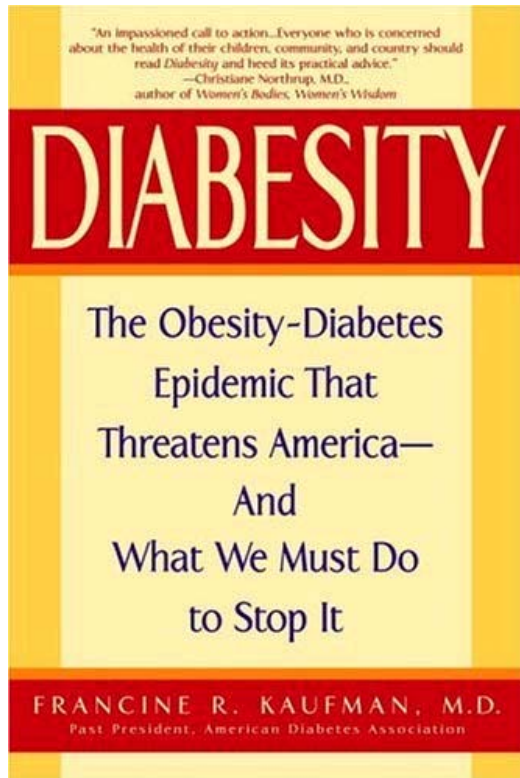




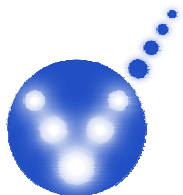
# Detecting Type 2 Diabetes With Noninvasive Skin Fluorescence Spectroscopy

Fifth Annual Diabetes Technology Meeting  
November 11, 2005

# Diabetes is a Huge and Growing Problem

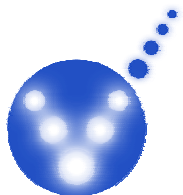
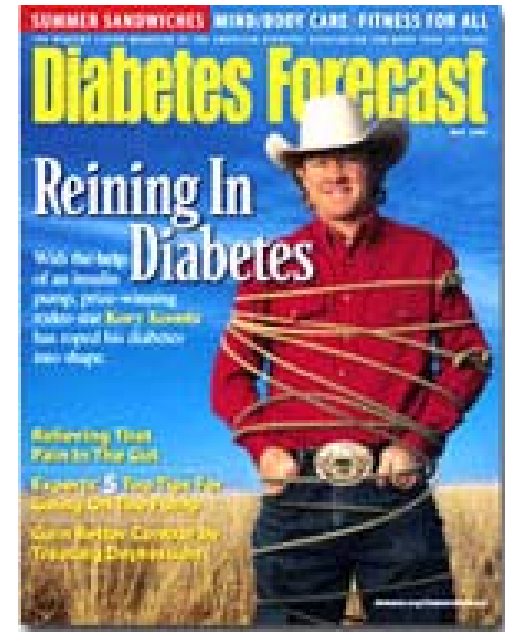


- A world-wide health problem affecting over 194 million people and expected to grow to over 333 million by 2025
- In the US, 20.8 million with diabetes and 41 million with pre-diabetes
- 2002 US direct and indirect costs of all diabetes exceeded \$132 billion
- One in three babies born in US today are projected to develop diabetes



# Good News in the War on Type 2 Diabetes

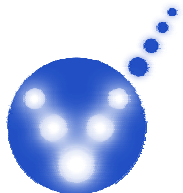
- Diabetes Prevention Program (DPP) and other studies have shown that lifestyle changes and/or medications can delay or prevent the progression to type 2 diabetes
- The United Kingdom Prospective Diabetes Study (UKPDS) showed that intensive glycemic control can reduce the risk of developing type 2 diabetes related complications
- The first step to any treatment or intervention is screening and diagnosis



