NONINVASIVE ECG IMAGING [ECGI] OF CARDIAC ARRHYTHMIAS

Disclosure: Y. Rudy is on the scientific advisory board and holds equity in CardioInsight Technologies (CIT). CIT does not support any research conducted by Y.R., including this work

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Cardiac arrhythmias are a major cause of death and disability
(prevalence: 3.9 million/yr ; mortality: about 325,000/yr in U.S. ; mortality is estimated at 7 million/yr worldwide)

Current Method for NonInvasive Diagnosis

- **ECG (or its extension to many torso surface electrodes) – Obtains and analyses data on the body surface, far away from the heart, and cannot resolve or locate electrical events in the heart**

- **Lacks sensitivity**
  Cannot detect arrhythmogenic substrate in many cases, or sufficiently early for preventive intervention

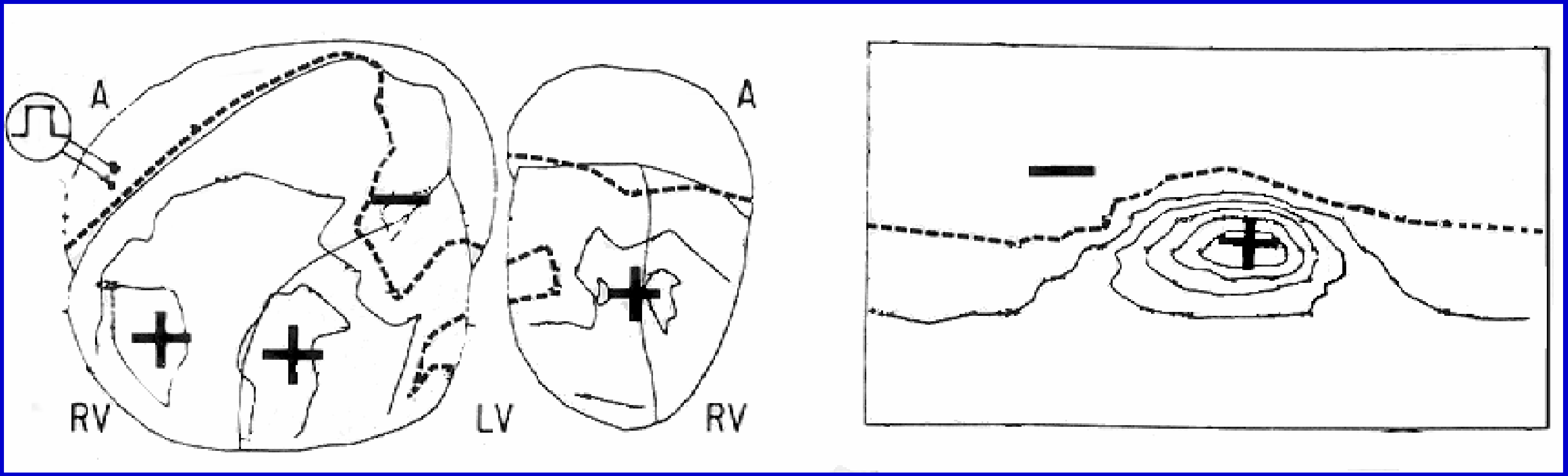
- **Lacks specificity**
  Cannot provide specific diagnosis of mechanism for specific therapy

How are Torso ECG Potentials Generated from Epicardial Potentials?

$$V_{ECG} = \frac{1}{4\pi}\int V_{EPI}\nabla\left(\frac{1}{r}\right)ds + [\text{Other Terms}]$$

Over Entire
Heart Surface

Epicardial Potentials **Torso Potentials**



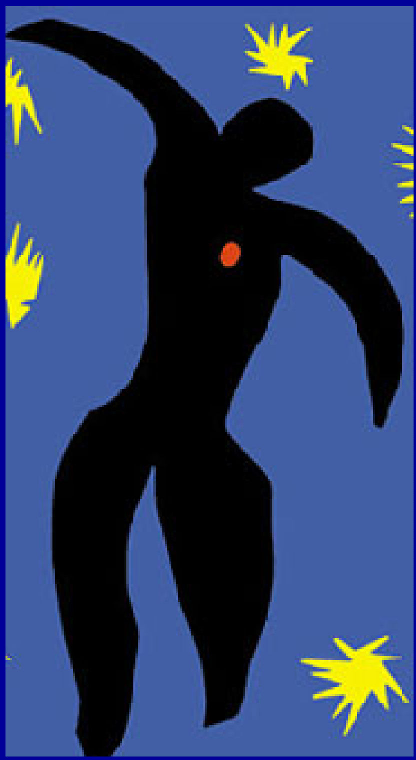
Ramsey *et. al.*, *Circ Res*, 1977

Electrocardiographic Imaging (ECGI)

- Noninvasive imaging is a corner stone of the practice of modern medicine (CT, MRI, Ultrasound). It is used for risk stratification, diagnosis, guidance of therapy, and follow-up

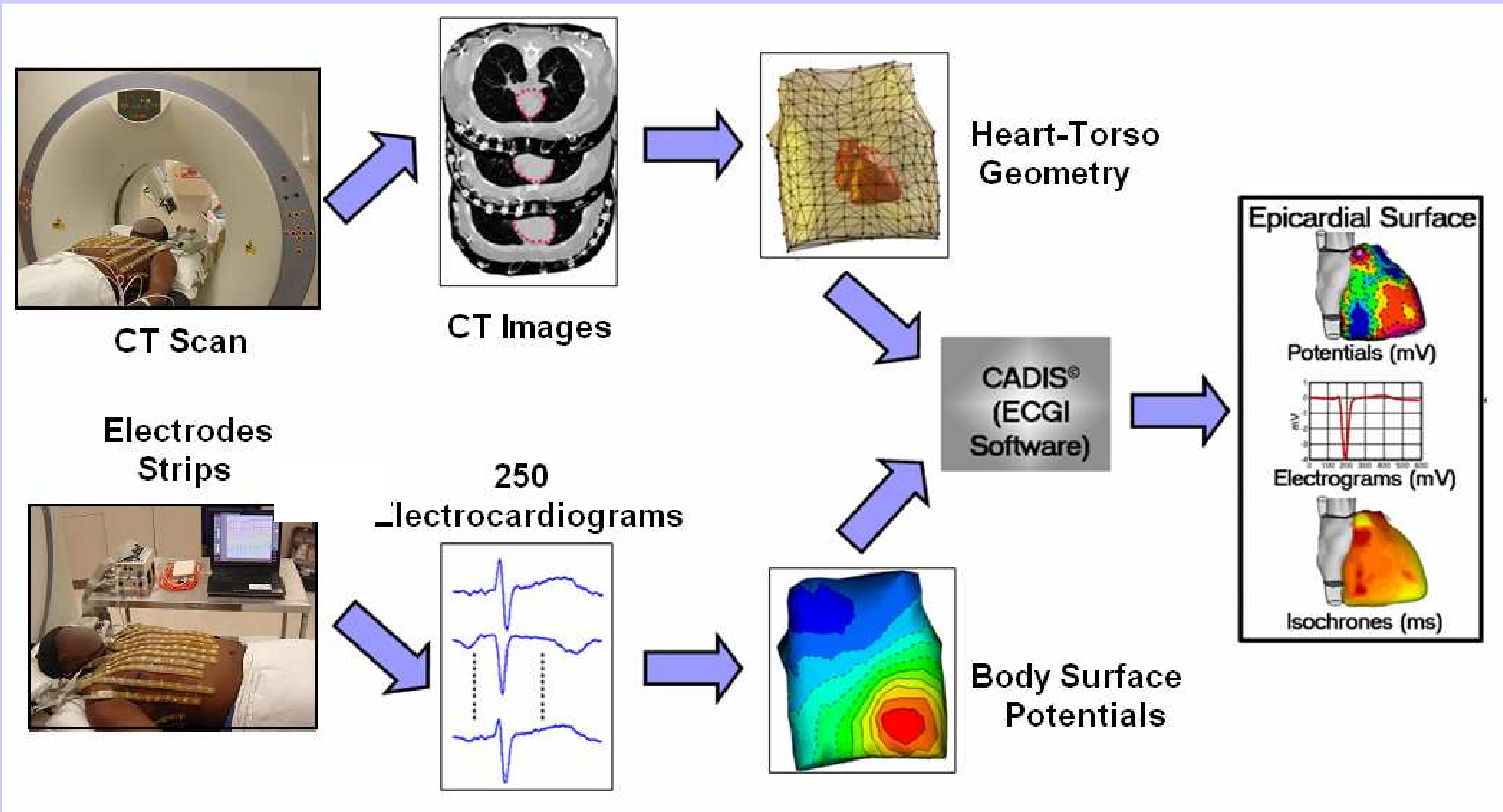
- Noninvasive imaging is also used extensively for research of disease processes in humans

