Séminaire
Winter Arrhythmia
School
Annual Cardiac Arrhythmia Meeting
Division of Cardiology, University of Toronto

ATLAS – Avoid Transvenous Leads in Appropriate Subjects

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Study Sponsor – Population Health Research Institute

Principal Investigators –

- Dr. Jeff Healey – Hamilton Health Sciences
- Dr. Blandine Mondesert – Montreal Heart Institute

AGENDA

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1. Rationale for the trial
2. Hypothesis
3. Objectives
4. Inclusions/exclusions
5. Design/timing
6. Primary outcomes
7. Secondary outcomes
8. Role of BSC
9. What happens next?

Rationale

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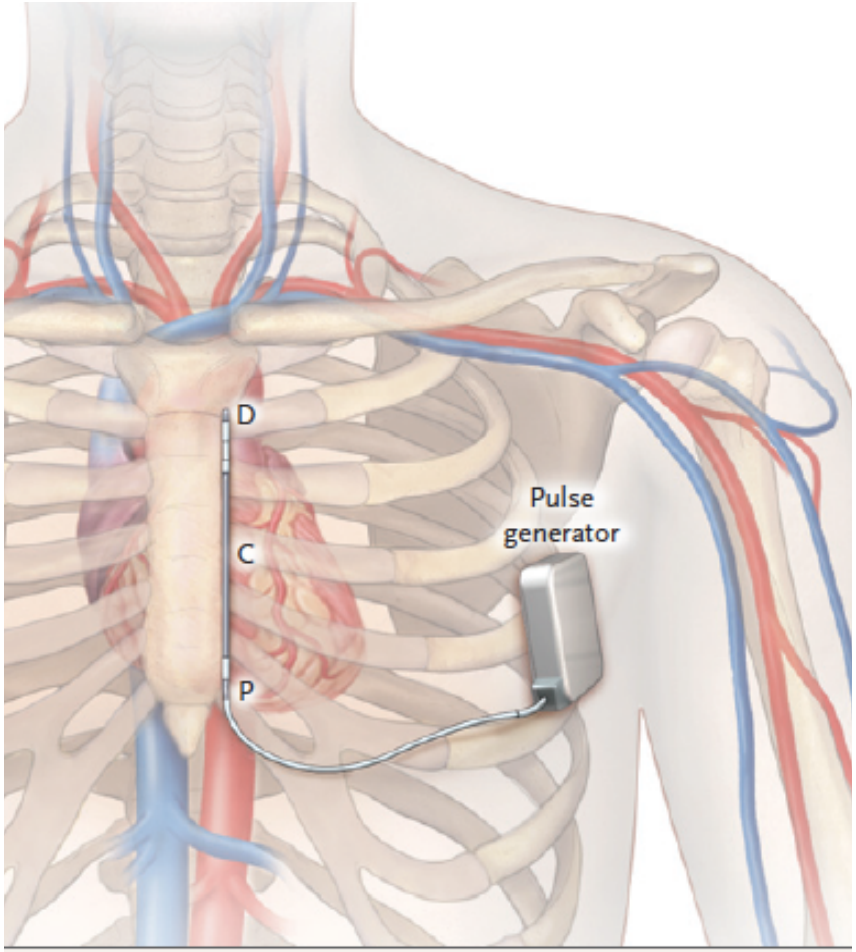
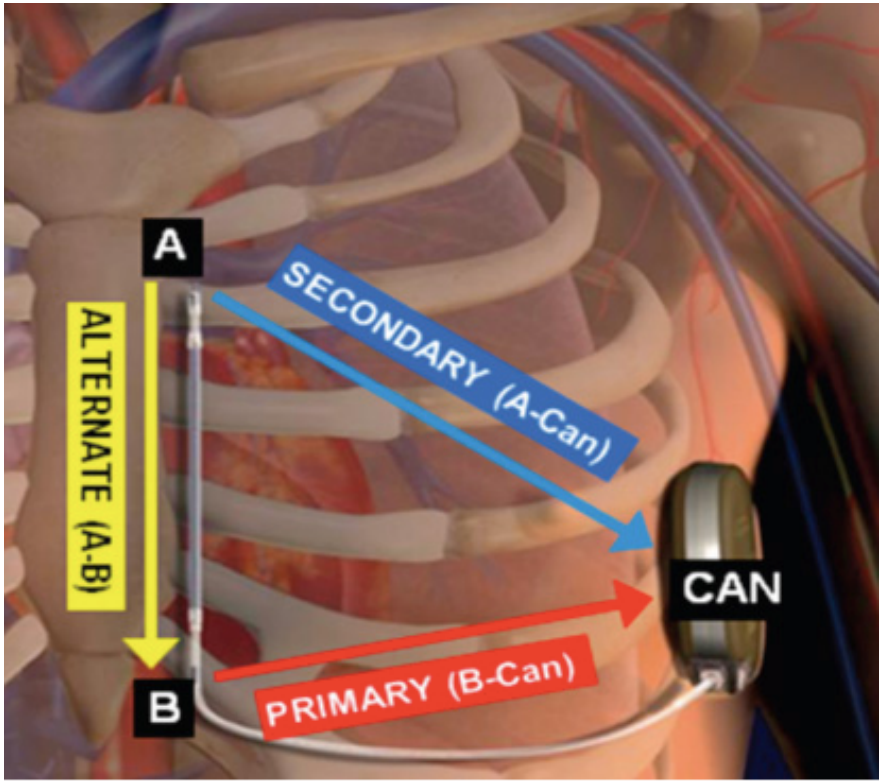
- The transvenous lead
  - The least reliable component of the ICD system
  - Premature revision of the system in 2-20% of patients during the typical lifespan of an ICD generator.
  - Many of these revisions and associated complications could be avoided if a lead was not placed in the vasculature or heart.

