

PAT Technology in Cardio-vascular and Sleep Applications



ICI meeting 2009
Innovations in Cardiovascular Interventions

Disclosures

I have the following financial relationships to disclose:

**Type of relation: Employee of Itamar Medical,
Senior Vice President CSO & CTO**

(level of remuneration)

**Type of relation: Consultancy, employment, honoraria, other compensation*

**Level of remuneration: high (over \$50,000 yearly), moderate (10-50,000), modest (under 10,000)*

Peripheral Arterial Tone (PAT)

- Measures changes in arterial pulsatile blood volume
- A window to two vaso-regulating systems:
 - *Arterial endothelial system*
 - *The autonomic nervous system*

Platform PAT Technology

- **Sensing technology**

- Sensitive
- Elimination of venous blood effects
- strong dynamic response
- Movement tolerant
- Comfortable during extended use

- **Application specific software**

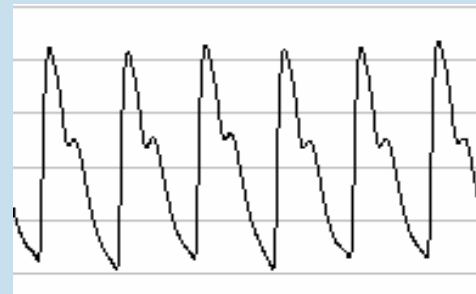
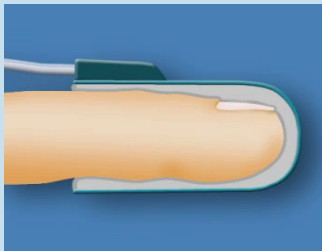
- Advanced signal processing
- Automatic analysis & reports

- **Publications**

- Over 100 manuscripts
- 200 abstracts

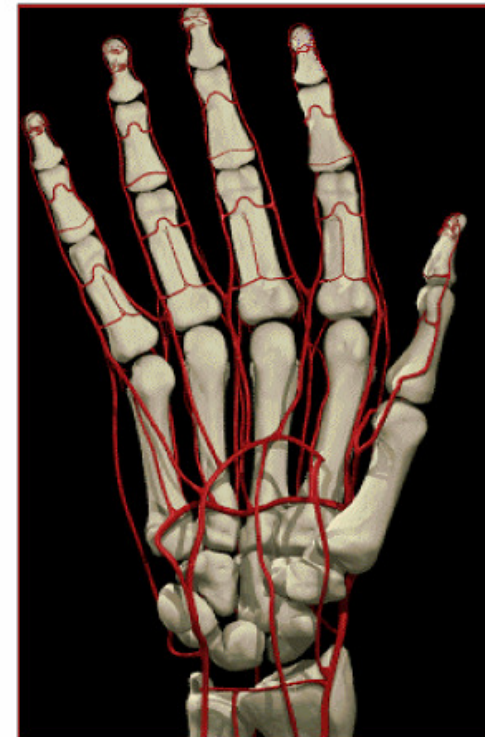
- **Patents**

- 40 issued
- 28 pending
- 4 provisional



The Finger – Unique Physiology

- Convenient site for measurement
- Highly vascular
- Tremendous dynamic range of blood flow (1-100ccm/100g/sec)



PAT Based Clinical Applications

Endo-PAT2000

- Endothelial dysfunction
- Arterial Stiffness

Watch-PAT200

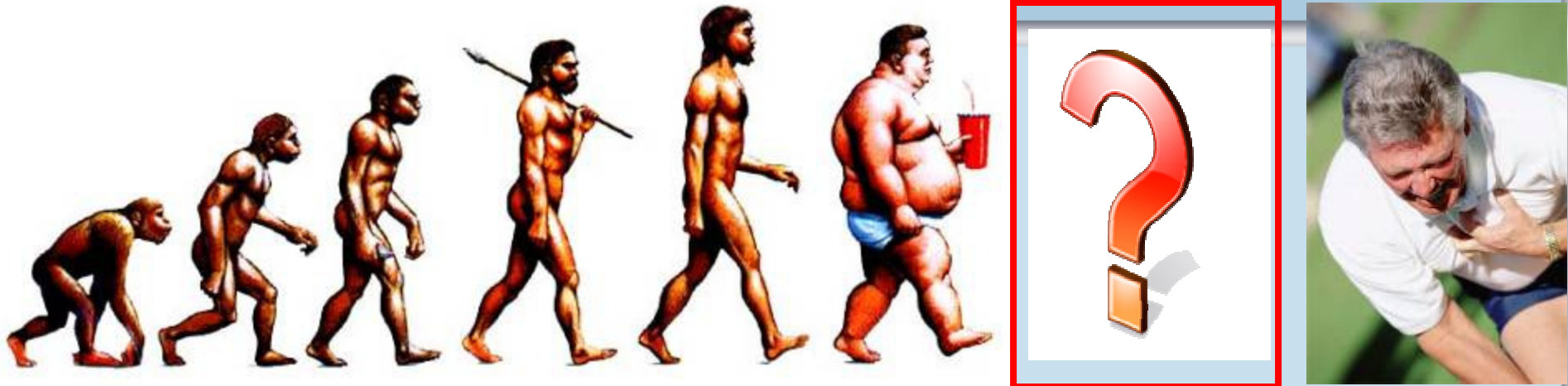
- Ambulatory device
- Sleep-related breathing disorders (i.e.OSAS)
- Sleep architecture (Wake/Light sleep/Deep sleep/REM)