# Current Screening Methods are Inadequate

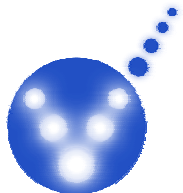
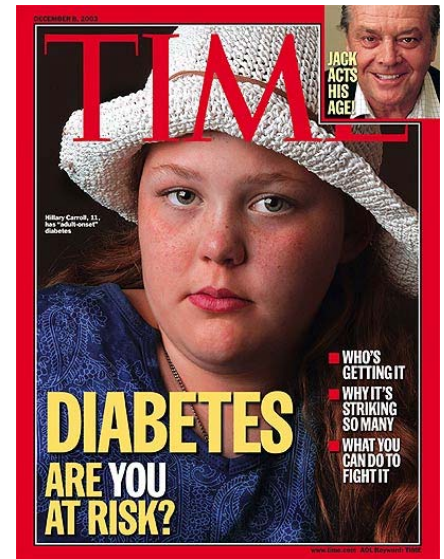


- The rarely used ‘gold standard’ for screening is the two hour oral glucose tolerance test (OGTT)
  - Very inconvenient
  - Poor reproducibility (CV ~17%)
- The fasting plasma glucose (FPG) is the most widely used screening test
  - Requires an overnight fast and a trip to a reference lab
  - It has a sensitivity of ~50%, i.e. ***it misses 1 out of every 2 patients with undiagnosed diabetes***
- Neither test has the convenience and accuracy needed for effective, point-of-service screening



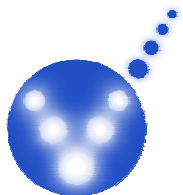
# As a Result...

- In the US, 6.2 million persons with diabetes are undiagnosed and untreated
  - a 24% increase since 2002
- Type 2 diabetes diagnosis usually occurs 5 to 10 years after onset
  - Half of all patients with newly diagnosed diabetes already have one or more complications
- Most patients with pre-diabetes are undiagnosed and untreated
  - Some patients with IGT develop early stage retinopathy and atherosclerosis



# The Scout Solution for Screening

- Noninvasive detection of type 2 diabetes and pre-diabetes based upon skin fluorescence
- 60 second measurement on underside of forearm
- No biohazards, minimal operator training
- No fasting – test anytime
- Enables point-of-service testing

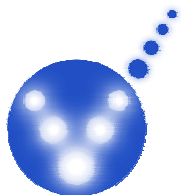


# Scout Measures Advanced Glycation Endproducts

- Elevated skin advanced glycation endproducts (AGEs) are a biomarker of diabetes and predictive of future diabetic retinopathy and nephropathy\*
- Persons with pre-diabetes and diabetes accumulate skin AGEs faster than individuals without diabetes
- Previously measured via punch biopsy
- Skin AGEs represent a metric for the integrated glycemic exposure
- A sensitive marker for improved diabetes screening



- 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)

