Has the transvenous ICD lead reached its zenith with new technologies such as S-ICD and leadless pacemaker?

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Disclosures:
Consultant, Clinical Trials, Speaking Fees- BSC, Medtronic, St Jude,

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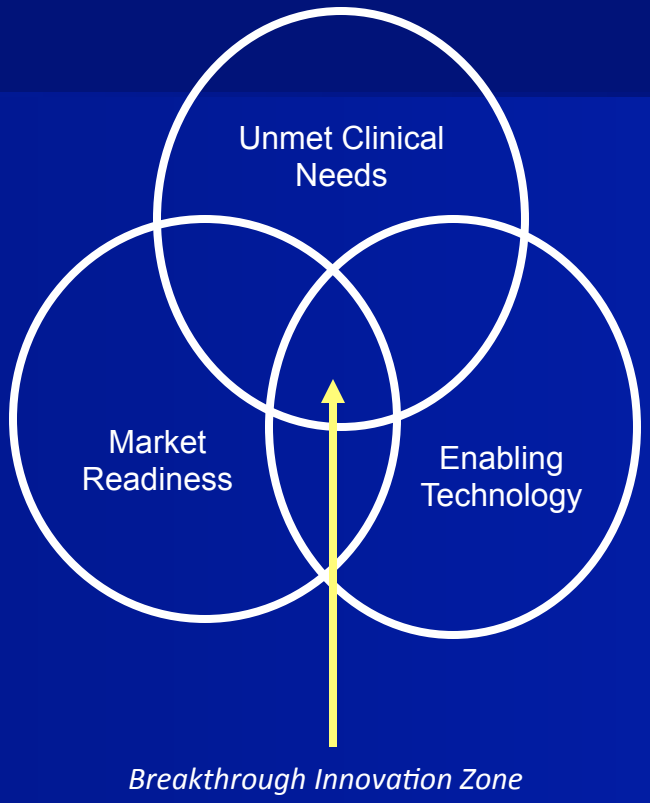
MY CONFLICTS OF INTEREST ARE

Consultant, Clinical Trials,
Speaking Fees-
BSC, Medtronic, St Jude

Breakthrough Innovation in Medical Devices

Requires alignment of:

- **Unmet clinical needs**
- **Societal/market readiness**
  - *Global Megatrends*
  - *Healthcare trends*
- **Enabling technology**



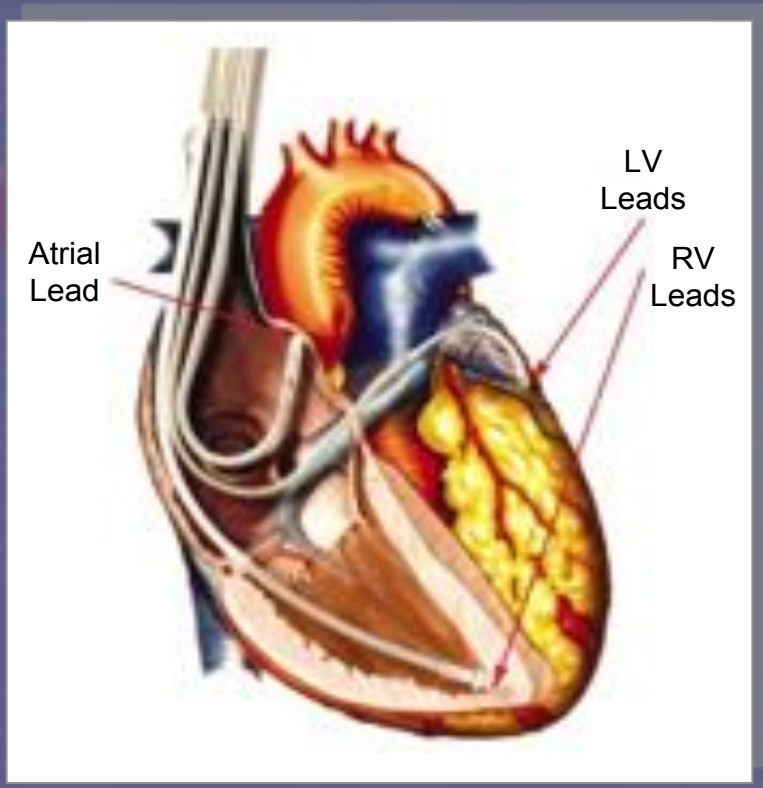
Introduction

- The ICD was first approved in 1985 as a simple shock box using epicardial patches with few if any programmable parameters
- It was shown to treat VT/VF effectively and reduce mortality in high risk cohorts
- Subsequent advances included pacing capabilities, transvenous leads and remote monitoring
- However, complications associated with these devices are one cause of under utilization