Endo-PAT2000



10⁷ 5,000,000 10⁶ 500,000 10⁵ 20th century 21st century



Cholesterol

**Risk FACTORS –
not the only missing
link!**

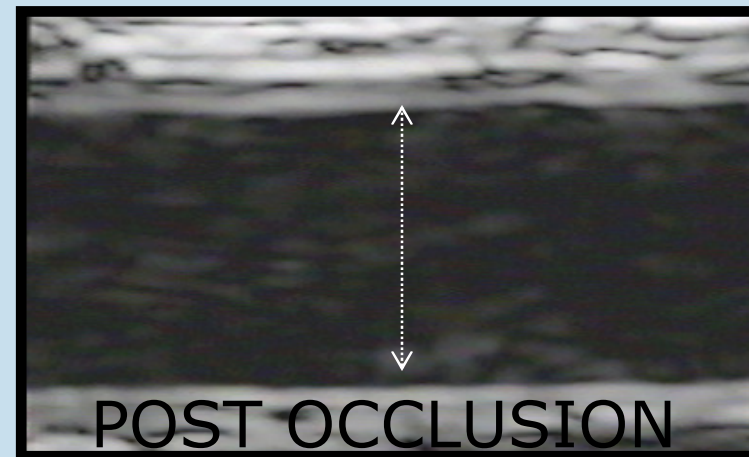
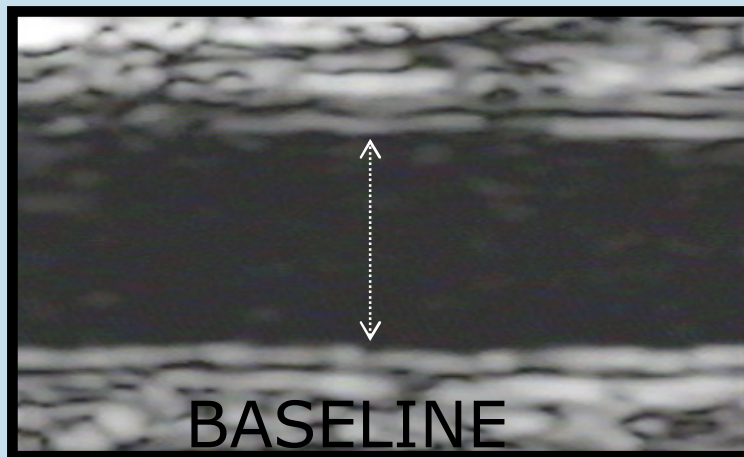
1950's