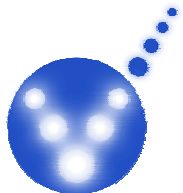


# Scout Development Progression

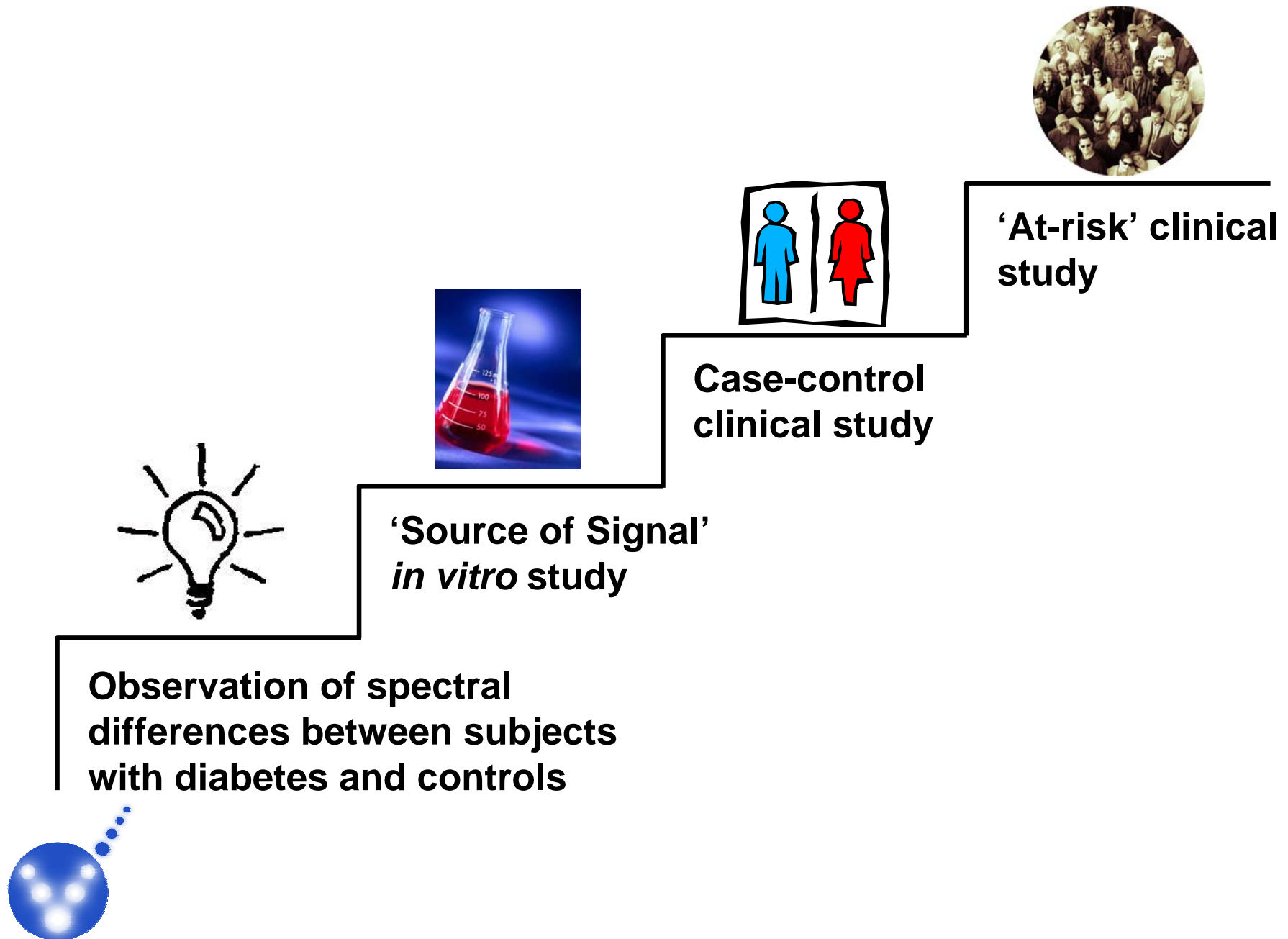
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**Observation of spectral  
differences between subjects  
with diabetes and controls**



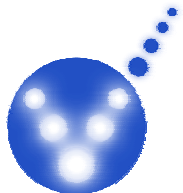
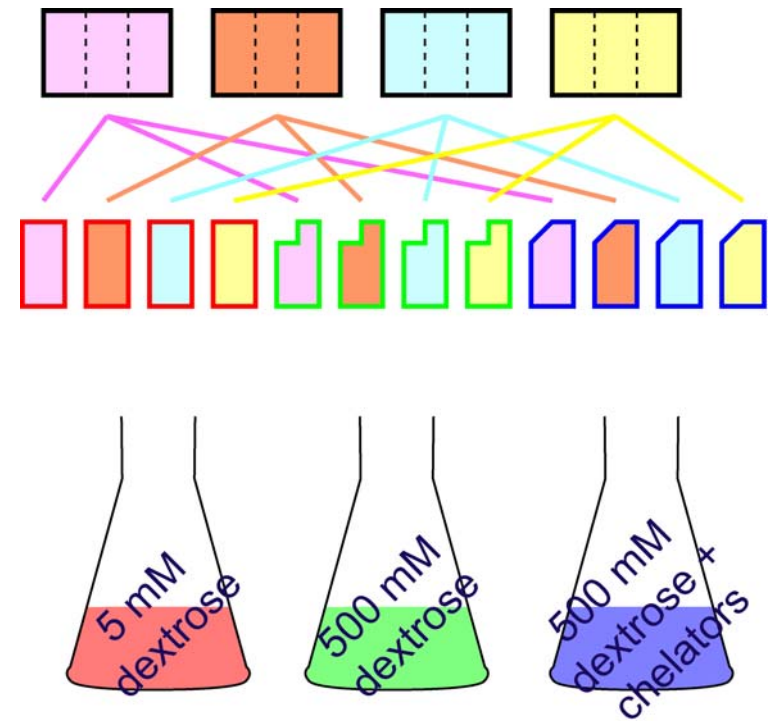
# Scout Development Progression



