New Implantable Devices for Heart Failure and Rhythm

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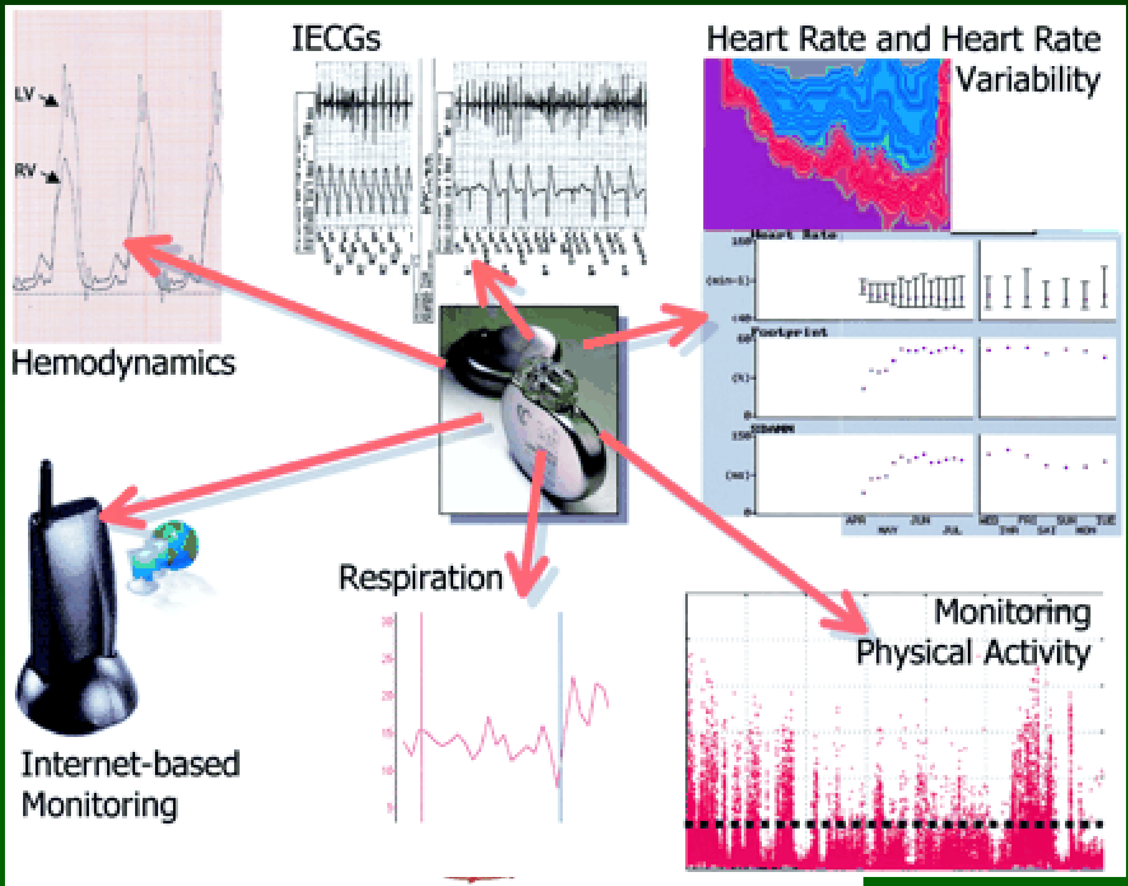
Status of Art: Heart Failure Device



CRT

+

ICD

+

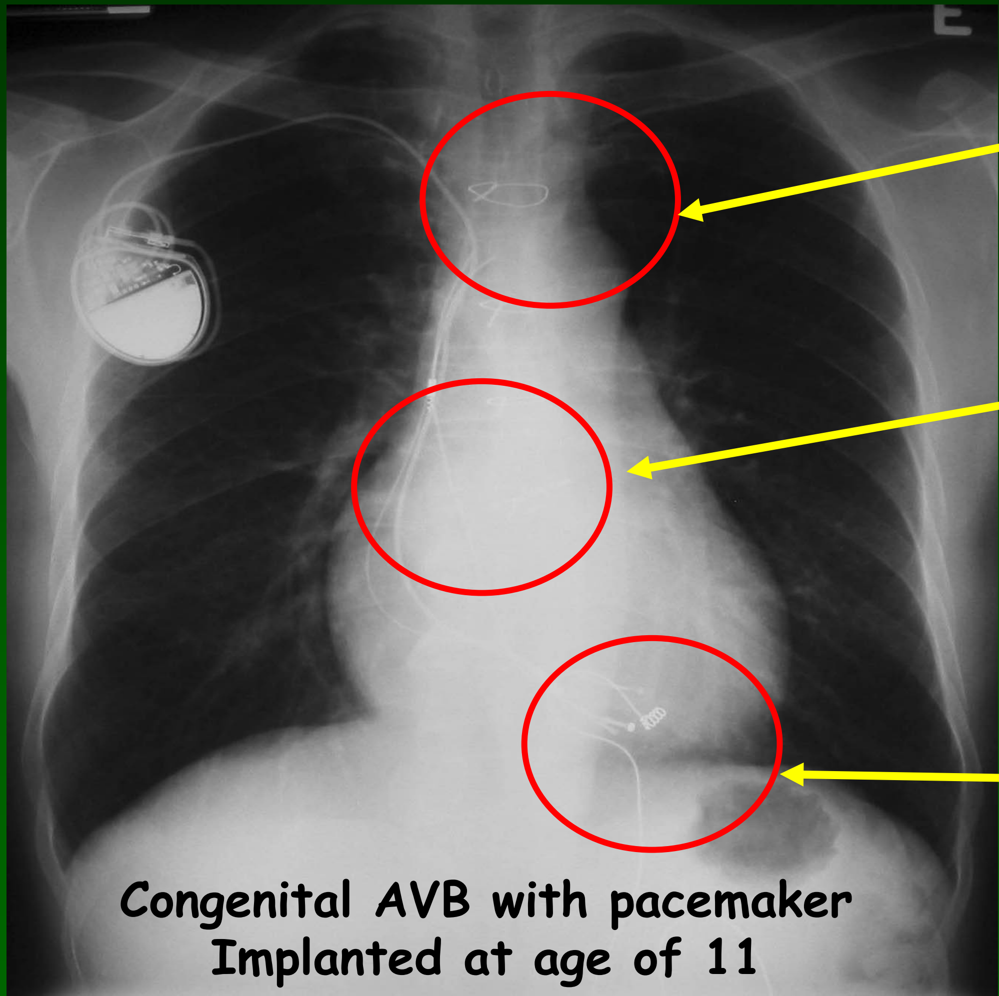
Monitoring

Auricchio & Abraham Circulation 2004;109:300-307

New Perspectives for Device Therapy

- Leadless
  - Defibrillation
  - Pacing
- Multiple Purpose Sensor Technologies

Problems with Transvenous Leads



Infection

Replacement of malfunction leads and pacemaker

Unable to meet the patients needs

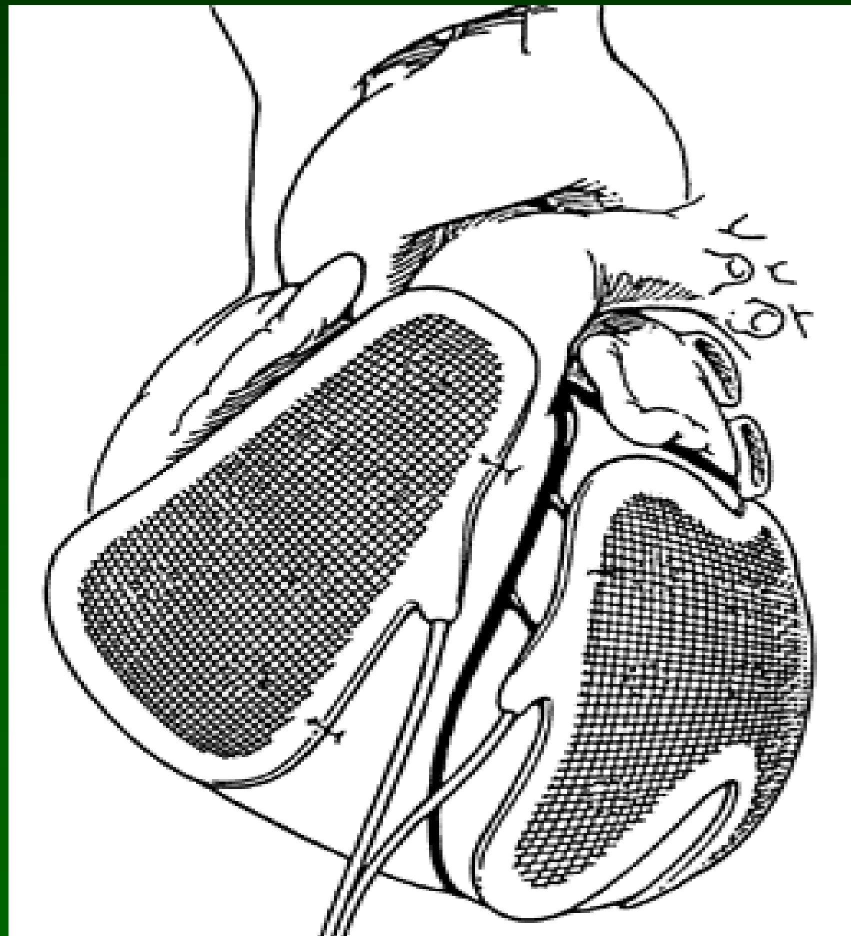
Novel ICD Systems

ICD systems without transvenous leads:

- Subcutaneous Lead System
- Cameron Health

ICD systems without generator:

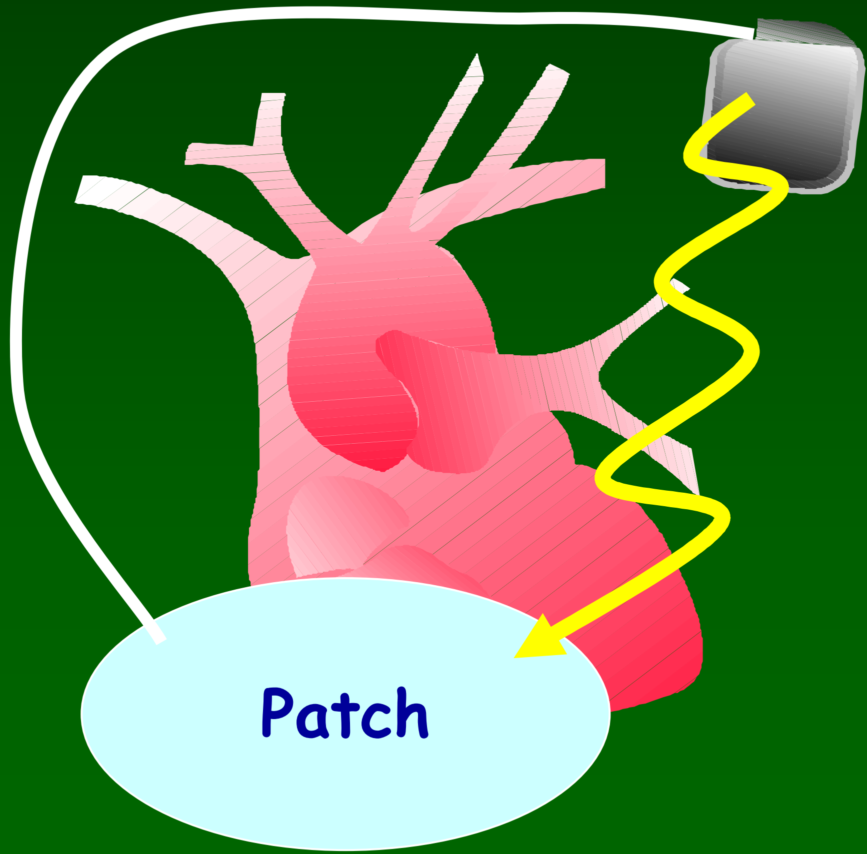
- CRM Generator is incorporated in lead



Leadless ICD Systems

Bardy GH, Late Breaking Trials HRS 2005:

- Subcutaneous System: one active shell and one subcutaneous elongated electrode
- Acute testing during ICD implantation
- Mean DFT=36.1J
- Cameron Health



Leadless ICD Systems

Advantage:

- Subcutaneous lead system only, avoid the problems related to transvenous lead
- Simplify implant procedure

Disadvantage:

- High DFT- need high energy device
- Limited pacing and sensing capacity
- Similar cost as existing ICD
- Long-term reliability of lead system

Leadless Pacing

- Cardiac stimulation without leads may enable major advancements in pacemaker therapy
  - Multisite pacing
  - Pediatric pacing
  - Reduce infection, lead failure, mechanical interference

Background: Leadless Pacing

- A new technology utilizing ultrasound-mediated electrical stimulation has been evaluated in acute porcine studies demonstrating:
  - Feasibility of endocardial, selected-site and multisite pacing
  - Safety of acute transthoracic ultrasound administration

Echt DS, et al. Heart Rhythm 2006

Technology

- Uses the mechanical-to-electrical properties of piezoelectric materials

Ultrasound Transmit Transducer

↓

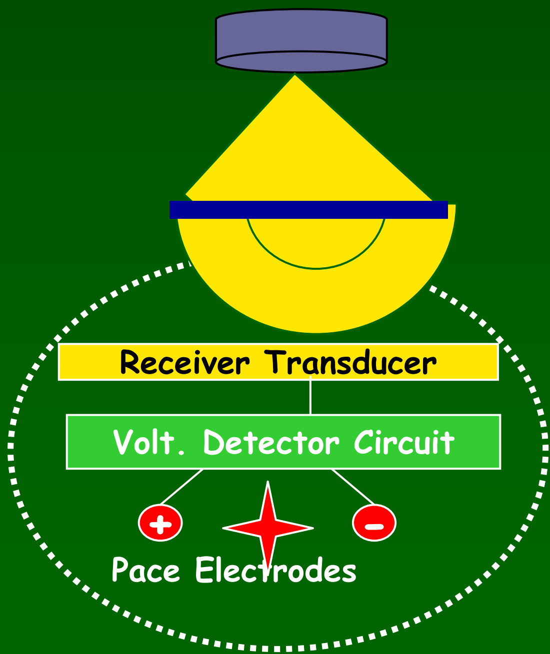
Acoustic Wave

↓

Receive Transducer

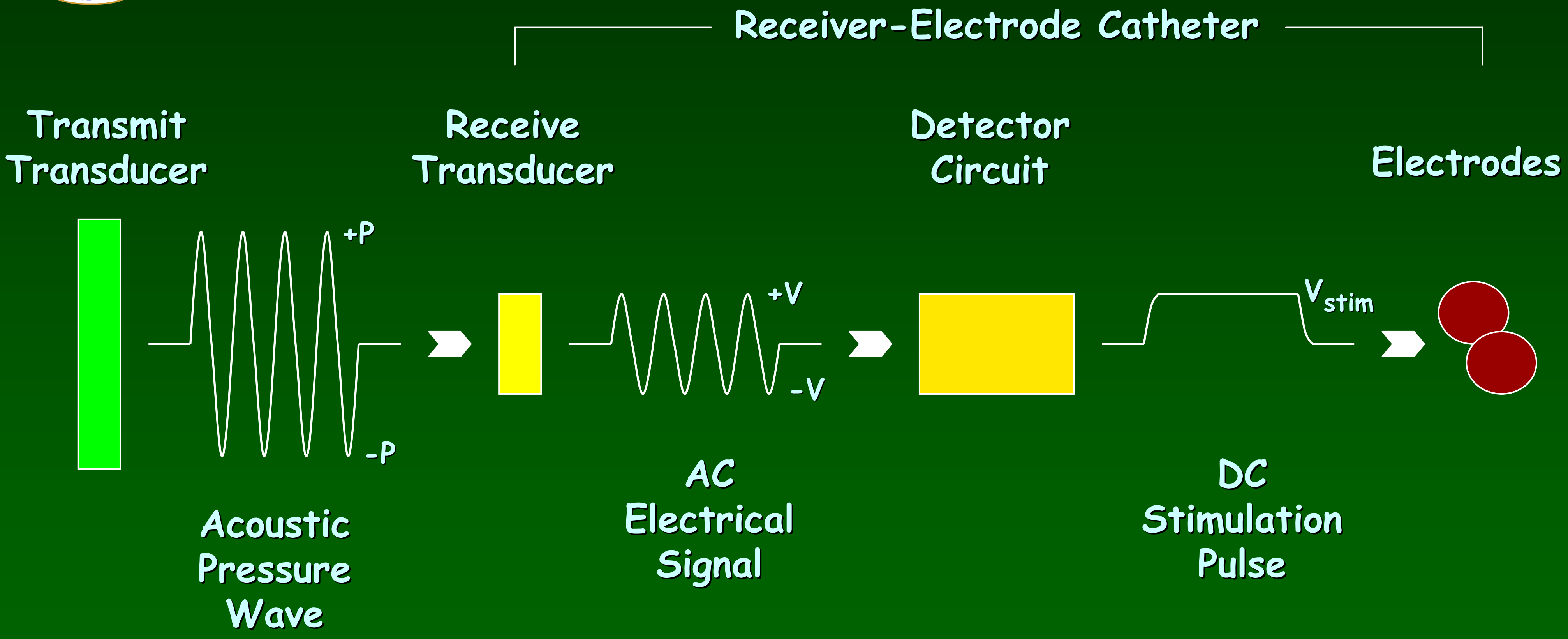
↓

Electrical Stimulation



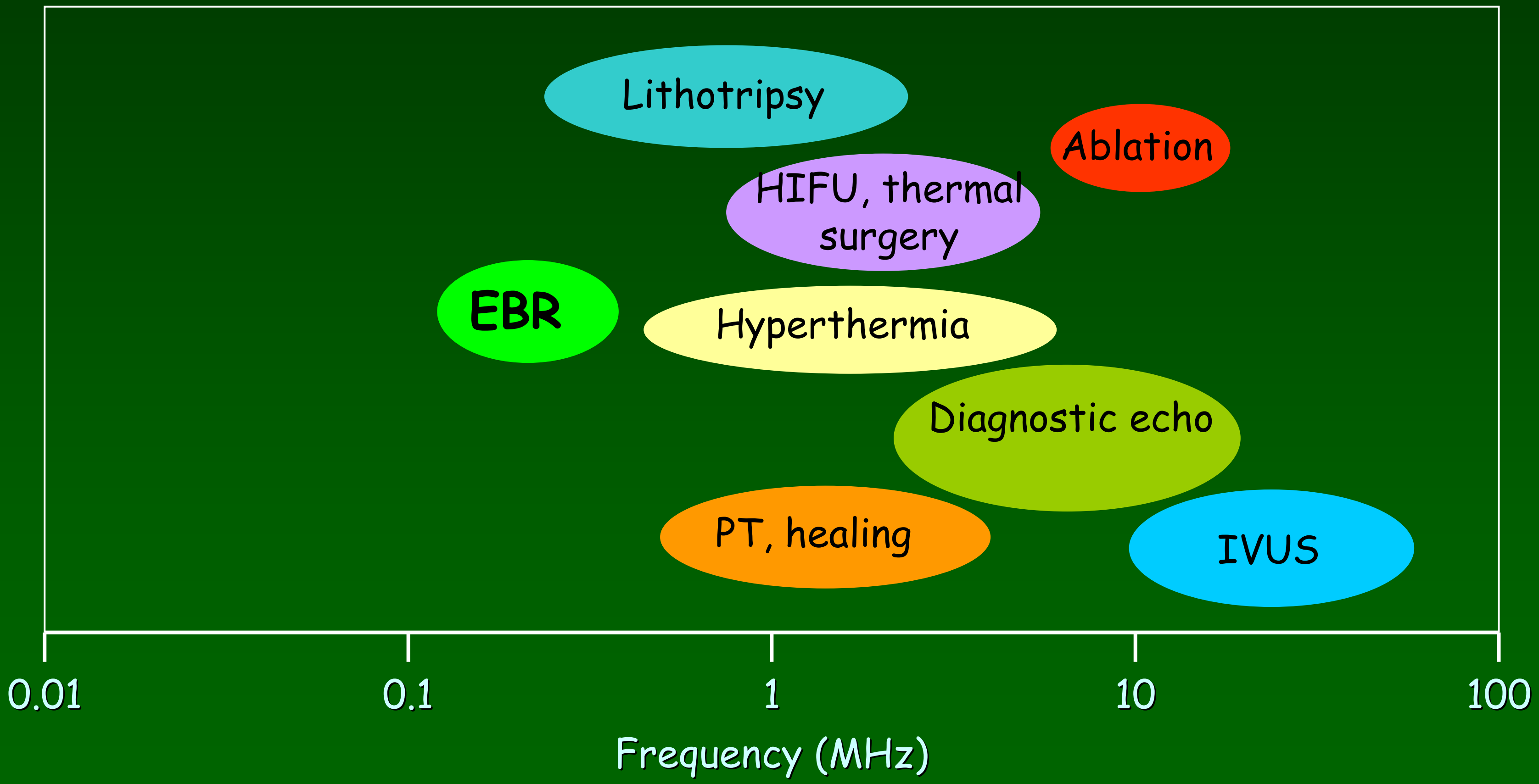
Echt DS, et al. Heart Rhythm 2006

Technology

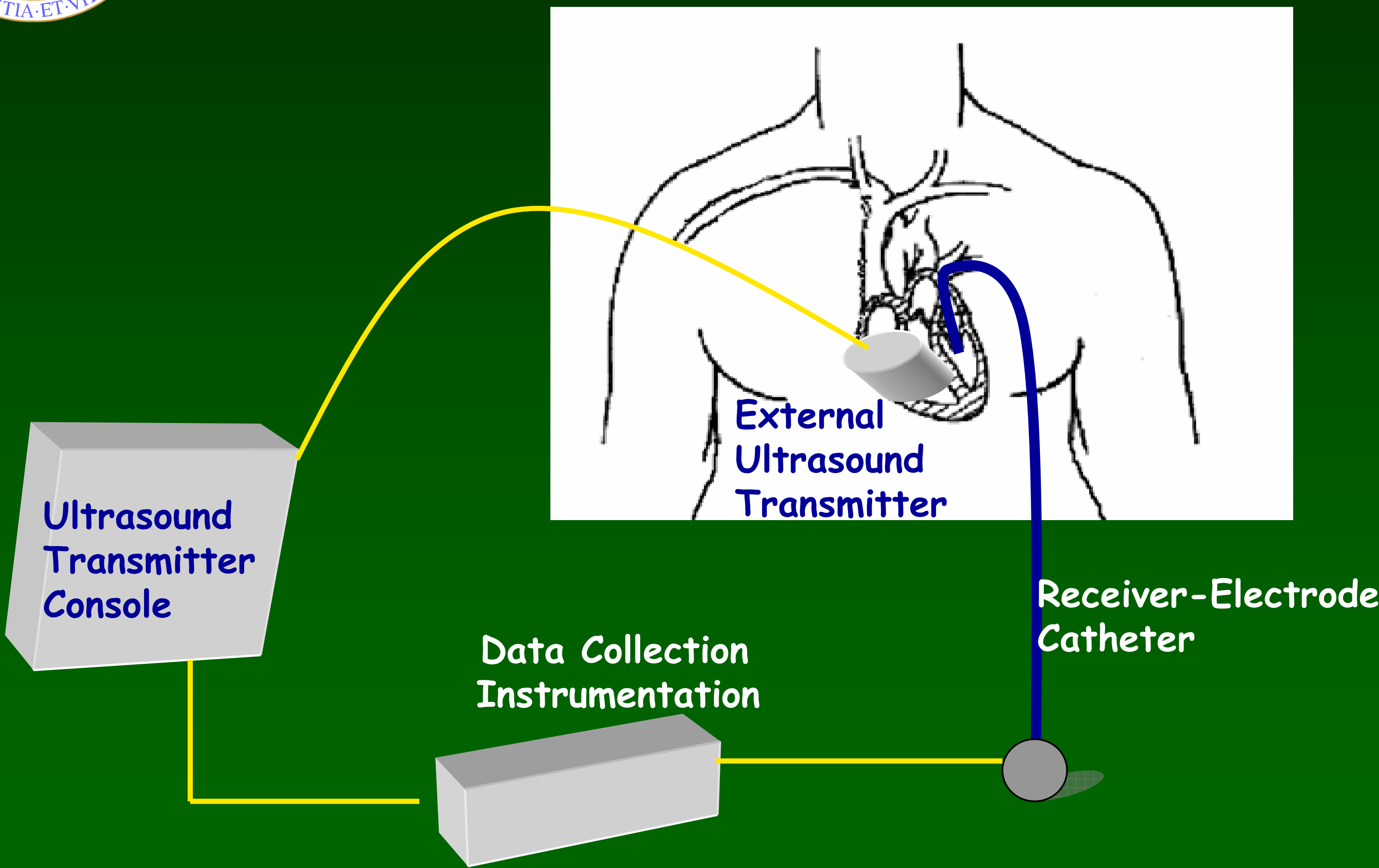


Echt DS, et al. Heart Rhythm 2006