1960's

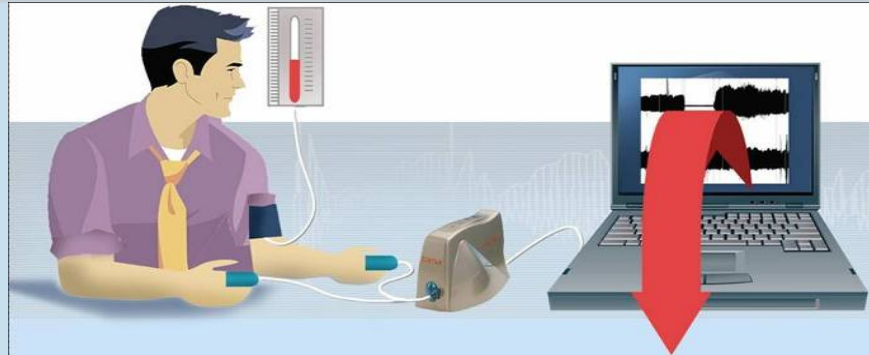
1970's

Brachial FMD

Response to Reactive Hyperemia



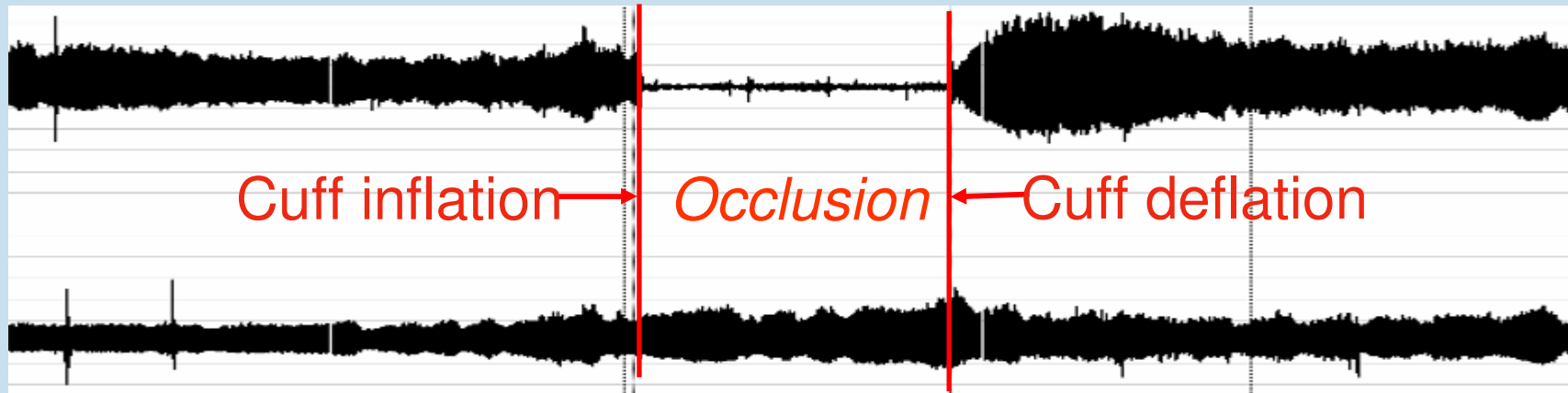
Endo-PAT Test Procedure



5 - 10 min

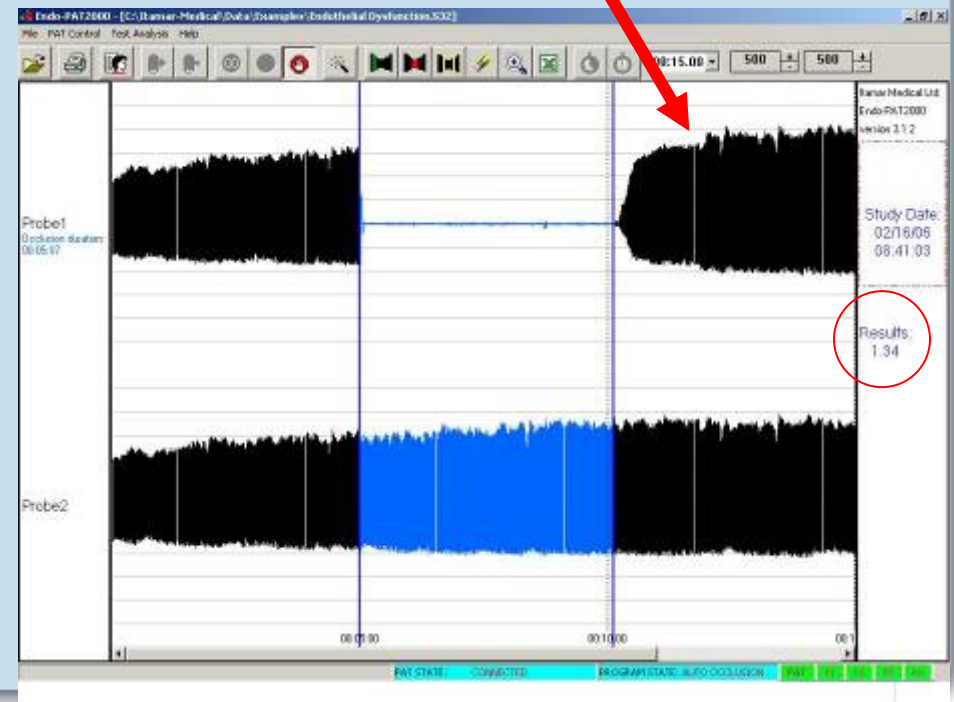
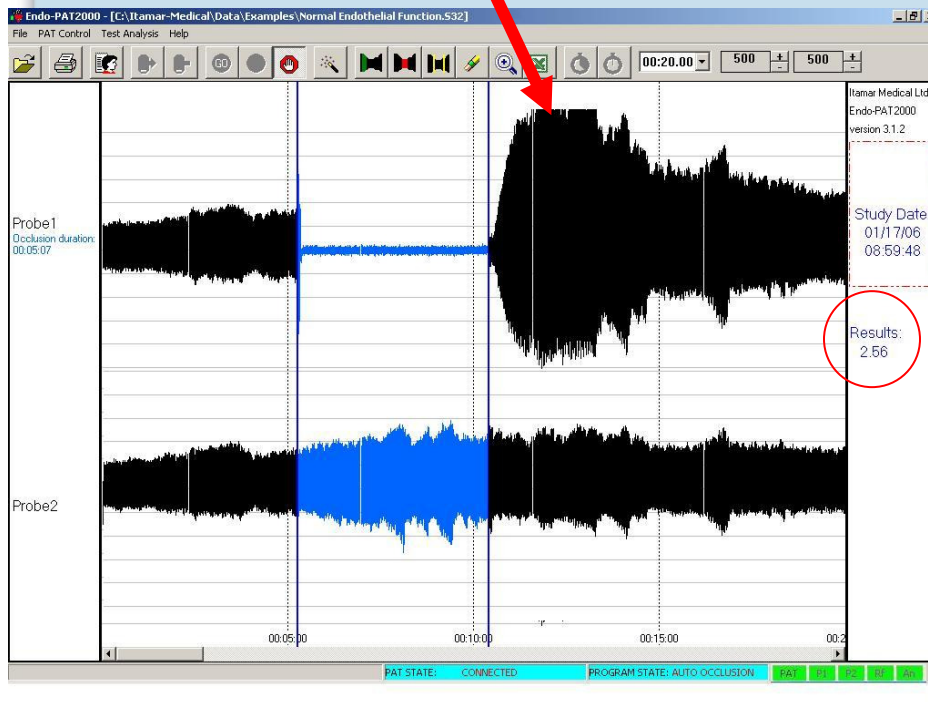
5 min

