# A preliminary investigation of EZSCAN<sup>™</sup> screening for impaired glucose tolerance and diabetes in a patient population

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Abstract. EZSCAN<sup>™</sup> is a non-invasive technology that evaluates sweat gland dysfunction using electrochemical skin conductance measurements, providing an opportunity to determine the risk of impaired glucose tolerance (IGT) and diabetes mellitus (DM). This study was conducted with the aims of detecting IGT and DM and investigating the efficacy and cut-off points of the EZSCAN test in a patient population. The traditional serum and plasma glucose tests were used as comparators. In this cross-sectional study, 270 previously undiagnosed patients (180 women and 90 men) with a high risk of glucose metabolism disorders (≥45 years old) were enrolled. All patients underwent an oral glucose tolerance test (OGTT) and hemoglobin A1c (HbA1c), fasting plasma glucose (FPG) and EZSCAN tests. Forty (14.8%) patients had newly diagnosed DM (NDM), 79 (29.3%) had IGT and 151 (55.9%) had normal glucose tolerance. The EZSCAN values of these groups were 48±11, 47±11 and 34±13%, respectively. For all patients, the correlation coefficient of EZSCAN was 0.462 with the OGTT (P<0.001), 0.182 with the FPG test (P<0.001) and 0.379 with the HbA1c test (P<0.001). The EZSCAN cut-off point for the detection of IGT was 37% [sensitivity, 82%; specificity, 62%; area under the curve (AUC), 0.778], and the cut-off point for NDM was 50% (sensitivity, 53%; specificity, 59%; AUC, 0.528). This study demonstrated that the non-invasive EZSCAN system is an effective screening tool for the detection of glucose dysfunction in the population tested, and that its performance in detecting previously undiagnosed IGT is superior to its performance in detecting DM.

### Introduction

Undiagnosed diabetes mellitus (DM) is characterized by persistently high glucose levels, which can lead to debilitating and life-threatening vascular-related secondary complications, such as blindness or heart and kidney failure. It is well known that early diagnosis is strongly associated with improved prognosis. The early detection of impaired glucose tolerance (IGT) may result in early lifestyle and/or pharmaceutical interventions that can delay the onset of DM and reduce the severity of secondary complications (1-3).

International health organizations recommend routine clinical screening for populations at a high risk of type 2 DM (4,5). A previous study revealed that, in the majority of cases, patients reported positive experiences with the type 2 DM screening procedure, regardless of the findings (6). The screening methods that are currently used include questionnaires, which identify behavioral risk factors, such as high-fat diets and sedentary lifestyles, and biochemical tests, which can identify IGT by examining body fluids. With regard to large-scale screening efforts, questionnaires are popular due to the low cost of their administration and their non-invasive nature, which enhances the probability of patient compliance; however, when used alone, questionnaires often perform poorly and numerous patients with IGT and/or DM remain undiagnosed (7).

Biochemical tests have higher performance rates than questionnaires but have a lower patient compliance rate due to the fact that they are invasive, inconvenient and require fasting samples for opportunistic testing. A survey on a series of opportunistic screenings showed that 95% of the screenings were conducted by random plasma glucose testing alone, which has the lowest sensitivity for detecting IGT and diagnosing DM. Only 3% of the screenings used the fasting plasma glucose (FPG) test, 2% used the hemoglobin A1c (HbA1c) test and <1% used the oral glucose tolerance test (OGTT) (8).

In the past decade, an EZSCAN<sup>™</sup> device (Impeto Medical, Paris, France) was developed to evaluate sweat-gland function by measuring electrochemical skin conductance (ESC) through chronoamperometry. This device has proven to be

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a promising, rapid, convenient and non-invasive diagnostic strategy for certain human diseases (9-11). This technology was first validated in patients with cystic fibrosis based on the high concentration of chloride in the sweat of patients with the disease (12), and was subsequently used as a method for measuring sudomotor dysfunction in patients with type 2 DM (10).

