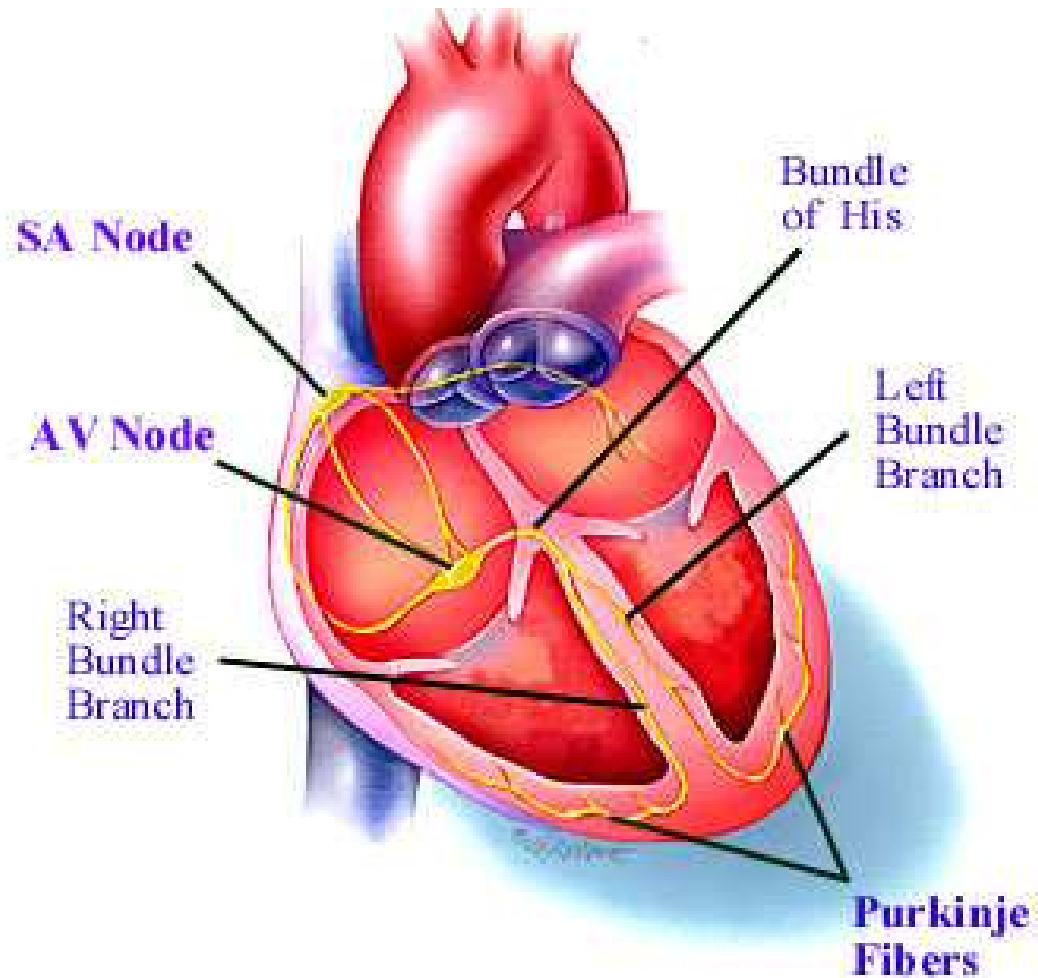# Predicting and Preventing Sudden Cardiac Death

Leon Glass
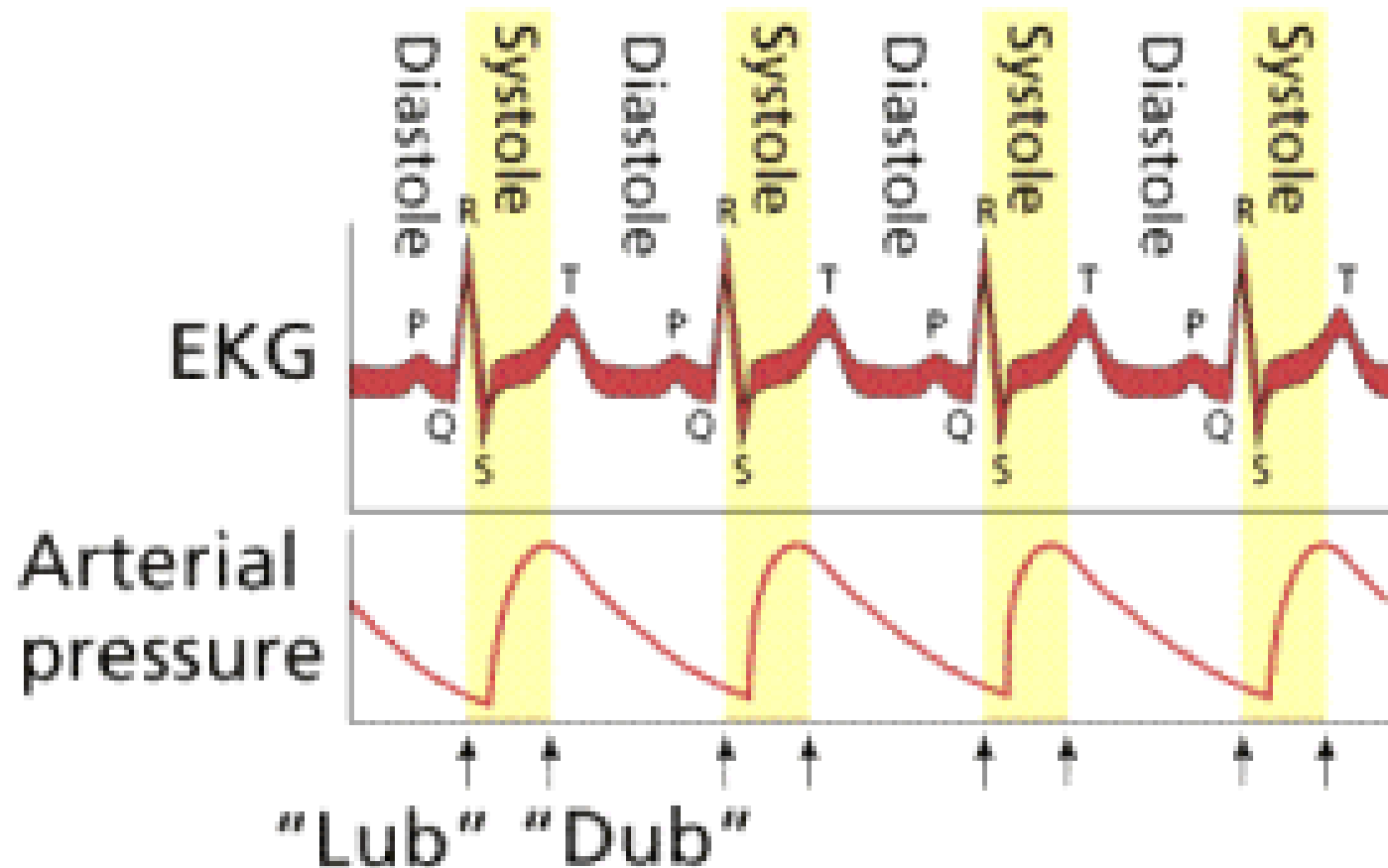
Isadore Rosenfeld Chair in Cardiology, McGill University, Montreal, Quebec