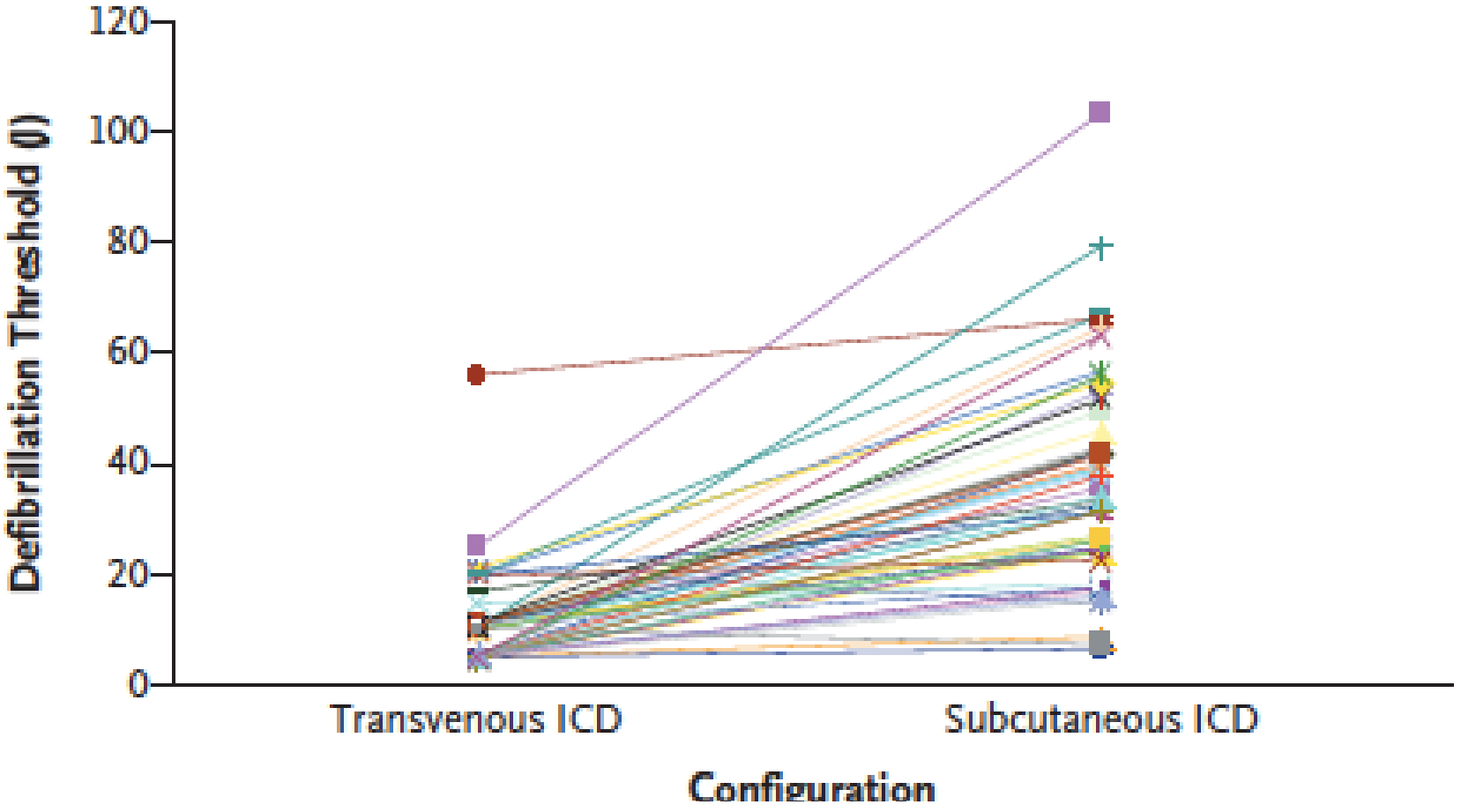
Complications due to Transvenous Leads

Complication	Estimated Rate	Source
Early avoidable, lead-related complications		
Pneumothorax/hemothorax	1.5% at 30-days	SIMPLE trial, Pacemaker meta-analysis, ICES ICD registry
Cardiac perforation, effusion, tamponade, pericarditis	1.0%	SIMPLE trial, ICD meta-analysis
Lead dislodgement, loss of sensing/pacing	3.0%	Pacemaker meta-analysis, clinical estimate, ICD meta-analysis
New, severe tricuspid insufficiency	3%	Sadreddini cohort
Ipsilateral upper extremity DVT	0.3%	Clinical estimate
Need to revise dialysis access	0.2%	Clinical estimate
Total	9%	
Other early complications		
Death	0.6%	SIMPLE trial
Myocardial Infarction	0.1%	SIMPLE trial
Stroke	0.2%	SIMPLE trial
Significant wound hematoma	2.3%	SIMPLE trial
Device-related infection	1.3%	SIMPLE trial, Pacemaker meta-analysis. Clinical estimate
Total	4.5%	

