Session 5. Device Therapy and Heart Failure

New Leadless ICD Technologies

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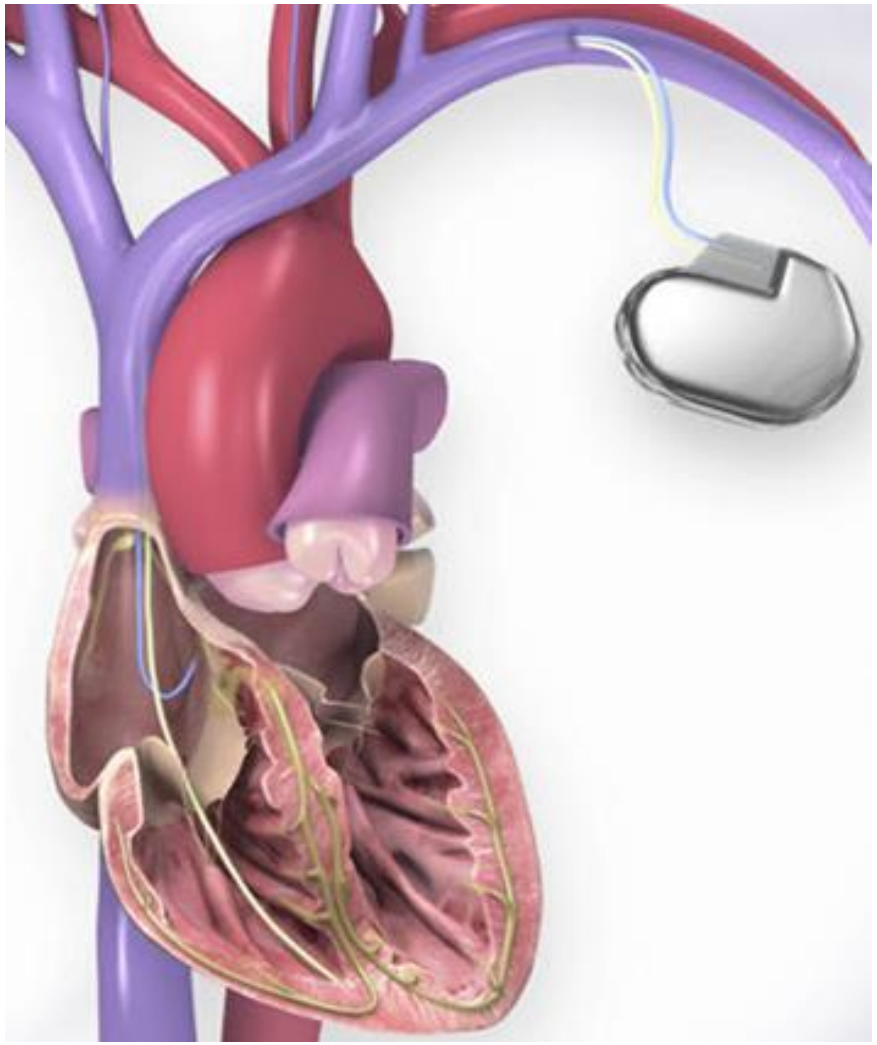
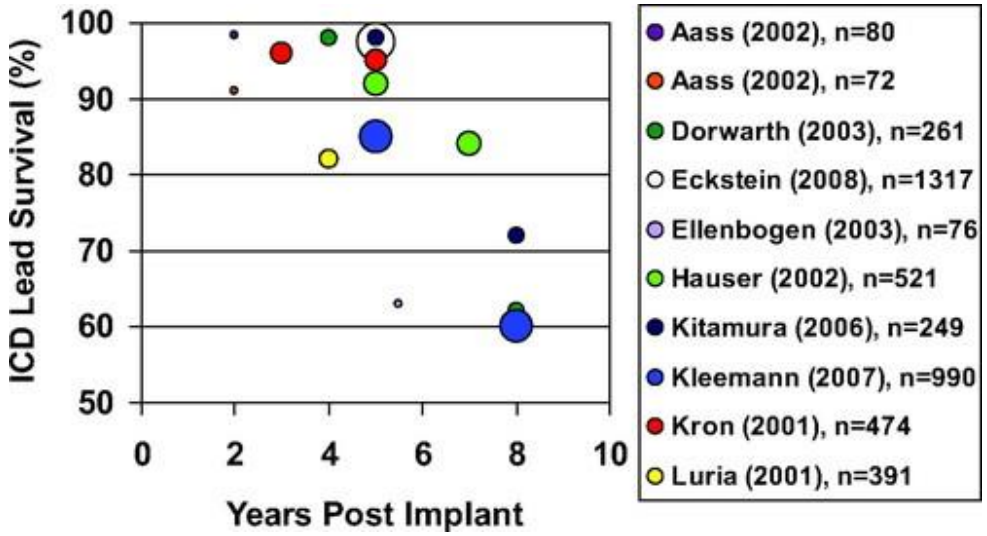
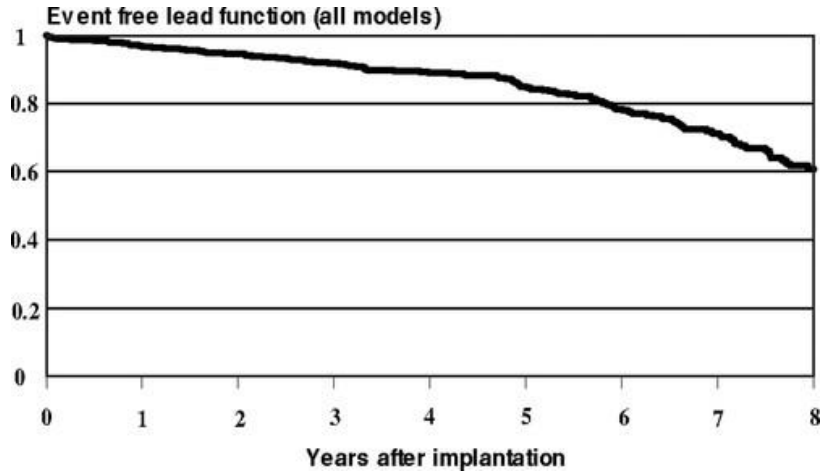
ICD with Transvenous leads

- Clear survival benefit in many RCTs
- Smaller devices, Longer battery life
- Rapid, simple, low risk implantation procedure
- Sophisticated VT/VF programming
- AF detection
- Remote monitoring
- Low rates of inappropriate shocks



Complication risk of transvenous ICD Mostly from TV-lead





- The Danish Registry demonstrated that up to 15% of ICD patients are at risk of a complication within the first 6 months of implant.
- The majority of complications requiring invasive intervention included:
  - Lead related issues: lead dislodgement, lead failure, etc.
  - Infection
  - Cardiac Perforation
  - Pneumothorax

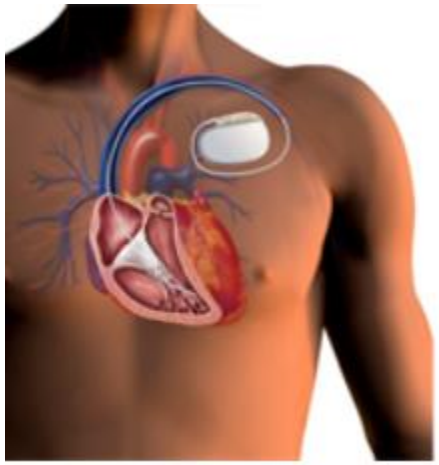
Maisel WH et al. Circulation 2008;117:2721-3
Kirkfeldt RE et al. Eur Heart J 2014;35:1186-94
Kleemann T et al. Circulation. 2007 May 15;115(19):2474-80

Venous stenosis after TV lead placement
: Venogram - mean time since implantation of 6.2 years

