CIEDS ieri oggi e domain: l'evoluzione della specie

GIUSEPPE STABILE

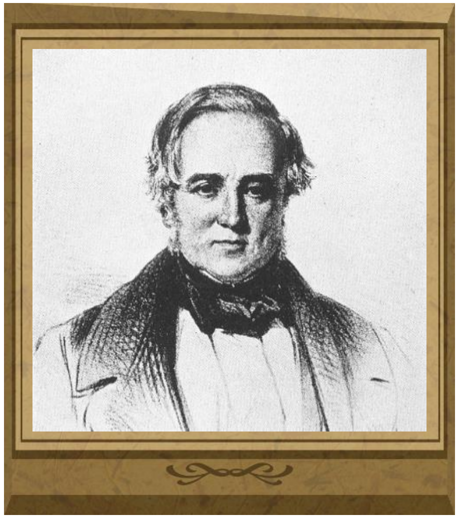
CLINICA MEDITERRANEA, NAPOLI; CLINICA MONTEVERGINE, MERCOGLIANO (AV); CLINICA SAN MICHELE, MADDALONI (CE); CLINICA DEL SOLE, SALERNO; CLINICA RUESCH, NAPOLI; ANTHEA HOSPITAL, BARI

Slow Pulse and Syncope

Hippocrates
467 - 377 BCE
Richards DW. *JAMA*. 1968; 206:377-378.

"Those who frequently feel very faint die suddenly from no discernable cause."

Aphorisms II:41 tr. P.B. Katz



Robert Adams
1791 – 1875
Willius FA, Keys TE, *Cardiac Classics*.

"[He had] remarkable slowness of the pulse, which generally ranged at the rate of 30 in a minute [and] not less than twenty apoplectic attacks… When they attacked him, his pulse would become even slower than usual …"

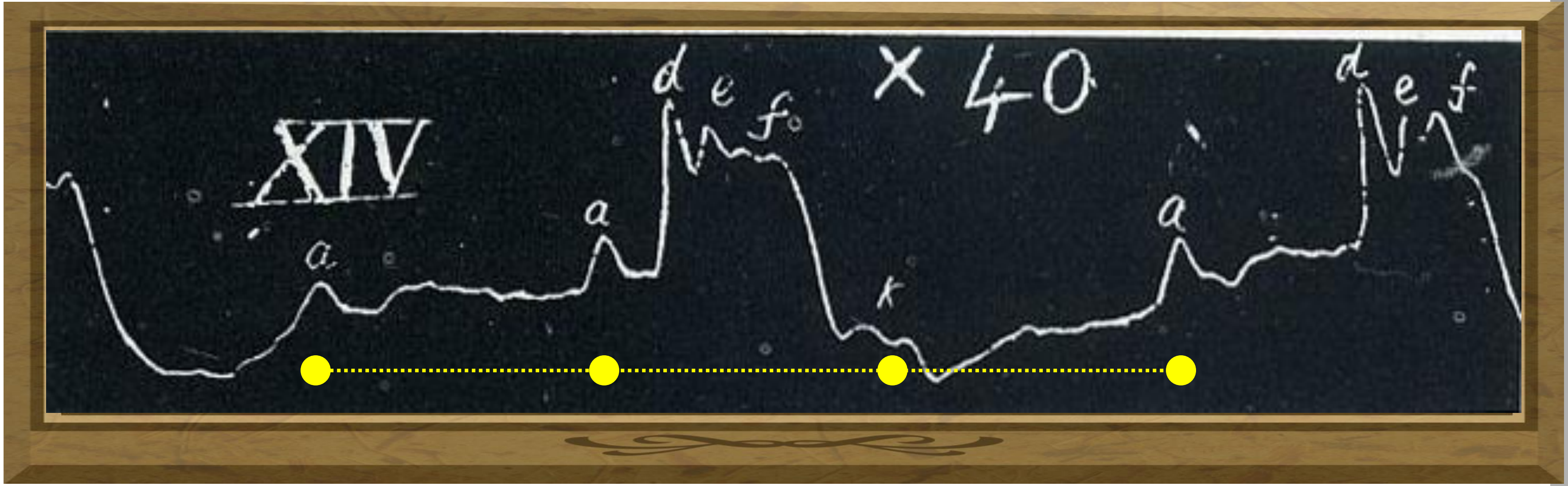
***Dublin Hosp Reports.* 1827;4:353-453.**

William Stokes
1804 - 1878
St. Louis, Mosby, 1941.

"[The combination] of permanently slow pulse [and] cerebral attacks of an apoplectic nature, though not followed by paralysis, [is] a very curious and… special combination of symptoms."

Dublin Quart *J Med Sci.* 1846;2:73-45.

Complete Atrioventricular Block Causing Slow Pulse Documented on Apex Cardiogram



"Richard B---, aet 34… 2 years before had been invalided on account of attacks of giddiness or faintness, and it was then noted that his heart beat very slowly.

