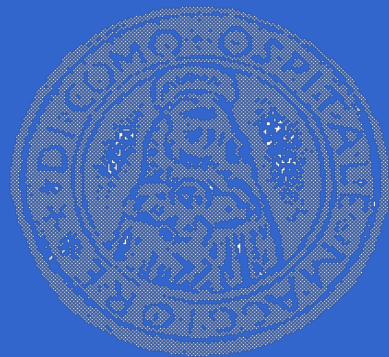




ADVANCES IN CARDIAC ARRHYTHMIAS

and

GREAT INNOVATIONS IN CARDIOLOGY

XXIX GIORNATE CARDIOLOGICHE TORINESI



UNIVERSITÀ DEGLI STUDI DI TORINO



Maria Pia Hospital



Ilva Caliper to Caliper



ARISTOTELIS
BY ARISTOTELIS

SUBCUTANEOUS ICD ITS JOURNEY FROM PROOF OF CONCEPT TO CURRENT EVOLUTION

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TURIN
OCTOBER
27-28,
2017

Centro Congressi
Unione Industriale
di Torino

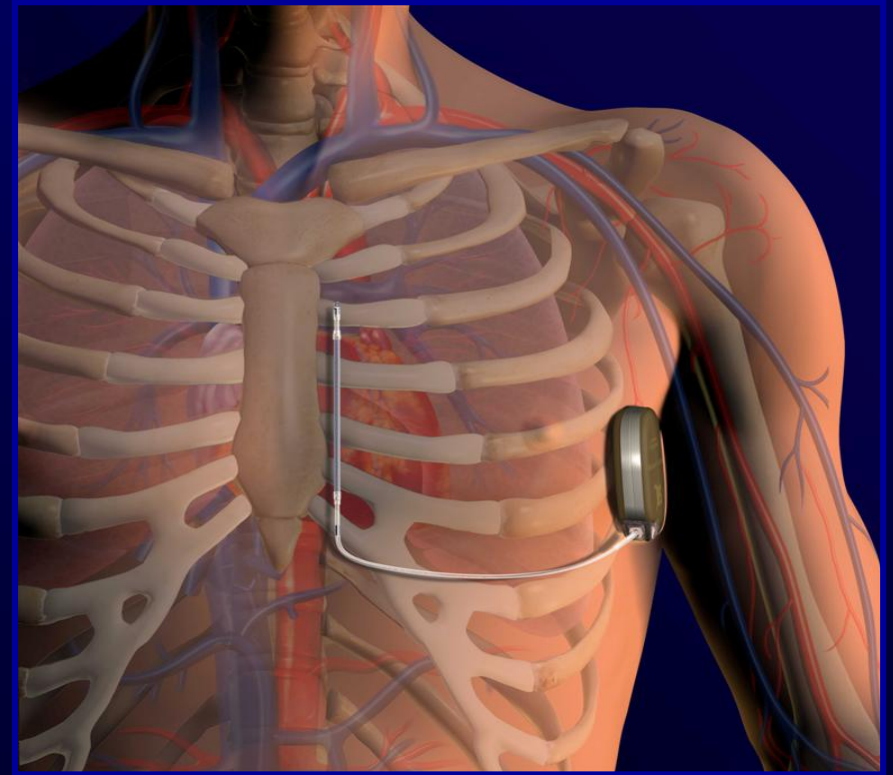
Presenter Disclosure Information

- Research support:
Boston Scientific, Medtronic; St., Bayer Healthcare, Gilead, Sanofi
- Advisory Board:
Biotronik, Medtronic; St. Jude Medical, MSD, Sanofi, Bayer Healthcare, Boehringer, BMS, Pfizer, Daiichi/Sankyo
- Speaker Fees:
Boston Scientific, Medtronic, St. Jude Medical, Sorin Group, Bayer Healthcare, Boehringer, BMS, Cardiome, Meda, MSD, Pfizer, Sanofi, Daiichi/Sankyo

The S-ICD System

The completely S-ICD was designed to avoid the complications associated with TV leads

- ▶ Limited pacing functionality with only transient post-shock, transthoracic pacing
- ▶ Studies have largely enrolled pts with “niche” indications and relatively few comorbidities from select, experienced centers

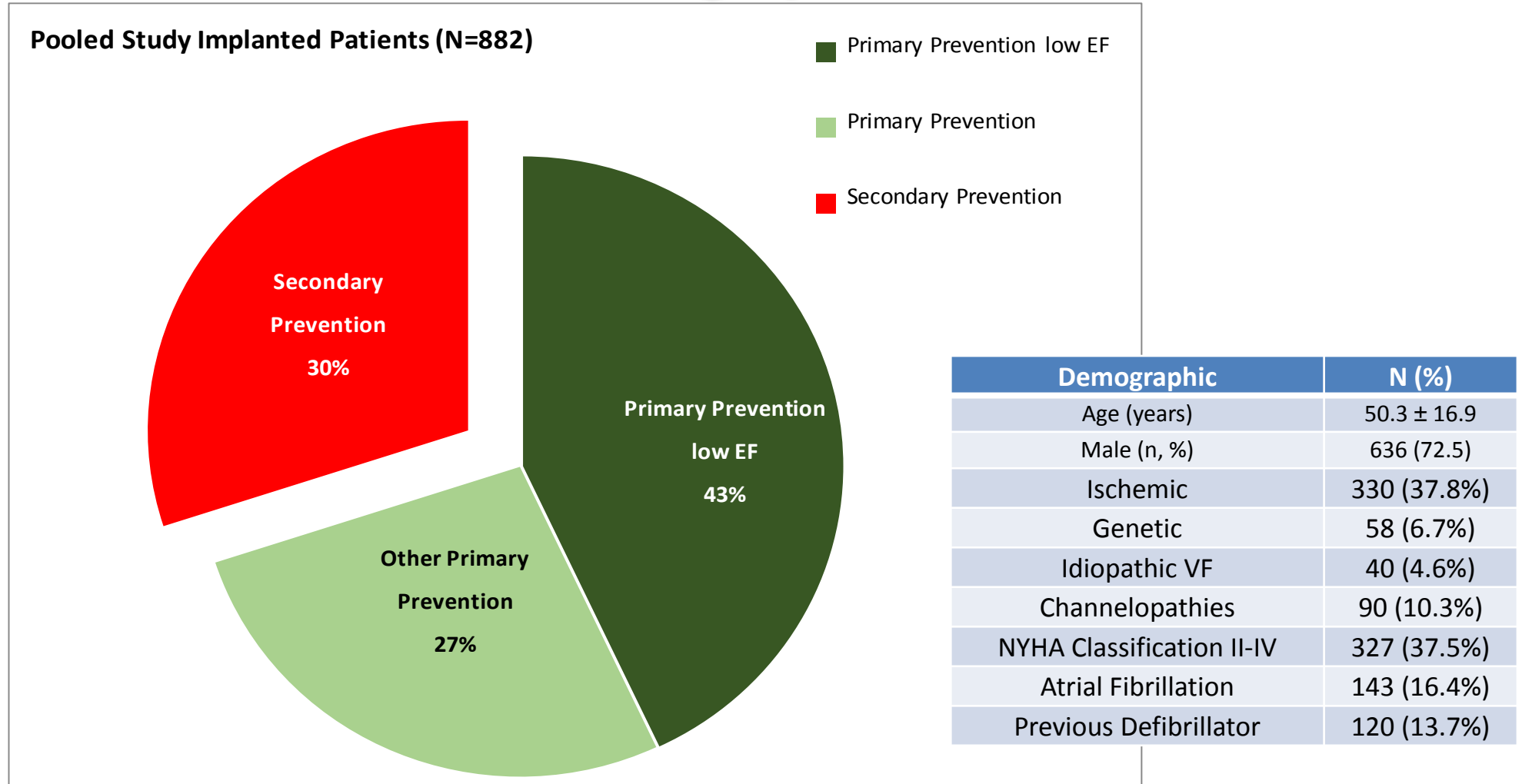


Summary of S-ICD Trials

	Bardy (n = 55)	Dabiri Abkenari (n = 31)	Aydin (n = 40)	Jarman (n = 111)	Olde Nordkamp (n = 118)	Köbe (n = 69)	Weiss (n = 330)	Lambiase (n = 472)	Burke (n = 883)
Age, yrs	56 ± 13	53 ± 4	42 ± 15	33	NA	46 ± 16	52 ± 16	49 ± 18	50 ± 17
Male	80	77	70	NA	75	72	74	72	72.5
Follow-up	10 ± 1 months	286 days	229 days	12.7 ± 7.1 months	18 ± 7 months	217 ± 138 days	330 days	558 days	651 ± 345 days
Ischemic cardiomyopathy	37 (67.0)	18 (58.0)	9 (22.5)	15 (14.0)	45 (38.0)	11 (15.9)	137 (41.4)	166 (37.0)	330 (37.8)
LVEF	35 ± 14	38 ± 15	47 ± 15	NA	41 ± 15	46 ± 16	36 ± 16	42 ± 19	39 ± 18
Primary prevention	43 (78.0)	21 (67.0)	17 (42.5)	55 (50.0)	71 (60.0)	41 (59.4)	262 (79.0)	282 (63.0)	610 (69.9)
Inappropriate shocks	5 (9.0)	5 (16.0)	2 (5.0)	17 (15.0)	15 (13.0)	3 (4.0)	41 (13.0)	32 (7.0)	14 (2.5)
Appropriate therapy (% successful)	3 (100.0)	4 (100.0)	4 (96.4)	13 (100.0)	8 (100.0)	3 (100.0)	21 (95.2)	33 (100.0)	111 (98.2)
Complications									
Infection	2 (3.6)	1 (3.2)	0	11 (9.9)	7 (5.9)	1 (1.4)	18 (5.6)	11 (2.3)	14 (1.5)
Lead migration	6 (10.9)	2 (6.4)	0	0	3 (2.5)	0	0	4 (0.8)	7 (0.8)
Device erosion	0	0	0	2 (1.8)	2 (1.7)	0	0	4 (0.8)	12 (1.4)
Hematoma	0	0	0	0	0	1 (1.4)	0	1 (0.2)	4 (0.4)
Patient characteristics									
Ischemic cardiomyopathy	37 (67.0)	18 (58.0)	9 (22.5)	15 (14.0)	45 (38.0)	11 (15.9)	137 (41.4)	166 (37.0)	330 (37.8)
Dilated cardiomyopathy	10 (18.0)	4 (13.0)	9 (22.5)	5 (5.0)	30 (25.4)	25 (36.2)	NA	43 (9.1)	277 (31.8)
HOCM	NA	NA	5 (12.5)	22 (20.0)	NA	10 (14.5)	NA	58 (12.2)	
Congenital heart disease	2 (4.0)	NA	NA	13 (12.0)	1 (0.8)	3 (4.4)	NA	33 (7.0)	
Brugada syndrome	NA	2 (6.5)	NA	14 (13.0)	NA	NA	NA		
Idiopathic VT/VF	NA	5 (16.1)	12 (30.0)	17 (15.0)	15 (13.0)	NA	NA	34 (8.0)	40 (4.6)
Ventricular noncompaction	NA	1 (3.0)	NA	NA	NA	NA	NA		
Valvular heart disease	NA	1 (3.0)	1 (2.5)	NA	NA	NA	NA		
Long QT	NA	NA	NA	10 (9.0)	NA	NA	NA		
CPVT	NA	NA	NA	7 (6.0)	NA	NA	NA		
Inherited channelopathy		5 (16.1)		31 (27.9)	27 (23.0)	14 (20.3)		60 (13.0)	90 (10.3)
Other	6 (11.0)	NA	13 (32.5)	13 (12.0)	57 (48.0)	NA	NA	14 (2.9)	

