UNIVERSITA DEGLI STUDI DI MILANO I.R.C.C.S. POLICLINICO SAN DONATO

CENTRO PER LO STUDIO E LA TERAPIA DELLLE MALATTIE CARDIOVASCOLARI

"E. MALAN"

Leadless ICD: How far from real life?!

Riccardo Cappato, MD
Pierpaolo Lupo, MD
Hussam Ali, MD

S-ICD Therapy

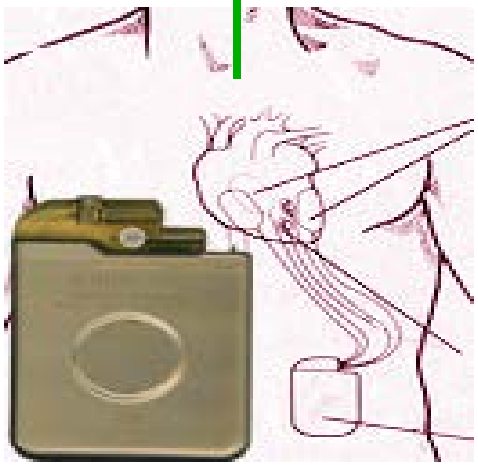
Aim of technology

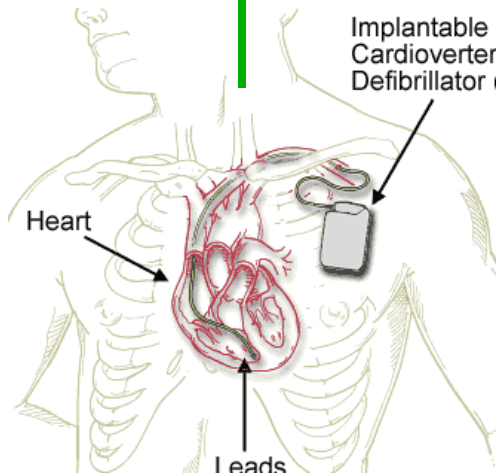
- The entirely Subcutaneous (S) -ICD is designed to provide the life-saving benefit of conventional ICDs whilst avoiding the shortcomings of transvenous leads

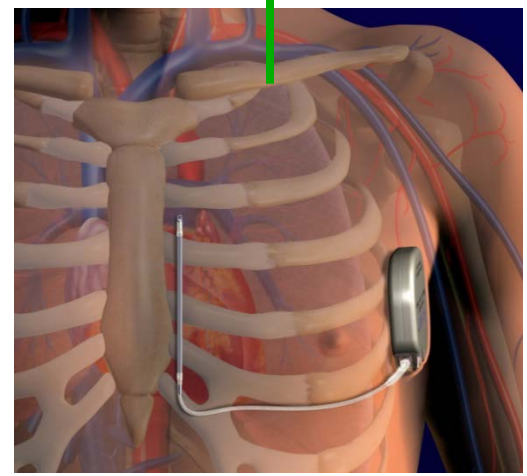
- By simplifying implant techniques, S-ICD is also meant to expand the use of ICDs in clinical practice

Evolving ICD Technologies

1980 **1989** **2008**







Epicardial ICD

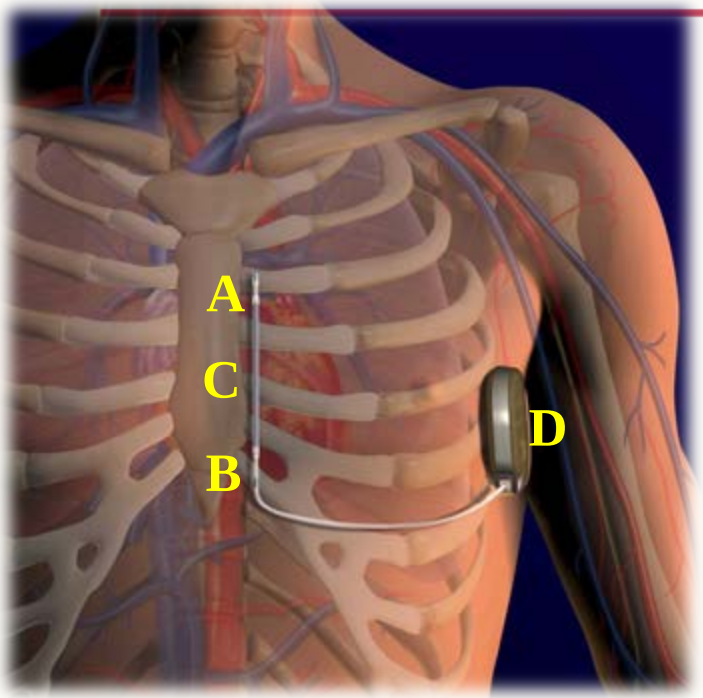
Transvenous ICD

Subcutaneous ICD

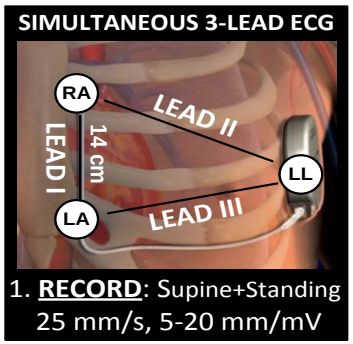
Invasiveness

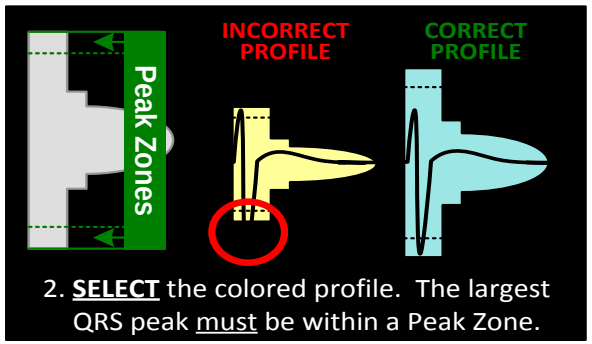
Most **Least**

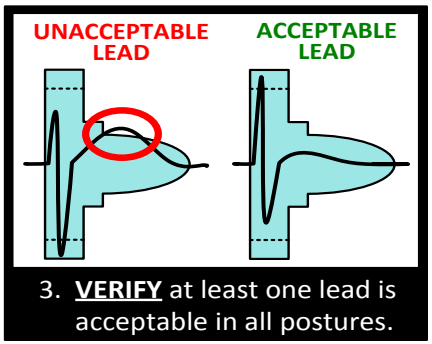
The S-ICD System:



- Entirely subcutaneous technology
- Treats malignant ventricular arrhythmias
- Fluoroscopy is not required for implant
- Final configuration: Canister D (left lateral thorax) connected to a single lead tunneled subcutaneously to the left parasternal line
- 3 sensing electrodes (A, B and D), Coil C
- A pre-operative screening tool to ensure adequate subcutaneous signals



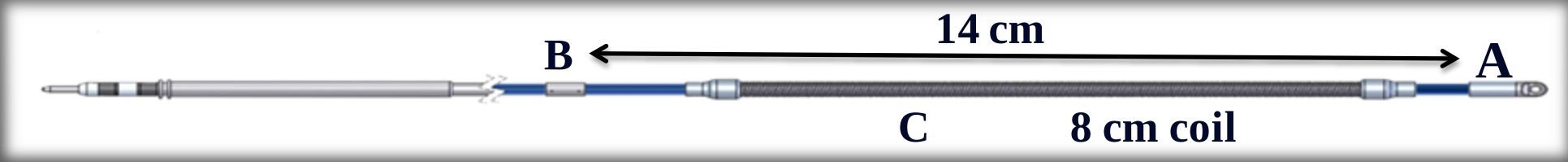




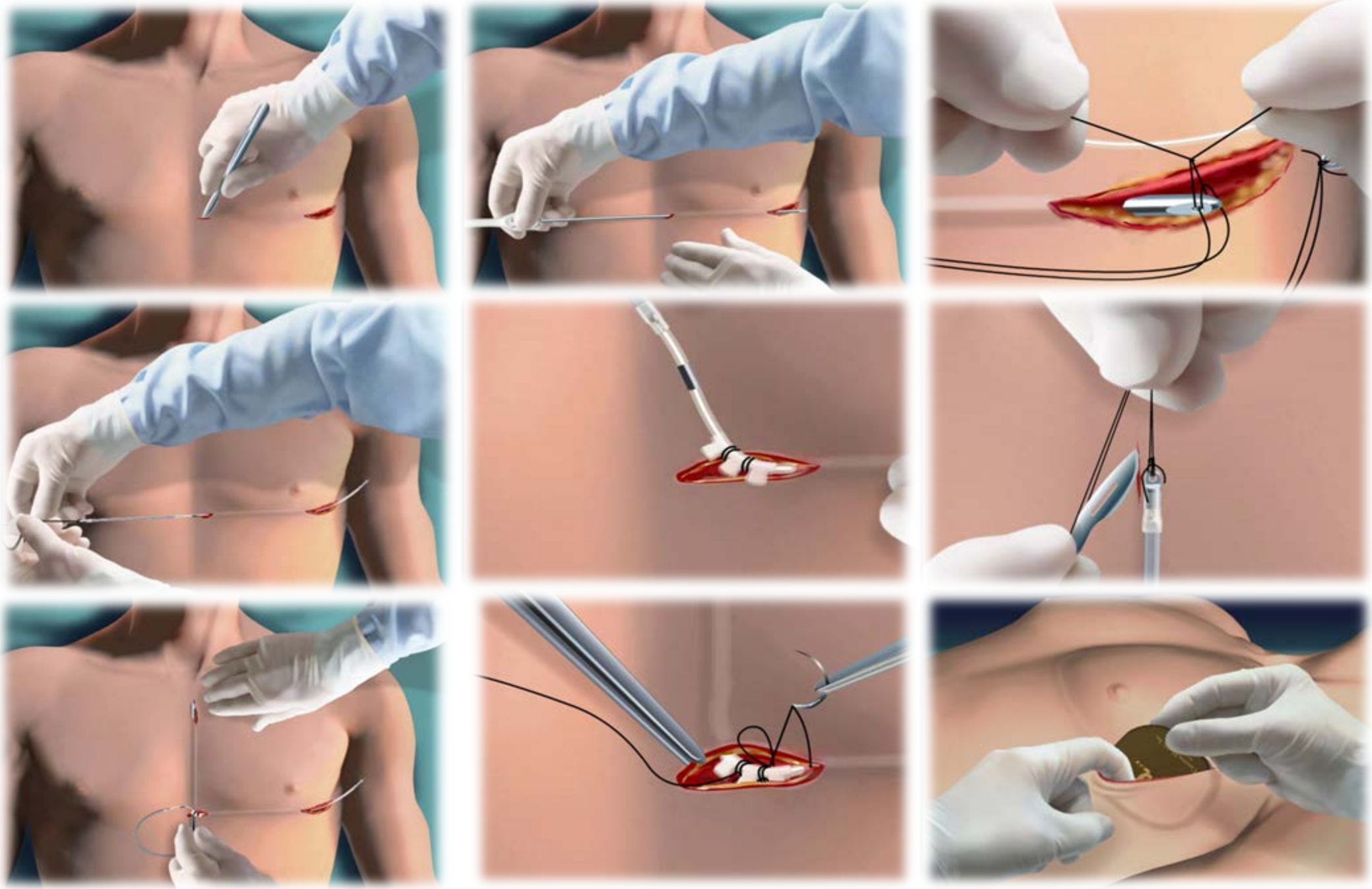
S-ICD Therapy

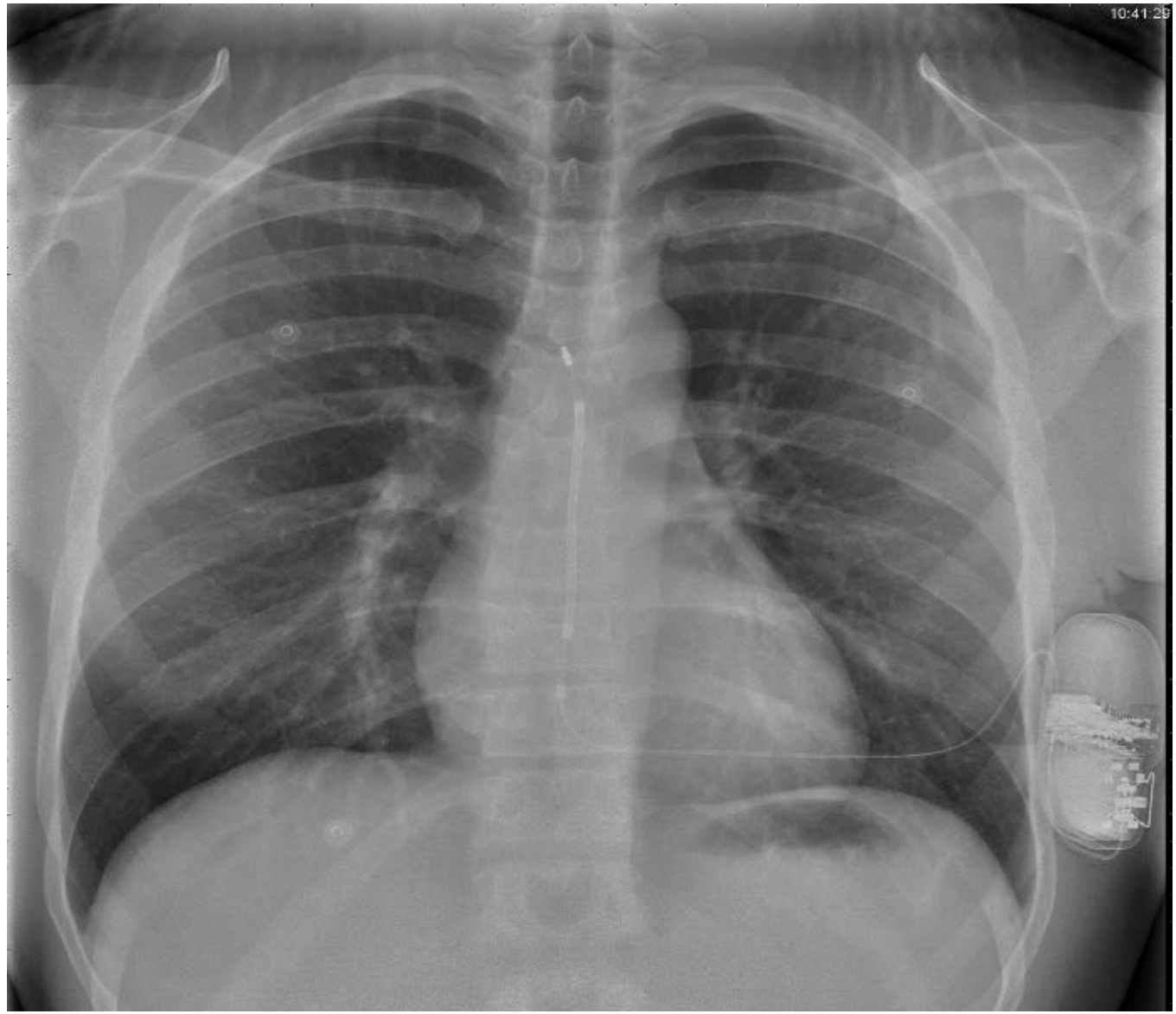
SQ-Rx Pulse Generator

Dimensions (mm): 78.2 x 65.5 x 15.7
Volume: 69.9 cc
Weight: 145 grams
Coating Material: Titanium Nitride,
Battery: Lithium MgO2
Energy: 80J (delivered)
Waveform: Biphasic, tilt 50%
Longevity: 5 years
Only post-shock pacing, 30 sec, 50 bpm



The subcutaneous lead *A tripolar parasternal electrode (polycarbonate-urethane 55D, 3 mm diameter, 45 cm length)*