Since dysglycemic patients present with reduced distributions of sweat glands and subepidermal nerve fibers, it has been suggested that the EZSCAN system is a useful screening tool for IGT and DM. Studies investigating the use of EZSCAN in the screening of patients for IGT and DM have shown that this test has a sensitivity of 70-85% and a specificity of 54-100% (10,11,13); however, the cut-off points for the EZSCAN values used to detect these disorders were specific to study populations from France (10) and India (11), and the 'thresholds' appeared to differ in different ethnic groups. Another tool for determining glucose status, the HbA1c test, has ethnic-specific optimal cut-off points for detecting DM (14). We hypothesized that an optimal cut-off point for EZSCAN results could also be ethnically specific.

The aim of this preliminary study, therefore, was to determine the optimal cut-off points for EZSCAN screening to detect previously undiagnosed IGT and DM in a Chinese population. Furthermore, the diagnostic performance of the EZSCAN system as a screening tool was compared to that of the FPG and HbA1c tests.

#### Materials and methods

Study population. The subjects were selected from individuals visiting the Xianghe Community Hospital (Xianghe, China) for routine health check-ups between May and June 2011. Subjects were included in the study only if they were at high risk of developing DM (age  $\geq$ 45 years) and did not meet the exclusion criteria. The exclusion criteria were as follows: Previous diagnosis of pre-DM or DM; cancer; severe psychiatric disturbance; epilepsy; pregnancy; consumption of drugs known to affect blood glucose levels (corticosteroids, diuretics, epinephrine, lithium, phenytoin); consumption of drugs known to affect the sympathetic nervous system ( $\beta$ -blockers); arm or leg amputation; electrical implantable device (pacemaker, defibrillator); or known allergy to nickel or to any other standard electrode materials.

Finally, 270 subjects (180 women and 90 men) were enrolled in the present study, and all provided informed consent prior to taking part. This study was approved by the Medical ethics Committee of Xianghe Community Hospital and was in accordance with the ethical standards of the Declaration of Helsinki.

Anthropometric and biochemical measurements. The study participants were invited to the clinic to complete a questionnaire on demographics, lifestyle, medications and medical history, and specially trained nurses performed the anthropometric examinations. The measurements taken included height, weight, waist circumference and blood pressure. Body mass index (BMI) was calculated using the following formula: BMI = weight (kg)/height (m)<sup>2</sup>. Blood pressure was measured three times on the right arm using a sphygmomanometer and with a 10-min rest period between each measurement. Blood pressure was recorded as the mean of these three measurements.

Following an overnight fast (8-10 h), blood samples were drawn from all subjects for FPG, HbA1c and lipid profile analyses. Each subject was then asked to consume 75 g liquid glucose for an OGTT. A second blood specimen was taken 2 h after administering the oral glucose load. All plasma and serum biochemistry tests were performed in the clinical laboratory of the Xianghe Community Hospital using standard operating procedures. Plasma glucose levels were measured by the glucose oxidase method. HbA1c levels were measured using high-performance liquid chromatography (15,16) and serum lipid profiles, including total cholesterol (TC), triglycerides, high-density lipoprotein (HDL)- and low-density lipoprotein (LDL)-cholesterol, were determined by standard enzymatic procedures.

EZSCAN values. As shown in the video tour of the device (http://www.impeto-medical.com/ezscan-demo-video/), the EZSCAN system was designed to perform precise evaluations of sweat gland functions through reverse iontophoresis and chronoamperometry. The system measures ESC based on chloride concentrations in sweat. The apparatus includes two sets of electrodes for the hands and feet and a headband comprising a total of six electrodes. The electrodes are connected to a computer, which serves for recording and data management.

During the test, electrodes were placed on the areas of a patient's skin known to be enriched in sweat glands, including the forehead, the palmar sides of the hands and the plantar sides of the feet. A continuous current of <4 V was induced and the electrochemical conductance (in  $\mu$ S; ratio between current generated and a constant DC stimulus) was determined for the face (left and right sides), hands (left and right), feet (left and right) and the whole body (global conductance). A time-ampere curve was recorded for each derivation. Since conductance is dependent upon the topographical distributions of sympathetic ganglions and nerve fiber lengths, different parts of the body exhibit different conductances. In each subject, identical electrochemical results will be generated in a specific zone, except when the function of the zone has been modified pathologically due to small fiber neuropathy. Following the placement of the electrodes on the hands and feet and the headband electrodes on the forehead of the patient, the patient was asked to stand still for 2-3 min. The EZSCAN scale ranged between 0 and 100% and was calculated using an algorithm that took into account different parameters, including demographic variables. The patient's details were displayed instantaneously in the form of a geometric figure, enabling a rapid, intuitive interpretation.