S-ICD Pooled Results

Demographics



S-ICD Pooled Results

S-ICD and TV-ICD Spontaneous Conversion Efficacy

S-ICD was as effective as TV-ICD in treating spontaneous arrhythmias

	Spontaneous Shock Efficacy	
	First Shock	Final Shock in episode
S-ICD Pooled Data*	90.1%	98.2%
ALTITUDE First Shock Study ¹	90.3%	99.8%
SCD-HeFT ²	83%	
PainFree Rx II ²	87%	
MADIT-CRT ³	89.8%	
LESS Study ⁴		97.3%

* Excluded VT/VF Storm events

S-ICD Pooled Data
100% Clinical conversion to normal sinus rhythm

Of two “unconverted” episodes

- One spontaneously terminated after the 5th shock
- In the other episode, the device prematurely declared the episode ended. A new episode was immediately reinitiated and the VF was successfully terminated with one shock

1 Cha YM. *Heart Rhythm* 2013;10:702–708.

3 Kutiyfa V. *J Cardiovasc Electrophysiol* 2013;24:1246-52.

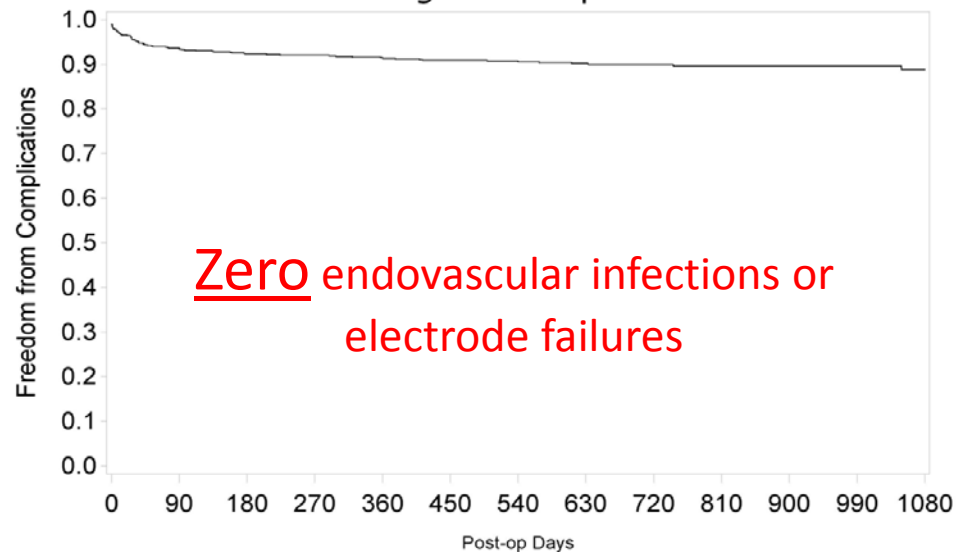
2 Swerdlow CD. *PACE* 2007; 30:675–700.

4 Gold MR. *Circulation* 2002;105:2043-2048.

S-ICD Pooled Results

Complications

Kaplan-Meier Estimate of Freedom from Complications Following S-ICD Implantation



No At Risk	878	791	731	707	650	591	525	414	303	217	162	123	105
K-M Estimate (%)	99.0	93.4	92.3	92.0	91.4	90.9	90.6	90.2	90.0	89.7	89.7	89.7	88.9

There were zero endovascular infections or electrode failures which could be a factor in the observed low mortality rate³

The acute major complication rate was lower when compared to studies with TV-ICD, likely because S-ICD doesn't require vascular access^{1,2}

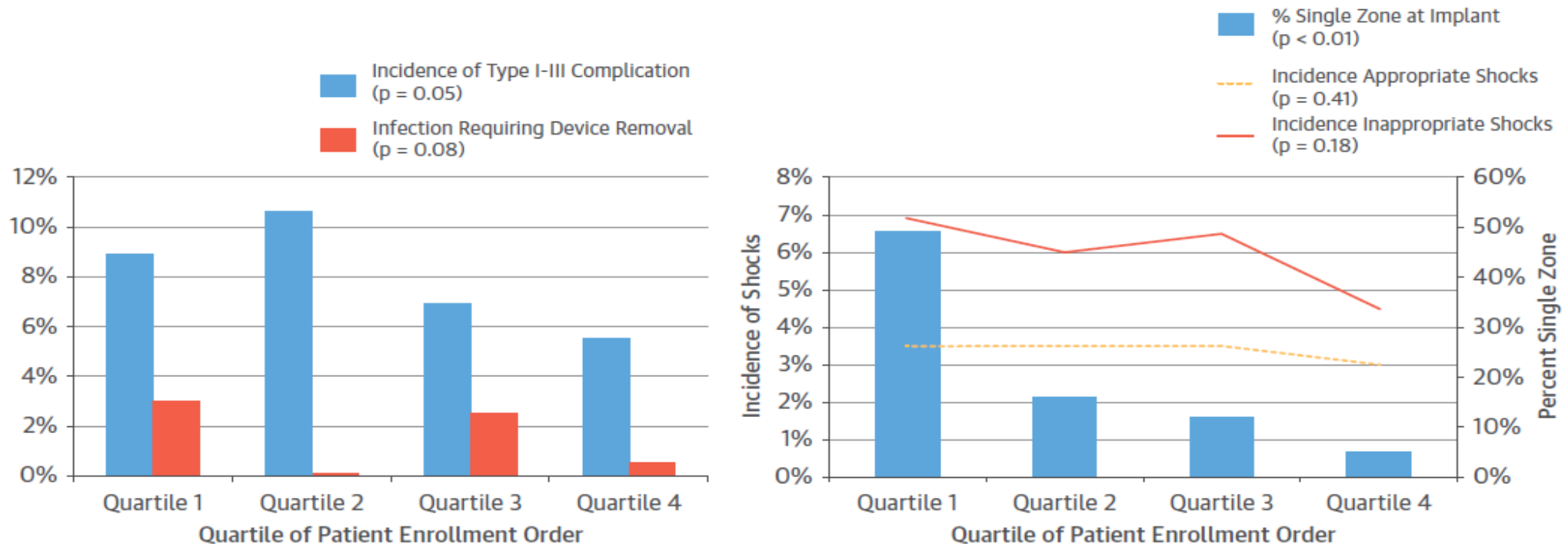
Acute Major Complications (% of patients)	<u>S-ICD</u> Pooled Data	<u>TV-ICD</u> NCDR Analysis (Peterson et al, JAMA 2013) ¹ Meta-analysis (van Rees et. al. JACC 2011) ²
	2 %	3 - 5 %
	(Hematoma, Lead or Device Mal-position or Displacement, Pneumothorax)	

1 Peterson PN. JAMA 2013; 309: 2025-2034. 2 Van Rees JB. JACC 2011; 58: 995-1000.

3 Tarakji KG. Europace 2014; 16: 490-495

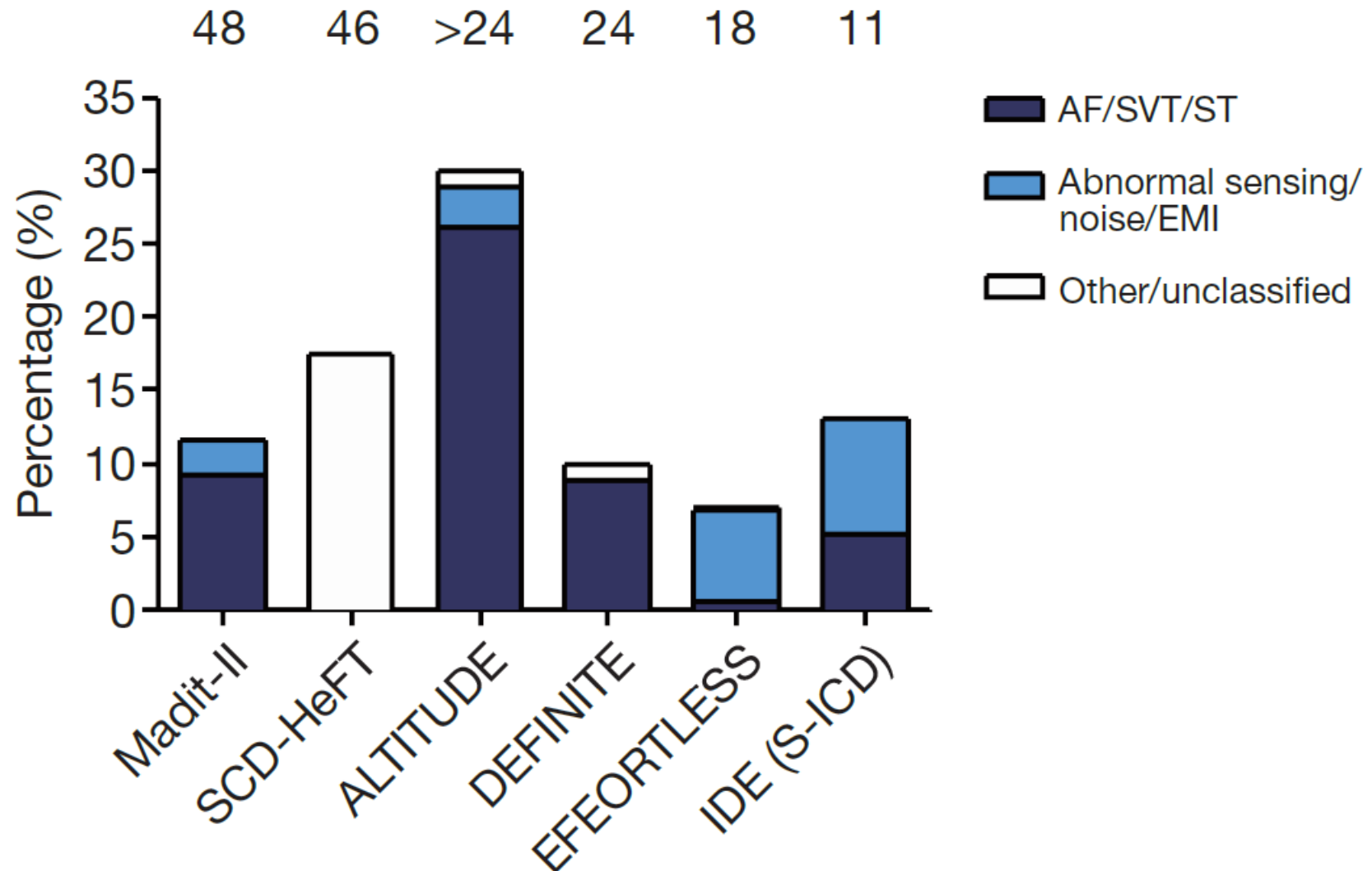
Safety and Efficacy of the Totally S-ICD