Technology - Ultrasound Frequencies



Methods

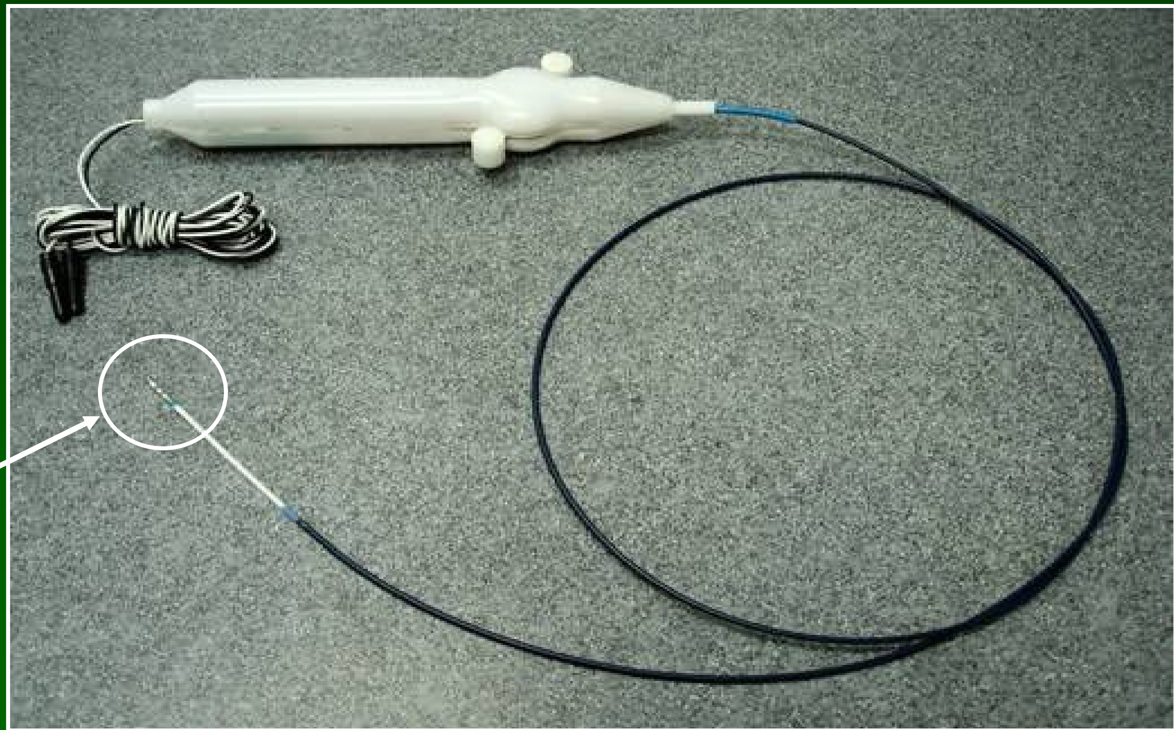


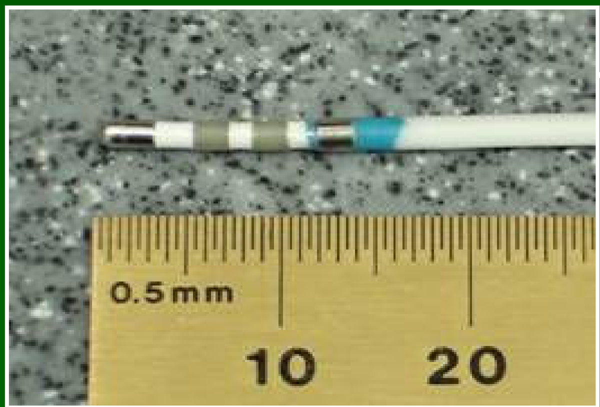
Lau CP, HRS Late Breaking Trials 2006
Lee KF, Lau CP, Tse HF, et al. J Am Coll Cardiol (in revision)

Methods

Transmit Transducer

Receiver-Electrode Catheter





Lau CP, HRS Late Breaking Trials 2006

Lee KF, Lau CP, Tse HF, et al. J Am Coll Cardiol (in revision)

Methods

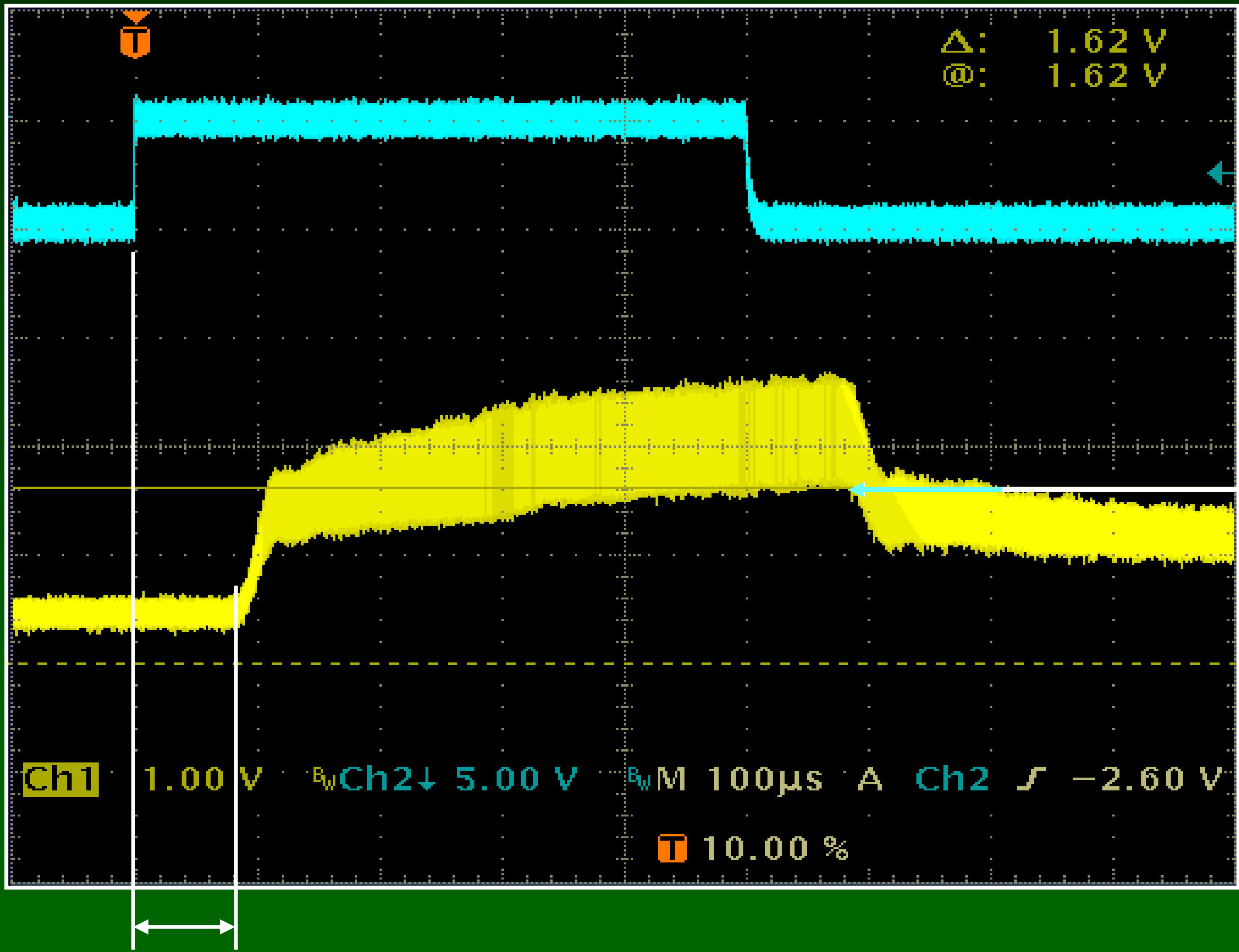
- Patients undergoing EP study for clinical indications
- Receiver-electrode catheter inserted into selected chamber and site
- Electrical pacing threshold documented (12 sec consistent pacing) with conventional stimulator
- Ultrasound transmitter placed on chest wall and positionally optimized for maximum receiver output
  - Ultrasound energy delivered at an identical rate and PW
  - Electrical output was monitored
  - Ultrasound-mediated pacing threshold documented (12 sec consistent pacing)
- Protocol was repeated at other intracardiac sites

Lau CP, HRS Late Breaking Trials 2006
Lee KF, Lau CP, Tse HF, et al. J Am Coll Cardiol (in revision)

Methods - Measurements

Transmit marker

Electrode output
(12-sec envelope)

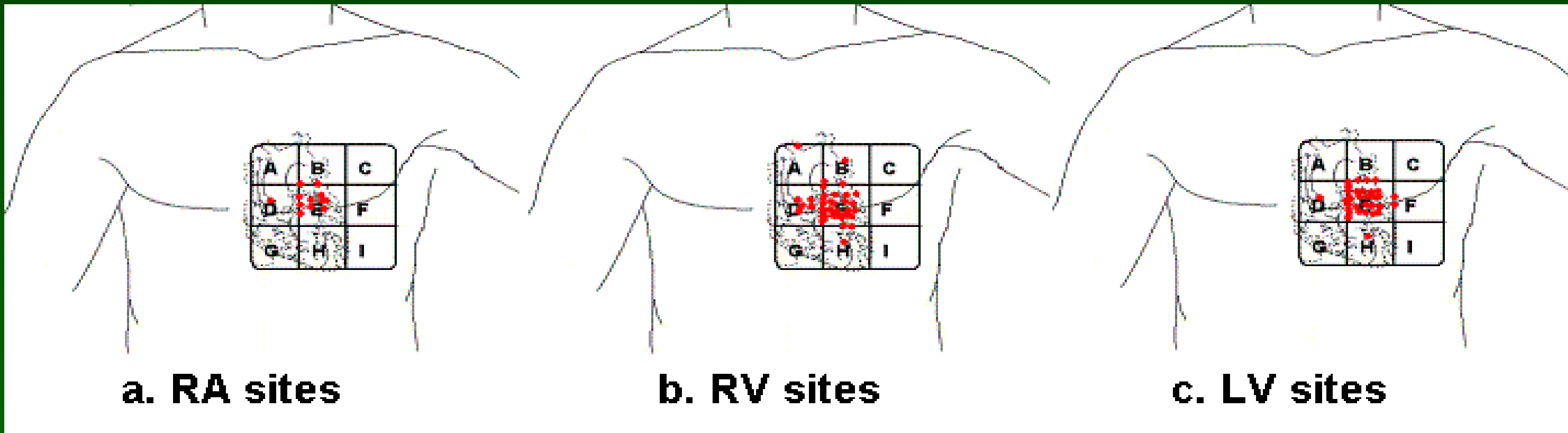


Recorded Threshold Voltage

Transmit Delay [transmit distance = delay (µs) x 1.5 mm/µs]

Results

Ultrasound Transmission Sites



Korean Society of Circulation 2007

Lee KF, Lau CP, Tse HF, et al. J Am Coll Cardiol (in revision)

