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Short Communication

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A Novel Approach for Device Dedicated to Non-Invasive Diabetes Control

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Introduction

John Whitehead, grandson of the founder of the world's largest clinical laboratory instrument company (Technicon Instruments), was visibly excited. The year was 1982, and the picture he was holding was a wristwatch, displaying" Blood Glucose = 107." "Wouldn't that be great!" he bubbled, "No more trips for diabetics to the doctor to measure blood sugar, no more need to stick a needle in your finger to make measurements at home."

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it products [1]. The number of people suffering diabetes is changing dramatically, and the summary of the global estimation is presented in Table 1 based on the International Diabetes Federation (IDF) forecast delivered in 2019 [2].

Region	Year	Diabetes [million]	Increase [%]	Remarks
North America & Caribbean	2019	48	33%	1 in 6 adults in the Region is at risk of type-2; 43% of global diabetes-related health expenditure occurs in this Region;
	2030	56		
	2045	63		
South & Central America	2019	32	55%	2 in 5 people with diabetes were undiagnosed; Only 9% of global diabetes-related health expenditure for diabetes is spent in this Region;
	2030	40		
	2045	49		
Europe	2019	59	15%	1 of 6 live births are affected by hyperglycaemia in pregnancy; The Region has the highest number of children and adolescents (0-19 years) with type 1 diabetes;
	2030	66		
	2045	68		
Africa	2045	47	143%	3 of 5 people diabetes are undiagnosed; 3 of 4 deaths due to diabetes were in people under the age of 60;
	2045	99		
	2045	19		
Middle East& North Africa	2019	55	96%	1in 8 people have diabetes; 1 in 2 deaths due to diabetes were in people under the age of 60;
	2030	76		
	2045	108		

South-East Asia	2019	88	74%	1 in 5adults with diabetes lives in this Region; 1 in 4 live births are affected by hyperglycaemia in pregnancy;
	2030	115		
	2045	153		
Western Pacific	2019	163	31%	1 in 3 adults with diabetes lives in the Region; 1 in 3 deaths due to diabetes occur in this Region;
	2030	197		
	2045	163		
WORLD	2019	463	51%	Diabetes affects people of all ages, typically showing higher prevalence with increasing age up to 60-69 years; 1 in 5 people older than 65 years have diabetes; 87% of diabetes-related deaths occur in low- and middle-income countries. But, only 35% of diabetes-related health expenditure is spent there.
	2030	578		
	2045	700		

Table 1: Global fact about number of adults (20-79 years) with diabetes worldwide based on the 9th edition 2019 delivered by International Diabetes Federation [2]

Figure 1: International Diabetes Federation. IDF Diabetes Atlas, 9th edn. Brussels, Belgium [Reprinted with permission from [2]: International Diabetes Federation, 2019].

A constantly increasing number of people of diabetes is a driving force for the diabetes monitoring devices market. The recently presented market report in 2020 is graphically presented in Figure 2. Briefly, according to report the Global Diabetes Monitoring Devices Market to grow at 5.4% CAGR and reach US$ 32.888.9 million value by 2026, for instance the diabetes monitoring market in Europe was valued at US$ 10,029.7 million in 2018 and based on the forecast is expected to dominate the global market. Based on the statistics presented by the International Diabetes Federation the main part of the market is filled by geriatric patients, therefore it is expected to deliver dedicated devices for this group. However, another group with special needs is young people, especially under 7-8 years old that require constant help from adults. Apart from the currently commercially available devices for autonomous glucose monitoring, such as GCMs (Glucose Continuous Monitoring), insulin pump equipped with the glucose sensors, novel devices focused on the non-invasive measurements are under investigation, such as exhaled breath analyzers dedicated to analyzing the volatile organic compounds named biomarkers, e.g. acetone.