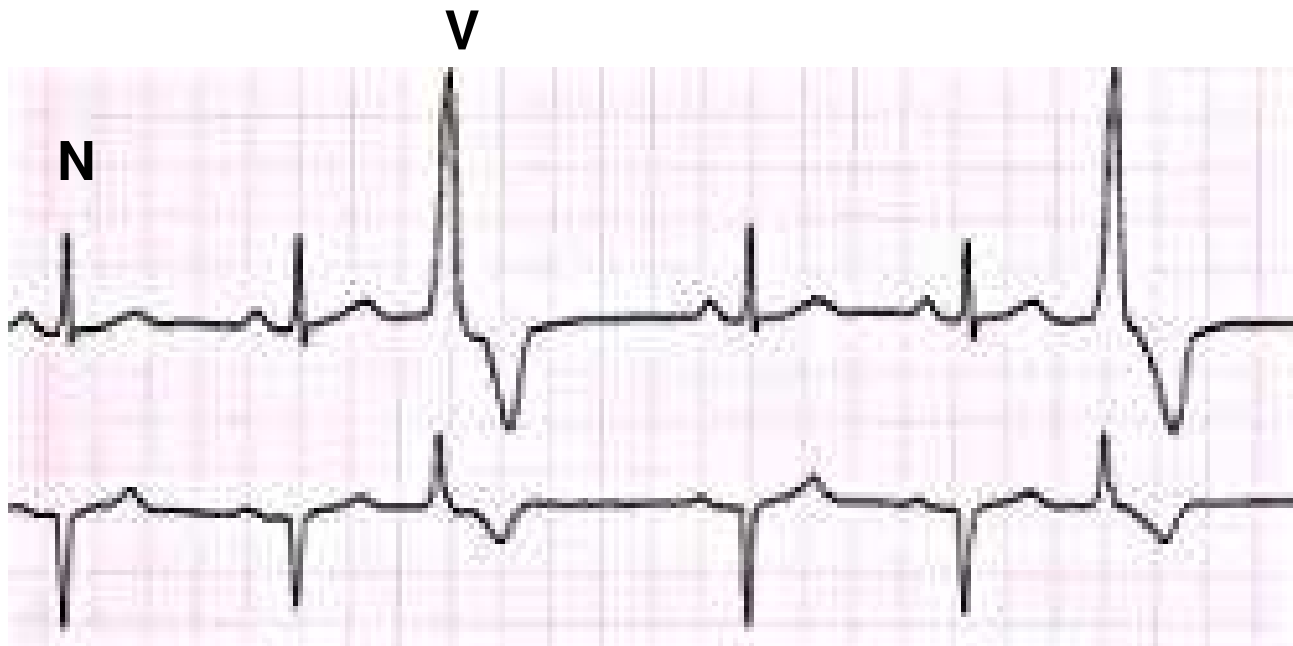- Introduction to cardiology
- The sudden cardiac death challenge
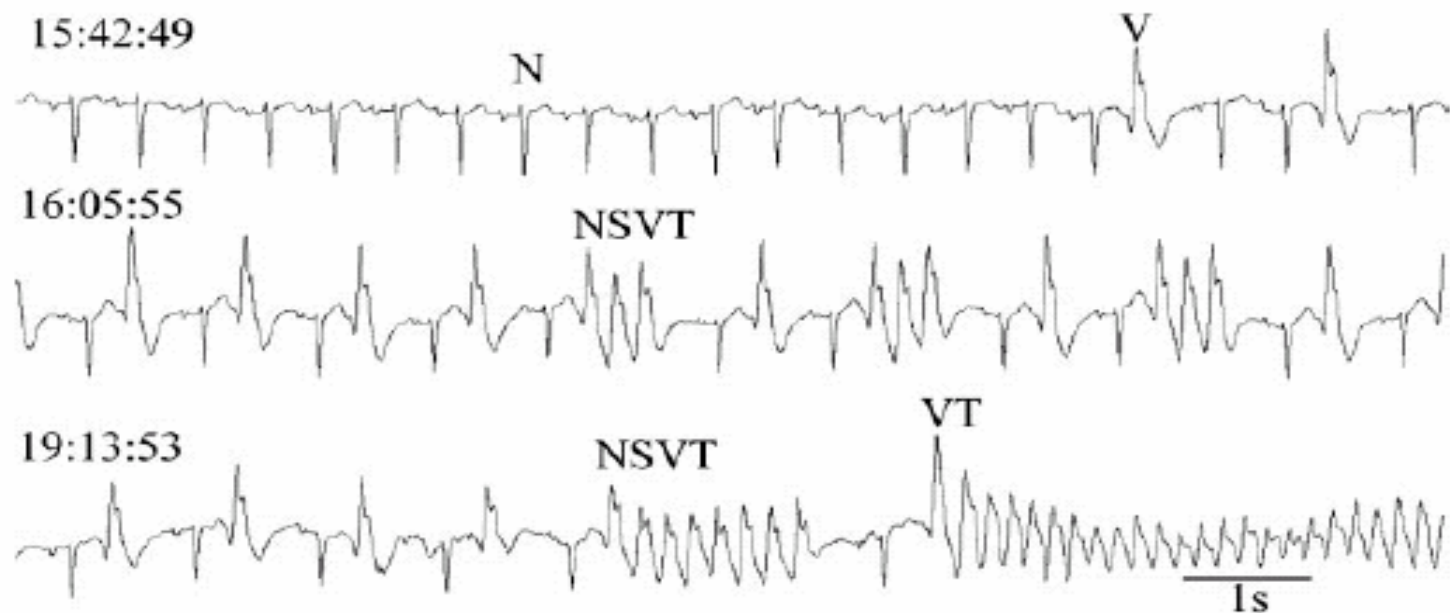
Conduction System of the Normal Heart