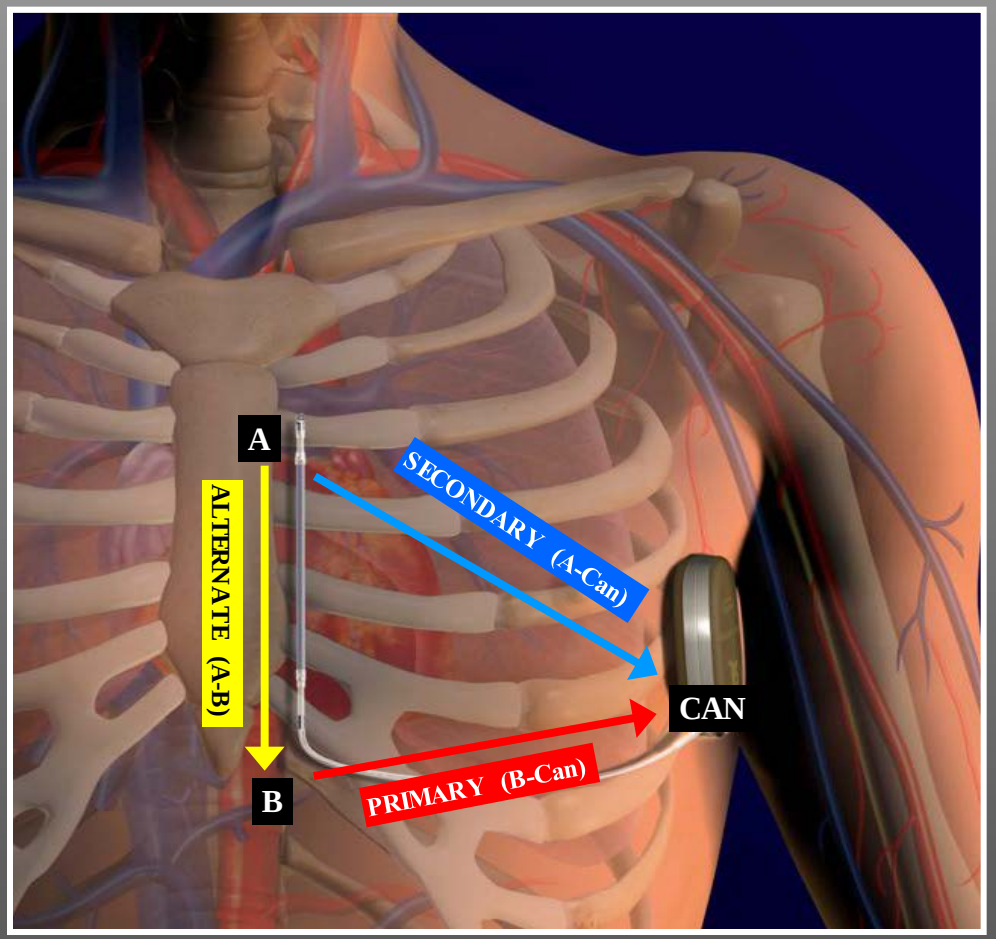



10:41:29

The fully S-ICD system

Sensing the subcutaneous signal….

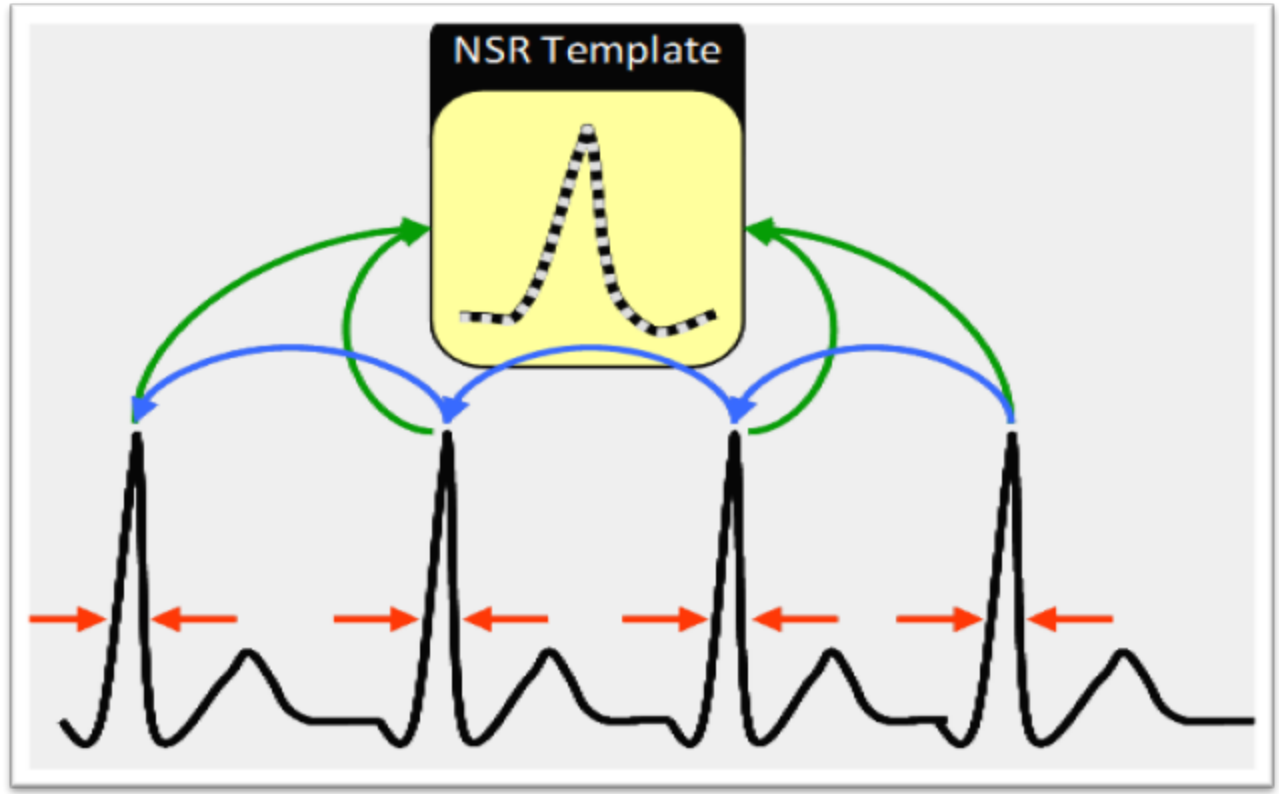
- Three bipolar sensing vectors provide maximum sensing flexibility.
- The ICD automatically selects the signals from the best vector for arrhythmia detection and to avoid double counting and T-wave oversensing



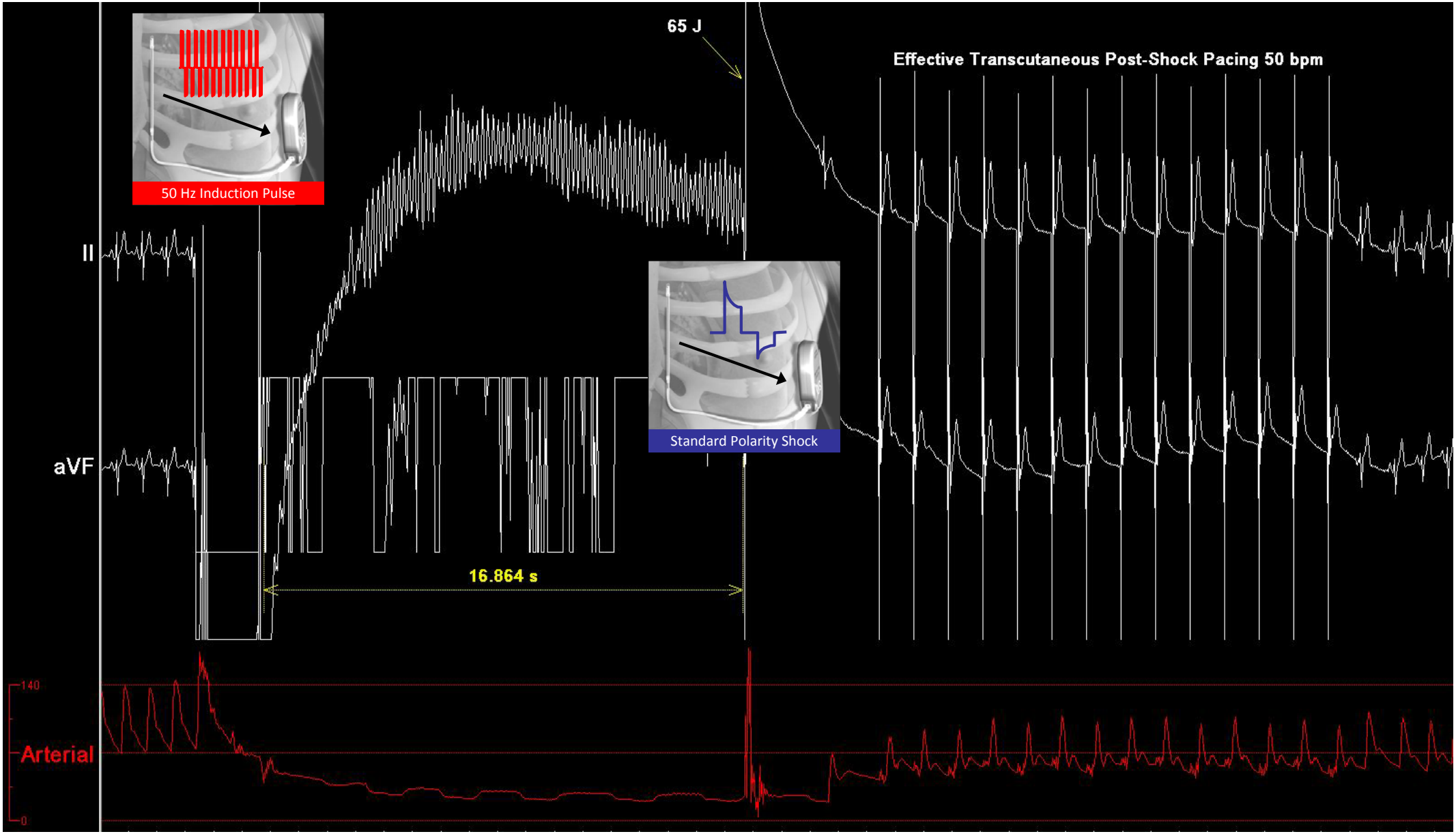
S-ICD

Rhythm Detection

- **All detection algorithms work together to identify S-ECG rhythm: heart rate, QRS width and dynamic template matching with learning from previous beats**

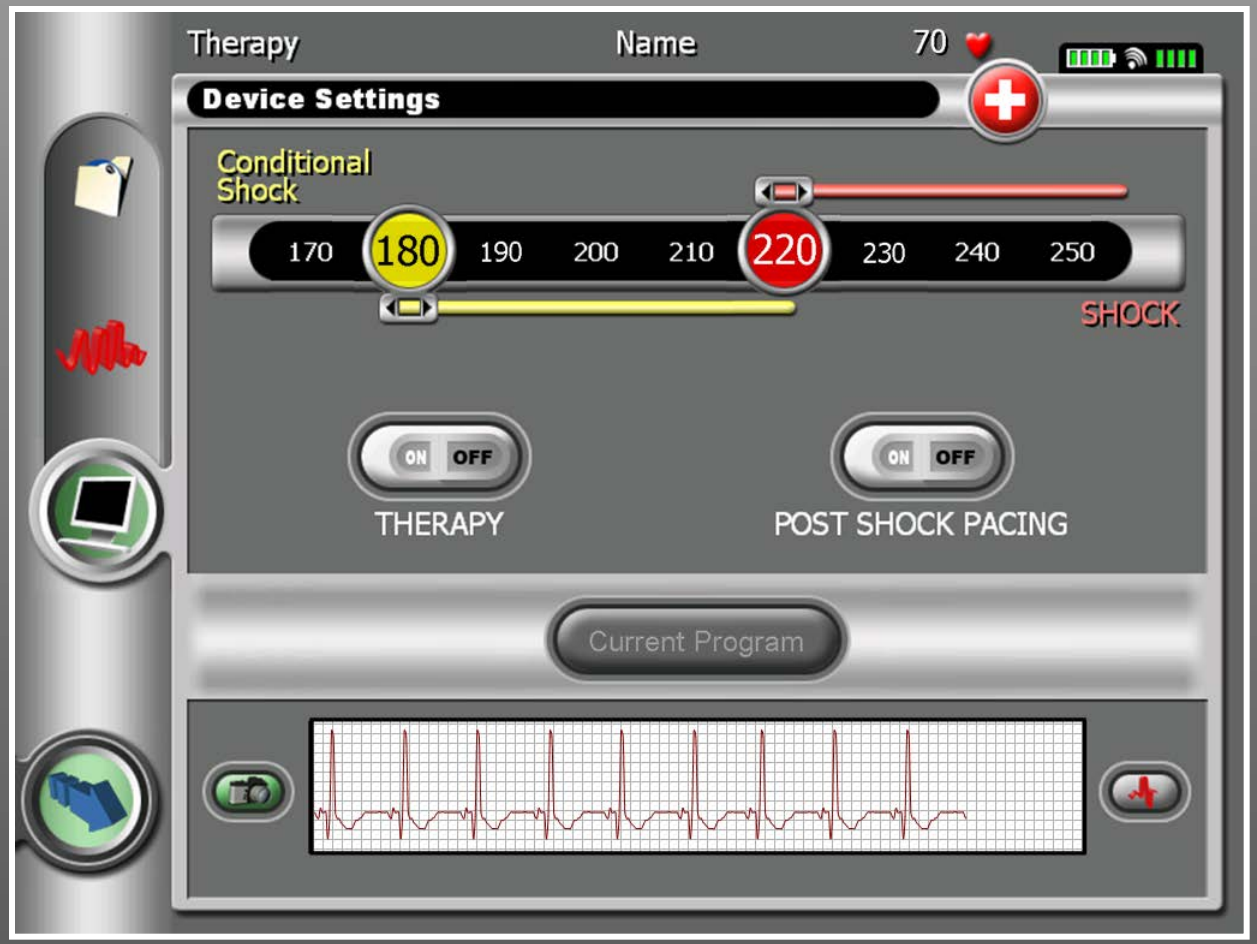


S-ICD Technical Manual


65 J
Effective Transcutaneous Post-Shock Pacing 50 bpm
50 Hz Induction Pulse
II
aVF
Standard Polarity Shock
16.864 s
140
Arterial
0

S-ICD Therapy

Programming Simplicity



Only few programmable parameters!
A programmable conditional shock zone (170-240 bpm)