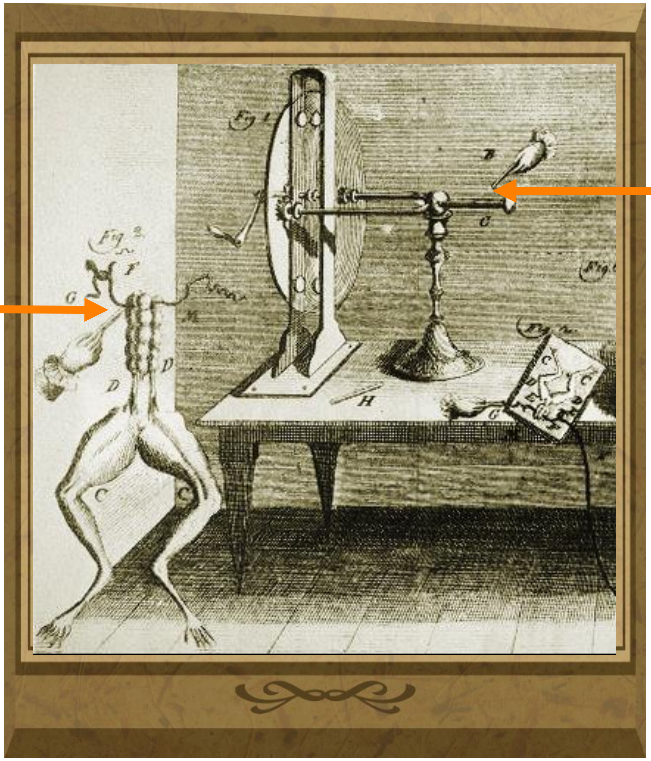
A tracing taken from this patient's heart in the fourth intercostal space is shown [above]. In listening… there could be heard between the strong pulsations either one or two faint beats which evidently corresponded to the elevations, a, [marked by yellow dots]… the feeble pulsations could not be heard at the apex, and were scarcely perceptible in the apex tracing… The conclusion seems clear that they were due to the contraction of the auricle only."Galiban AL. *Guy's Hosp Rep.* 1875;20:261; cited by Schechter et al. *Dis Chest.* 1969;55 (Suppl 1):535-579.

In this diagram, the first two and last yellow dots correspond to the "faint beats" described by Galiban and labeled "a"; the third yellow dot has been interpolated assuming constant timing.

Muscular Contraction in Frogs Can Be Induced By Electrical Impulses

Luigi Galvani 1737-1798

A



B

"I… applied the point of the scalpel [A] first to one and then the other [nerve], while at the same time one of the assistants produced a spark [B]… Violent contractions were induced in the individual muscles of the limbs…"

Galvani L. De viribus electricitatis in motu musculari commentarius.
De Bononiensi Scientarium et Atrium Instituto atque Academia Commentarii. **1791;7:363-418.**
(Tr. Acierno LJ. *The History of Cardiology*. London, Parthenon 1994)

Electrical Impulses Can Stimulate Human Hearts to Contract

Giovanni Aldini 1762-1834

(Nephew and assistant of Galvani who studied the effects of electrical stimulation on the bodies of executed criminals)

"Upon Galvanic stimulation, the heart [of an executed criminal]… which possessed a great deal of vitality, was immediately very visibly contracted."

Aldini J. *General Views on the Application of Galvanism to Medical Purposes.* London, J. Callow, 1819

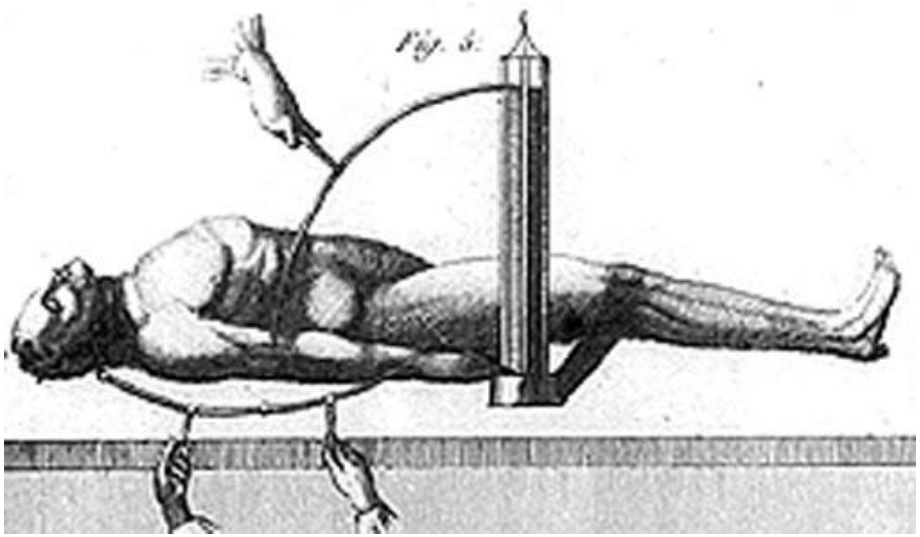
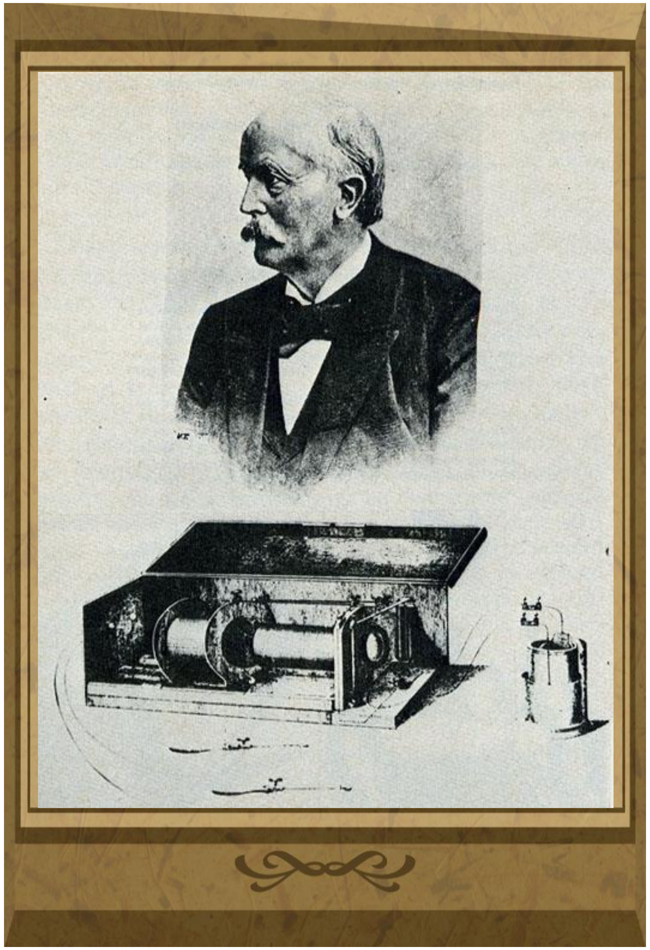


Figure from Aldini J. *Essai Théoretique et Experimental pour le Galvanisme.* Paris, Fournier Fils. 1804.