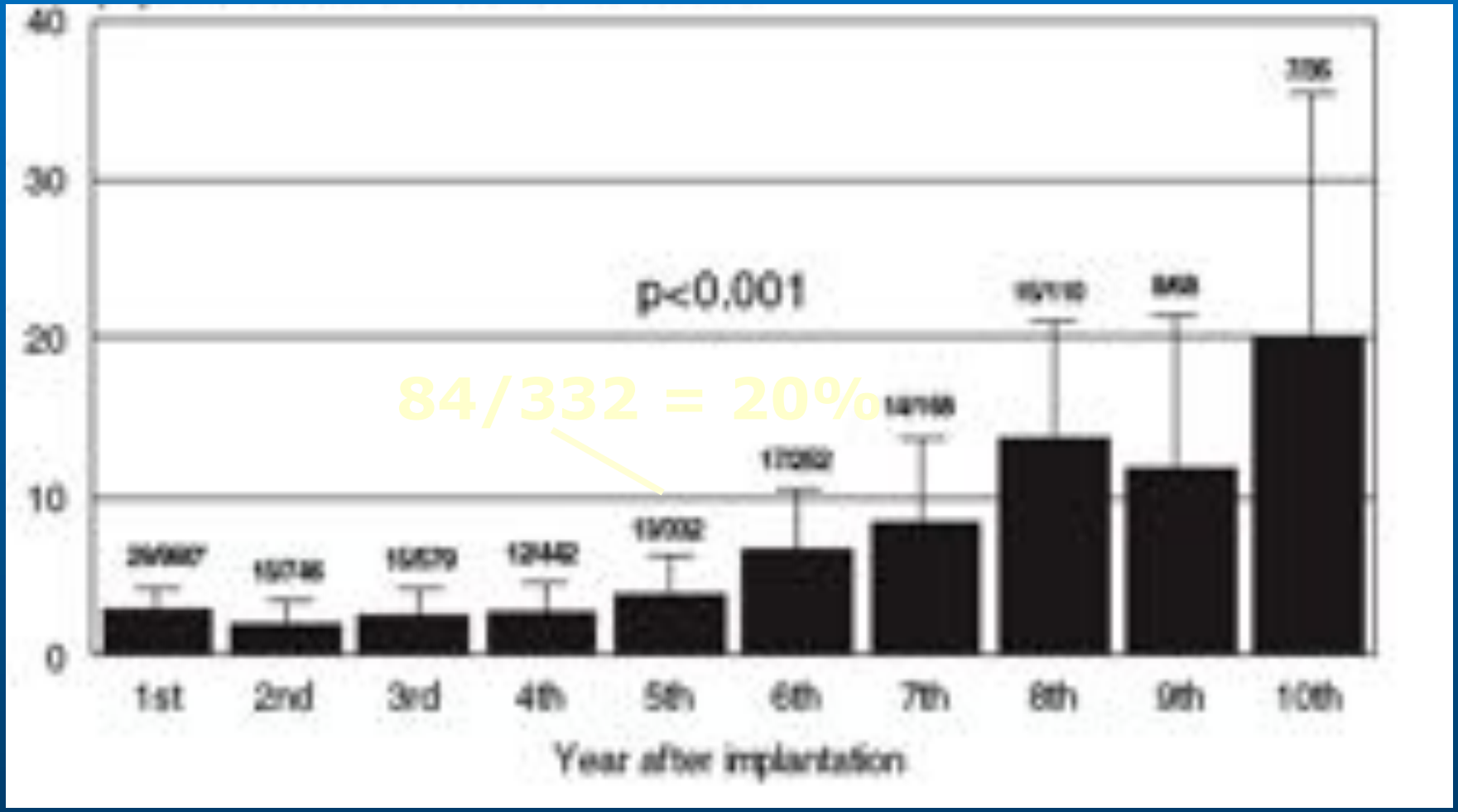
ICD Systems

The current ICD approach while effective, is not without significant risks

- 11% ICD patients suffer complications during or shortly after implant
- Acute complications add significant costs to the healthcare system (>$7000/pt.)
- Infection rates are rising (one of the most serious complications)

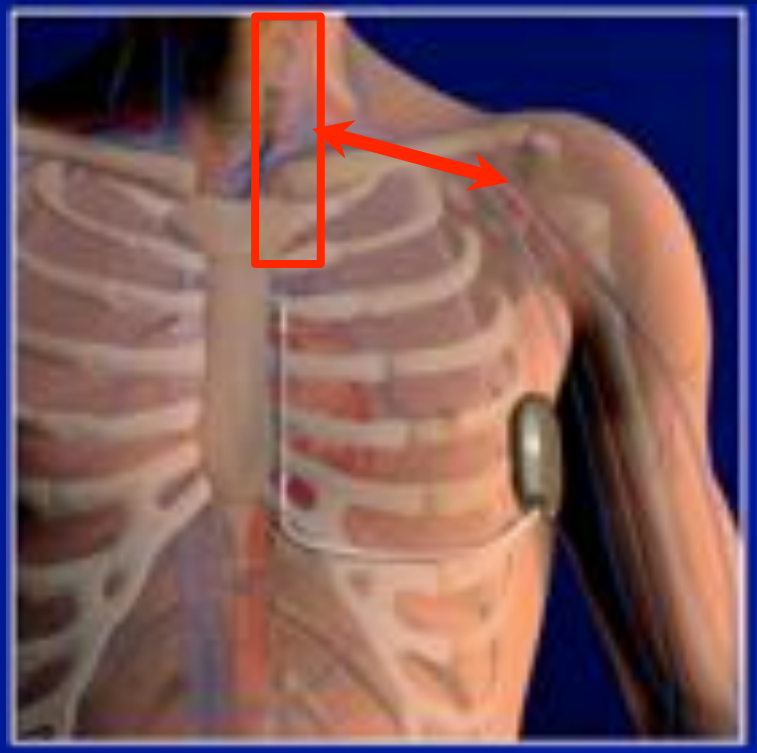


Incidence of Lead Failures in Defibrillation Systems



Kleemann *et al.* Circulation May 2007

S-ICD Lead
Structural Differences



- No lumen
  - –Greater Tensile Strength
- Less Torque/Stress
- 8cm Parasternal Coil
- Shock vector can ↔ coil (reversible)

S-ICD System Study Design
Prospective, Single-Arm

Enrollment (N=330)
- 33 Sites in the US, NZ, NL, UK

1º Efficacy Endpoint: Acute VF Conversion Rate
- 2 consecutive successes out of 4 attempts
- Lower Bound of 2-sided $CI_{95\%}$ > 88%

Optional Sub-Study: VF Conversion Rate at ≥150 Days

1º Safety Endpoint: 180-Day System Complication Free Rate
- Lower Bound of 2-sided $CI_{95\%}$ > 79%