2-Y Results From a Pooled Analysis of the IDE Study and EFFORTLESS Registry



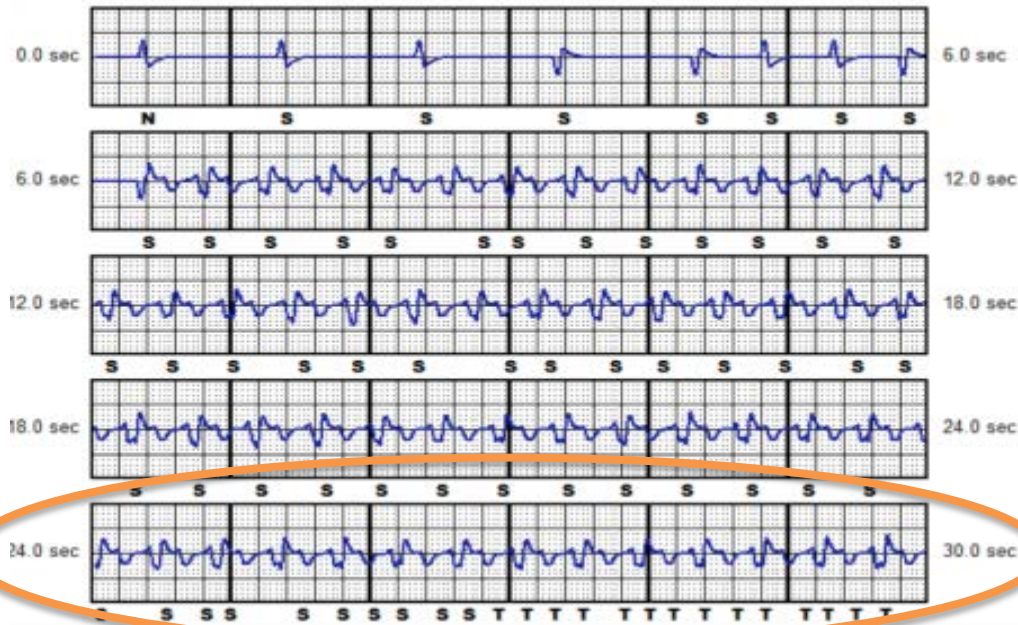
Inappropriate Shock Rate

T-ICD vs S-ICD in Different Clinical Setting

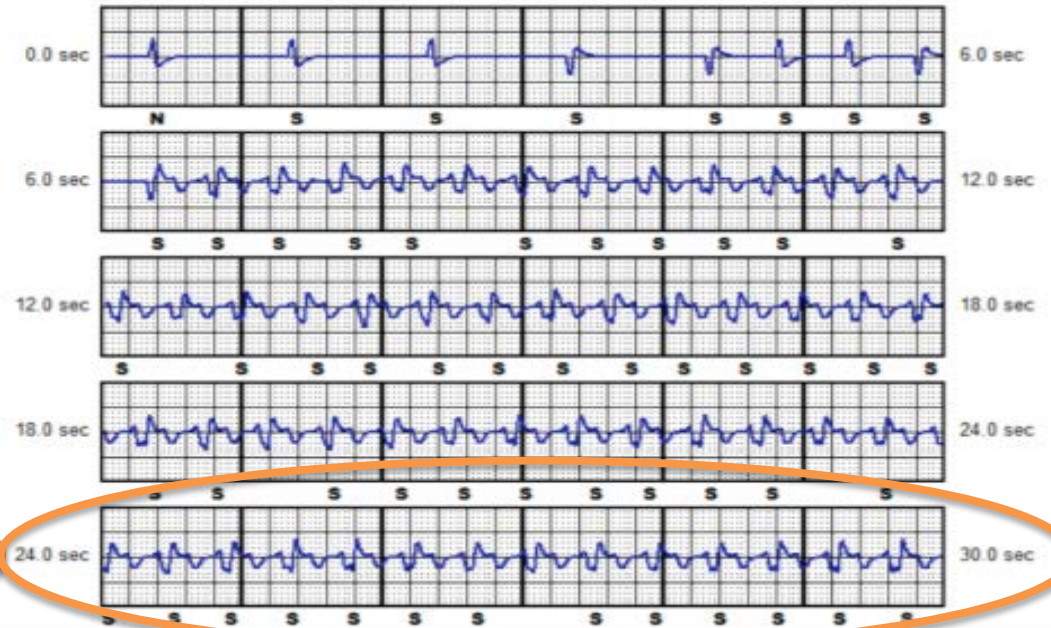


SMART Pass Example

SMART Pass **OFF**



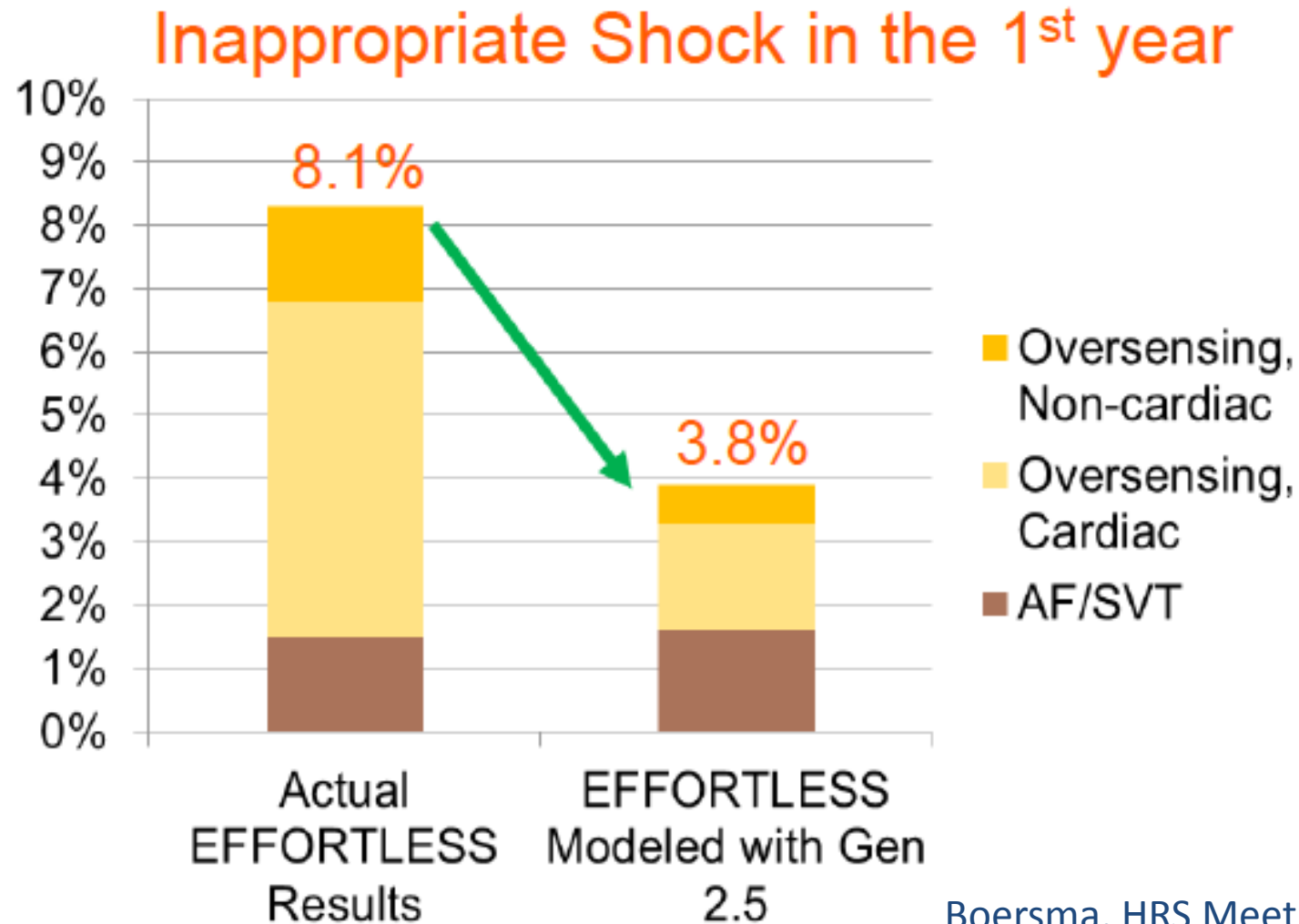
SMART Pass **ON**



Difference in sensing when comparing SMART Pass OFF versus ON*.