The Cardiac Cycle and Electrocardiogram

Normal Heartbeats and Premature Ventricular Complexes (PVCs)

Sudden death. Why did this 82 yr old woman die at 19:13:53 and not earlier?


www.physionet.org

Sudden Cardiac Death (definition)

- Sudden cardiac death (SCD), or **cardiac arrest**, is the sudden, abrupt loss of heart function in a person who may or may not have diagnosed heart disease. The time and mode of death are unexpected.

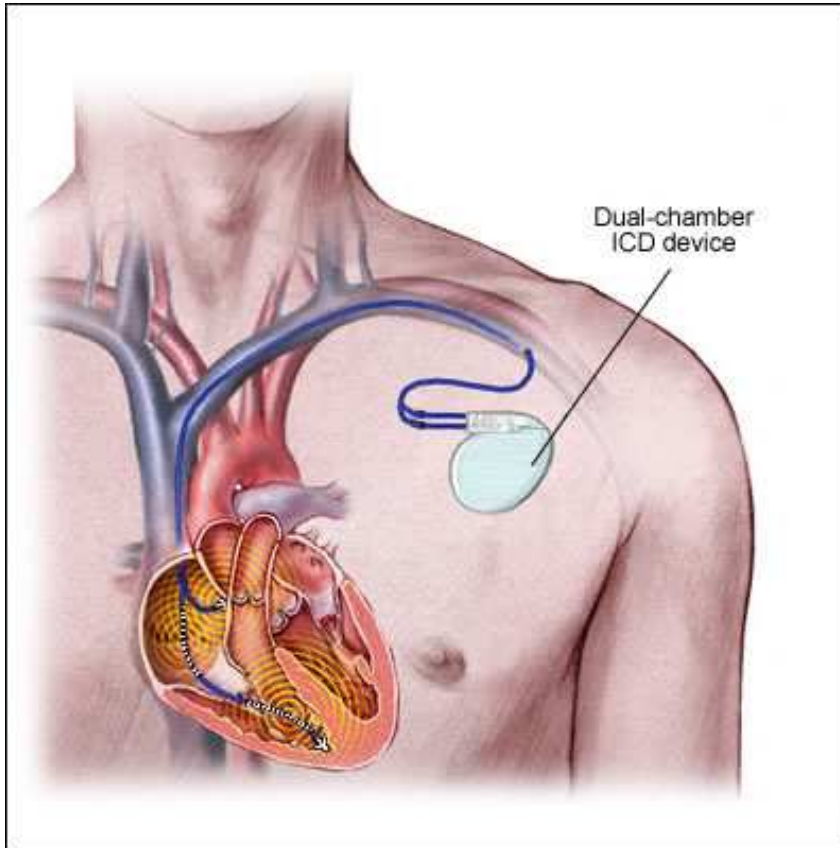# Questions?

- Can we predict who has a high risk of sudden cardiac death?

- If we could, could we prevent the sudden cardiac death?

Implantable Cardioverter Defibrillators (ICD) reduce the incidence of sudden death
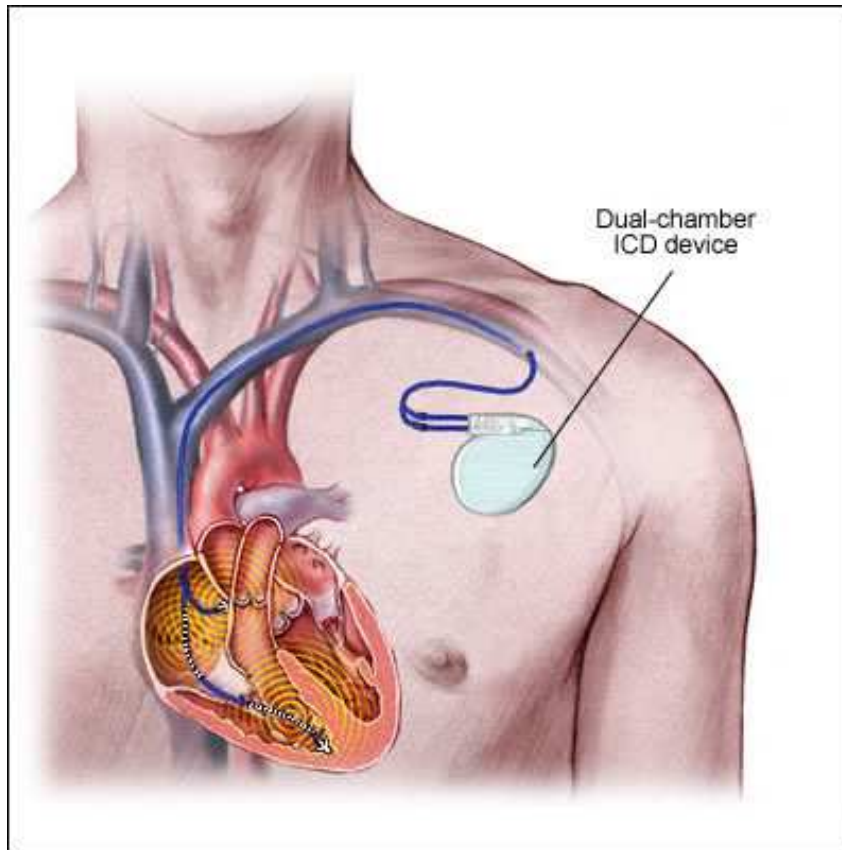
Dual-chamber ICD device

