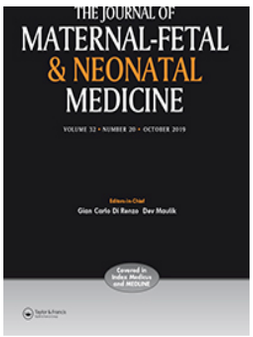

The Journal of Maternal-Fetal & Neonatal Medicine

ISSN: 1476-7058 (Print) 1476-4954 (Online) Journal homepage: https://www.tandfonline.com/loi/ijmf20

Noninvasive, continuous, real-time glucose measurements compared to reference laboratory venous plasma glucose values

Eran Hadar, Rony Chen, Yoel Toledano, Kinneret Tenenbaum-Gavish, Yuval Atzmon & Moshe Hod

To cite this article: Eran Hadar, Rony Chen, Yoel Toledano, Kinneret Tenenbaum-Gavish, Yuval Atzmon & Moshe Hod (2019) Noninvasive, continuous, real-time glucose measurements compared to reference laboratory venous plasma glucose values, The Journal of Maternal-Fetal & Neonatal Medicine, 32:20, 3393-3400, DOI: 10.1080/14767058.2018.1463987

To link to this article: https://doi.org/10.1080/14767058.2018.1463987

THE JOURNAL OF MATERNAL-FETAL & NEONATAL MEDICINE
2019, VOL. 32, NO. 20, 3393–3400
https://doi.org/10.1080/14767058.2018.1463987

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Noninvasive, continuous, real-time glucose measurements compared to reference laboratory venous plasma glucose values

Eran Hadar[a,b,c], Rony Chen[a,b,c], Yoel Toledano[a,b], Kinneret Tenenbaum-Gavish[a,b], Yuval Atzmon[c] and Moshe Hod[a,b]

[a]Helen Schneider Hospital for Women, Rabin Medical Center, Petach-Tikva, Israel; [b]Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [c]Dan Petach-Tikva District, Clalit Health Services, Petach-Tikva, Israel

ABSTRACT

Purpose: Current modalities for glucose monitoring are invasive and inconvenient. The search for a noninvasive technique is still ongoing, without a clinically viable product. The aim of our study was to evaluate the safety and accuracy of a novel non-invasive continuous glucometer – the Wizmi™ device.

Methods: Prospective, observational, controlled clinical trial. We included healthy pregnant women designated to undergo a 3-hour oral glucose tolerance test. Each participant underwent synchronous and simultaneous glucose measurement by venous sampling of plasma glucose and non-invasive glucose by Wizmi device. Primary outcome was the accuracy of the Wizmi device as assessed by comparing between paired measurements, i.e. non-invasive glucose measurements by Wizmi versus standard plasma glucose levels, which were taken at the exact same time.

Results: Thirty-two women underwent oral glucose tolerance test (OGTT), contributing 224 paired glucose measurements. Of the 224 paired measurements, all were within the clinically appropriate zones of the Clarke error grid analysis zones −208 (93%) in Zone A and 16 (7%) in zone B. Mean absolute relative difference of the Wizmi non-invasive glucose versus plasma glucose laboratory reference was 7.23% or 9.66 mg/dl. Overall, for all 224 paired measurements, across all Wizmi glucose ranges, the agreement was 86.6, 92.0, 97.8 and 99.5% for deviations within ±15, 20, 30, 40% (if glucose >80 mg/dl) or mg/dl (if glucose ≤80 mg/dl).

Conclusions: Wizmi device is novel non-invasive continuous glucose monitor, safe to use, with overall high accuracy compared to a gold standard reference of plasma glucose.

ARTICLE HISTORY
Received 4 April 2018
Accepted 9 April 2018

KEYWORDS
Diabetes; glucose; monitoring; non-invasive; continuous

Introduction

Optimal glycemic control in patients with all types of diabetes – Type 1, Type 2, gestational and others – is a pivotal therapeutic goal, indispensable for preventing hypo- and hyperglycemic related morbidity and mortality [1]. For this to be accomplished, it is paramount to monitor glucose by any of several available methods, including: plasma glucose thru venous blood sampling, capillary plasma glucose via finger-pricking glucometers and continuous glucose monitoring by electrochemical sensing of interstitial fluid glucose. While plasma venous sampling is considered as the reference gold standard, only the latter two modalities allow for frequent and practical self-monitoring of glucose [2–5]. Nonetheless, all these methods are invasive and inconvenient, potentially leading to undermotivation and low compliance for glucose surveillance [6,7].