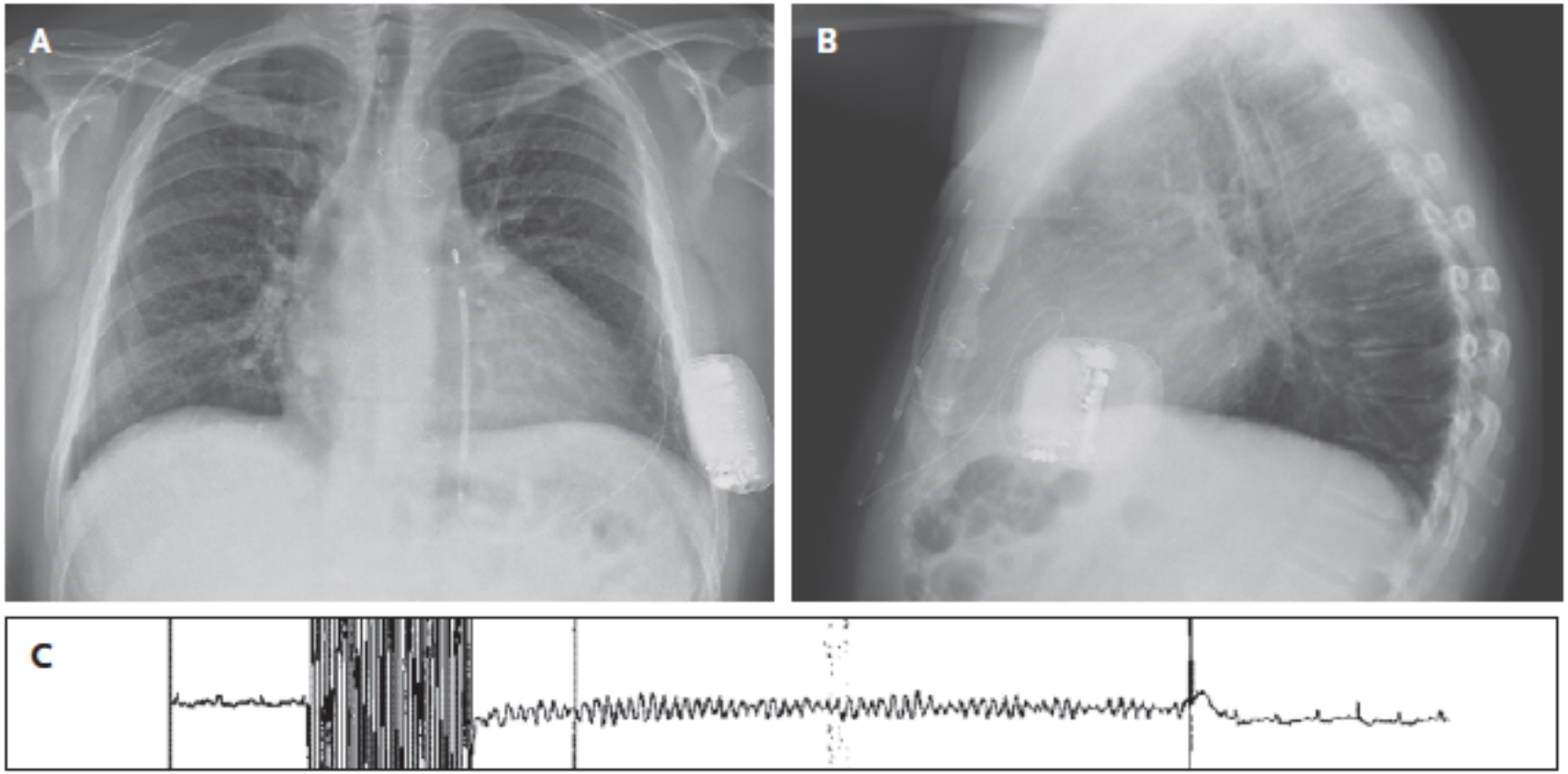


- D- distal electrode
- P- proximal electrode
- C- coil





Bardy GH, et, NEJM 2010