Inappropriate Shocks

Effortless Registry: 985 patients (follow-up 3.1 years)



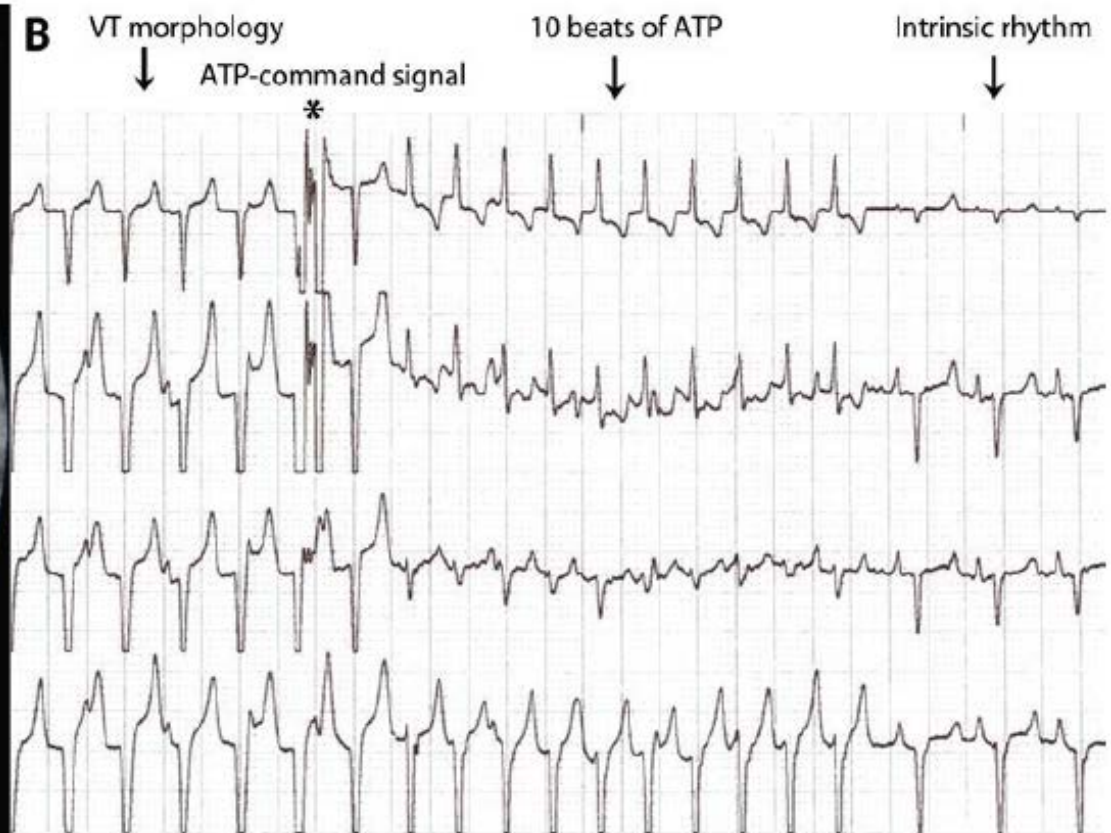
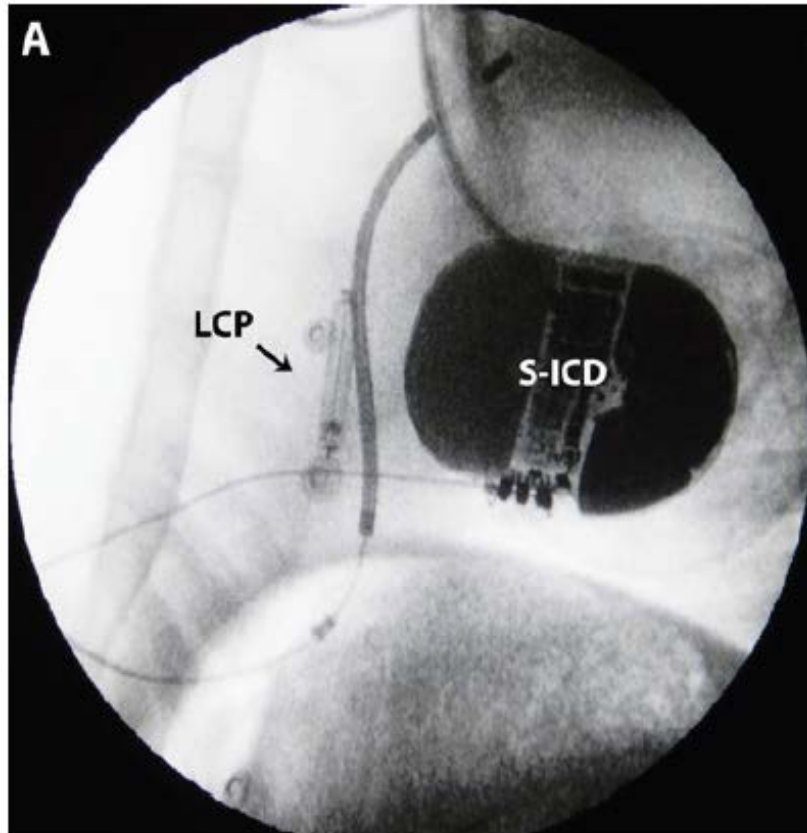
S-ICD Pooled Results

Device Extraction for Pacing

Extraction for pacing occurred in 0.4% of pts

Reason	Number (Percent)
New Pacing Indication	1 (0.1%)
ATP	1 (0.1%)
Ventricular overdrive pacing	1 (0.1%)
CRT Indication	1 (0.1%)

And if it is ...
The Future is Coming



2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death



The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC)

4.3.2 Subcutaneous implantable cardioverter defibrillator

Subcutaneous implantable cardioverter defibrillator

Recommendations	Class ^a	Level ^b	Ref. ^c
Subcutaneous defibrillators should be considered as an alternative to transvenous defibrillators in patients with an indication for an ICD when pacing therapy for bradycardia support, cardiac resynchronization or antitachycardia pacing is not needed.	IIa	C	157, 158
The subcutaneous ICD may be considered as a useful alternative to the transvenous ICD system when venous access is difficult, after the removal of a transvenous ICD for infections or in young patients with a long-term need for ICD therapy.	IIb	C	This panel of experts

ICD = implantable cardioverter defibrillator.

^aClass of recommendation.

^bLevel of evidence.

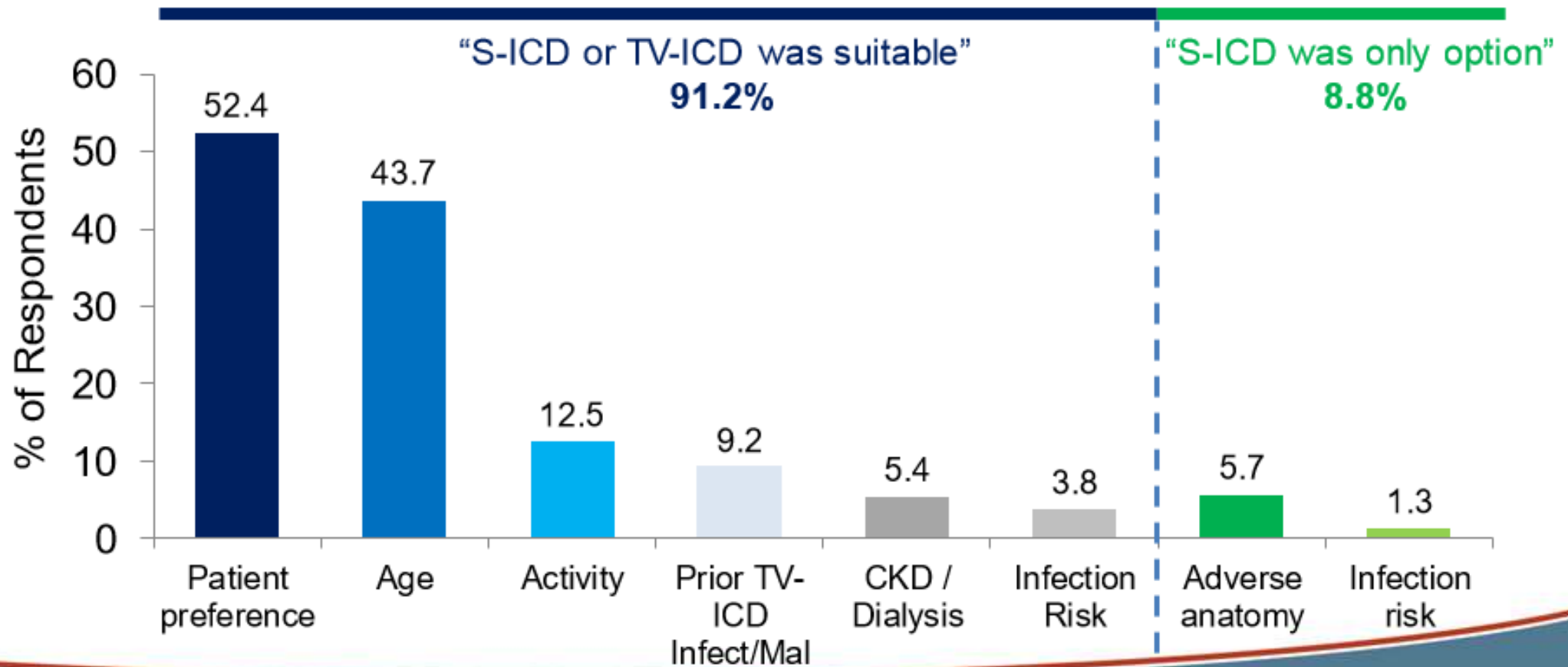
^cReference(s) supporting recommendations.

S-ICD Post-Approval Study

Evaluate A More Real World US Population

Reasons for S-ICD Device Choice

(Multiple reasons could be chosen)



**Selecting The Right Device For Each Patient Is Essential To
Preserve The Long-term Benefit By Avoiding The Complications
Of ICD Therapy**

S-ICD

**High Risk for
lead-related and
infectious
complications**



TV-ICD

**Need for TV-ICD
Pacing/sensing
options**



The Italian subcutaneous implantable cardioverter-defibrillator survey: S-ICD, why not?

