

**Performance Characteristics & Evaluation of an
Immunochemical, Automated Developed
& Quantitative
Fecal Occult Blood Screening Test**

P. Rozen

**Gastroenterology Dept.
Rabin Medical Center,
Professor (Emeritus) of Medicine
Tel Aviv University**

**Chairman of OMED
(World Organization for Digestive Endoscopy)
Colorectal Cancer Screening Committee**

Background

- Standard guaiac FOB CRC screening tests (G-FOBT) are faulted for **low** sensitivity & specificity due to:
 - non-specificity for human Hb
 - non-standardized development
- Immunochemical, automated-developed & quantitative human Hb FOBT (I-FOBT):
 - eliminates diet restrictions
 - allows selection of a Hb level for colonoscopy

OC Sensor Evaluation: Aims

1. Evaluate test characteristics:
 - FOB measurement **reproducibility**
 - effects of FOB sample **storage** in a hot climate:
 - in refrigeration (4°C)
 - at 20°C temperature
 - at ambient room temperature (30°C)
 - number of samples needed to best identify neoplasia (3 days, 2 days, 1 day collections).
2. Determine true **sensitivity** & **specificity** by evaluating OC-Sensor against colonoscopy.
3. Determine what **level of FOB** detected will provide best sensitivity & specificity for our medical services.

I-FOBT OC-Sensor

(Eiken)

(Latex Agglutination Test
Human Hb AO Antibodies)

*Courtesy of
ALFA WASSERMANN,
Milan, Italy*

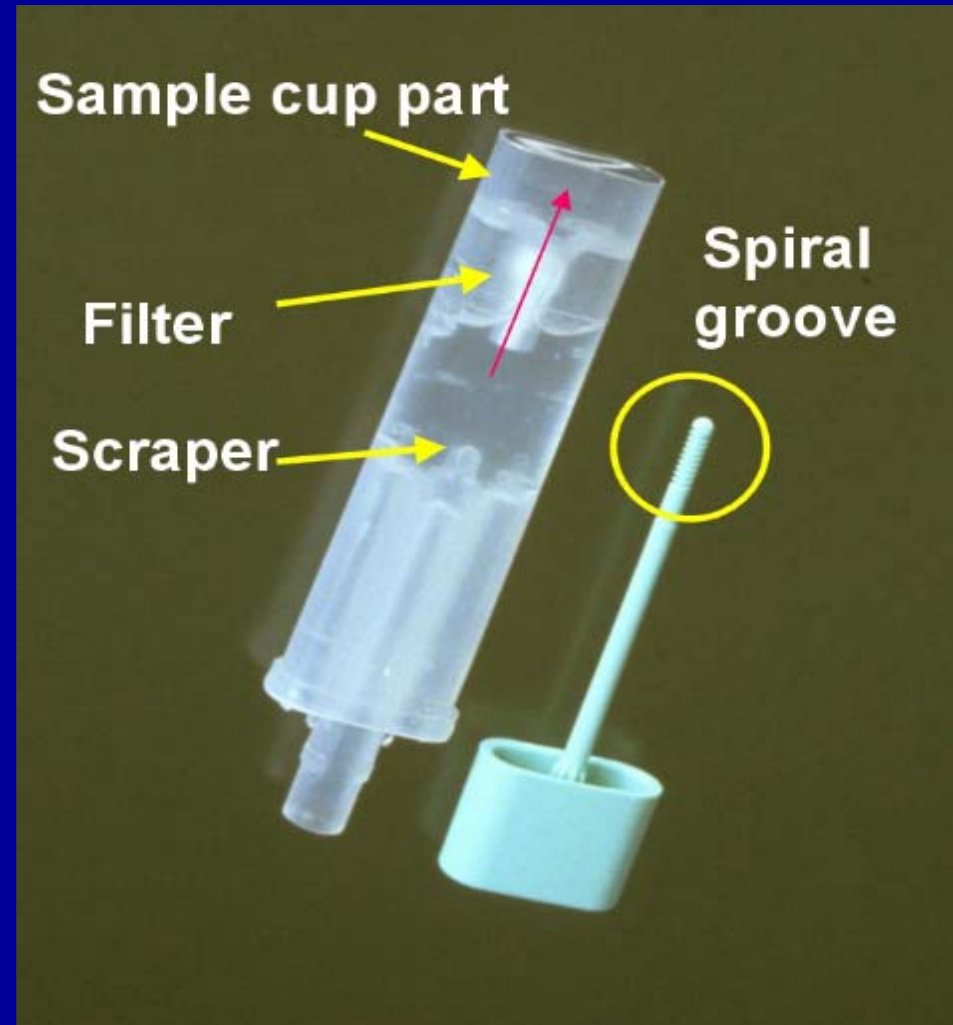
- Photometric quantitative determination of Hb
- Completely automated