Electric Shock Can Pace the Human Heart

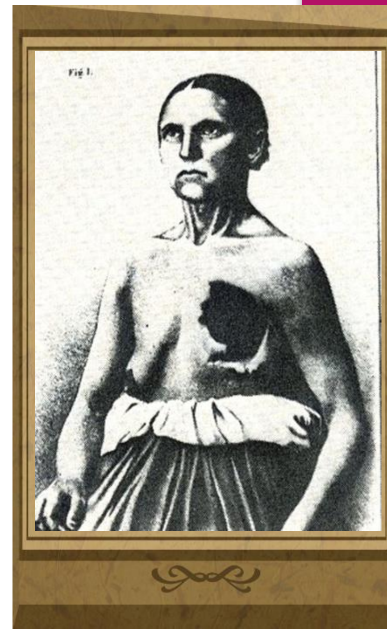


Hugo van Ziemessen and his electrical stimulator.

Schechter DC. *NY State J Med.* 1972;72:395.

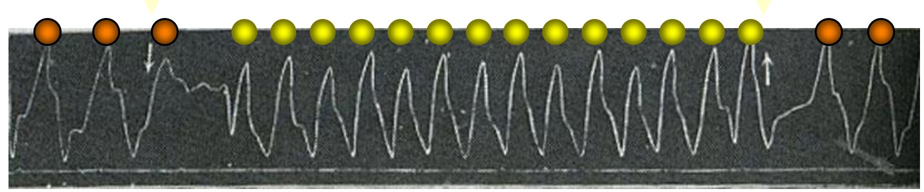
Catherina Serafin after removal of an enchondroma of her chest wall.

van Ziemessen H. *Arch Klin Med*. 1882;30:270.



Onset of Electrical Stimulation

Cessation of Electrical Stimulation



Sphygmic responses to pacing by repetitive electrical stimuli applied through the skin directly over a human heart.

Intrinsic beats: Paced beats:

Electric Shock Can Pace the Human Heart

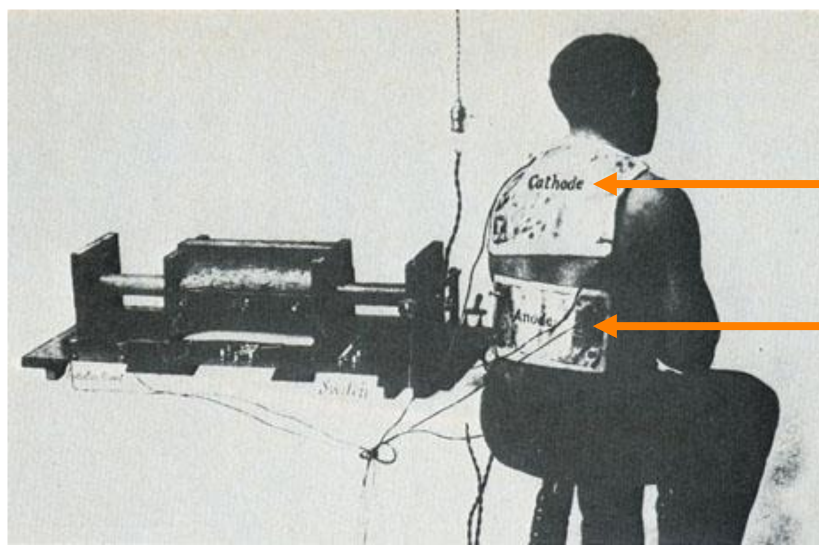
… a young woman, a chronic morphine eater, was admitted to the Ste.-Anne asylum, Paris. [when] deprived of her daily dose of morphine she had a sudden attack of syncope, the pulse was almost imperceptible, and her face was blue - almost black-blue…

We practiced rhythmic [electrical] excitations [and] as the excitations were being repeated, it was astonishing to see the accompanying change in color of the patient's face; the dark blue color changed to pale, then to almost natural color; at the end of the thirty seconds of rhythmic excitations, the patient took a spontaneous breath, opened her eyes, and said: "Oh, I feel so cold in my back." The cold she felt was the wet cotton of the electrodes… with our method we cause artificial heart beats, as well as artificial respirations, to take place…"

Robinovitch LG. *J Ment Path.* 1907-1909;8:180.

Disposition of electrodes favored by Robinovitch who laid stress on exclusion of the brain from electric field.

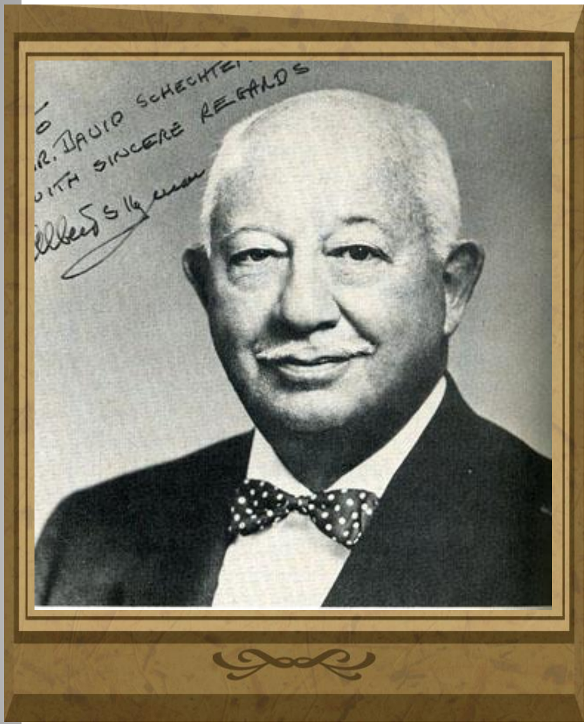
Schechter DC. *NY State J Med.* 1972;72:395.