*Study groups*. The study subjects were categorized into three groups based on the World Health Organization (WHO) criteria of 1999 (17): i) The normal glucose tolerance (NGT) group (fasting glucose <6.1 mmol/l and 2-h plasma glucose <7.8 mmol/l); ii) the IGT group (2-h plasma glucose of 7.8 to <11.1 mmol/l) and iii) the newly diagnosed DM (NDM) group (fasting glucose >7 mmol/l and/or 2-h plasma glucose >11.1 mmol/l).

| Characteristic              | Total population    | NGT              | IGT                           | NDM                           | P-value |
|-----------------------------|---------------------|------------------|-------------------------------|-------------------------------|---------|
| Subjects, n                 | 270                 | 151              | 79                            | 40                            | -       |
| Age, years                  | 58.6 (10.2)         | 55.7 (10.2)      | 62.2 (8.5) <sup>b</sup>       | 62.5 (9.4) <sup>b</sup>       | < 0.001 |
| Male, %                     | 31.6                | 31.1             | 35.4                          | 37.5                          | 0.378   |
| Weight, kg                  | 66.8 (12.3)         | 65.7 (12.7)      | 69.1 (12.0)                   | 66.2 (11.1)                   | 0.134   |
| BMI, kg/m <sup>2</sup>      | 25.6 (4.7)          | 25.2 (4.8)       | 26.2 (4.9)                    | 25.7 (3.8)                    | 0.354   |
| Waist, cm                   | 90.8 (10.2)         | 89.1 (10.9)      | 93.3 (8.8) <sup>b</sup>       | 92.7 (8.6)                    | 0.006   |
| SBP, mmHg                   | 130.0 (120.0-150.0) | 130.0 (21.8)     | 137.6 (21.3)                  | 145.3 (25.5) <sup>b</sup>     | < 0.001 |
| DBP, mmHg                   | 79.5 (11.2)         | 78.7 (11.8)      | 79.9 (11.2)                   | 81.7 (8.6)                    | 0.291   |
| TC, mmol/l                  | 5.02 (1.03)         | 4.90 (0.96)      | 5.24 (1.14)                   | 5.03 (1.03)                   | 0.610   |
| TG, mmol/l <sup>a</sup>     | 1.61 (1.14-2.42)    | 1.44 (1.06-1.89) | 1.85 (1.32-2.63) <sup>b</sup> | 1.87 (1.29-3.43) <sup>b</sup> | < 0.001 |
| HDL, mmol/l                 | 1.32 (1.20-1.38)    | 1.29 (0.20)      | 1.31 (0.20)                   | 1.31 (0.23)                   | 0.684   |
| LDL, mmol/l                 | 2.78 (1.05)         | 2.83 (0.94)      | 2.82 (1.23)                   | 2.53 (0.98)                   | 0.255   |
| FPG, mmol/l                 | 5.59 (5.21-6.16)    | 5.47 (0.58)      | 5.89 (0.98) <sup>b</sup>      | 8.04 (3.40) <sup>b,c</sup>    | < 0.001 |
| 2-h postload plasma         | 7.44 (6.18-9.72)    | 6.16 (0.98)      | 9.17 (0.91) <sup>b</sup>      | 14.52 (3.81) <sup>b,c</sup>   | < 0.001 |
| glucose mmol/l              |                     |                  |                               |                               |         |
| HbA1c, %                    | 6.0 (5.7-6.4)       | 5.9 (0.5)        | 6.0 (0.5)                     | 7.3 (1.8) <sup>b,c</sup>      | < 0.001 |
| EZSCAN <sup>TM</sup> , $\%$ | 42 (26-51)          | 34 (13)          | 47 (11) <sup>b</sup>          | 48 (11) <sup>b</sup>          | < 0.001 |

| Table I. Characteristics of the study subject | Table I. | Characteristics | of the | study | subjects |
|---|----------|-----------------|--------|-------|----------|
|---|----------|-----------------|--------|-------|----------|

Values are presented as the mean standard deviation, median (25-75th percentiles) or as a percentage. <sup>a</sup>Log-transformed prior to testing. <sup>b</sup>Significantly different from IGT. NGT, normal glucose tolerance; IGT, impaired glucose tolerance; NDM, newly diagnosed diabetes mellitus; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglycerides; FPG, fasting plasma glucose; BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; HbA1c, hemoglobin A1c.