- Despite the need, a noninvasive imaging modality for cardiac arrhythmias does not exist yet



ECGI is a new imaging approach that reconstructs potentials, electrograms, isochrones and repolarization patterns on the heart surface from body-surface electrocardiographic measurements, noninvasively

The ECGI Procedure



Nature Medicine 2004;10:422-428

PNAS 2006;103:6309-6314

http://rudylab.wustl.edu

ECGI Theory

- **Volume between the heart and the body surface is source free - governed by Laplace's Equation:**

$$\nabla^2\Phi=0$$

$$\nabla^2 \phi = 0$$

Green's 2nd theorem: integrals of Φ over the heart and torso surfaces

(Governing Equation Laplace's equation)

Boundary Element Method

Forward Problem

$$[\Phi_T] = [\mathbf{A}][\Phi_E]$$

Torso potential

Heart (epicardial) potential

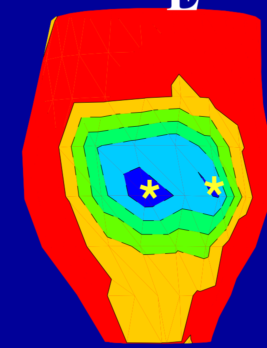
Cardiac Inverse Potential Problem

Φ_T

Inverse Problem

The reconstruction of Φ_E from Φ_T is an ill-posed inverse problem.

Φ_E



Cannot simply invert

$$\left[\Phi_T\right] = \left[A\right]\left[\Phi_E\right]$$

because A is ill-conditioned and A^{-1} is close to singular

Cardiac Inverse Problem - Methods

I. Tikhonov regularization

Laplace's equation **constraint**

$$\min_{\Phi_E}\left[\left\|A\Phi_E - \Phi_T\right\|^2 + t\left\|L\Phi_E\right\|^2\right]$$

t = regularization parameter

L = Unity, Gradient

or Laplacian operator

II. Generalized Minimal Residual Method (GMRes) – an iterative approach

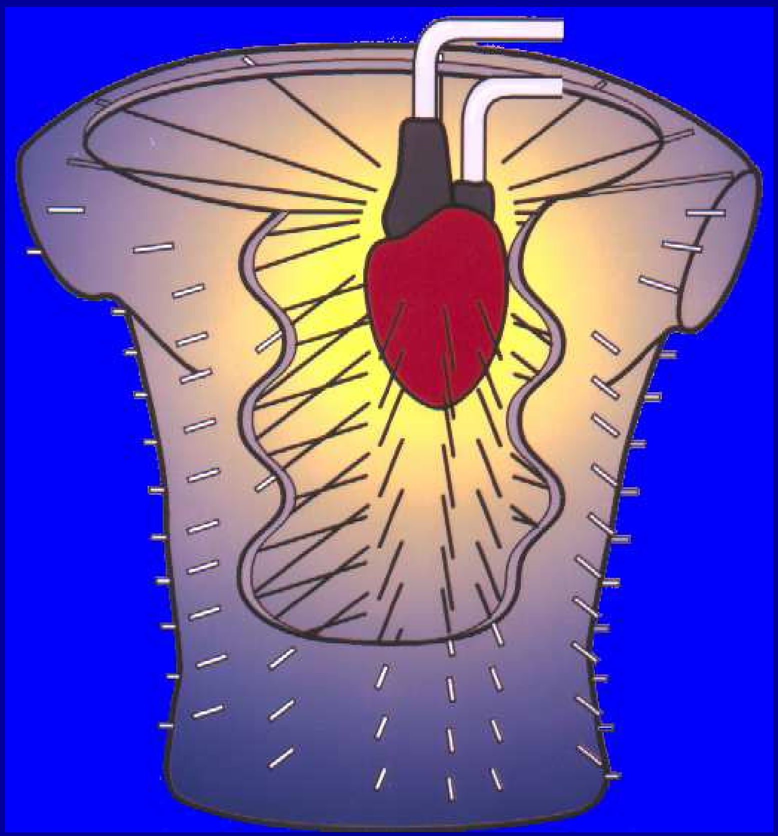
- A^{-1} is approximated by polynomial $p(A)$

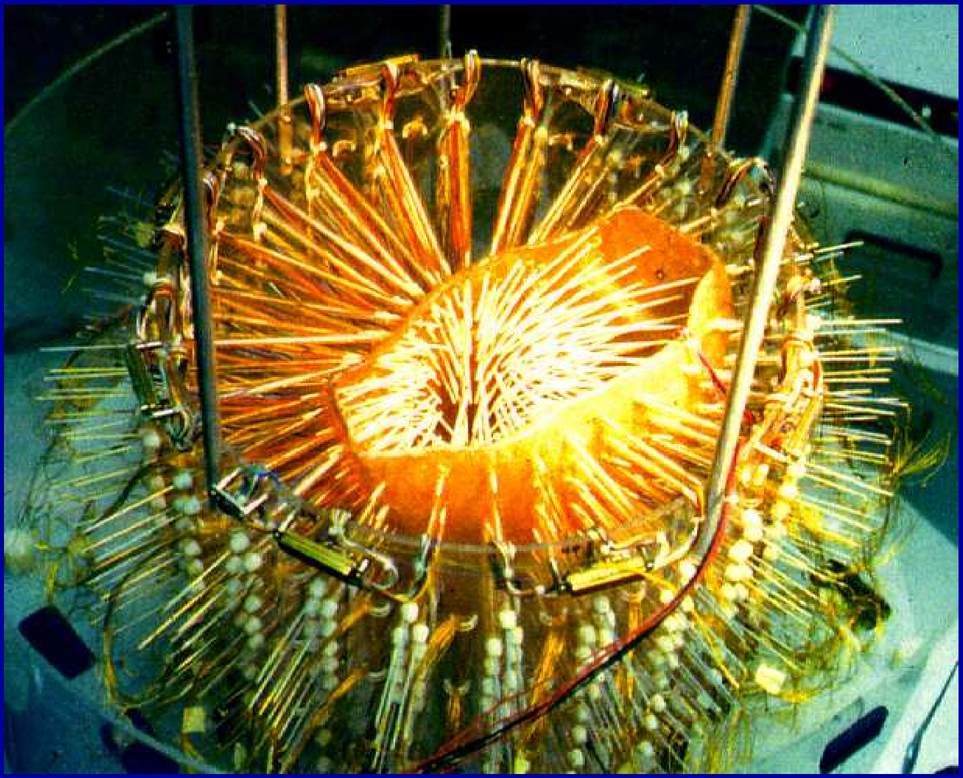
$$\boxed{\Phi_E = p(A)\,\Phi_T}$$

  - $p(A)\,\Phi_T$ defines a Krylov subspace, K
  - For n iterations, $K_n = \text{span}\{\Phi_T, A\,\Phi_T, A^2\,\Phi_T, \ldots\ldots A^{n-1}\,\Phi_T\}$
  - The order of $p(A)\,\Phi_T$ increases with each iteration
  - Residual $\|A\,\Phi_E - \Phi_T\|$ decreases with each iteration
  - Iteration stops when: residual < specified tolerance **or** number of iterations exceeds a specified maximum
  - Best iterate is chosen as the solution