# An *In Vitro* Study: Source of the Signal



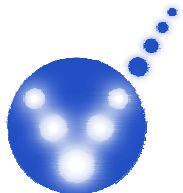
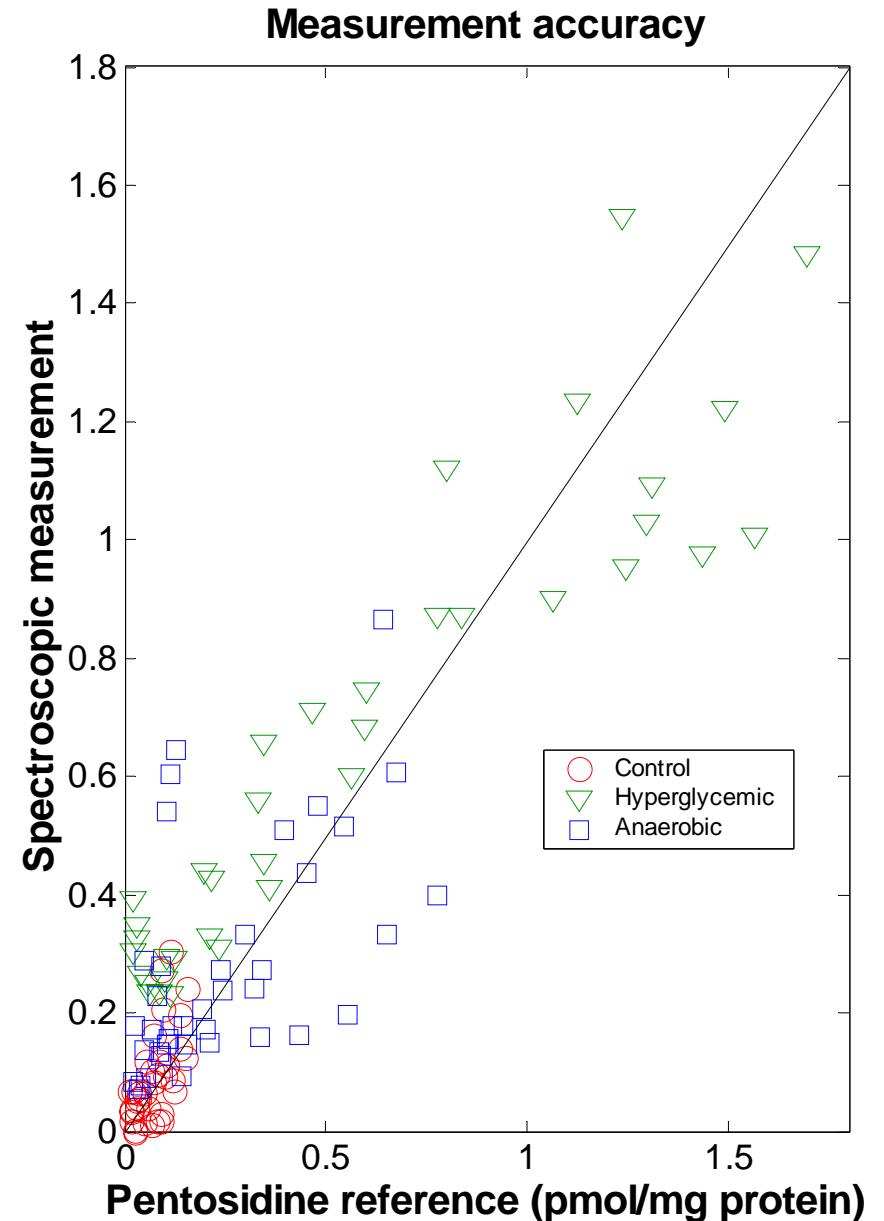
- *In vitro* study designed to test hypothesis that AGEs are the source of the spectral signal
- Freshly-harvested porcine dermis
- Specimens subdivided and placed into 1 of 3 incubation media:
  - Normoglycemic
  - Hyperglycemic
  - Hyperglycemic, anaerobic
- 5 week duration