Intensive glucose monitoring, with tight glycemic control, is associated with reduction of long term diabetes complications, but requires multiple daily glucose measurements [8,9]. A glucose monitoring system which will provide frequent and comfortable glucose indices, will enhance glucose control and diminish adverse clinical outcome for patients with diabetes [10]. Consequently, there is unmet clinical need for the utopic glucometer – accurate, user-friendly, low maintenance, pain-free, and truly noninvasive.

Non-invasive glucose monitoring refers to a measurement of blood glucose levels, without bloodletting and while avoiding skin puncturing, pain, or trauma. The search for an appropriate non-invasive technique is ongoing for half a century, without a practical, clinical, commercially available product to answer all such requirements [11].

CONTACT Eran Hadar eranh42@gmail.com Helen Schneider Hospital for Women, Rabin Medical Center, 39 Zabotinski Street, Petach-Tikva 4941492, Israel

Multiple technical approaches have been explored to achieve non-invasive glucose measurement, including: spectroscopy-based techniques (near- or mid-infrared wavelengths, bioimpedance, thermal emission, absorbance, photoacoustic or Raman), transdermal reverse iontophoresis (pulling glucose through the skin using either chemicals or electricity), optical polarimetry (quantifying polarized light which is rotated by glucose in the ocular aqueous humor), ultrasound technology, fluorescence, electromagnetic sensing, temperature regulated localized reflectance, optical coherence tomography and metabolic heat conformation [12,13]. Only few such devices have been approved for commercial use by the FDA (United States Food and Drug Administration) or CE (Conformité Européenne) via dermal, sweat and interstitial fluid approaches [14,15].

Therefore, the aim of our study was to evaluate the safety and accuracy of a novel non-invasive glucometer – the Wizmi™ device, developed by Wear2b Ltd – as a pilot, proof of concept evaluation. Wizmi is based on near-infrared spectroscopy, designated to provide non-invasive, real-time, continuous glucose measurements.

Methods

We conducted a prospective, diagnostic, observational, open label, controlled clinical trial to assess the safety and accuracy of a novel non-invasive glucometer. The study was conducted from September 2017 to February 2018, at the maternal-fetal medicine unit of the Rabin Medical Center. The study was approved by the local institutional review board (approval No. 0657-16) and was implemented in accordance with the ICH-GCP (International Conference on Harmonization and Good clinical practice) guidelines for the conduct of clinical trials, following written, signed and dated informed consent from all participants.

Population

Healthy pregnant women, 18 years old and above, designated to undergo a 3-hour oral glucose tolerance test (OGTT), at all gestational weeks. Eligible women were referred to the maternal-fetal medicine outpatient clinic at the Rabin Medical Center to perform an OGTT, while performing simultaneously all study related procedures.

We excluded from study participation, women with skin damage or discoloration, known psoriasis or eczema and/or the presence of a tattoo, at the optical sampling zone, i.e. at the wrist of the designated arm.

Conduct

All glucose measurements – plasma and non-invasive – started while the participant was in the fasting state, following an 8-hour overnight fasting, as required beforehand to an OGTT. Prior to initiating glucose measurements, a venous catheter was placed at the participant's forearm and the opposing wrist was dressed with the Wizmi device. The Wizmi sensor set was placed by a designated technician and a series of fast calibration measurements were performed prior to venous blood sampling.

Each participating woman underwent synchronous and simultaneous glucose measurement by two distinct methods in parallel, during a single clinic visit: (1) plasma glucose *via* venous blood sampling; considered as the gold standard laboratory reference measurement; (2) non-invasive, continuous, glucose assessment by the Wizmi device.

Standard plasma glucose, extracted from venous blood sampling, was performed every 30 minutes for up to 3 hours, with the first measurement taken at the fasting state, and the following six measurements made after ingestion of 100 g glucose, along the routine course of the planned OGTT. Glucose measurements were performed at the hospital's biochemistry laboratory, by routine standard technique, using the Cobas 8000 analyzer (Roche Diagnostics, Indianapolis, IN, USA).

Non-invasive glucose was measured by the Wizmi device (Wear2b, Israel). The device is a wrist bracelet, in contact with participant's skin, located above the superficial veins of the wrist – the superficial palmar venous arch draining into the cephalic and basilica veins of the forearm. Measurements were performed consecutively, and continuously, starting shortly prior to glucose ingestion and up to the final glucose assessment, 180 minutes following glucose intake. A 10-minute break, per hour, was allowed if requested, for each participant.