Ann Biomed Eng 2003;31:981-994

Validation: Torso-Tank Experiments



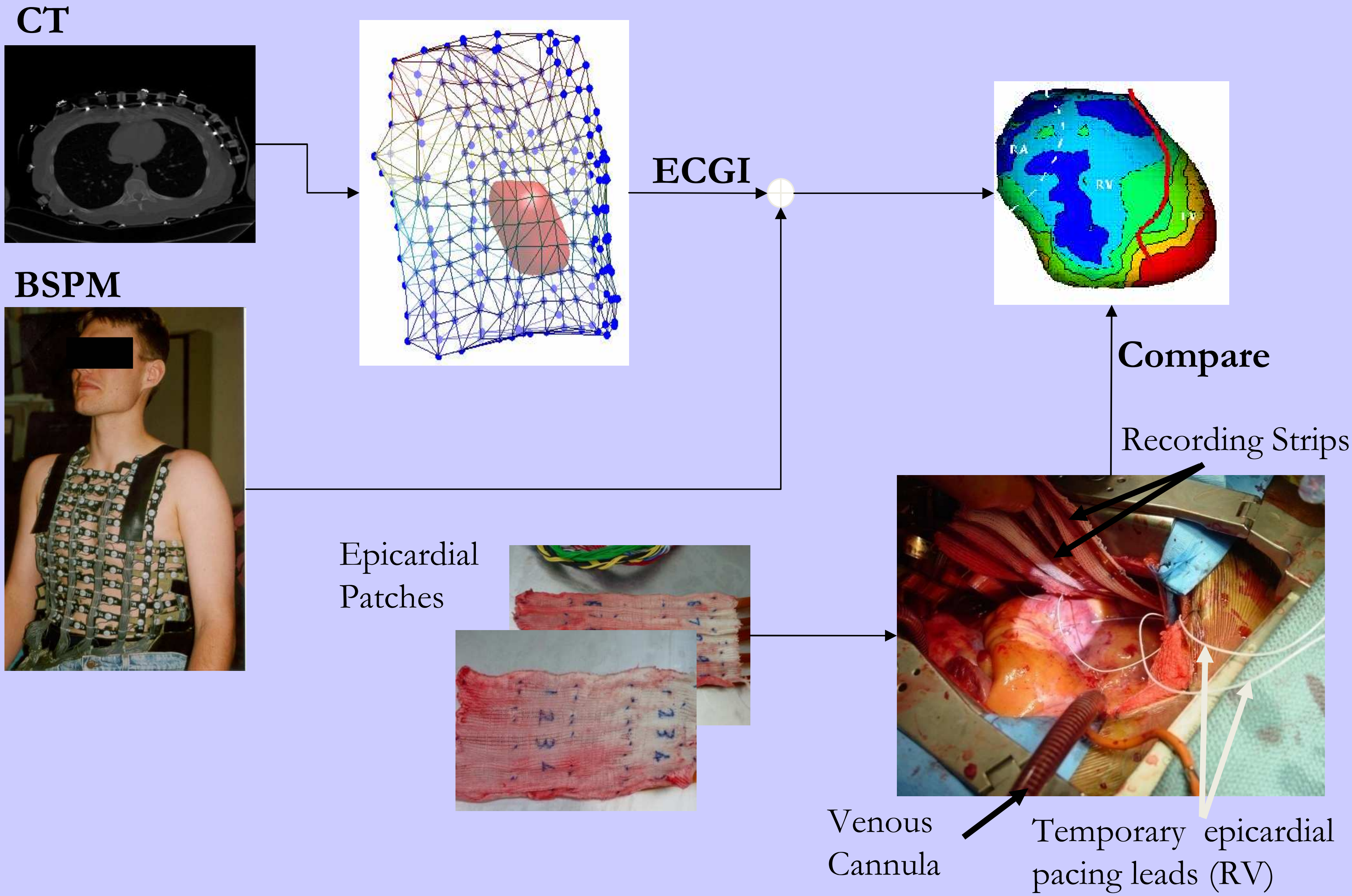


The approach was validated extensively in torso-tank and animal experiments in normal and infarcted hearts

Circulation; Circ Res; JACC; and http://rudylab.wustl.edu

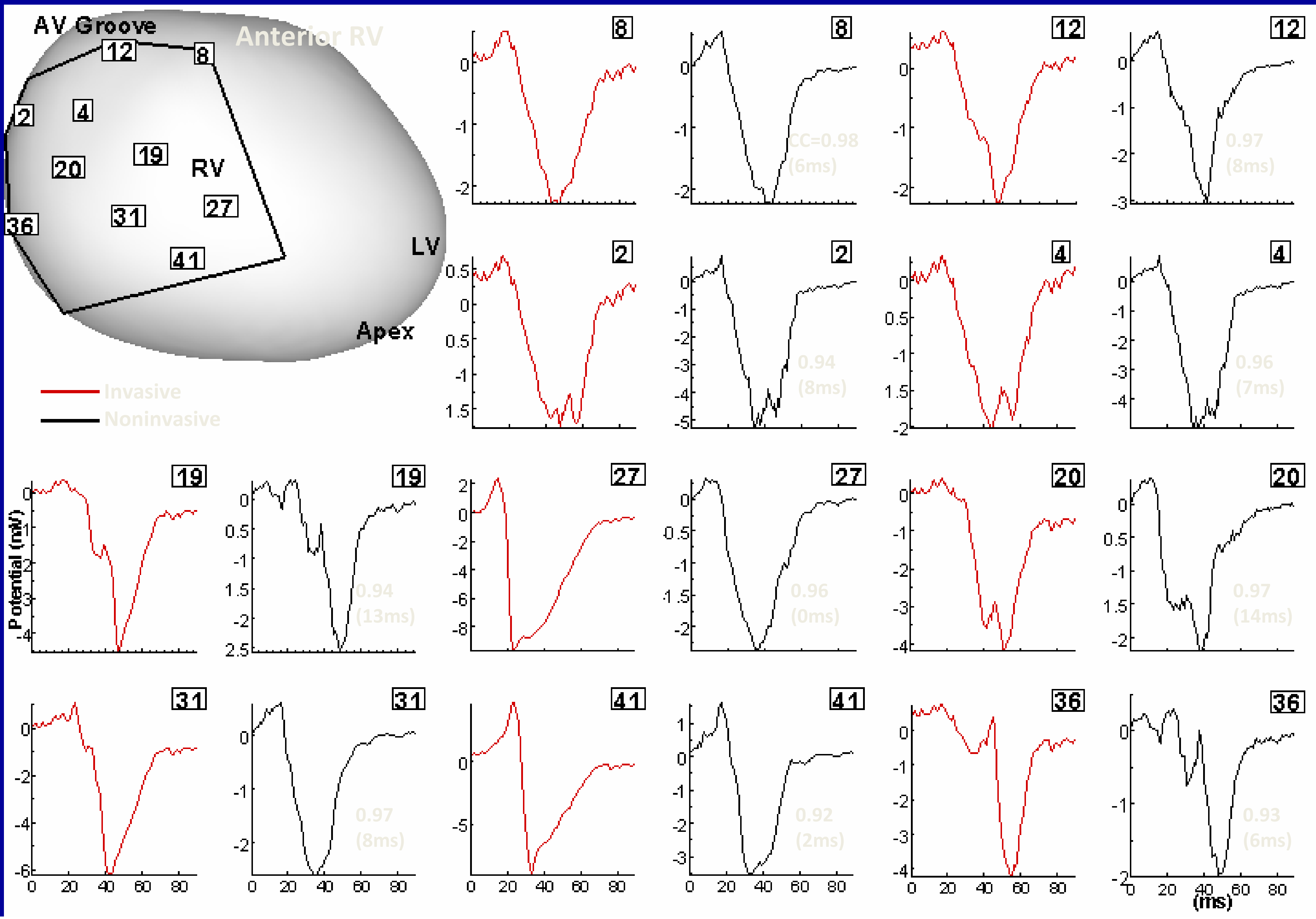
Validation by Invasive Surgical Mapping

Heart Rhythm 2005;2:339-354



Noninvasive Electrograms (Sinus Rhythm)