Bar code labels
on collection tubes.



OC-Sensor: Stool sampling

- Feces collected at home, using the collecting stick.
- 10 mg of feces attach on to stick
- Stick reinserted into tube, pushed thru a scraper & membrane
- Feces then dissolved in 2 ml buffer & stable ~21d at 4°C



OC-Sensor

Automated development & Hb quantified (1)

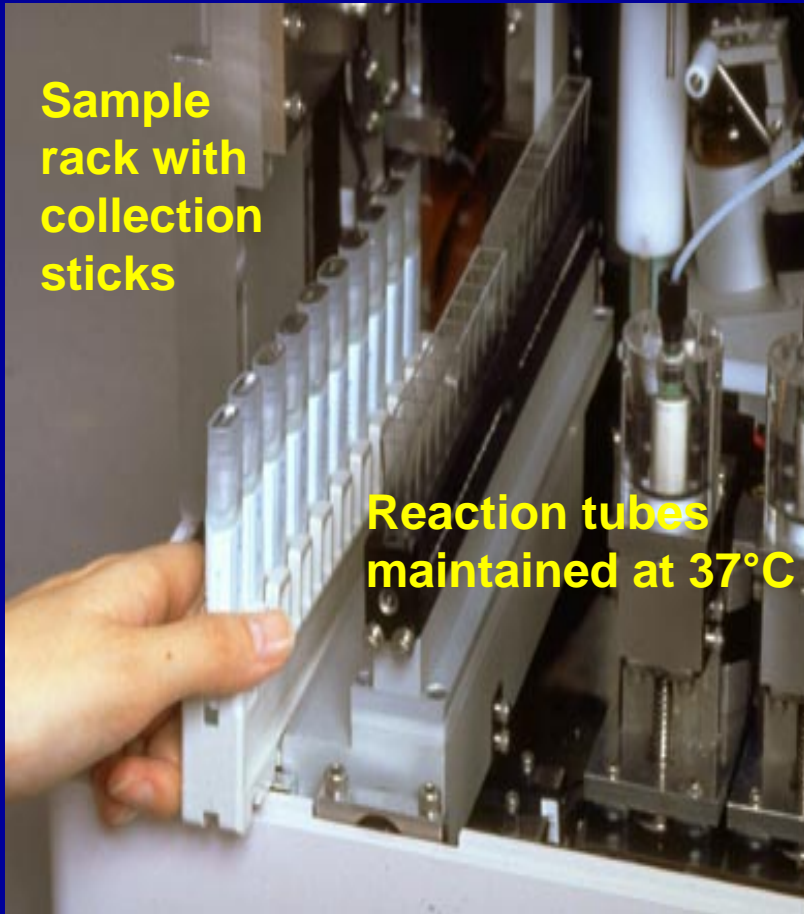


- Bar code labels are on collection tubes.
- Tubes loaded in sample rack
- Sample rack has an identification read-out

*Courtesy of ALFA WASSERMANN,
Milan, Italy*

OC-Sensor

Automated development & Hb quantified (2)