5 - 10 min



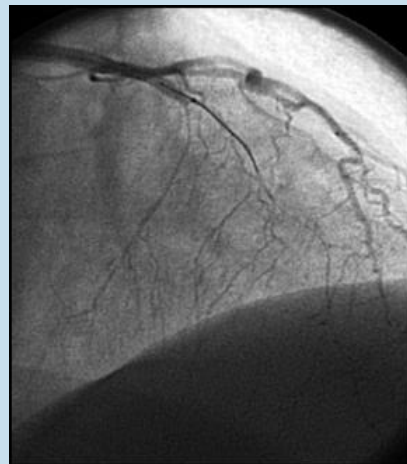
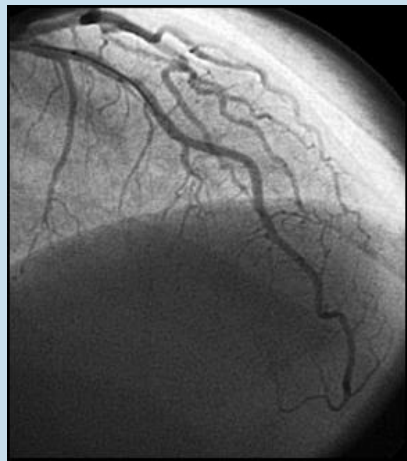
Normal Endothelial Function