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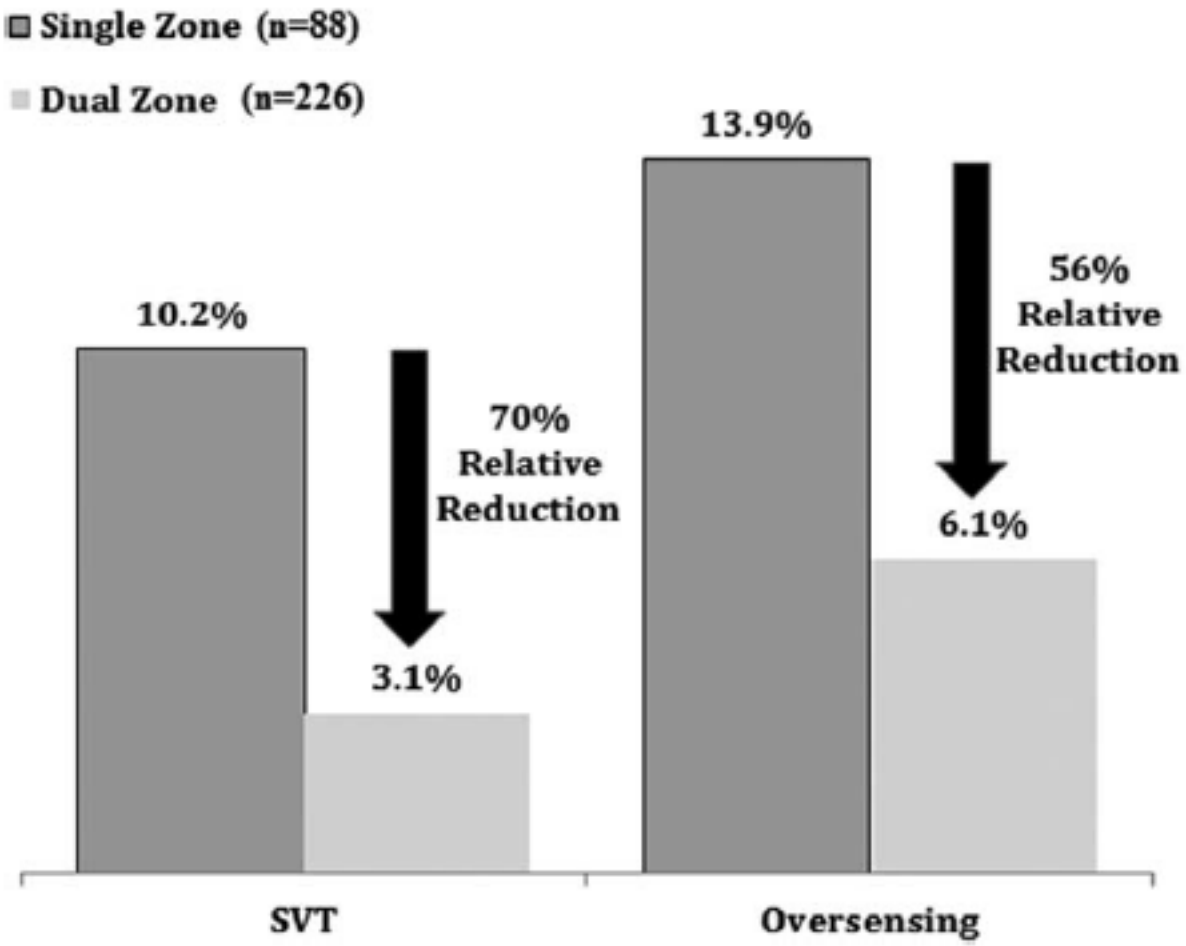
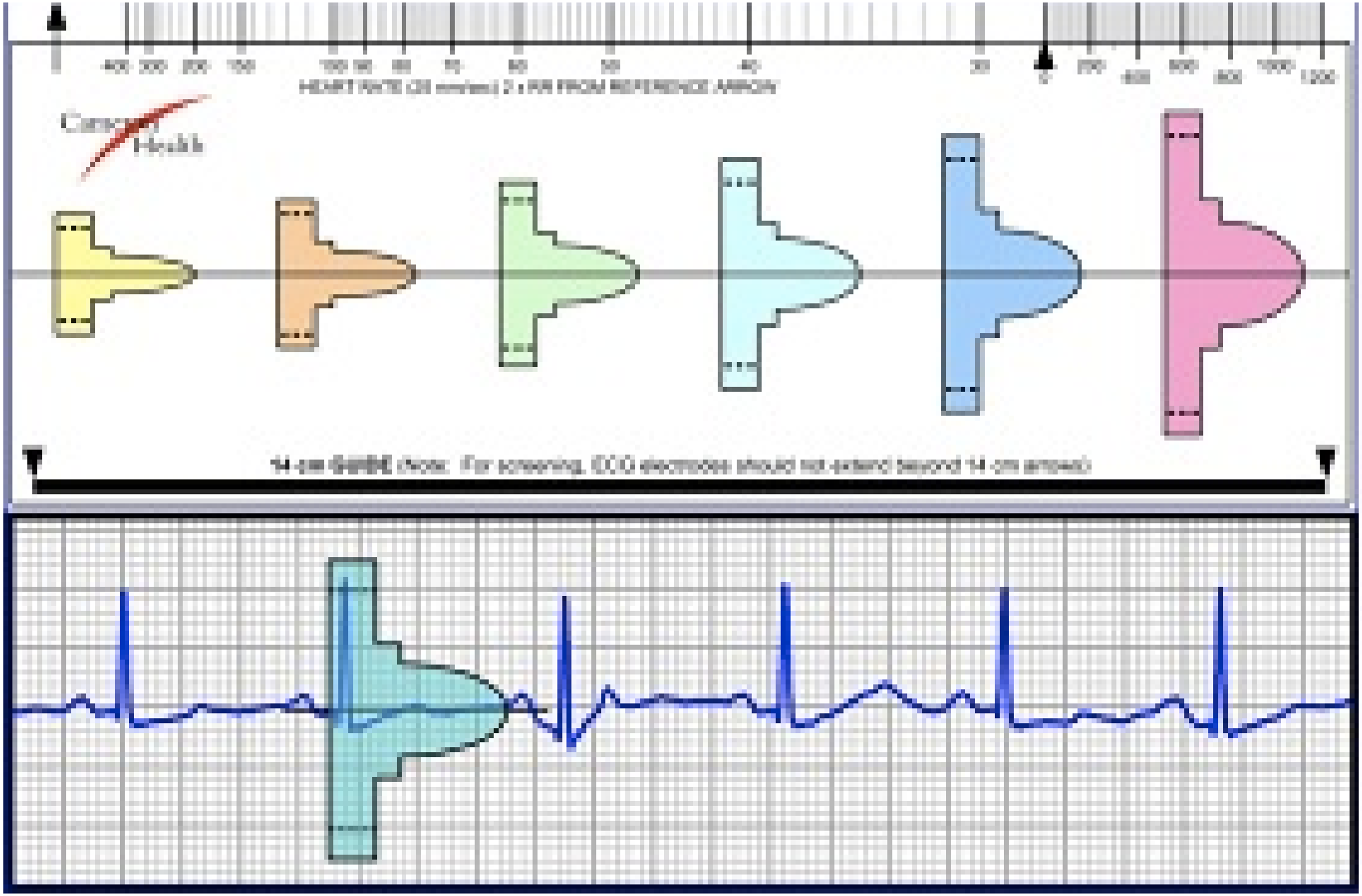


