Development of Noninvasive Technology for Type 2 Diabetes Screening

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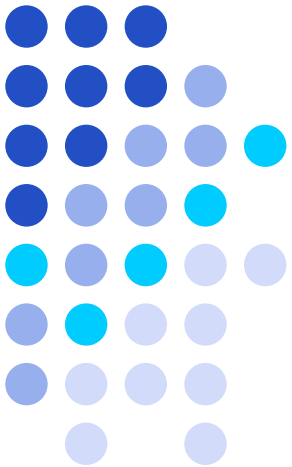
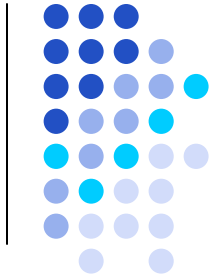
International Diabetes Federation
19th World Diabetes Congress
December 7, 2006

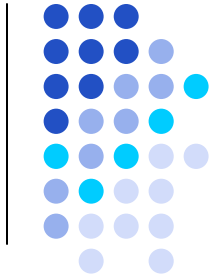


Motivation



- Crushing problem
  - WHO estimates 221 million worldwide diabetes cases by 2010
- Diabetes complications are preventable
- Current screening methods are inadequate
  - Inconvenient: requires fasting and blood draw
  - Inaccurate: fasting plasma glucose sensitivity is poor
  - Therefore, patients often present with one or more complications at diagnosis