Wizmi device

Wizmi is based on Wear2b proprietary, patent pending, novel, non-invasive opto-bio sensor. It uses diffusive spectroscopy, biology, electro-optics, cloud computing and mathematical algorithms to build a unique multitrajectories analysis using proprietary elements' reduction technology, to achieve superior signal-to-noise (SNR) ratio and read multiple arrays of

data for better and improved accuracy. Wizmi is equipped with spectroscopy technology, utilizing near-infrared light wavelength, which is a non-ionizing harmless radiation (similar to any TV remote controller light), able to penetrate through the skin and blood vessels of the wrist up to 5-mm depth.

The Opto-bio sensor set is placed as a wrist bracelet, in touch with skin surface. An open stand for wrist placement was equipped with a stopper and a wrist band, to allow for repeated and accurate placement of the sensor set on the wrist's blood vessels (Figure 1).

The complete optical system is powered by a 7.4 V battery and is hard wired to a laptop computer (for the current study configuration, while future versions will transmit on-line results to the user's smartphone *via* a designated application).

Endpoints

Study endpoints included safety and accuracy of the Wizmi device. Accuracy was determined at variable glucose levels, hence was the choice of women performing OGTT to allow for both low and high glucose levels. Primary outcome was the accuracy of the Wizmi device as assessed by comparing between paired measurements, i.e. non-invasive glucose measurements by Wizmi versus standard plasma glucose levels, by venous blood sampling, which were taken at the exact same time. The safety of the Wizmi device was evaluated by the number of participants with any adverse or serious adverse events, as reported while using the device.

Figure 1. Real life photo of the Wizmi™ device.

Data collection

Other than the glucose measurements, as detailed above, the following demographic and clinical data were ascertained and collected from all participants: age, ethnicity, gestational week according to last menstrual period, prior and concomitant illnesses and/or medications, vital signs (body temperature, respiratory rate, pulse, systolic, and diastolic blood pressure), weight, height, wrist circumference; as well as the skin color and tone (Figure 2), which was evaluated by the Fitzpatrick scale [16].

Data analysis

Clinical accuracy was evaluated and presented by the Clarke error grid analysis [17]. Shortly, the grid contains five zones representing different clinical accuracy significance risk levels, with values in zones A and B are considered as clinically acceptable – (1) Zone A: clinically accurate (No risk); (2) Zone B: appropriate for benign decisions or no treatment (slight risk); (3) Zone C: Over corrections of normal glucose levels, leading to unnecessary treatment (moderate risk); (4) Zone D: failure to detect and treat high or low levels (significant risk); (5) Zone E: erroneous treatment decisions, treating hypoglycemia for hyperglycemia and vice versa (dangerous).

Numerical differences between paired measurements was assessed by calculation of the mean and the median absolute and relative differences between paired measurements, expressed by percentage and mg/dl.

Figure 2. Fitzpatrick Skin Type Scale. Numerical classification schema for human skin color: Type I (light, pale, white), Type II (fair, white), Type III (cream white to olive), Type IV (olive, moderate brown), Type V (Brown, dark brown) Type VI (Very dark brown, black).

Agreement between the two measurements – Wizmi non-invasive results versus plasma glucose reference values – was also made per different glucose cutoffs – within 15, 20, 30, 40, >40 mg/dl (for glucose values ≤80 mg/dl) or percentage (for glucose values >80 mg/dl).

Table 1. Basic demographic and medical characteristics, $n = 32$.

Parameter	Mean ± standard deviation or *n* (%)	Median (range)
Age, years	33.8 ± 5.1	34 (25–44)
Gestational age at inclusion, weeks	26.7 ± 5.9	27.1 (11.1–39.6)
Weight, kilograms	79.8 ± 19.6	74.7 (53.0–132.0)
Height, meters	1.64 ± 0.06	1.65 (1.50–1.76)
Wrist circumference, centimeters	16.5 ± 1.92	16.1 (14.6–24.0)
Body mass index, kg/m^2	28.8 ± 6.1	26.6 (20.2–45.0)
Underweight	0	
Normal weight	7 (22%)	
Overweight	12 (37%)	
Obese	13 (41%)	
Skin tone, Fitzpatrick scale (1–6)	2.38 ± 1.04	2 (1–6)
Grade 1	4 (13%)	
Grade 2	18 (56%)	
Grade 3	6 (19%)	
Grade 4	3 (9%)	
Grade 5	0 (0%)	
Grade 6	1 (3%)	
Ethnicity		
Caucasian	28 (90.6%)	
Asian	1 (3.1%)	
Black	2 (6.3%)	

Data presented as mean ± standard deviation and median (range) for continuous variables or *n*(%) for categorical variables.