**Giovanni Luca Botto^{1*}, Giovanni B. Forleo², Alessandro Capucci³,
Francesco Solimene⁴, Antonello Vado⁵, Giovanni Bertero⁶, Pietro Palmisano⁷,
Ennio Pisanò⁸, Antonio Rapacciuolo⁹, Tommaso Infusino¹⁰, Alessandro Vicentini¹¹,
Miguel Viscusi¹², Paola Ferrari¹³, Antonello Talarico¹⁴, Giovanni Russo¹,
Giuseppe Boriani¹⁵, Luigi Padeletti¹⁶, Mariolina Lovecchio¹⁷, Sergio Valsecchi¹⁷,
Antonio D'Onofrio¹⁸**; on behalf of 'AIAC S-ICD Why Not' Survey Investigators



Associazione Italiana Aritmologia e Cardioritmo

S-ICD® System: why not? AIAC SURVEY

OBIETTIVO:

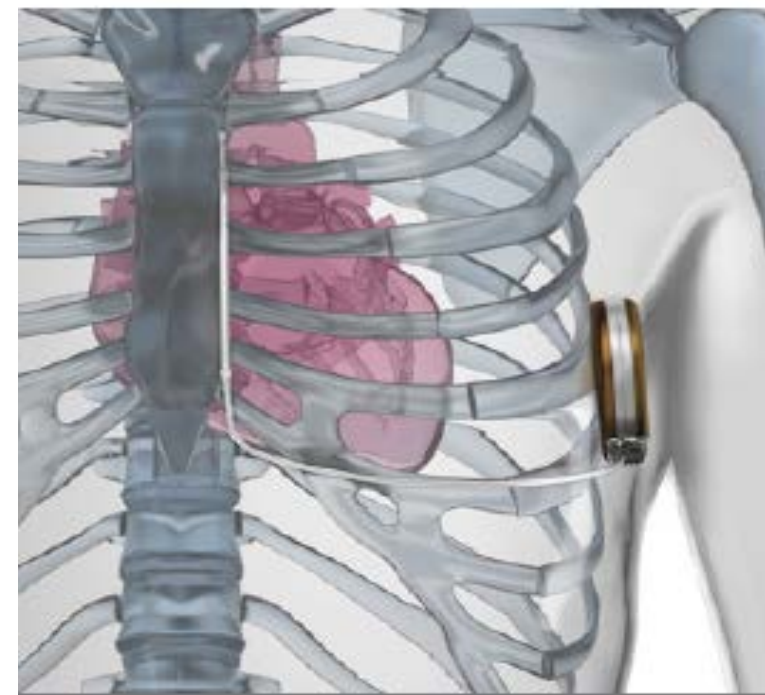
- Valutare le caratteristiche cliniche di base e le indicazioni all'impianto di un'ampia popolazione di pazienti consecutivi sottoposti ad impianto di ICD nella pratica clinica attuale.
- Indagare sui principali driver di scelta di S-ICD o T-ICD nella pratica clinica attuale
- Valutare tali driver alla luce delle evidenze cliniche esistenti (motivazioni supportate da dati)

PROGETTO:

- I centri coinvolti costituiranno un campione rappresentativo dei centri AIAC
- Il periodo di osservazione sarà di 3 mesi (Set, Ott, Nov 2015)

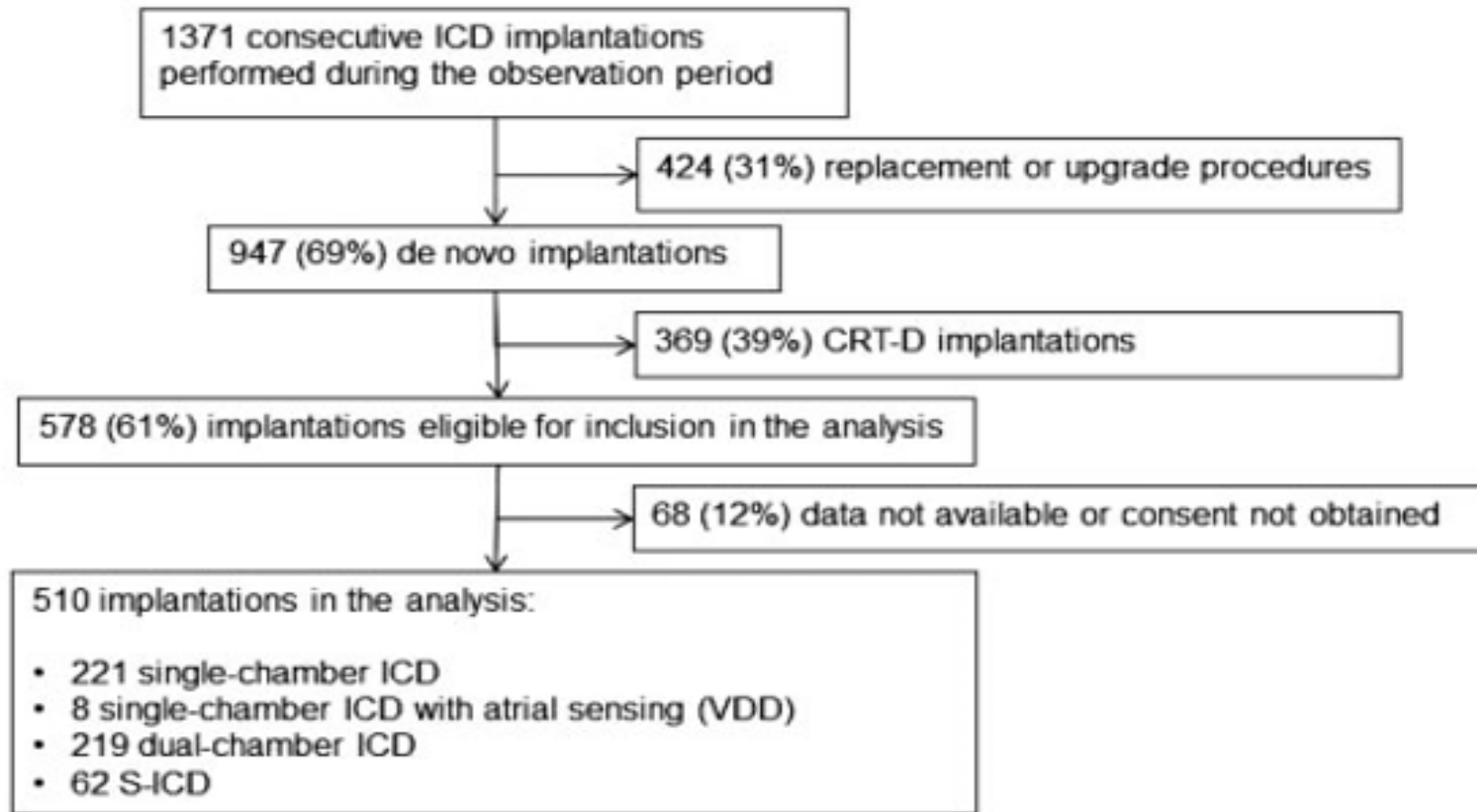
MODALITÀ DI RACCOLTA DATI:

- Si potranno usare CRF Cartacee o direttamente una piattaforma Web-based



S-ICD: Why Not?

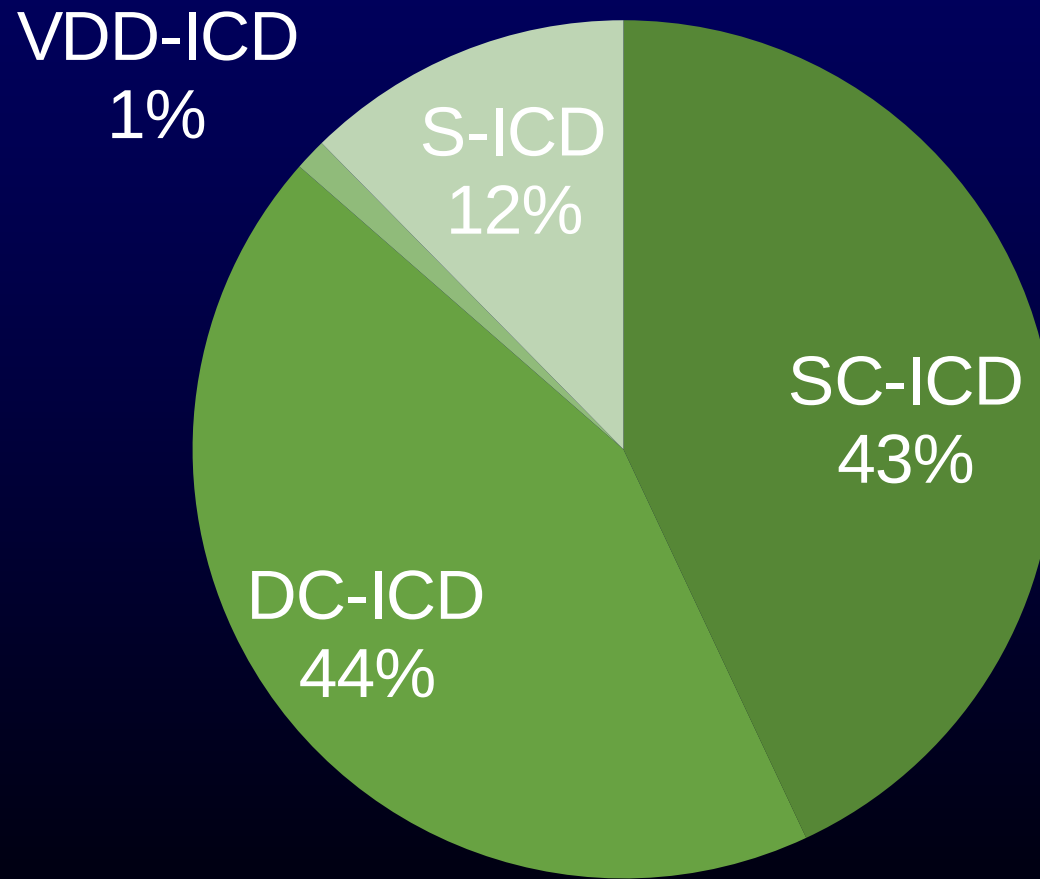
Diagram of the Study: N° of Cases in Analysis



S-ICD : Why Not ?