Results – Patient Demographics

- 24 patients
  - Mean age 48 ± 12 years
  - 12 F, 12 M
  - Concurrent EP study
    - Ablation: AVNRT (8), AVRT (6), AF (2), A*fl* (3), VT (2)
    - Diagnostic (4)
  - Underlying cardiac disease
    - None (18)
    - AR, HCM, HF, HTN, CAD, CVA (6)
    - Mild atrial enlargement (4)
    - Moderate LV dysfunction (1)

Lee KF, Lau CP, Tse HF, et al. J Am Coll Cardiol (in revision)

Results

- 80 of 82 sites evaluated had consistent electrical pacing capture
  - RA (12)
  - RV (35)
  - LV endocardial (31)
  - CS/LV epicardial (2)
- 80 sites ultrasound-mediated pacing capture
  - 77 sites consistent ultrasound-mediated pacing capture
    - Two RA sites had possible lung interference
    - One LV site in CS had electrical threshold of 5 mA

Lee KF, Lau CP, Tse HF, et al. J Am Coll Cardiol (in revision)

Results

Parameter	N	Mean ± 1 sd
Electrical pacing threshold	70	1.0 ± 0.7 V *
Receiver-electrode output threshold Minimum Maximum	59	 1.04 ± 0.6 V 2.16 ± 1.10 V
Mechanical Index	80	0.51 ± 0.31
Transmit-to-receive distance	80	11.3 ± 3.2 cm (5.3-22.5 cm)

p =NS

* 1.6 ± 1.1 mA measured, assumes impedance of 605 Ohms

Lee KF, Lau CP, Tse HF, et al. J Am Coll Cardiol (in revision)

Results - Safety

- No ultrasound-related adverse events
  - One femoral artery false aneurysm successfully repaired with thrombin
  - Minimal elevations in CPK, CK-MB in patients undergoing concomitant ablation
- No audible sensation perceived with ultrasound transmission
- No tactile discomfort perceived with ultrasound transmission

Lee KF, Lau CP, Tse HF, et al. J Am Coll Cardiol (in revision)

Leadless Pacing

- Ultrasound-mediated pacing without leads was demonstrated acutely:
  - At 80 sites in the left and right heart
  - With consistent pacing at 77 of 80 sites
  - At distances of up to 22.5 cm
  - At a mean Mechanical Index of 0.51
  - With no safety issues
  - With no patient discomfort

↓

Safe and feasible method for cardiac stimulation

Multiple Purpose Sensor Technologies

Sensor Applications

Rate Adaptation ↔ Monitoring

Implantable Sensors

Technology	Examples
Accelerometer / piezoelectric crystal	Activity sensing Positional sensing
Paced QRS	QT, Evoked R wave
Impedance	MV, RR, pulmonary fluid, contractility and SV
Special lead sensors	SaO2, RVP, PEA

Tse HF, Lau CP. In Clinical Cardiac Pacing, Defibrillation, and Resynchronization Therapy. *3rd Edition 2007*

Rate Adaptive Pacing

Rate Adaptive Pacing in HF

- In patients with HF, pharmacologic treatment with β-blockers and/or co-existing chronotropic incompetence frequently limit an increase in HR during exercise, which may have negative effect on their exercise capacity.
- Due to the limited ability to increase stroke volume in patients with HF, HR augmentation is a major determinant of cardiac output during exercise.
- Appropriate rate adaptation with CRT may therefore provide incremental benefit to patients with HF during exercise.
- Conversely, inappropriate use of rate-adaptive pacing with excessive tachycardia in patients with HF may lead to adverse outcome.

Incremental Benefit of Rate-Adaptive Pacing on Exercise Performance during Cardiac Resynchronization Therapy

- 20 patients with HF, chronotropic incompetence (<85% age-predicted HR [AP-HR] and <80% HR reserve) and implanted with CRT.
- All patients underwent cardiopulmonary exercise treadmill test using:

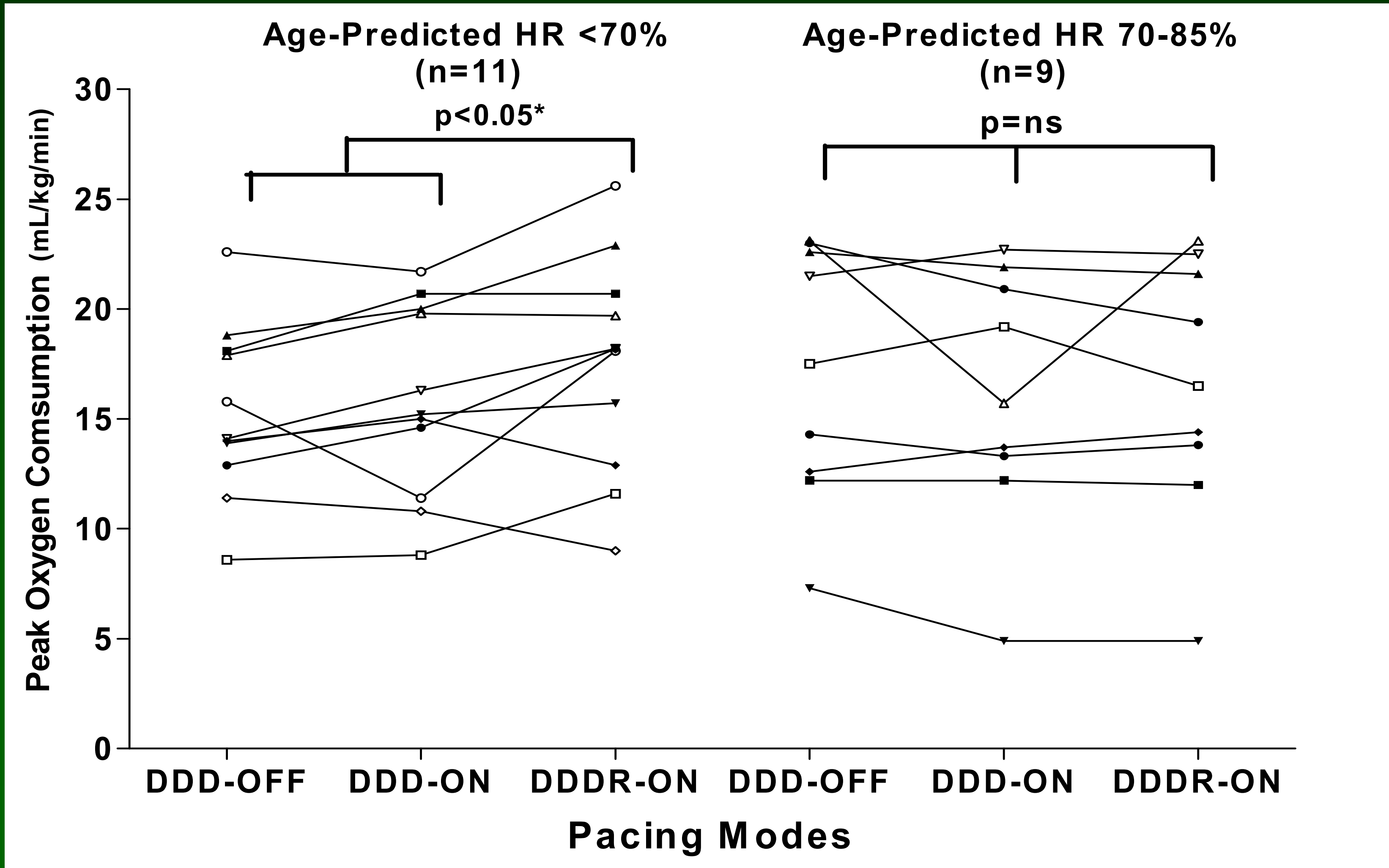
  1) DDD mode with fixed AVI (DDD-OFF);

  2) DDD mode with adaptive AVI on (DDD-ON)

  3) DDDR mode with adaptive AVI on (DDDR-ON)

Tse HF, et al. JACC 2005

Exercise Capacity and Rate Adaptive Pacing in HF Patients



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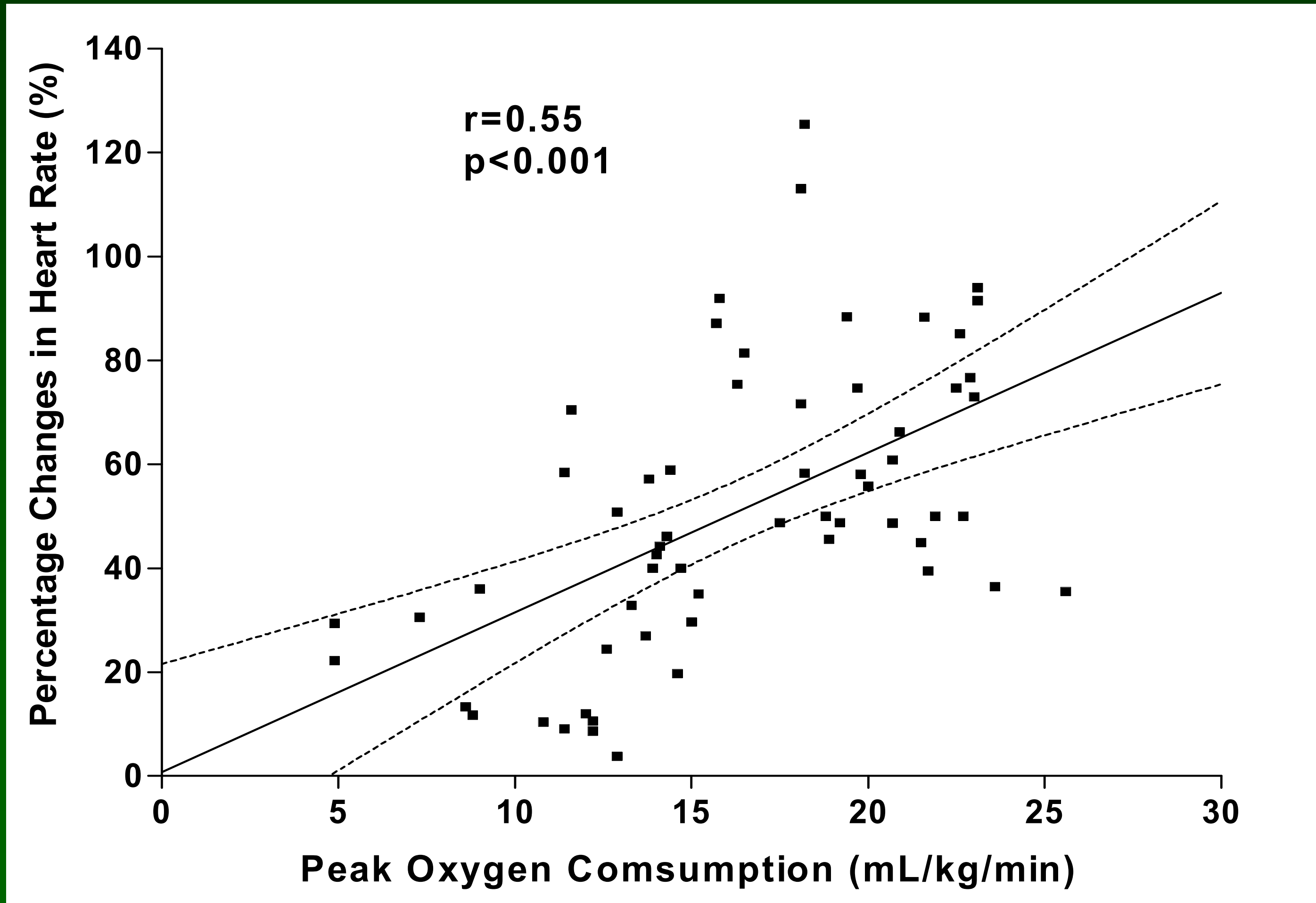
Tse HF, et al. JACC 2005

Relationship Between Exercise Capacity and HR in HF Patients



Tse HF, et al. JACC 2005

Incremental Benefit of Rate-Adaptive Pacing on Exercise Performance during Cardiac Resynchronization Therapy

Conclusions:

- In patients with HF implanted with CRT, chronotropic incompetence is one of the potential causes for impaired exercise capacity.
- Therefore, these patients should undergo exercise testing to assess the HR response during exercise after stabilization of medical therapy.
- In patients with severe chronotropic incompetence as defined by failure to achieve 70% of AP-HR, appropriate use of rate- adaptive pacing with CRT provide incremental benefit on exercise capacity during exercise.