Results

Overall, 32 women underwent OGTT, contributing 224 paired glucose measurements, plasma and noninvasive. Basic demographic and clinical characteristics of the participants are presented in Table 1. The overall accuracy, between paired measurements, is presented in the Clarke error grid analysis (Figure 3). Of the 224 paired measurements, all were within the clinically appropriate zones −208 (93%) in Zone A and 16 (7%) in Zone B.

Numerical differences between paired glucose measurements of Wizmi non-invasive glucose and venous blood glucose sampling are presented in Table 2. As measure of overall performance, in a single particular parameter, mean absolute relative difference (MARD) of the Wizmi non-invasive glucose versus plasma glucose laboratory reference was 7.23% or 9.66 mg/dl.

The agreement between paired glucose measurements of Wizmi non-invasive glucose and venous blood glucose sampling are presented in Table 3 and Figure 4. Overall, for all 224 paired measurements, across all Wizmi glucose ranges, the agreement was 86.6, 92.0, 97.8 and 99.5% for deviations within ±15, 20, 30, 40% (if glucose >80 mg/dl) or mg/dl (if glucose ≤80 mg/dl). The proportion of paired measurements,

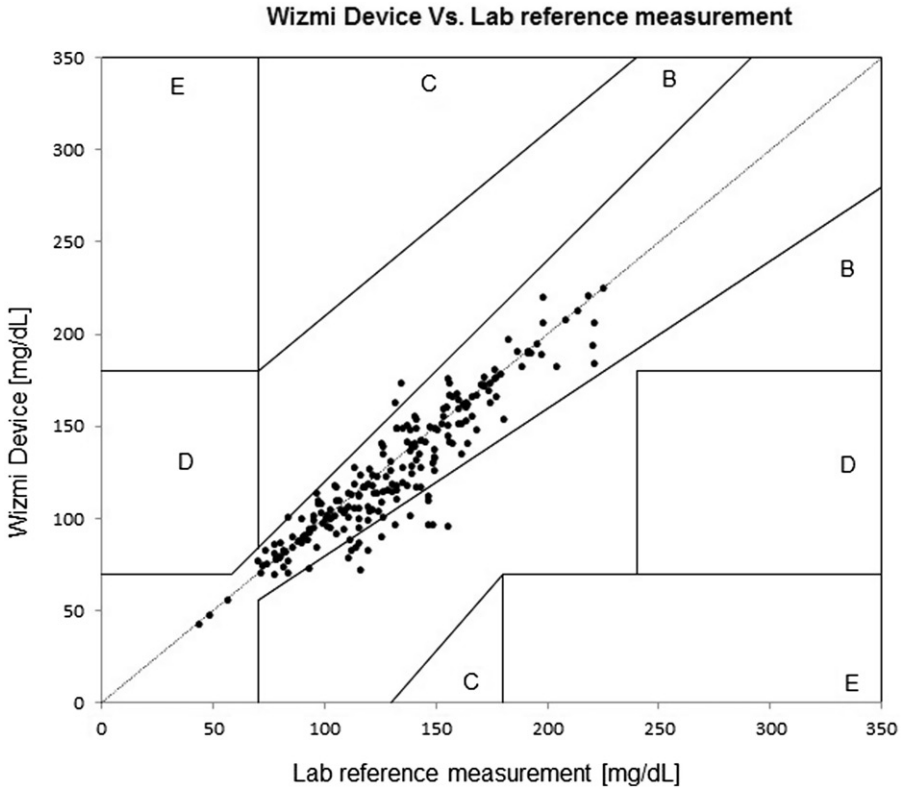

Figure 3. Clarke error grid analysis Noninvasive glucose measurements (Wizmi device [mg/dl]) versus plasma blood glucose (Lab reference measurement [mg/dl]), categorized into A through E zones across the grid.

Table 2. Differences between Wizmi device glucose and reference plasma blood glucose measurements.

Units	No. of paired measurements	Mean difference	Median difference	Mean absolute difference	Median absolute difference
mg/dl	244	−3.77	0	9.66	7.0
Percent (%)		−2.4	0	7.23	5.04

Table 3. Wizmi device agreement with laboratory reference glucose measurements, within Wizmi glucose ranges.