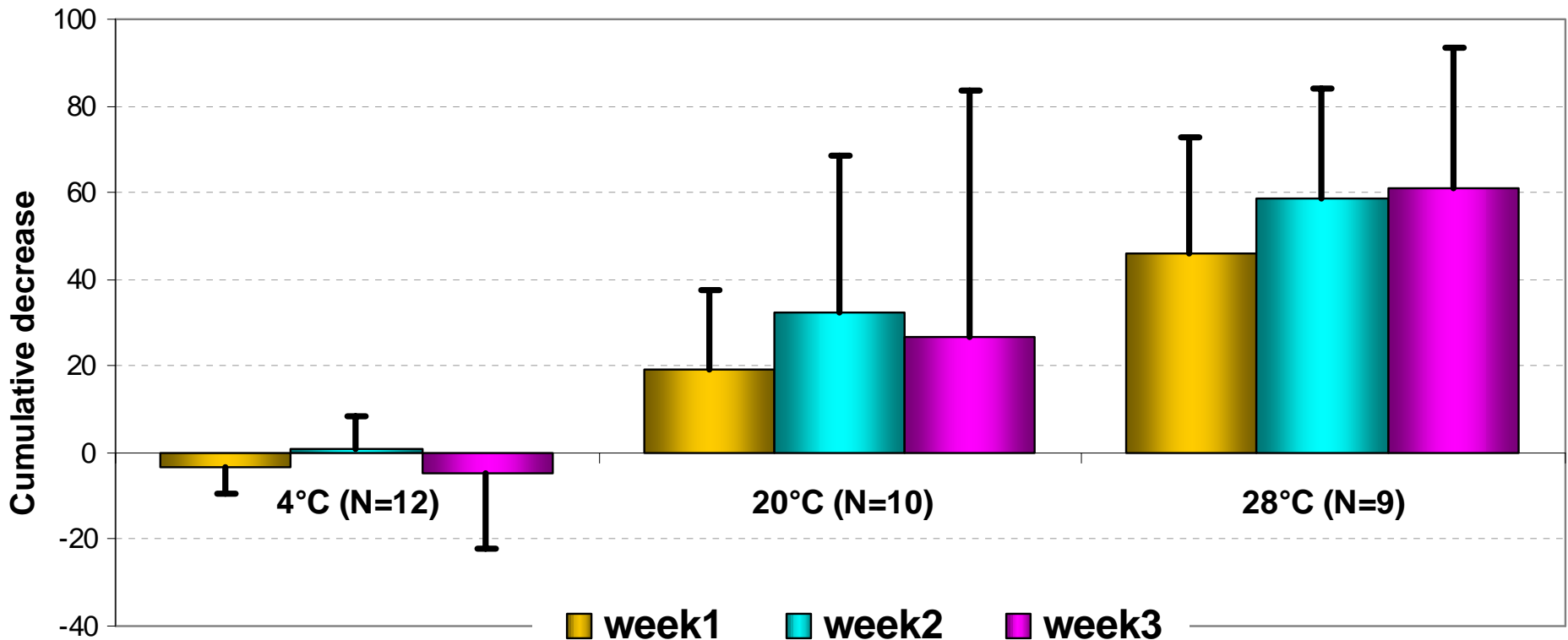
- Collection tubes automatically punctured, 1 drop extracted & dripped into reaction tube.
- Latex-Ab particles & buffer mixed.
- Flocculation measured by LED & Hb concentration calculated.
- Range 50-2000 ng Hb/ml = 10-400 μ g Hb/g feces.
- 50 specimens/hr.
- Print-out:Hb measurements, ID numbers, error messages.