# In Vitro Study: Outcomes



- *In vitro* tissue fluorescence driven by AGE accumulation
- Spectroscopy can quantify glycemic damage to collagen\*
  - SEP = 0.18 pmol/mg
  - $R^2 = 0.79$
  - Reference assay CV of 22%

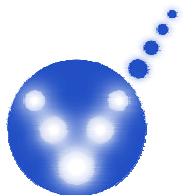
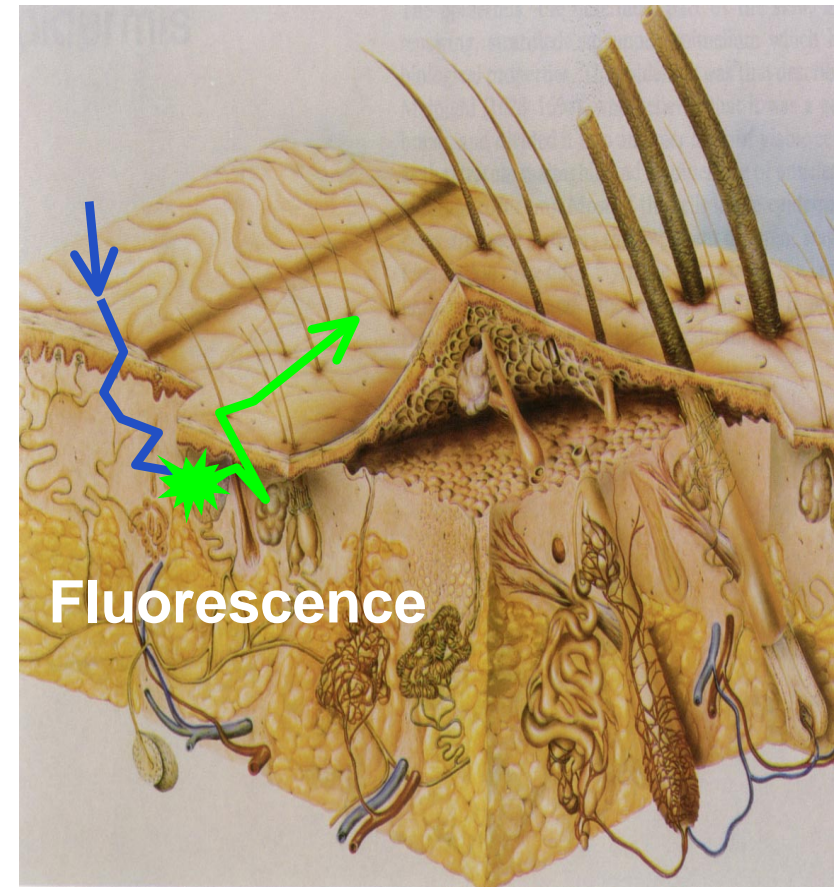


\* Hull et al., "Noninvasive, optical detection of diabetes: model studies with porcine skin," *Optics Express*, 12(19), 4496-4510 (2004).

# Challenges for *In Vivo* Optical Measurement



- Pigment, blood and scattering distort true dermal fluorescence
- Tissue heterogeneity will impact measurement accuracy
- Scout incorporates a custom optical probe and correction algorithms to minimize these effects