Heart Rhythm
2005;2:339-354



Atrial Arrhythmias

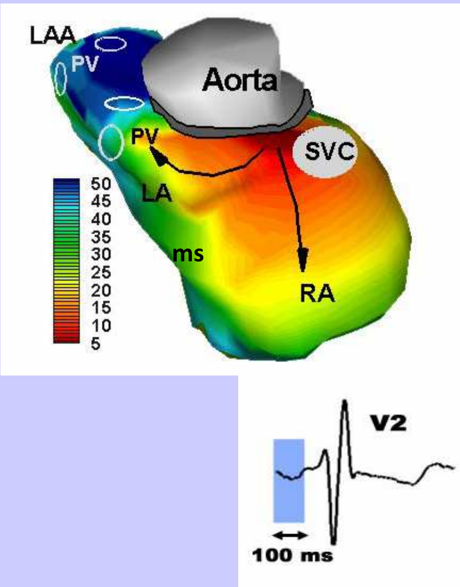
Atrial Flutter

Atrial Fibrillation

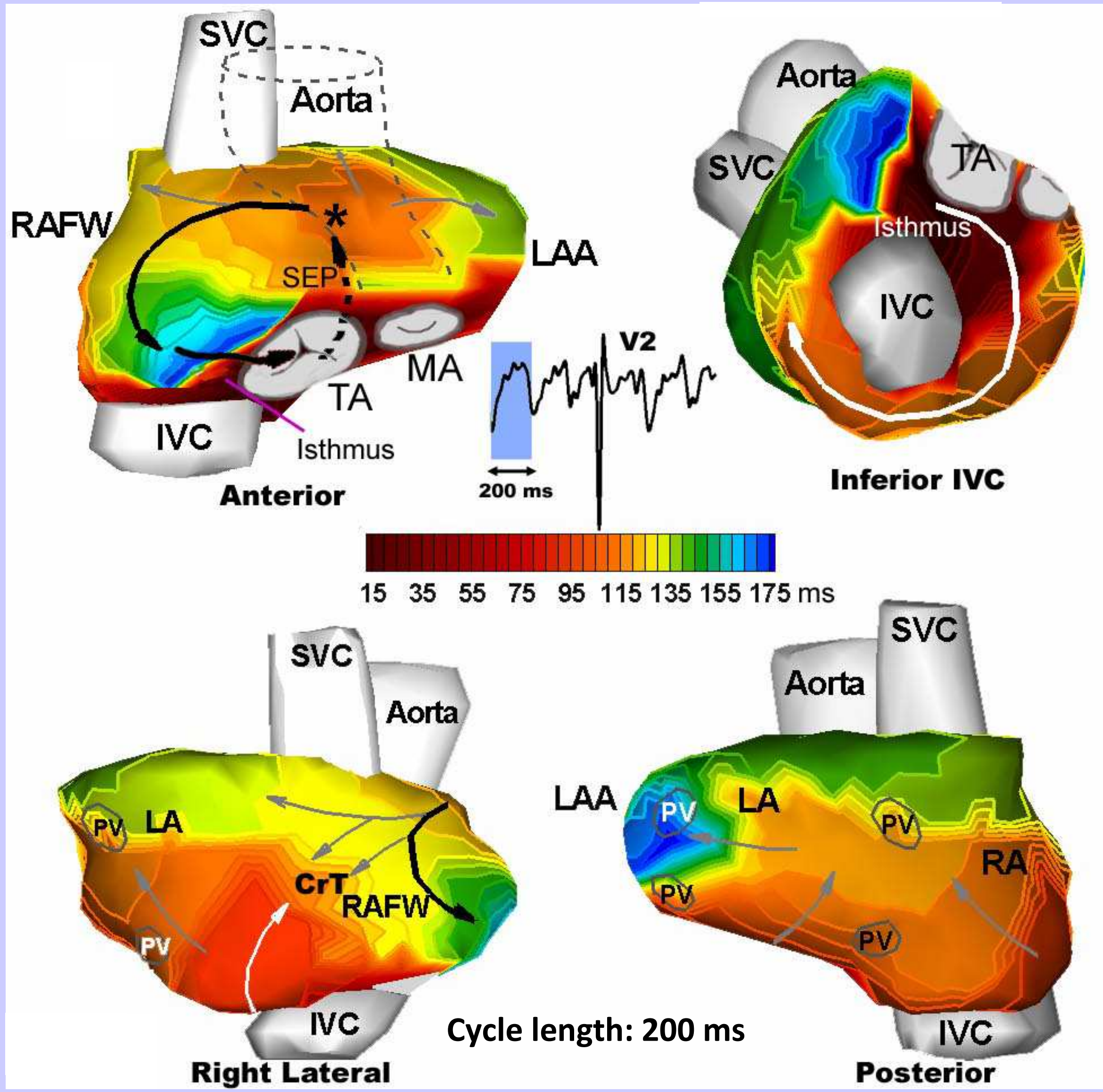
TYPICAL ATRIAL FLUTTER

Nature Medicine 2004;10:422-428

Normal Isochrones



Flutter Isochrones



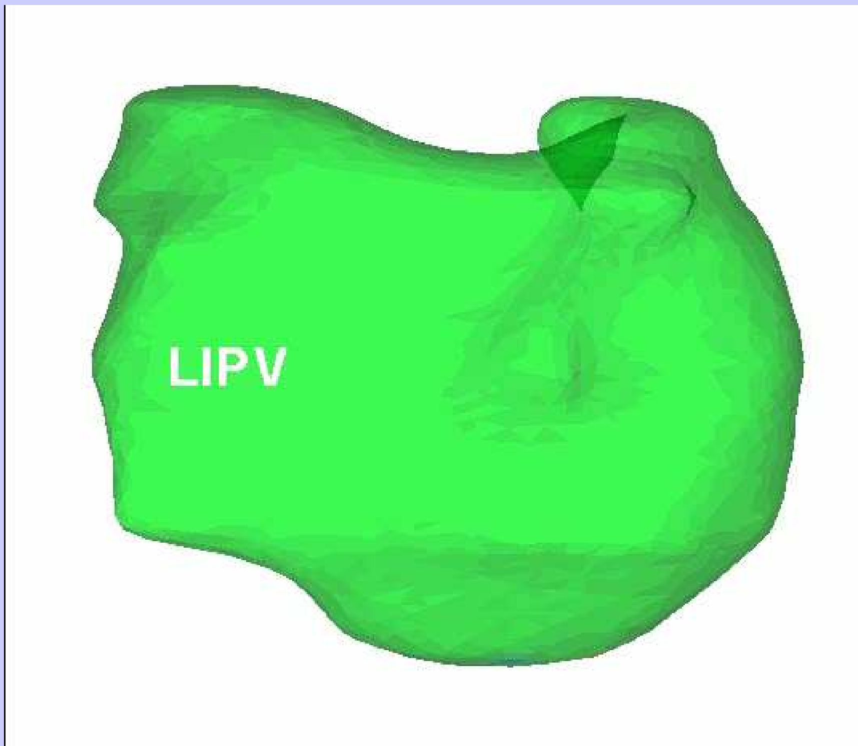
LAA: Left atrial appendage
IVC: Inferior vena cava
SVC: Superior Vena cava
TA: Tricuspid Annulus
MA: Mitral Annulus
PV: Pulmonary vein
RAFW: Right atrial free-wall
SEP: Septum
CrT: Crista terminalis.