Glucose (mg/dl)	No. of paired measurements	Within ±15% or 15 mg/dl	Within ±20% or ±20 mg/dl	Within ±30% or 30 mg/dl	Within ±40% or ±40 mg/dl	Outside ±40% or ±40 mg/dl
40–300	224 (100%)	86.6%	92.0%	97.8%	99.5%	0.5%
40–50	2 (0.9%)	100%	100%	100%	100%	0
51–80	18 (8.0%)	83.3%	88.9%	88.9%	94.4%	5.6%
81–180	185 (82.6%)	85.9%	91.9%	97.8%	100%	0
181–300	19 (8.5%)	94.7%	100%	100%	100%	0

For glucose >80 mg/dl, the absolute percent difference between paired measurements was assessed by calculating the percentage of Wizmi readings that were within 15, 20, 30, 40% and more than 40% from the reference values.
For glucose ≤80 mg/dl, the absolute difference between paired measurements was assessed by calculating the percentage of Wizmi readings that were within 15, 20, 30, 40 mg/dl and greater than 40 mg/dl from the reference values.

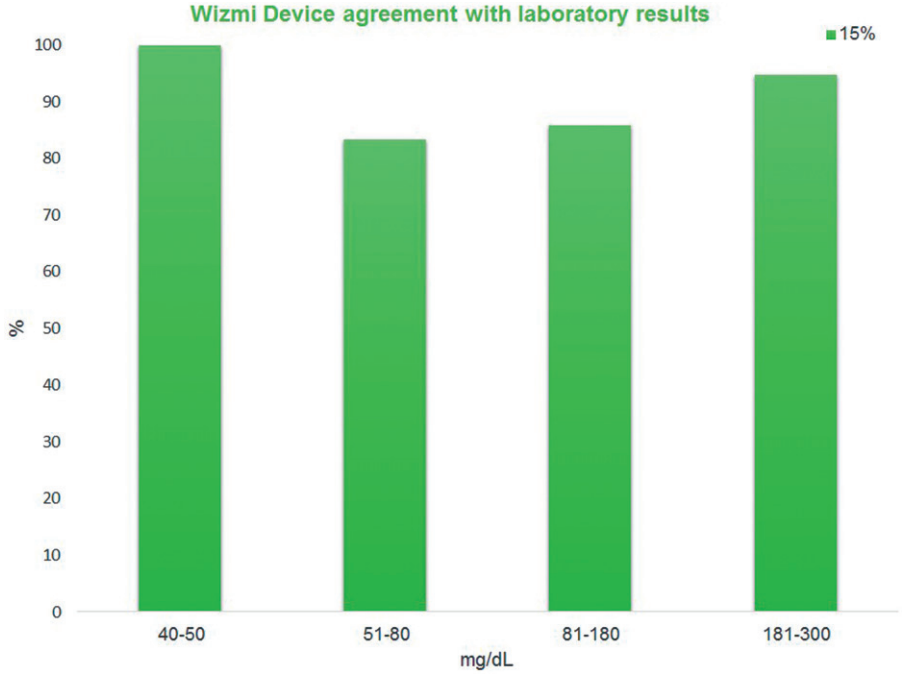

Figure 4. Wizmi device agreement with laboratory reference glucose measurements, within Wizmi glucose ranges.

within close agreement to the reference (±15% or 15 mg/dl), even at extreme values of both hyper- and hypo-glycemia, <180 mg/dl and <50 mg/dl, respectively, is 100 and 94.7%.

Graphical comparison of paired glucose values, among several selected participants, is presented in Figure 5. The Wizmi glucose measurements are presented as continuous values over 180 minutes, and their counterpart reference values, are presented as single, point values.

In terms of safety outcomes, none of the participants experienced or reported any local or systemic adverse or serious adverse events, during study participation. By the end of all study related procedures and removal of the Wizmi bracelet, no side effects were documented, including: local redness, burns, pain or other complications. The procedure was well tolerated by all participants, without any discomfort, and without any of the participants requesting to prematurely terminate the use of the bracelet, prior to study completion.