Weiss R, et al Circulation 2013

Pre Operative Screening



EFFORTLESS - International Participation[1]

985 patients implanted w/ S-ICD at *42 study sites, Europe and New Zealand*

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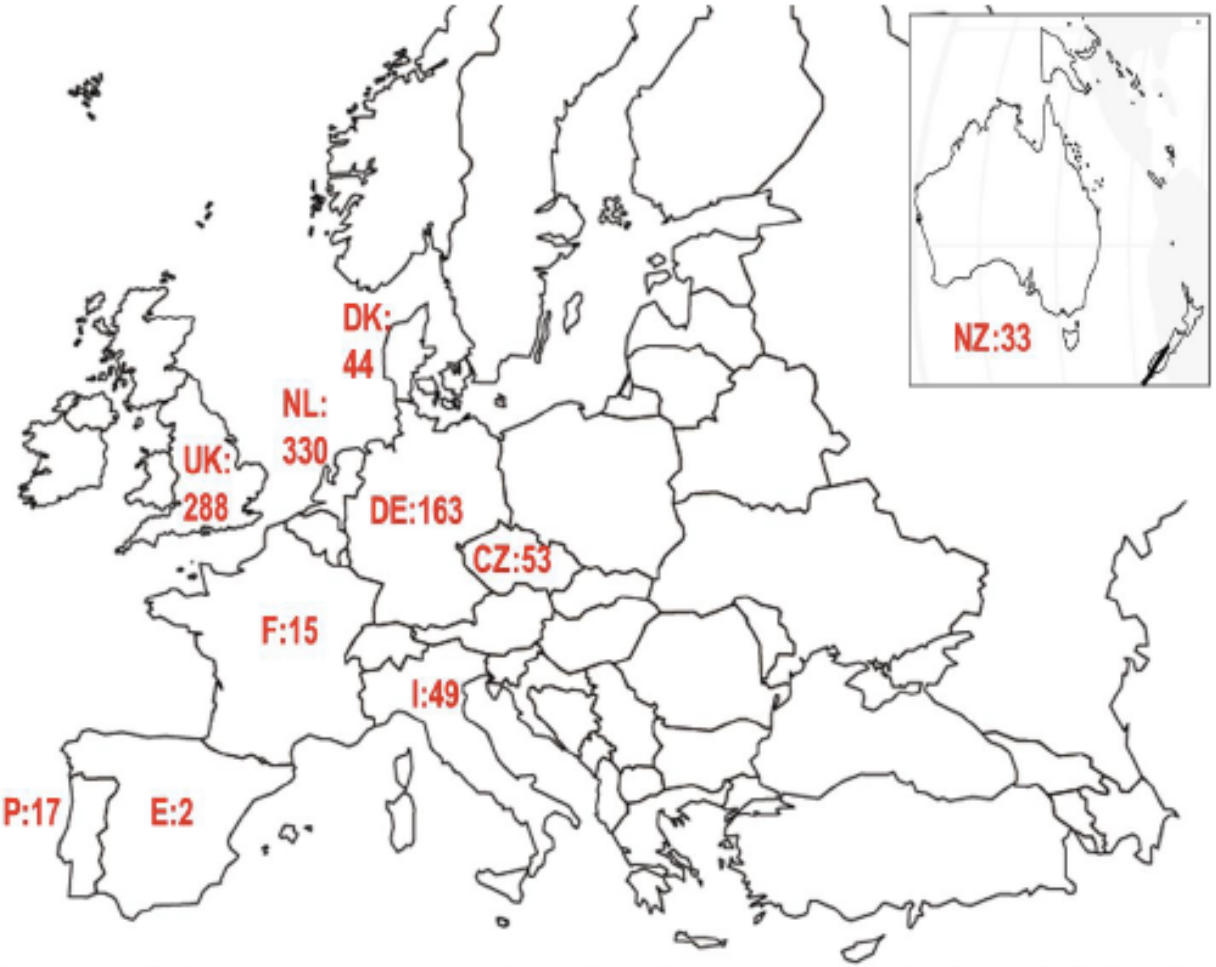
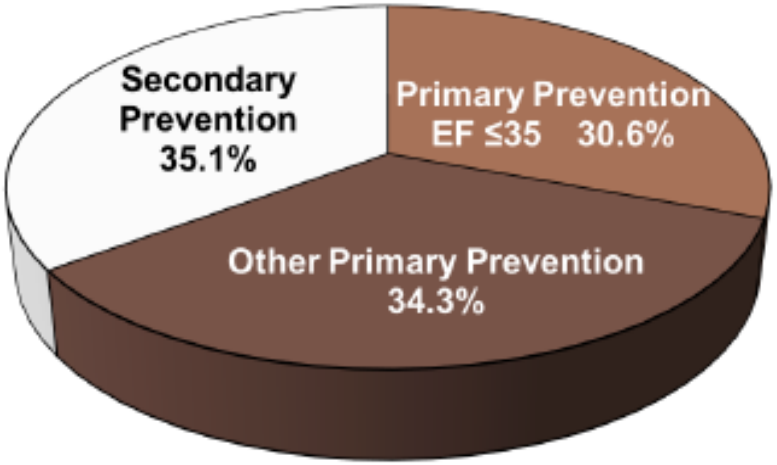


3.1 year average follow-up

Boersma et al Performance and outcomes in patients with the Subcutaneous Implantable Cardiac Defibrillator Mid-term follow-up. May 6th 2016 HRS LBCT[1]

Demographics[1]

Boston Scientific



Variable	Percent
Average Age	48 ± 17
Percent Male	72%
Ejection Fraction	43% ± 18%
QRS width, msec	106 ± 25
BMI	27 ± 6

Primary Cardiac Disease		Percent
Non-ischaemic		38.5%
	ARVC	3.5%
	Congenital	2.1%
	Dilated	9.3%
	HCM	11.7%
	Unspecified/Other	11.9%
Ischemic		31.1%
Inherited		18.6%
Idiopathic VF		6.0%
Valvular Disease		2.3%
Other		2.2%
CHF		1.2%

Effortless registry at 3 years , HRS 2016

S-ICD was as effective as TV-ICD in treating spontaneous arrhythmias when compared to studies with TV-ICD

Boston Scientific

	Spontaneous Shock Efficacy	
	First Shock	Final Shock in episode
S-ICD* EFFORTLESS 3 year Analysis[1]	88.5%	97.4%
S-ICD Pooled 2 year Analysis[2]	90.1%	98.2%
SIMPLE Testing Group [3]	88.5%	95.7%
SIMPLE No Testing Group [3]	92.0%	94.8%
SCD-HeFT[4]	83%	
PainFree Rx II[5]	87%	
MADIT-CRT[6]	89.8%	
LESS Study[7]		97.3%

* S-ICD Pooled Data excluded VT/VF Storm events

S-ICD Data	Of 4 "unconverted" episodes in Pooled & EFFORTLESS
100% Clinical conversion to normal sinus rhythm	• Two spontaneously terminated after the 5th shock • In another 2 episodes, the device prematurely declared the episode ended. A new episode was immediately reinitiated and the VF was successfully terminated with one shock