Semi-Annual Follow-Up Visits Through Study Close

Implant Attempts

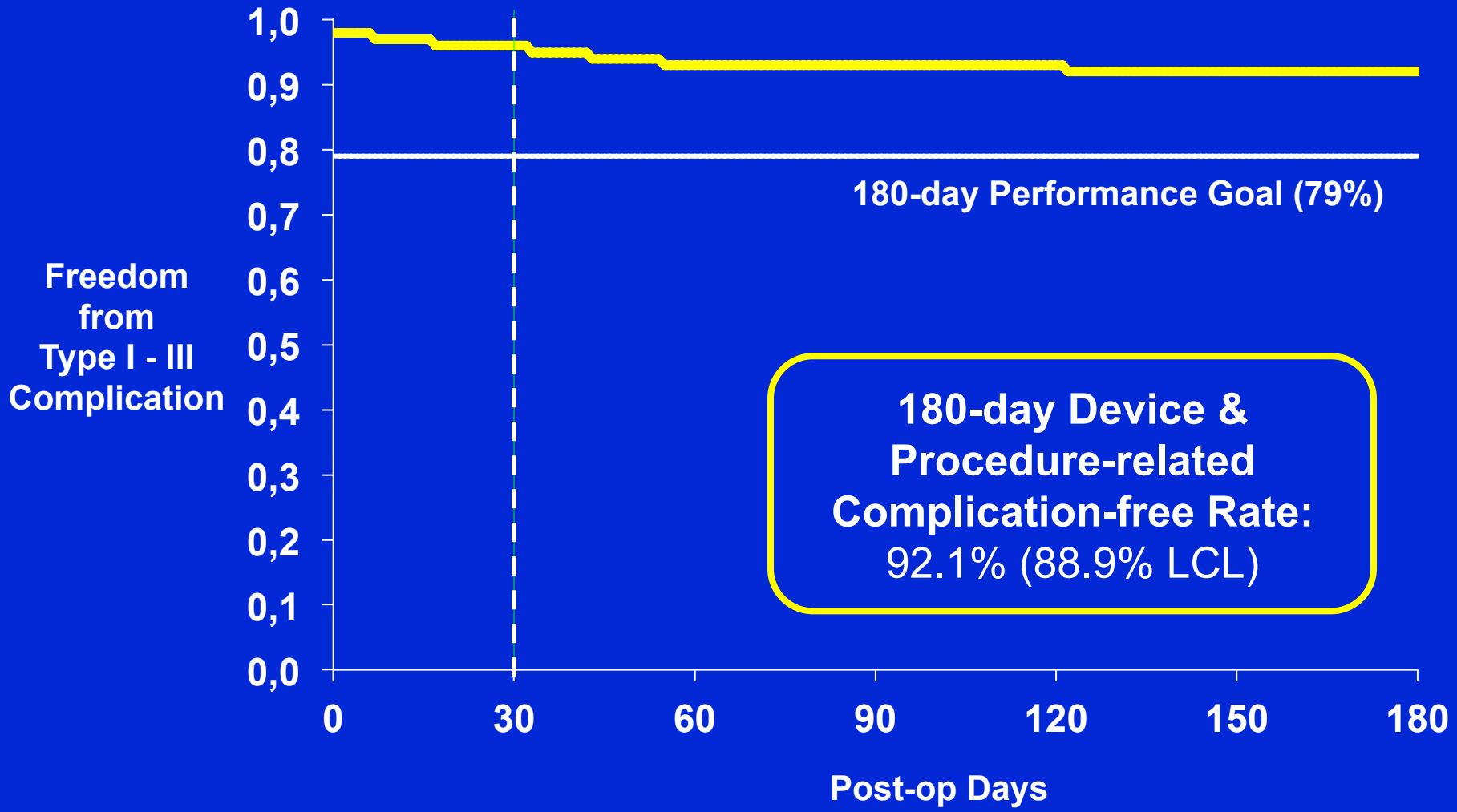
- 321 patients underwent implant procedure
  - 95% implanted using only anatomical landmarks (no medical imaging)
- No electrode or pulse generator movement in 99% of implanted patients throughout follow-up period

Primary Effectiveness Endpoints

- **Acute VT/VF Sensitivity**
  - VT/VF Inductions: 809
  - Successful detections: 808 (99.9%)

- **Conversion with 65 J Shocks (2 consecutive times out of 4 attempts**
  - **100% Successful**

Freedom from all Device-, Labeling-, & Procedure-related Complications



S-ICD System Clinical Investigation

Annualized Mortality of ICD Studies

Clinical Study	Annualized Mortality Rate
S-ICD System IDE Study[1]	3.7%
MADIT[2]	5.8%
MADIT II[3]	6.2%
AVID[4]	8.2%
SCD-HeFT[5]	5.8%

[1]S-ICD System Clinical Investigation. Study not prospectively designed to evaluate mortality,
[2]Moss, NEJM 1996
[3]Goldenburg, Circulation 2010
[4]AVID Investigators, N Engl J Med 1997;337:1576-83
[5]Bardy, NEJM 2005

Incidence and Efficacy of Shocks With the S-ICD: Pooled Long Term Results from the IDE and EFFORTLESS Studies