Discussion

We conducted a proof of concept clinical trial to assess feasibility and performance of the *Wizmi* continuous non-invasive glucometer. Our main results demonstrate that among 32 women and 224 paired

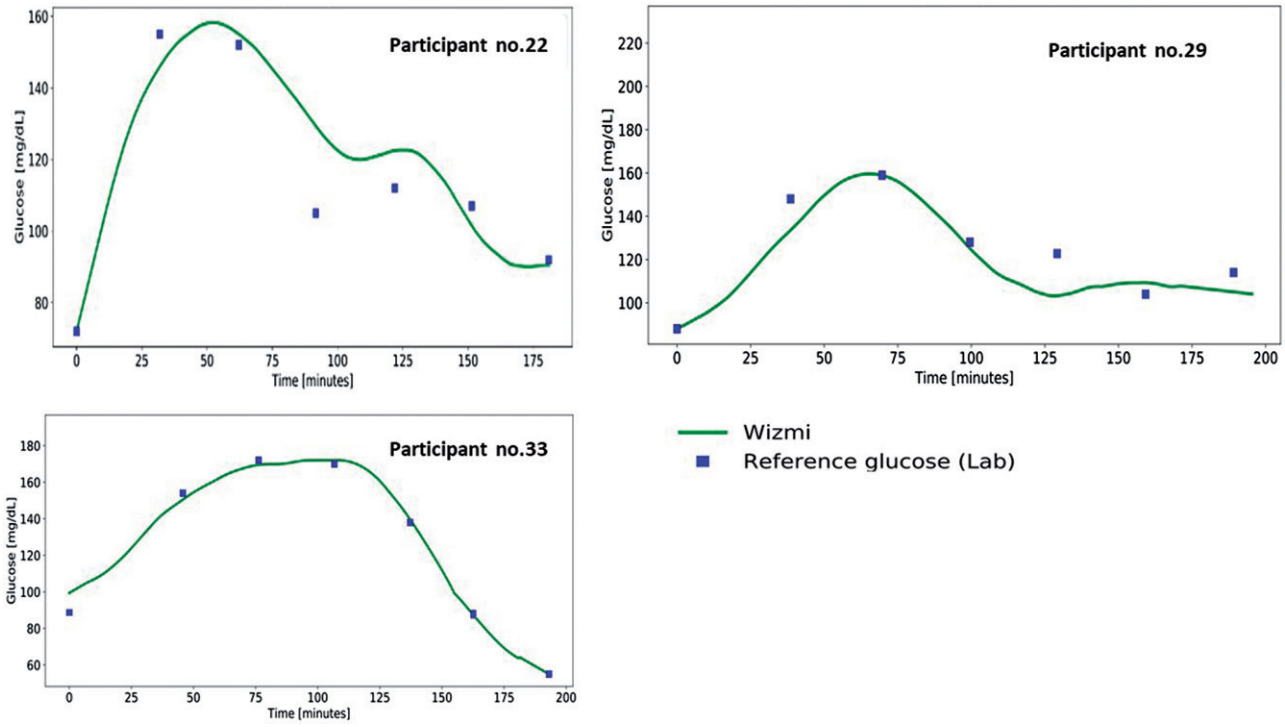

Figure 5. Correlation between Wizmi noninvasive glucose measurements and plasma blood glucose measurements, presented for selected participants.

measurements: (1) the device is well tolerated and safe to use; (2) the Clarke grid error analysis indicates that 100% of the measurements are within the clinically acceptable zones; (3) accuracy is well maintained in hypo- and hyper-glycemic values.

Most of the current blood glucose monitoring devices are based on a combination of electrochemical sensor, automated lancets and a minimal amount of blood derived by finger pricking to perform the actual measurement. This modality is still invasive, although minimal, and certainly painful to a level which disallows intensive, pain free, glucose follow up. The primary alternative for such glucometers is a subcutaneous continuous glucose sensor. These devices measure glucose in the interstitial fluid, and are considerably less painful and invasive. However, they are still limited by discomfort and the need for repeated calibrations. Therefore, non-invasive glucose monitoring is the only true, pain free, absolutely non-invasive alternative, with a revolutionary potential in glucose monitoring systems. The currently investigated device is such a novel non-invasive glucometer.

In comparison to other non-invasive glucometers, none of which has reached a standard of care status [14,15], the current study shows the *Wizmi* device to be superior to them – with all measurement to be within the clinically acceptable zones A (93% of measurements) and B (7% of measurements) in the Clarke error grid analysis.

GlucoWatch [18], was the first FDA and CE approved, non-invasive glucometer. It is a wrist-watch device, based on reverse iontophoresis, as such it is not purely non-invasive. It was discontinued from commercial marketing at 2007, due to inappropriate efficacy and safety issues. Furthermore, several disadvantages were related to calibration procedures and inadaptability to changing conditions, such as temperature, water and sweat. Clinical trials have demonstrated that the Clarke Error grid analysis is set at 94% of GlucoWatch readings to be with zones A and B. Importantly, this was compared to a finger-pricking capillary glucometer and not to an appropriate reference of plasma glucose [19].