Endothelial Dysfunction



PAT Estimation of Coronary Endothelial Dysfunction

Coronary Angiography



Baseline

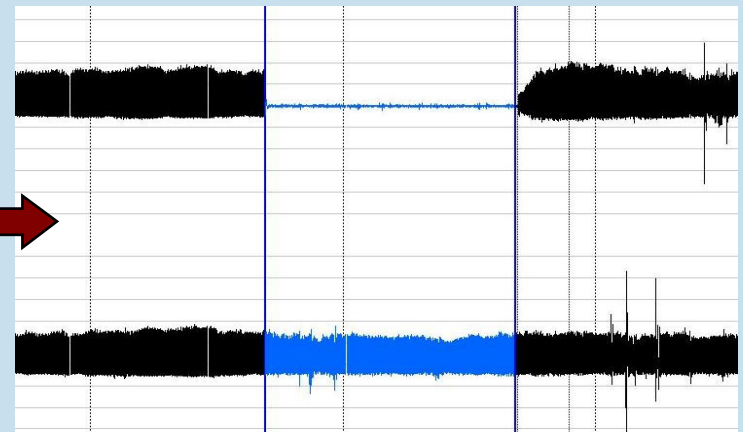
Acetylcholine

Bonetti et al. JACC 2004

Courtesy of Prof. Lerman, Mayo Clinic

Endo-PAT

{24 hrs}



- Sensitivity=82%
- Specificity=77%

Summary of studies on the relationship between Endo-PAT and BAUS

Group (ref)	N	Population	r	p	Comments
Kuvin <i>et al.</i> ⁵	89	Chest pain	0.55	<0.0001	
Kuvin <i>et al.</i> ⁶	60	CAD(+) and CAD(-)	0.3	<0.05	
Dhindsa <i>et al.</i> ⁷	40	Apparently healthy	0.47	<0.01	
Grutu <i>et al.</i> ⁸	246	Apparently healthy, IBD and CAD(+)	--		Only Endo-PAT index significantly lower in CAD group
Erbs <i>et al.</i> ⁹	15	Obese adolescents	0.9		

[5] Kuvin et al. **Assessment of Peripheral Vascular Endothelial Function with Finger Arterial Pulse Wave Amplitude.** *AHJ* 2003; 146: 168-74

[6] Kuvin et al. **Assessment of Peripheral Vascular Endothelial Function in the Ambulatory Setting.** *Vascular Medicine* 2007; 12:13-16

[7] Dhindsaa et al. **Inter-relationships Among Noninvasive Measures of Postischemic Macro- and Micro-Vascular Reactivity** *Journal of Applied Physiology* 2008; 105:398-9

[8] Gurtu et al. **Peripheral Arterial Tonometry (Pat-Index) As A Determinant Of Vascular Function And Cardiovascular Health** *Canadian Cardiovascular Congress Oct 2008*

[9] Erbs et al. **Vascular Dysfunction in Obese Children** *ESC 2008*

Summary of Endo-PAT reproducibility data

Group	n	Cohort	Time interval	Statistical Parameter	Result	Comments
Reisner <i>et al.</i> ¹⁰	113	Adult volunteers	24 hours	ICC*	0.56 (p<0.001)	Classification of normal vs. dysfunction maintained in 75% of males and 70% of females between days (p<0.01)
Selamet Tierney <i>et al.</i> ¹¹	30	Young adult volunteers	1 to 7 days	ICC*	0.78 (p<0.001)	
Tomfohr <i>et al.</i> ¹²	12	Young adult volunteers	1 to 7 days	ICC*	0.73 (p<0.001)	
JT Kuvin – Tufts Medical Center	47	Adults with chest pain	24 hours	ICC*	0.59 (P=0.001)	Part of FDA submission - unpublished data
Haller <i>et al.</i> ¹³	44	Type 1 Diabetes adolescents	4 weeks	Coefficient of variation	14.8%	

[10] Reisner et al. **Reproducibility of endothelial function and arterial stiffness assessed using finger peripheral arterial tonometry** *EHJ* 2007; 28 (Suppl.):484

[11] Tomfohr et al. **Symptoms of depression and impaired endothelial function in healthy adolescent women.** *J Behav Med* 2008; 31:137–143

[12] Selamet-Tierney ES, Newburger JW, Gauvreau K, Geva J, Coogan E, Colan SD, Ferranti SD **Endothelial Pulse Amplitude Testing: Feasibility and Reproducibility in Adolescents** *J Pediatr.* 2009 Feb 12. [Epub ahead of print]

[13] Haller et al. **Peripheral Artery Tonometry Demonstrates Altered Endothelial Function In Children With Type 1 Diabetes.** *Pediatric Diabetes* 2007; 8:193–198