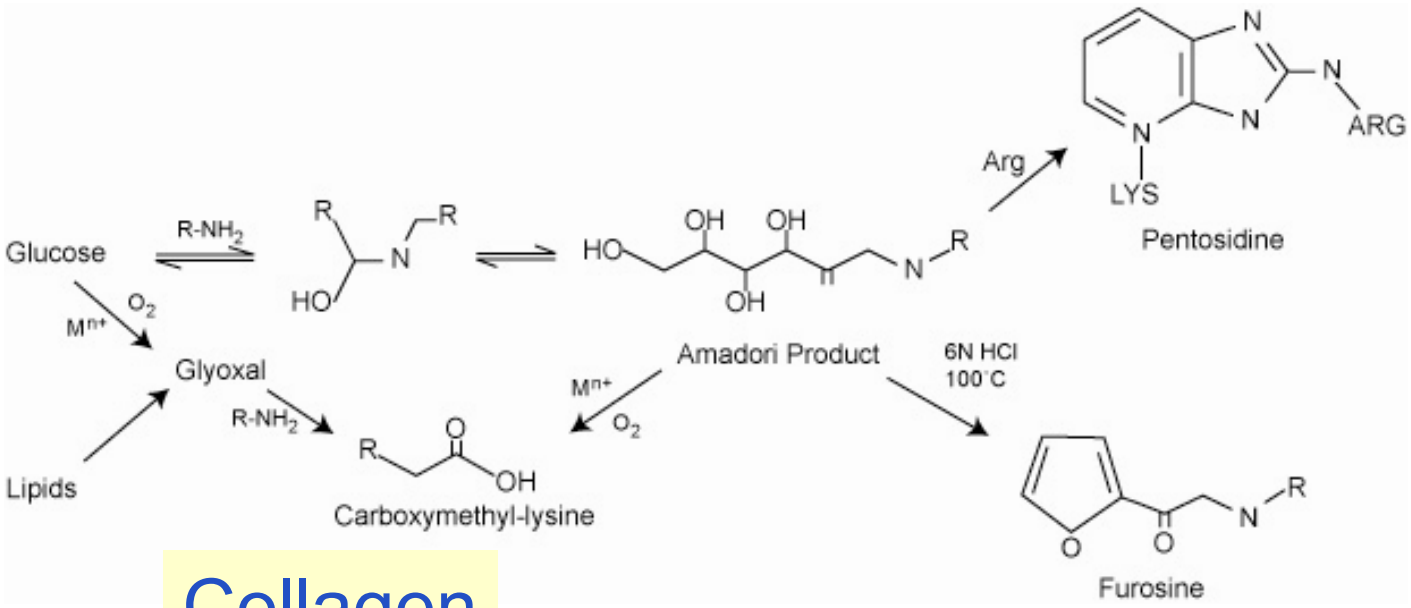
A new approach



- Skin Advanced Glycation Endproducts (AGEs)
  - Known biomarkers for diabetes (DCCT[1] and EDIC[2])
  - Better predictor of future complications than HbA1c[2]
  - Sensitive summary metric of integrated glycemic exposure
- Noninvasive measurement
  - Dermal fluorescence: well correlated to skin AGE levels[3]
  - Rapid results: ~1 minute
  - No fasting: test anytime
  - No biohazards: no blood draws
  - Enables point-of-service testing

[1] *DCCT Skin Collagen Ancillary Study Group, Diabetes* ***48****: 870-880 (1999)*
[2] *Genuth et al., Diabetes,* ***54****, 3103-3111 (2005)*
[3] *Mulder et al., Diabetes Technology & Therapeutics,* ***8****, 523-535 (2006)*