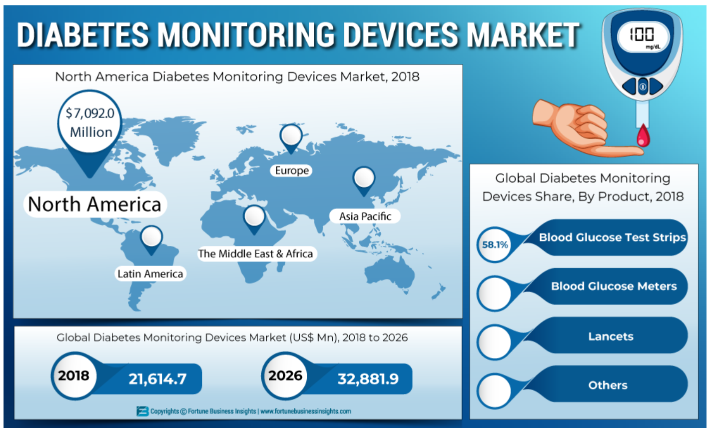

Figure 2: Diabetes Monitoring Devices Market Report 2020 Size, Share, Growth, Business Analysis, and Regional Forecast to 2026 is latest research report on Global Diabetes Monitoring Devices Market published by "Fortune Business Insights" [3].

The rising adoption of the technologically advanced blood glucose meters and higher demand for insulin delivery devices will further boost the growth of the diabetes monitoring market; such as t:Slim X2TM insulin pump from DiaMonTech GmbH, which received the FDA approval. Moreover, the technical developments of insulin patches, blood glucose monitoring devices for self-diabetes management is also influencing the diabetes monitoring devices market trend. The novel non-invasive devices that can support the conventional ones, and in future replace them, can pivot the investors' attention. It is well-known, that non-invasive devices are under investigation for over 40 years, but there is no commercially available device that can be used in the clinical routine. However, based on the number of papers and patents released in the near past can suggest that the revolution in this field is coming. The authors focused only on exhaled breath analysis as one of the potential tools for diabetes monitoring. The number of papers dealing with exhaled breath analysis to detect or monitor several diseases increased exponentially over the last twenty years. Briefly, exhaled human breath is a composition of major compounds such as CO_2, O_2, N_2, and Volatile Organic Compounds (VOCs), which are continuously generated in the human body and are partially emitted via exhaled breath, through the skin, and by urine and feces [1-3]. VOCs are mainly in the ppm–ppt (part per million to part per trillion) range, thus, laboratory methods based on the spectrometry measurements are used for their detection in breath: GC-MS, PTR-MS, IMS-MS just to name a few [4-11]. Almost 3500 different VOCs have been detected in the human breath [12], and a single breath consists of around 500 various VOCs [13]. Among them, one of the VOC that was found is acetone, which is considered as a biomarker of diabetes, since patients with diabetes tend to have higher acetone levels in their breath than non-diabetics [28]. The technical challenge for using exhaled acetone levels to monitor the blood glucose monitoring was the acetone concentration, which is in the range of 0.2–0.9 ppm for non-diabetics, and in the range of 1.25-2.5 ppm for people with diabetes [14], and the limit of detection for commercially available acetone sensors is 50 ppm (TGS822, Figaro, Inc). The latest achievement of gas sensors for enhanced acetone detection in the ppb and sub-ppm range are reviewed and discussed in [15-17].

Devices description

Three types of devices for glucose level determination from diabetes marker measurements in exhaled air are designed, developed, and presented [18,19]. All important components were developed and patented. The first one dedicated to hospitals and medical centre presented in Figure 3. It has a stable form and is easy to transport and there is no external restriction for permanent use for a desirable number of patients. An important advantage is that o calibration is not required after each treatment [20]. The gas sensor is the most important component of all types of devices. Particularly gas sensor array.

(a) (b)

Figure 3: (a) Diabetomat dedicated to hospitals, (b) device display with result of measurement.

