

Noninvasive Prediabetes and Diabetes Screening Using Skin Fluorescence: Clinical Validation in an At-Risk Cohort

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Study Aims

- Prospectively compare the performance of the noninvasive SCOUT DS[®] Diabetes Score to fasting plasma glucose and A1C for detection of abnormal glucose tolerance (impaired glucose tolerance or undiagnosed diabetes) in a cohort at risk for development of type 2 diabetes

Background

- Noninvasive skin fluorescence (SF) measurements of dermal advanced glycation end products (AGEs) and oxidative stress markers have been proposed to screen subjects for pre-diabetes and type 2 diabetes¹
- SF measurements contain multiple sources of information related to the development of pre-diabetes and type 2 diabetes
 - ❖ Multiple spectral signatures from fluorophores in the epidermis and dermis (e.g. fluorescent AGEs, NADH, flavoproteins)
 - ❖ Light scattering and absorption due to microvascular damage and cross-linking of collagen and elastin
- The SCOUT DS device measures skin fluorescence noninvasively and produces a SCOUT Diabetes Score (SDS) on a scale of 0 to 100
 - ❖ SDS produced by a multivariate algorithm that utilizes LED excited fluorescence, white light reflectance, and subject age / gender
 - ❖ The higher the SDS, the more likely the patient has pre-diabetes or diabetes
- SCOUT DS is licenced (#85875) in Canada for noninvasive diabetes screening at the point-of-care

Study Design

- The ENGINE clinical study recruited subjects at risk for type 2 diabetes but without an existing diagnosis of diabetes at 12 clinical sites across the USA
- Each clinical site had a dedicated SCOUT DS device
- Study participation required three separate visits to the clinic
- Visit 1 required an overnight fast (> 8 hours) and occurred in the morning
 - ❖ Obtained informed consent, health history and physical measurements
 - ❖ Fasting plasma glucose (FPG), A1C and SCOUT DS measurements
 - ❖ 75 gram, 2 hour oral glucose tolerance test (OGTT) performed
- Visit 2 did not require fasting and occurred anytime of day
 - ❖ Two consecutive SCOUT DS measurements performed
- Visit 3 required an overnight fast (> 8 hours) and occurred in the morning
 - ❖ FPG and SCOUT DS measurements

Inclusion Criteria

- Age greater than or equal to 45 years; OR
- Age 18 to 44 years and a BMI \geq 25 kg/m² with one or more of additional risk factors for type 2 diabetes²

Exclusion Criteria

- Diagnosed with any type of diabetes, including type 1 or 2
- Taking glucose lowering medications
- Prior bariatric surgery
- Known to be pregnant
- Receiving dialysis or having known renal compromise
- Conditions that cause secondary diabetes including Cushing's syndrome, acromegaly, hemochromatosis, pancreatitis, or cystic fibrosis
- Scars, tattoos, rashes or other disruptions on the left volar forearm
- Recent (within past month) or current oral steroid therapy or topical steroids applied to the left forearm; inhaled steroid therapy is not excluded
- Current chemotherapy, or chemotherapy within the past 12 months
- Known to have, or at risk for, photosensitivity reactions
- Receiving medications that fluoresce

Cohort Demographics

	NGT ¹	AGT ²	P Value
Number of Subjects	299 (73%)	109 (27%)	n/a
Males	127 (42%)	46 (42%)	0.98
Ethnicity	183 (61%) White 52 (17%) Latino 58 (19%) Afr. Amer. 6 (2%) Other	71 (65%) White 24 (22%) Latino 7 (6%) Afr. Amer. 7 (6%) Other	0.47
Age (yrs)	50.2 \pm 13.7	55.5 \pm 12.4	< 0.001
OGTT (mmol)	5.8 \pm 1.1	10.8 \pm 4.0	<0.0001
A1C (%)	5.6 \pm 0.3	6.2 \pm 1.1	<0.0001
FPG (mmol)	5.2 \pm 0.5	6.1 \pm 2.0	<0.0001
SCOUT Diabetes Score	49.1 \pm 9.3	55.9 \pm 9.7	<0.0001

Table 1: Demographic characteristics of the ENGINE cohort expressed as either number (%) or mean \pm standard deviation

¹ Normal glucose tolerance, i.e. had OGTT < 7.8 mmol (140 mg/dL) during the trial