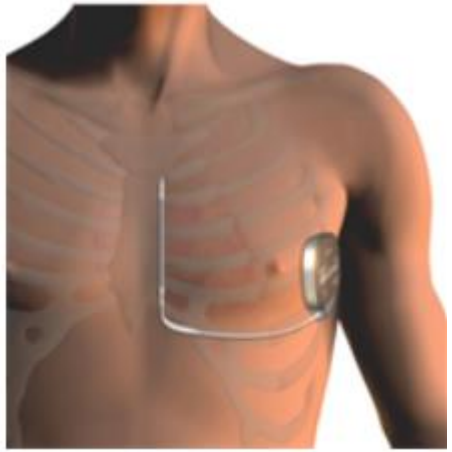
Variable	Percent of Patients
Venous Stenosis	61%
Percent stenosis	
0%	39%
20-49%	10%
50-74%	16%
75-99%	9%
100%	26%

J Am Heart Assoc. 2015 Jul 31;4(8):e001878

TV-ICD vs S-ICD



- Brady pacing
- ATP for patients with VT
- Provides atrial diagnostics (in presence of A lead)
- Rapid, Simple, Familiar implant technique

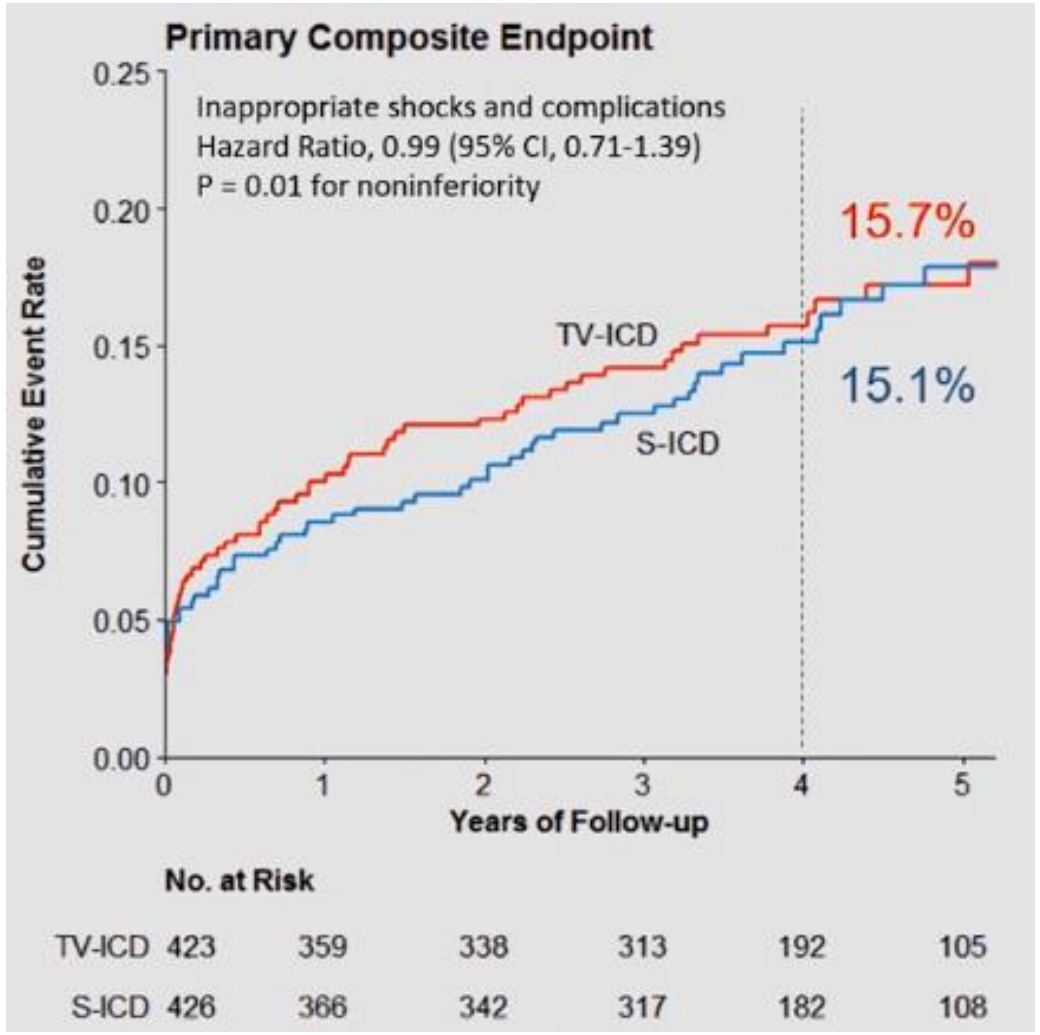


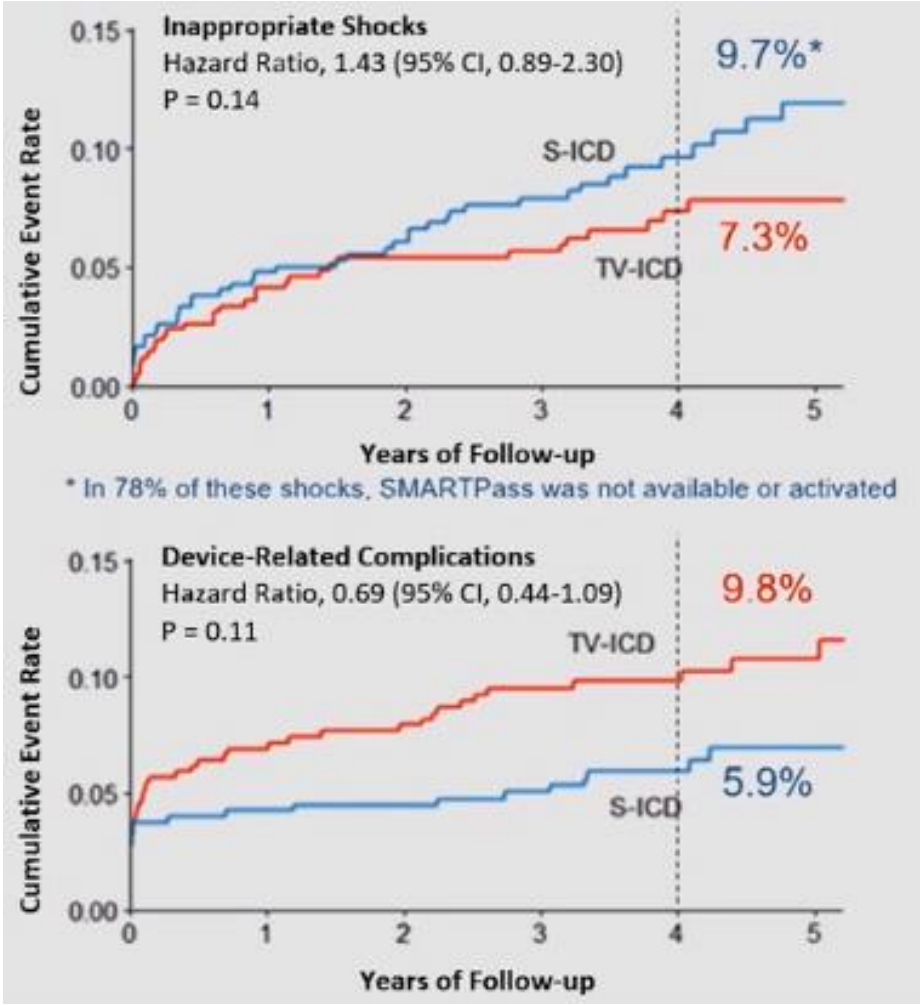
- No risk of vascular injury
- Low risk of systemic infection
- Preserves venous access
- Avoid risk of endovascular lead extraction
- Fluoroscopy not required

PRAETORIAN trial

: S-ICD vs. TV-ICD, N=849 (Class I or IIa indication for ICD, no need for ATP/pacing)