Effortless registry at 3 years , HRS 2016

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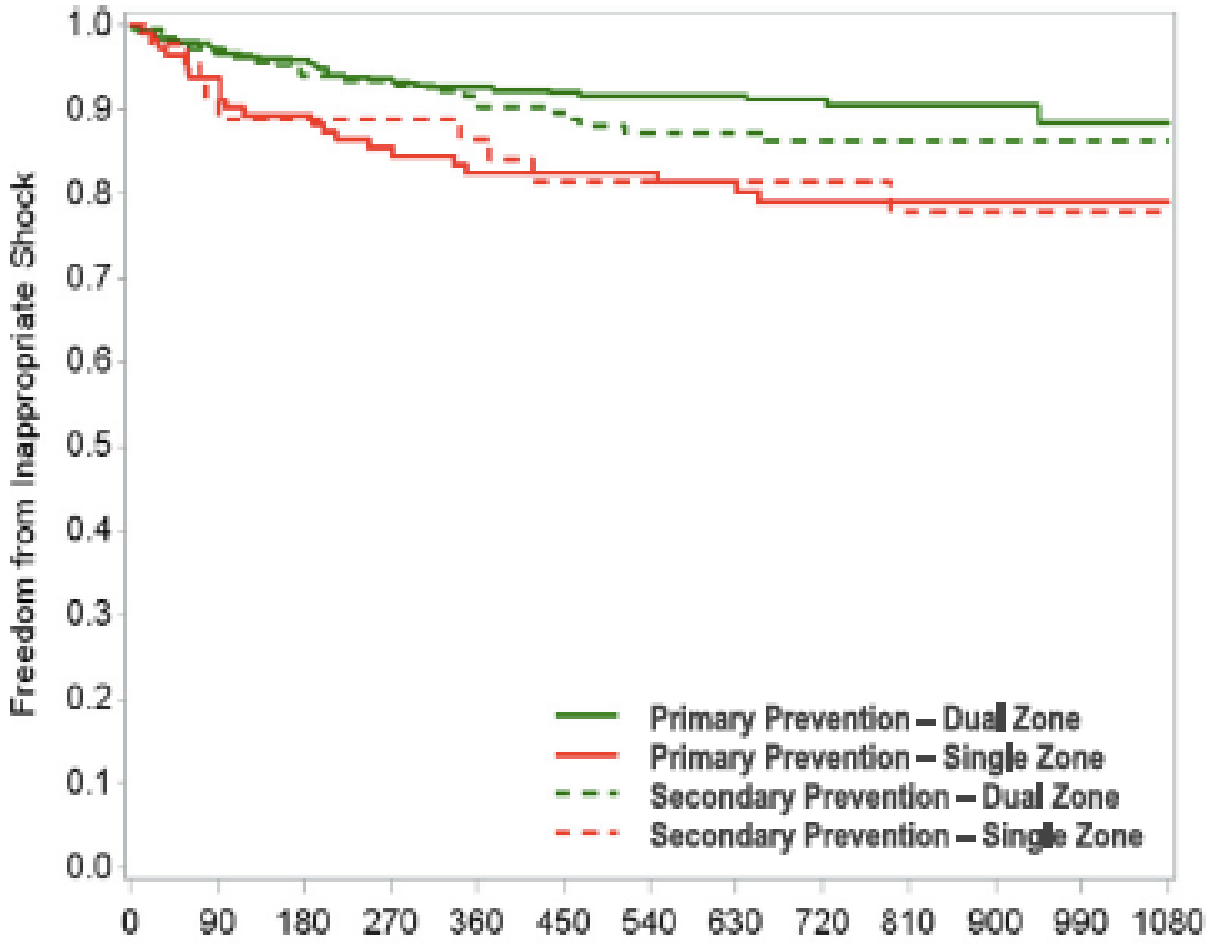
PP vs SP



Boersma LV, et al, Heart Rhythm 2016

This 3 year follow up data demonstrates that the need for pacing after implant of the S-ICD continues to be low

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	EFFORTLESS[1]	S-ICD Pooled Data[2] Number/ (% of Patients)
Extraction of S-ICD for new Pacing Indication	1/ (0.1%)	1/(0.1%)
Extraction of S-ICD for new ATP Indication	5 (0.5%)	1/(0.1%)
Extraction of S-ICD for new CRT Indication	4 (0.4%)	1/(0.1%)

1 Boersma et al. EFFORTLESS 3 year results May 6th 2016 HRS LBCT. 2 Burke MC et al. Pooled Analysis of the EFFORTLESS and IDE Registry.