Result From AIAC Survey

ICD Type



S-ICD: why not? – AIAC Survey

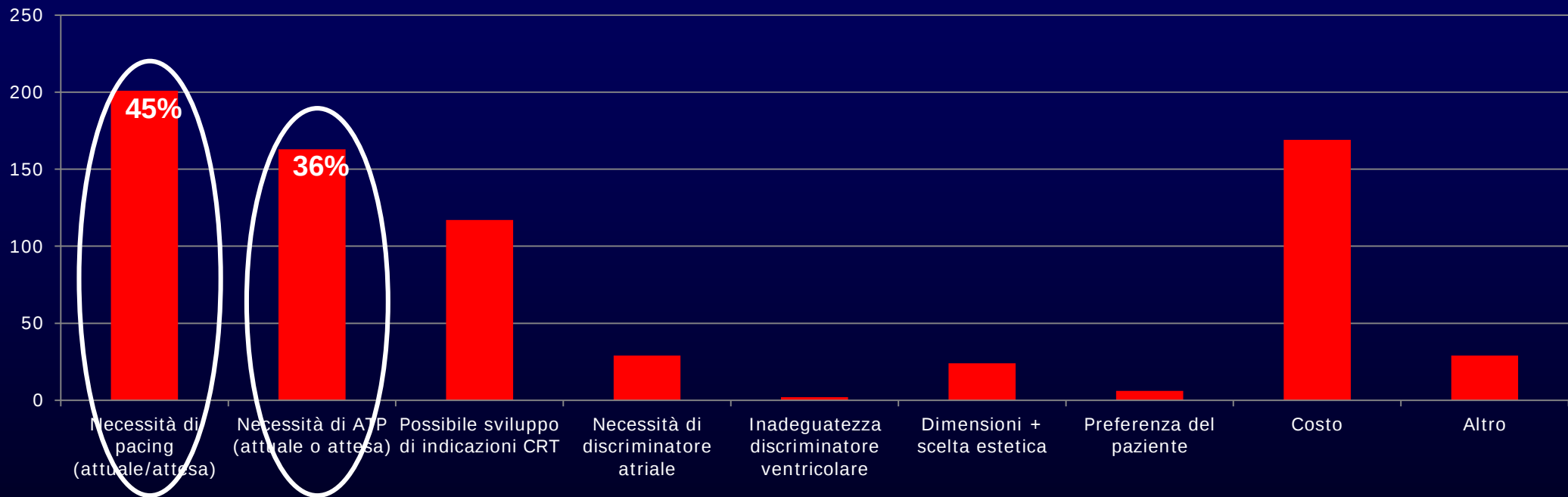
Parameter	All patients (n=510)	Transvenous ICD (n=448)	Subcutaneous ICD (n=62)
Male gender, n (%)	399 (78)	354 (79)	45 (73)
Age, years	65±13	67±11	47±13*
BMI classification			*
Underweight, n (%)	10 (2)	10 (2)	0 (0)
Normal weight, n (%)	189 (37)	154 (34)	35 (56)
Overweight and Obese, n (%)	311 (61)	286 (64)	25 (40)
LV ejection fraction, %	36±11	34±10	49±14*
New York Heart Association			*
Class I, n (%)	107 (21)	66 (15)	41 (66)
Class II, n (%)	270 (53)	256 (57)	14 (23)
Class III, n (%)	128 (25)	121 (27)	7 (11)
Class IV, n (%)	5 (1)	5 (1)	0 (0)
Secondary prevention of SCD, n (%)	123 (24)	91 (20)	32 (52)*
Cardiomyopathy			
Ischemic, n (%)	286 (56)	268 (60)	18 (29)*
Dilated, n (%)	97 (19)	94 (22)	3 (5)*
Hypertrophic, n (%)	25 (5)	16 (4)	9 (15)*
Hypertensive, n (%)	16 (3)	15 (3)	1 (2)
Valvular, n (%)	20 (4)	18 (4)	2 (3)
ARVD, n (%)	10 (2)	7 (2)	3 (5)
Congenital, n (%)	5 (1)	4 (1)	1 (2)
Other, n (%)	5 (1)	3 (1)	2 (3)
Channelopathies/Other			
Idiopathic VF, n (%)	20 (4)	13 (3)	7 (11)*
Brugada, n (%)	15 (3)	2 (0.4)	13 (21)*
Long QT syndrome, n (%)	5 (1)	3 (1)	2 (3)
Other, n (%)	6 (1)	5 (1)	1 (2)
Coronary artery disease, n (%)	293 (57)	275 (61)	18 (29)*
Myocardial infarction, n (%)	269 (53)	252 (56)	17 (27)*
Coronary artery bypass graft, n (%)	97 (19)	92 (21)	5 (8)*
PTCA, n (%)	194 (38)	181 (40)	13 (21)*
Chronic kidney disease, n (%)	87 (17)	83 (19)	4 (6)*
Diabetes, n (%)	134 (27)	127 (28)	7 (11)*
Chronic obstructive pulmonary disease, n (%)	82 (16)	80 (18)	2 (3)*

BMI: Body Mass Index; LV: Left ventricular; SCD: Sudden Cardiac Death; ARVD: Arrhythmogenic Right Ventricular Dysplasia; VF: Ventricular Fibrillation; PTCA: Percutaneous Transluminal Coronary Angioplasty. *: p<0.05 versus Transvenous ICD.

S-ICD : Why Not ?