*Courtesy of ALFA WASSERMANN,
Milan, Italy*

Test Characteristics

- **Reproducibility:**
5 I-FOBTs re-examined 5x in 1 day showed no significant differences in measurements.
- Effects of **duration of storage & temperature** on 30 tests stored >21days:
 - at 4°C, decay/day of $0.3\% \pm 0.4$ (NS)
 - at 20°C, decay/day of $2.2\% \pm 1.7$ (NS)
 - at 28°C, decay/day of $3.7\% \pm 1.8$
($P < 0.05$)

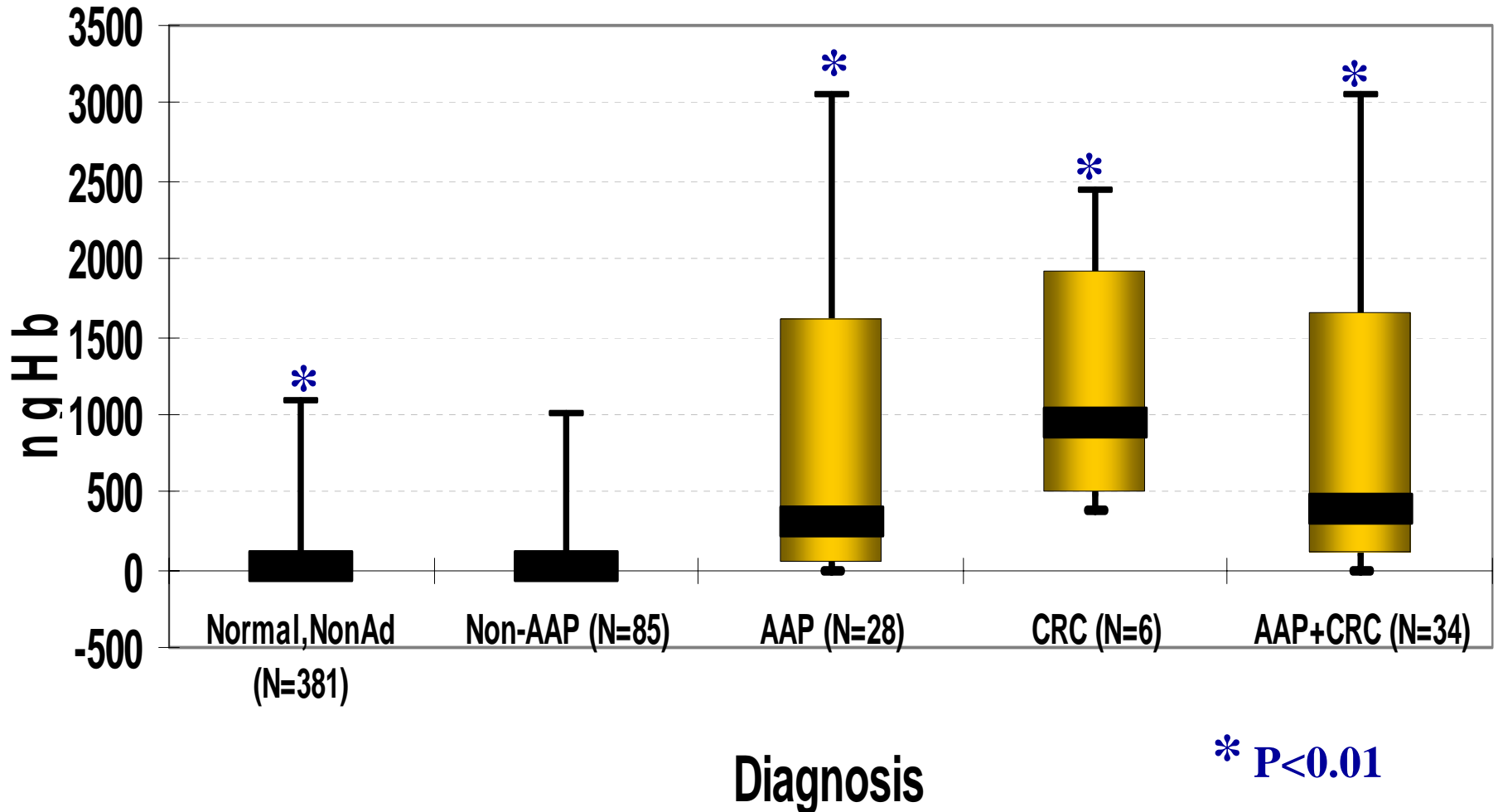
Effects of Storage Duration & Temperature: Cumulative % Decrease in FOBT Hb of Lowest Weekly Measurements from Initial Values (means \pm SD, $P < 0.05$ at 28°C)