Tse HF, et al. JACC 2005

Monitoring

Purpose of Monitoring

Cardiovascular
- Arrhythmia
- Exercise
- Hemodynamics
- Heart muscles & ischemia

Non-Cardiovascular
- Posture
- Respiration

Pacemaker house keeping
- Lead integrity
- Pacing & sensing
- Programming

Tse HF, Lau CP. In Clinical Cardiac Pacing, Defibrillation, and Resynchronization Therapy. *3rd Edition 2007*

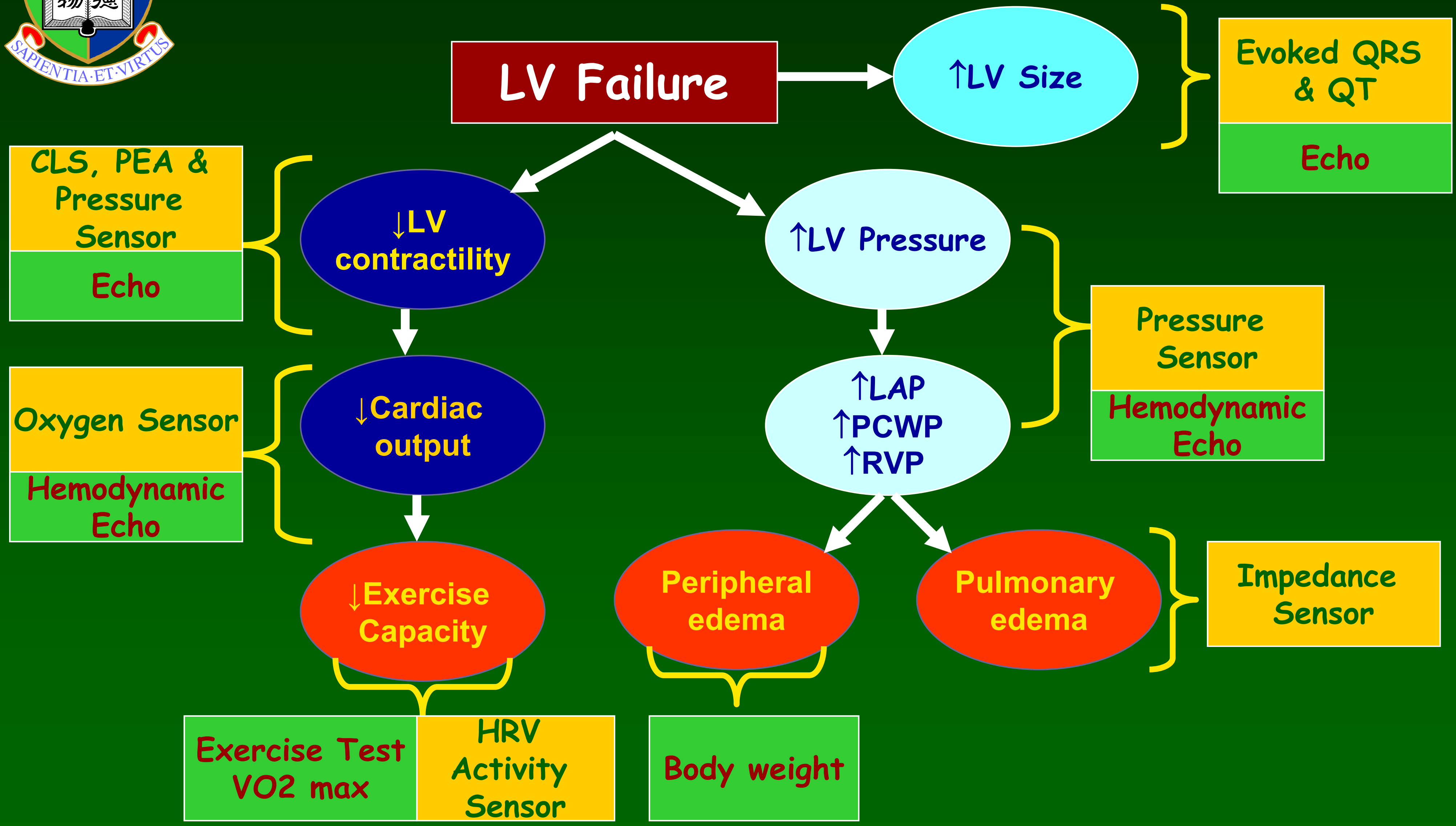
Can Hospitalization of HF be Prevented with Close Monitoring?

Philbin EF et al J Gen Intern Med 1999; 14: 130-135

- 7 randomized controlled trials on the role intensive monitoring / home visits :

Authors	Hospital Readmission	Economic Impact ($ pt/m)
Fonarrow	-85%	-$1591
Kornowski	-62%	-
Rich	-56%	-$153
Sheh	-50%	-
Tilney	-60%	-
Weinberger	-36%	-
West	-74%	-

Pathophysiology of HF vs. Monitoring



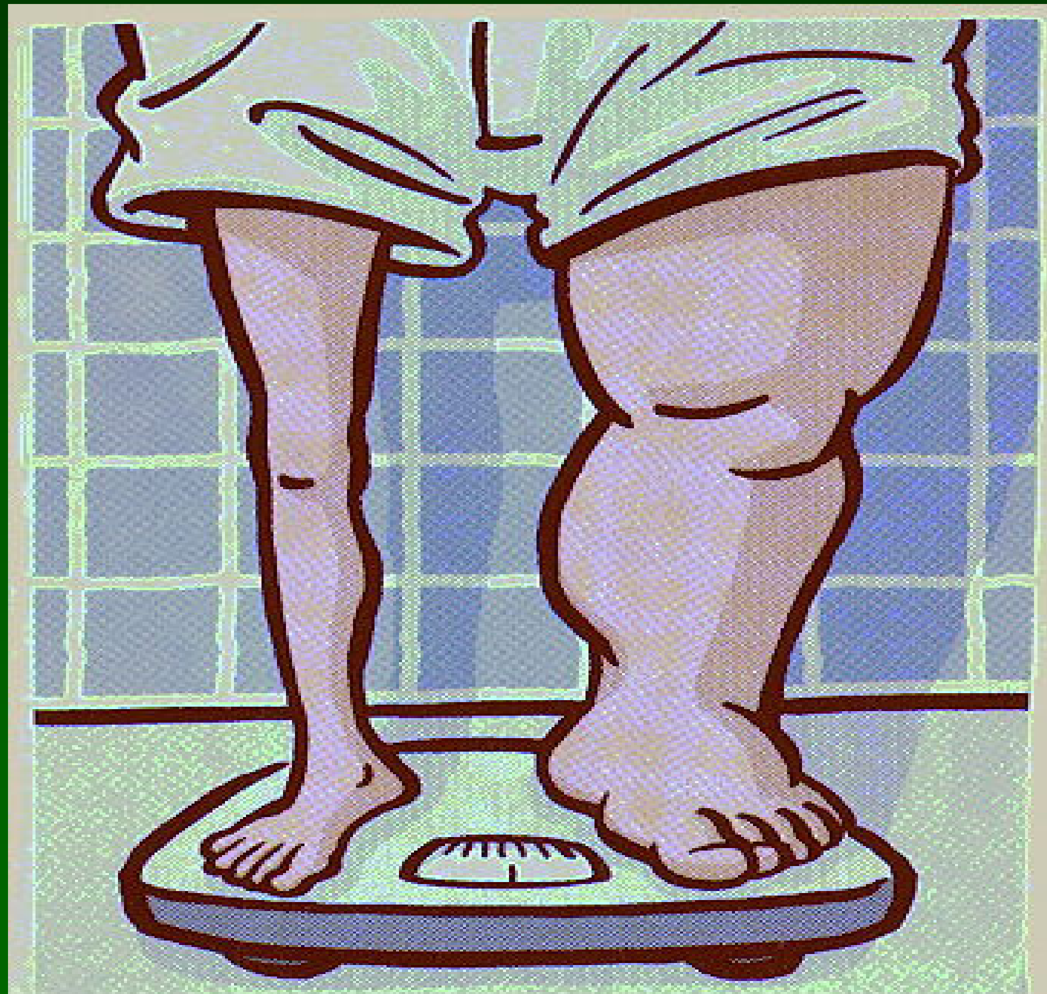
Weight and Edema are Unreliable for HF monitoring over Time

Weight may stay stable when fluid increases, if appetite decreases.

Weight may increase despite stable fluid status over longer period when patients eat better

Edema usually indicates > 2 L of fluid retention

Many patients never get edema despite severe volume overload



Why Implantable Sensors to Monitor HF?

- Worsening HF and hospitalization can be prevented by close monitoring and expedite intervention
- Symptoms and signs (including body weight) may be too late or unreliable
- External monitoring such as Holter, pedometers and accelerometers are unreliable and cumbersome
- Implantable monitors while involving the risk of surgical implantation are attractive, and mode more widely applicable by the expended indications of device use in HF (ICD and CRT)

Issues in Monitoring

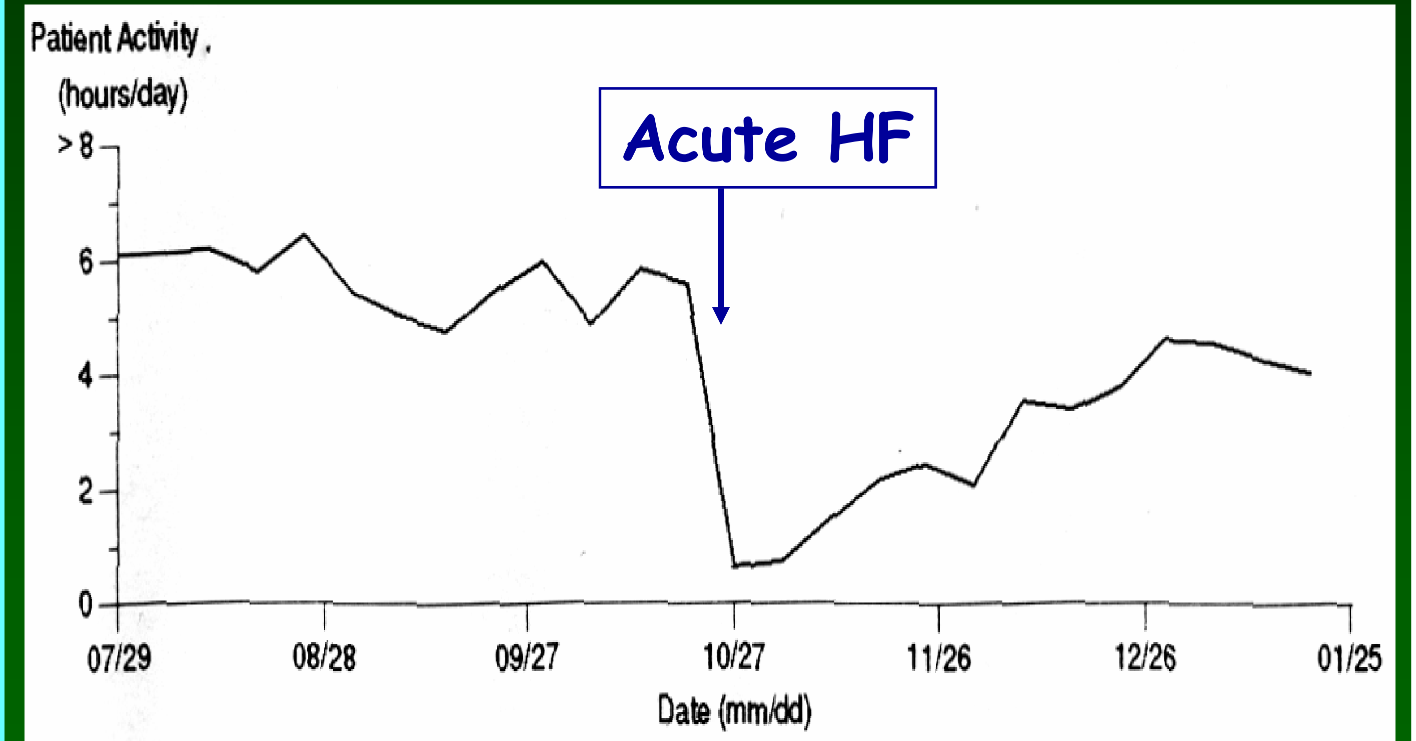
- Compatible with an implantable system
- Acceptable battery energy consumption
- Changes in Parameter should antedate the onset of clinical heart failure so that corrective measures can be taken
- Sensor data should be readily available (web base)
- Acceptable low false alarm rate
- Clinical proof