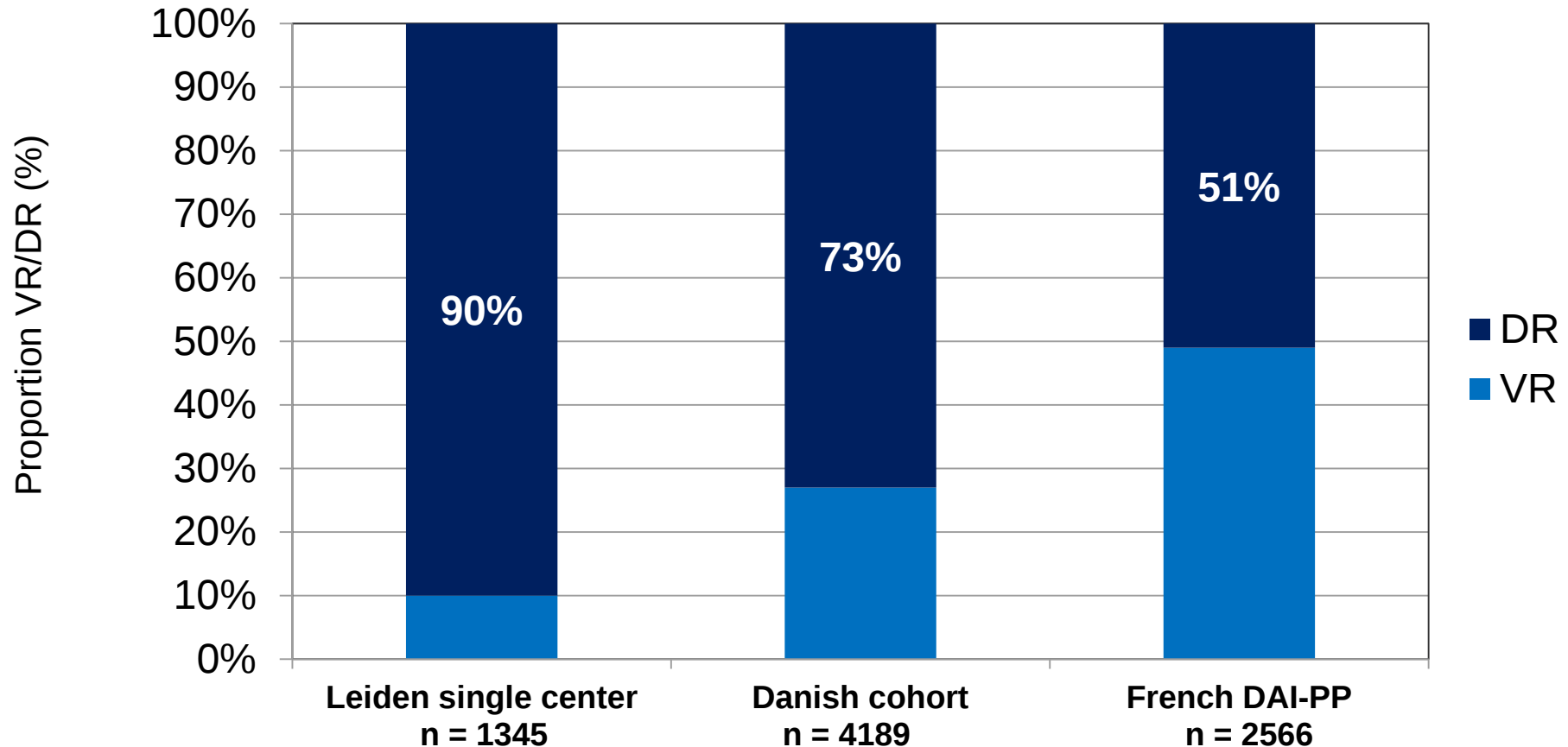
Result From AIAC Survey

Unsuitability for S-ICD



Current Single or Dual Chamber ICD Use

Range of 50-90% use of dual chamber TV-ICD



Indication for pacing in patients with persistent bradycardia

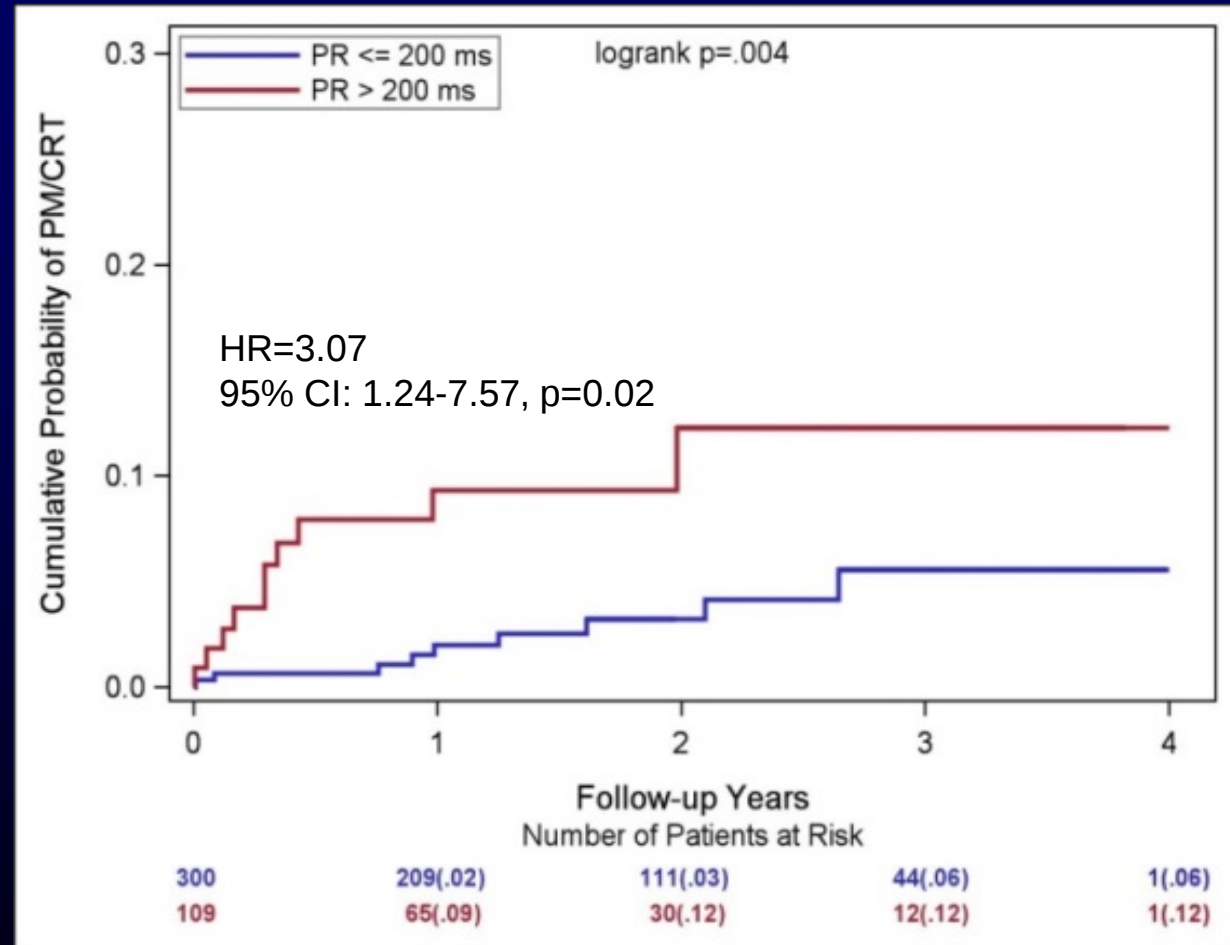
Recommendations	Class	Level
1) Sinus node disease. Pacing is indicated when symptoms can clearly be attributed to bradycardia.	I	B
2) Sinus node disease. Pacing may be indicated when symptoms are likely to be due to bradycardia, even if the evidence is not conclusive.	IIb	C
3) Sinus node disease. Pacing is not indicated in patients with sinus bradycardia which is asymptomatic or due to reversible causes.	III	C
4) Acquired AV block. Pacing is indicated in patients with third- or second-degree type 2 AV block irrespective of symptoms.	I	C
5) Acquired AV block. Pacing should be considered in patients with second-degree type 1 AV block which causes symptoms or is found to be located at intra- or infra-His levels at EPS.	IIa	C
6) Acquired AV block. Pacing is not indicated in patients with AV block which is due to reversible causes.	III	C

Predictors of Bradycardia Pacing Need Development ?

- ▶ 458 pts from MADIT II control arm
- ▶ 20 month median follow-up

Baseline PR interval >200 ms significant predictor of subsequent PM/CRT implantation

- ▶ Total PM rate is ~2% per year
- ▶ Need for PM in MADIT-II pts is low, especially in those with normal PR interval (≤ 200 ms)



S-ICD: why not? – AIAC Survey

Risultati - Controindicazioni all'uso di S-ICD :

necessità di pacing

ECG all'impianto	N = 510	ESC 2013
Malattia nodo del seno, n(%)	28 (5)	I o IIb (*)
Incompetenza cronotropa, n(%)	32 (6)	#
BAV II Mobitz II or BAV III, n(%)	8 (2)	I
BAV II Mobitz I, n(%)	5 (1)	IIa (*)
Altro	7 (1)	IIa o IIb (*)

*: in base sintomi; #: non raccomandato

Indicazioni ESC

Classe I: 36 (7%)

Classe II: 12 (2%)

sviluppo indicazioni pacing

ECG all'impianto	N = 510
BAV I (PR > 200ms), n(%)	61 (12)
Durata PR, ms	174 ± 37

Indication for pacing in patients with persistent bradycardia

Recommendations	Class ^a	Level ^b	Ref. ^c
1) Sinus node disease. Pacing is indicated when symptoms can clearly be attributed to bradycardia.	I	B	1, 6-9
2) Sinus node disease.			

Indication for cardiac pacing in patients with BBB

Recommendations	Class ^a	Level ^b	Ref. ^c
1) BBB, unexplained syncope and abnormal EPS. Pacing is indicated in patients with syncope, BBB and positive EPS defined as HV interval of ≥70 ms, or second- or third-degree His-Purkinje block demonstrated during incremental atrial pacing or with pharmacological challenge.	I	B	25, 31
2) Alternating BBB. Pacing is indicated in patients with alternating BBB with or without symptoms.	I	C	-
3) BBB, unexplained syncope non diagnostic investigations. Pacing may be considered in selected patients with unexplained syncope and BBB.	IIb	B	32
4) Asymptomatic BBB. Pacing is not indicated for BBB in asymptomatic patients.	III	B	26, 33, 34

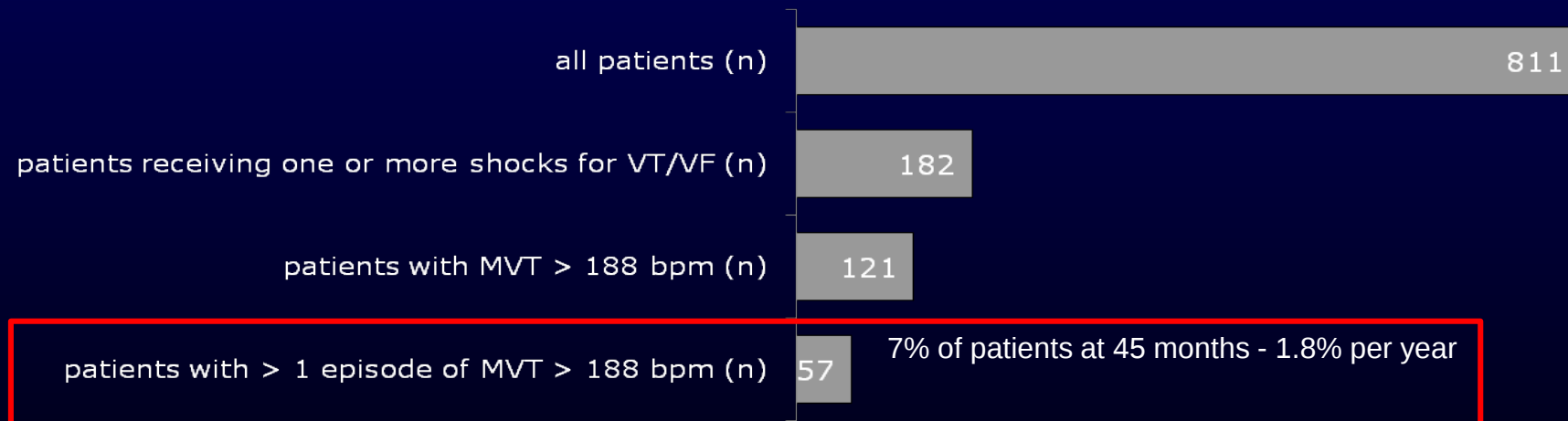
Eur Heart J. 2013; 34: 2281-329.

PR > 200ms: 61 (12%)

How Critical is ATP for the Avoidance of Shocks with TV-ICD?

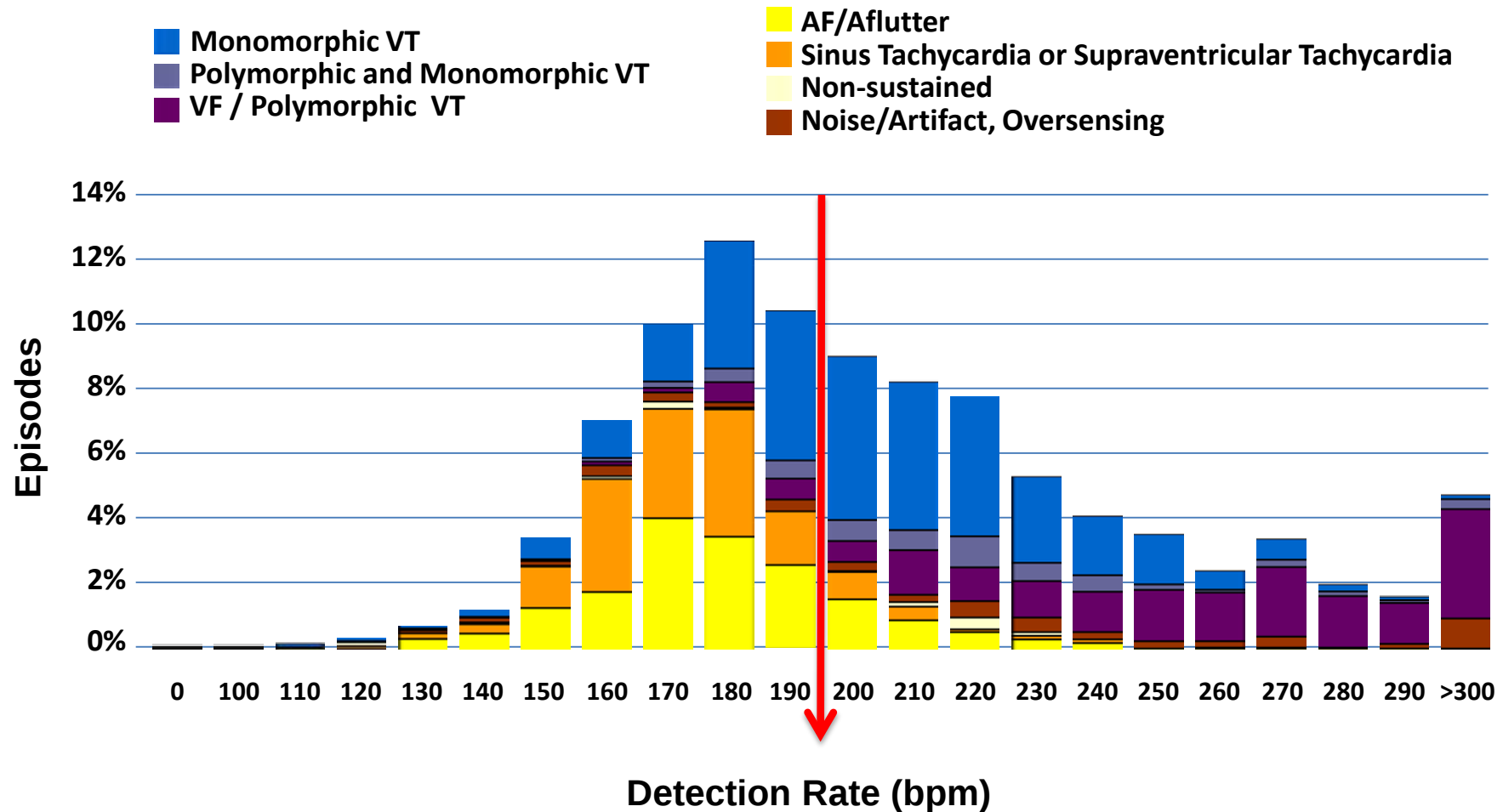
Recurrent fast MVT > 188 bpm (18/24 NID) in SCD-HeFT