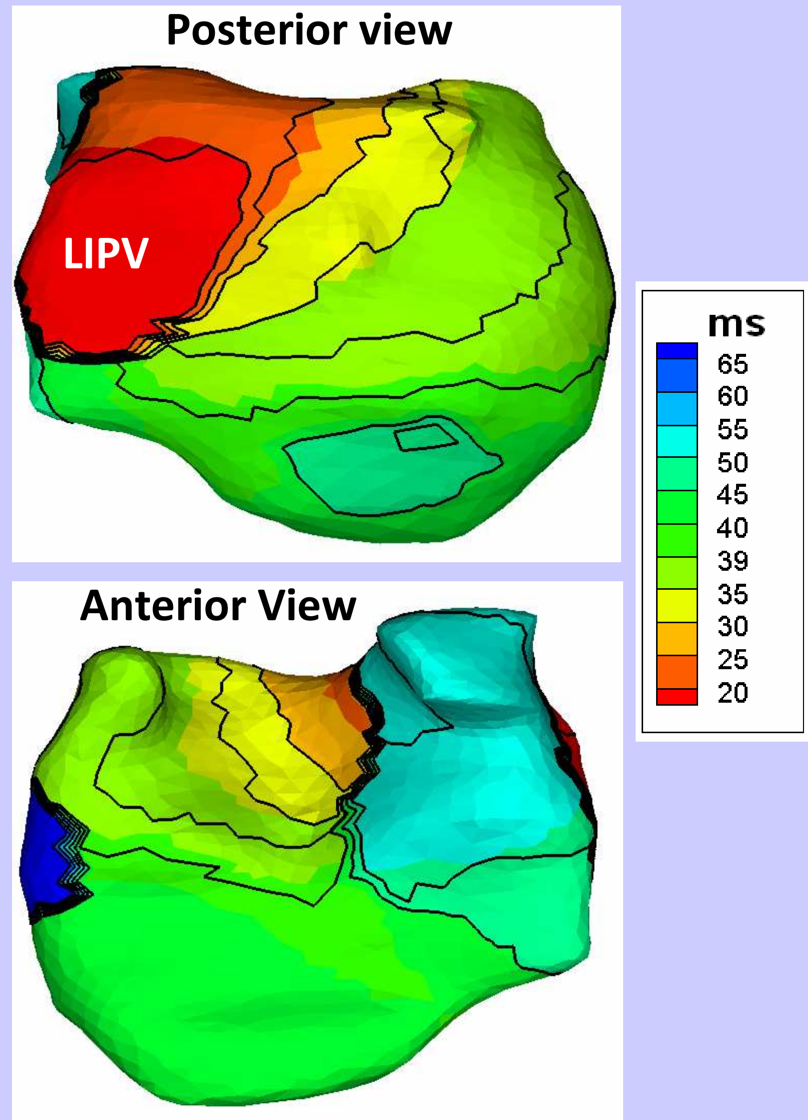
Example: PAROXYSMAL ATRIAL FIBRILLATION

CIRCULATION 2010;
22:1364-1372

Posterior View

Red: Activation Front





Both focal triggers and spiral waves are observed.