AGEs: the Maillard reaction



Collagen

+

Glucose

Time

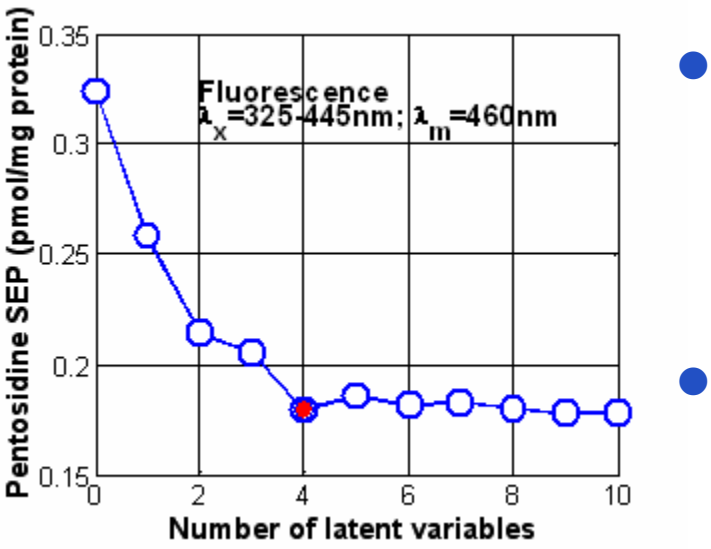
+

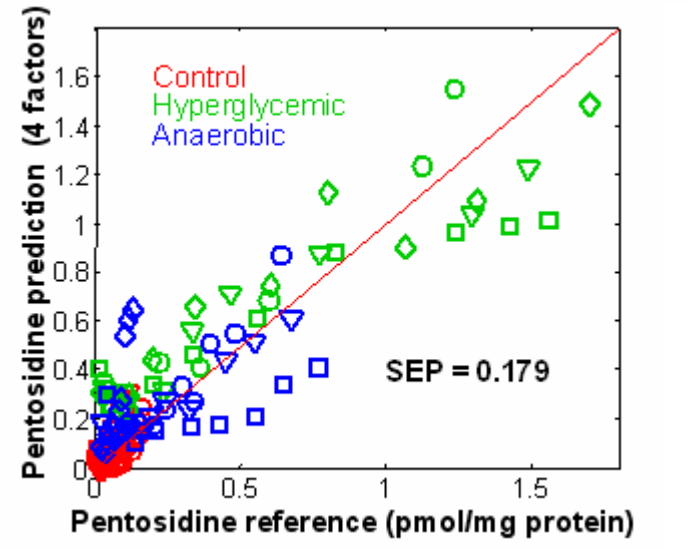
Glucose

$\propto$

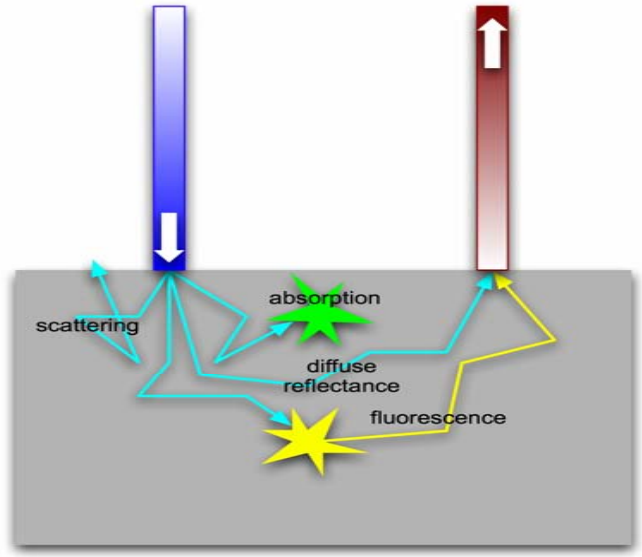
Skin AGEs

Source of Signal: Dermal Fluoresence

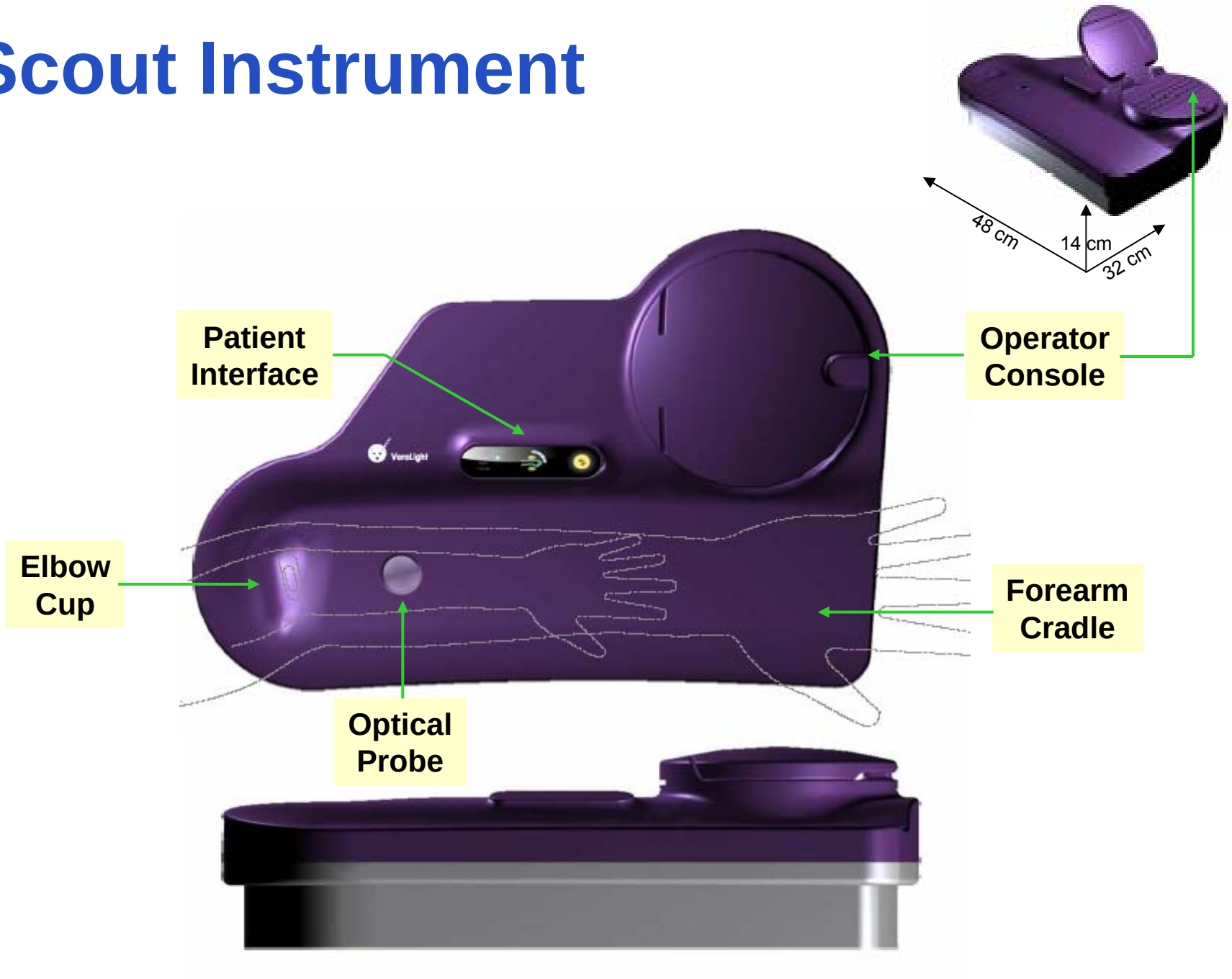




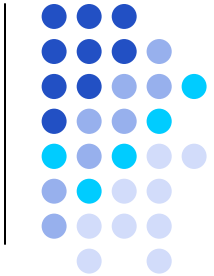
- In vitro studies demonstrated noninvasive fluorescence spectroscopy can quantify dermal AGEs (left)
- Fiber optic probe designed to collect fluorescence of dermal AGEs and cross-links (below)



Scout Instrument

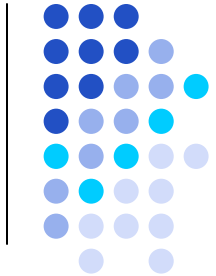


Experimental design



- Head-to-head evaluation of noninvasive skin measurement against *Fasting Plasma Glucose* (FPG) and *HbA1c* tests
- Two hour *Oral Glucose Tolerance* (OGT) test used to adjudicate truth
- Naïve population
  - Selection criteria were 1+ risk factors for diabetes
  - Individuals with previous type 2 diagnosis excluded
  - Ethnic/racial composition reflects local demographics