◆Median FU for 48months

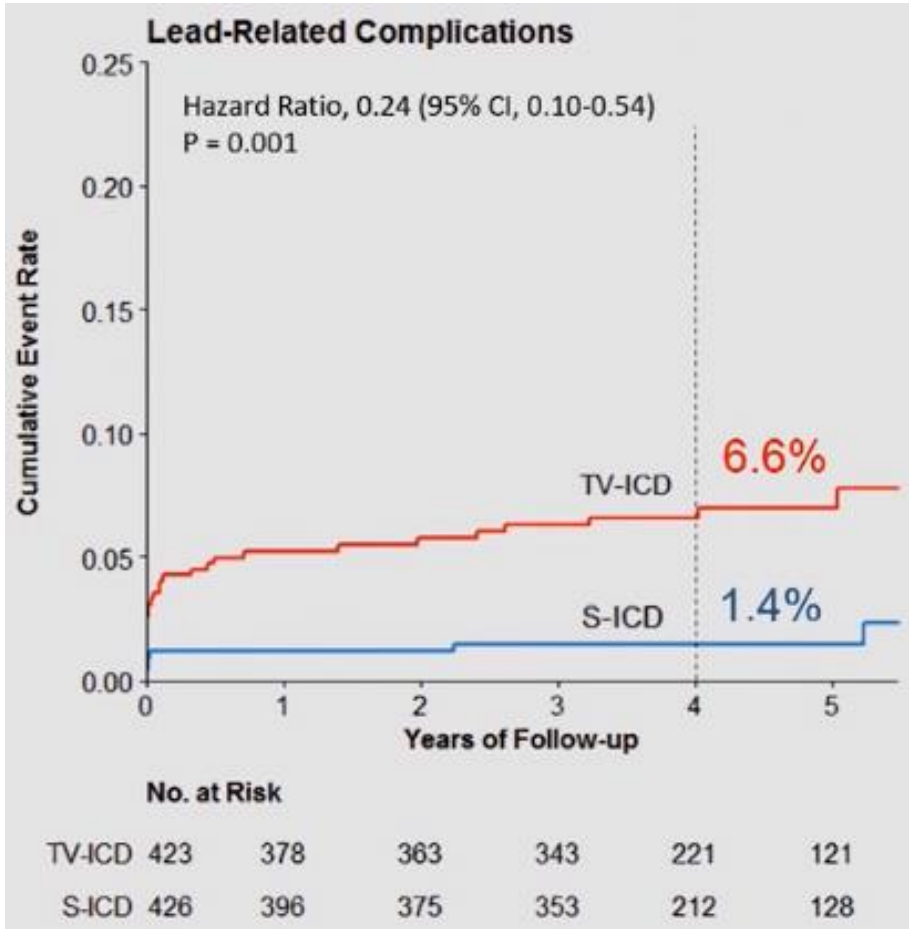




Knops RE et al. N Engl J Med 2020; 383:526-536

PRAETORIAN trial
: S-ICD vs. TV-ICD, N=849 (Class I or IIa indication for ICD, no need for ATP/pacing)

	S-ICD (N = 426)	TV-ICD (N = 423)
Primary composite endpoint	68 (15.1%)	68 (15.7%)
Device-related complications (P = 0.11)	31 (5.9%)	44 (9.8%)
– Infection	4	8
– Bleeding	8	2
– Thrombotic event	1	2
– Pneumothorax	0	4
– Lead perforation	0	4
– Lead repositioning	2	7
– Other	19	20
• Lead replacement	3	9
• Device or sensing malfunction	8	6
• Pacing indication	5	1
• Implantation or DFT failure	3	3
• Pain or discomfort	2	3



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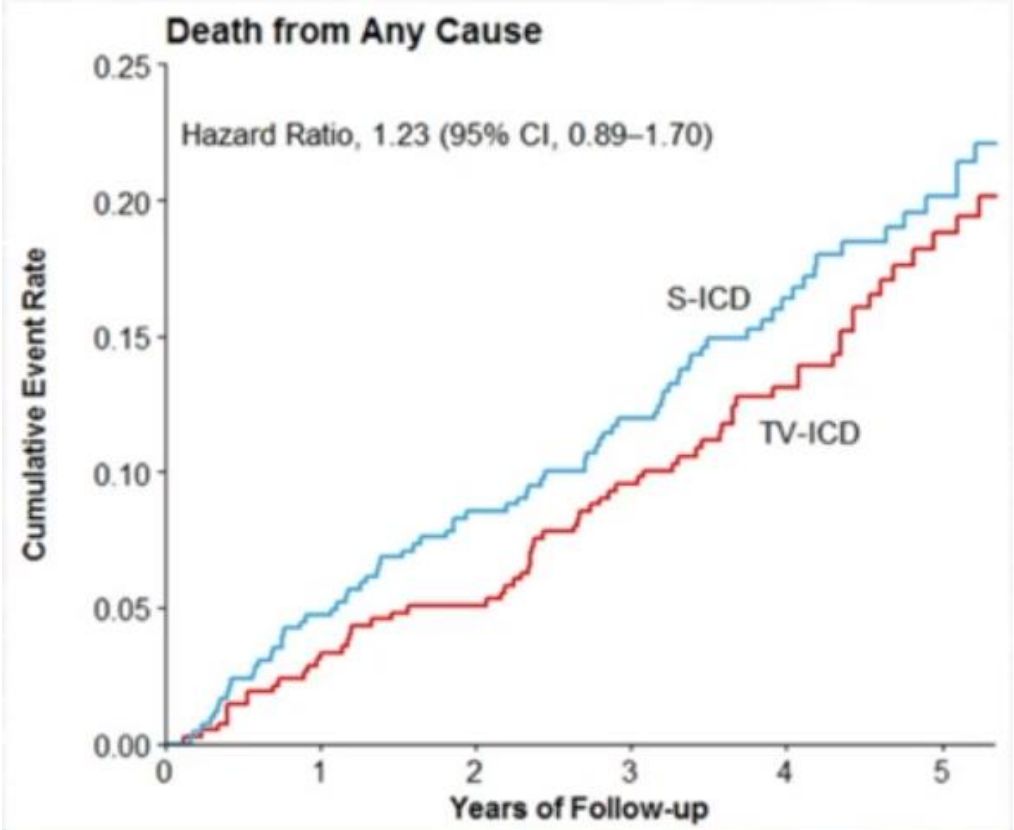