Implantable Cardioverter Defibrillators (ICD) reduce the incidence of sudden death

Dual-chamber ICD device

Estimated ICD statistics (Canada 2006/2007)

- Total number meeting implantation criteria 103,100
- Total number treated 15,021
- Total number untreated 88,079
- New implants in 2006/2007 4500
- New implants/million   141

(Simpson et al., Can J Cardiol 2005)

Clinical trials are used to assess risk and therapy efficacy for sudden cardiac death

- Trials are essential for physicians who are treating patients
- Trials have led to improved therapies
- But, they are somewhat crude and there are problems….

Strategy 101 to investigate Sudden Cardiac Death (SCD)

- Observation: Premature Ventricular Complexes (PVCs) often occur with increasing frequency before SCD

- Hypothesis: Decrease of PVCs will lead to decreased SCD

- Experiment: Give 750 people a drug that reduces the number of PVCs and give 750 people a placebo. Count the number of people that die as a function of time.

Cardiac Arrhythmia Suppression Trial (CAST).
NEJM 321:406 (1989); 324:781 (1991)
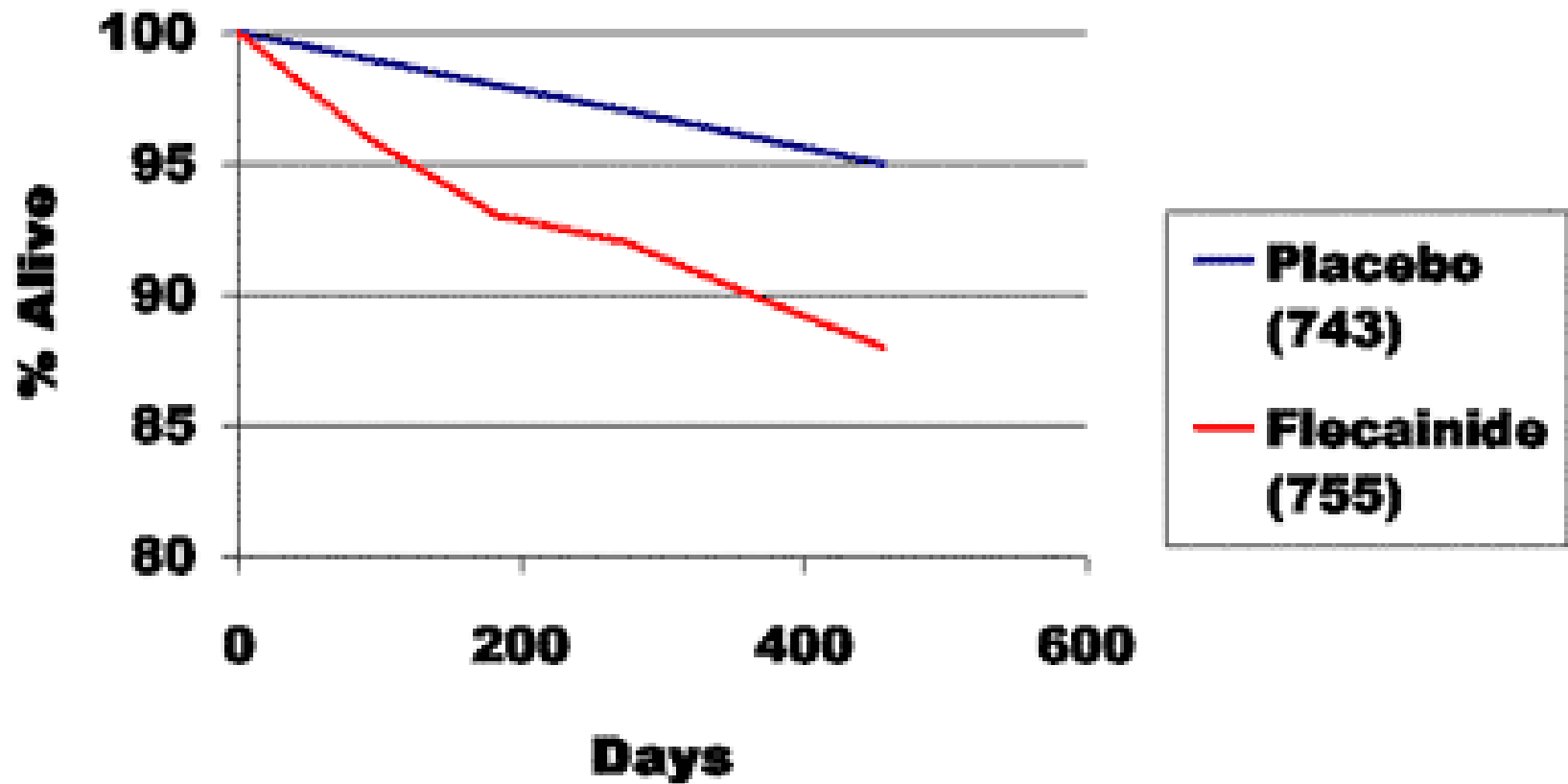
Cardiac Arrhythmia Suppression Trial (CAST).
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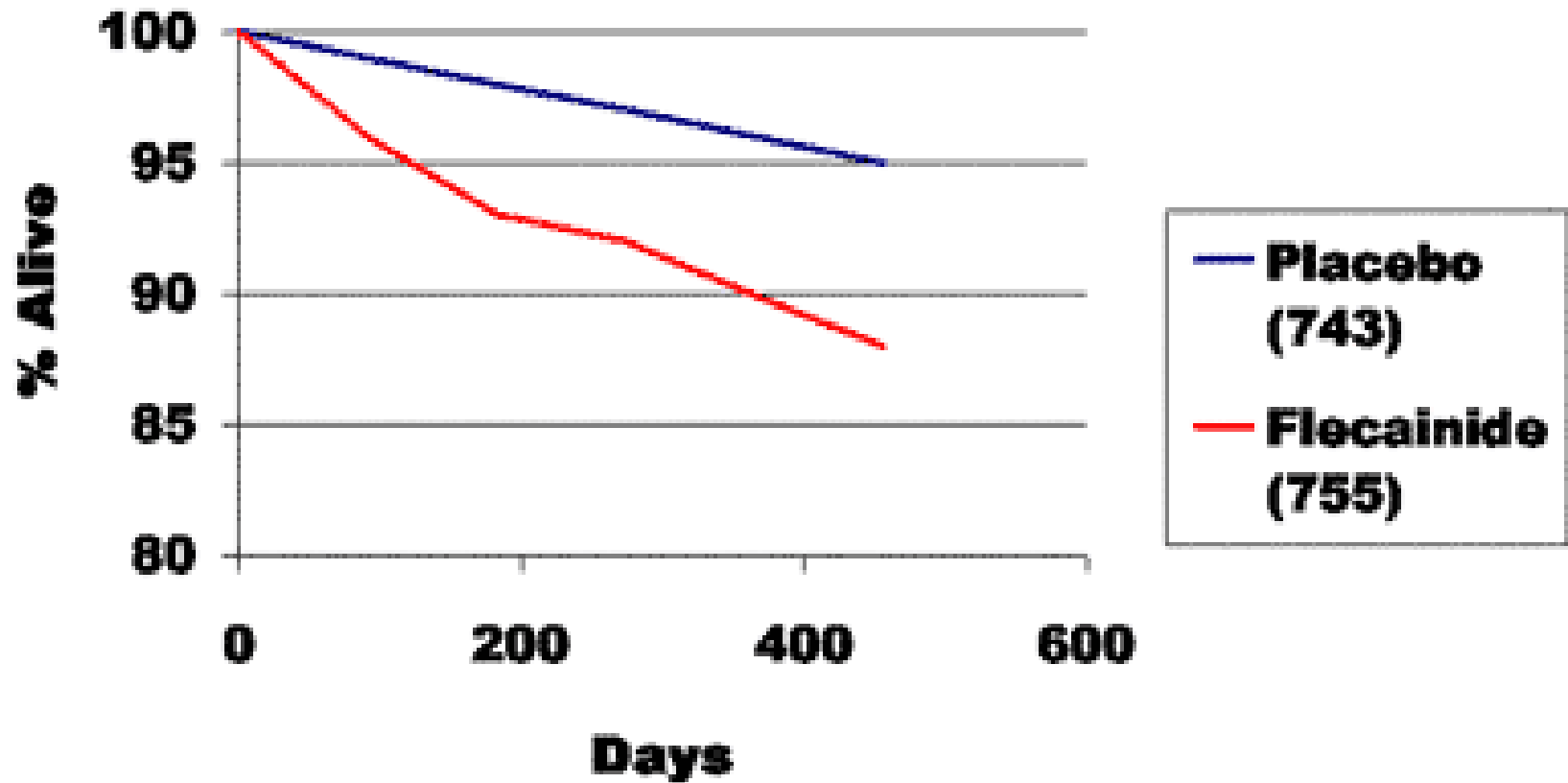
- That is: the hypothesis was disproved.

