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Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☒	☐	A description of all covariates tested
☒	☐	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	Raman spectra are acquired by mμSORS system developed in this study. Venous blood glucose (VBG) is measured by an autoanalyzer (AU5800, BECKMAN). DEJ Depth of human thenar was determined by optical coherence tomography system(Ganymede SD-OCT System, Thorlabs). Bright field image and Raman spectra of ex-vivo human skin were obtained from WITec alpha 300 imaging system (Germany).
Data analysis	Python version 3.9.13 is used with the base packages and the following additional packages: numpy (1.21.5), matplotlib (3.5.2), scipy (1.9.1), pandas (1.4.4), and seaborn (0.11.2). A standard PLS algorithm is used to build the regression models. The analysis codes used in the current study are available upon reasonable request addressed to the corresponding authors

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

Data and code showed in figures can be found with the link: https://doi.org/10.6084/m9.figshare.25750602. All data used in the current study are available upon reasonable request addressed to the corresponding authors

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	In all basic experimental studies with humans (BESHs), the sex of the participants was reported as a number and percentage of the total number of participants. Sex or birth gender of participants was determined based on self-report and government-issued personal Identity Card (ID). We performed sex-based analyses and showed no significant difference in accuracy between female and male subjects.
Reporting on race, ethnicity, or other socially relevant groupings	All participants in the study were Chinese.
Population characteristics	In the preliminary BESH (No. NCT05504005): 1) Male or female, healthy or previously diagnosed type 2 diabetes. 2) Aged between 30 and 60 years. 3) For healthy subjects without diabetes history, fasting blood glucose (FPG) < 6.1 mmol/L and glycated hemoglobin (HbA1c) < 5.7% during the screening period?and for patients with type 2 diabetes, FBG ≥ 6.1 and < 13.3 mmol/L. 4) There are no scars, obvious pigmentation and other factors that interfere with the detection of the palm skin to be tested. In the expanded BESH (No.NCT05921344): 1) Male or female, previously diagnosed type 2 diabetes. 2) Aged larger than or equal to 18 years old. 3) There are no scars, obvious pigmentation and other factors that interfere with the detection of the palm skin to be tested. In the expanded BESH (No.NCT06512077): 1) Male or female, without diabetes history. 2) Aged larger than or equal to 18 years old. 3) Fasting blood glucose (FPG) < 6.1 mmol/L and glycated hemoglobin (HbA1c) < 5.7% during the screening period. 4) There are no scars, obvious pigmentation and other factors that interfere with the detection of the palm skin to be tested.
Recruitment	All BESHs were open, participants were recruited from Ruijin hospital. For the enrollment of T2D subjects, it is required that no acute complications of diabetes within 3 months before enrollment, or severe chronic complications of diabetes and comorbidities [including severe structural heart disease, chronic congestive heart failure (NYHA≥III), and history of severe liver or kidney dysfunction, etc] were observed.
Ethics oversight	All ethics approvals were obtained from the RuiJin Hospital Ethics Committee, affiliated with Shanghai JiaoTong University School of Medicine. All the subjects have provided written informed consent and were compensated for the travel reimbursement and sampling.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	35 participants in the preliminary BESH (No. NCT05504005). 200 participants in the expanded BESH (No.NCT05921344). 30 participants in the expanded BESH (No.NCT06512077). No sample-size calculations were performed. Sample sizes were chosen based on similar previously published studies of non-invasive glucose blood monitoring (Stefan Pleus et al. J Diabetes Sci Technol. 15,11-18 (2020) & Anders Pors et al. ACS Sens. 2024 https://doi.org/10.1021/acssensors.2c02756). The numbers of samples are large enough to capture normal variation and glucose feature from Raman spectra according to the published data in this field.
Data exclusions	In the preliminary BESH (No. NCT05504005): Among all 420 sets of data, 5 spectra are lost due to technical issues.

Data exclusions	In the expanded BESH (No.NCT05921344): Among all 4800 sets of data, 24 from both hands of subject D016 were lost because the subject quit the BESH. 8 sampling points of subject D119 were lost due to technical problems. In the expanded BESH (No.NCT06512077): Among all 540 sets of data, no data lost.
Replication	We have demonstrated the replication with three independent BESHs.
Randomization	N/A - No randomization was used in this study, and all enrolled subjects were treated the same.
Blinding	N/A - Blinding was not necessary since there was no randomization nor experimental groups.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☒ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	https://clinicaltrials.gov/, No. NCT05504005, No. NCT05921344 and No.NCT06512077.
Study protocol	https://clinicaltrials.gov/
Data collection	We recruited all the participants, performed the study and collected all the data in Ruijin Hospital affiliated with Shanghai JiaoTong University School of Medicine in Shanghai of China. The data in preliminary BESH (No. NCT05504005) was collected from August to December in 2022. The data in expanded BESH (No. NCT05921344) was collected from July to September in 2023. The data in expanded BESH (No.NCT06512077) was collected in August of 2024.
Outcomes	Primary outcome: 1) Mean absolute relative deviation (MARD) of venous plasma glucose and glucose values measured by mμSORS at each time point of OGTT. 2) Consensus Error Grid (CEG) for venous plasma glucose and glucose values measured by mμSORS at each time point of OGTT. Secondary Outcome: 1) MARD for two measurement methods in different blood glucose ranges. 2) Incidence of treatment-emergent adverse events.

Plants

Seed stocks	N/A.
Novel plant genotypes	N/A.
Authentication	N/A.