Statistical analysis. SPSS software version 16.0 (SPSS, Inc., Chicago, IL, USA) was used for the statistical analysis. Results are presented as the mean (standard deviation), median (25th-75th percentiles) or percentages, as appropriate. One-way analysis of variance and  $\chi^2$  tests were used to compare the results for the groups with different glycemic states. Pearson correlation analysis was used to assess the correlation between the EZSCAN values and the results from the FPG and HbA1c tests and the OGTT. Receiver operating characteristic (ROC) curves were generated to evaluate the performance of EZSCAN for IGT and DM detection as compared to the FPG and HbA1c results. The areas under these ROC curves (AUCs) and the corresponding 95% confidence intervals (CI) were calculated and used to determine maximum sensitivity and specificity at optimal cut-off points. P<0.05 was considered to indicate a statistically significant difference.

## Results

Subject characteristics and the correlations between EZSCAN scores and blood glucose metabolism variables. A total of 270 subjects were enrolled in this study. None of the subjects had been previously diagnosed with any glucose metabolism disorder. The demographic characteristics of the study population are shown in Table I. Based on the WHO criteria of 1999 (17), the subjects included 151 (55.9%) with NGT, 79 (29.3%) with IGT and 40 (14.8%) with NDM. No significant differences were found among these three groups in terms of weight, BMI, diastolic blood pressure, TC, HDL-cholesterol or LDL-cholesterol; however, compared with subjects with

NGT, those with IGT and NDM were older, had greater waist circumferences, higher systolic blood pressures and higher FPG and HbA1c levels. Furthermore, the EZSCAN scores were significantly higher for subjects with IGT ( $47\pm11\%$ ) and NDM ( $48\pm11\%$ ) than those for subjects with NGT ( $34\pm13\%$ ). Thus, the EZSCAN values corresponded to other abnormalities in subjects with IGT and NDM.

For all subjects, the correlation coefficients of the EZSCAN value were 0.462 with the 2-h post-glucose load OGTT (P<0.001), 0.182 with FPG (P<0.001) and 0.379 with HbA1c (P<0.001). Although these correlations were moderate, they were statistically significant and indicated that the EZSCAN values paralleled changes in markers associated with IGT and or NDM.

*Diagnostic performance of the EZSCAN values.* ROC curves were generated for the EZSCAN values and FPG and HbA1c levels for subjects with IGT (Fig. 1A) and those with NDM (Fig. 1B). Again, the subjects for whom these curves were generated had, according to the WHO classification, either IGT or NDM. Based on these curves, the optimal cut-off points of these three variables were determined and were used to assess their diagnostic performance. Table II summarizes the results.

For those patients with IGT, the optimal cut-off point for EZSCAN was 37%, which gave a sensitivity of 82%, a specificity of 63% and an AUC of 0.778. This AUC for EZSCAN was significantly higher than that for FPG (0.639; P=0.0164) and HbA1c (0.540; P<0.001). For those patients with NDM, the optimal cut-off point was 50%, which gave a sensitivity

| Table II. Diagnostic performances | of EZSCAN <sup>™</sup> . FPC | and HbA1c testing | for the detection c | of IGT and NDM. |
|-----------------------------------|------------------------------|-------------------|---------------------|-----------------|
|                                   |                              |                   |                     |                 |