Endo-PAT studies demonstrating improvement in Endothelial Function

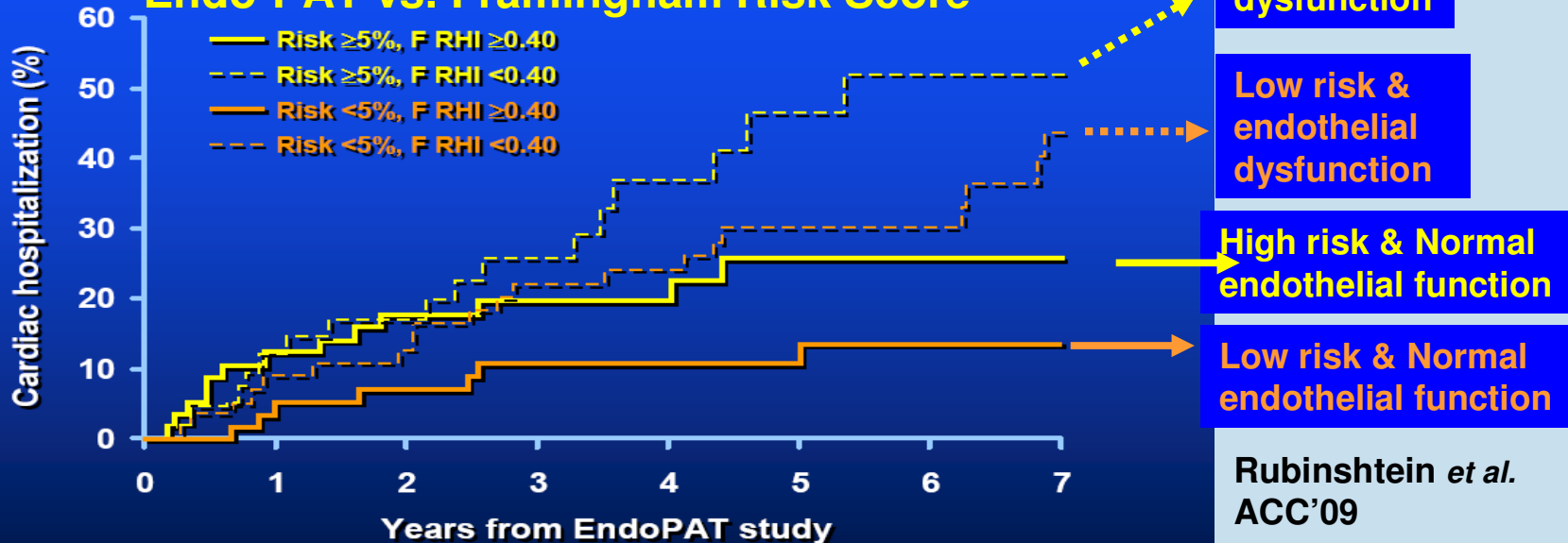
Category	Intervention	Reference
Lifestyle modification	Smoking cessation	Komatsu <i>et al.</i> ³²
Dietary changes	Flavonoids	Schroeter <i>et al.</i> ³³ , Fisher <i>et al.</i> ³⁴ , Barringer <i>et al.</i> ³⁵ , Fisher <i>et al.</i> ³⁶ , Hollenberg <i>et al.</i> ³⁷
	Omega 3	Dangardt <i>et al.</i> ³⁸
	Low carb/fat diet	Davis <i>et al.</i> ³⁹
	Conjugated Linoleic Acid	Fielitz <i>et al.</i> ⁴⁰
Devices for co-morbidity	EECP	Bonetti <i>et al.</i> ⁴¹
	Oral Appliances	Ithzhaki <i>et al.</i> ⁴² Pillar ⁴³
	CPAP	Ithzhaki <i>et al.</i> ⁴⁴ , Morgenthaler <i>et al.</i> ⁴⁵
Drugs	PDE5-I	Prince <i>et al.</i> ⁴⁷ Aversa <i>et al.</i> ⁴⁸
	BH4	Hsu <i>et al.</i> ⁴⁶
	L-Arginine	Yeo <i>et al.</i> ^{49,50}
	Eplerenone	Thum <i>et al.</i> ⁵¹
	Clopidogrel	Luu <i>et al.</i> ⁵²