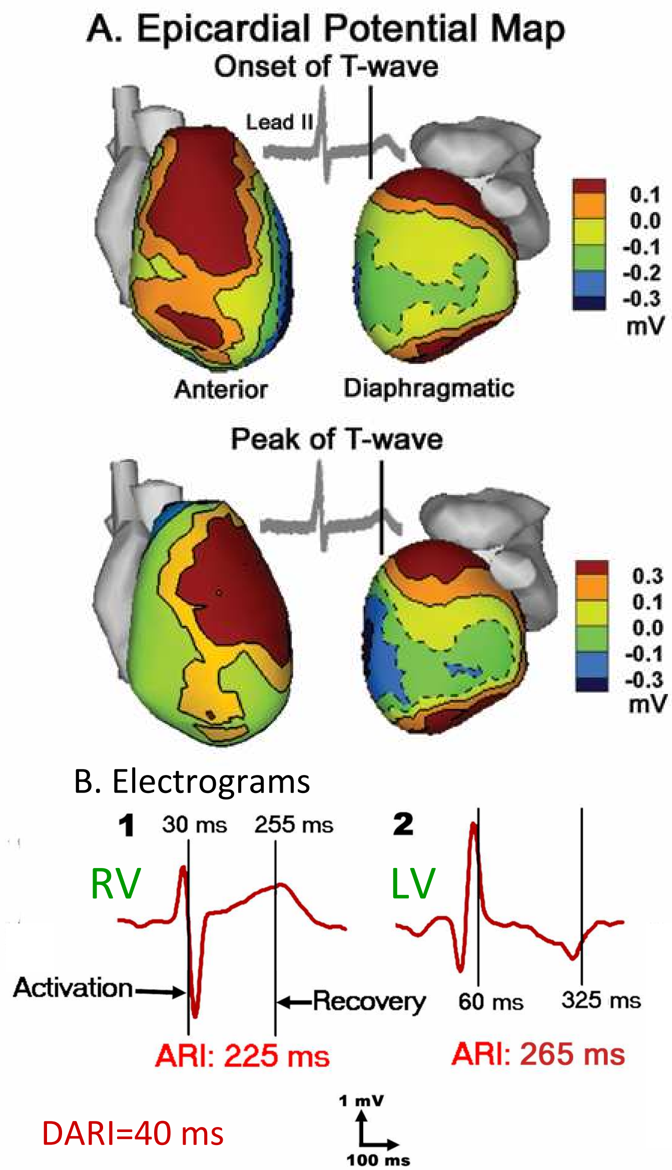
Abnormal Ventricular Repolarization

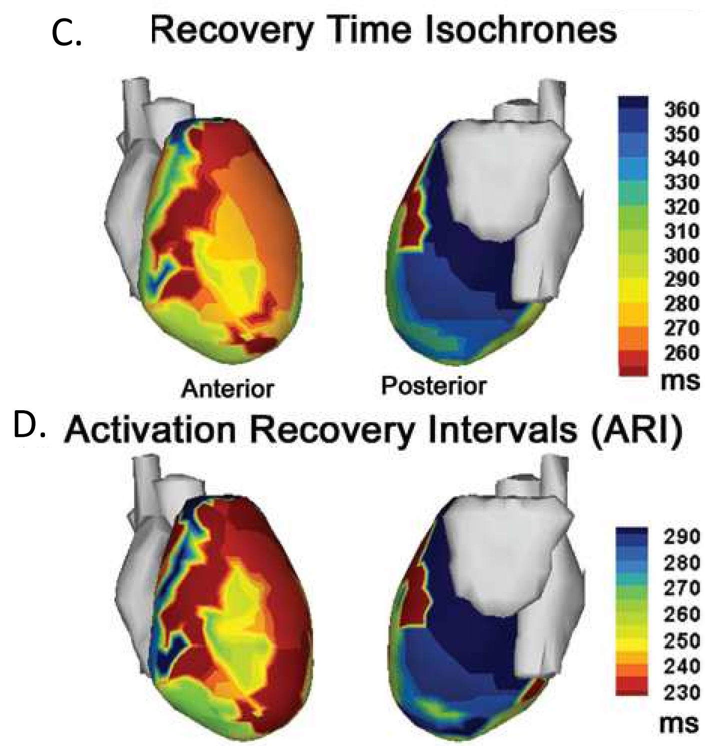
Early Repolarization Syndrome

Normal Ventricular Repolarization

Nature Medicine 2004;10:422-428

PNAS 2006;103:6309-6314



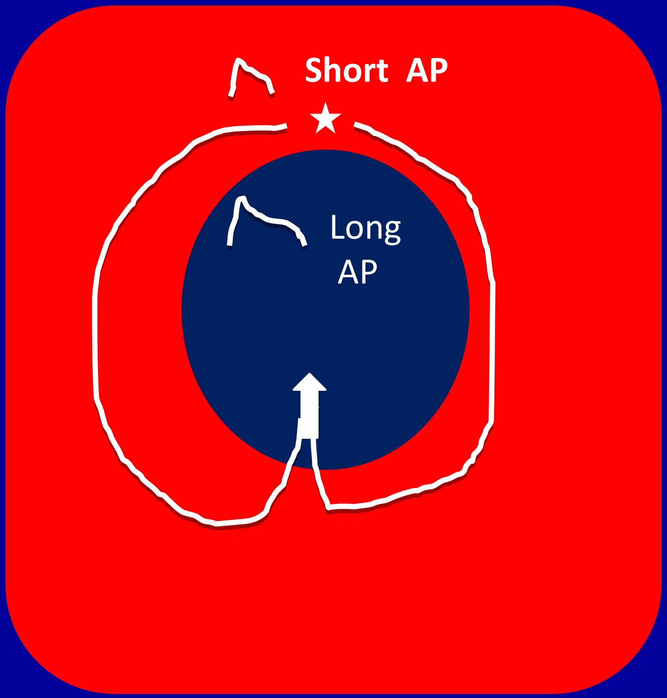


<u>7 SUBJECTS</u>

Mean ARI=235 ms

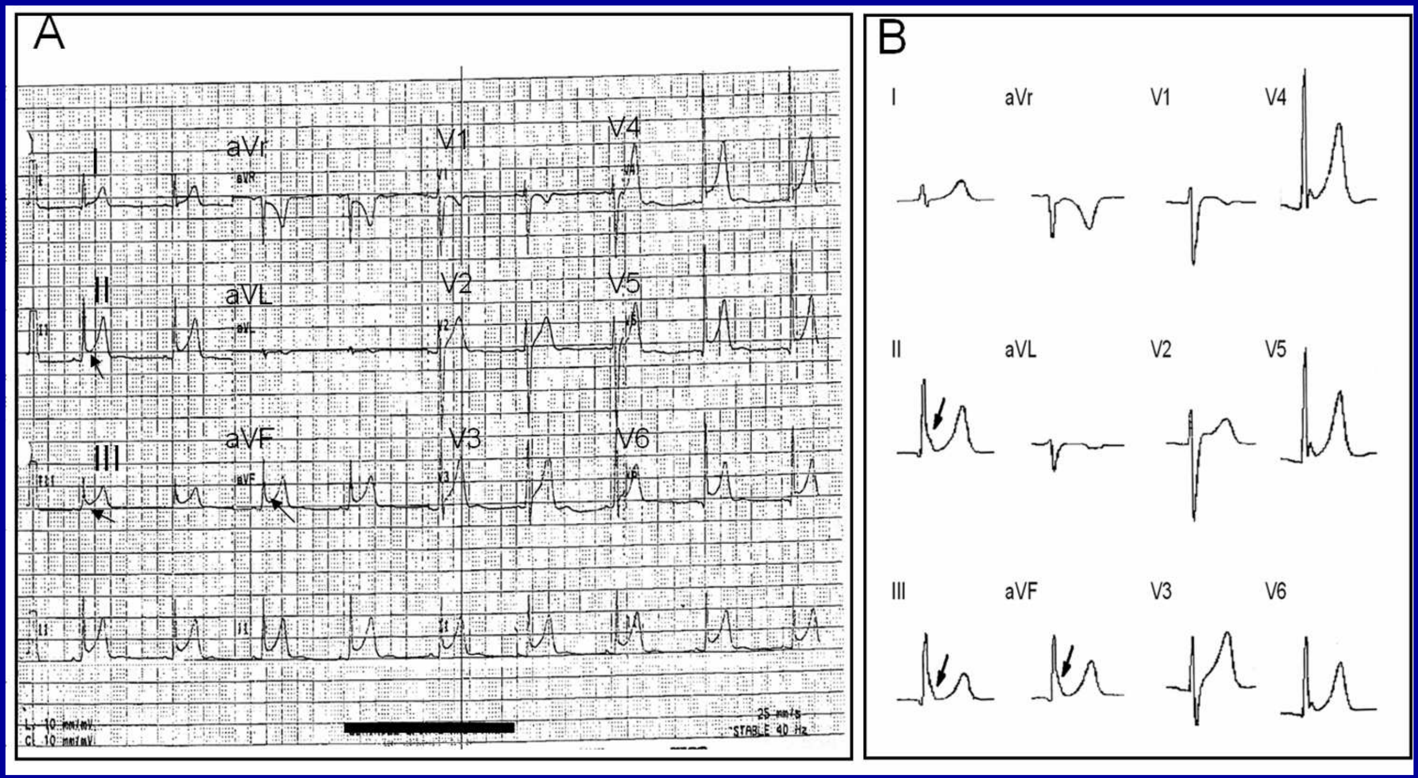
Mean LV
apex-to-base
ARI dispersion=37 ms

Repolarization abnormalities create substrate for reentry and arrhythmia



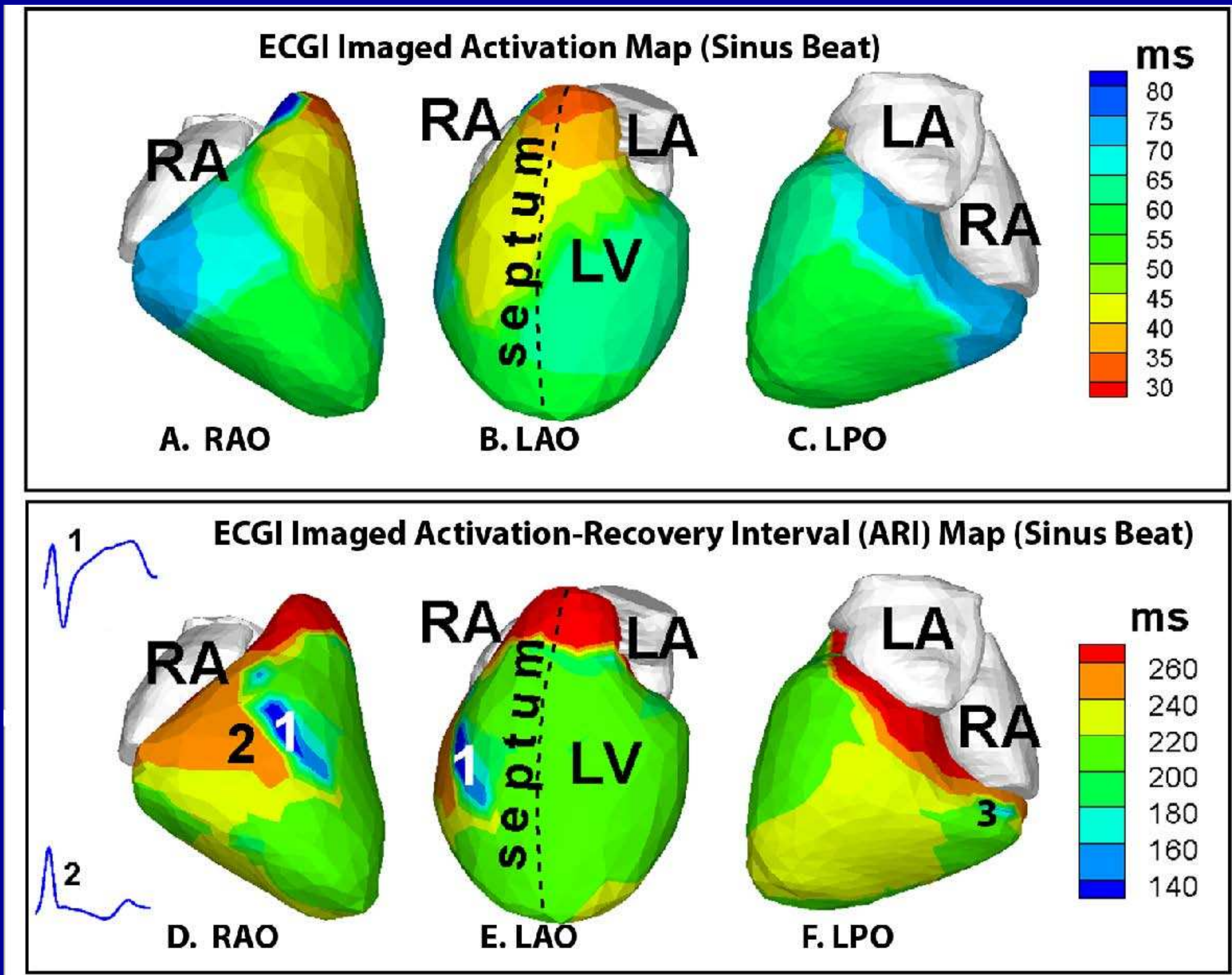
Can this substrate be detected noninvasively?