| Screening method | Cut-off | Sensitivity      | Specificity      | PPV              | NPP              | AUC                 |
|------------------|---------|------------------|------------------|------------------|------------------|---------------------|
| IGT              |         |                  |                  |                  |                  |                     |
| EZSCAN, %        | 37      | 82 (72.1-90.0)   | 63 (55.1-71.0)   | 54 (44.8-63.3)   | 87 (79.3-92.8)   | 0.778 (0.718-0.830) |
| FPG, mmol/l      | 6.1     | 35.9 (25.3-47.6) | 88.9 (82.7-93.6) | 63.6 (47.8-77.6) | 72.1 (64.9-78.5) | 0.639 (0.572-0.702) |
| HbA1c,%          | 6.0     | 46 (34.1-57.2)   | 64 (55.1-71.3)   | 40 (29.4-50.8)   | 69 (60.1-76.4)   | 0.540 (0.472-0.607) |
| NDM              |         |                  |                  |                  |                  |                     |
| EZSCAN, %        | 50      | 53 (36.1-68.5)   | 59 (47.3-70.0)   | 40 (26.5-54)     | 71 (58.2-81.4)   | 0.528 (0.433-0.622) |
| FPG, mmol/l      | 7.0     | 45.0 (29.3-61.5) | 89.7 (80.8-95.5) | 69.2 (47.8-86.0) | 76.1 (66.1-84.4) | 0.772 (0.685-0.845) |
| HbA1c, %         | 6.5     | 59 (42.1-74.4)   | 82 (71.4-89.7)   | 62 (44.4-77.7)   | 80 (69.2-88.0)   | 0.759 (0.671-0.834) |

IGT, impaired glucose tolerance; NDM, newly diagnosed diabetes mellitus; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; PPV, positive predictive value; NPP, negative predictive value; AUC, area under the curve.

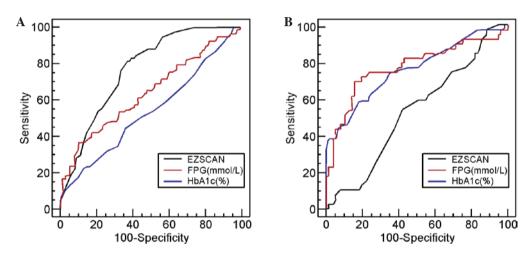


Figure 1. Receiver operating characteristic curves created for the evaluation of the diagnostic performances of the EZSCAN<sup>TM</sup>, FPG and HbAlc tests for subjects with (A) IGT and (B) NDM. IGT and NDM diagnoses were defined based on the World Health Organization classifications of 1999 (18). FPG, fasting plasma glucose; HbAlc, hemoglobin Alc; IGT, impaired glucose tolerance; NDM, newly diagnosed diabetes.

of 53%, a specificity of 59% and an AUC of 0.528. This AUC for EZSCAN was significantly lower than that for FPG (0.772; P=0.001) and HbA1c (0.759; P=0.0012). A superior performance in detecting IGT was recorded for the EZSCAN values, compared to those of FPG or HbA1c; however, the EZSCAN values did not perform as well in detecting NDM in this study population. In addition, the gender-specific diagnostic performance of the EZSCAN values was evaluated. Table III shows the sensitivities, specificities and EZSCAN values for women and men with IGT and NDM. No significant difference in sensitivity or specificity between the genders was observed for either an EZSCAN cut-off point of 37% for those patients with IGT (P>0.05) or an EZSCAN cut-off point of 50% for those patients with NDM (P>0.05). In addition, the mean EZSCAN values for women and men were not significantly different (P>0.05). Thus, the diagnostic performance of EZSCAN was similar for women and men.

Table IV shows the percentages of patients with NGT, IGT and NDM that were identified when different EZSCAN value cut-off points were used. Based on the WHO criteria of 1999 (17), when the 37% cut-off point was used, 82.1% of patients with IGT were correctly identified. When the 50%

cut-off point was used, 57.5% of patients with NDM were correctly identified; however, this higher cut-off point also misclassified 19.3% of patients with NGT and 51.3% of patients with IGT. Again, the EZSCAN values performed well in detecting previously undiagnosed IGT, but their performance in detecting NDM was marginal, at best.