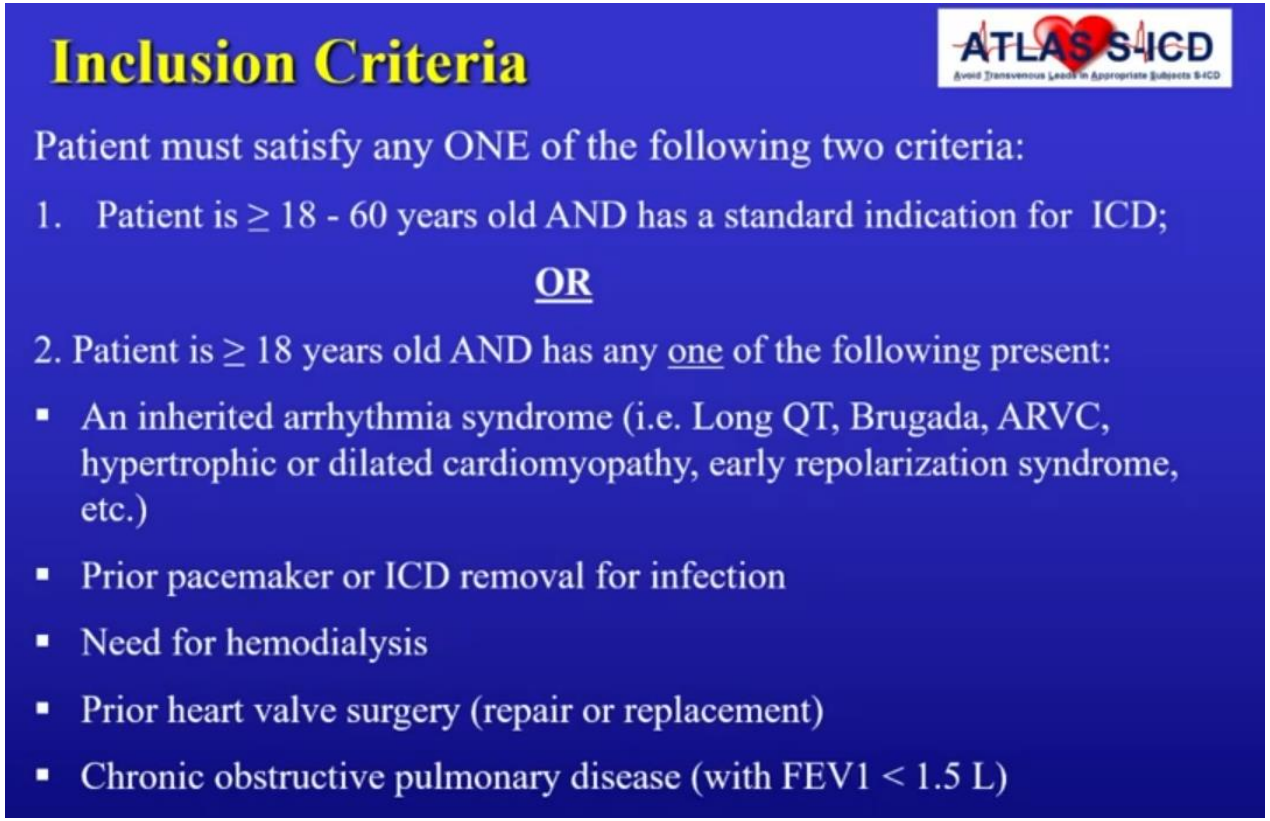
	S-ICD (n = 426)	TV-ICD (n = 423)
Death from any cause	83 (16.4%)	68 (13.1%)
– Sudden cardiac death	18	18
– Other cardiovascular death	34	28
– Noncardiovascular death	31	22

Knops RE et al. N Engl J Med 2020; 383:526-536

Current status of non TV-ICD

- High shock efficacy : similar to TV-ICD
- Low rate of inappropriate shocks; now approaching to TV-ICD
- Survival rate appears similar to TV-ICD (2nd RCT at early 2022)
- Comparative device complication rate, better lead complication rate

Upcoming RCTs : S-ICD vs TV-ICD

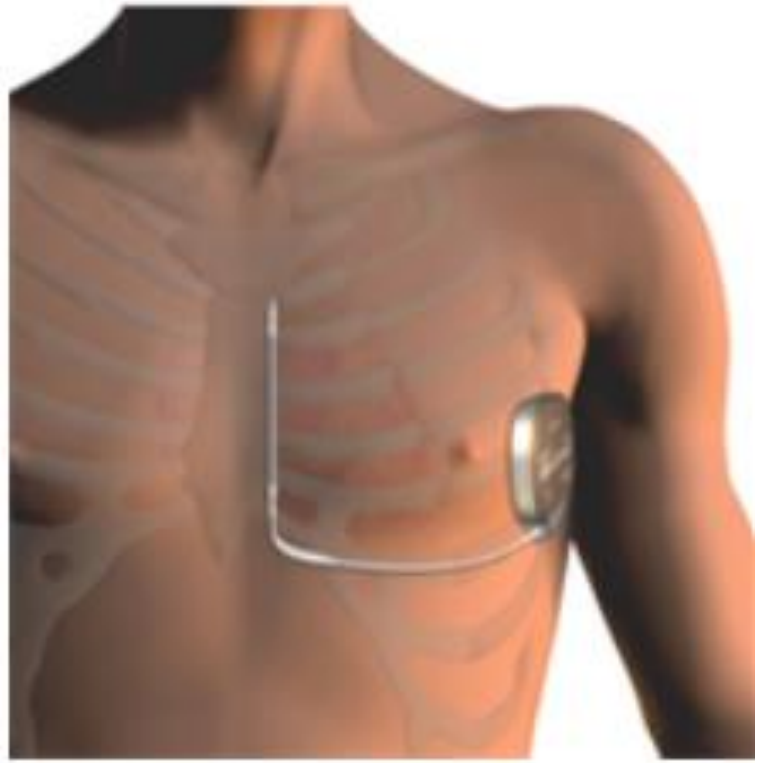


Study Design

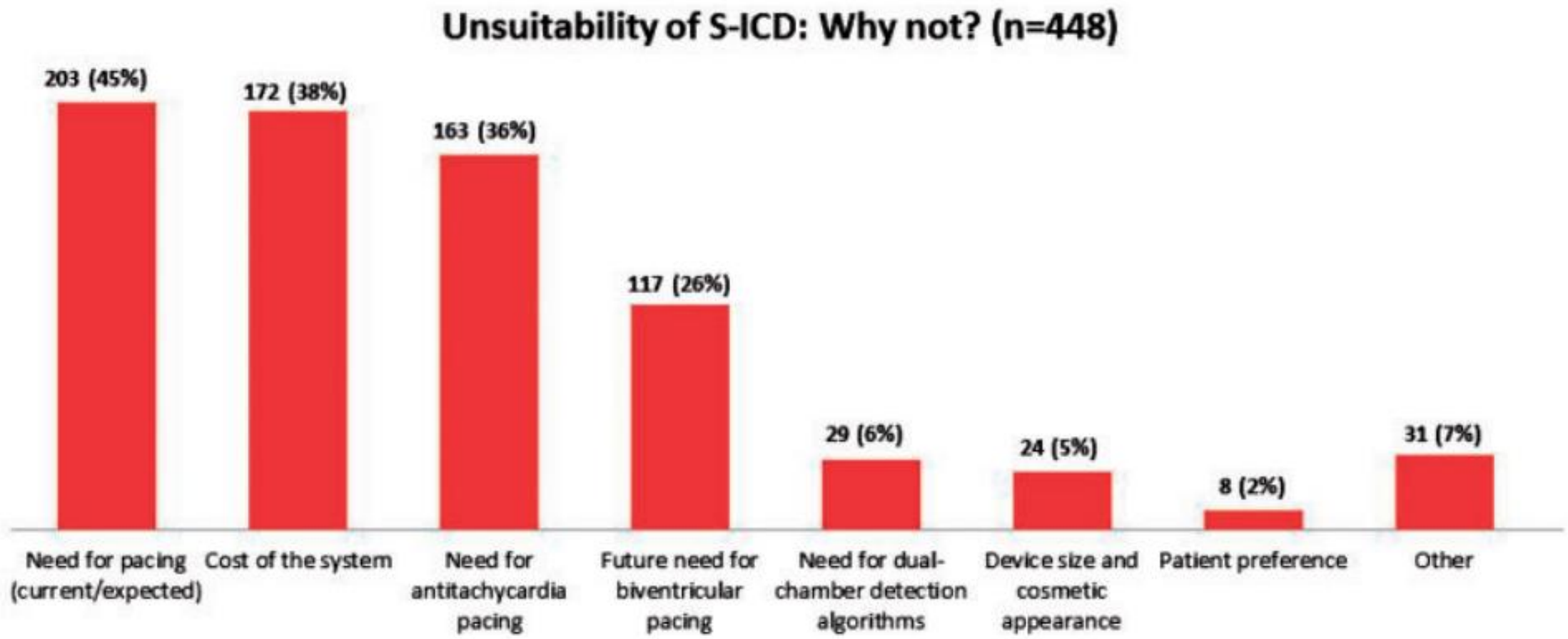
Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	500 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	None (Open Label)
Primary Purpose:	Prevention
Official Title:	Avoid Transvenous Leads in Appropriate Subjects
Actual Study Start Date :	February 22, 2017
Estimated Primary Completion Date :	December 31, 2021
Estimated Study Completion Date :	February 28, 2022