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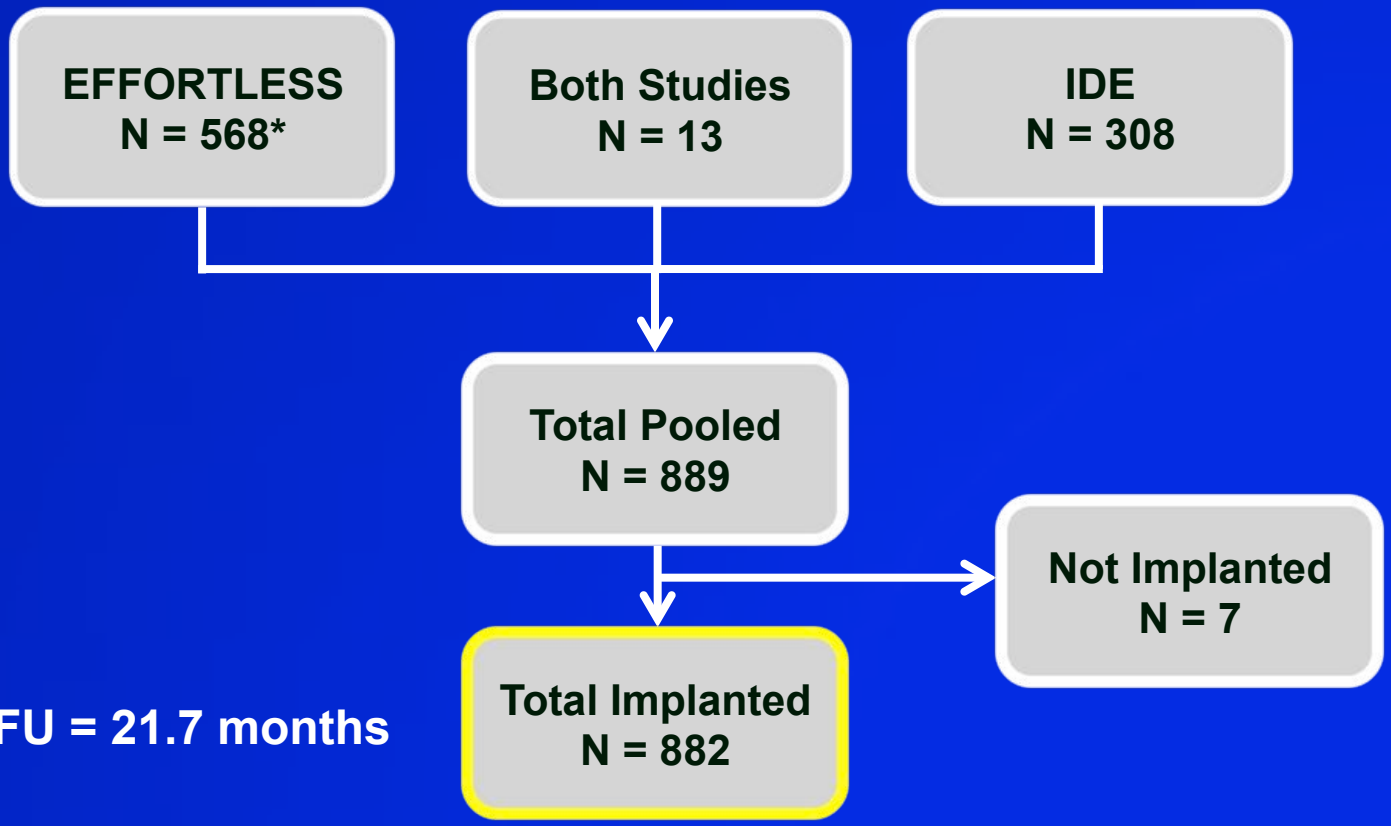
Pooled Analysis Cohort



Mean FU = 21.7 months

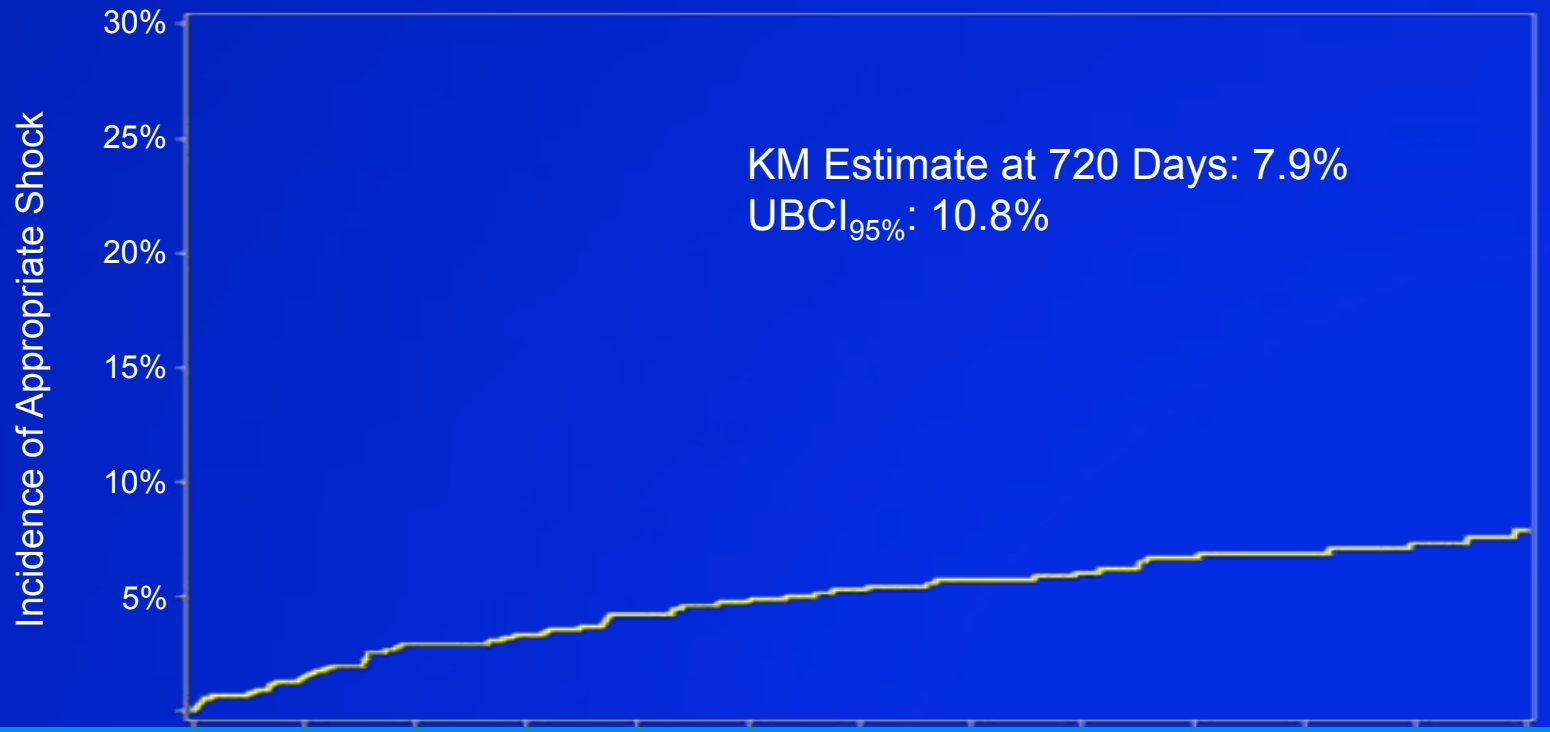
** Includes 314 enrolled prospectively and 254 enrolled retrospectively*