## Discussion

The results of this preliminary investigation suggested that an EZSCAN cut-off point of 37% was optimal for detecting previously undiagnosed IGT, as this gave a sensitivity of 82% and a specificity of 62%. A cut-off point of 50% was optimal for detecting DM, with relatively low sensitivity and specificity (53 and 59%, respectively). The present results are in accordance with the hypothesis that the EZSCAN system is an acceptable tool for screening patients with IGT and DM. In addition, this study is the first, to the best of our knowledge, to demonstrate the efficacy of the EZSCAN system in the screening of a specific Chinese population.

Two previous studies using the EZSCAN system to detect IGT and DM were conducted with French (10) and

|         | IC                          | ĴΤ                           | NI                           | DM                           |                           |
|---------|-----------------------------|------------------------------|------------------------------|------------------------------|---------------------------|
| Gender  | Sensitivity <sup>a</sup> ,% | Specificity <sup>a</sup> , % | Sensitivity <sup>a</sup> , % | Specificity <sup>a</sup> , % | EZSCAN value <sup>b</sup> |
| Female  | 81 (66.9-90.2)              | 63 (52.9-72.1)               | 44 (24.4-65.1)               | 57 (42.2-70.7)               | 39±13.3                   |
| Male    | 75 (55.1-89.3)              | 65 (49.8-78.6)               | 53 (26.6-78.7)               | 60 (49.8-89.2)               | 41±13.7                   |
| P-value | >0.05                       | >0.05                        | >0.05                        | >0.05                        | 0.26                      |

| Table III. EZSCAN <sup>™</sup> | diagnostic | performances | for | female | e and | male pa | atients. |
|--------------------------------|------------|--------------|-----|--------|-------|---------|----------|
|                                |            |              |     |        |       |         |          |

<sup>a</sup>Presented as the median (range); <sup>b</sup>presented as the mean ± standard deviation. IGT, impaired glucose tolerance; NDM, newly diagnosed diabetes mellitus.

| Table IV. Identification of subjects | with NGT, IGT and NDM using different EZSC. | AN <sup>™</sup> cut-off points. |
|--------------------------------------|---|---------------------------------|
|                                      |   |                                 |

| EZSCAN cut-off points, % | NGT, n (%) | IGT, n (%) | NDM, n (%) |
|--------------------------|------------|------------|------------|
| ≥25                      | 107 (73.8) | 78 (100.0) | 40 (100.0) |
| ≥31                      | 60 (41.4)  | 66 (84.6)  | 35 (87.5)  |
| ≥37                      | 56 (38.6)  | 64 (82.1)  | 33 (82.5)  |
| ≥43                      | 47 (32.4)  | 54 (69.2)  | 29 (72.5)  |
| ≥50                      | 28 (19.3)  | 40 (51.3)  | 23 (57.5)  |
| ≥56                      | 12 (8.3)   | 17 (21.8)  | 6 (15.0)   |
| ≥62                      | 2 (1.4)    | 6 (7.7)    | 4 (10.0)   |

NGT, normal glucose tolerance; IGT, impaired glucose tolerance; NDM, newly diagnosed diabetes mellitus.

Indian (11) study populations. The investigation that took place in France, where the device was developed, demonstrated that the EZSCAN system had 75% sensitivity and 100% specificity for diagnosing DM (10). The investigation conducted in India also showed that EZSCAN had a high sensitivity for detecting both IGT and DM. Using a cut-off point of 50% for this Asian Indian population, the device showed a sensitivity of 75% for detecting DM and 70% for detecting IGT (11). A third study testing the EZSCAN device was conducted with patients in Hong Kong, China; however, its aim was to determine the optimal cut-off point (i.e., 55%) for detecting DM-associated kidney disease (18). A fourth study (13) was conducted with a Chinese population to establish the efficacy of EZSCAN screening for detecting DM; however, the cut-off point used was provided by the French manufacturer and was based on a French population (13). Despite this, and consistent with our recent report (19), a good reproducibility of the EZSCAN test was suggested in the Chinese population.

The present study provided novel information regarding the ethnic-specific cut-off values for the EZSCAN system in a Chinese population. These values were determined by ROC curves, which were generated following the classification of the subjects based on their OGTT results, the gold standard test for the diagnosis of IGT and DM according to the WHO recommended guidelines (17). It was found that, in this Chinese population, the EZSCAN cut-off points of 37 and 50% were optimal for detecting IGT and DM, respectively.