Presented in Figure 4 together with the final shape of the portably personal device, which is under the final clinical test. Therefore, the dream of John Whitehead will be available for everybody in the nearest future. The presented gas sensor consists of three layers. The top one is the thin-film semiconducting capacitor. The middle one is a layer of the heater and the bottom one is a layer of electrical path and contacts. All thin and thick films are deposited on LTCC. This design could be used for different gas sensing materials like WO_3 [21-23], CuO [24], SnO_2 [25], etc. and we can detect different gas markers of diabetes. The level of all 4 diabetes markers has to be measure as well as CO_2 and water vapour levels. This matrix was mounted in a standard IC case. Also, an insulin pump could be integrated with these devices. However, it is not the end of our innovation. The final one is presented in figure 5. One of the most dynamical of developing electronics parts is electronics on flexible substrates. Thin film technology is able to fulfil the requirement of such design and there are lot of applications of the devices prepared using this technology. One of them will be a portable personal exhaled air analyzer presented in figure 5. The advantage is that it could have desired shape like this presented in figure 5 but also any other which one could fix to watch, cloths or mobile.

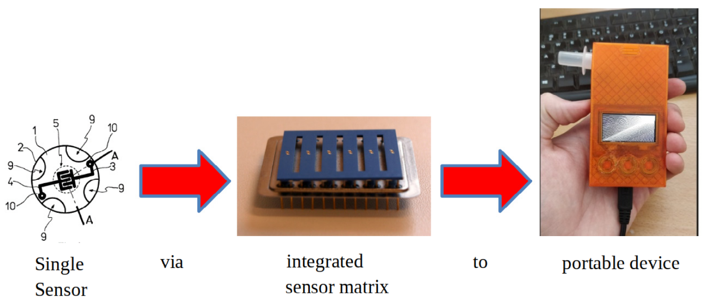

Figure 4: From gas detection to diagnosis [18,26,27].

Presented in Figure 5 model was dedicated to under collar installation. It will be not visible but easy to use by patients. The model consists also of Bluetooth Low Energy (BLE) for the device –mobile communication. This opportunity open all possibilities of result storage in mobile memory or transmission data to medical centre or personal doctor for on line analysis and diagnosis. Such design has to be more tricky especially in the case of integrated gas sensor matrix and gas leading channels but problems were solved and detail included in the patent [28,29]. Some details of sensor design were presented in a paper published by authors in Electronic Material Letters. Such design will be probably the most desirably by patients model because of comfort use and discreet "Installation" under the collar or in a pocket etc. Of course, to fulfil the sensor requirements we develop quite a new GLAD magnetron sputtering method, which increases the sensitivity of gas-sensing layers based on the doped metal oxides.

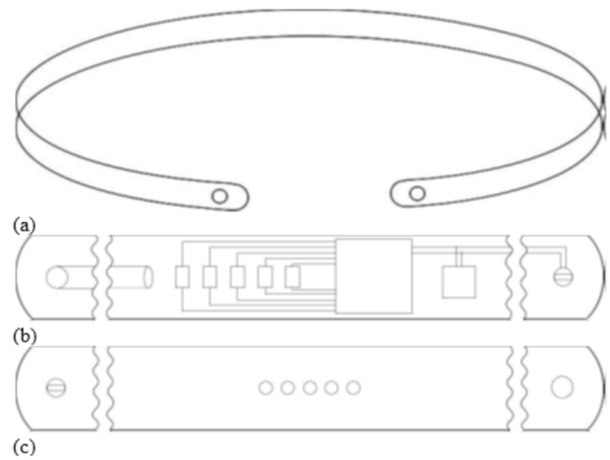

Figure 5: Design of personal, portable device for exhaled air content monitoring: (a) general overview (b) cross section with sensors (c) back side view [27].

Conclusions

The paper present state of art diabetes todays and next 20 years. One could conclude how large and important problem is to detect and develop investigation tools for diabetics. The authors have developed and patented diagnostic method and several different tools for diabetes diagnosis. Three of them were presented in this paper. Some of them are in final clinical test so we believe it is last step before entering to the market and much more important to all patients around the world. Fast and exact diagnosis is one of the important step in the war with this disease.

Founding Source: Advanced Diagnostic Equipment Sp. z o.o.

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