Early Repolarization Syndrome associated with Sudden Death: ECG of Identical Twins



Heart Rhythm 2010;7(4):534-537

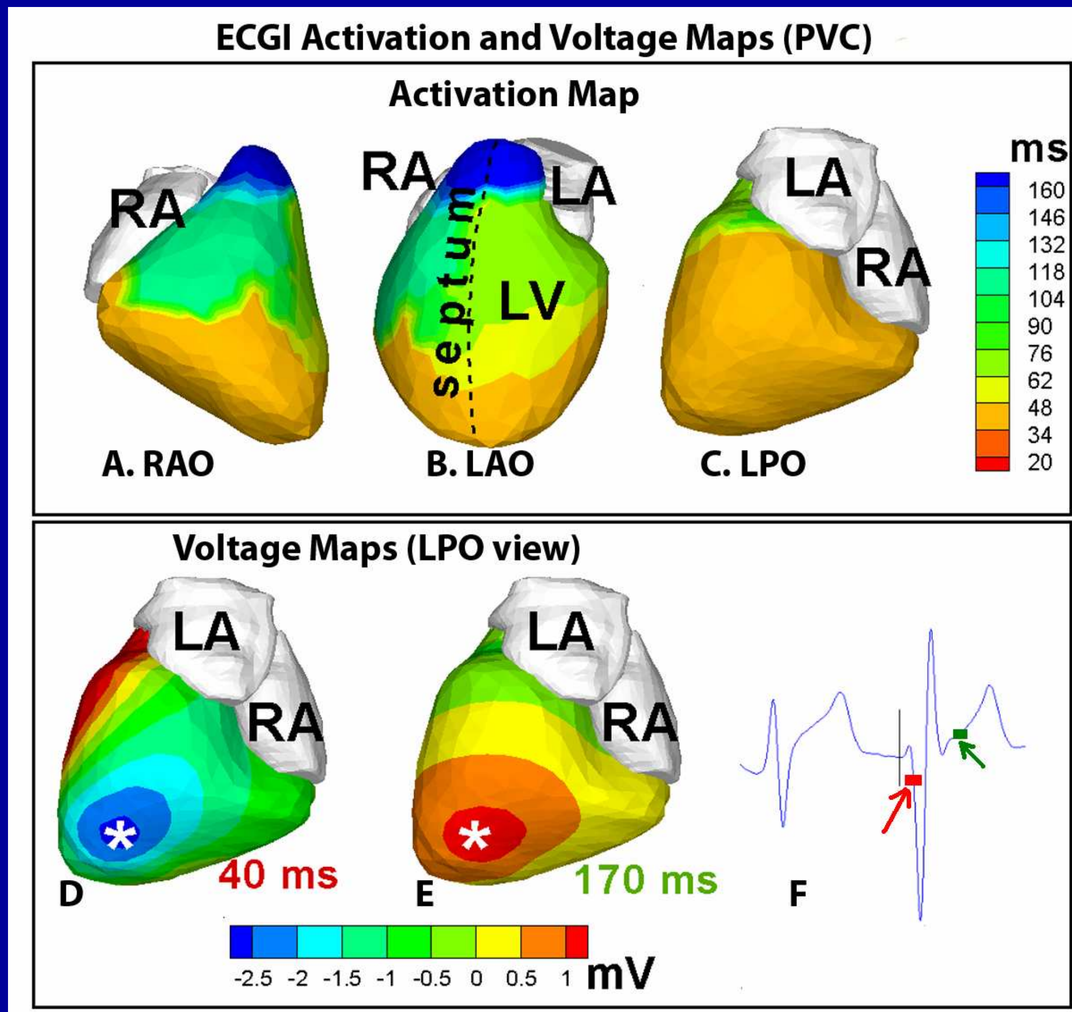
Early Repolarization associated with Sudden Death: Activation and Repolarization Maps of Surviving Twin [Sinus Rhythm]



- Islands of very short ARI=140ms (normal is 235ms)
- Extremely large local repolarization gradients: DARI=107ms/cm (normal is 11ms/cm)

Heart Rhythm 2010;7(4):534-537

Activation during Premature Ectopic Beat

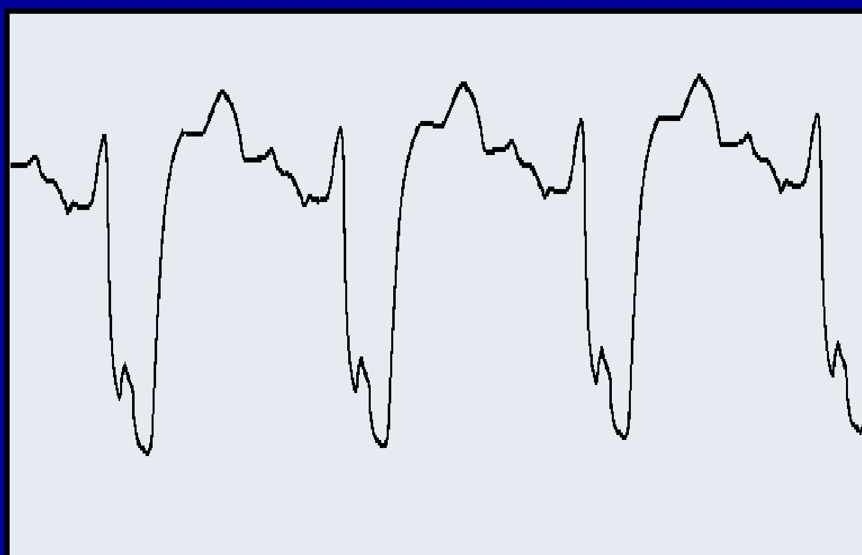


Heart Rhythm 2010;7(4):534-537

Electrocardiographic Imaging (ECGI) of Cardiac Resynchronization Therapy in Heart-Failure Patients:
Observation of
Variable Electrophysiological Responses

Heart Rhythm 2006;3:296-310

Heart failure ⟶ LV conduction delay (LBBB pattern)



Electrical Dyssynchrony

↓

Mechanical Dyssynchrony

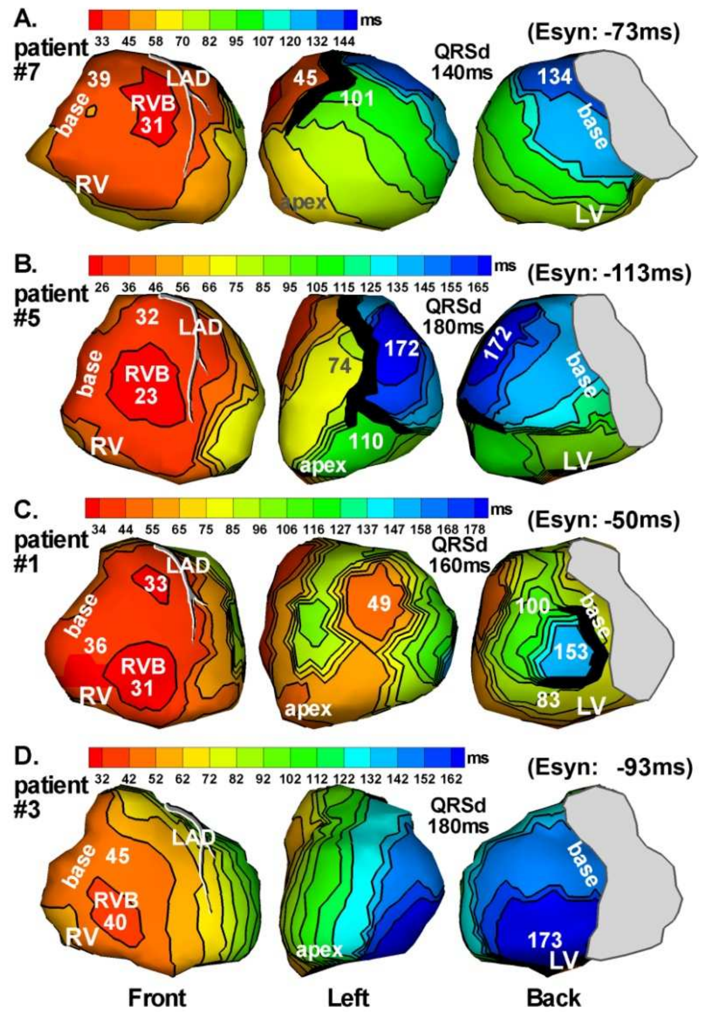
↓

↓ Pump Function

HEART - FAILURE SUBSTRATE

Native Rhythm (NR)

- **Heterogeneous LBBB activation patterns**
- **Relatively normal RV activation**
- **LV activation is delayed 90ms relative to RV (normal is less than 40ms)**
- **Anterior lines of block/slow conduction, U-shaped activation around block**
- **Latest activation region varies; lateral LV base is most common**