Study demographics

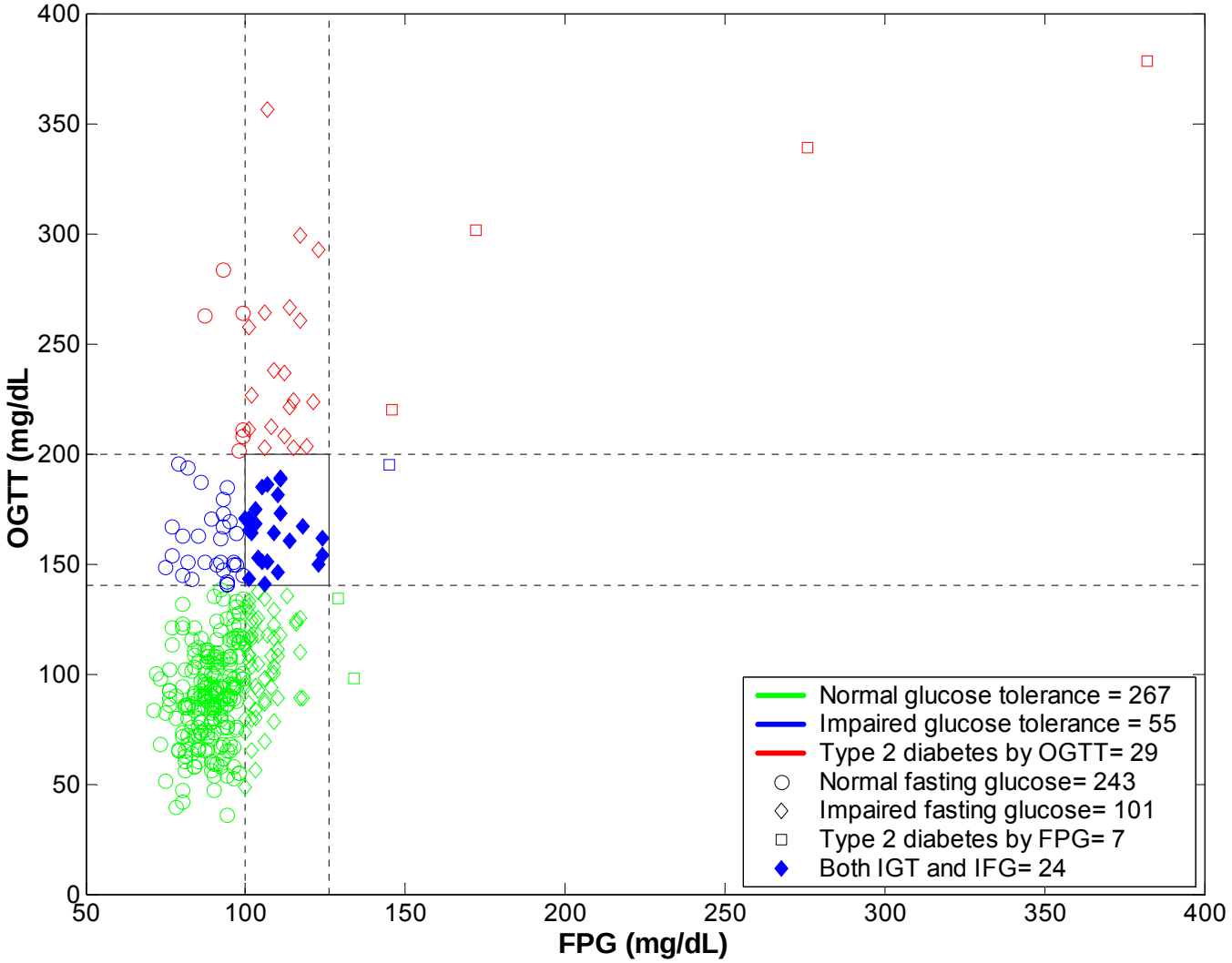


N = 351					
Age		**Gender**		**Race/Ethnicity**	
21-30	4.8%	Male	36.5%	Caucasian	53.3%
31-40	14.8%	Female	63.5%	Hispanic	36.5%
41-50	28.2%			African Am	3.1%
51-60	25.1%			Native Am	4.8%
61-70	18.5%			Asian	0.9%
71-80	6.3%			East Indian	0.3%
81+	2.3%			Other	1.1%