Main Flaws of CAST and Similar Clinical Trials

- They do not elucidate the mechanisms of arrhythmias
- A significant improvement in one arm of the trial would lead to that treatment for all individuals meeting selection criteria, ignoring individual physiologic differences (i.e. there is a strong economic incentive for broadly defined classes)

Strategy 102. Use nonlinear dynamical models and experimental models to analyze mechanisms of arrhythmia by confronting theory and experiment (one problem at a time).

- AV heart block
- Dynamics in heart cell aggregates: alternans
- Dynamics in heart cell aggregates: resetting and entrainment
- Parasystole
- Reentrant rhythms. Universal patterns of spatio-temporal dynamics
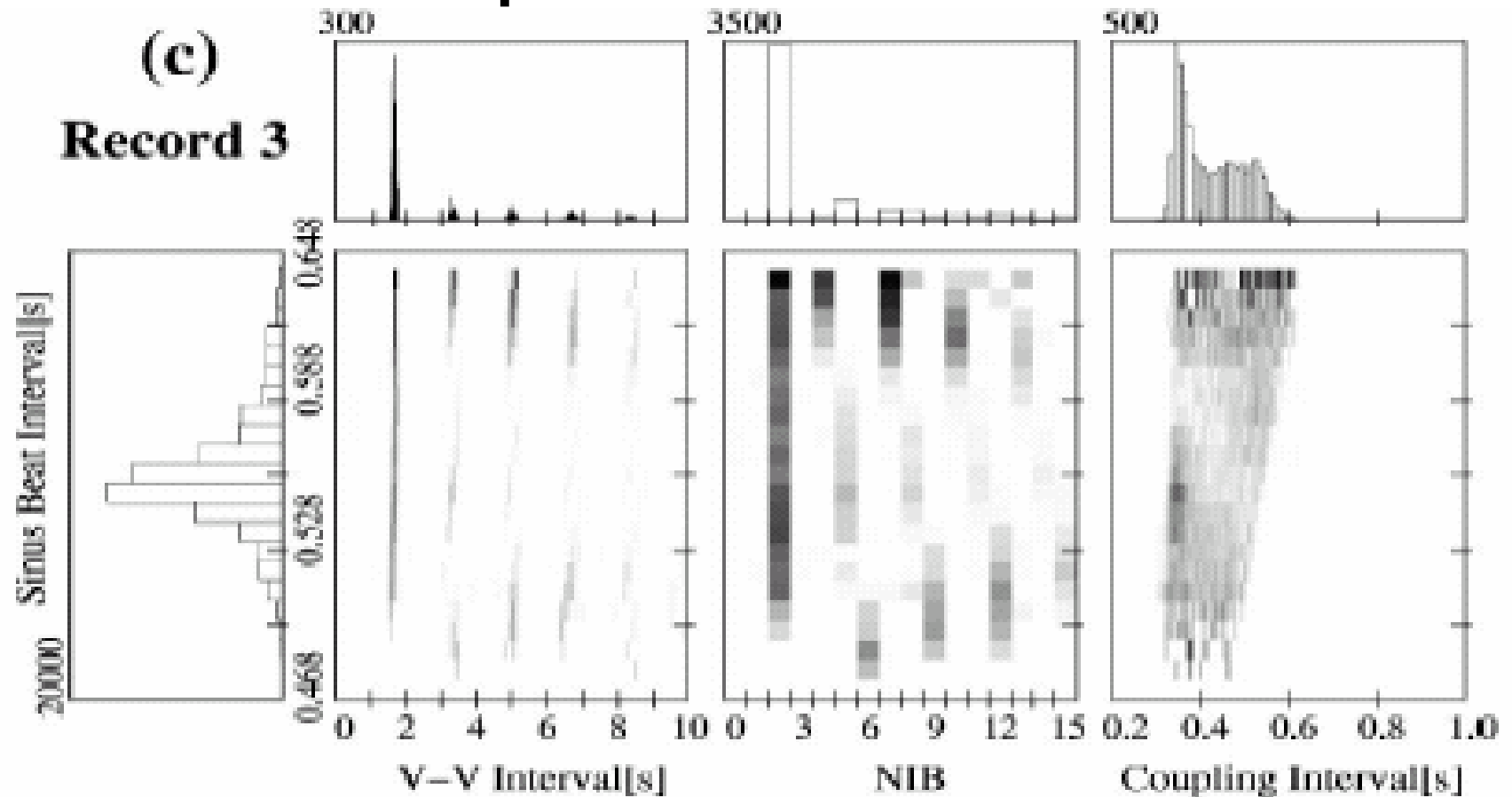
Pure Parasystole

Rules of Pure Parasystole

Count the number of sinus beats between ectopic beats.
In this sequence: (1) there are 3 integers; (2) one is odd;
(3) the sum of the two smaller is one less than the largest.
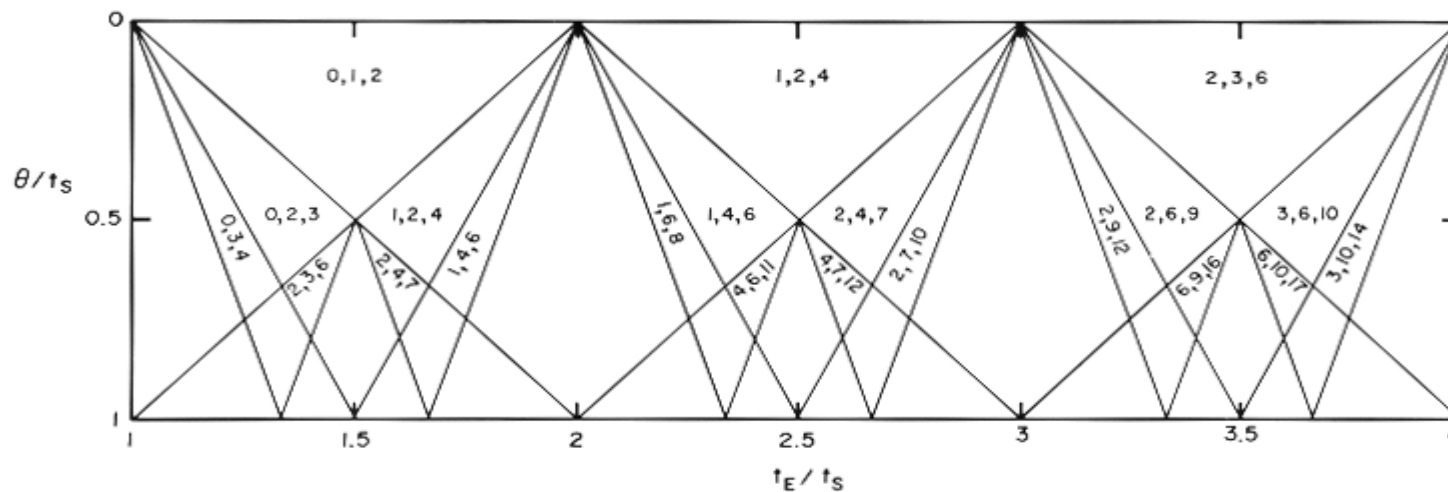
Glass, Goldberger, Belair (1986)

Heartprint of a Patient

Complex patterns of abnormal heartbeats

Verena Schulte-Frohlinde,[1,2,*] Yosef Ashkenazy,[1,3] Ary L. Goldberger,[2] Plamen Ch. Ivanov,[1] Madalena Costa,[2] Adrian Morley-Davies,[4] H. Eugene Stanley,[1] and Leon Glass[5]

Good news – bad news

- I think we really understand parasystole
- It is generally considered a benign arrhythmia (e.g. it does not kill people)
- Only a small percentage (<10%?) of records with frequent PVCs appear to have a parasytolic mechanism