S-ICD Therapy

CE Trial; 55 Patients

Europe/New Zealand

- Enrolment: 55 pts 12 Dec 2008 → 13 Feb 2009

Detection of VF

- 137/137 episodes: Sensitivity 100%
- Time-to-therapy: 14 ± 2 sec

Conversion of VF @ 65J

- 52/53 (>98%) pts met the primary conversion endpoint

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

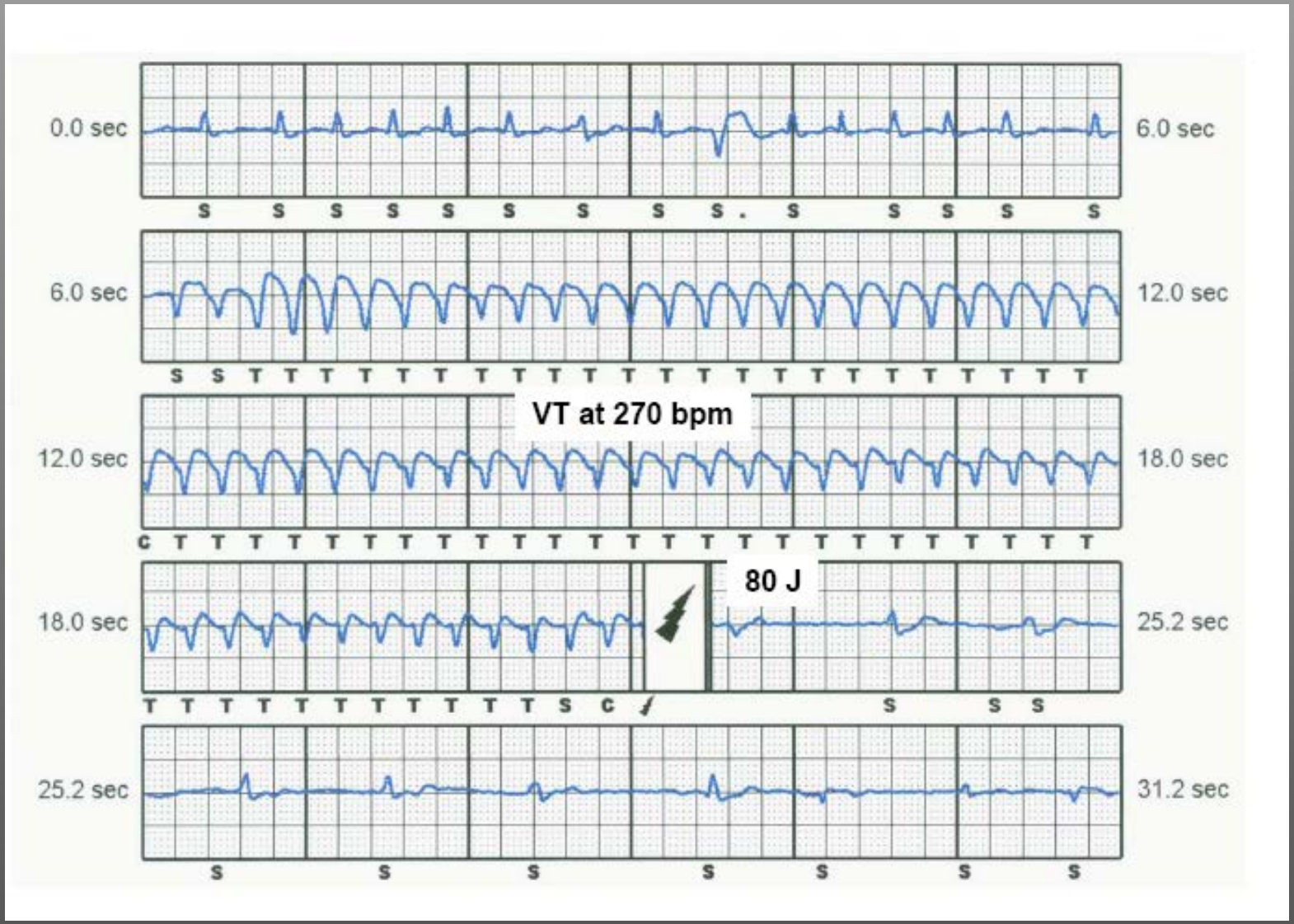
An Entirely Subcutaneous Implantable Cardioverter–Defibrillator

CONCLUSIONS

In small, nonrandomized studies, an entirely subcutaneous ICD consistently detected and converted ventricular fibrillation induced during electrophysiological testing. The device also successfully detected and treated all 12 episodes of spontaneous, sustained ventricular tachyarrhythmia. (ClinicalTrials.gov numbers, NCT00399217 and NCT00853645.)

Bardy, Cappato et al, NEJM 2010;363:36

Spontaneous Events



S-ICD Therapy

EFFORTLESS

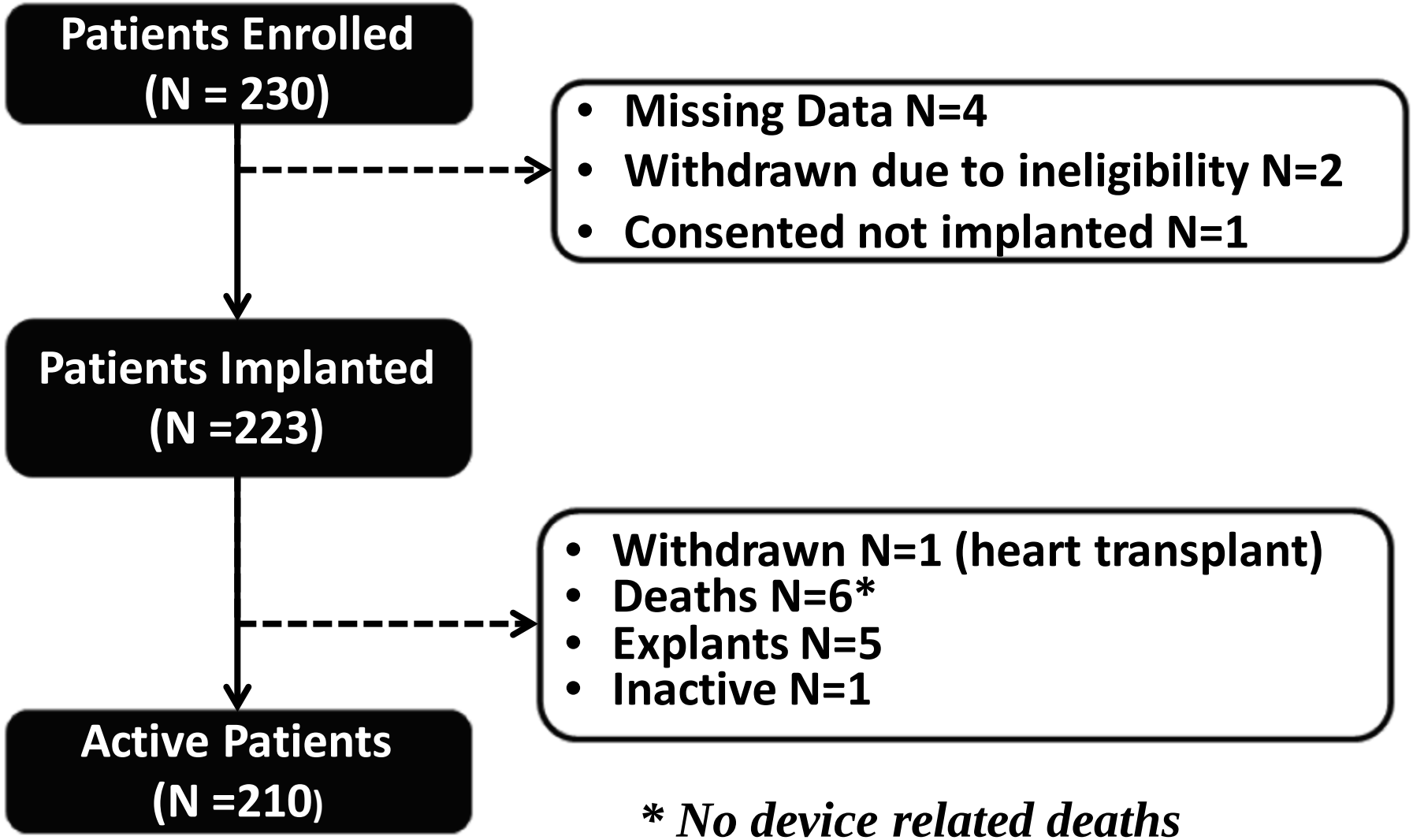
Evaluation oF FactORs AffecTing the CLinical Outcome and Cost EffectiveneSS of the S-ICD

The EFFORTLESS S-ICD Registry Design

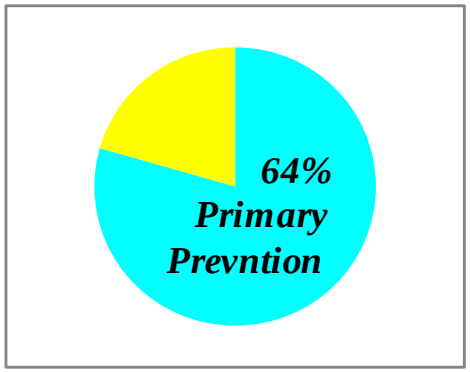
- International, standard of care Registry to collect short, mid and long-term operational and clinical outcome data on the Cameron Health S-ICD system
- Retrospective and prospective patients implanted since CE mark
- Aiming to recruit up to 1000 patients
- 5 year data post implant
- Centers to be included from all current commercial countries

Patient Status as of April 27, 2012

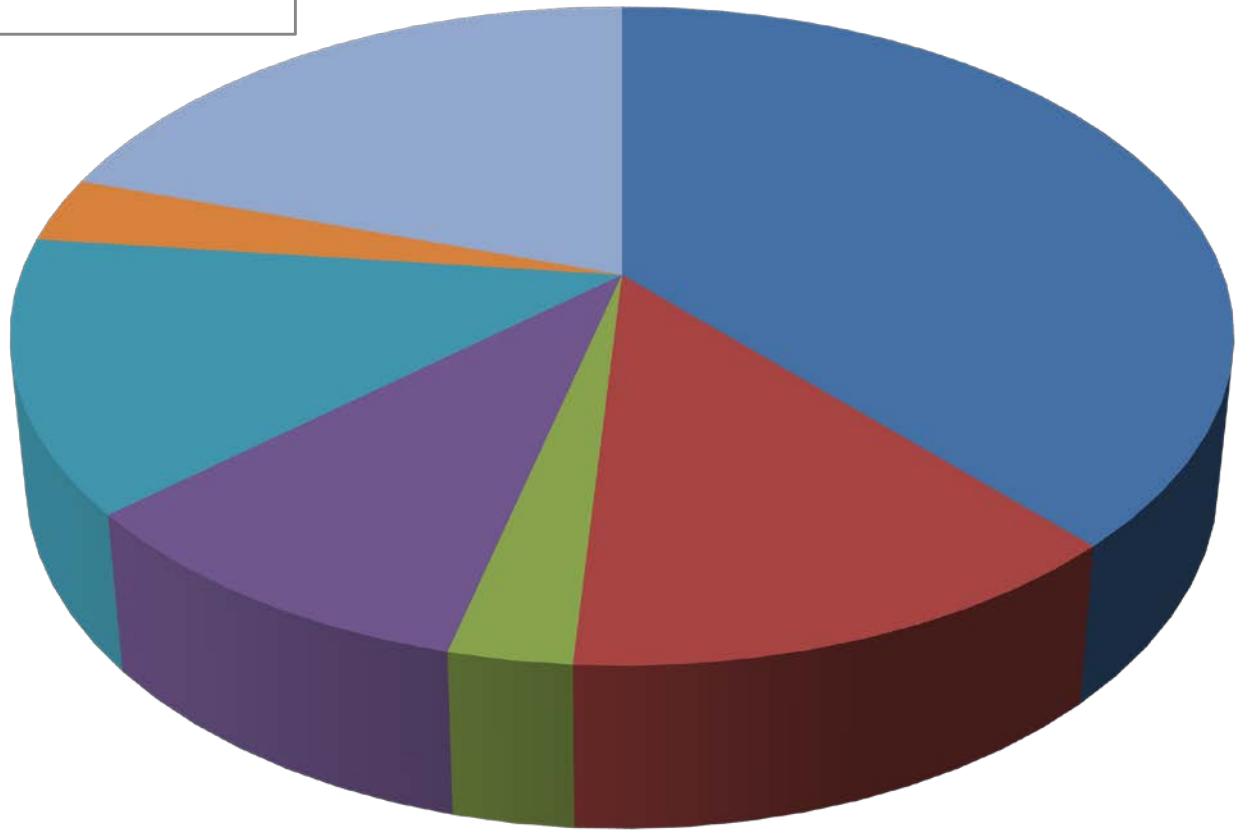
Average FU 389±282 days, max 981 days



** No device related deaths*



Broad Range of ICD Indications



- Ischemic (38%)
- Channelopathy (13%)
- Congential (3%)
- Non ischemic CM (10%)
- HCM (13%)
- ARVD (3%)
- Idiopathic VF (20%)

Effective Conversion of Induced VT/VF

Patient Data	n	%
Implant Conversion test data available	204	
Successful conversion within 1 procedure	201	98.5
-Successful at 65J	197	96.5
-Successful at ≤80J	201	98.5
Patients requiring repositioning		1.5
-Successful conversion following repositioning	1	
-Awaiting retesting (non inducible)	2	

Mean time to therapy: 15.9 ± 3.8 sec (93% within 21 sec)

100% Conversion of Spontaneous VT/VF

- 16 discrete VT/VF episodes from 11 patients

		EPISODES		
Discrete Episodes	Patients	spontaneous Termination	1st S-ICD System Shock Conversion	2nd S-ICD System Shock Conversion
16	11	2	13	1

- 32 VT/VF storm episodes from 2 patients both with electrolyte imbalances (post dialysis and post surgery)

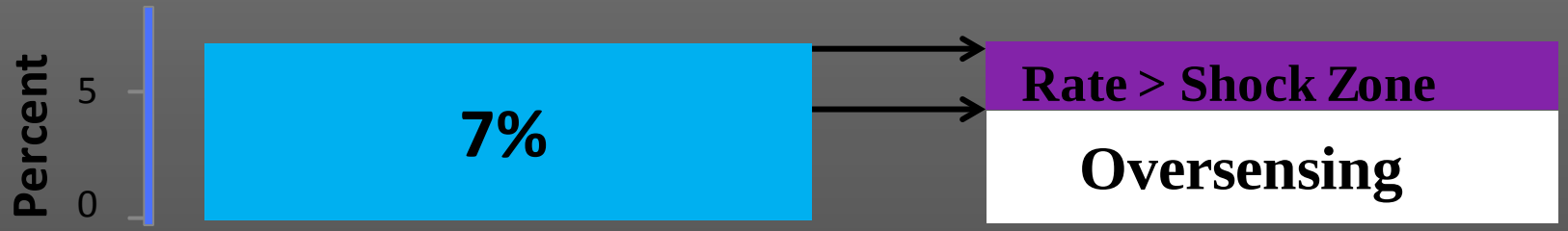
			EPISODES
Storm Events	Episodes	Patients	S-ICD System Shock Conversion
4	32	2	32 (100%)

Device & Procedure-Related Events

Category	Complications	Observations
Device-related	2	16
Procedure-related	15	19
	17 (7%)	

Annual Inappropriate Shock Rate of 7%

- 15 patients received inappropriate shocks (7%)
- No inappropriate shocks have been recorded for AF/SVT within a programmed conditional shock zone



The START Study:
Subcutaneous vs Transvenous Arrhythmia Recognition Testing

Head-To-Head Comparison of Arrhythmia Discrimination Performance of Subcutaneous and Transvenous ICD Arrhythmia Detection Algorithms: The START Study

MICHAEL R. GOLD, M.D., PH.D.,* DOMINIC A. THEUNS, PH.D.,†
BRADLEY P. KNIGHT, M.D.,‡ J. LACY STURDIVANT, M.D.,* RICK SANGHERA, B.S.E.E.,§
KENNETH A. ELLENBOGEN, M.D.,¶ MARK A. WOOD, M.D.,¶ and MARTIN C. BURKE, D.O.**

From the *Medical University of South Carolina, Charleston, South Carolina, USA; †Erasmus MC, Rotterdam, the Netherlands; ‡Northwestern University, Chicago, Illinois, USA; §Cameron Health Inc., San Clemente, California, USA; ¶Virginia Commonwealth University, Richmond, Virginia, USA; and **University of Chicago, Chicago, Illinois, USA

