

## Noninvasive Type 2 Diabetes Screening More Sensitive Than Standard Tests **CME**

**News Author:** Laurie Barclay, MD  
**CME Author:** Désirée Lie, MD, MEd  
[Disclosures](#)

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May 3, 2007 — Spectroscopic measurement of dermal advanced glycation end products (AGEs) is a more effective and noninvasive technology for prediabetes and diabetes screening compared with fasting plasma glucose and glycosylated hemoglobin (A<sub>1c</sub>) tests, according to the results of a study published in the May issue of *Diabetes Care*.

"This study compared the performance of a novel noninvasive technology to fasting plasma glucose (FPG) and A<sub>1c</sub> tests for detecting undiagnosed diabetes and impaired glucose tolerance," write John D. Maynard, MS, from VeraLight in Albuquerque, New Mexico, and colleagues. "Current screening methods for type 2 diabetes and pre-diabetes are inadequate due to their inconvenience and inaccuracy.... A more accurate and convenient screening method could dramatically improve early detection of type 2 diabetes and its precursors, facilitating interventions that can prevent or at least delay the development of type 2 diabetes and its related micro- and macrovascular complications."

Elevated skin AGEs are biomarkers of diabetes, are highly correlated with the complications of diabetes, and predict future diabetic retinopathy and nephropathy. Individuals with diabetes accumulate skin AGEs faster than do individuals with normal glucose regulation. Until the recent development of novel noninvasive technology to measure AGEs, a punch biopsy was needed to quantify skin AGE levels. Spectroscopic measurement of dermal AGEs (SAGE) measures skin fluorescence caused by AGEs and provides a quantitative diabetes risk score. It does not require fasting, creates no biohazards, automatically compensates for subject-specific skin differences, and provides an immediate result.

This head-to-head evaluation in a naive population of 351 subjects compared results from FPG and A<sub>1c</sub> tests with results from testing with a noninvasive device that detects the fluorescence of skin AGEs.

The positive screening class was defined as subjects with 2-hour oral glucose tolerance test (OGTT) values of 140 mg/dL or greater (n = 84; prevalence, 23.9%). The performances of the noninvasive device, FPG, and A<sub>1c</sub> were evaluated for sensitivity and specificity using the OGTT results as the gold standard.

At the impaired fasting glucose threshold of FPG of 100 mg/dL, sensitivity of FPG was 58% and specificity was 77.4%. At that same specificity, the sensitivity for A<sub>1c</sub> testing was 63.8%, whereas the noninvasive testing sensitivity was 74.7%. The increase in sensitivity of the noninvasive device compared with both blood tests for detecting diabetes and prediabetes was statistically significant ( $P < .05$ ).

"The noninvasive technology showed clinical performance advantages over both FPG and A<sub>1c</sub> testing," the authors write. "The sensitivity differential indicated that the noninvasive device is capable of identifying 28.8% more individuals in the OGTT-defined positive screening class than FPG testing and 17.1% more than A<sub>1c</sub> testing. The combination of higher sensitivity and greater convenience — rapid results with no fasting or blood draws — makes the device well suited for opportunistic screening."

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### Clinical Context

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According to the authors of the current study, 20.6 million individuals in the United States have diabetes and 30% are undiagnosed, with 54 million having prediabetes. Current screening methods using serum testing are inaccurate and require an overnight fast and blood draw. Specifically, according to the authors, FPG has a sensitivity of only 40% to 60%, contributing to late diagnosis of type 2 diabetes. Elevated skin AGEs are biomarkers of diabetes that have been shown to be highly correlated with diabetes complications and predictive of retinopathy and nephropathy, according to the authors, and can be used to screen for diabetes. AGEs can be measured by spectroscopic detection of skin fluorescence to provide a quantitative score, with compensation for individual skin color and pigmentation. Dermal AGEs represent the

integrated damage caused by hyperglycemia, and noninvasive measurement of these biomarkers using spectrometry (SAGE) is a potentially convenient method of screening for diabetes.

This is a study of patients identified by a 2-hour OGTT with abnormal/impaired glucose tolerance and diabetes to compare the sensitivity of SAGE with that of FPG and A<sub>1c</sub> for diabetes screening.

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### Study Highlights

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- 351 participants aged 21 to 86 years from 1 US state who responded to a newspaper advertisement and had at least 1 risk factor for diabetes using American Diabetes Association guidelines were screened using the OGTT.
- Excluded were those with a previous diagnosis of diabetes.
- The OGTT was used as a gold standard against which the SAGE, FPG, and A<sub>1c</sub> performances were judged.
- The threshold for impaired glucose tolerance was a 2-hour OGTT of 140 mg/dL or greater.
- All 3 tests were evaluated at the specificity corresponding to an FPG value of 100 mg/dL or higher for impaired fasting glucose.
- For type 2 diabetes, the threshold was a 2-hour OGTT of 200 mg/dL or greater.
- Subjects were diverse in ethnicity with 20% Caucasian, 28% Hispanic, 35% Native American, and 33% Asian.
- 84 of 351 subjects with abnormal glucose tolerance were identified, with a prevalence of 23.9%.
- Of these subjects, 55 subjects had impaired glucose tolerance and 29 had frank type 2 diabetes.
- Subjects fasted overnight for 8 hours and then had blood drawn for clinical assays.
- The SAGE instrument was used at 2 sessions, once to derive values after the overnight fast and once in a nonfasting state, 1 hour after ingestion of a glucose load.
- For SAGE screening, the subject sat in a chair beside the instrument and rested the forearm in a cradle.
- A fiberoptic probe that coupled input from near-UV and blue-light emitting diodes to the volar forearm collected skin fluorescence and diffuse reflectance measurements.
- The optical radiation emitted from the skin was dispersed in a modified research-grade spectrometer and detected by a charge-coupled device array.
- Subject skin pigmentation was objectively quantified from diffuse reflectance measurements and classified as light and dark.
- The test took only minutes to conduct and results were available immediately.
- The risk for erythema from the SAGE device was negligible.
- The screening performances of FPG, A<sub>1c</sub>, and SAGE were assessed by comparing their respective sensitivities at a relevant clinical threshold.
- The impaired fasting glucose threshold of 100 mg/dL corresponded to an FPG specificity of 77.4%.
- At 77.4% specificity, the FPG sensitivity was 58%, the A<sub>1c</sub> sensitivity was 63.8%, and the SAGE sensitivity was 74.7%.
- The sensitivity differences between SAGE and the FPG and A<sub>1c</sub> tests were statistically significant ( $P < .05$ ).
- The absolute sensitivity advantage of the SAGE screen vs FPG and A<sub>1c</sub> were 16.7 and 10.9 percentage points, respectively.
- The SAGE identified 28.8% more individuals with OGTT-defined positive screening than FPG and 17.1% more than A<sub>1c</sub> testing.
- For subjects with light skin, sensitivity for detecting abnormal glucose tolerance was 70.1%; for subjects with dark skin it was 82.1%.
- SAGE sensitivity was not impaired by intersubject skin variations.
- SAGE performance was independent of ambient blood glucose level.
- The authors concluded that the combination of higher sensitivity and greater convenience (rapid results) of the SAGE technique make it an alternative for diabetes screening in clinical practice.

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### Pearls for Practice

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- The SAGE technique is a noninvasive measure of skin fluorescence to detect glycation end products associated with diabetes risk.
- The sensitivity of the SAGE technique is higher than that of FPG and A<sub>1c</sub> for detection of type 2 diabetes and impaired glucose tolerance.