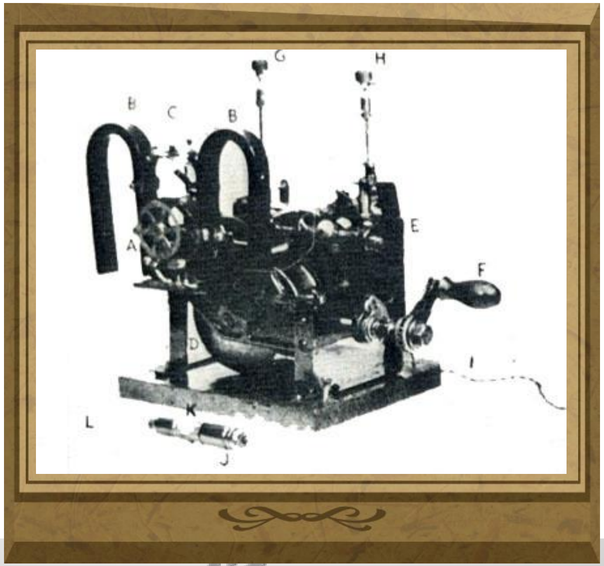
Electric Shock Can Pace the Human Heart

“… a retired engine room officer aged 76 with ECG evidence of complete atrial and ventricular dissociation… In one spot the ventricular rate got down to 12 bpm.
He was totally unconscious. Dr. Hyman and I applied the needle electrodes… the artificial pacemaker started to work and the ventricular complexes [sped up] to about 76 bpm. However, when we stopped the pacemaker, the ventricular idiopathic rate went back down to the 20’s.”Unpublished proceedings of a conference held on February 16, 1942 by the Brooklyn Naval Hospital Clinical Society.

Cited by Schechter DC. *NY State J Med*. 1972;72:953.

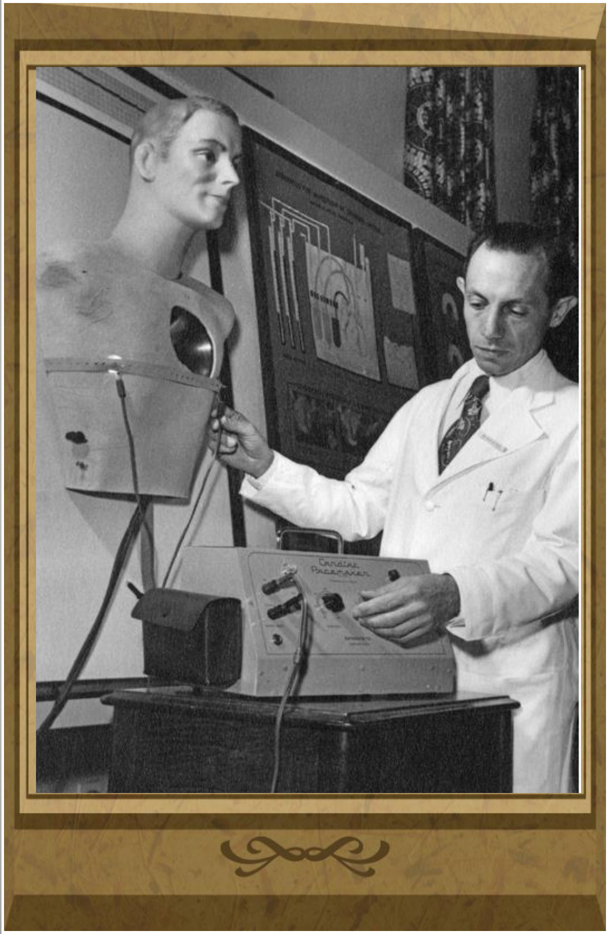


Albert Hyman

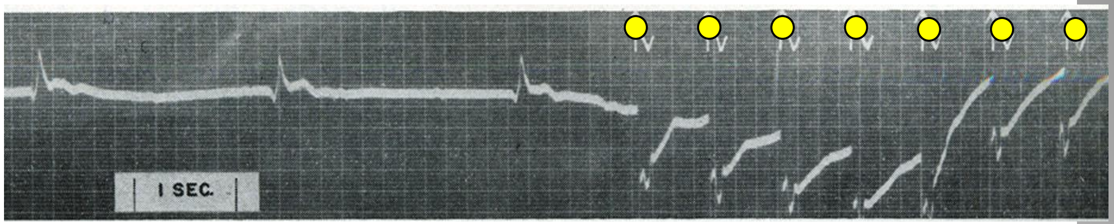


Artificial pacemaker designed by Hyman in the 1930s.

Paul Zoll and an Early Pacemaker



Paul Zoll



Electrocardiogram from a man with complete heart block and an idioventricular rate of 38/min. : External pacemaker impulses.

"During the first few hospital days the ventricular rate was between 30 and 40 beats per minute. At noon on the 6th hospital day, episodes of prolonged asystole with syncope and convulsions began… and electric shocks [from the external pacemaker] were employed… Constant ventricular responses to the electrical stimuli were observed in the electrocardiograms.

For 3 days the electrical stimulator was turned on for repeated episodes of ventricular standstill… [After] a persistent spontaneous idioventricular rate of 44 per minute appeared that was adequate to maintain satisfactory cerebral and peripheral blood flow… the electrical stimulator was turned off… No further episodes of syncope or asystole occurred…

[Two days later] his blood pressure remained stable at 110/70… no neurologic or other ill effects of the 5 days of ventricular standstill and external electrical stimulation were evident."