Good news – bad news

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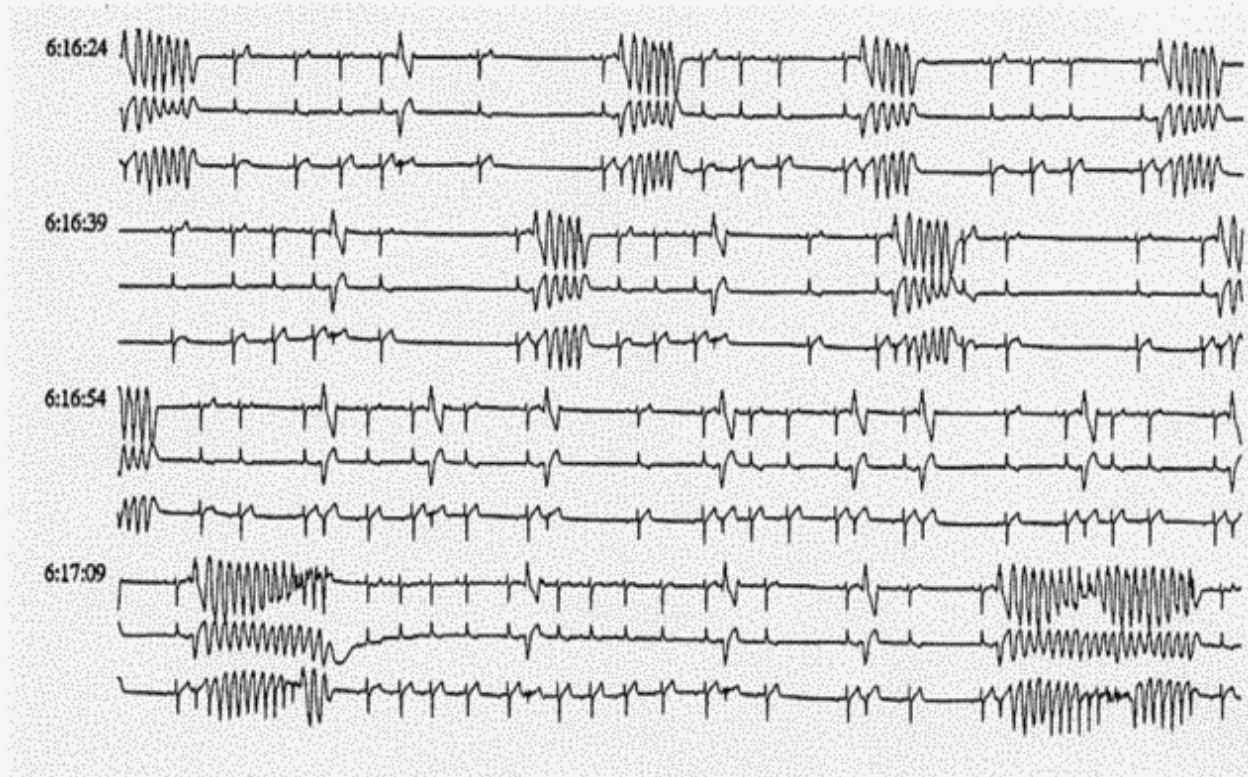- Cardiologists do not care about this arrhythmia (at all!)