GlucoTrack is a hand-held, non-invasive, glucose monitor, combining three techniques – ultrasound, electromagnetic and heat capacity, to enhance accuracy and reduce SNR. It is CE-certified, but it was not intended for continuous use, as its sensor is ear-lobe attached. Clinical trials demonstrated that 92–98% of the measurements were within Clarke grid zones A and B [20,21]. These trials also used capillary blood as a reference and not plasma glucose. Importantly, as calibration is a major technical aspect, for all non-invasive devices, GlucoTrack requires calibration procedures versus invasive blood glucose references, prior to first use.

Pendra, is another wrist-watch configured glucometer, with CE certification [22]. It was discontinued from

commercial applications due to wide variations in the readings among individuals, and an elaborate calibration process to compensate for this. Moreover, Clarke error grid analysis indicated that only 84.9% of the reading are with the clinically safe zone, and 4.3% are in E zone, which is the high-risk danger zone.

Another device is the *NBM-200G* [23], also a CE-certified, non-invasive device, intended for glucose, hemoglobin and oxygen saturation assessments. It is based on near-infrared occlusive spectroscopy. It has several technical advantages such as ease of use, infrequent calibrations, nevertheless it is actually designed as point of care tool, not as a continuous, hand-held, personal device. Clarke's grid yielded 95.3% that of all measurements are within A-B zones, 4.7% were in C-D zones and none in zone E.

Even when considered versus commercially available continuous, invasive, glucose monitors, the Wizmi device, according to our data yielded at least as good, and at times better accuracy. Several studies have evaluated the recently introduced *Freestyle Libre* compared to reference laboratory measurements, among diverse populations of adults and children, including type 1, type 2, and gestational diabetics [24]. Reported results for the Clarke error grid analysis demonstrated a range of 85.5–88.1% of the reading within zone A and 99.0–99.8% of the readings within zones A and B, with MARD stretching from 11.8 to 13.9%.

Calibration is one of the key issues in both invasive and non-invasive glucometer. *Wizmi* is ready to go, as was demonstrated in this study, following a short calibration devoid of invasive referencing for its setting. This is an exceptionally short calibration period, compared to other noninvasive devices, which require calibration periods of up to 3 hours [12–15].

Safety is another important advantage of the current system, as is for all noninvasive testing. There is no risk of blood-borne pathogen transmission, which is a major concern for both capillary and interstitial fluid-based device.

The ongoing quest for a precise, wearable, continuous, non-invasive, user-friendly glucose monitor is one of high importance, as it may revolutionize management of diabetes. The technical challenges associated with such devices needs to triumph issue such as accuracy (versus laboratory references), calibration (short, simple, and without invasive counterpart), and ease of use for on-line reading, operating, and alarm policy of the monitor.

Wizmi may answer some if not all of these challenges. Our data demonstrated the combination of several sensors and data management by mathematical algorithms leads to a highly accurate device, with the potential of performing superiorly to other currently available devices, be it invasive or noninvasive, as demonstrated by the MARD and Clarke Error grid analysis scores.

Although, innovative and encouraging results, our study is limited by a relatively small sample size. This was planned as a proof of concept, and accordingly future studied will have to be conducted to allow stratification for possible confounders, as well as to investigate daily, long term usage, and compare relevant clinical outcomes versus current standard of care glucose monitoring schemes. Nevertheless, we have compared a relatively large number of paired measurements, in a heterogeneous population, at a wide range of glucose values.

It has now become quite clear that many pregnancy complications, among them gestational diabetes mellitus (GDM), can be predicted at an integrated first trimester visit at 11–13 weeks by combining data from maternal characteristics and history with findings of biophysical, biochemical, and highly sophisticated genetic tests. We believe that the Wizmi device with its potential production of limitless continuous data on glucose metabolism in these early stages of pregnancy (throughout the first trimester) will provide an opportunity to predict GDM and lead the way towards preventive measures.

In conclusion, Wizmi device is novel non-invasive glucose monitor, safe to use with overall high accuracy compared to a gold standard reference plasma glucose. As such, it may provide a superior modality for glucose surveillance, which will be pain free and continuous, possibly improving diabetes management.

Disclosure statement

No potential conflict of interest was reported by the authors.