Limitation of Subcutaneous ICD

- High DFT - lower Battery longevity
- Larger device – position sensitive discomfort
- High oversensing rate – higher inappropriate shock
- No pacing option (no brady back up/no ATP)



Expected need for pacing : prefer TV-ICD



Botto GL et al. Europace. 2017 Nov 1;19(11):1826-1832

Brady pacing need in patients with ICD over time

S-ICD studies

- **EFFORTLESS : 2.0%**
- **PRAETORIAN : 1.2%**
- **UNTOUCHED : 0.0%**

****Selected population without conduction problems at baseline**

Boersma et al. JACC 2017
Gold et al. Circulation 2021
Knops et al. NEJM 2020

TV-ICD studies

- **MVP trial ; 5.5%**
- **SCD-HeFT trial : 3.0%**
- **DAVID-I trial : 4.0%**
- **DAVID-II trial : 14.0%**
- **MADIT-II trial : 4.1%**

Sweeney et al Heart Rhythm 2010
Brady et al. NEJM 2005
Wilkoff et al. JAMA 2003
Wilfoff et al. JACC 2009
Kutyifa et al HRS 2015

ATP for S-ICD studies

- **EFFORTLESS : 50% of all episodes were sustained VT, 2.2% of all pts had >1 treated monomorphic VT episode**

- **UNTOUCHED : 62% of patients experienced 42 monomorphic VT**
  - **1 170bpm**
  - **205 200-230bpm**
  - **15 >230bpm**

- **PRAETORIAN : Appropriate ATP in 12.9% of TV-ICD → 55% terminated**

Boersma et al. JACC 2017
Gold et al. Circulation 2021
Knops et al. NEJM 2020

Extravascular ICD with substernal lead

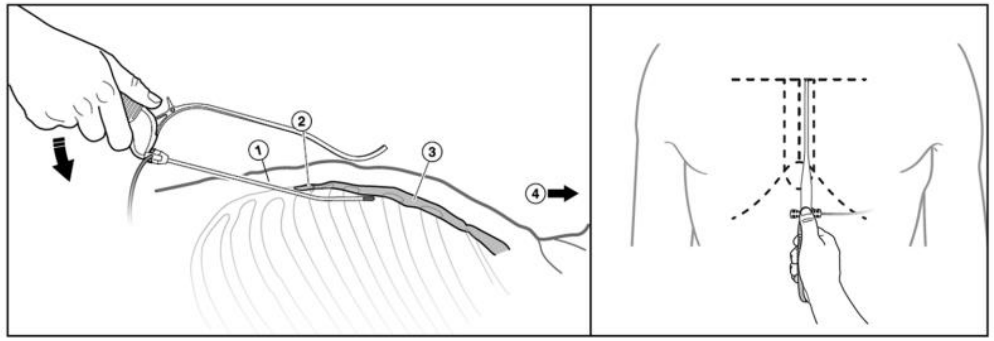
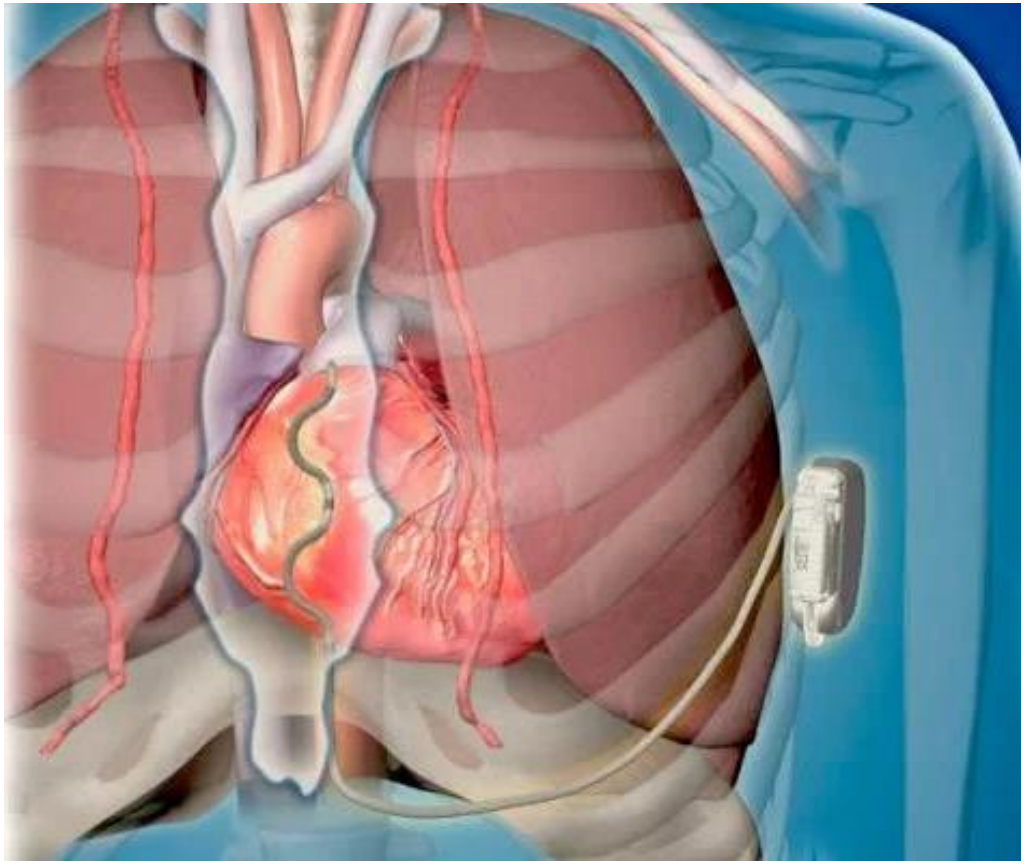


FIGURE 2 EV ICD implant overview. Left panel: Lateral view. Tunneling rod tip at the top of the cardiac silhouette (1, Tunneling Rod, 2, Xiphisternal Junction, 3, Sternum, 4, Head). Right panel: Exterior view: tunneling rod tip at the top of the cardiac silhouette. EV, extravascular; ICD, implantable cardioverter defibrillator



- Lower DFT (only 1.5 times higher than TV ICD)
- Smaller device size
- Greater Longevity
- Pacing (Brady, ATP)

Crozier I et al. JACC EP 2020

Extravascular ICD with substernal lead : The ASD2 study

Therapy From a Novel Substernal Lead

The ASD2 Study

Lucas V.A. Boersma, MD, PhD,[a,b] Béla Merkely, MD, PhD,[c] Petr Neuzil, MD, PhD,[d] Ian G. Crozier, MD,[e] Devender N. Akula, MD,[f] Liesbeth Timmers, MD,[g] Zbigniew Kalarus, MD, PhD,[h,i] Lou Sherfesee, PhD,[j] Paul J. DeGroot, MS,[j] Amy E. Thompson, MS, MBA,[j] Daniel R. Lexcen, PhD,[j] Bradley P. Knight, MD[k]