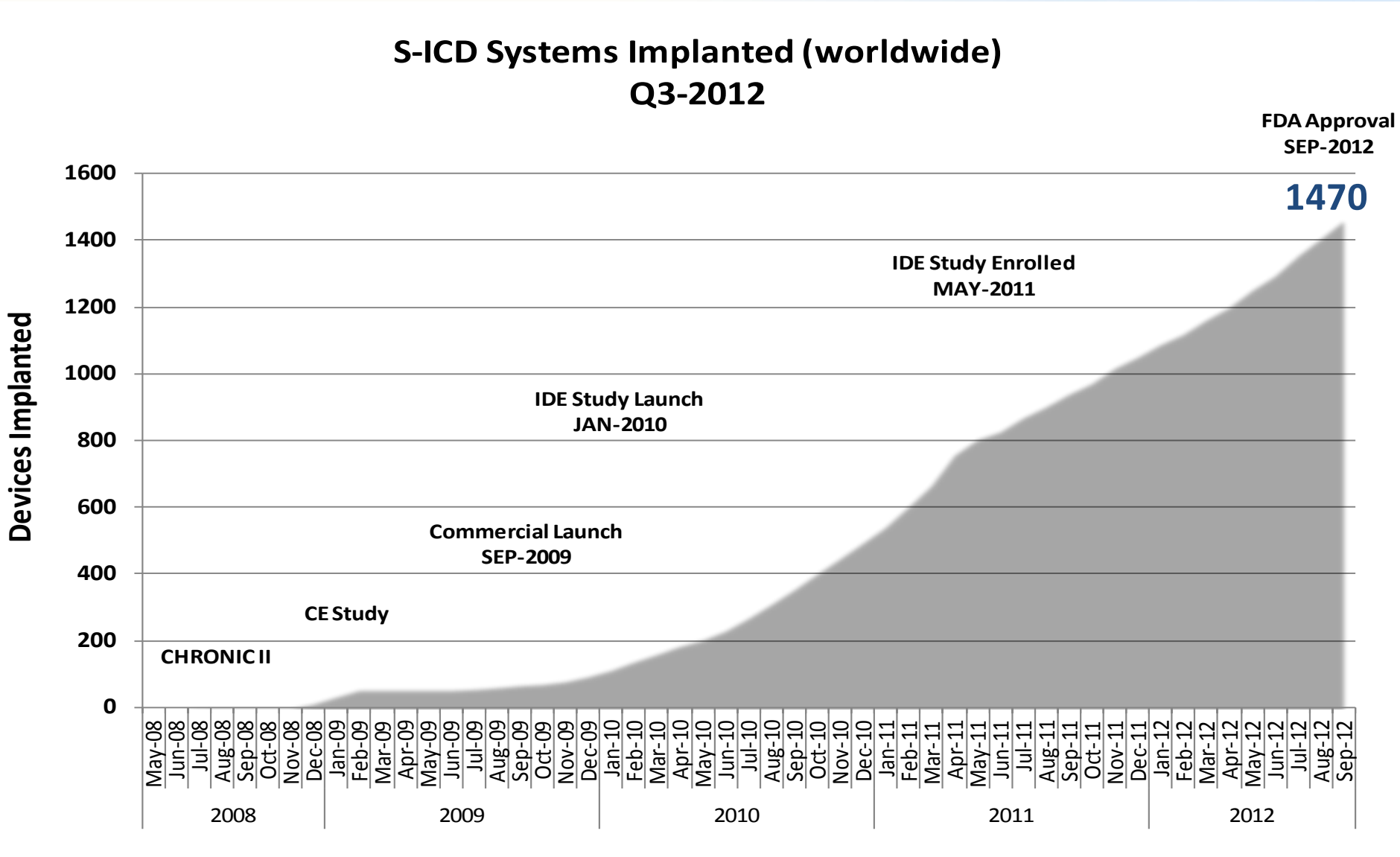
Results: **Appropriate detection of ventricular tachyarrhythmias for subcutaneous and TV devices in single- and dual-zone configurations was 100% and >99%, respectively. Specificity for supraventricular arrhythmias was significantly better for the S-ICD system compared to 2 of 3 TV systems, as well as the composite of TV devices (98.0% [S-ICD] vs 76.7% [SC-TV range: 64.0–92.0%] vs 68.0% [DC-TV range: 32.7–89.8%; P < 0.001]).**

Conclusion: **Appropriate ventricular arrhythmia detection is excellent for all ICD systems evaluated; however, specificity of supraventricular arrhythmia discrimination by the S-ICD system is better than discrimination by 2 of 3 TV systems.** *(J Cardiovasc Electrophysiol, Vol. 23, pp. 359-366, April 2012)*