² Abnormal glucose tolerance, i.e. had OGTT \geq 7.8 mmol (140 mg/dL) during the trial

Measurement Methods

- Blood for the FPG, A1C and 2 hour post challenge glucose was drawn from a vein on the right arm and assayed at local reference laboratories
- The SCOUT DS device (Figure 1) measures light in the range of 360 to 660 nm and excites skin fluorescence with light emitting diodes (LED) centered at 375, 405, 417, 435 and 456 nm
- The SCOUT DS device also measures skin reflectivity with a white LED to account for subject specific melanin and hemoglobin content
- SCOUT DS measurement performed on the left volar forearm (Figure 2)
- The SCOUT DS device requires the subject to place their arm on the device twice before the SDS is reported



Figure 1: SCOUT DS device



Figure 2: Forearm on device

Analysis

- Abnormal glucose tolerance was defined as a 2 hour post challenge glucose \geq 7.8 mmol (140 mg/dL) after the OGTT
- Receiver operating characteristics (ROC) curves were calculated for SDS, FPG and A1C by sweeping the test threshold from the entire range of values and computing the corresponding sensitivities and specificities
- The partial area under the ROC curve index (pAUCi) was computed for the area of the ROC curve between 20% and 50% false positive rates
- The inter-day coefficient of variation for SF and FPG was calculated by the method reported in the Hoorn study³

Results

- Figure 3 shows the ROC, test threshold sensitivity/false positive rate (FPR) pairs and pAUCi results for the ability of SDS, FPG and A1C to detect abnormal glucose tolerance in the ENGINE cohort
- The inter-day Hoorn CV for SCOUT DS was 7.7% while it was 8.1% for FPG

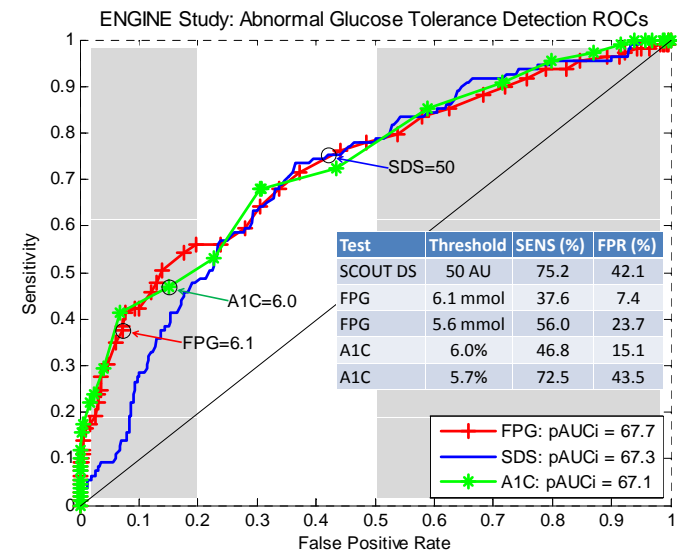


Figure 3: Analysis Showing Detection of Abnormal Glucose Tolerance

Summary

- 408 subjects had complete data of which 109 had abnormal glucose tolerance
- There was a representative distribution of age, gender and ethnicity
- The SCOUT DS pAUCi was similar to both FPG and A1C for detection of abnormal glucose tolerance
- The SCOUT DS threshold favors test sensitivity at the expense of a moderate FPR while the A1C and FPG thresholds of 6.0% and 6.1 mmol, respectively, favor lower FPR at the expense of sensitivity

Conclusion

The point-of-care SCOUT DS device was demonstrated to be non-inferior to laboratory-based FPG and A1C for detection of abnormal glucose tolerance in an at-risk population. In addition, SCOUT DS had a comparable inter-day Hoorn CV to FPG. The SCOUT DS threshold of 50 identifies 60% more individuals with AGT than an A1C threshold of 6.0% and 100% more than an FPG threshold of 6.1 mmol. The noninvasive, non-fasting nature of SCOUT DS coupled with higher sensitivity than traditional blood-based screening tests make it an option for opportunistic prediabetes and diabetes screening in the at risk population.

References

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3. Mooy JM et al. Intra-individual variation of glucose, specific insulin and proinsulin concentrations measured by two oral glucose tolerance tests in a general caucasian population: The Hoorn study. *Diabetologia*. 1996;39:298-305.