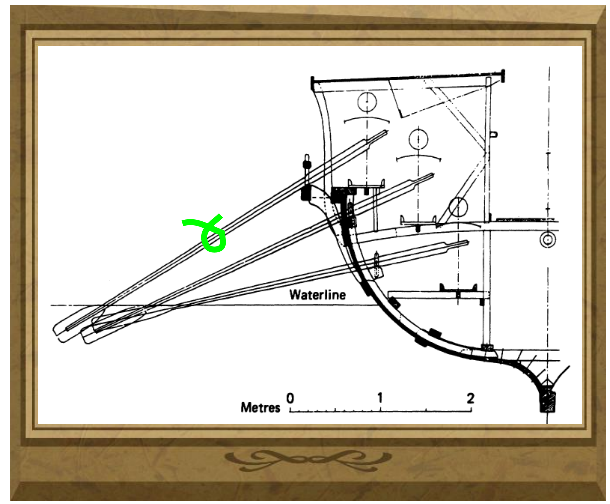
New Engl J Med. 1952;247:768.

Nei primi mesi del 1958, un giovane cardiologo statunitense, Seymour Furman, applicò il primo impianto di pacemaker provvisorio a un paziente anziano affetto da blocco atrioventricolare. Il sistema, costituito da un singolo elettrocatetere fatto passare dalla vena femorale fino al cuore, funzionò correttamente, ma aveva il non trascurabile svantaggio di richiedere un generatore di impulsi esterno delle dimensioni di una lavatrice.

La strada era aperta e solo pochi mesi dopo i danesi Rune Elmqvist e Ake Senning (rispettivamente ingegnere e cardiologo) svilupparono il primo pacemaker interamente impiantabile. Il primo paziente a essere sottoposto all’intervento fu un altro ingegnere quarantenne, di nome Arne Larsson, e la sua storia sarà indissolubilmente legata a quella della moderna elettrofisiologia.

Restoring Homogeneous Contraction Does Improve Performance in Failing Hearts

Serge J. Cazeau



"[In] eight subjects with widened QRS and end-stage heart failure despite maximal medical therapy, biventricular pacing increased the mean cardiac index by 25%… and decreased pulmonary capillary wedge pressure by 17%."

Cazeau S et al. *PACE*. 1994;17(PT II):1974.

Electric Shock Can Restart Stopped Human Hearts

1774: “*Electricity Restored Vitality*”

“Sophia Greenhill, on Thursday last, fell out of a… window [and was] to all appearance dead. The surgeons at Middlesex Hospital, and the Apothecary, declared that nothing could be done for the child.

Mr. Squires tried the effects of electricity.

… upon transmitting a few shocks through the thorax, he perceived a small pulsation; after a few minutes the child began to breathe with great difficulty, and after some time she vomited. A kind of stupor… remained for several days, but, by the proper means being used, her health was restored.”

Registers of the Royal Humane Society of London. **London, Nichols & Sons, 1774-1784.**
(Cited by **Acierno LJ.** ***The History of Cardiology*****. London, Parthenon 1994).**

Electric Shock Can Restart Stopped Human Hearts

1872: Electric Shock Can Reverse Chloroform-Induced Cardiac Arrest

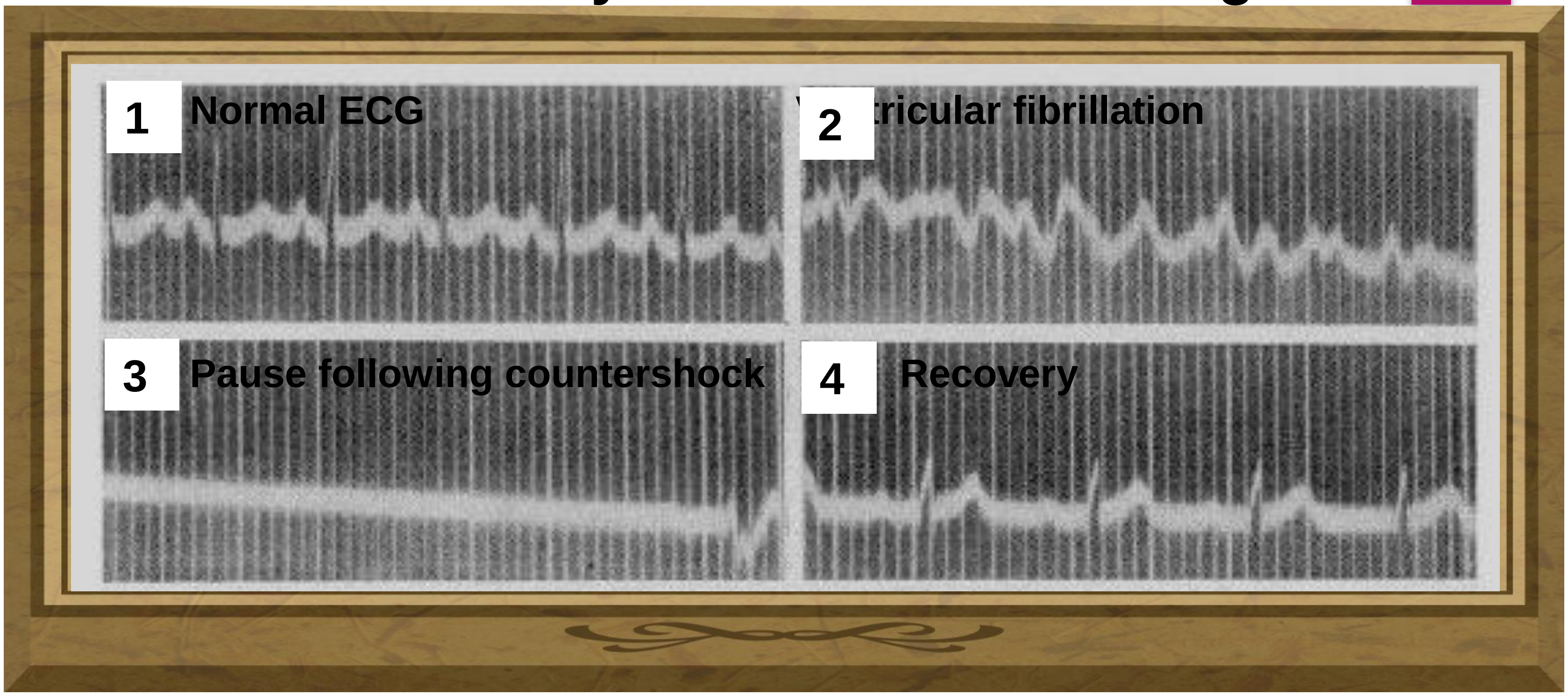
"I had operated on a small boy for stone, under chloroform. The operation was over… when Mr. Webster called after me to say the pulse had stopped. On turning around I found the boy deadly pale and pulseless, and his breathing stopped. The galvanic battery was in the theatre ready for use and it was instantly applied. After a few seconds, both pulse and breathing returned, and the patient entirely recovered.