FIGURE 1 Tunneling Tool

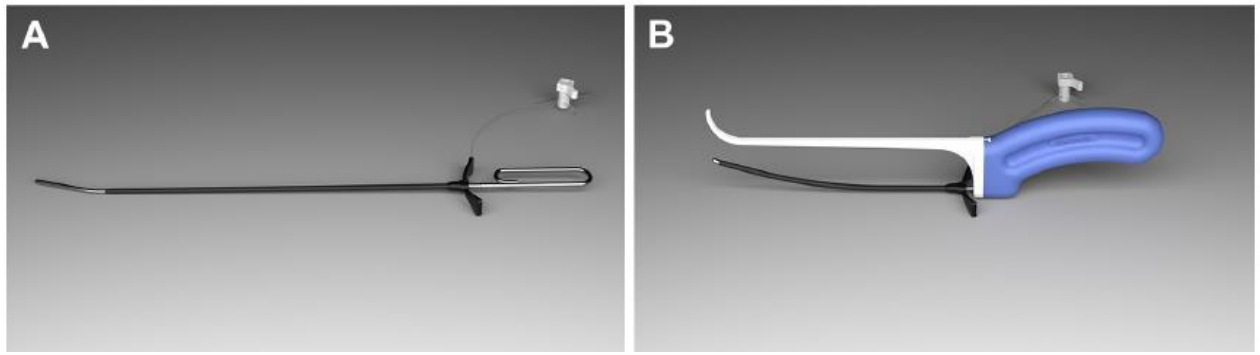
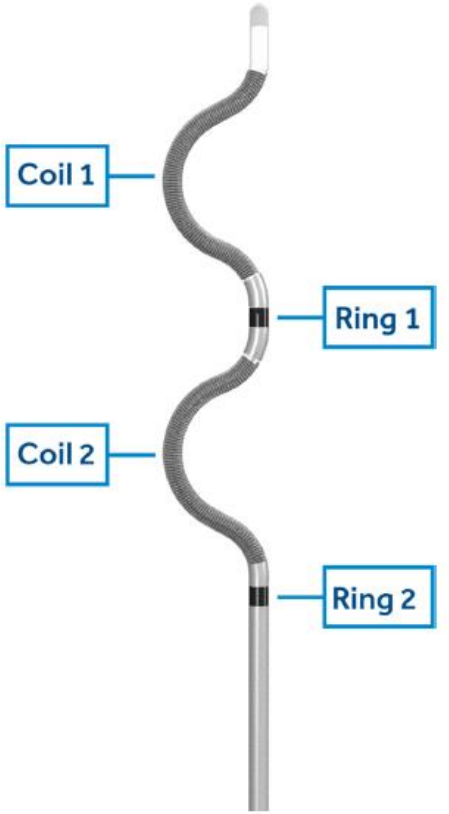


FIGURE 2 Investigational Lead

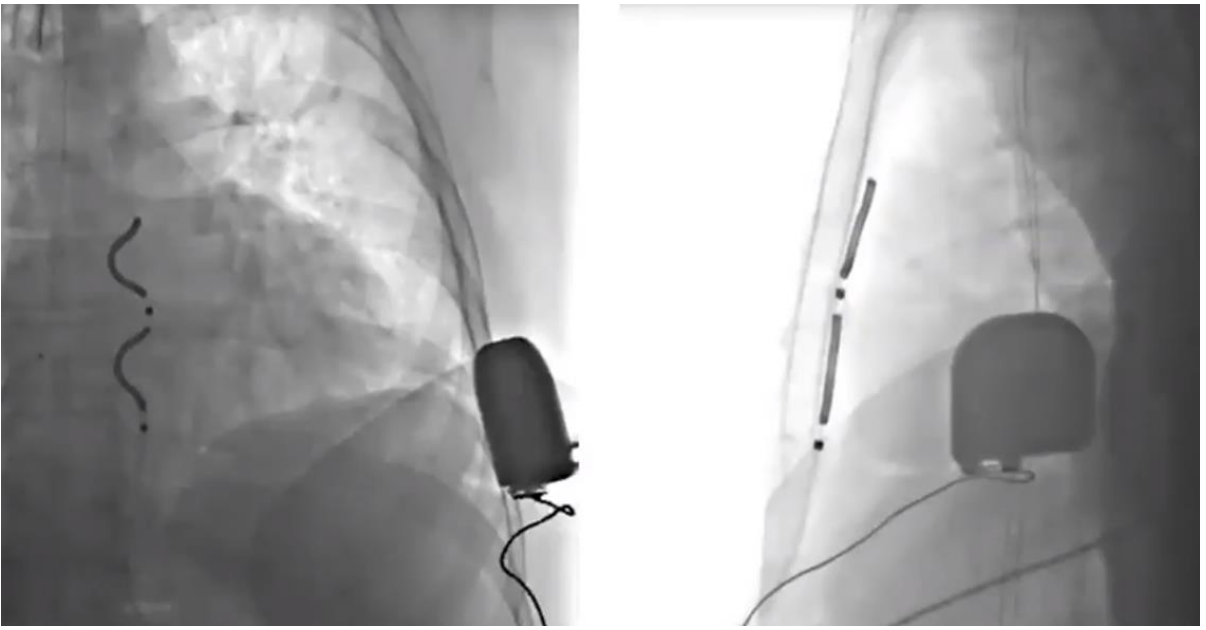


- **Procedure**
  - ✓ Minimal invasive sub-xiphoid approach
  - ✓ Substernal lead advancement via blunt tunneling rod

- **Lead**
  - ✓ Designed for substernal therapy delivery
  - ✓ Overall 8cm defib coil
  - ✓ Two pace/sense rings

Boersma et al. J Am Coll Cardiol EP 2019;5:186–96

Extravascular ICD with substernal lead
: The ASD2 study



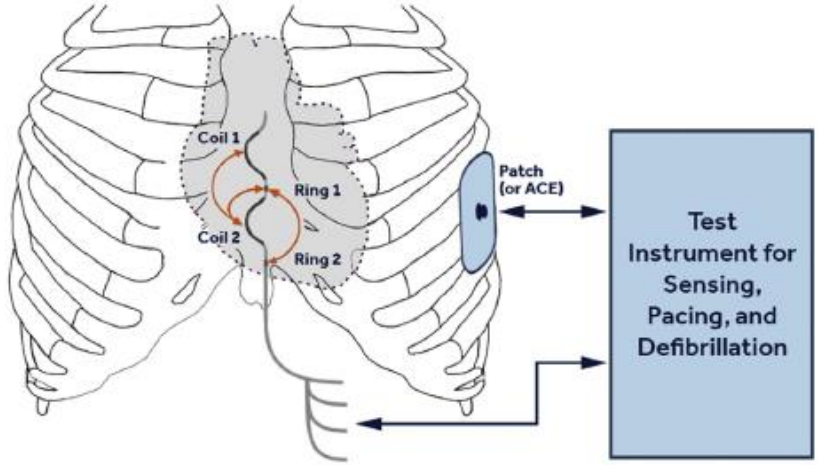
- Total median lead placement time : 12.0 ± 9.0min
- 7 adverse events (bleeding, erythema, anesthesia reaction, transient AF & VF, pericarditis, tamponade)

Enrollment
n = 87

16	Cardiothoracic Surgery
12	SQ ICD (re)placement
56	TV ICD (re)placement
1	Other
2	Unknown (no baseline form)

Data Collection
n = 79

71	Pacing & Defibrillation Testing
7	Pacing Testing Only
1	Tunneling Procedure Only



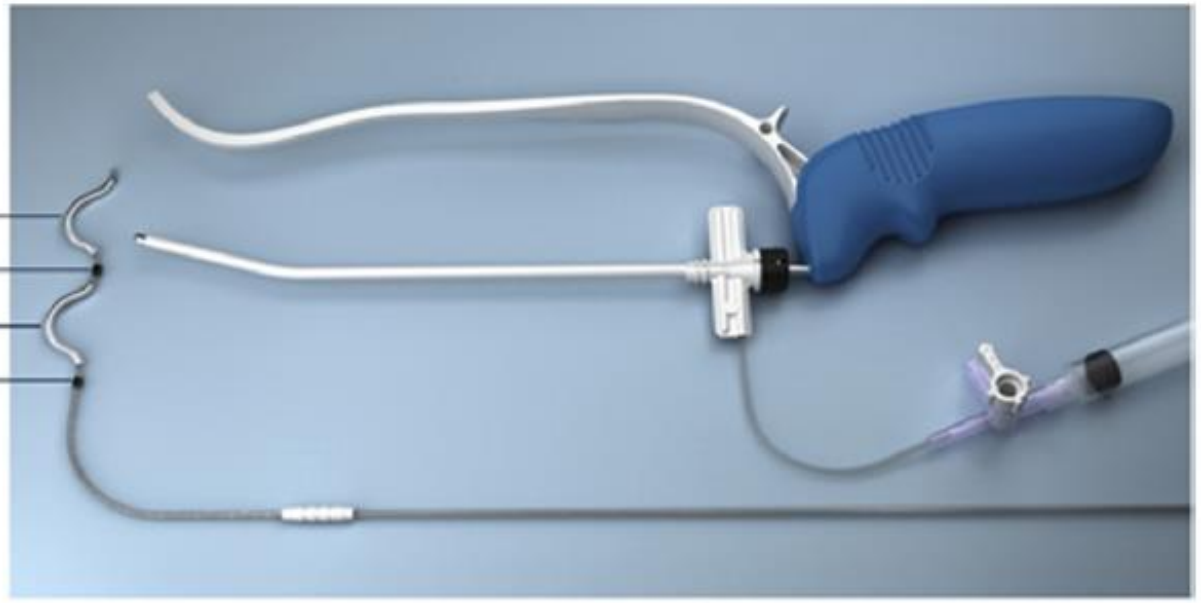
Pacing	Sensing	Defibrillation
76 of 78 patients (97.4%) with successful ventricular pacing capture in ≥1 vector	Median R-wave amplitude: 2.4 mV IQR: 1.8 – 3.6 mV	104 of 128 (81.3%) episodes of VF terminated with a single 30 J shock