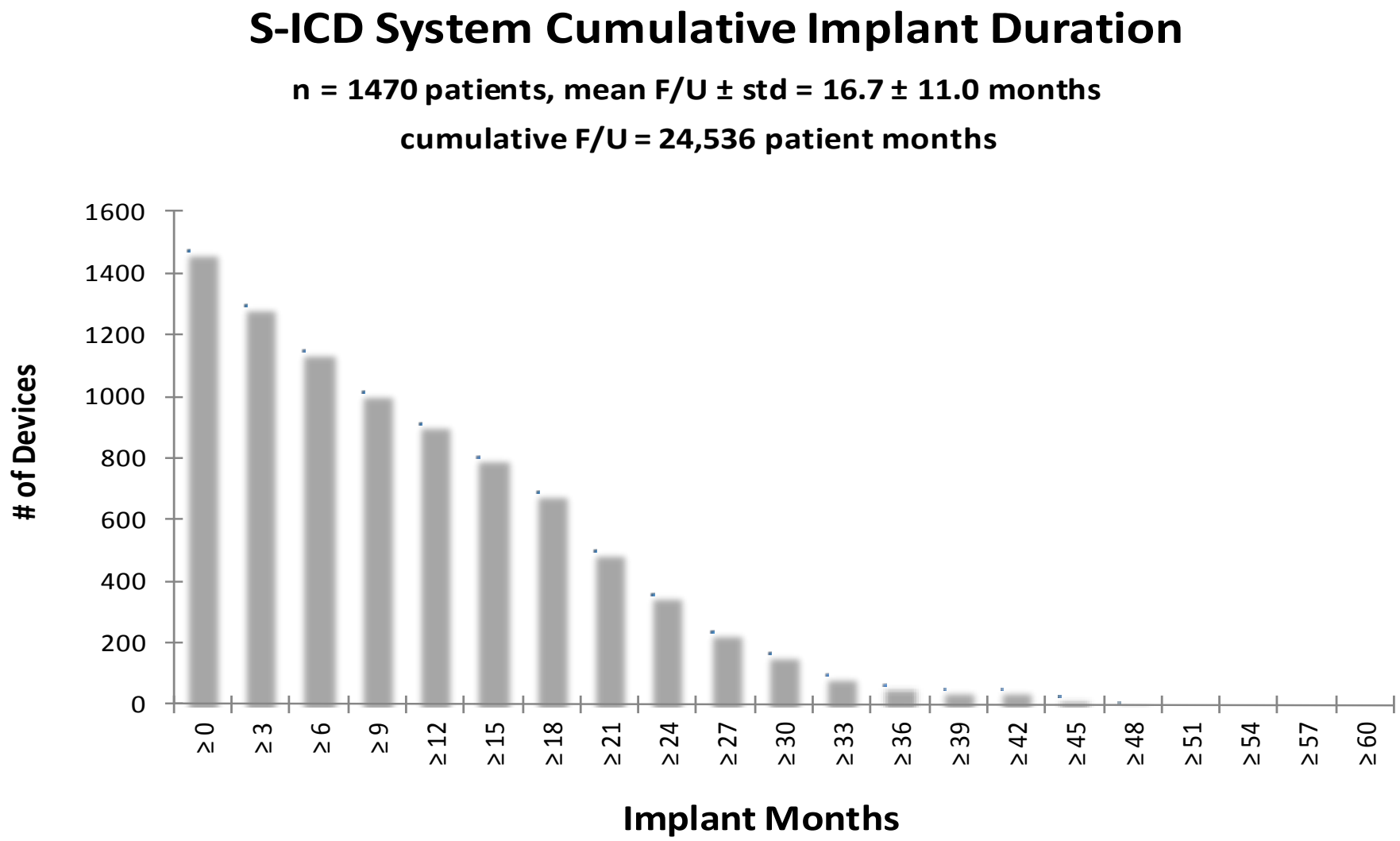
S-ICD System Performance

- Implanted Systems & Duration
- Commercial Use
- Therapy Delivery Analysis

S-ICD System Performance:
Implanted Systems…

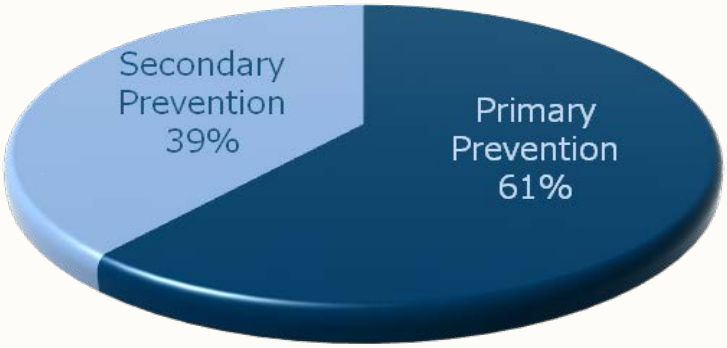


S-ICD System Performance:
Implant Duration (cumulative)…

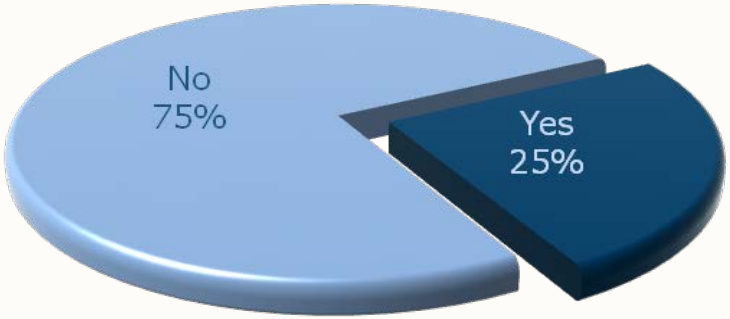


S-ICD System Performance:
Commercial Use…

S-ICD System Indictation

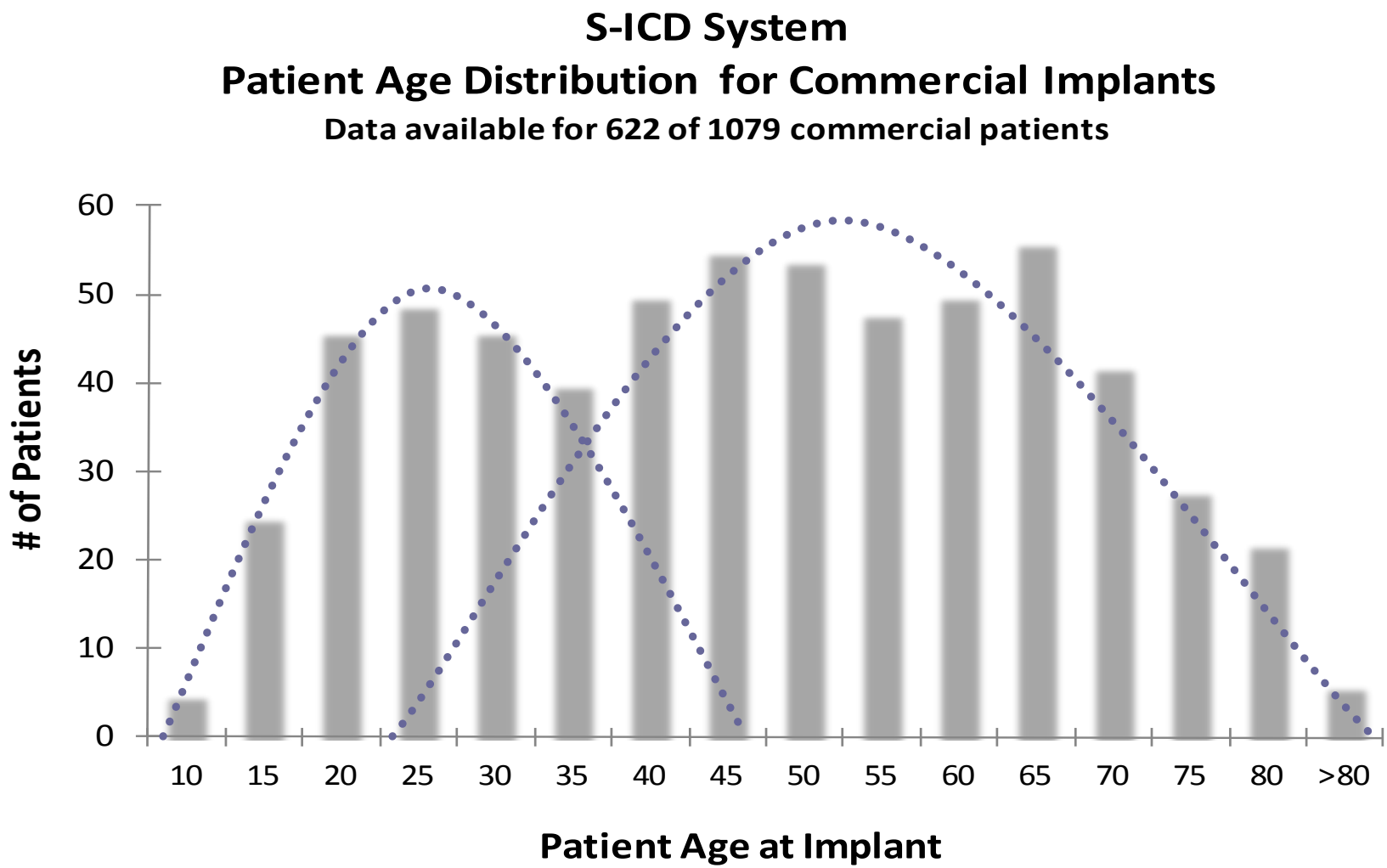


Prior TV-ICD

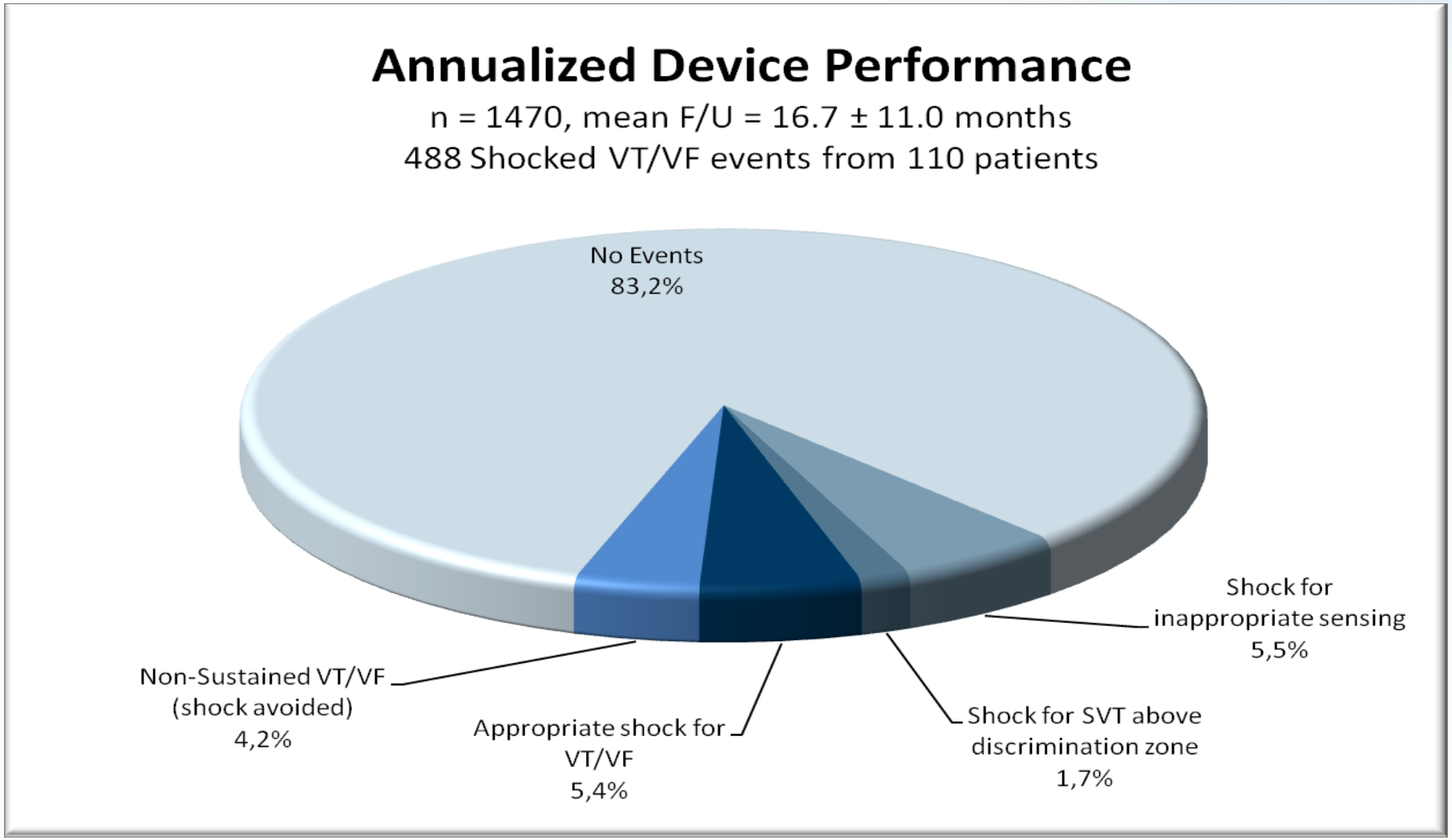


COMMERCIAL (n = 1079)			
AGE (years)		**PRIOR TV-ICD**	
Sample size (n)	622	Sample size (n)	582
Mean (SD)	45 (19)	Yes	145 (25%)
Median	45	No	437 (75%)
Range	10 - 91		
GENDER (%)		**INDICATION (%)**	
Sample size (n)	612	Sample Size (n)	588
Male	74%	Primary	61%
Female	26%	Secondary	39%
HEIGHT (cm)		**TYPES OF PATIENTS TREATED**	
Sample size (n)	494	Sample size (n)	582
Mean (SD)	175 (11)	ARVC	1.0%
Median	175	Brugada	11.2%
Range	100 - 208	CPVT	0.9%
WEIGHT (kg)		DCM	11.0%
Sample size (n)	506	HOCM/HCM	12.5%
Mean (SD)	81 (21)	ICM	5.3%
Median	80	Long QT	4.8%
Range	30 - 180	Situs Inversus	0.3%
BMI		TGV	1.5%
Sample size (n)	493	TOF	1.5%
Mean (SD)	26.5 (5.8)	VF arrest	16.2%
Median	25.6	Other	33.7%
Range	13.8 - 54.0		

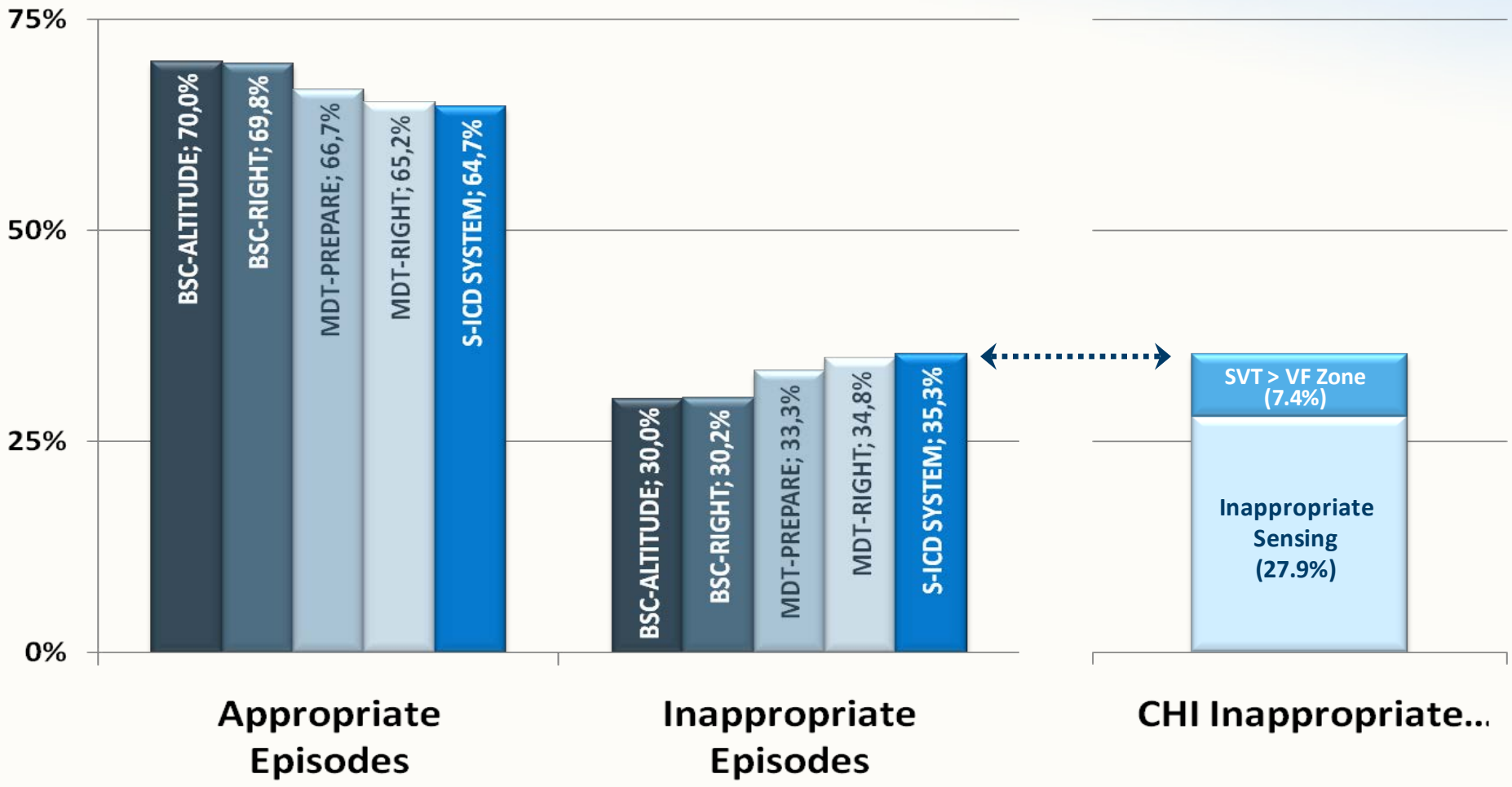
S-ICD System Performance:
Commercial Age Distribution…



S-ICD System Performance:
Therapy Delivery (patient analysis)…



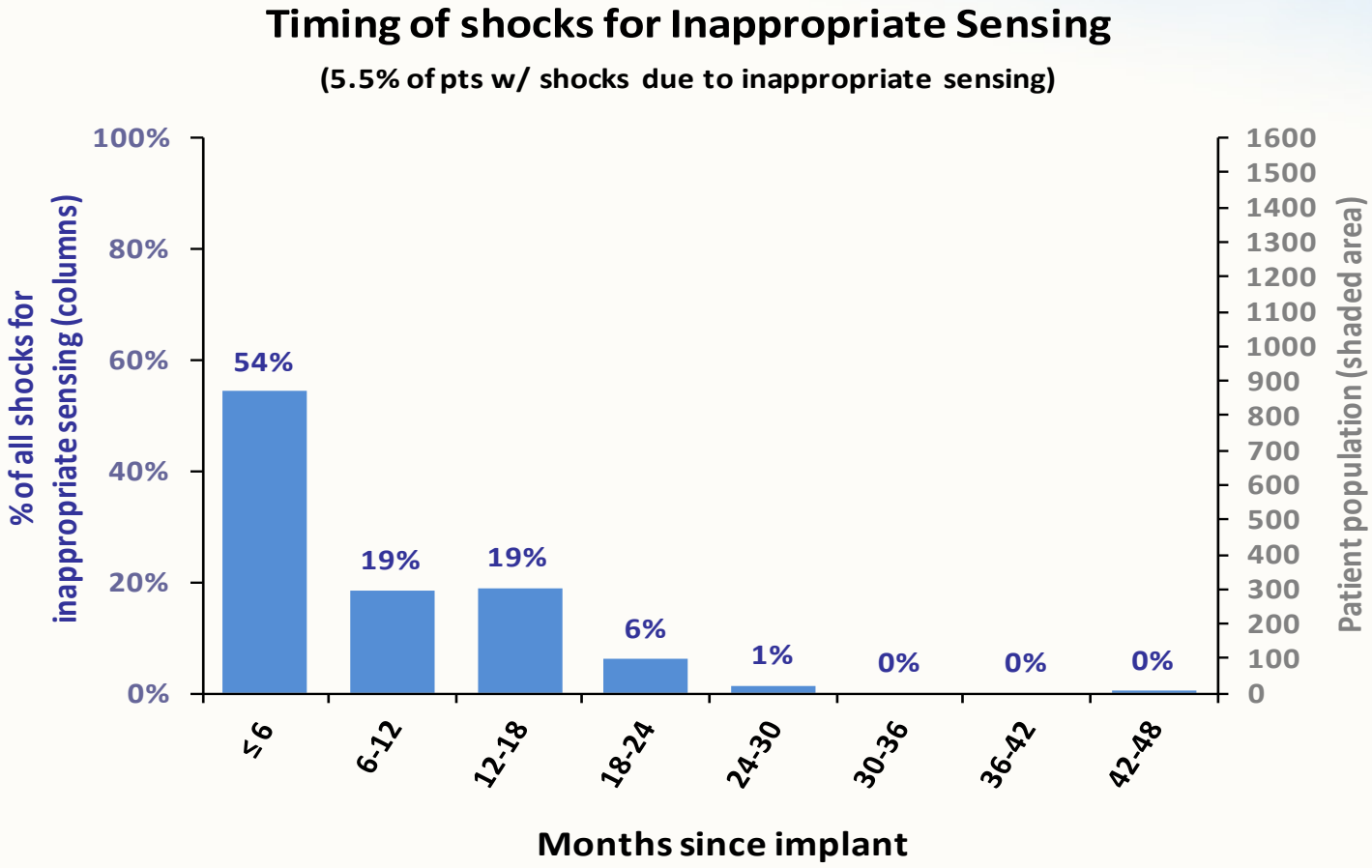
S-ICD System Performance:
Therapy Delivery (episode analysis)…



EPISODE ANALYSIS

S-ICD System Performance:
Therapy Delivery (inappropriate therapy)…

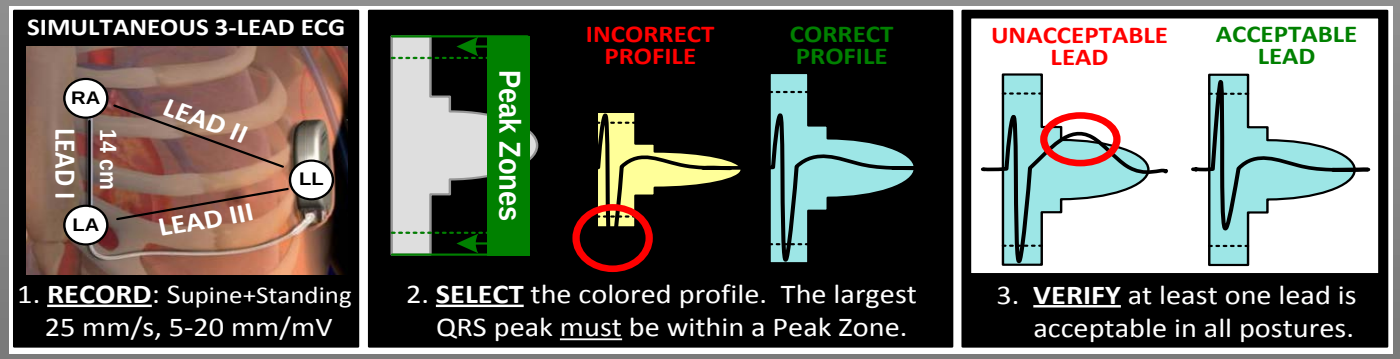
- **Inappropriate Therapy:**
  - Low annual inappropriate shock rate
  - Reprogramming has been very successful at mitigating further events
  - Of the inappropriate therapy delivered, the majority occurred within the first six months from implant and was subsequently managed with reprogramming



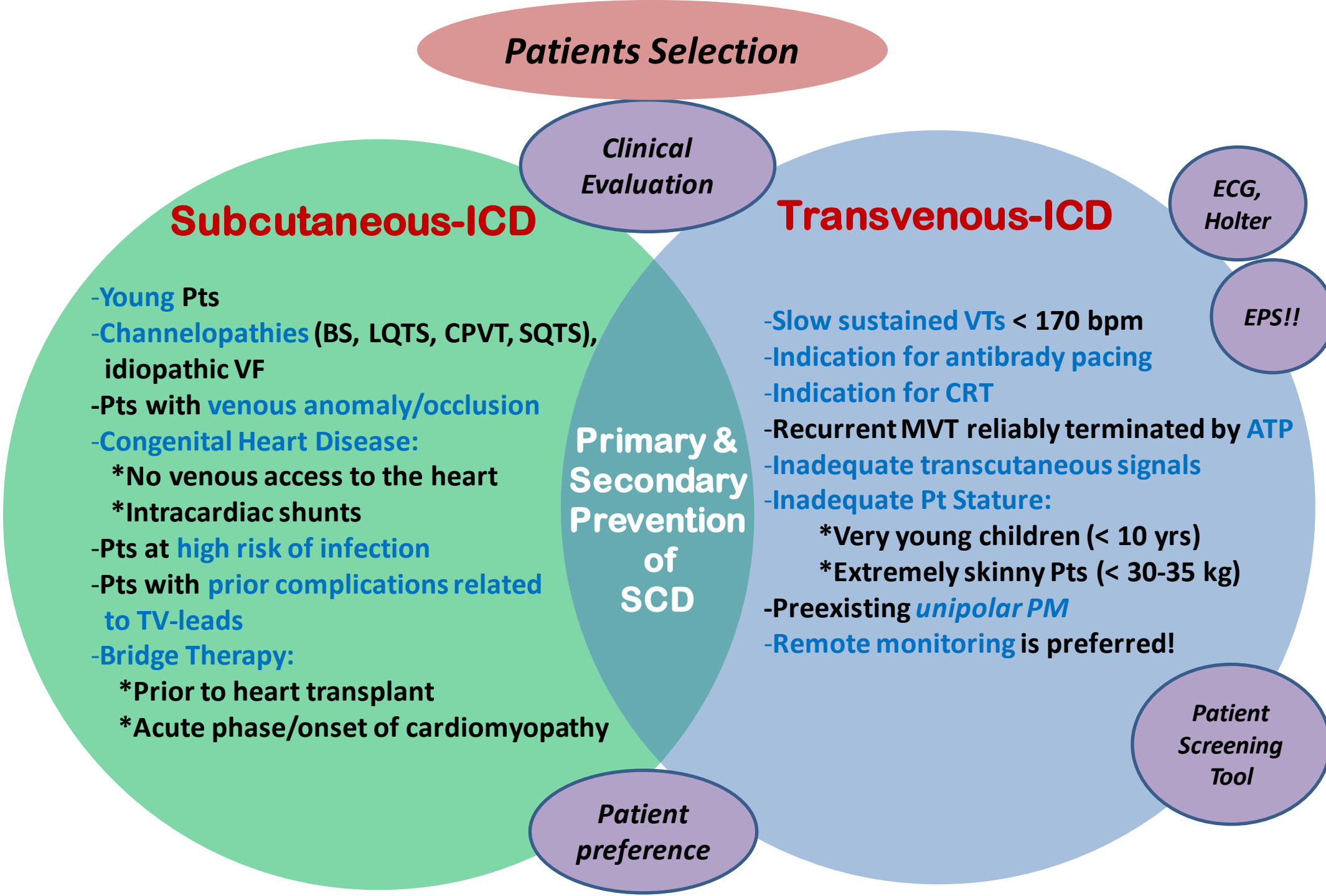
The fully S-ICD system

How to minimize inappropriate shocks in S-ICD Pts?!