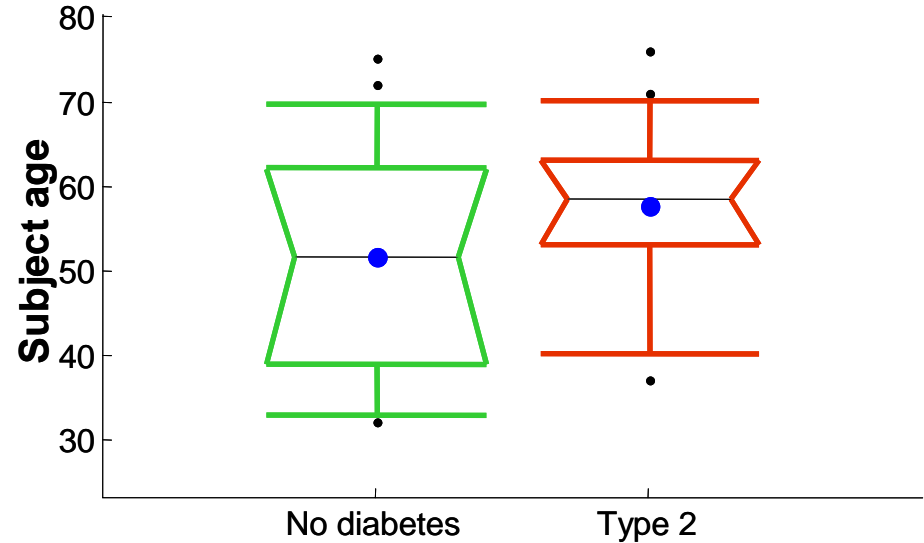


# Scout vs. FPG: Case-Control Study

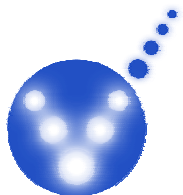
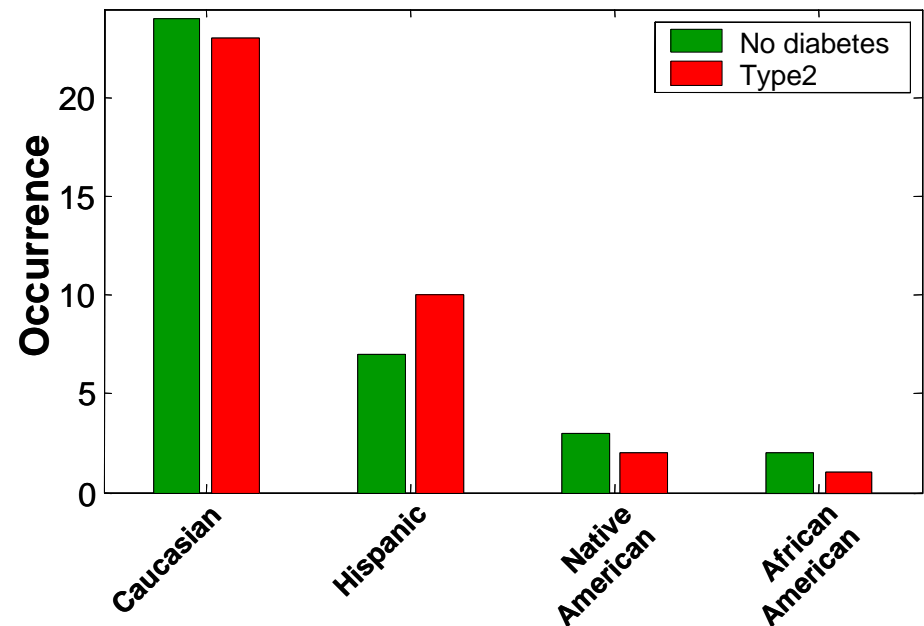


- 72 subjects: 36 subjects with type 2 diabetes and 36 controls
- Attempted to match cohort for age, ethnicity and gender
- Evaluate new probe and correction algorithm
- Compare Scout classification with FPG