Since there is strong evidence that lifestyle management can reduce the rate of progression from IGT to DM, it is important to identify all individuals with pre-DM so that prevention efforts may be implemented in a timely manner (20). The present results have shown that, when using the 37% cut-off point, the EZSCAN test had a higher sensitivity and a significantly greater AUC for detecting IGT than either the FPG or the HbA1c test. The EZSCAN test may therefore be the most effective screening method and the most efficient way to ensure early intervention in the Chinese population; however, further studies with larger groups of patients would assist in refining the cut-off point in order to more accurately detect this pre-diabetic state.

It was also observed that the AUC for the detection of NDM in the Chinese population using EZSCAN was significantly lower than that for either the FPG or the HbA1c test. The EZSCAN system did, however, have a relatively high sensitivity. We speculate that the EZSCAN test may be a more effective screening tool for the detection of IGT than for the detection of DM. A possible explanation for this may be that the nerves associated with the sweat glands are in a phase of hypersensitivity during the IGT phase, but in a phase of hypersensitivity in DM (21); however, further studies are required to confirm this speculation, as the EZSCAN values of the subjects with IGT ( $47\pm11\%$ ) and those with NDM ( $48\pm11\%$ ) were virtually identical.

It is a fact that the distribution of hyperglycemic states can vary based on ethnicity. For example, Western and Chinese populations have different proportions of patients with elevated FPG concentrations (40 vs. 19%, respectively), elevated 2-h post-load plasma glucose concentrations (31 vs. 44%) and elevated FPG with elevated 2-h post-load plasma glucose concentrations (29 vs. 37%) (22,23). In the present study population, the IGT state was the more frequently represented compared with FPG. Since the results indicated that the EZSCAN test had a higher sensitivity for detecting IGT, we hypothesize that EZSCAN may be more suitable for detecting IGT in Chinese populations. Future studies should investigate this possibility.

As noted previously in the study, the EZSCAN test has several advantages over traditional biochemical tests. Firstly, an EZSCAN test can be performed without fasting or other patient preparation (24). Secondly, this test is non-invasive and rapid, which promotes patient comfort and compliance. Thirdly, the test is highly sensitive, and is likely to diagnose cases that may fall below the detection thresholds of other methods. The major limitation of EZSCAN is its relatively low specificity, and future studies should address this issue in order to develop an improved EZSCAN strategy. It has been suggested in previous studies (12,13) that the EZSCAN values may also be affected by the environment, such as temperature and humidity, and the age of the subjects; however, the subjects in the present study were tested in a dehumidified room with air-conditioning, the temperature of which was maintained at 20°C. The subjects were neither extremely old nor extremely young. Consequently, none of the factors mentioned above played a significant role in this particular study; however, further studies are warranted for a definite conclusion.

The present study had several limitations. Firstly, due to the fact that this was a preliminary study investigating screening efficacy, the sample size was relatively small, preventing direct extrapolations of the observations to the general population. Larger population-based studies comprising composite population groups from different regions of China are required to better evaluate the capabilities of EZSCAN in diagnosing IGT and DM. Secondly, continuous glucose monitoring during the test day was not possible in the present study population, and only one OGTT was performed on each subject. The moderate correlations that were observed between the EZSCAN values and blood glucose concentrations were, in part, due to the rather high variability of the 2-h post-load plasma glucose levels between individuals. A study with an extensive dataset for temporal glucose monitoring may provide more meaningful insights into these correlations.

In conclusion, the EZSCAN optimal cut-off points for detecting IGT and DM in Chinese patients, independently of other tests, were determined to be 37 and 50%, respectively. These cut-off points were different from those recorded in previous studies, whose subjects were of different ethnic groups, and may aid clinicians in interpreting EZSCAN results for patients of different ethnicities. Although the EZSCAN test is a promising approach for performing non-invasive, convenient screenings for IGT and DM in Chinese populations, further studies, focusing on larger, more diverse Chinese sub-populations, are necessary. Despite this, the results of the present study provide a foundation for conducting future studies on the cost-effectiveness of EZSCAN versus plasma glucose testing and for investigating the potential of EZSCAN to predict future DM or micro- and macrovascular complications.

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