- *Patient screening* prior to the implant to insure adequate transcutaneous signals (pre-operating screening tool)



- *Device optimizing* to select the best sensing vector (supine/orthostatic positions)
- *Dual zone programming* is preferred (ex: conditional shock zone 180-220 bpm, shock zone >220 bpm)
- *Exercise test* maybe helpful to evaluate the occurrence of myopotential oversensing/functional BBB during excercise


Patients Selection
Clinical Evaluation
Subcutaneous-ICD
-Young Pts
-Channelopathies (BS, LQTS, CPVT, SQTS), idiopathic VF
-Pts with venous anomaly/occlusion
-Congenital Heart Disease:
*No venous access to the heart
*Intracardiac shunts
-Pts at high risk of infection
-Pts with prior complications related to TV-leads
-Bridge Therapy:
*Prior to heart transplant
*Acute phase/onset of cardiomyopathy
Primary & Secondary Prevention of SCD
Transvenous-ICD
ECG, Holter
EPS!!
-Slow sustained VTs < 170 bpm
-Indication for antibrady pacing
-Indication for CRT
-Recurrent MVT reliably terminated by ATP
-Inadequate transcutaneous signals
-Inadequate Pt Stature:
*Very young children (< 10 yrs)
*Extremely skinny Pts (< 30-35 kg)
-Preexisting unipolar PM
-Remote monitoring is preferred!
Patient Screening Tool
Patient preference

The PRAETORIAN Trial

A Prospective, RAndomizEd comparision of subcuTaneOus & tRansvenous ImplANTable cardiovertor-defibrillator therapy

Louise R. A. Olde Nordkamp, MD,[a,n,o] Reinoud E. Knops, MD,[a,n,o] Gust H. Bardy, MD,[b,n] Yuri Blaauw, MD, PhD,[c,n] Lucas V. A. Boersma, MD, PhD,[d,n] Johannes S. Bos, MD, PhD,[e,n] Peter Paul H. M. Delnoy, MD, PhD,[f,n] Pascal F. H. M. van Dessel, MD, PhD,[a,n] Antoine H. G. Driessen, MD,[g,n] Joris R. de Groot, MD, PhD,[a,n] Jean Paul R. Herrman, MD, PhD,[h,n] Luc J. L. M. Jordaens, MD, PhD,[i,n] Kirsten M. Kooiman, CCDS,[a,n] Alexander H. Maass, MD, PhD,[j,n] Mathias Meine, MD, PhD,[k,n] Yuka Mizusawa, MD,[a,n] Sander G. Molhoek, MD, PhD,[l,n] Jurjen van Opstal, MD, PhD,[m,n] Jan G. P. Tijssen, PhD,[a,n] and Arthur A. M. Wilde, MD, PhD[a,n] *Amsterdam, Maastricht, Nieuwegein, Nijmegen, Zwolle, Rotterdam, Groningen, Utrecht, Breda, and Enschede, The Netherlands; and Seattle, WA*

Study Design The PRAETORIAN trial is an investigator-initiated, randomized, controlled, multicenter, prospective 2-arm trial that outlines the advantages and disadvantages of the subcutaneous ICD. Patients with a class I or IIa indication for ICD therapy without an indication for bradypacing or tachypacing are included. A total of 700 patients are randomized to either the subcutaneous or transvenous ICD (1:1). The study is powered to claim noninferiority of the subcutaneous ICD with respect to the composite primary endpoint of inappropriate shocks and ICD-related complications. After noninferiority is established, statistical analysis is done for potential superiority. Secondary endpoint comparisons of shock efficacy and patient mortality are also made.

The fully S-ICD system

CONCLUSIONS

- **After more than a decade of continuous research/studies, the S-ICD has become a *real life* clinical practice for primary/secondary prevention of SCD unless pacing is required**
- **S-ICD avoids procedural difficulties/complications associated with transvenous leads, and does not require routine fluoroscopy use**
- **Further technology innovations as *Leadless Pacing*, if integrated with the S-ICD might offer an attractive therapeutic approach in the future**
- **Considering the simplicity of its implantation/removal, the S-ICD may fill the gap between the current indications for ICD therapy and the clinical practice**

It might expand indications for ICD therapy in the future?!

The Subcutaneous ICD

Thanks for your attention!

I.R.C.C.S . POLICLINICO SAN DONATO, MILAN

Patients Selection

Subcutaneous ICD

- Young Pts with long life expectancy *who are more prone to lead failure*
- Channelopathies (BS, LQTS, CPVT, SQTS), idiopathic VF *(the initial arrhythmia is usually PVT/VF unresponsive to ATP)*
- Pts with venous anomaly/occlusion
- Congenital Heart Disease:
  - *No venous access to the heart *(Fontan)*
  - *Intrcardiac shunts *(thromboembolic risk with TV-leads)*
- Pts at high risk of infection:
  - *Immunosuppressive therapy
  - *Pts on dialysis
  - *HIV
- Pts with prior complications related to TV-leads:
  - *endocarditis *venous thrombosis
  - *multiple lead failures/extractions)
- Non obstructive HCM
- Bridge Therapy, similarly to WCD:
  - *Prior to heart transplant
  - *Acute phase/onset of cardiomyopathy

Primary & Secondary Prevention of SCD

Clinical Evaluation

Patient preference

Transvenous ICD

EPS!!

- Slow sustained VTs < 170 bpm
- Indication for antibrady pacing
- Indication for CRT
- Recurrent MVT reliably terminated by ATP
- Inadequate transcutaneous signals
- Unipolar PM

Patient Screening Tool

- High probability to develop pacing indication:
  - *PQ > 300 ms, Bi/tre-fascicular Block
  - *LBBB ± low EF%
  - *Marked sinus bradycardia with BB therapy is still to be optimized
  - *Specific cardiopathies (Sarcoidosis, OHCM, Amyloidosis, Muscular Dystrophy, LQTS3)
  - *Chronic AF!
  - *Very old Pts (> 75 yrs)

ECG, Holter

Cardiac Immaging

- Inadequate Pt Stature:
  - *Very young children (< 10 yrs)
  - *Extremely skinny Pts (< 35 kg)
  - *Extremely obese Pts (BMI > 40),↑DFT?
- Remote monitoring is preferred!
- Contraindication to ICD test in secondary prevention

Advantages and Limits of S-ICD Therapy

What is the real clinical utility of ATP?

- 6% of SCD-HeFT patients had >1 shock/year
- 3% of SCD-HeFT patients had >1 episode MMVT/year
- PainFree Rx ll indicated ATP success rate of 72%
- Accordingly ATP likely to be clinically beneficial in ~2% of these primary prevention patients

SCD-Heft investigators, Heart Rhythm Society, Boston 2006

Utility of ATP for Fast VT

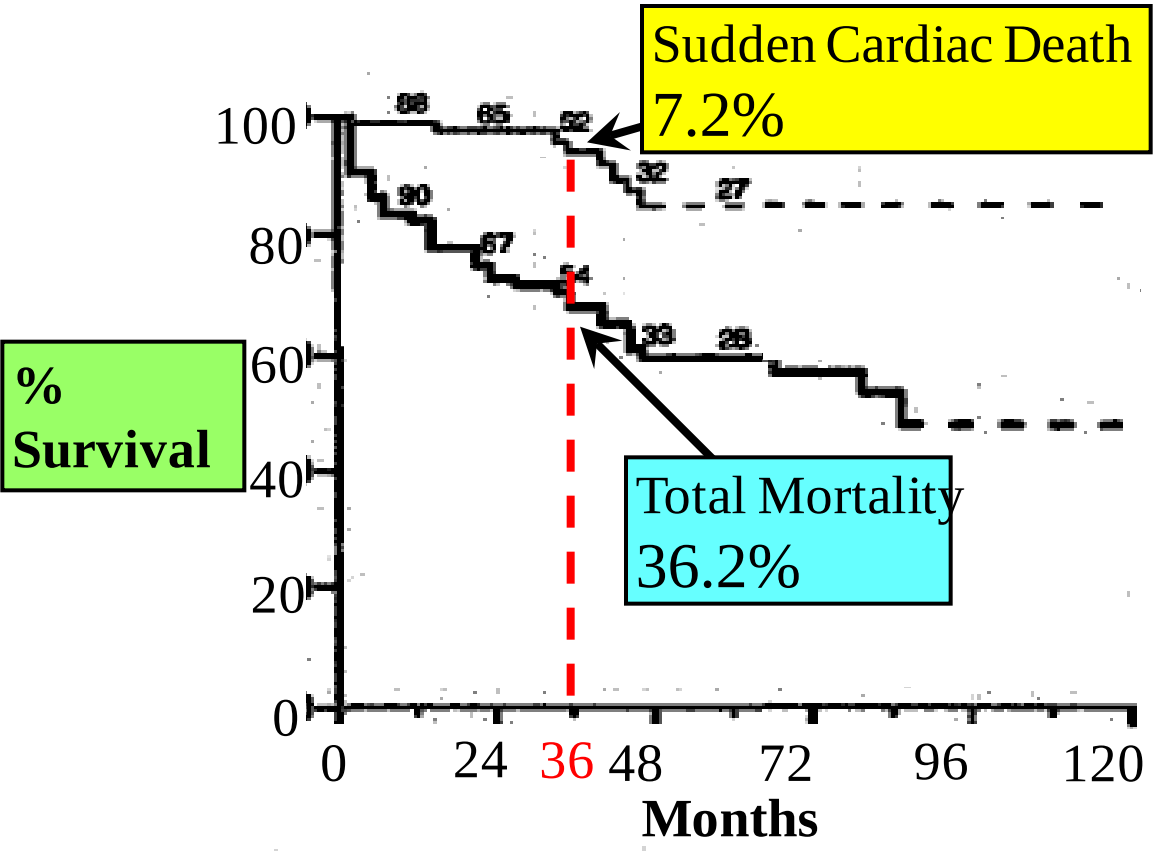
PainFREE RxII

- Shock vs. ATP for VT 188-250 bpm
- 634 patients, 11±3 months follow up
- 1837 analyzed "VT" events, 431 FVT, (134 VF)
- Shock limb; 147 events in 51 patients
  - 110 shocks delivered (if arrhythmia HR > 188 bpm!)
  - 34% spontaneous conversions in arm
- ATP limb; 284 events in 47 patients
  - 2 pts accounted for 131 (46%) of episodes
  - 72% success with ATP, 229/284 episodes
  - 62 shocks delivered
  - No spontaneous conversions in ATP arm
- QOL; Some scores better with ATP, (FVT event patients)

Mortality; Shock 7%, ATP 10%, p=0.22

Wathen et al, 2004

Risk of Sudden Cardiac Death in Patients with "Hemodynamically Stable Sustained VT" After Myocardial Infarction



(Sarter et al. JACC, 1996; 28: 122-9)

- 124 pts: 78 pts - AAD
  46 pts - surgical ablation
- Follow-up: 36 ± 30 month
- ICD in only 6 /124 pts

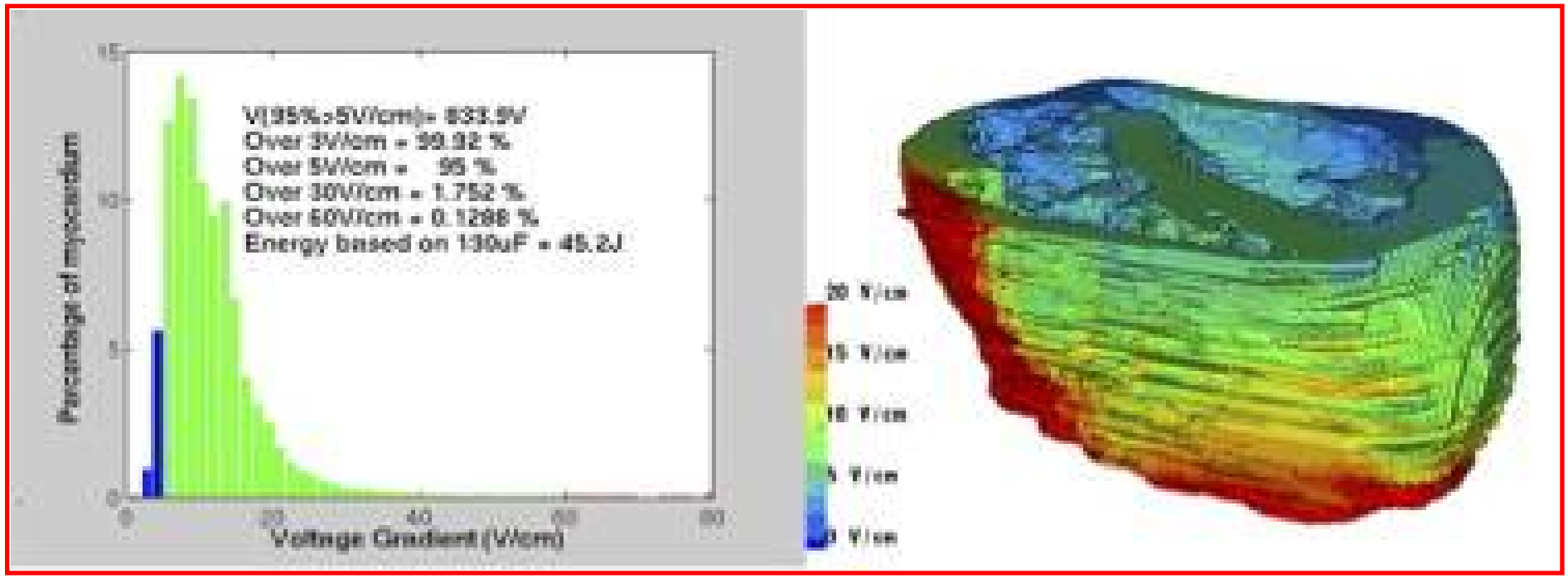
Total mortality: 45/124 (36.2%)

- Sudden Cardiac Death:
  9 pts (7.2%)
  (Average 2.4% / year)
- Heart failure/ Recurrent MI
  20 pts (23.4%)
- Perioperative death 9 pts
  (20% operative mortality)

Defibrillation Voltage Gradients

S-ICD

- Jolley M…Triedman J.
- Computer Modelling, ICD systems
- Subcutaneous ICD, abdominal-right posterior @ DFT