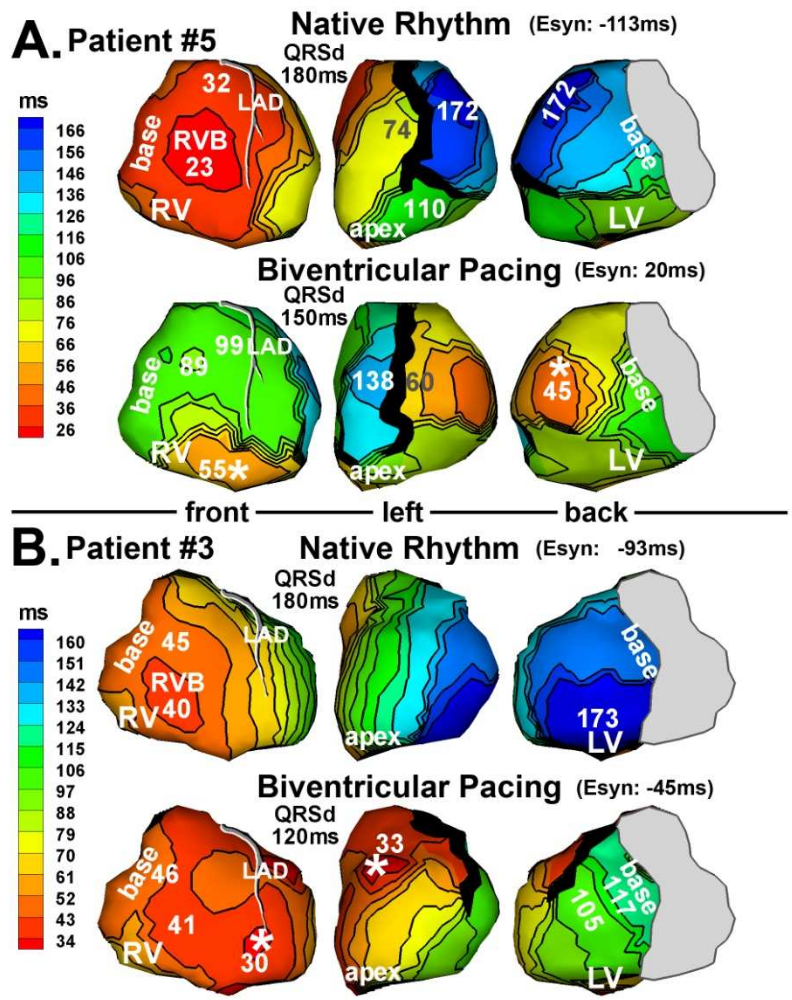


Heart Rhythm 2006;3:296-310

Esyn = lateral (RV – LV) activation

Native Rhythm and BiV Pacing
(2 responders)

- **Large inter-patients variability in activation patterns and synchrony**
- **Patient 5: Lateral LVP; BiV improved Esyn from -113 to 20ms**
- **Patient 3: Anterior LVP; BiV improved Esyn from -93 to -45ms**

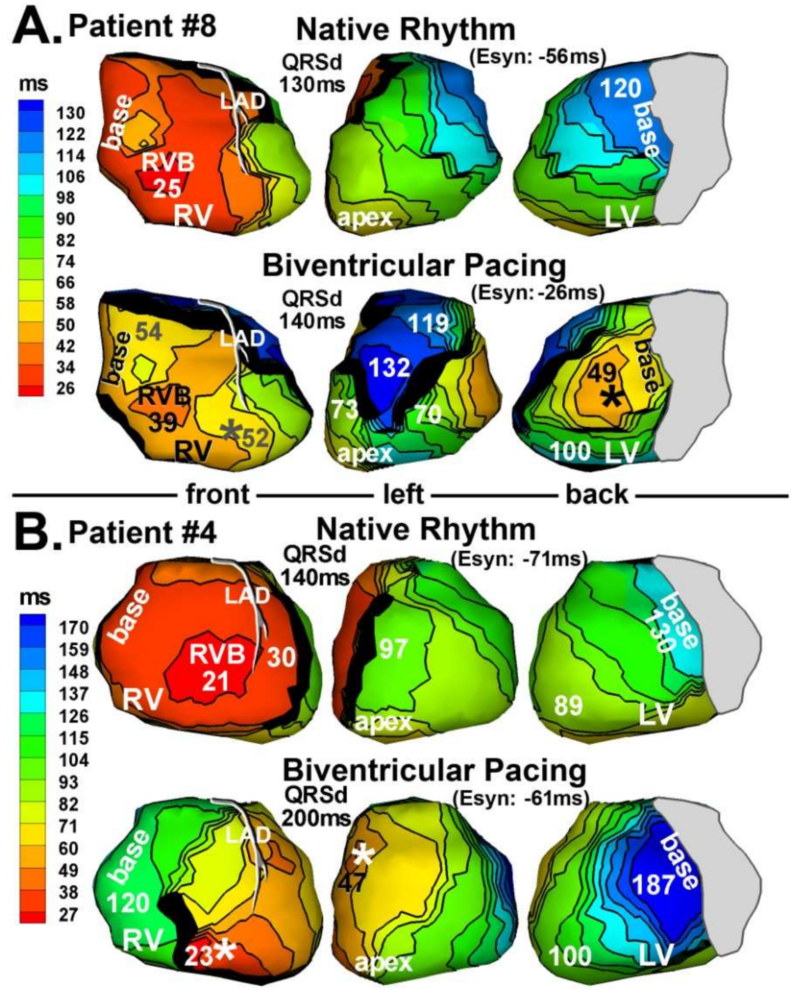


Heart Rhythm 2006;3:296-310

Native Rhythm and BiV Pacing
(2 non-responders)

- **Patient 8: Lateral LVP; BiV improved Esyn from -56 to -26ms (QRS did not shorten); Latest activation in anterior LV (132ms)**

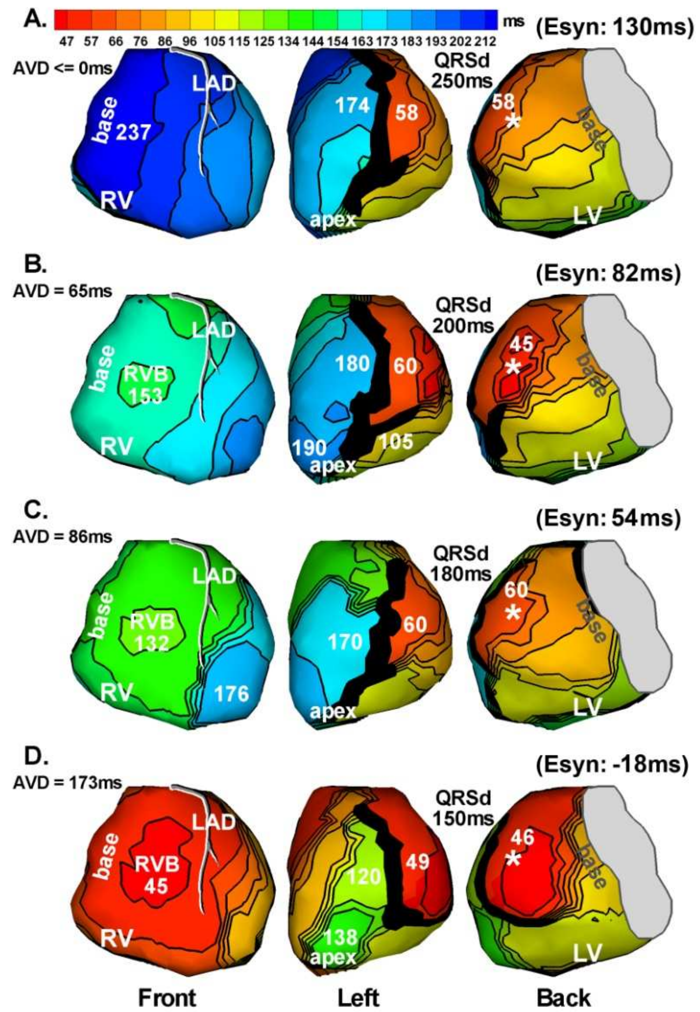
- **Patient 4: Anterior LVP; lateral LV activation was greatly slowed relative to NR**



Heart Rhythm 2006;3:296-310

Fusion Beats during LV Pacing

- 3 of 4 patients with intact AV conduction showed fusion with intrinsic excitation during LV pacing with optimal AV delay
- Degree of fusion increased with increase of AV delay (delay from atrial pacing to LV pacing), because intrinsic RV activation occurred progressively earlier relative to LV pacing
- Esyn improved as fusion increased



Heart Rhythm 2006;3:296-310

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Case Western Reserve and others