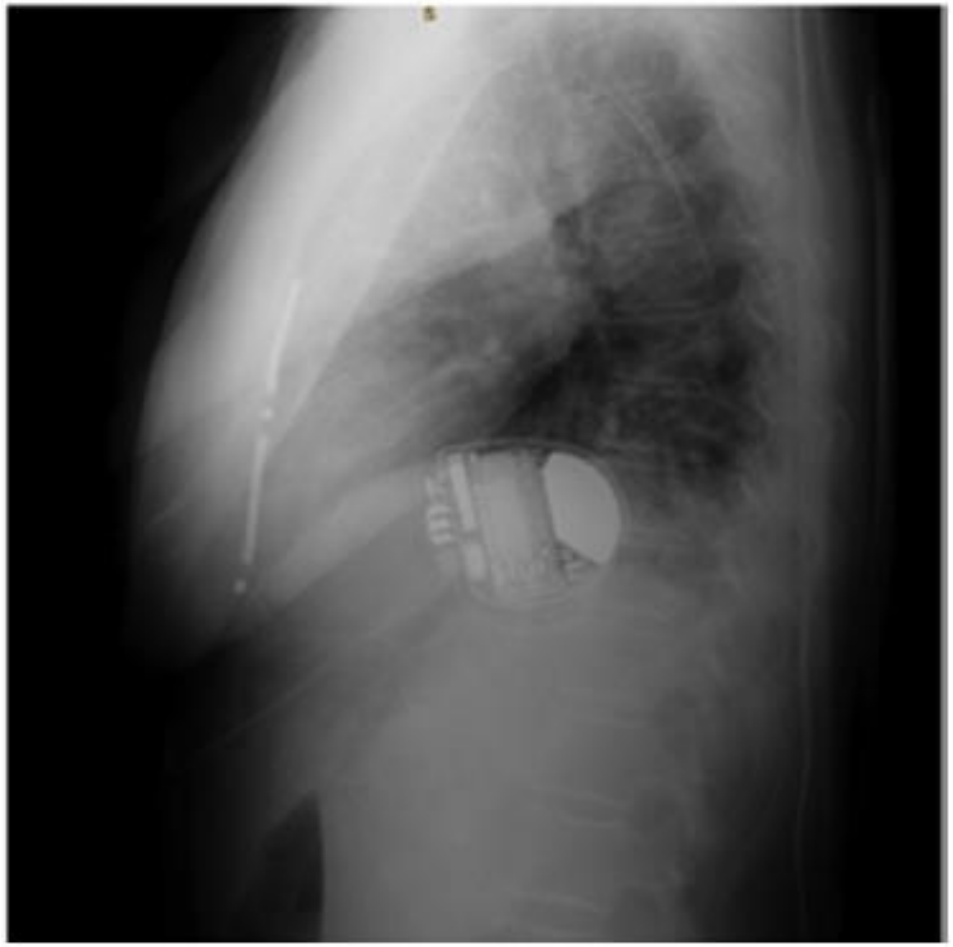
Boersma et al. J Am Coll Cardiol EP 2019;5:186–96

Extravascular ICD with substernal lead

First-in-Human Chronic Implant Experience of the Substernal Extravascular Implantable Cardioverter-Defibrillator

Ian Crozier, MB ChB,[a] Haris Haqqani, MBBS, PhD,[b] Emily Kotschet, MBBS,[c] David Shaw, MB ChB,[a] Anil Prabhu, MCh,[b] Nicholas Roubos, MBBS, BMedSci,[d] Jeffrey Alison, MBBS,[c] Iain Melton, MB ChB,[a] Russell Denman, MBBS,[b] Tina Lin, MBBS,[d] Aubrey Almeida, MBBS,[c] Bridget Portway, BS,[e] Robert Sawchuk, BSEE, MBA,[e] Amy Thompson, MS, MBA,[e] Lou Sherfesee, PhD,[e] Samuel Liang, MBiomedE,[e] Linnea Lentz, DVM, PhD,[e] Paul DeGroot, MS,[e] Alan Cheng, MD,[e] David O'Donnell, MBBS[d]





Crozier I et al. JACC EP 2020

Extravascular ICD with substernal lead

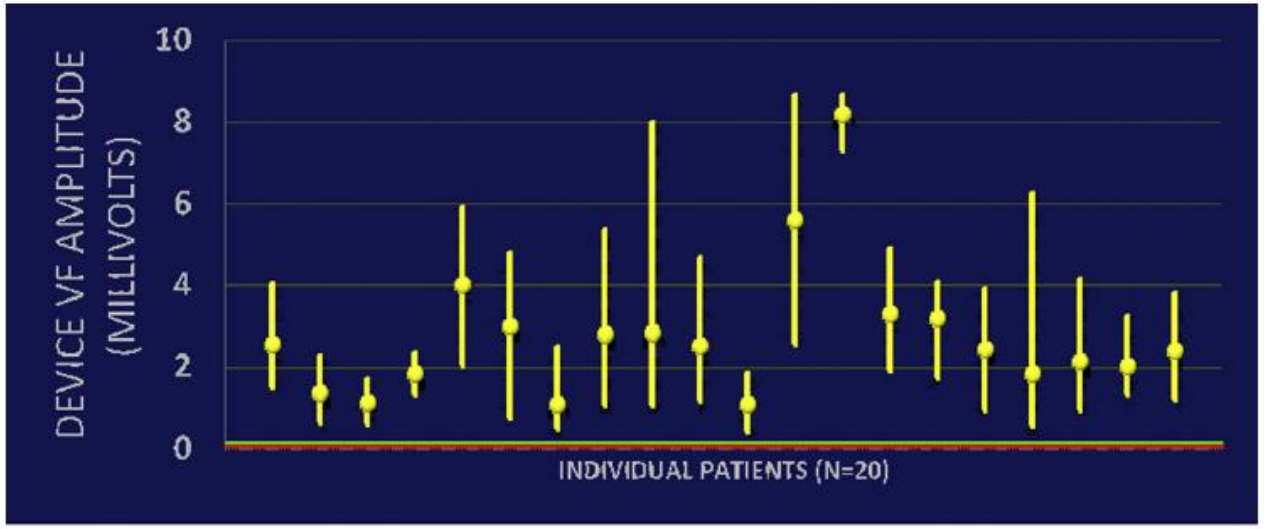
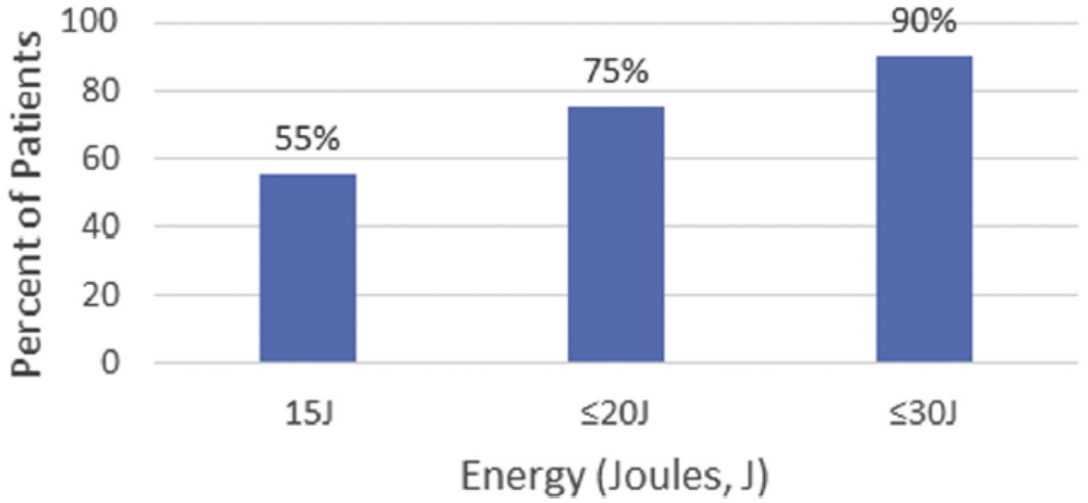