OC Sensor Results by Diagnosis

(N=500 high-risk colonoscopies)

Maximum of 3 FOBTs, ngHb/ml



Sensitivity & Specificity for Colorectal Neoplasia (N=500)

Fecal Hb/ml	Cancer	Advanced adenomas	Cancer & advanced adenomas	
			Sensitivity	Specificity
50ng	6/6	21/28	79.4%	89.7%
100ng	6/6	20/28	76.5%	95.3%
200ng	6/6	16/28	64.7%	96.3%

Sensitivity & Specificity for Colorectal Neoplasia (N=500)

Fecal
Hb/ml

Cancer &
advanced adenomas (34)

Sensitivity

Specificity

PPV

NPV

50ng

79.4%

89.7%

36.0

98.3

100ng

76.5%

95.3%

54.2

98.2

200ng

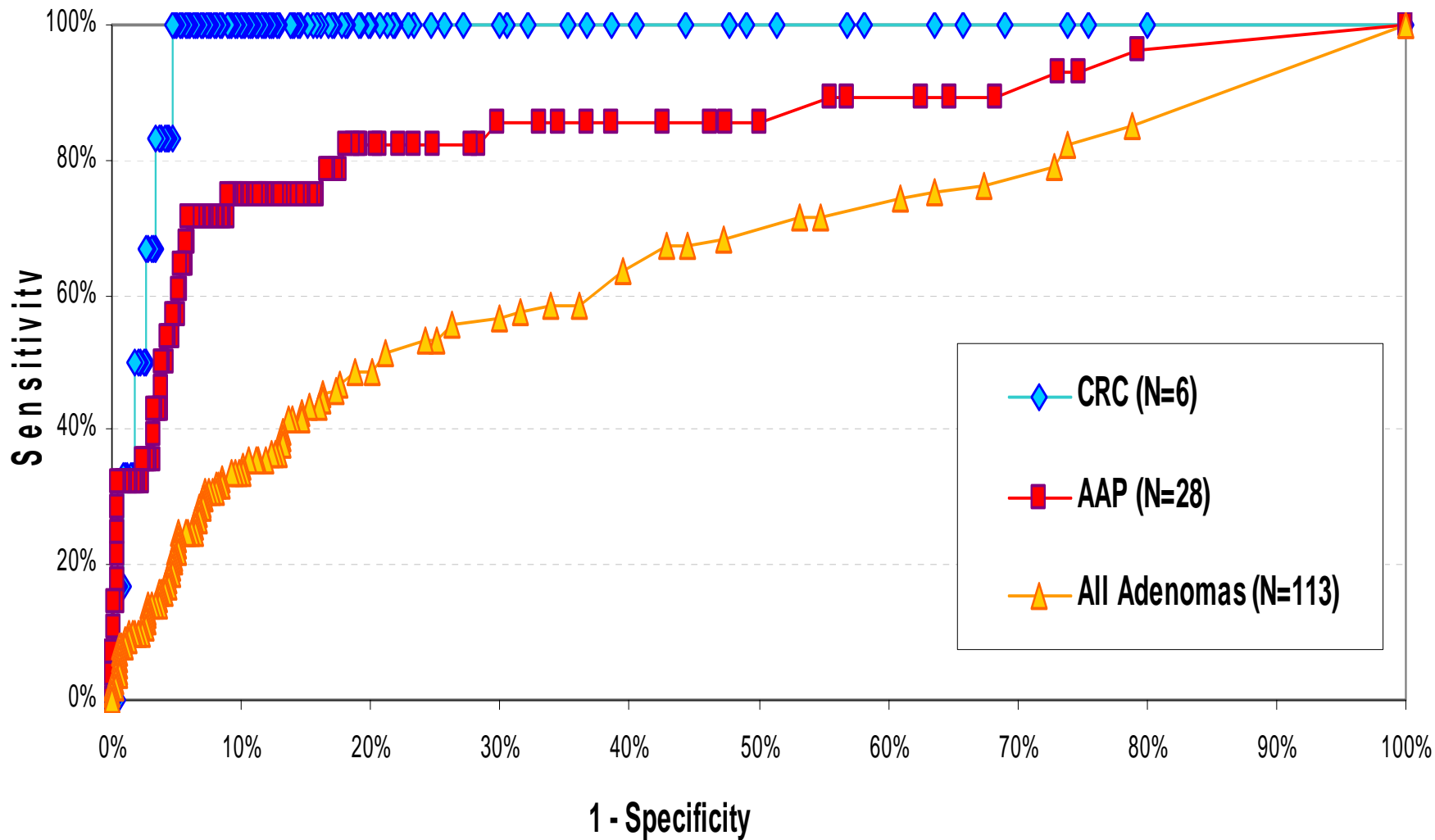
64.7%

96.3%

56.4

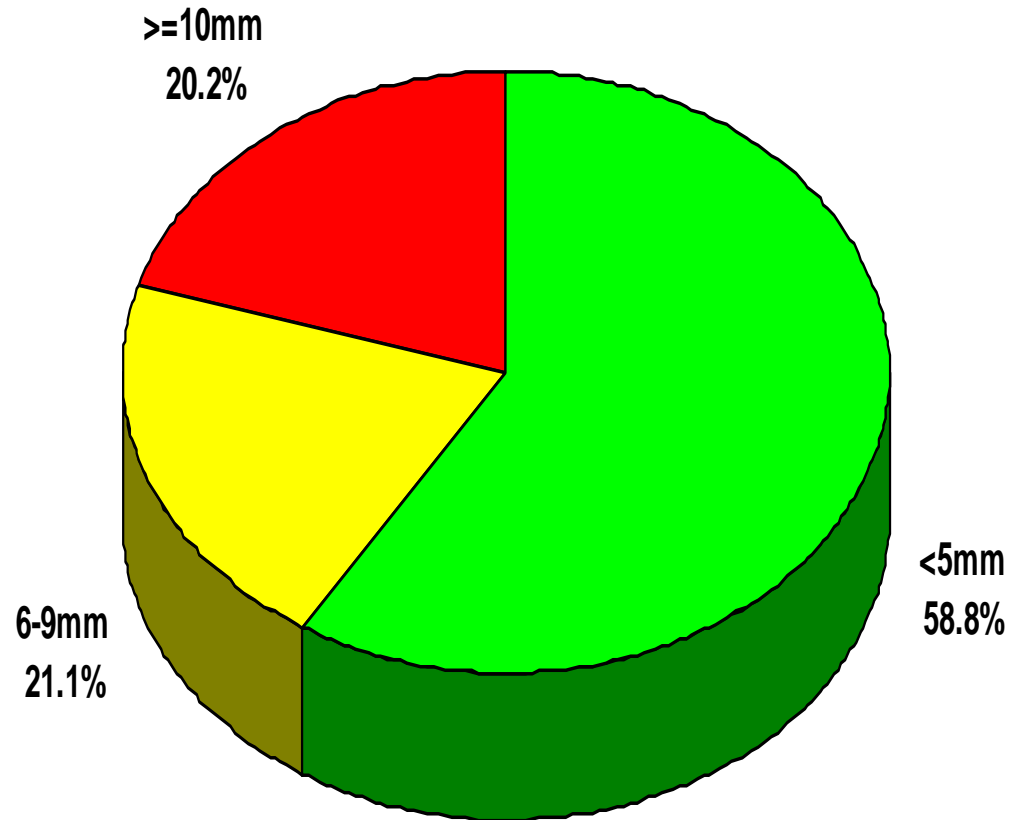
97.4

ROC Curves: Analysis for OC Sensor (100ngHb/ml)