Induced VT/VF Conversion

	Patients (N = 771)*	
Category	**n**	**%**
Successful Conversion ≤ 65 J	**728**	**94.4**
Successful Conversion ≤ 80 J	**760**	**98.6**

** Includes all available conversion tests.*

Incidence of Appropriate Shocks at 2 years



Post Op Days	0	60	120	180	240	300	360	420	480	540	600	660	720
Pts w/Episodes (Cum)	0	13	25	28	35	40	43	46	48	52	53	55	57
No at Risk	882	837	798	755	738	704	664	625	586	535	453	378	303
K-M Estimate (%)	0.0	1.5	2.9	3.3	4.2	4.9	5.3	5.7	6.0	6.7	6.9	7.3	7.9
95% LBCI (%)	0.0	2.3	4.1	4.6	5.6	6.4	6.9	7.5	7.9	8.7	9.1	9.9	10.8

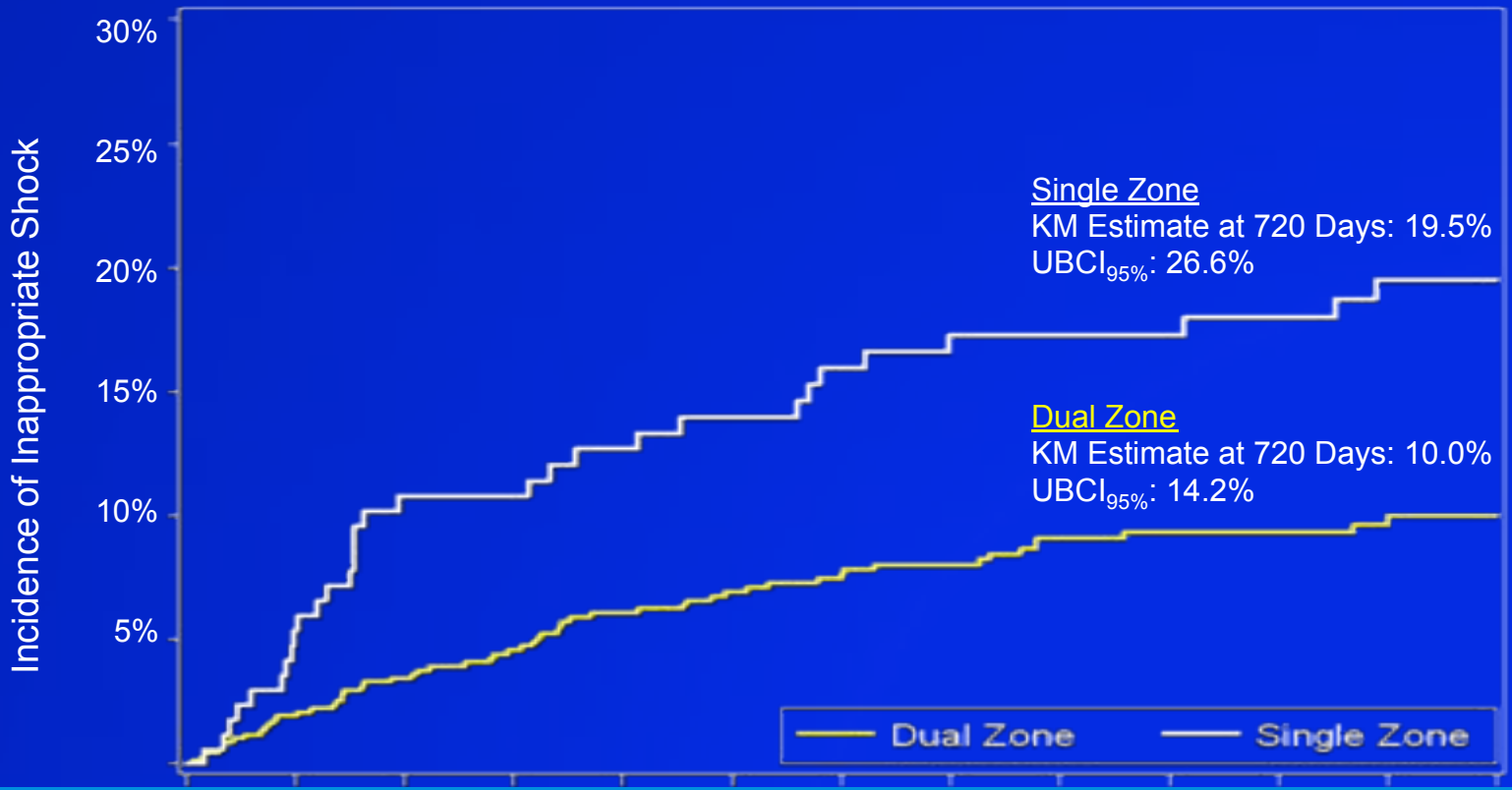
Conversion of Spontaneous VT/VF

Rhythm	Episodes N (Pts)	DISCRETE EPISODES	
		1st Shock Conversion (%)	≥ 1 Shock Conversion (%)
MVT	60 (40)	55 (91.7)	60 (100.0)
PVT/VF	51 (32)	45 (88.2)	49 (96.1)
All	111 (59)	100 (90.1)	109* (98.2)

*Of two unconverted episodes, one terminated after the 5th shock but beyond the time frame of EGM recording. In the other episode, the device prematurely declared the episode ended after 2 shocks due to undersensing. A new episode was immediately reinitiated and the VF was successfully terminated with one additional shock.