… The last five cases here related can leave no doubt as to the fact that galvanism saved life in each of them; that the pulsations of the heart stopped in an instant, and were instantly restored by this agent.

… [galvanic stimulation is] the most powerful agent known to restore animation when [the heart beat] is suspended by chloroform… to be successful it must be ready for instantaneous use – on that depends its success… when galvanism is employed… one pole should be applied to the neck, and the other over the ribs at the left side"

Green T. On death from chloroform; its prevention by galvanism. *Br Med J*. 1872;1:551-553.

ECG Documented Reversal of Ventricular Fibrillation by Electric Shock in Dogs



“With the electrodes applied directly to the heart, currents of 0.4 ampere for five seconds will cause fibrillation and currents of 0.8 ampere or more will stop fibrillation…

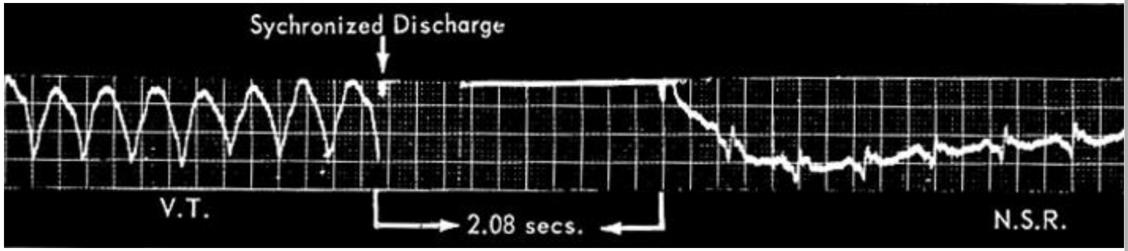
Following the countershock the ventricles are quiescent for a brief period. When contractions begin they are very feeble but quickly increase in vigor and the circulation is reestablished if fibrillation has not continued for long. If fibrillation has lasted for two minutes or more, spontaneous recovery of effective beats will not follow. Under these circumstances cardiac massage may be of signal benefit.”

Hooker DR, Kouwenhoven WB, Langworthy OR. *Am J Physiol.* 1933;103:444-454.

Bernard Lown and an Early Cardioverter

Bernard Lown

Shock applied by an external defibrillator



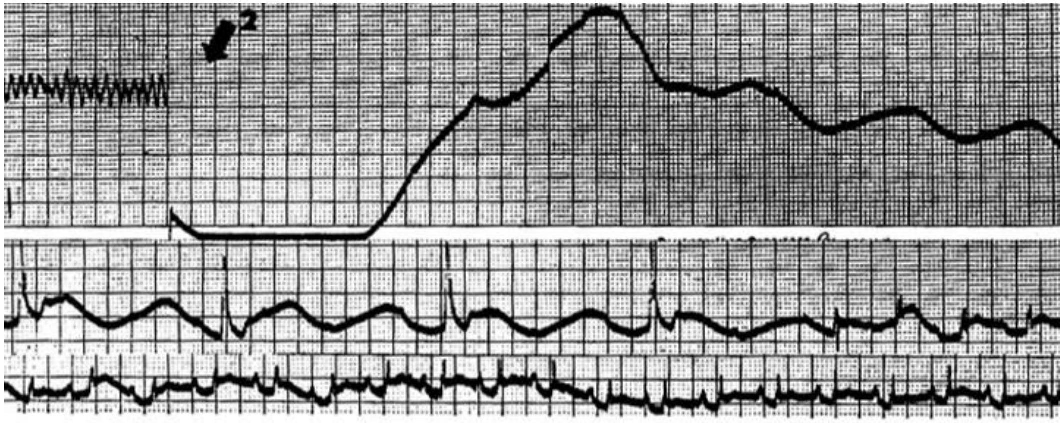
"All 9 episodes of ventricular tachycardia were successfully reverted with a single synchronized DC discharge… a normal sinus mechanism was observed in each patient within 2 to 3 seconds."

Lown B et al. *JAMA*. 1962;182:548.

Michel Mirowski and the Implantable Defibrillator

Michel Mirowski

Shock applied automatically
by an implanted defibrillator



“A laboratory model of an automatic defibrillator has been designed, developed, and tested successfully on dogs… For use outside the hospital, this device might be implanted on a permanent basis in selected patients with coronary heart disease identified as belonging to high-risk population.”

Mirowski M et al. *Arch Int Med*. 1970;126:158.