FIGURE 4 Defibrillation Performance



Defibrillation

90% successful with ≥ 10 J safety margin

Median energy for defibrillation: 15 J

Pacing

5.4 ± 2.2 V mean pacing threshold (acute)

95% of patients with successful pacing capture at ≤ 10 volts

Sensing

3.4 ± 2.0 mV mean R-wave amplitude

Successfully detected VF with ≥ 0.3 mV sensitivity in all patients

Crozier I et al. JACC EP 2020

Extravascular ICD with substernal lead

Received: 15 March 2021 | Revised: 23 May 2021 | Accepted: 8 June 2021

DOI: 10.1111/jce.15190

CLINICAL TRIAL STUDY DESIGN

WILE

The extravascular implantable cardioverter-defibrillator: The pivotal study plan

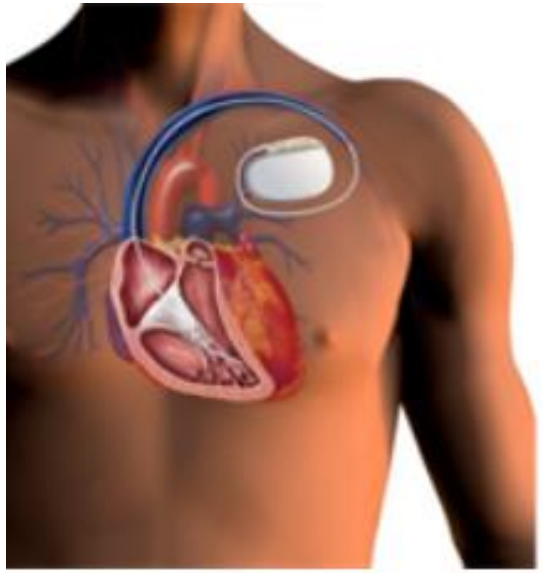
Ian Crozier MB, CHB[1] | David O'Donnell MBBS[2] | Lucas Boersma MD, PhD[3] | Francis Murgatroyd FRCP[4] | Jaimie Manlucu MD[5] | Bradley P. Knight MD[6] | Ulrika Maria Birgersdotter-Green MD[7] | Christophe Leclercq MD, PhD[8] | Amy Thompson MS, MBA[9] | Robert Sawchuk BSEE, MBA[9] | Sarah Willey MPH[9] | Christopher Wiggenhorn PhD[9] | Paul Friedman MD, FHRS[10]

Study Design: The EV ICD pivotal study is a prospective, multicenter, single-arm, nonrandomized, premarket clinical study designed to examine the safety and acute efficacy of the system. This study will enroll up to 400 patients with a Class I or IIa indication for implantation of an ICD. Implanted subjects will be followed up to approximately 3.5 years, depending on when the patient is enrolled.

Objective: The clinical trial is designed to demonstrate safety and effectiveness of the EV ICD system in human use. The safety endpoint is freedom from major complications, while the efficacy endpoint is defibrillation success. Both endpoints will be assessed against prespecified criteria. Additionally, this study will evaluate antitachycardia pacing performance, electrical performance, extracardiac pacing sensation, asystole pacing, appropriate and inappropriate shocks, as well as a summary of adverse events.

Conclusion: The EV ICD pivotal study is designed to provide clear evidence addressing the safety and efficacy performance of the EV ICD System.

TV-ICD vs Subcutaneous ICD vs Substernal ICD



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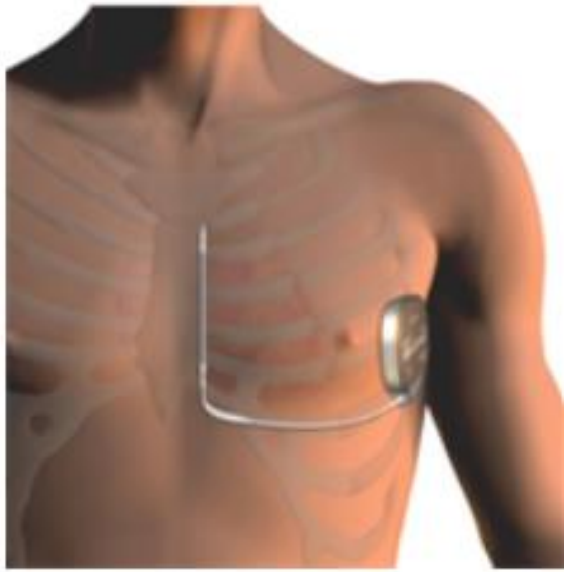
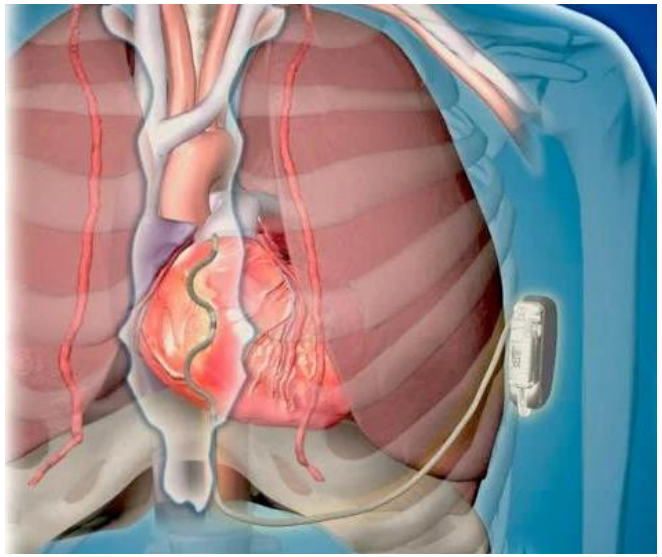


- No risk of vascular injury
- Risk of systemic infection ↓
- Preserves venous access
- Risk of lead extraction ↓
- Fluoroscopy not required



- No risk of vascular injury
- Risk of systemic infection ↓
- Preserves venous access
- Risk of lead extraction ↓
- Fluoroscopy not required
- Brady pacing
- ATP for patients with VT
- Lower (Acceptable) DFT

Conclusions

- Extravascular (non-TV) ICD can avoid many lead-related complications
- S-ICD : only extravascular ICD with FDA and CE approval, **but has limitations (pacing, ATP, higher DFT, shorter battery longevity)**
- Second RCT for S-ICD to present in early 2022

- Substernal ICD can allow
  - ✓ Lower DFT with smaller can
  - ✓ ATP and brady-pacing
  - ✓ **More data are needed** - Outcomes expected 2022

Thank You For Your Attention