Endo-PAT adds incremental value over FRS

outcomes = cardiac mortality, revascularization,

Outcomes response curve

Endo-PAT vs. Framingham Risk Score

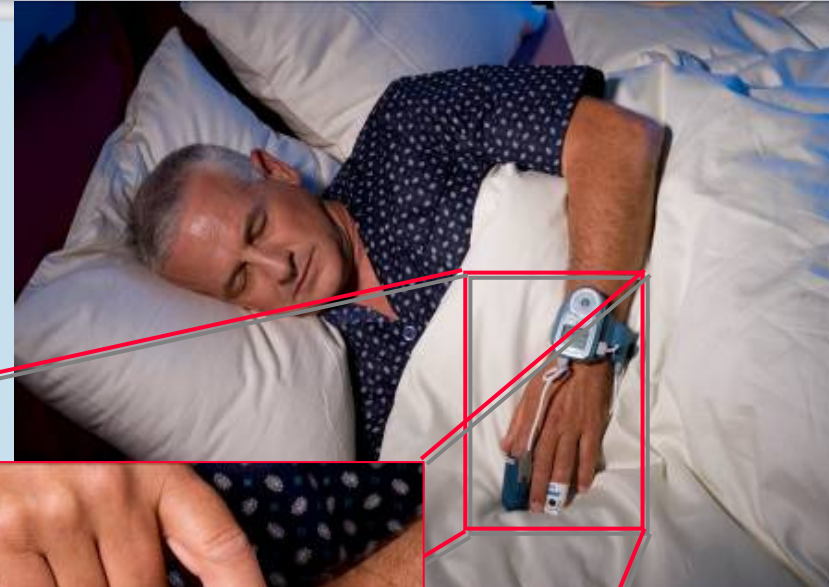


n=270, Intermediate risk patients
Mayo Clinic & Tufts Medical Center


Rubinshtein *et al.*
ACC'09
Oral presentation
0917-7,
Room W308C
Tuesday, 11:30-45

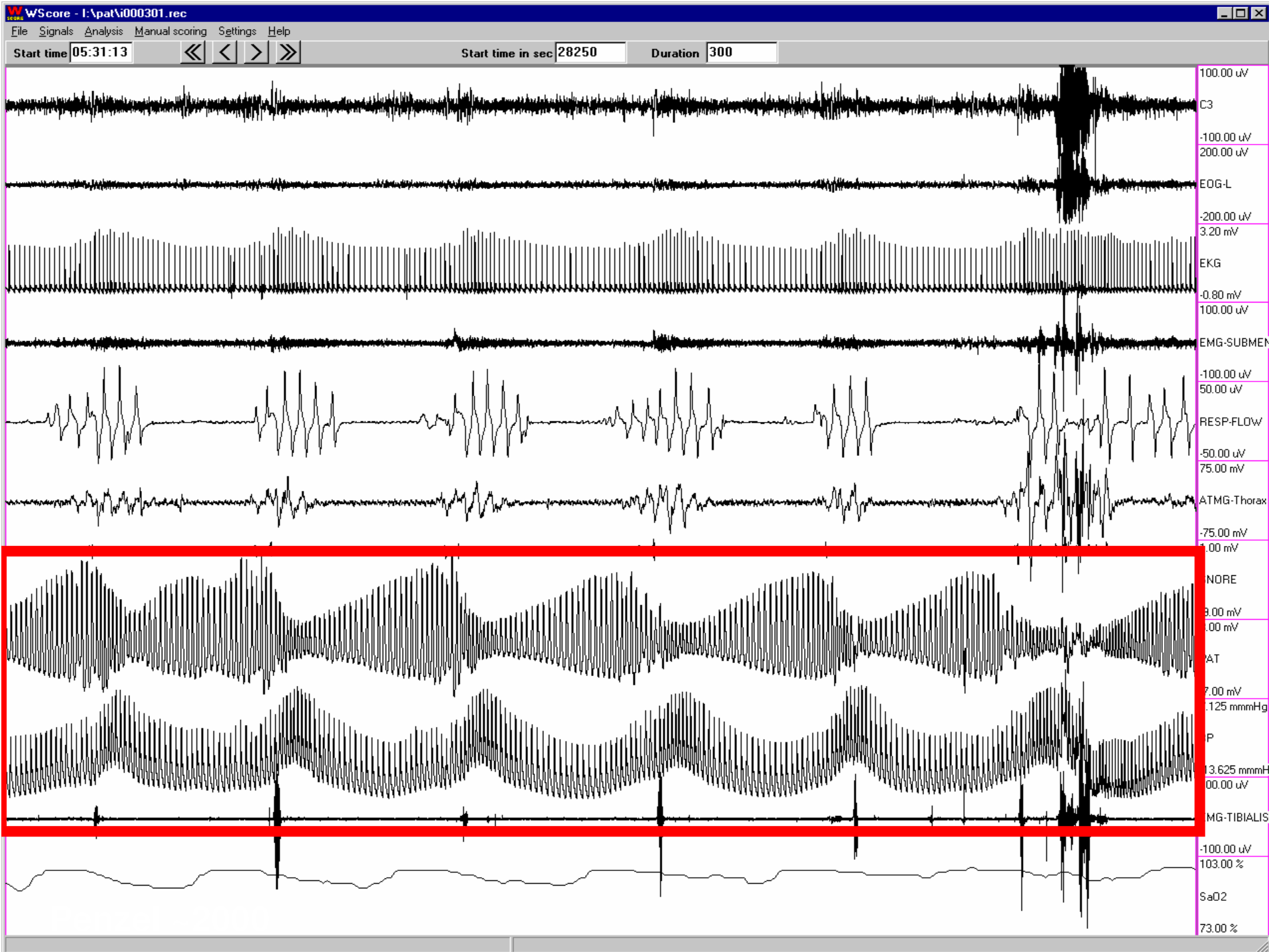
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Watch-PAT200