REGISTRI

Registro Italiano Pacemaker e Defibrillatori

Bollettino Periodico 2019

Associazione Italiana di Aritmologia e Cardiostimolazione

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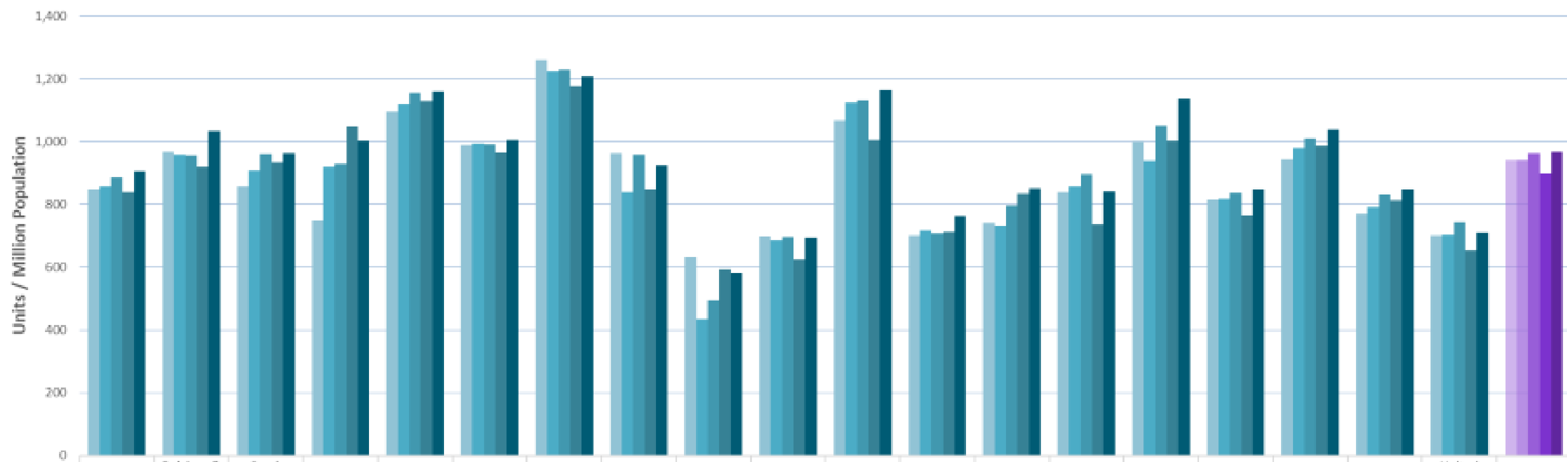
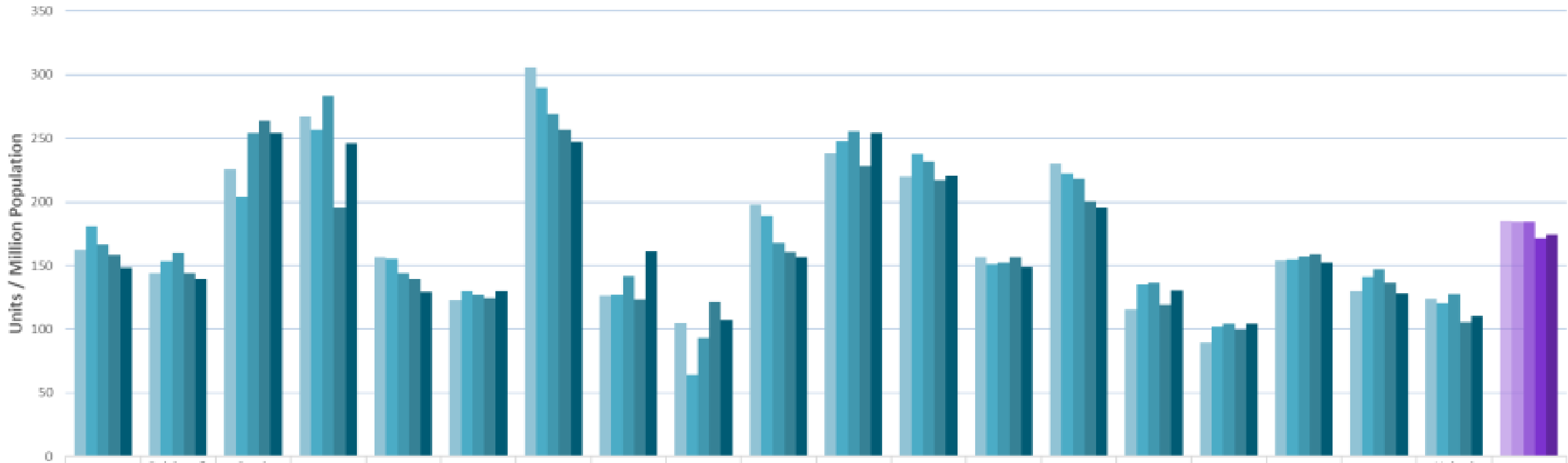
Pacemakers - Units per million inhabitants