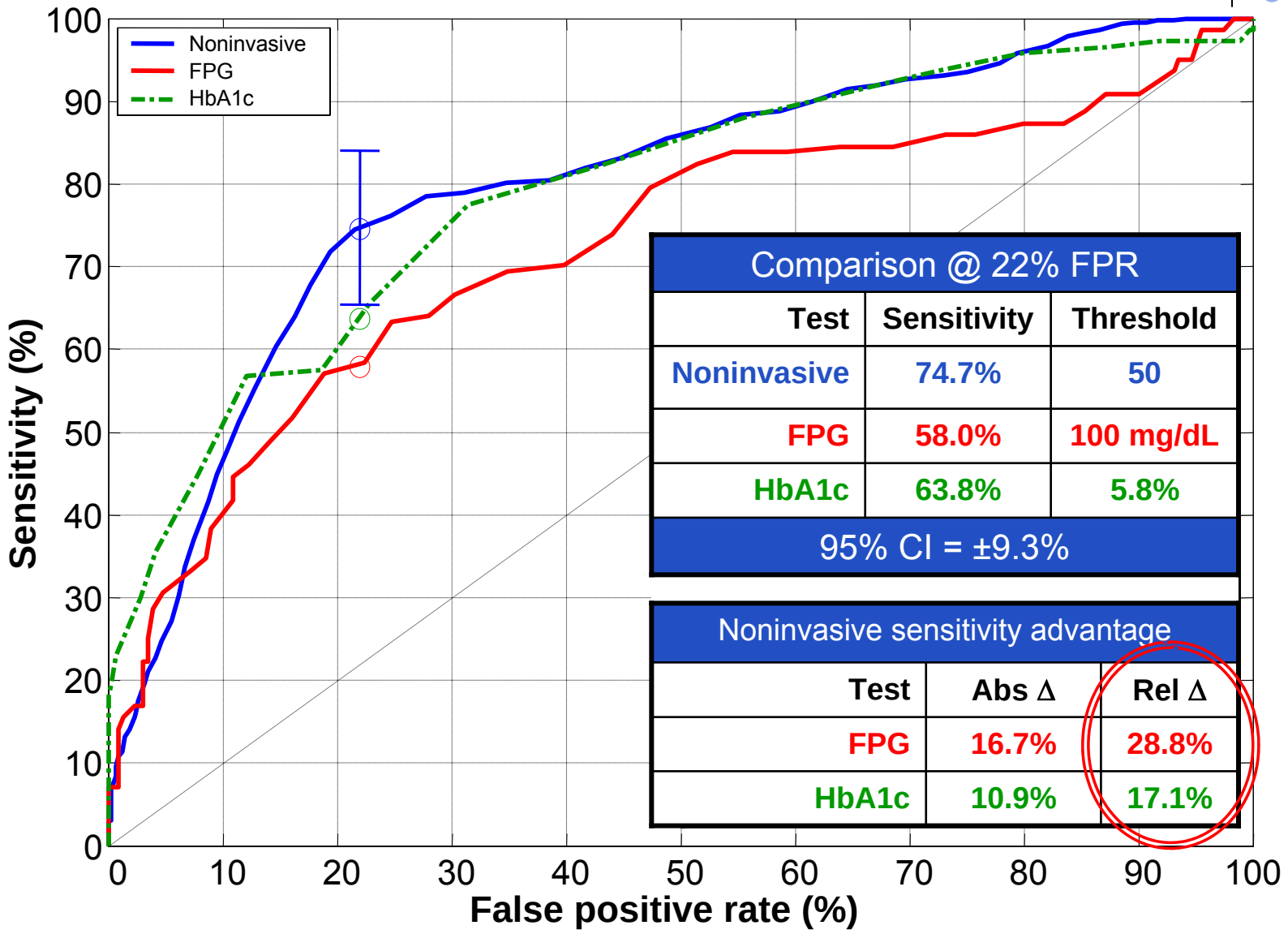
Methods

- Positive screening class
  - 2 hour OGT ≥ 140 mg/dL
  - *Abnormal Glucose Tolerance*
- Noninvasive measurement
  - Illuminate volar forearm with harmless near-UV and blue light
  - Collect dermal fluorescence
  - Multivariate algorithm generates diabetes risk score (0 to 100) for each subject

OGT vs FPG


OGTT (mg/dL)
FPG (mg/dL)
0
50
100
150
200
250
300
350
400
50
100
150
200
250
300
350
400
Normal glucose tolerance = 267
Impaired glucose tolerance = 55
Type 2 diabetes by OGTT= 29
Normal fasting glucose= 243
Impaired fasting glucose= 101
Type 2 diabetes by FPG= 7
Both IGT and IFG= 24