Patients	Storms	Device Episodes	VT/VF STORMS
			Final Storm Conversion (%)
7	12	88	S-ICD Shock: 10 (83.3%)
			External Shock: 1 (8.3%)
			No Conversion: 1 (8.3%)

Incidence of Inappropriate Shocks at 2 years



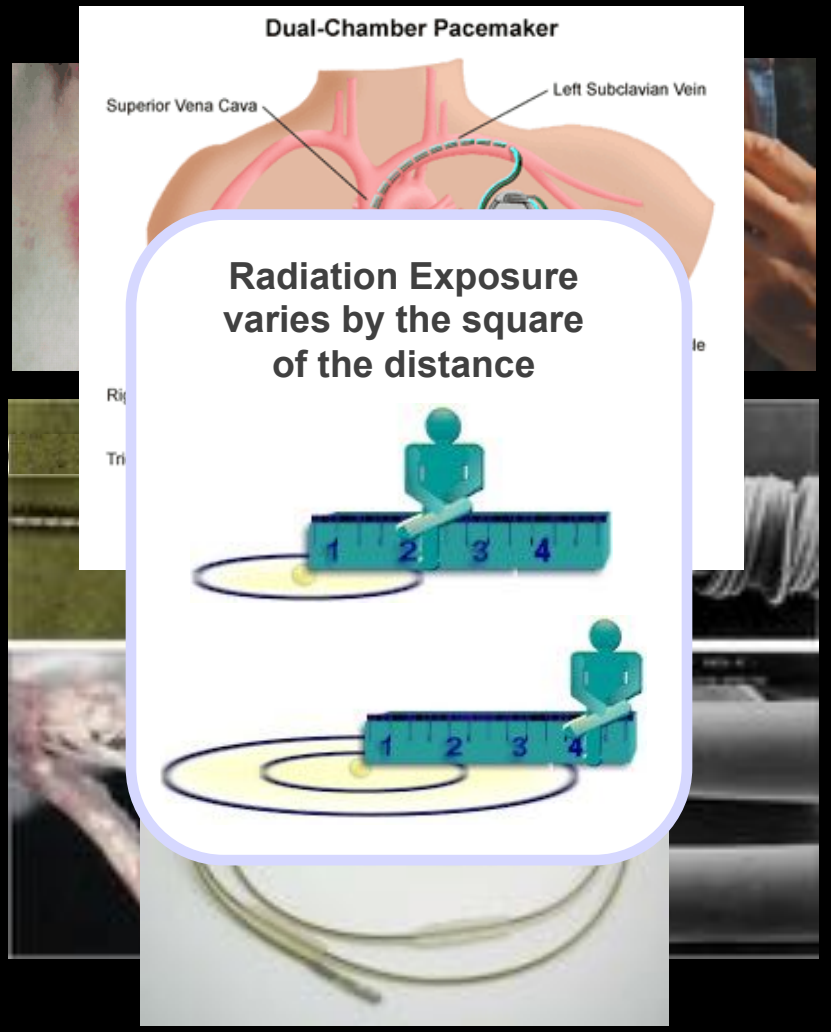
Post Op Days		0	60	120	180	240	300	360	420	480	540	600	660	720
Dual Zone	No at Risk	688	649	617	576	558	531	494	460	423	378	307	239	180
	K-M Est. (%)	0.0	1.9	3.5	46	6.1	6.9	7.7	8.0	9.1	9.3	9.3	10.0	10.0
Single Zone	No at Risk	170	158	147	141	137	133	126	123	121	117	111	103	96
	K-M Est. (%)	0.0	5.4	10.8	10.8	12.7	14.0	15.9	17.3	17.3	17.3	18.0	19.5	19.5

S-ICD Lead

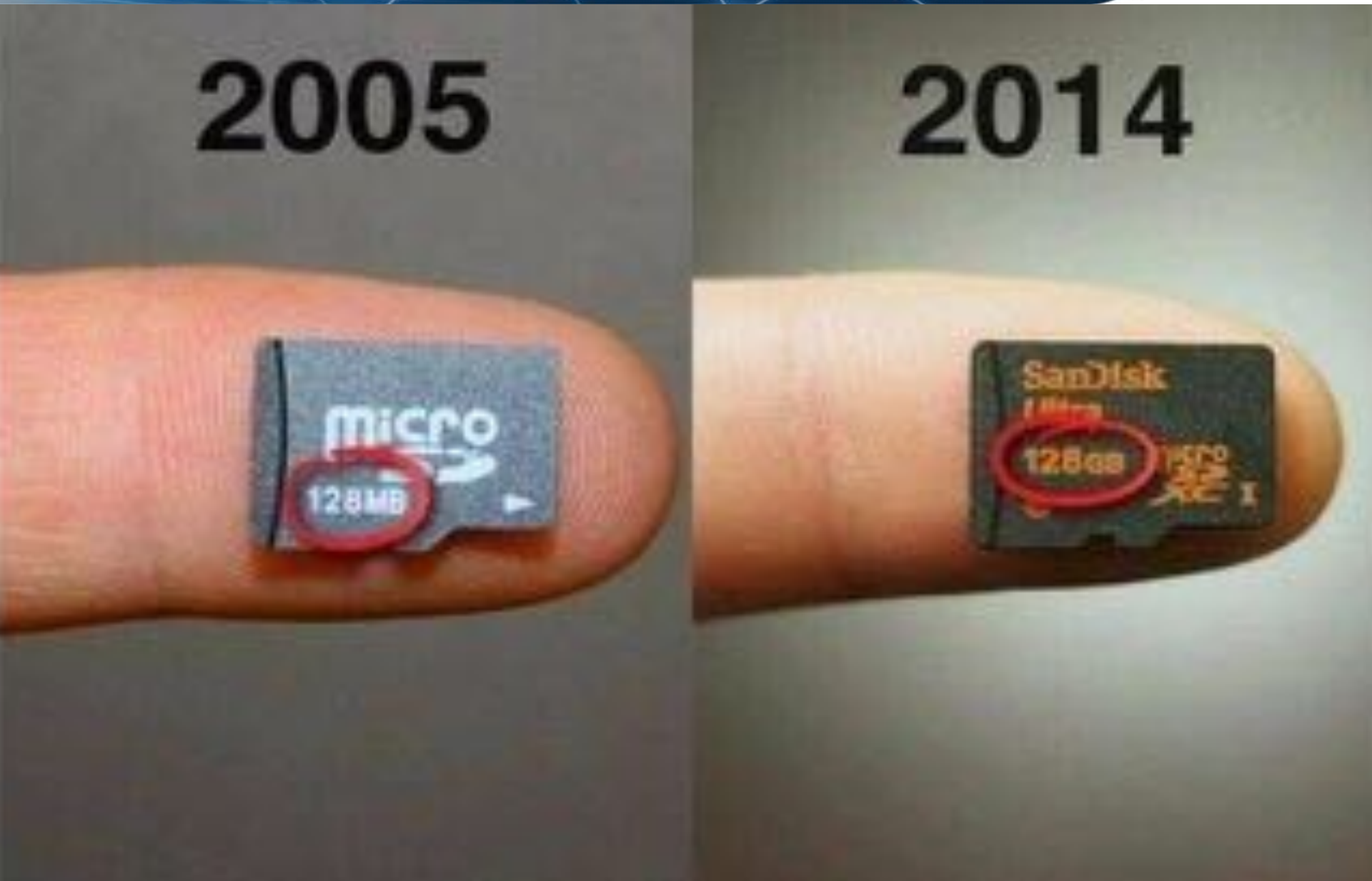
- 1 reported lead failure in US trials when lead inadvertently cut with scapel during implant
- Longest series from Netherlands showed no failures at mean follow-up of 4.5 years