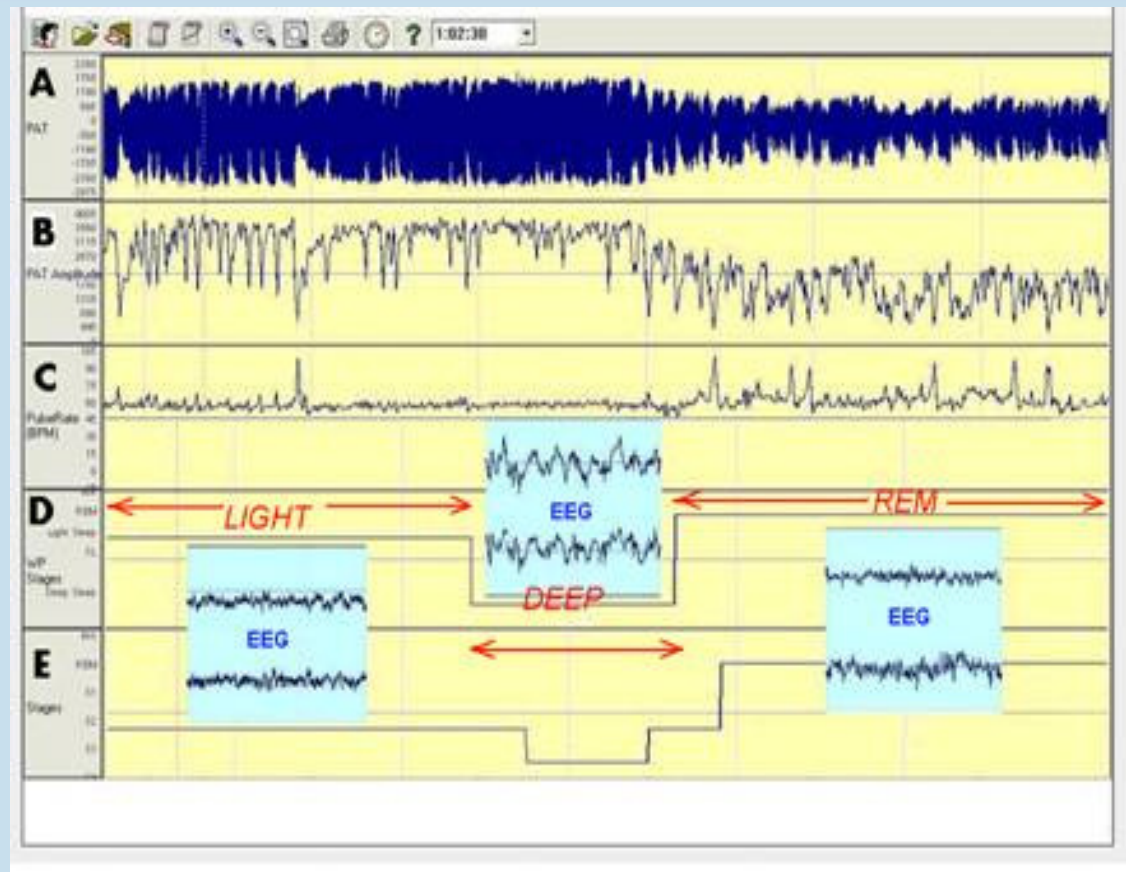


Sympathetic Activation in Sleep Apnea

- Reduced Upper Airway Muscle Tone
 - ⇒ Upper Airway Walls collapsed
 - ⇒ Upper Airways obstruction
 - ⇒ Respiratory event
 - Respiratory Event
 - ⇒ Feedback mechanisms
 - ⇒ Sympathetic activation
 - ⇒ Vasoconstriction & Heart Rate acceleration
 - ⇒ PAT attenuation
- 
- Recovery sleep
- Apnea termination
- Recovery upper airway muscle tone



Sleep stages



Watch-PAT200

- **Automatic analysis**

- **Clinical parameters:**

- RDI (Respiratory Disturbance Index)
- AHI (Apnea Hyperpnoea index)
- ODI (Oxygen disaturation index)
- Wake/Sleep Analysis
- REM/NREM/Light/Deep sleep
- Snoring
- Body Position

- **Comprehensive Report**

- **Treatment follow up**

- **User Friendly, easy to use**

- **Comfortable - minimal sleep interference**



Thank you !

Red bloom, the Judean Hills

Spring 2007

Anemone Coronaria L. & Asphodelus