Current Sensors for Moniting HF

Type	Activity	HRV	SaO2	PAP	PEA	Impedance
Special lead	-	-	+	+	+	-
Energy Consumption	L	L	M	M	M	M
Changes precedes HF Web-based	-	16 days	?	4-5 days	-	18 days
Data Availability	-	-	-	Yes	-	Pending
False-positive	N/A	2.4/yr	N/A	N/A	N/A	1.5/yr
Clinical proof	-	-	-	+	-	-

Monitor HF: Patient Activity

- Logs patient activity above a sedentary level
- Correlates to change in 6-min walk test[1]
- Daily for a week weekly for a year



Khadiresan V, et al., AJC, 2002

Changes in HRV Predicts Hospitalization

Adamson PB et al Circ 2005; 110: 2389-2394

Background :

HRV indirectly measures autonomic tone and may be of prognostic importance

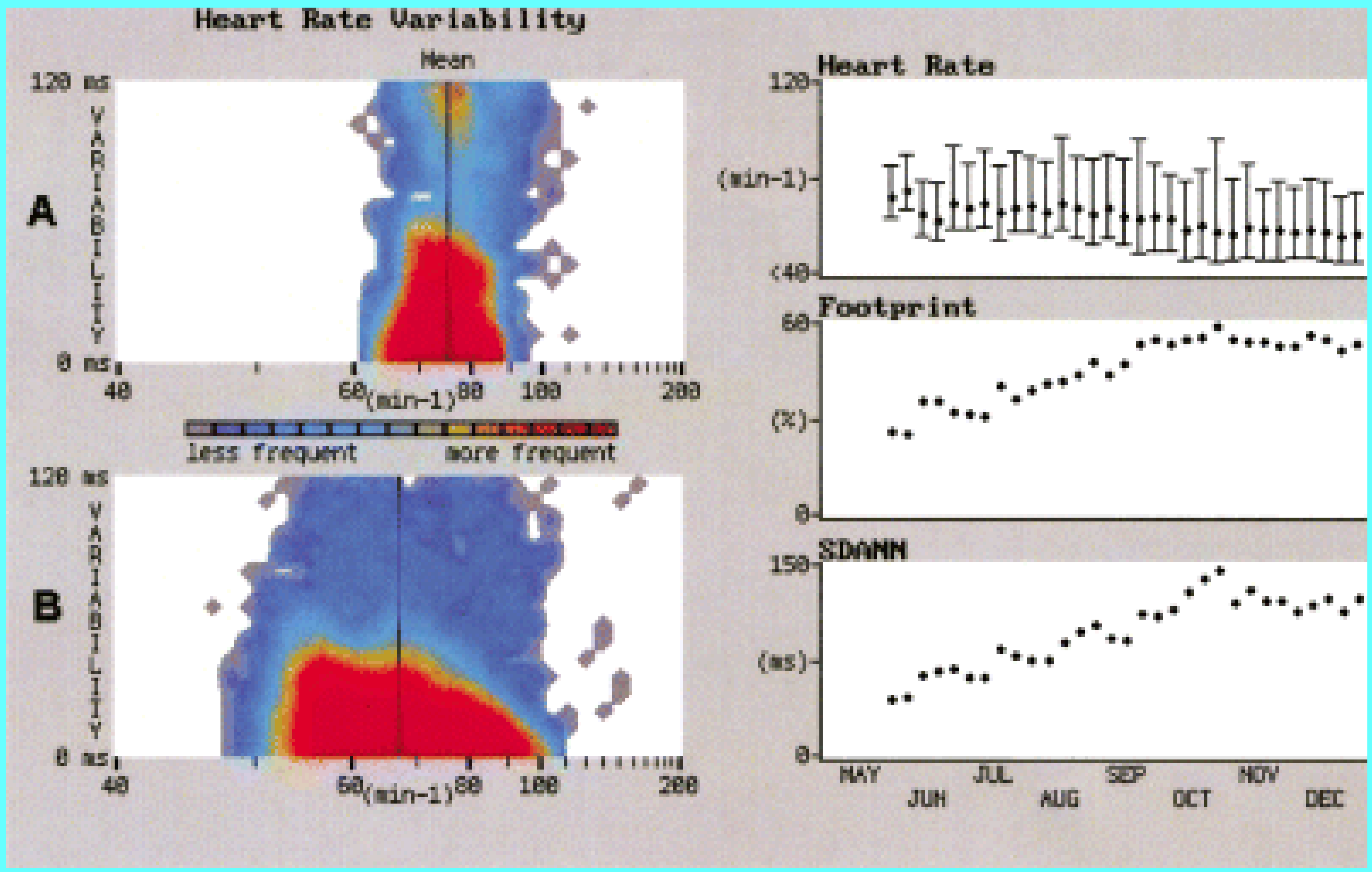
Pts & Methods :

397 pts with NYHA III/IV HF received Insync III device. Data on 5-minute median atrial-atrial intervals (SDAAM), activity and right time heart rate were related to clinical events

Results :

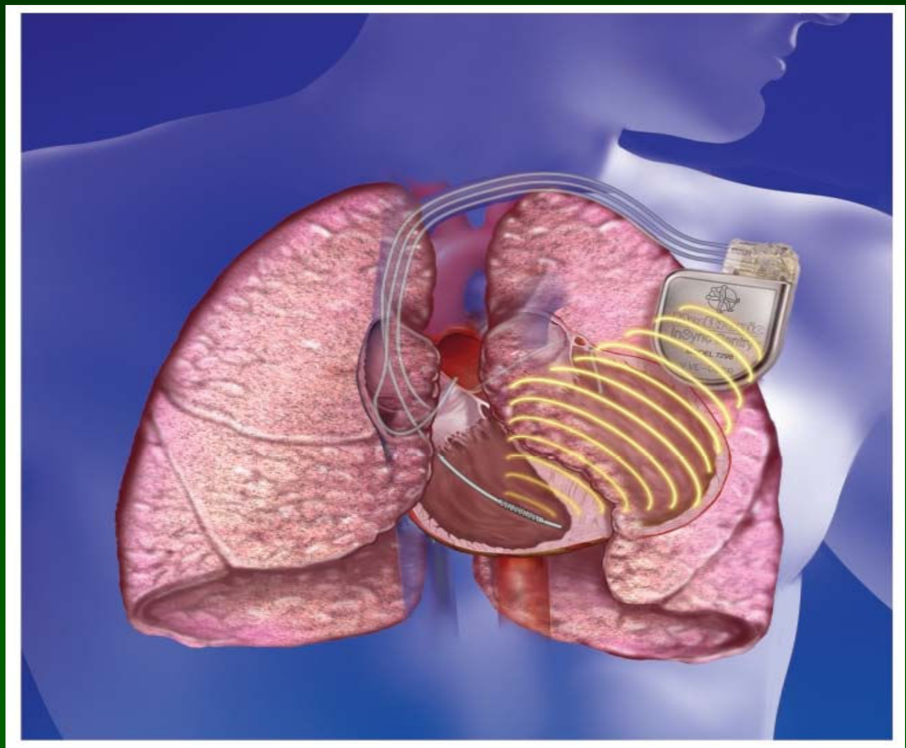
SDAAM <50ms over 4 weeks identified high risk for death and hospitalization. SDAAM is 70% sensitive in predicting hospitalisation at 16days before, with 2.4 false-positive alarm/yr

HRV Trending



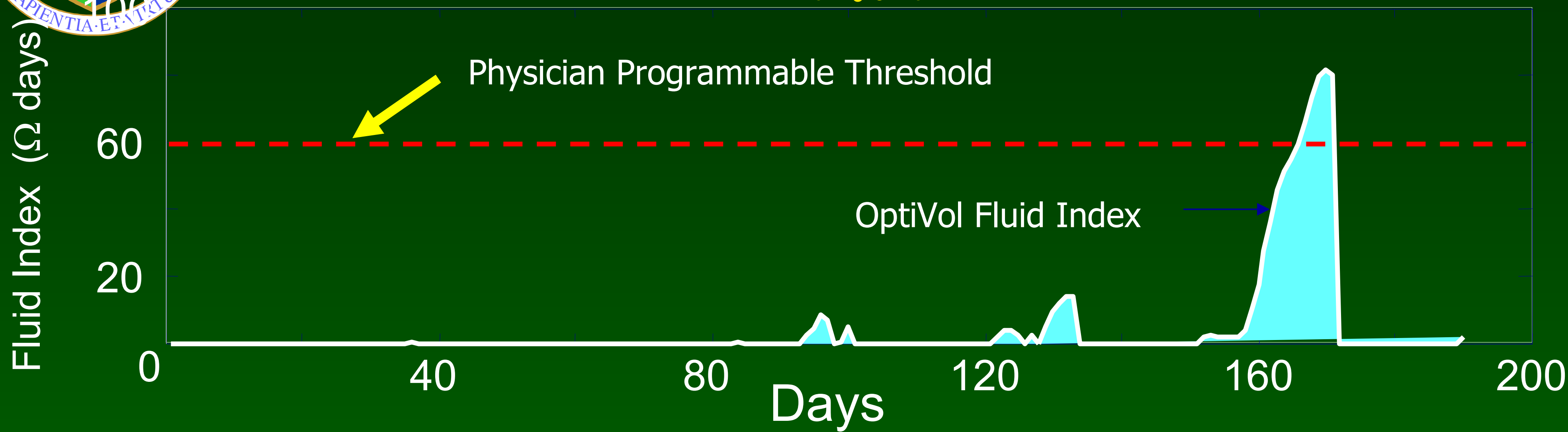
Carlson G, et al JCE 2005

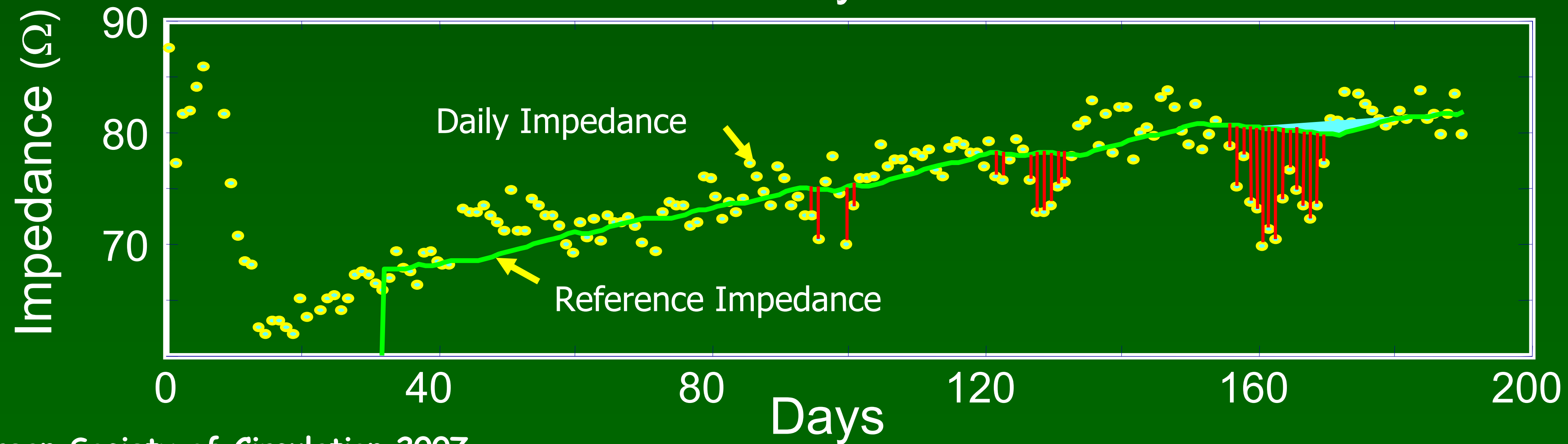
OptiVol™ Intrathoracic Impedance Measurements