References

[1] Standards of Medical Care in Diabetes – 2017. Diabetes Care. 2017;40:S1–S2.

[2] Schütt M, Kern W, Krause U, et al. Is the frequency of selfmonitoring of blood glucose related to long-term metabolic control? Multicenter analysis including 24,500 patients from 191 centers in Germany and Austria. Exp Clin Endocrinol Diabetes. 2006;114:384–388.

[3] Towfigh A, Romanova M, Weinreb JE, et al. Selfmonitoring of blood glucose levels in patients with type 2 diabetes mellitus not taking insulin: a meta-analysis. Am J Manag Care. 2008;14:468–475.

[4] Raman P, Shepherd E, Dowswell T, et al. Different methods and settings for glucose monitoring for

gestational diabetes during pregnancy. Cochrane Database Syst Rev. 2017;10:CD011069:CD011069.
[5] Moy FM, Ray A, Buckley BS, et al. Techniques of monitoring blood glucose during pregnancy for women with pre-existing diabetes. Cochrane Database Syst Rev. 2017;11:CD009613.
[6] Vincze G, Barner JC, Lopez D. Factors associated with adherence to selfmonitoring of blood glucose among persons with diabetes. Diabetes Educ. 2004;30:112–125.
[7] Moström P, Ahlén E, Imberg H, et al. Adherence of selfmonitoring of blood glucose in persons with type 1 diabetes in Sweden. BMJ Open Diabetes Res Care. 2017;5:e000342.
[8] Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet. 1998;352:837–853.
[9] Langer O, Rodriguez DA, Xenakis EM, et al. Intensified versus conventional management of gestational diabetes. Am J Obstet Gynecol. 1994;170:1036–1046.
[10] Ginsberg BH. An overview of minimally invasive technologies. Clin Chem. 1992;38:1596–1600.
[11] Smith J. The pursuit of noninvasive glucose: hunting the deceitful turkey. [Internet] [cited 2018 Mar 21]; Available from: http://www.mendosa.com/The%20Pursuit%20of%20Noninva-sive%20Glucose%203rd%20Edition.pdf
[12] Tura A, Maran A, Pacini G. Non-invasive glucose monitoring: assessment of technologies and devices according to quantitative criteria. Diabetes Res Clin Pract. 2007;77:16–40.
[13] Yadav J, Rani A, Singh V, et al. Prospects and limitations of non-invasive blood glucose monitoring using near-infrared spectroscopy. Biomed Signal Process Contr. 2015;18:214–227.
[14] Vashist SK. Non-invasive glucose monitoring technology in diabetes management: a review. Anal Chim Acta. 2012;750:16–27.
[15] Kim J, Campbell AS, Wang J. Wearable non-invasive epidermal glucose sensors: a review. Talanta. 2018;177:163–170.
[16] Fitzpatrick TB. The validity and practicality of sun-reactive skin types I through VI. Arch Dermatol. 1988;124:869–871.
[17] Clarke WL, Cox D, Gonder-Frederick LA, et al. Evaluating clinical accuracy of systems for selfmonitoring of blood glucose. Diabetes Care. 1987;10:622–628.
[18] Chase HP, Beck R, Tamborlane W, et al. A randomized multicenter trial comparing the GlucoWatch Biographer with standard glucose monitoring in children with type 1 diabetes. Diabetes Care. 2005;28:1101–1106.
[19] Tierney MJ, Tamada JA, Potts RO, et al. Clinical evaluation of the GlucoWatch biographer: a continual, non-invasive glucose monitor for patients with diabetes. Biosens Bioelectron. 2001;16:621–629.
[20] Horman K, Mayzel Y, Gal A, et al. Performance and user experience evaluation of a non-invasive glucose monitoring device. Int J Diabetes Metab Disord. 2016;1:1–7.
[21] Harman-Boehm I, Gal A, Raykhman AM, et al. Noninvasive glucose monitoring: a novel approach. J Diabetes Sci Technol. 2009;3:253–260.
[22] Wentholt IM, Hoekstra JB, Zwart A, et al. Pendra goes Dutch: lessons for the CE mark in Europe. Diabetologia. 2005;48:1055–1058.
[23] Amir O, Weinstein D, Zilberman S, et al. Continuous noninvasive glucose monitoring technology based on "occlusion spectroscopy". J Diabetes Sci Technol. 2007;1:463–469.
[24] Leelarathna L, Wilmot EG. Flash forward: a review of flash glucose monitoring. Diabet Med. 2018;35:472–482.