

Introduction

Abstract

In the US, the estimated number of people having undiagnosed type 2 diabetes grew by over 20% from 2002 to 2005, underscoring concern that current screening methods are inadequate. In addition, an estimated 41 million in the US have pre-diabetes. Conventional blood tests are not only inconvenient – requiring an overnight fast and a reference lab trip – but also have performance issues that render them inefficient and ineffective for diabetes screening.

In a recent NIDDK-funded case-control study, a novel fluorescence spectroscopic technique showed considerable promise for quick, accurate diabetes screening that does not require patient fasting. A next generation instrument was developed to assess the clinical utility of this technology. The device illuminates the volar forearm skin with low-intensity light at multiple near-ultraviolet and visible wavelengths. A specially designed fiber-optic probe couples the excitation light to the subject and relays resulting skin fluorescence to a detection module. Multivariate techniques are applied to the spectra to obtain a diabetes risk score.

The study presented is a head-to-head evaluation of the noninvasive technology and fasting plasma glucose (FPG) test in an at-risk population. The oral glucose tolerance (OGT) test is applied as the adjudicating test. The 401 subjects in the study cohort range in age from 21 to 88 years old with a nearly equal gender split. The receiver-operator characteristics of the tests for detecting impaired glucose tolerance (2hr OGT > 139 mg/dl) yield area-under-the-curve (AUC) values of 64.9% for FPG and 75.9% for the noninvasive method ($\pm 7.1\%$). At the impaired fasting glucose threshold of 100 mg/dl, the FPG sensitivity is 51.8% with a specificity of 79.0%. At that specificity, the noninvasive sensitivity is 65.2%.

Comprehensive study findings and the implications for further development of noninvasive screening for type 2 diabetes and pre-diabetes will be presented.

Background of Advanced Glycation Endproducts

- DCCT and other studies have demonstrated that elevated skin advanced glycation endproducts (AGEs) are a biomarker of diabetes and are predictive of future diabetic retinopathy and nephropathy [1,2]
- Persons with pre-diabetes and diabetes accumulate skin AGEs faster than individuals without diabetes
- Skin AGEs are a sensitive, summary metric for the integrated glycemic exposure the body has endured
 - Analogous to a 'diabetes odometer'
- The noninvasive device, **SCOUT**, measures skin fluorescence due to AGEs *in vivo* and provides a quantitative diabetes risk score
 - No fasting - skin fluorescence is insensitive to acute glucose levels
 - No blood draws or biohazards
 - Measurement time ~ 1 minute



Summary of Previous Studies

- In-vitro study of Advanced Glycation Endproducts (AGEs)
 - Confirmed relationship between skin AGEs and the SCOUT signal
 - Verified ability to spectroscopically quantify carboxymethyl lysine and pentosidine – biomarkers that correlate with disease state and are predictive of future complications
- Case-control clinical study
 - Supported by a grant from NIH/NIDDK
 - Evaluated new optical probe, optimized for dermal fluorescence
 - Demonstrated optical disease classification in a dichotomous population
- Evaluate the role of low-molecular weight serum AGEs in skin fluorescence
 - Test premise that serum AGEs diffuse into dermal interstitial space and potentially corrupt the noninvasive SCOUT measurement
 - Negligible correlation between spectral scores and AGE assay results
 - Partial-least-squares analysis confirms lack of relationship between serum AGEs and skin fluorescence

At-Risk Clinical Study

Experimental Design

328 naïve subjects with risk factors for type 2 diabetes or pre-diabetes

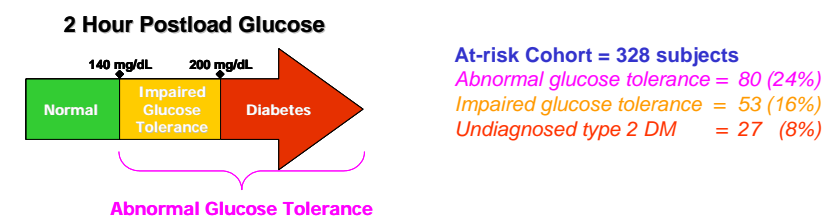
- Risk factors included age, first degree relative with type 2 diabetes, hypertension, dyslipidemia, body mass index > 25, ethnicity with higher disease prevalence, previous gestational diabetes, baby weighing more than 9 lbs at birth and/or polycystic ovary syndrome
- Most subjects had two or more risk factors

- Head-to-head test of SCOUT's noninvasive technology and fasting plasma glucose (FPG)
- Oral glucose tolerance (OGT) used to adjudicate truth