Results – Detecting Abnormal Glucose Tolerance

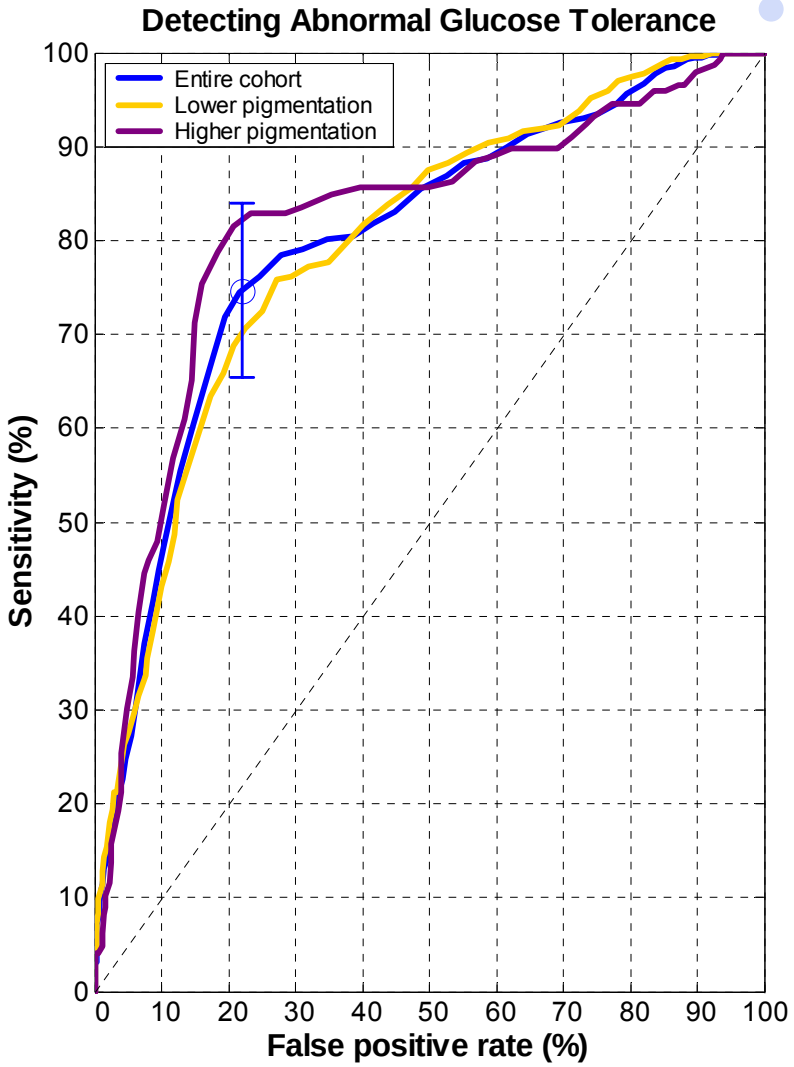


Comparison @ 22% FPR		
Test	Sensitivity	Threshold
Noninvasive	74.7%	50
FPG	58.0%	100 mg/dL
HbA1c	63.8%	5.8%
95% CI = ±9.3%		

Noninvasive sensitivity advantage		
Test	Abs Δ	Rel Δ
FPG	16.7%	28.8%
HbA1c	10.9%	17.1%