Distribution of ages



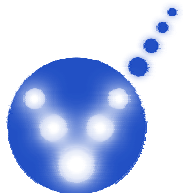
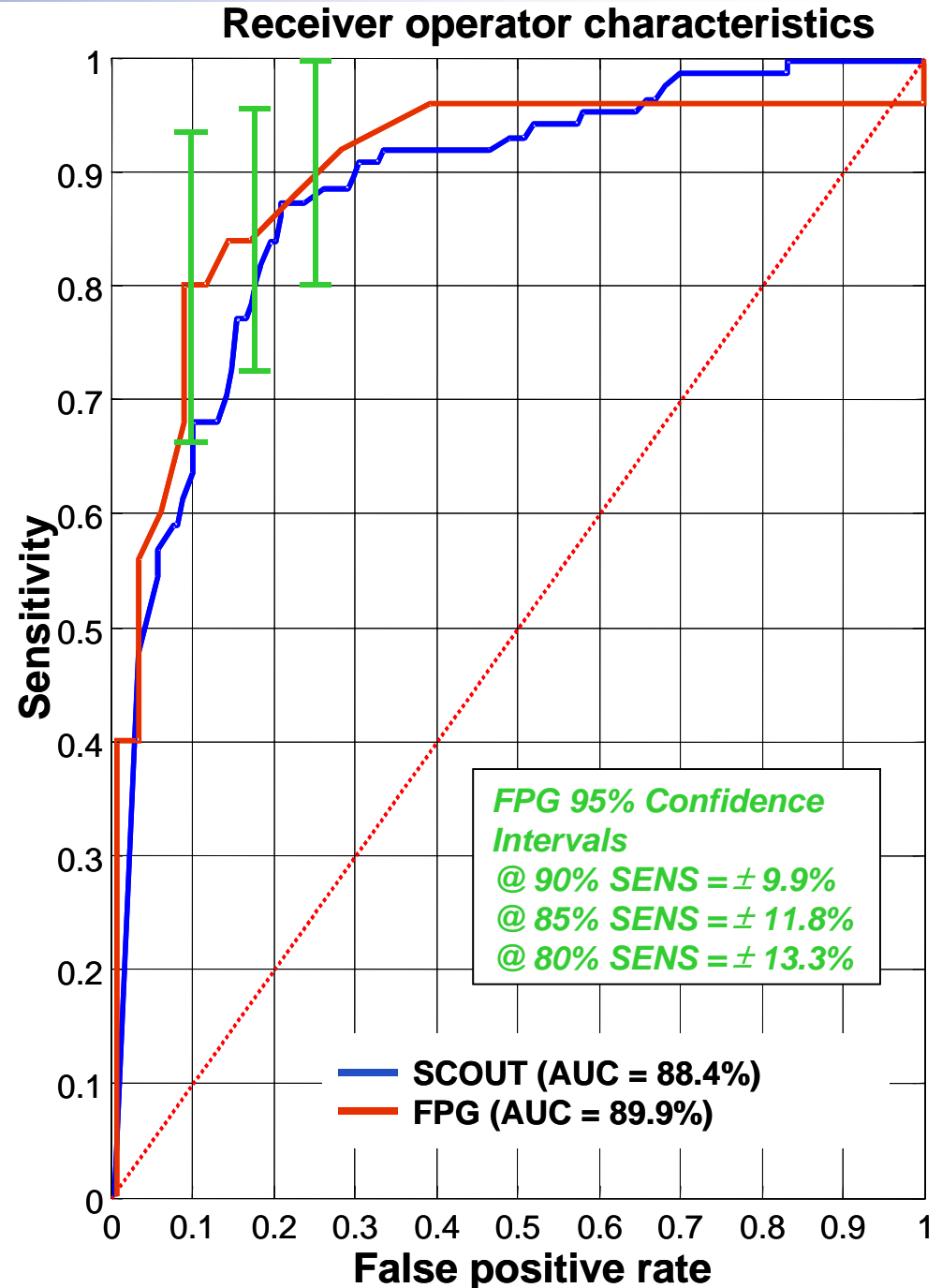
Distribution of ethnicities



# Case Control Study: Outcomes



- In case-control, Scout comparable to FPG
- Instrument performance objectives were defined as it relates to
  - Signal/noise
  - Spectral resolution
  - Spectral regions





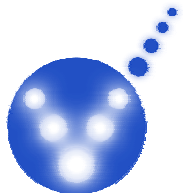
# Next step – an ‘at risk’ study

- New instrument design with improved signal/noise
- Assess performance in ‘at risk’ subjects
  - ADA criteria used to define ‘at risk’
- Test pivotal clinical trial design
  - Single site
  - Head-to-head with FPG
  - OGTT adjudication of positives and random sampling of negatives
  - 700 subjects



Scout

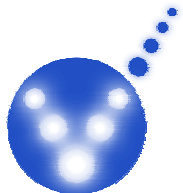
		—	+
FPG	—	—	+
	+	—	+



# A New Tool in the War on Diabetes

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- Scout is an innovative noninvasive device that will address the need for effective, point-of-service screening
- Next steps
  - Complete clinical study of ‘at-risk’ cohort
  - Develop and test clinical prototypes
  - Implement multi-center, pivotal trial



# Acknowledgements

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