of such noise is by using a combination approach, where three independent, NI technologies are used: ultrasound, conductivity and heat capacity.

Each technology measures different tissue parameters that are affected by the same PP. The response of the tissue to changes in glucose concentrations, for example increase in osmolarity in hyperglycemia, is accompanied by movement of ions and water across the cell membrane from the tissue and erythrocytes into the vascular compartment [6, 7] (Fig. 2). The ion and water flux are in the opposite direction in hypoglycemia but are not of equal magnitude. However, the glucose is not transported out of the cell during hypoglycemia.

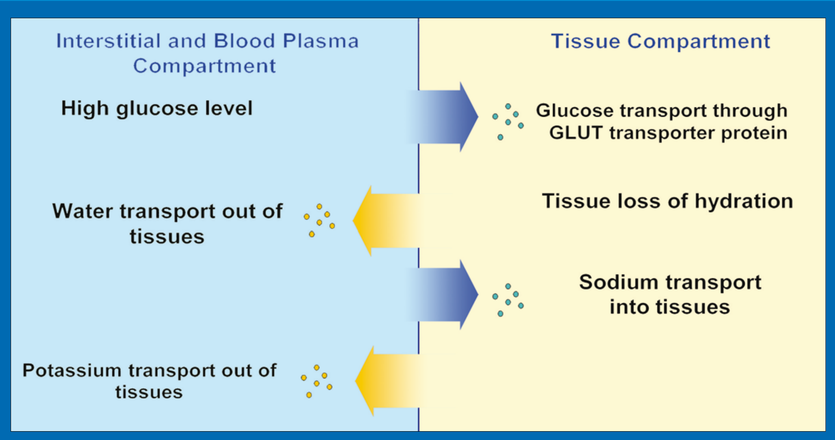

Fig. 2: Ion and water movement between Interstitial and Tissue Compartments due to hyperglycemia.

Ion transport through the membrane or the "membrane leakiness" is altered, which leads to a change in other transporters (e.g., ion pumps). The alteration of the membrane permeability or activity of the ion pumps result in changes in the permittivity, conductivity, acoustic impedance, and heat transfer characteristics of the tissue and interstitial compartments due to changes in ion concentration, density, compressibility and hydration of the interstitial and cellular compartments. [6]

Each technology (of the three mentioned above) measures the effect of glucose and the disturbance factors (noise). However, the sensitivity of each technology to the noise is different. By combining all three, the weighed average reading reflects the blood glucose value, with smaller impact of interferences, thus allowing more accurate results.

In the proposed method, spot measurement is performed by a clip (containing sensors), attached to the earlobe. This location, not only has a large blood supply, but is also an easily accessible site that doesn't interfere with routine activities.

GlucoTrack (Model DF-F)
US Patent 6,954,662

Caution:
Investigational device.
Limited by federal law to investigational use only.

An Individual calibration is required to be performed prior to glucose measurements, so that the structure of the tissue and other factors that don't change frequently can be eliminated. The calibration is performed against invasive basal and post-prandial blood glucose references. The procedure is valid for a long period of time (relative to other known procedures) – current recalibration intervals are one month.

Methods:

Clinical trials were performed at Diabetes Unit, Soroka University Medical Center, Beer-Sheva, Israel. 94 subjects were tested by the end of August 2007 (400 data pairs): 14 T1DM (7F, 7M), 70 T2DM (18F, 52M) and 10 healthy subjects (7F, 3M). Average age: 56.0±24.5 years, BMI: 28.5±12.0 Kg/M^2. Calibration was performed individually against invasive basal and post-prandial blood glucose references and measurements were evaluated with Abbott FreeStyle® and HemoCue Glucose 201$^+$ Analyzer, using capillary fingertip blood sample.

The trial was performed in 2 stages. The first included 50 patients who performed at least 1 measurement pair for initial method validation. The second (current) stage was performed for further validation of the method on broader range of patients and a more variable glucose range. This stage so far includes 44 patients, 24 of whom performed 4-6 measurement pairs in a 1.5 hour period, and 20 people who were evaluated for a full day - 8 to 10 hours daytime session, during which 9-12 pairs were taken. All values within the last group were measured on a different day than the calibration process.

Results:

Clarke Error Grid analysis of the results shows 93% of the points falling into zones A+B, of which 57% are in zone A (Fig 3).

Clinical trials still take place in Israel, to be followed by Europe and the USA.

Zone A	Zone B	Zone C	Zone D	Zone E
229	143	17	10	1
57%	36%	4%	3%	0%

MARD (mean): 25.47% **MARD (median): 17.12%**

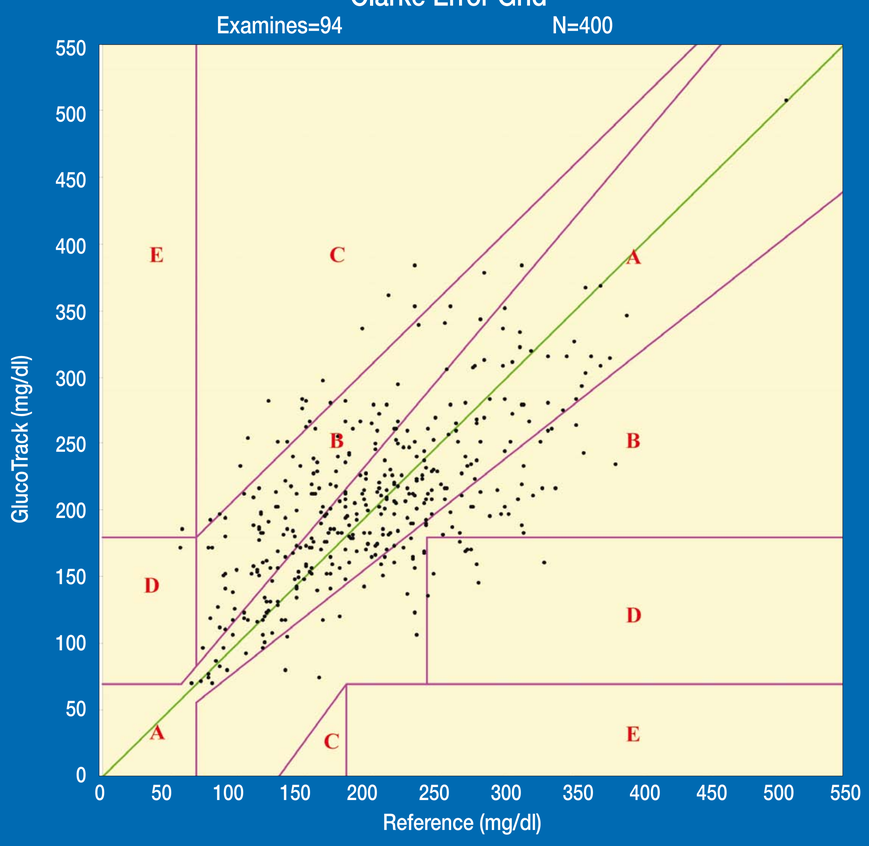

Fig. 3: Clarke Error Grid analysis for both stages of the clinical trial

Conclusions:

Although the present version of GlucoTrack gives promising results, further improvements of the device's characteristics have been set as a goal, and are currently in process. A key issue for the device's accuracy level is the quality of calibration for the entire dynamic range of readings. Thus, present emphasis is set on improving the calibration procedure and the data processing algorithm.

References:

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