Polyps Detected in OC Sensor Study (N=500 high-risk colonoscopies)

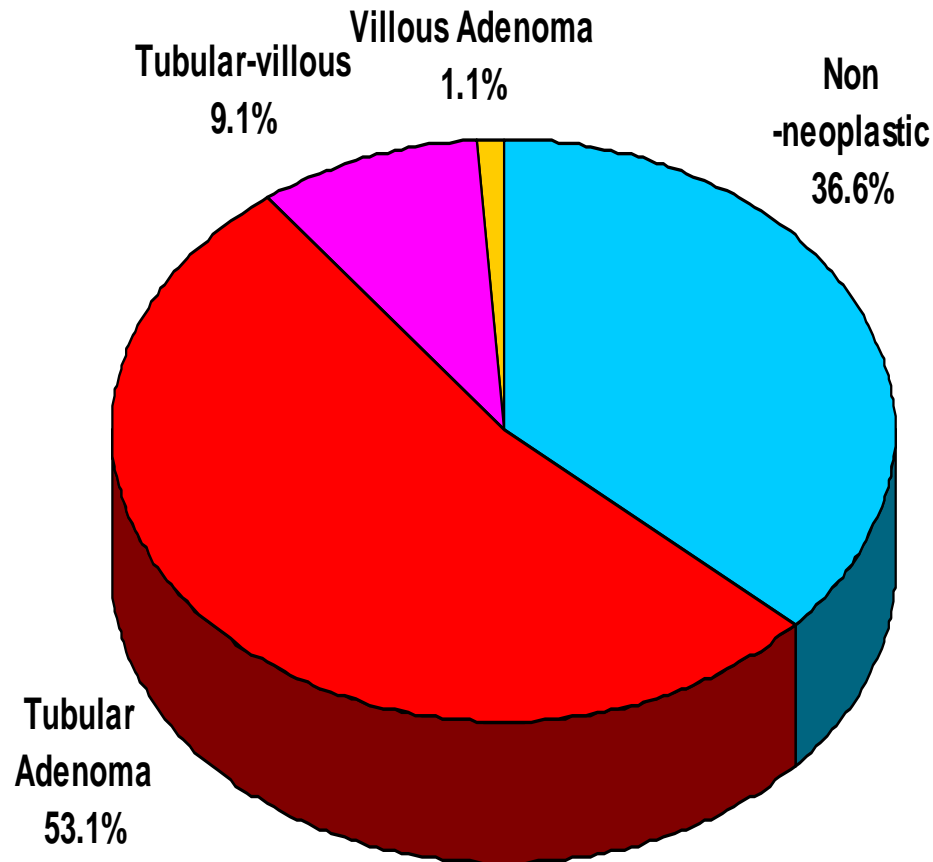
Polyp size (largest), N=114



Polyps Detected in OC Sensor Study

(N=500 high-risk colonoscopies)

Polyp pathology (all), N=175



Conclusions- OC-Sensor

- Is an **easy** to prepare & automatically develop, quantified I-FOBT.
- Prepared fecal samples are **stable** at least 21 days at **4°C**.
- Hb quantification is **reproducible**.
- **3** fecal samples provides the best sensitivity.
- Provides a highly **significant & specific** FOBT for clinically significant neoplasia with a **high negative predictive value**.

Acknowledgments

Researchers	Laboratory/ Coordinator	Associated Endoscopy Units
Dr A Vilkin	A Waked	Dr E Maoz & colleagues
Dr Z Levi	Z Levi	Dr S Birkenfeld & colleagues
Dr Y Niv		
Pharmatrade-Israel, Alpha Wasserman-Italy, Eiken-Japan		