Voltage Metrics @ DFT 42.5 J

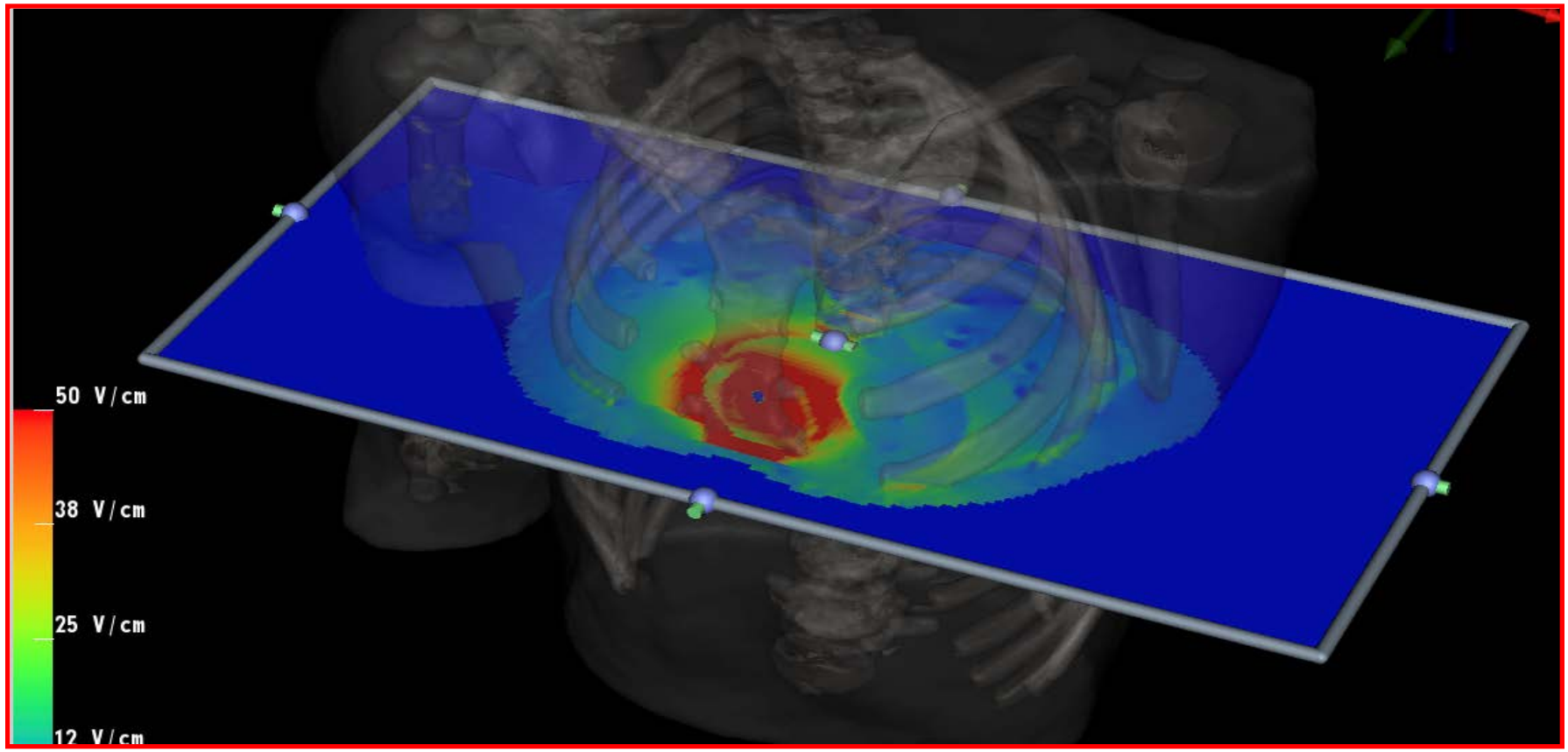
Myocardial Voltage Gradients

Jolley et al Heart Rhythm 2008;5:565

Defibrillation Voltage Gradients

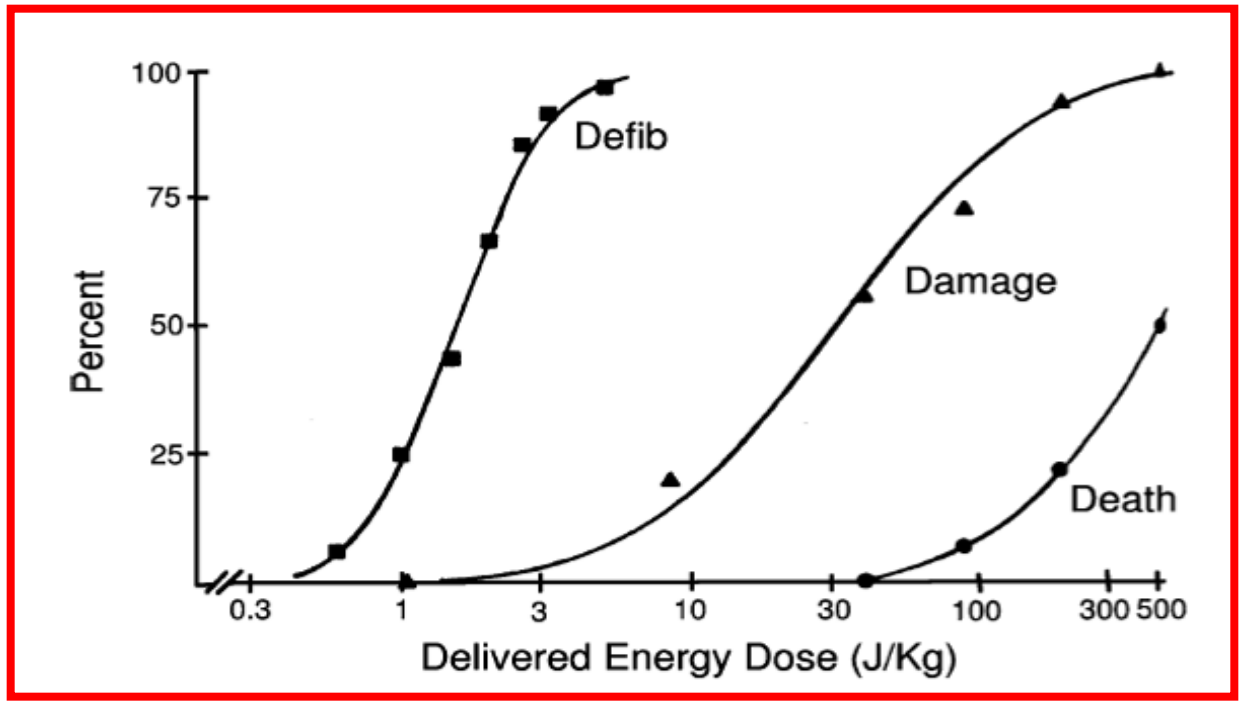
TV-ICD

- Transvenous ICD, Dual Coil, Active Can
- Modelled by Matthew Jolley



Myocardial Voltage Gradients @ DFT

High Defibrillation Shock Strengths Cause Myocardial Damage



Walcott & Ideker

Resuscitation 2003;59:59

Myocardial Voltage Gradients

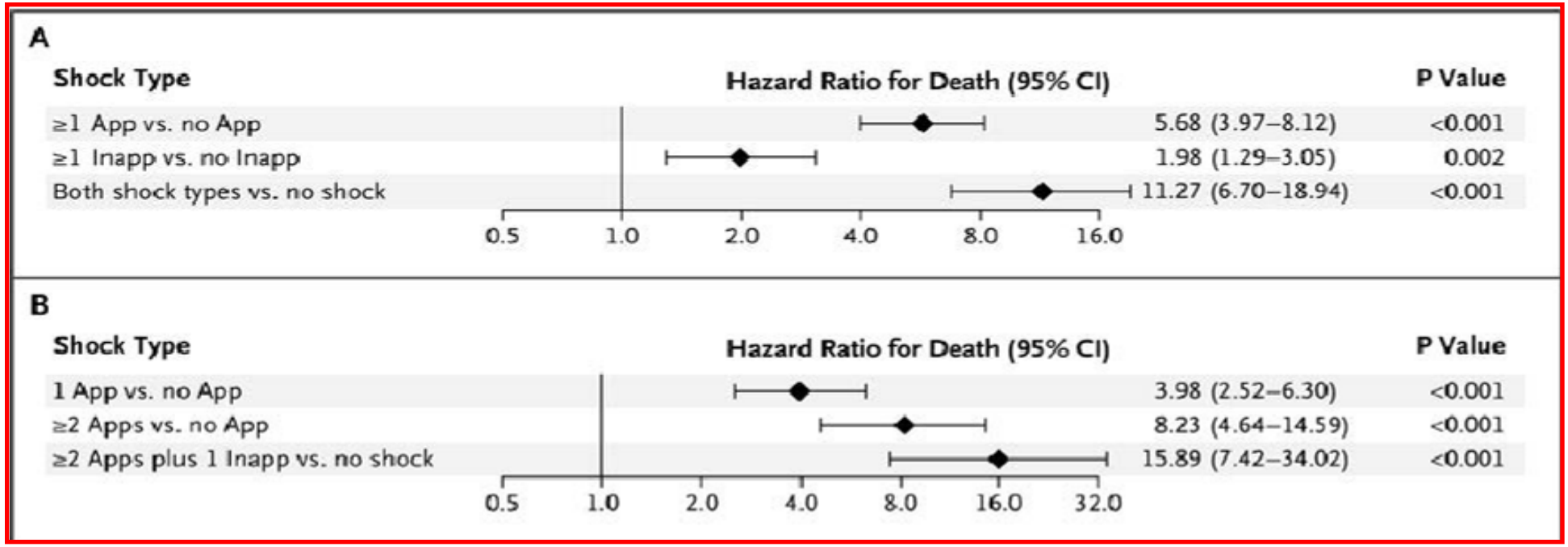
- Defibrillation 5 V/cm
- Electroporation >30 V/cm (Leaky myocyte membranes)
  - Decreased contractility
- Ventricular stunning >50 V/cm
  - Ventricular proarrhythmia

Jones et al Circ Res 1980
Weaver et al NEJM 1988
Bardy et al Circ 1995
Xie et al Circ 1997
Strickberger et al JCEP 1998/9

ICD Shocks Associated with Higher Risk of Death

SCD-HeFT

Hazard Ratios for the Association of ICD Shock with the Risk of Death, According to Shock Type

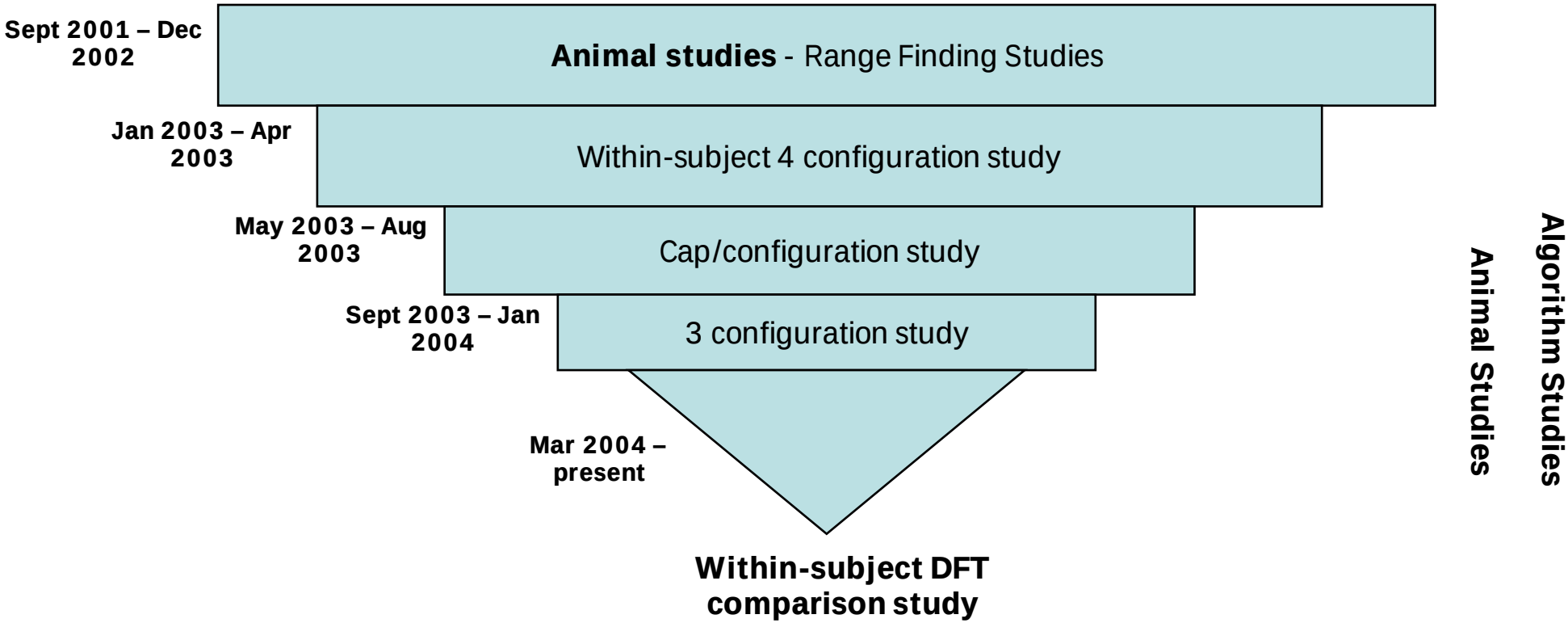


Appropriate and Inappropriate Shocks were *associated* with a Higher Risk of Death

Poole et al NEJM 2008;359:1009

Progress in Device Technology: Subcutaneous ICD

Preclinical and Clinical Research Timeline



Subcutaneous Pacing

Leadless Pacing Technologies

Concept

- Use of ultrasound energy transmission through the chest to a receiver-electrode in contact with the myocardium that converts the ultrasound energy into electrical energy sufficient to pace the myocardium

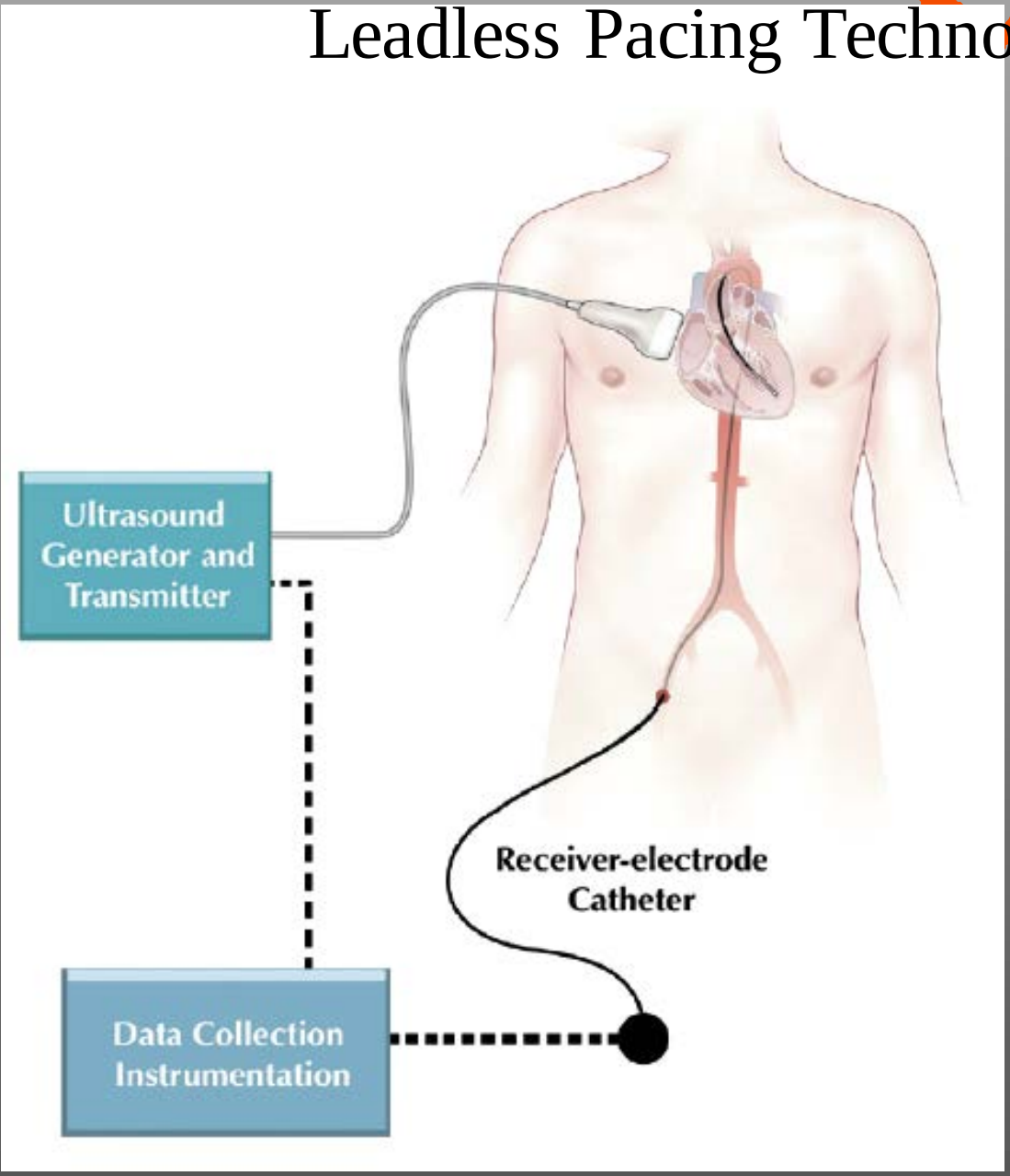
Echt et al, 2006

Leadless Pacing Technologies

Methods

- Ultrasound energy transmitted at 313 to 385 kHz
- Transmitter moved on the chest wall to target the receiver (circuitry to convert ultrasound energy into electrical energy)