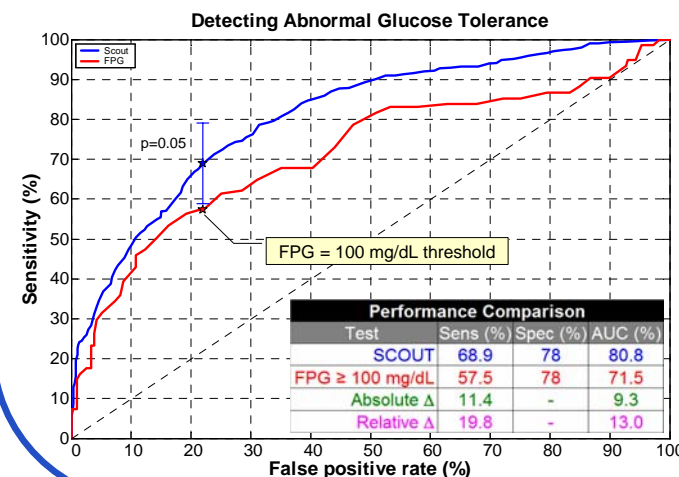
Study Demographics

Age		Gender		Ethnicity	
21-30	17	Male	105	Caucasian	177
31-40	49	Female	223	Hispanic	118
41-50	88	Total	328	African Am	10
51-60	84			Native Am	15
61-70	62	Smokers		Asian	3
71-80	20	Yes	122	East Indian	1
81+	8	No	206	Other	4
Total	328	Total	328	Total	328

Disease Classification

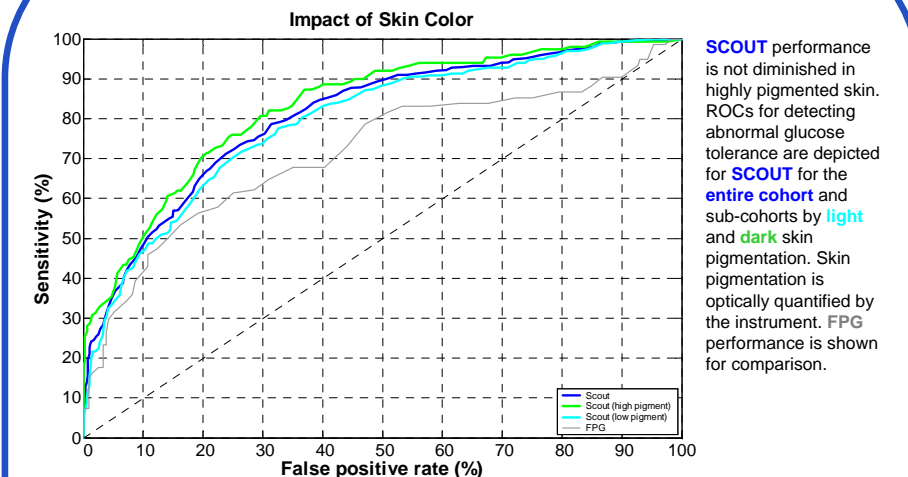


Results



Receiver-operator curves demonstrating the performance advantage of **SCOUT** over **FPG** in the at-risk population of this study. The **SCOUT** vs **FPG** differential is statistically significant both in area-under-the-curve (AUC) and at the **FPG** clinical screening threshold (100 mg/dL).

Results, continued



Clinical Study Summary

- SCOUT significantly outperforms fasting plasma glucose as a screening test
 - SCOUT finds ~20% more patients with disease or precursors than current test
- SCOUT is unaffected by skin pigmentation
- Lack of a fasting requirement, overall convenience and superior accuracy for SCOUT will facilitate opportunistic diabetes and pre-diabetes screening at the point-of-service

Next Steps

- Construction of clinical prototypes
- Multi-center calibration
- Pivot trials for regulatory clearance
- Product launch



Conceptual clinical prototype

References

- DCCT Skin Collagen Ancillary Study Group, "Skin collagen glycation, glycoxidation, and crosslinking are lower in subjects with long-term intensive versus conventional therapy of type 1 diabetes," *Diabetes* 48: 870-880 (1999).
- Genuth et al., "Glycation and Carboxymethyllysine Levels in Skin Collagen Predict the Risk of Future 10-Year Progression of Diabetic Retinopathy and Nephropathy in the DCCT and EDIC Participants with Type 1 Diabetes," *Diabetes*, 54, 3103-3111 (2005).

Additional information

Copies of publications, posters and presentations providing additional detail are available at www.veralight.com