Pacemaker State-of-the-Art

- **Procedure:**
  - Radiation exposure
  - Surgical pocket + Transvenous leads
- **Device issues – Pocket:**
  - Discomfort
  - Hematomas
  - Infections
  - Cosmetic concerns
- **Leads**
  - Mechanical failures
  - Infections; Extractions
  - Mobility restrictions
  - Challenge in compatibility with MRI



Pace of Innovation



Incidence of Lead & Pocket Complications

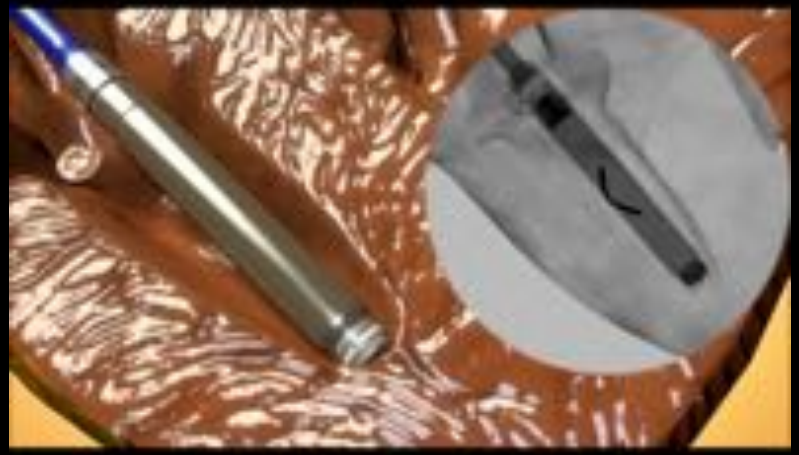
- Over 700,000 people are implanted annually worldwide
  - Nearly 50,000 experience post-implant related problems
- Over 4.4 million people WW currently have pacemaker
  - 65,000 chronic lead related problems annually

Pacing complication	Average of Incremental cost per intervention in 2009
Infection	$ 49,652
Lead revision	$ 16,285
Pneumothorax	$ 16,411
Pocket revision	$ 12,560

1: Didier Klug, *Circulation*, 2007
2; MDT, STJ, BSX Product Performance Reports
3: Danish Pacemaker Registry, www.pacemaker.dk