Leadless Pacing Technologies

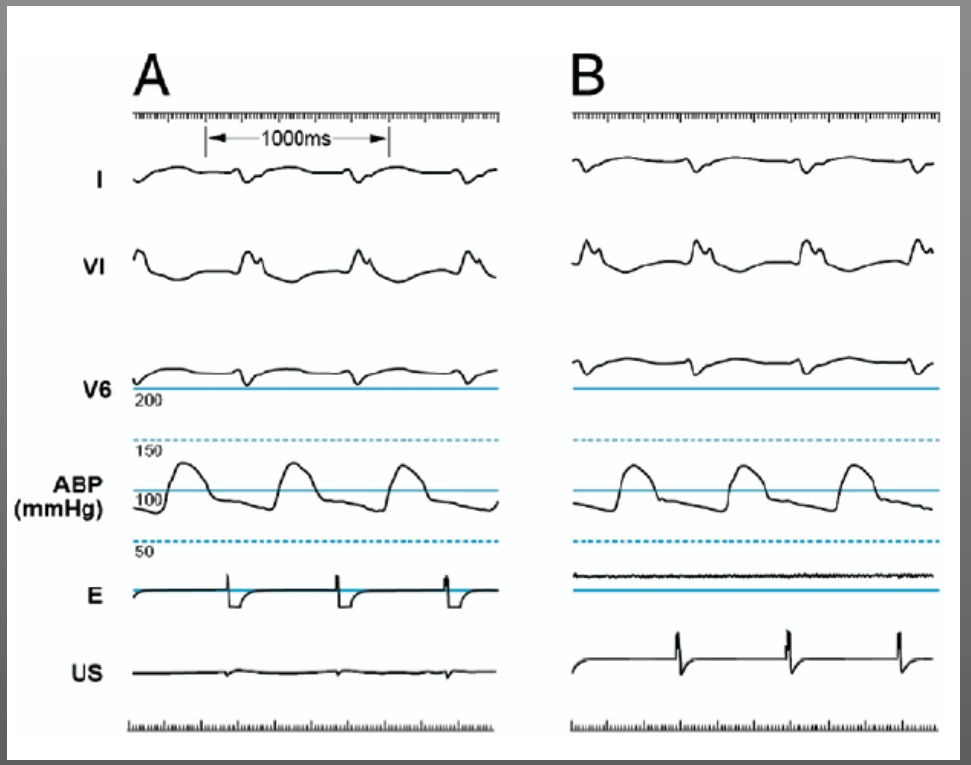


Leadless Pacing Technologies

Results

Human studies

- 24 pts (48 ± 12 yrs)
- 80 pacing sites tested (3.3 / pt)
- Ultrasound mediated pacing achieved at all sites, w/ capture at 77 (96%)
- No adverse events, no pt discomfort



Lee et al, 2007

Leadless Pacing Technologies

Temporary leadless pacing in heart failure patients with ultrasound-mediated stimulation energy and effects on the acoustic window

Kathy L. Lee, MBBS,* Hung-Fat Tse, MD, PhD,* Debra S. Echt, MD, FHRS,† Chu-Pak Lau, MD, FHRS*

*From the *Cardiology Division, Department of Medicine, University of Hong Kong, Hong Kong Special Administrative Region, China, and †EBR Systems, Inc., Sunnyvale, California.*

Heart Rhythm, Vol 6, No 6, June 2009

RESULTS Ten pts were studied. Ultrasound-mediated pacing was successful in all pts.

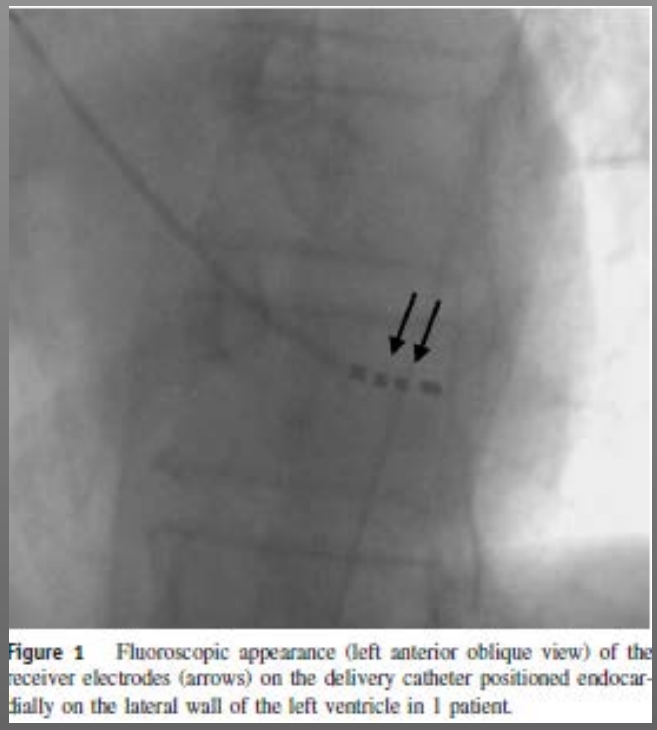


Figure 1 Fluoroscopic appearance (left anterior oblique view) of the receiver electrodes (arrows) on the delivery catheter positioned endocardially on the lateral wall of the left ventricle in 1 patient.

Leadless Pacing Technologies

EDITORIAL COMMENTARY

The leadless ultrasonic pacemaker: A sound idea?

David G. Benditt, BScEE, MD, FACC, FRCPC, FHRS, MaryAnn Goldstein, MD,
Andres Belalcazar, BSEE, PhD

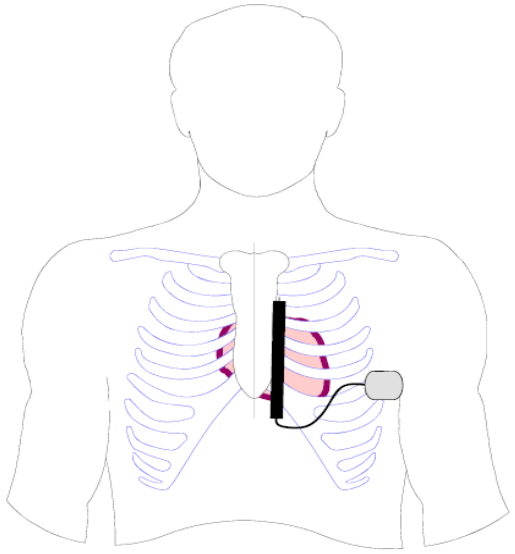
From The Cardiac Arrhythmia Center, University of Minnesota Medical School, Minneapolis, Minnesota.

Heart Rhythm, Vol 6, No 6, June 2009

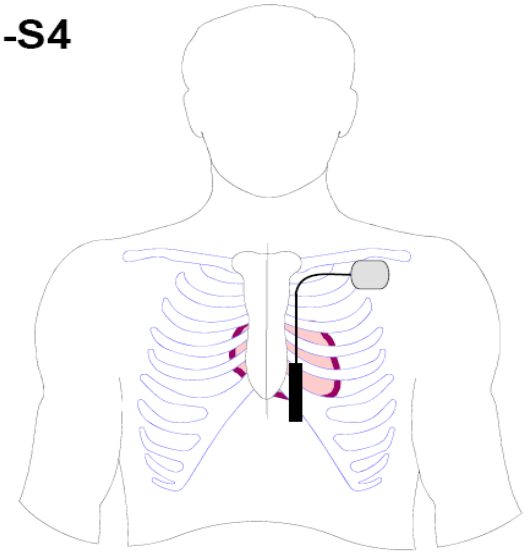
" However…many obstacles remain to be overcome…and it is much too early to determine whether it is indeed a sound idea"

S-ICDs: Development to First Chronic Human Implant

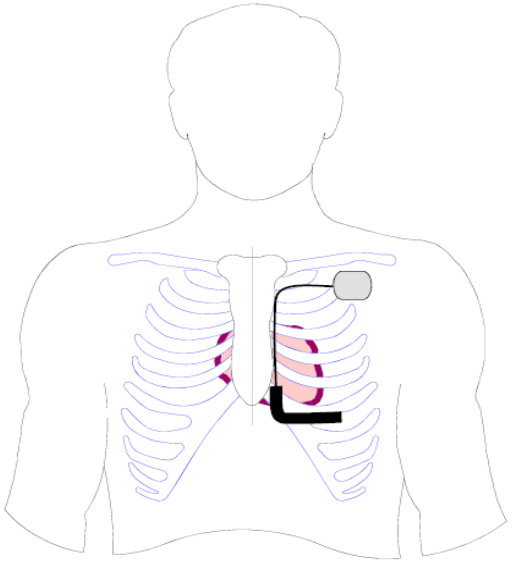
1. LCan-S8



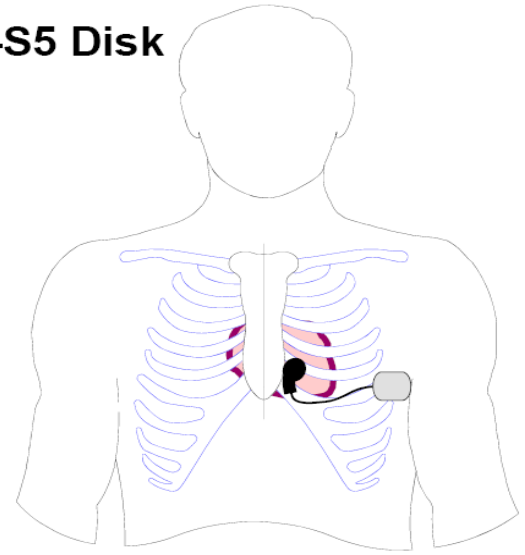
2. PCan-S4

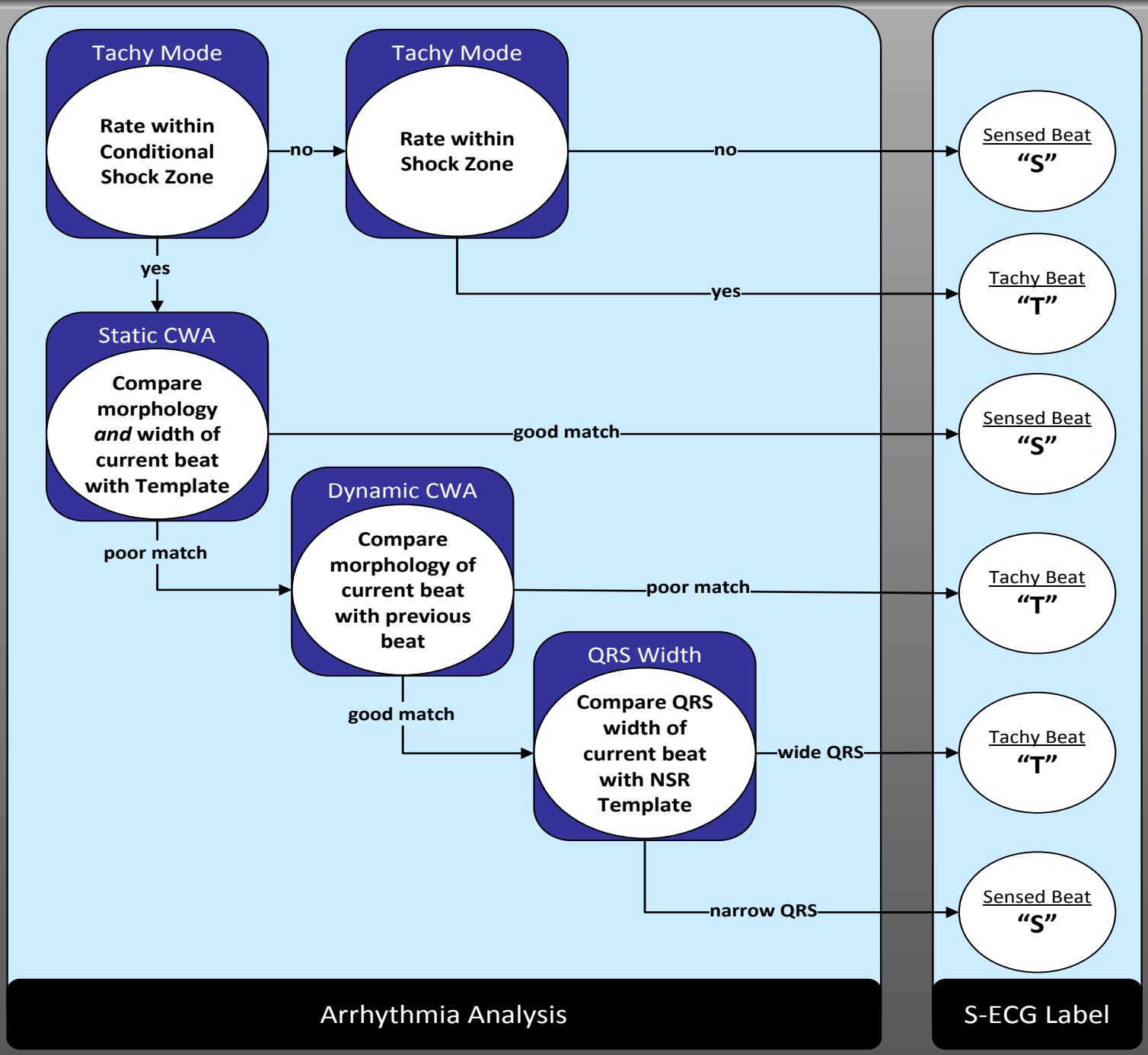


3. PCan-C8



4. LCan-S5 Disk




Tachy Mode
Rate within Conditional Shock Zone
no
Tachy Mode
Rate within Shock Zone
no
Sensed Beat
"S"
yes
yes
Tachy Beat
"T"
Static CWA
Compare morphology *and* width of current beat with Template
good match
Sensed Beat
"S"
poor match
Dynamic CWA
Compare morphology of current beat with previous beat
poor match
Tachy Beat
"T"
QRS Width
good match
Compare QRS width of current beat with NSR Template
wide QRS
Tachy Beat
"T"
narrow QRS
Sensed Beat
"S"
Arrhythmia Analysis
S-ECG Label