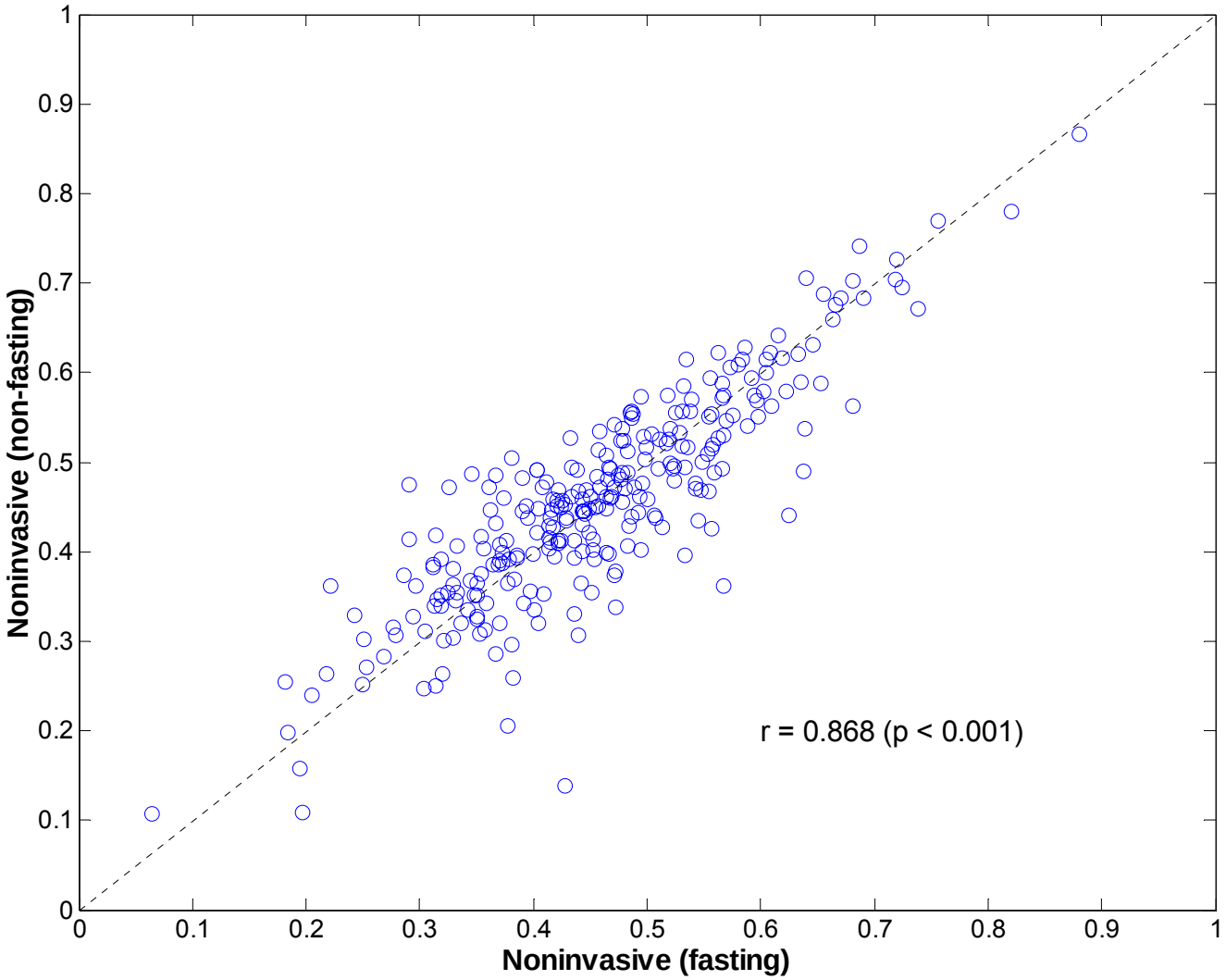
Results – Impact of skin color

- Algorithm based on skin reflectance compensates for individual skin optics[1]
- Assess impact of skin pigmentation on measurement sensitivity
  - Cohort sub-divided by skin reflectance model
  - Compare sub-cohort detection performance

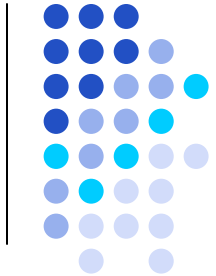


[1] Hull et al., Opt. Express, **12**, 4496-4510 (2004)

Results – noninvasive reproducibility



Conclusions



- Noninvasive measurement significantly out-performs conventional blood tests
  - Sensitivity differences are statistically significant
  - Detects ~30% more undiagnosed abnormal glucose tolerance than FPG
- Facilitates point-of-service testing
  - No fasting: test anytime
  - No biohazards or blood draws
  - Rapid results: ~1 minute
- Superior tool for early detection of type 2 and pre-diabetes