- Over the course of the 45.5 mos of follow up 7% of all pts had more than a single episode of fast MVT
- This corresponds to a incidence of 1.8% per year
it is unknown how many are self-terminable events, or would have been treated successfully b ATP



ATP Works Perfectly Well For Episodes Within The "SVT" Range

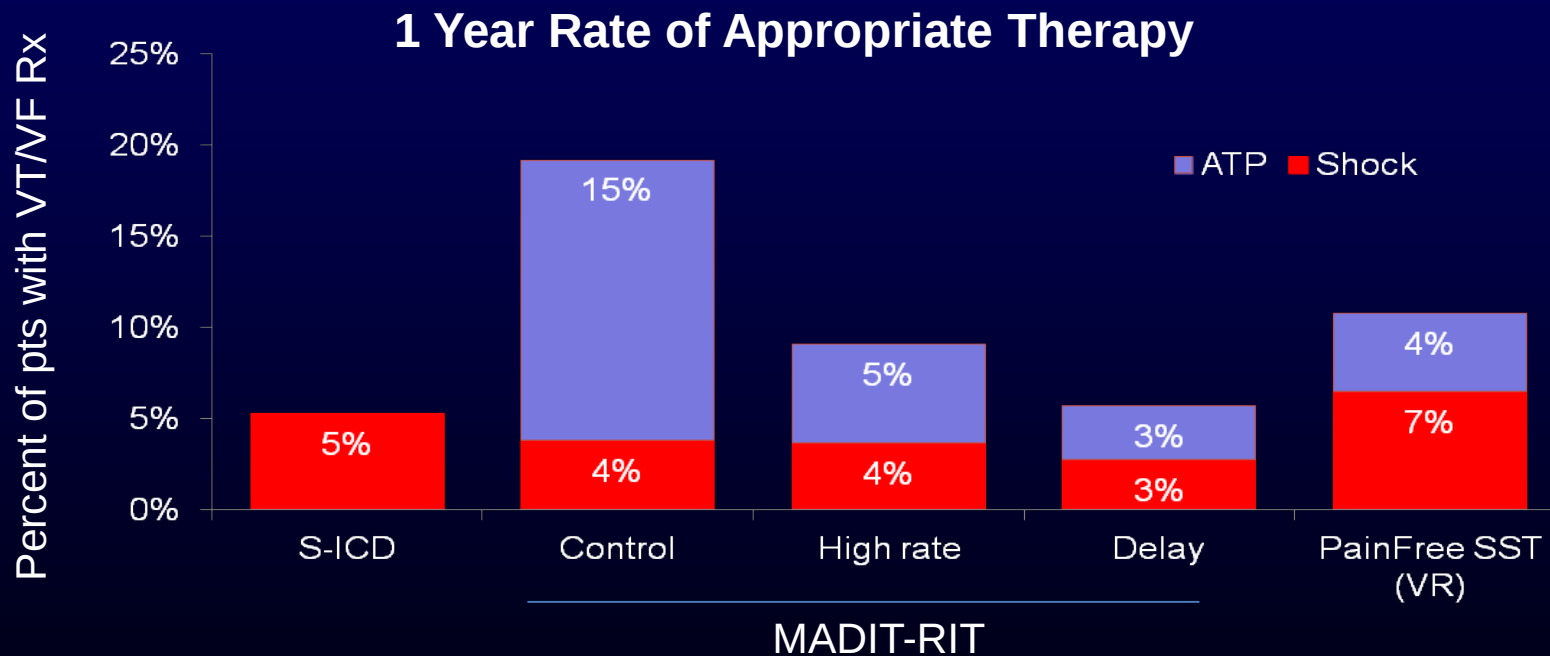
Altitude Registry: 2345 1st shock episodes



Avoiding Unnecessary Shocks for fast VT

Duration Delay and Spontaneous Termination

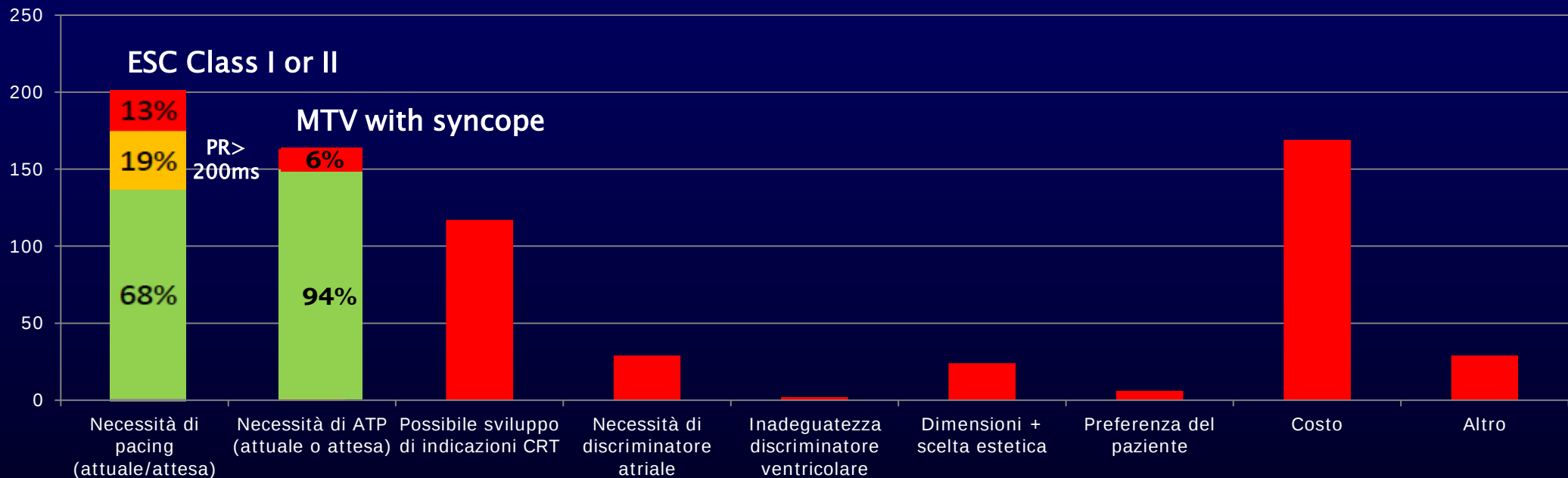
- ▶ MADIT RIT (primary prev pts): same incidence of appropriate shocks despite large reductions in unnecessary ATP
- ▶ PainFree SST (secondary prev pts): same incidence of appropriate shocks despite reduction in unnecessary ATP



1 year Kaplan Meier incidence shown for S-ICD and PainFREE SST. 1 year rate for MADIT-RIT annualized at an average follow-up of 1.4 years.

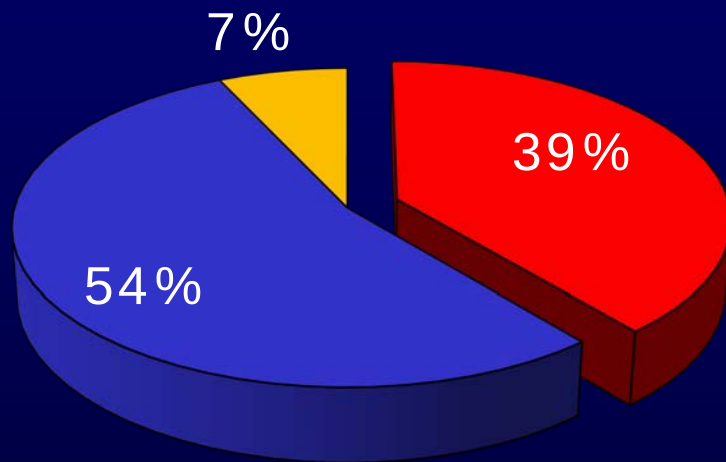
S-ICD : Why Not ?

Result From AIAC Survey



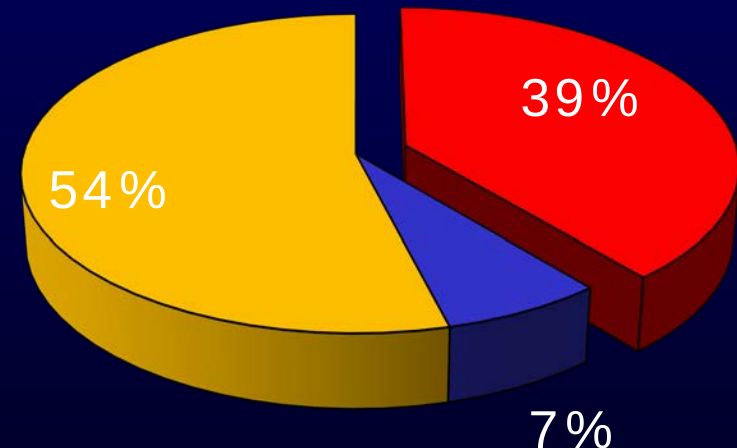
S-ICD : Why Not ?

Conclusion From AIAC Survey



■ CRT-D ■ ICD ■ S-ICD

No pacing
No ATP:
88 % of ICD



■ CRT-D ■ ICD ■ S-ICD

S-ICD Therapy

Take –Away Points (1)

- Excellent **efficacy** (similar to TV-ICD)
- Low rate of **inappropriate** shocks
- Less **complication** rate ?
long term data to come...
- Alternative to TV-ICD when
no pacing or CRT, no ATP (Class IIa)
*difficult venous access, in young pts, or
when risk of infection* (Class IIb)

S-ICD Therapy

Take –Away Points (2)

- Indication to pacing need by TV-ICD should be reconsidered
- Cost issues and/or lack of reimbursement limit the uptake in daily practice
- Implantation-rates expected to significantly increase

Which Pts Would Benefit From A TV-ICD?

Needs for Paradigm Shift

**TV system only if there is a strong reason
Balance between the benefit and the risk**