Conclusions

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- The EFFORTLESS registry provides the largest S-ICD database in the world
- Primary Endpoints of the full 985 pt cohort with 1-yr follow-up show:
  - ✓ Freedom from complications caused by the S-ICD was high (97.9%)
  - ✓ Inappropriate Shock rate for AF/SVT was low (1.5%)
- All cause complications were low across cohorts, declining with experience
  - ✓ Zero electrode failures in this study
  - ✓ Zero endovascular or systemic infections
- Acute conversion efficacy for induced VT/VF episodes was high (99.5%)
- Appropriate therapy was clinically effective in all but 1 pt with VF storm
  - ✓ Ischemic etiology was not a predictor for repeated MVT episodes
- The S-ICD continues to show adequate clinical performance
- 3.8% modeled rate of IAS with SmartPass is similar to rates seen in patients with a TV-ICD

TABLE 2 Clinical Endpoints*

Complications	S-ICD	KM Rate, %	TV-ICD	KM Rate, %
Appropriate therapy	12	17.0	39	31.3
ATP			28	21.8
Shock	12	17.0	24	21.3
Inappropriate shocks	20		22	
Oversensing	17	17.1	1	1.2
Supraventricular tachycardia	3	4.2	21	17.6
Deceased	2		6	
Noncardiac	1	2.0	3	2.6
Cardiac	1	2.0	2	1.7
Unknown	0	0	1	0.9

*Crude number of patients in the first 5 years and the adjusted Kaplan-Meier rate

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Hypothesis:

Compared to standard, single-chamber transvenous implantable cardioverter defibrillators (TV-ICDs), the use of a sub-cutaneous ICD (S-ICD) will result in fewer perioperative and long-term device-related complications, and will have a similar rate of failed appropriate clinical shocks and arrhythmic death.

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Objectives

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Primary Objective:

To compare the rate of perioperative complications, measured at 30-days following implant, between patients receiving an S-ICD compared to those receiving a TV-ICD.

Secondary Objectives:

- 1. To determine if the S-ICD is associated with fewer long-term device-related complications.
-
- 2. To determine if the S-ICD has a similar effectiveness for the treatment of ventricular arrhythmias and is associated with a similar risk of failed appropriate ICD shock and/or arrhythmic death

Inclusions

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Any standard ICD indication with

- Age 14 - 60 years old with; OR
- Patients ≥ 14 years old with:
  - An inherited arrhythmia syndrome (i.e. Long QT, Brugada, ARVC, hypertrophic or dilated cardiomyopathy, early repolarization syndrome, idiopathic ventricular fibrillation, etc.)
  - Prior pacemaker or ICD removal for infection
  - Need for hemodialysis
  - Prior heart valve surgery (repair or replacement)
  - Chronic obstructive pulmonary disease (with FEV_1 < 1.5 L)

Exclusion Criteria

- Mechanical tricuspid valve
- Fontan repair
- Ventricular septal defect with right-to-left shunt
- Known lack of upper extremity venous access
- Need for cardiac pacing for bradycardia indication
- PR interval of > 240 msec

Trial Design

- Patients will be randomized to receive either a TV-ICD (control arm) or an S-ICD (experimental arm).
- S-ICD implantation will be performed by investigators with a minimum experience of 5 implants.
- Safety will be assessed by comparing a composite of safety parameters measured at 30 days following implant.
- Patients will be followed for between 12 and 72 months to measure:
  - late device-related complications;
  - mortality (total and arrhythmic death);
  - the rate and success of appropriate ICD therapies.

- All patients will have standardized programming of ICD therapies to allow comparison between treatment arms.

Trial Design

- 500 patients enrolled in any interested Canadian centre meeting the participation criteria.
- Patients will be enrolled over a 24 month period with the primary outcome assessed 30 days after the last patient is enrolled.
- Analysis of the primary results will be completed within the following 6 months.
- Patients will then enter a long-term follow-up phase for an additional 48 months. Remote monitoring.
- Any device-related complications (i.e. infection, lead fracture) will be captured by an in-person special visit.

Primary Outcome

30 – day composite of lead-related perioperative complications, including:

- Hemothorax or pneumothorax
- Cardiac perforation, tamponade, pericardial effusion or pericarditis
- Lead dislodgement or loss of pacing/sensing requiring revision
- New moderate-severe or severe tricuspid insufficiency (3+ or 4+)
- Ipsilateral upper extremity deep venous thrombosis

A secondary 30-day safety composite will include the following, in addition to the above complications:

- Device-related infection requiring surgical revision, Significant wound hematoma (requiring evacuation or interruption of oral anticoagulation)
- Myocardial infarction, Stroke, Death

Secondary Outcomes

- Late (> 30 days post-operative), device-related complications, including:
  - Lead dislodgement or fracture, or loss of adequate sensing or pacing
  - Device-related infection
  - Pericarditis or pericardial effusion
  - New severe tricuspid insufficiency
  - Ipsilateral upper extremity deep venous thrombosis
  - Need to revise dialysis access
  - Need to revise ICD to deliver pacing or ICD revision for any reason
- Occurrence of failed appropriate shock or arrhythmic death
- Hospital or clinic visits for ICD therapy (shocks or ATP, both appropriate and inappropriate), device-related complications, arrhythmia or heart failure
- Any inappropriate shock