Worsening Heart Failure → Pulmonary Congestion → Decreased Intrathoracic Electrical Impedance

Algorithm Developed to Track Fluid Accumulation





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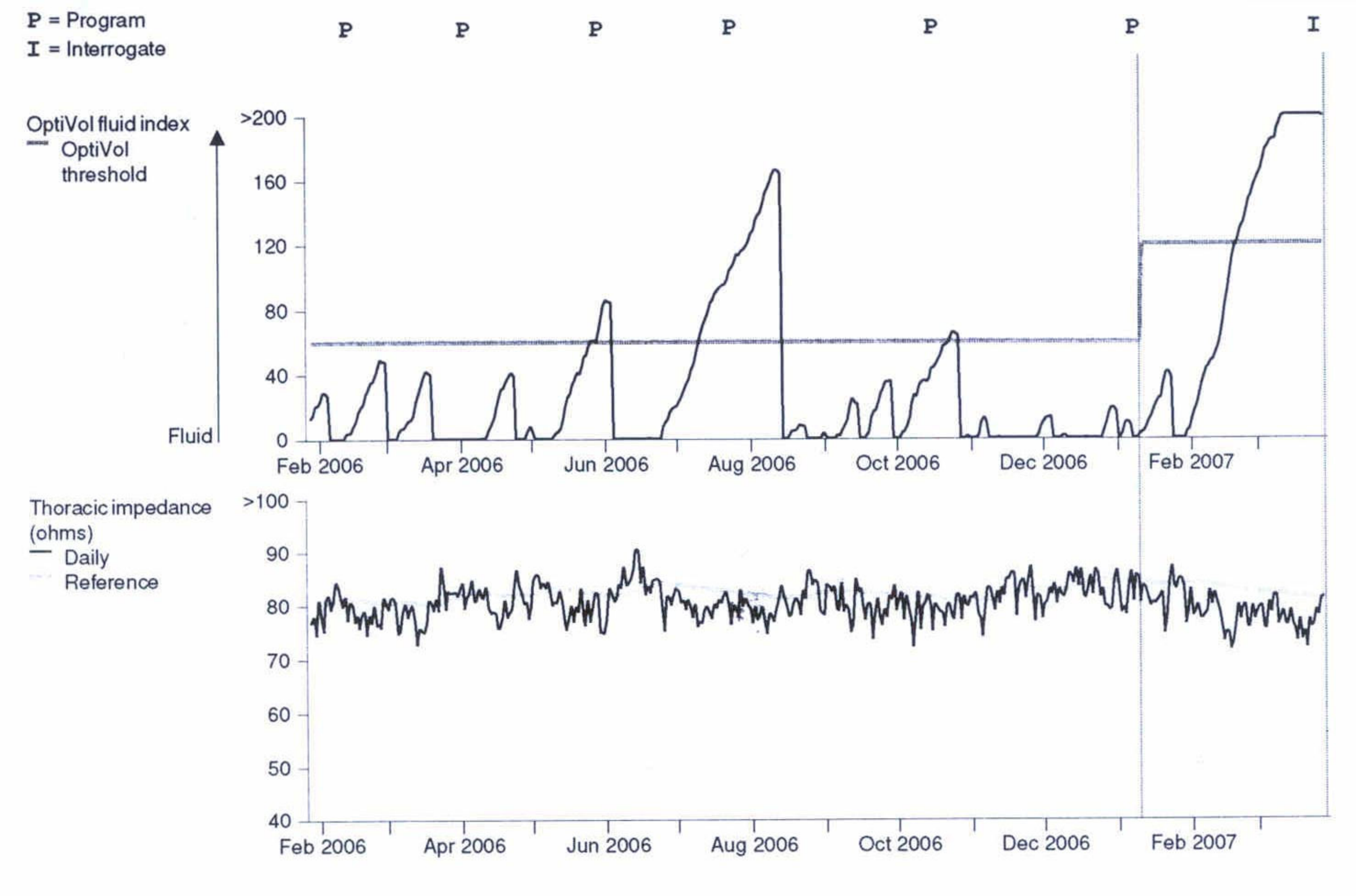
Medtronic data on file


P = Program
I = Interrogate
P
P
P
P
P
P
I
OptiVol fluid index
OptiVol threshold
Fluid
>200
160
120
80
40
0
Feb 2006
Apr 2006
Jun 2006
Aug 2006
Oct 2006
Dec 2006
Feb 2007
Thoracic impedance (ohms)
Daily
Reference
>100
90
80
70
60
50
40
Feb 2006
Apr 2006
Jun 2006
Aug 2006
Oct 2006
Dec 2006
Feb 2007

Impedance for Fluid Status

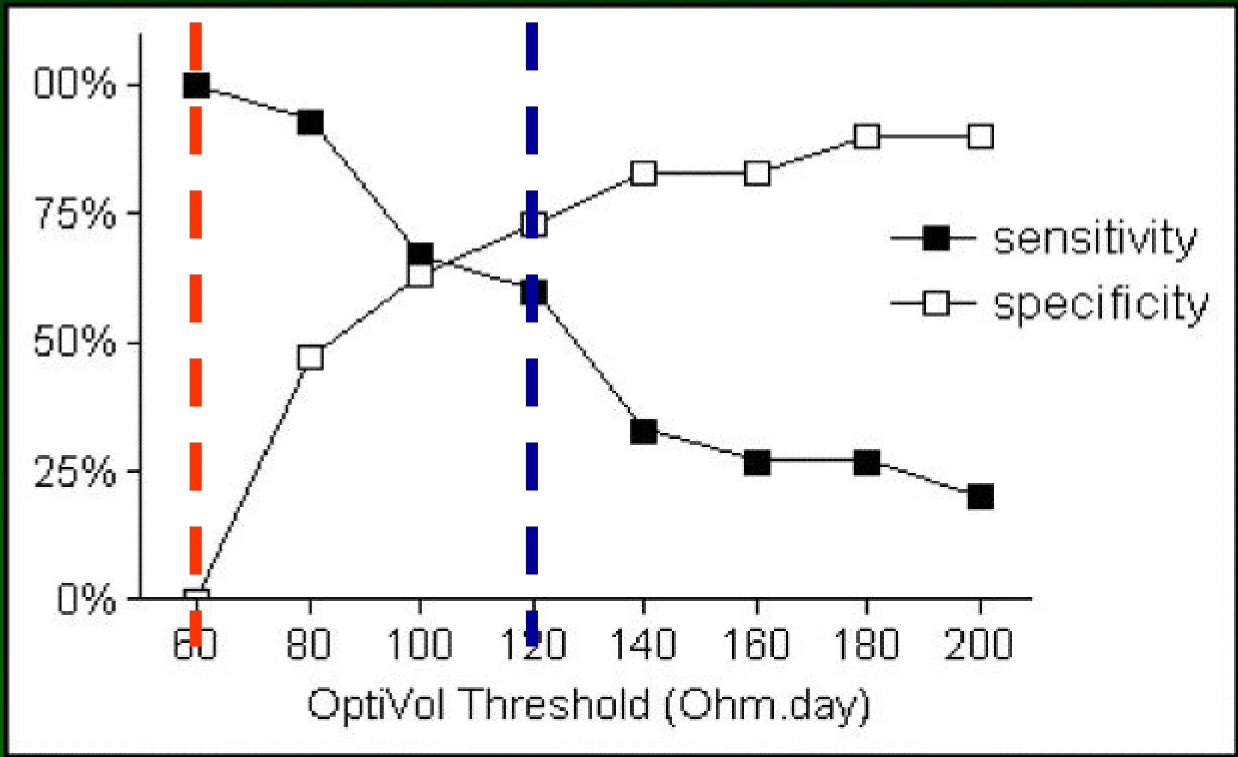
Advantages :

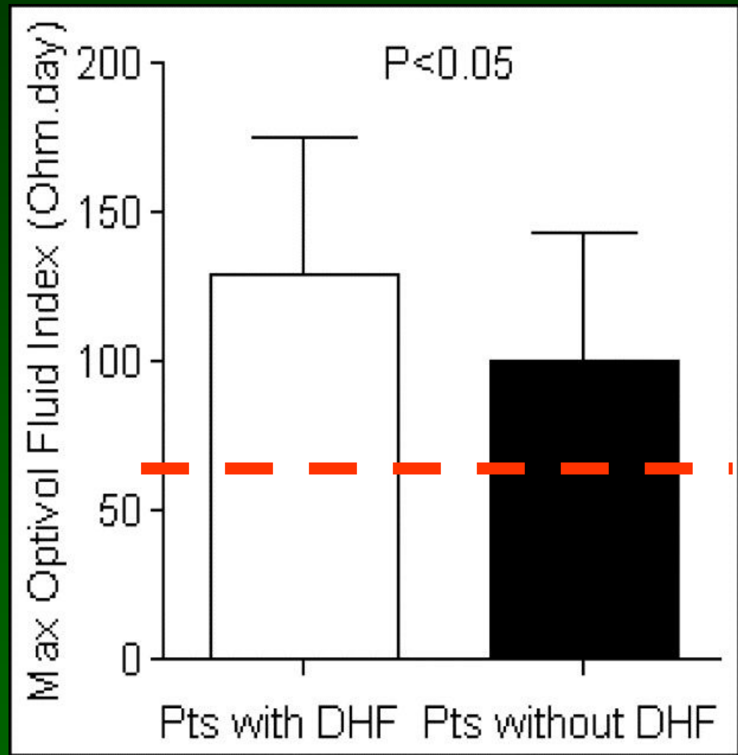
- Compatible with standard ICD coil
- Acceptable false alarm level

Disadvantages :

- Lung disease (pneumonia, COAD)
- Other changes of HF not detected
- Variable threshold level

Impedance for Fluid Status



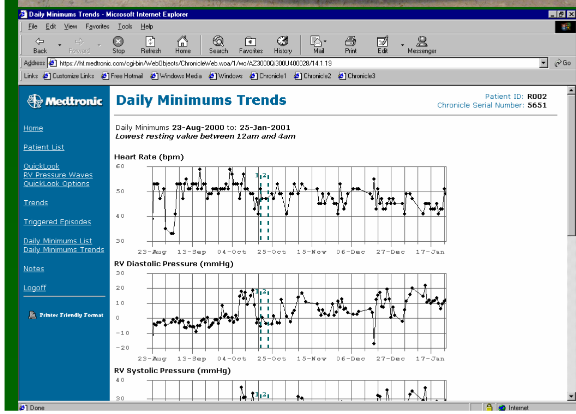


- -115 ICD pts with OptiVol monitoring for 9 months
- - only 15/45 alert events were true +ve