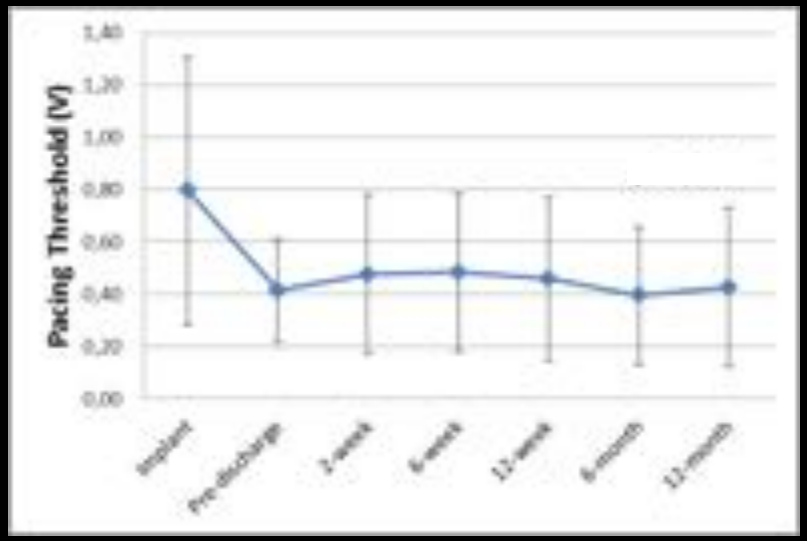
Pacemaker Minutarization

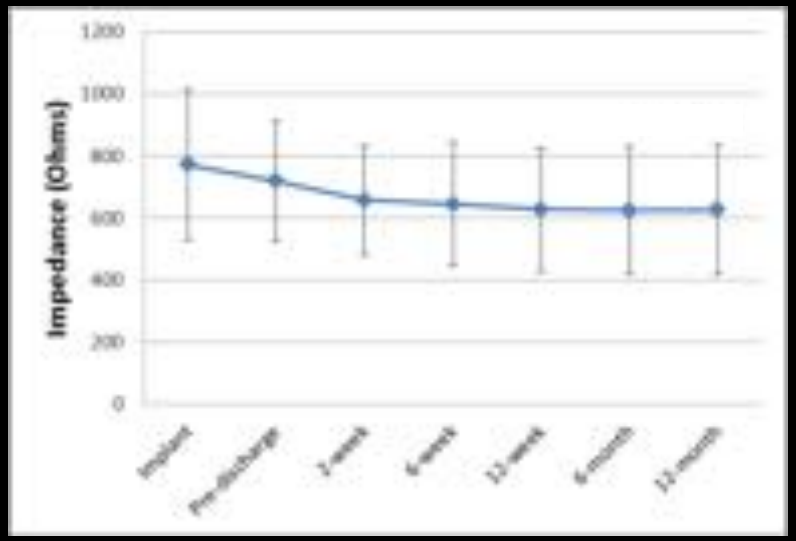
- **Percutaneous femoral vein delivery**
  - 18F introducer /steerable catheter
- **Self-contained device in right ventricle**
  - No lead or surgical pocket
  - VVIR w/ Hysteresis
  - Inherently MRI compatible
- **Replacement options**
  - Catheter-based retrieval
  - Deliver additional leadless pacemakers
  - Revert to conventional pacing lead

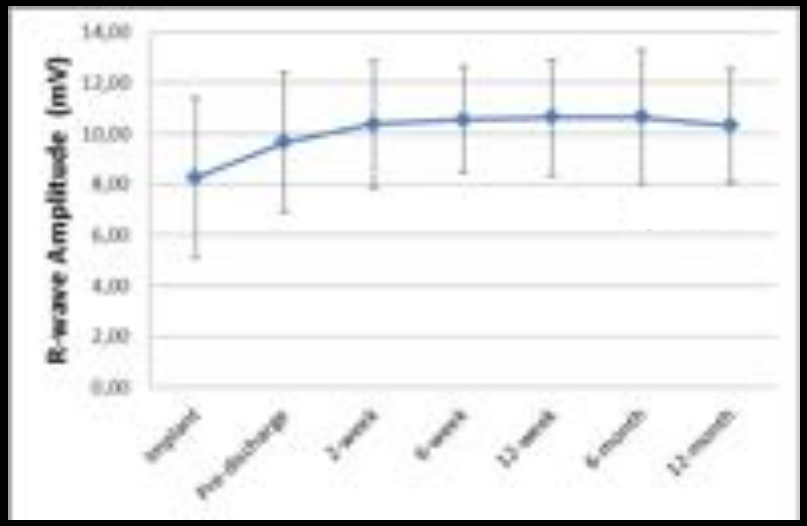


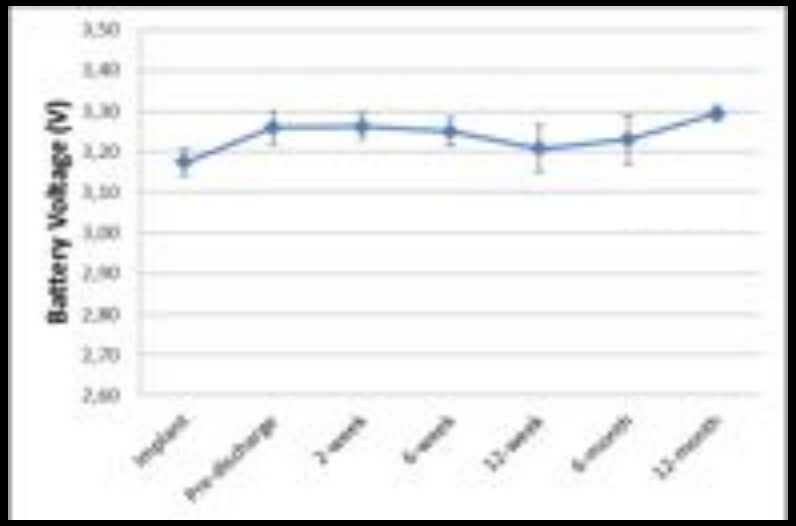
LCP Long-Term Outcome:

Summary of Pacing/Sensing Parameters









LEADLESS Study

Safety Events

- Early Safety Events:
  - 1 inadvertent placement in LV (across PFO) → promptly removed and device placed in RV
  - 1 Tamponade → Surgery → f/u: Fatal stroke
  - 1 Minor Groin Hematoma → no treatment
  - 1 w/ VT 2 days after implant → LCP removed and ICD placed → ICD shock 2 wks later (same CL)
- Safety Events in follow-up:
  - No device migration / dislodgements
  - No infection
  - No mechanical failures / early battery depletion
  - No pro-arrhythmia

Current Status of Leadless Pacemaker

- *Pacemaker System*:
  - Leadless right ventricular cardiac pacing is feasible
  - Can eliminate the weak link in pacemaker systems: the lead
- Proof of Principle for acute / sub-acute LCP retrieval
- Potential Limitations:
  - Single-chamber (RV) pacing only
  - Potential risk for device embolization (not seen in *LEADLESS*)
  - Large venous sheath (18- 24F):
    - Now increasingly common used for EP procedures
  - How to manage device after battery depletion?
    - Retrieval ***vs*** Abandonment

SUMMARY

- Intravascular leads remain the “weak link” of both pacing and ICD systems
- The S-ICD is approved therapy and effective in patients without pacing requirements. It has been used most commonly in young patients with low risk of monomorphic VT or bradycardia
- Leadless pacing is a new therapy for RV only pacing that will likely be used primarily in AF patients or those with limited access
- Ultimately, multi-chamber leadless pacemakers or pellets will be combined with subcutaneous ICDs to allow for leadless CRT or other systems