PhysioBank's Sudden Cardiac Death Database

Heartprint from a patient who had sudden cardiac death
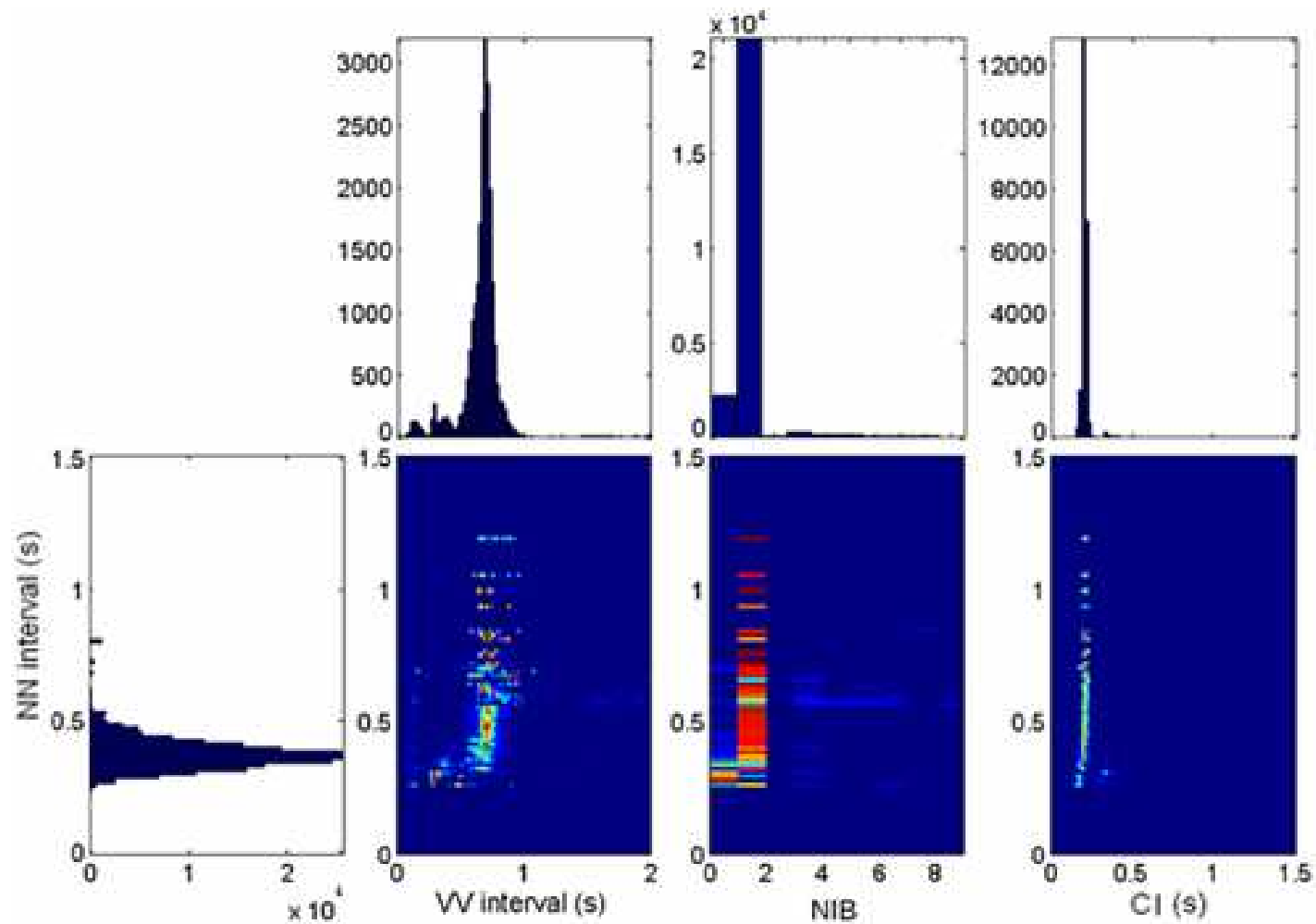### - Record 47 -
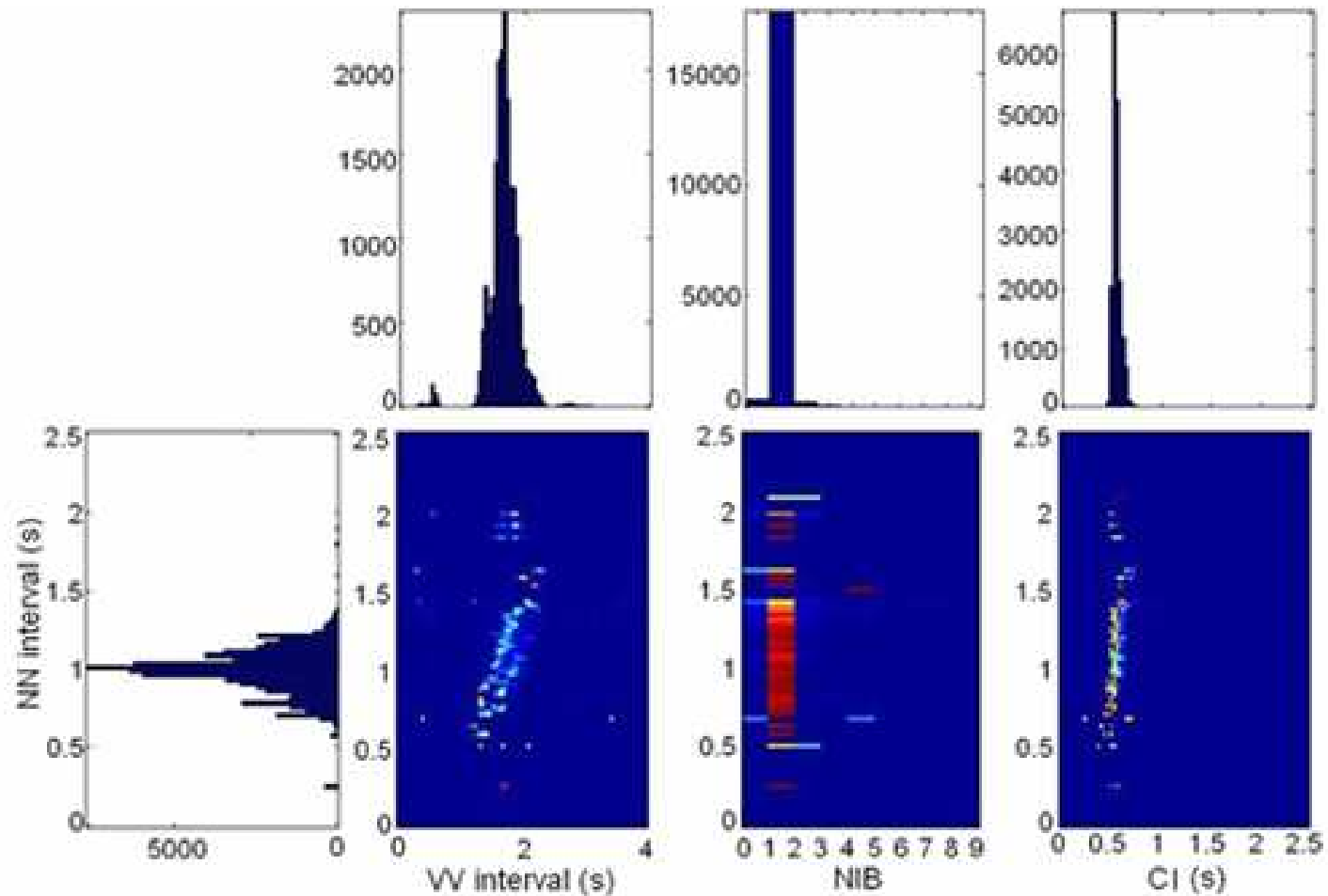
Spontaneous VT in German shepherd dogs

Sydney Moise, DVM and Robert Gilmour, PhD,
Cornell University College of Veterinary Medicine

Record from Dog # 4 who suffered sudden cardiac death -

Striking ECG characteristics from dynamical analysis in 6/15 SCD patients

Analysis using the PhysioNet Sudden Cardiac Death Holter Database

(i)   Frequent ventricular bigeminy (>5% of total ventricular arrhythmias)

(ii)   Long QTc > 0.5 s

(iii)   Fixed CI

(iv)   Onset of torsade de pointes after a long-short RR sequence

Consistent with a mechanism of early afterdepolarizations leading to SCD

(Lerma , Goldberger, Glass, J. Electrocardiol.2007)

Challenge for cardiology

- Develop deeper understanding of events that precede fatal arrhythmias with a view of better predicting those at risk for sudden cardiac death
- Since the bifurcations to fatal arrhythmias may be different in different people, this requires analysis of ECG records of many individual patients (this is a highly maligned activity – i.e. it is hard to fund and hard to publish)
- The role of mathematical models and simple model experimental systems is not yet evident

Acknowledgments