Ypenburg et al. Am J Cardiol. 2007

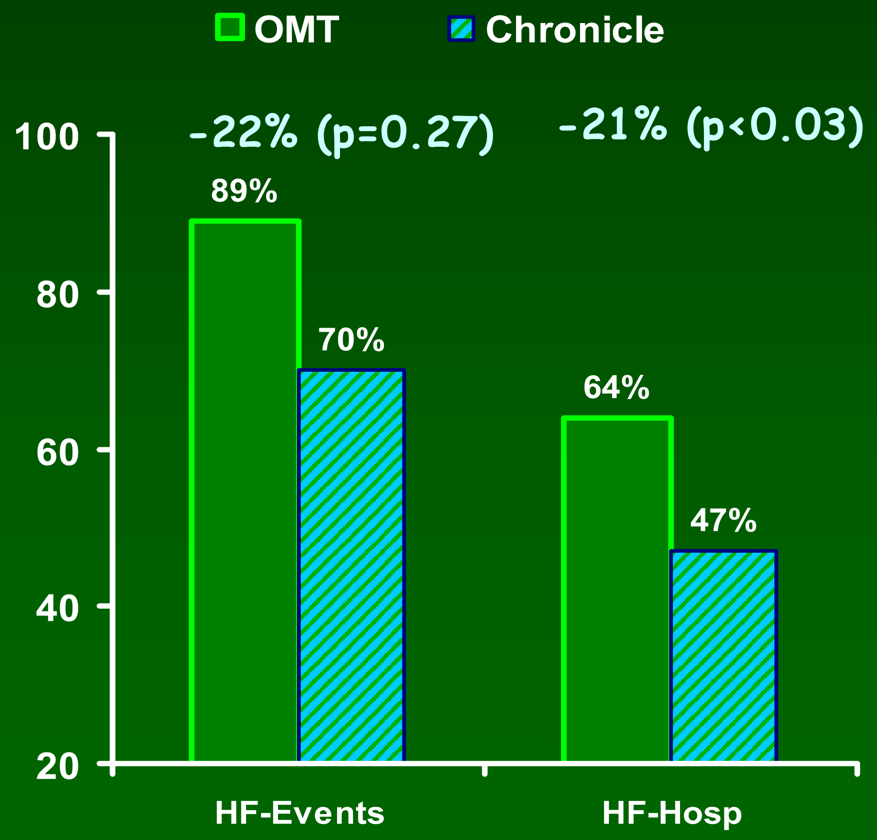
Chronicle® System Components

- Implantable Hemodynamic Monitor
- Pressure Sensor Lead
- External Pressure Reference
- Programmer and software
- Remote Monitor
- Patient Management Information Network

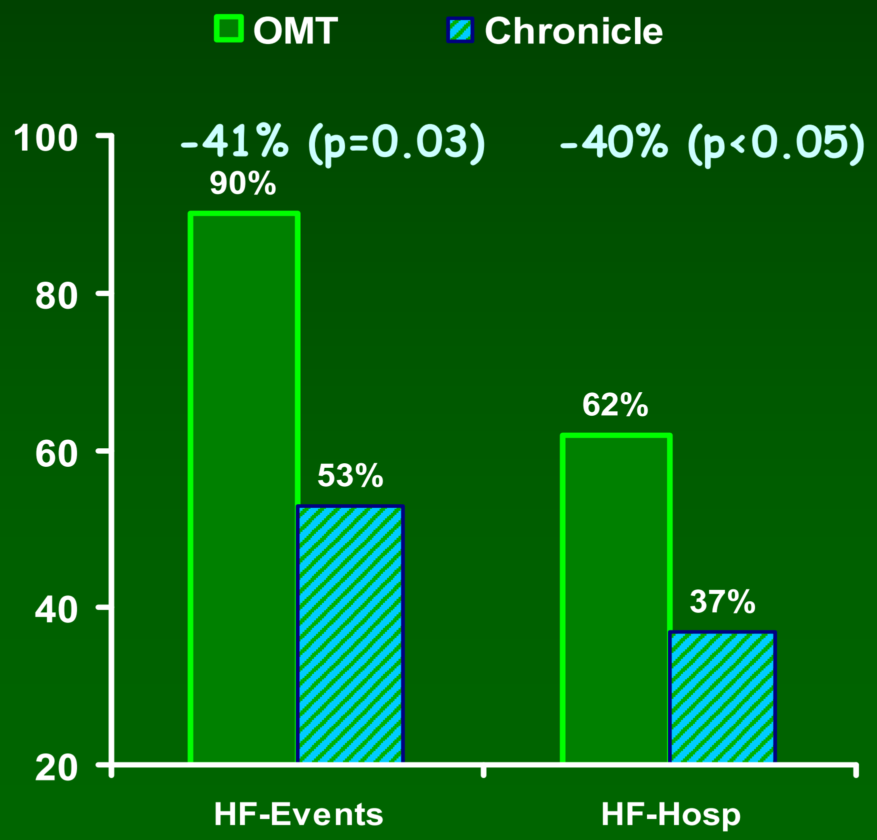


Chronicle Offers Management to Patient with Advanced Signs and Symptoms of Heart Failure (COMPASS-HF) trial.

All patients



Class III pts



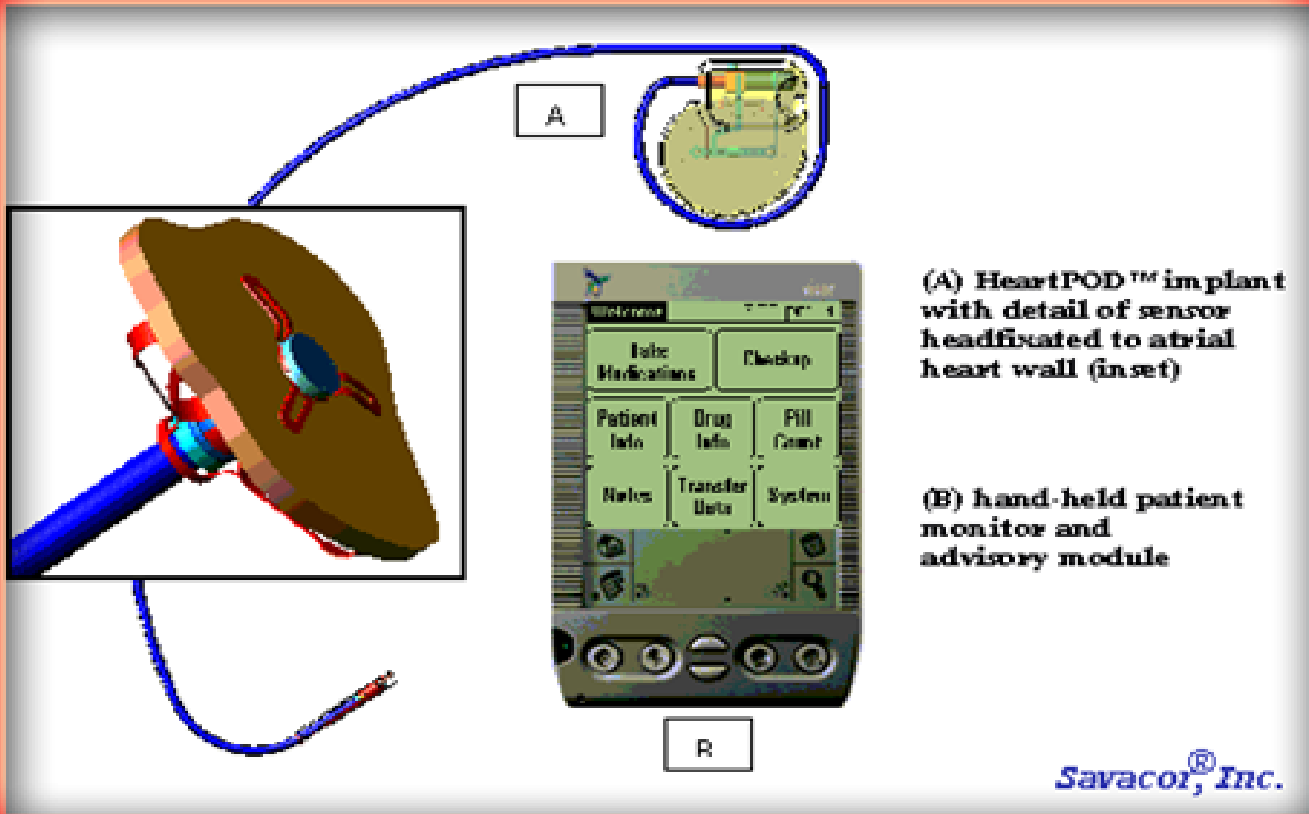
Bourge RC. Late Breaking New ACC 2005

Chronicle Offers Management to Patient with Advanced Signs and Symptoms of Heart Failure (COMPASS-HF) trial.

- Prolonged time to heart failure in Class III Chronicle patient
- There was no lead failure, and <10% system complications
- Reduced hospitalization on top of OMT + HF specialist care (21%)
- 33% reduction in proportion of pts
- Estimated saving for Class III pts based on 500,000 HF hospitalization, $3 Billion, 41% reduction resulted in $1.2 billion / yrs (Dr. Jamie Conti)

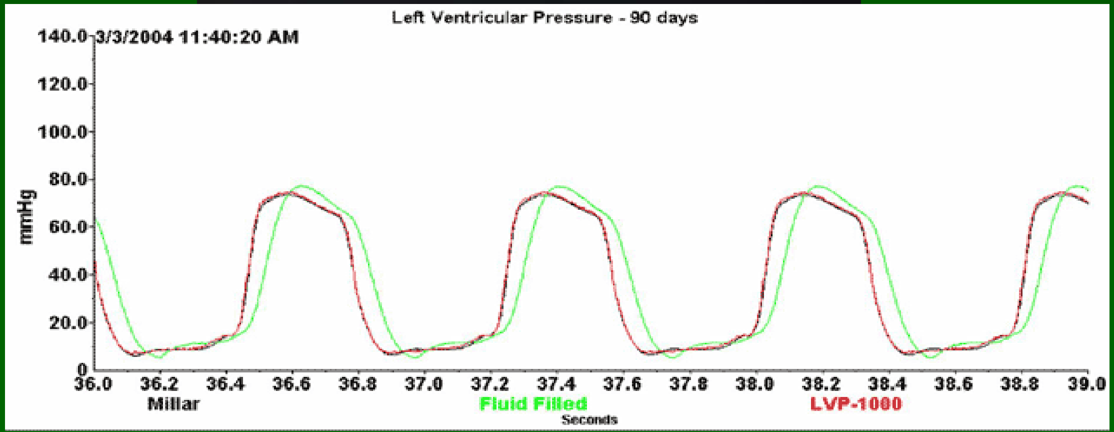
Bourge RC. Late Breaking New ACC 2005

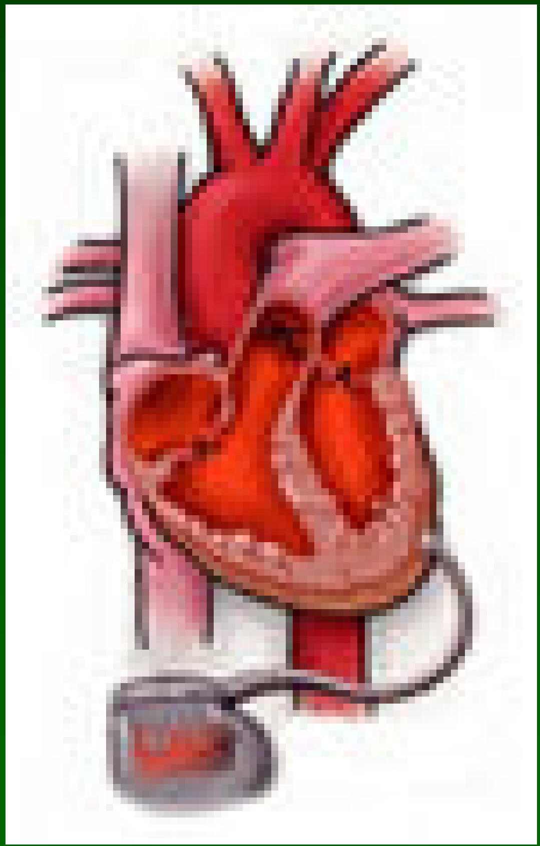
Homeostasis 1 trial: HeartPOD™- LA Pressure



Left Ventricular Pressure Monitoring

LVP-1000 Transmitter





Transoma Medical (St. Paul, MN)

Conclusions

- Leadless defibrillation and pacing are feasible, but the clinical implications remains unclear
- In selected patients with HF, rate adaptive pacing with CRT improved exercise capacity. ? Role in Non-CRT pts
- ? Optimal types of sensors for HF monitoring

Conclusions

- Implanted sensors have potentials to provide useful cardiovascular and non-cardiovascular data in HF.
- However, those sensors information remained open-loop
- ? Role of combined sensors data for HF monitoring
- ? Which data provide better prediction for HF