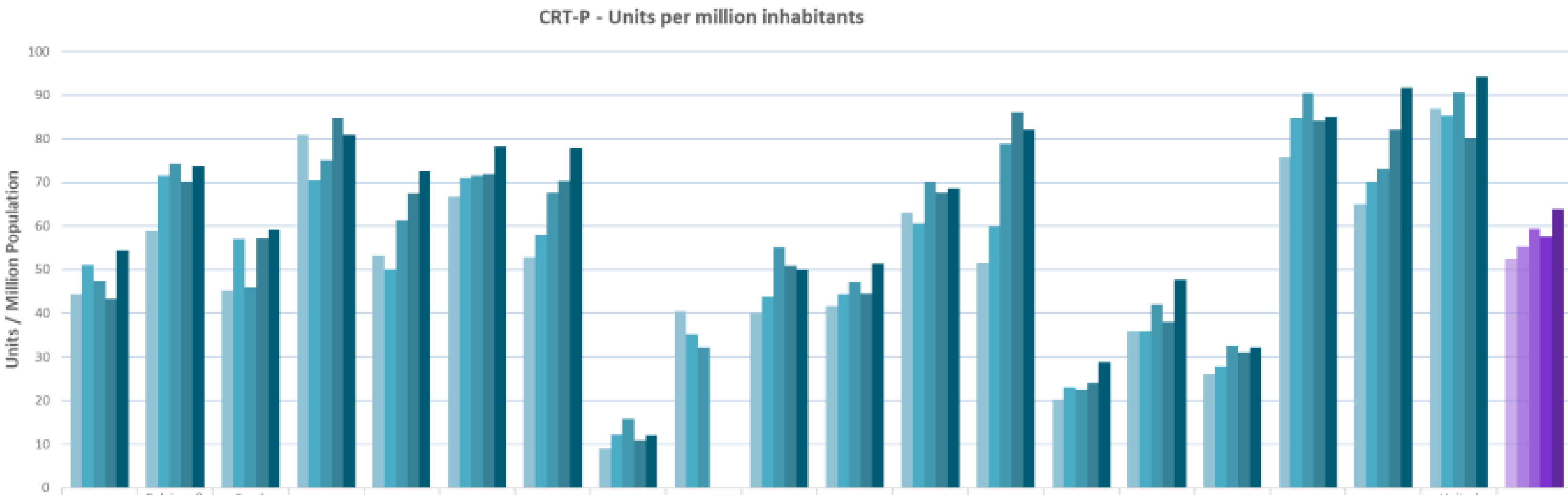
	Austria	Belgium & Lux	Czech Republic	Denmark	Finland	France	Germany	Greece	Hungary	Ireland
2017	849	968	858	748	1,096	989	1,260	963	632	699
2018	858	958	907	919	1,119	994	1,224	840	436	686
2019	887	956	961	928	1,155	990	1,230	958	495	696
2020	839	920	935	1,048	1,130	965	1,176	847	593	624
2021	905	1,035	963	1,003	1,160	1,005	1,207	925	583	694

	Italy	Netherlands	Norway	Poland	Portugal	Spain	Sweden	Switzerland	United Kingdom	Europe*
2017	1,068	702	741	839	1,000	816	942	769	701	941
2018	1,124	718	732	859	940	818	979	792	703	942
2019	1,132	708	795	895	1,051	837	1,011	832	744	963
2020	1,006	713	833	736	1,003	766	987	812	654	899
2021	1,164	764	851	841	1,136	849	1,040	847	710	966

Defibrillators - Units per million inhabitants

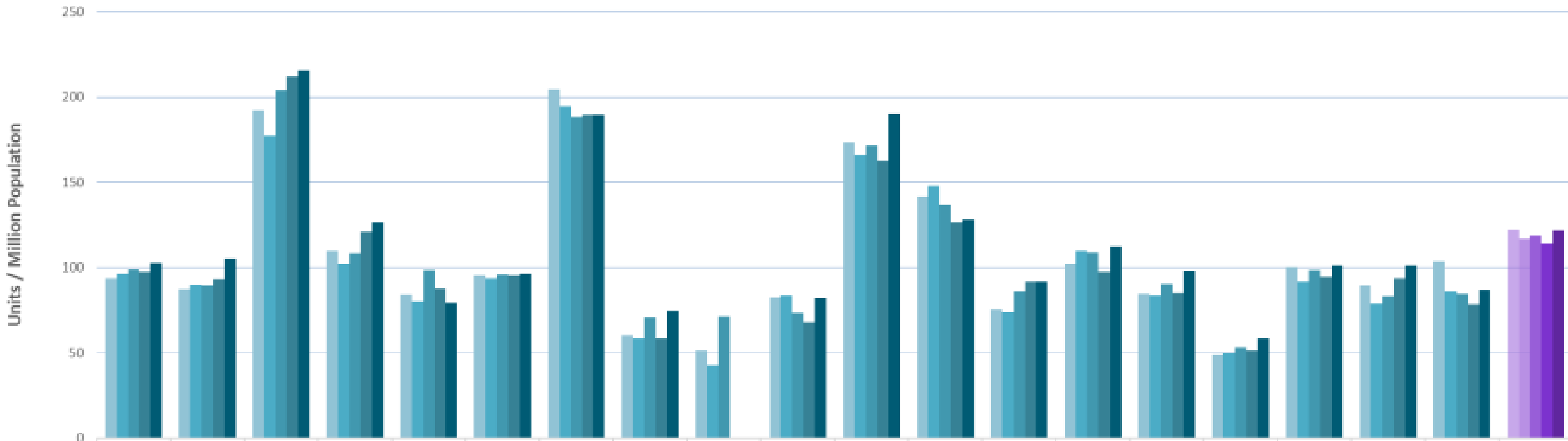


	Austria	Belgium & Lux	Czech Republic	Denmark	Finland	France	Germany	Greece	Hungary	Ireland	Italy	Netherlands	Norway	Poland	Portugal	Spain	Sweden	Switzerland	United Kingdom	Europe*
2017	163	144	226	268	157	123	306	126	105	198	238	220	156	230	116	89	154	130	124	185
2018	181	154	204	257	155	130	290	127	64	189	248	237	151	222	135	102	155	141	121	185
2019	167	160	254	283	144	127	269	142	93	168	255	232	153	218	136	104	157	147	127	184
2020	158	144	264	196	140	125	257	123	122	160	229	217	157	201	119	100	159	136	106	171
2021	148	139	254	246	129	130	247	161	107	157	254	220	149	196	131	105	152	128	110	174



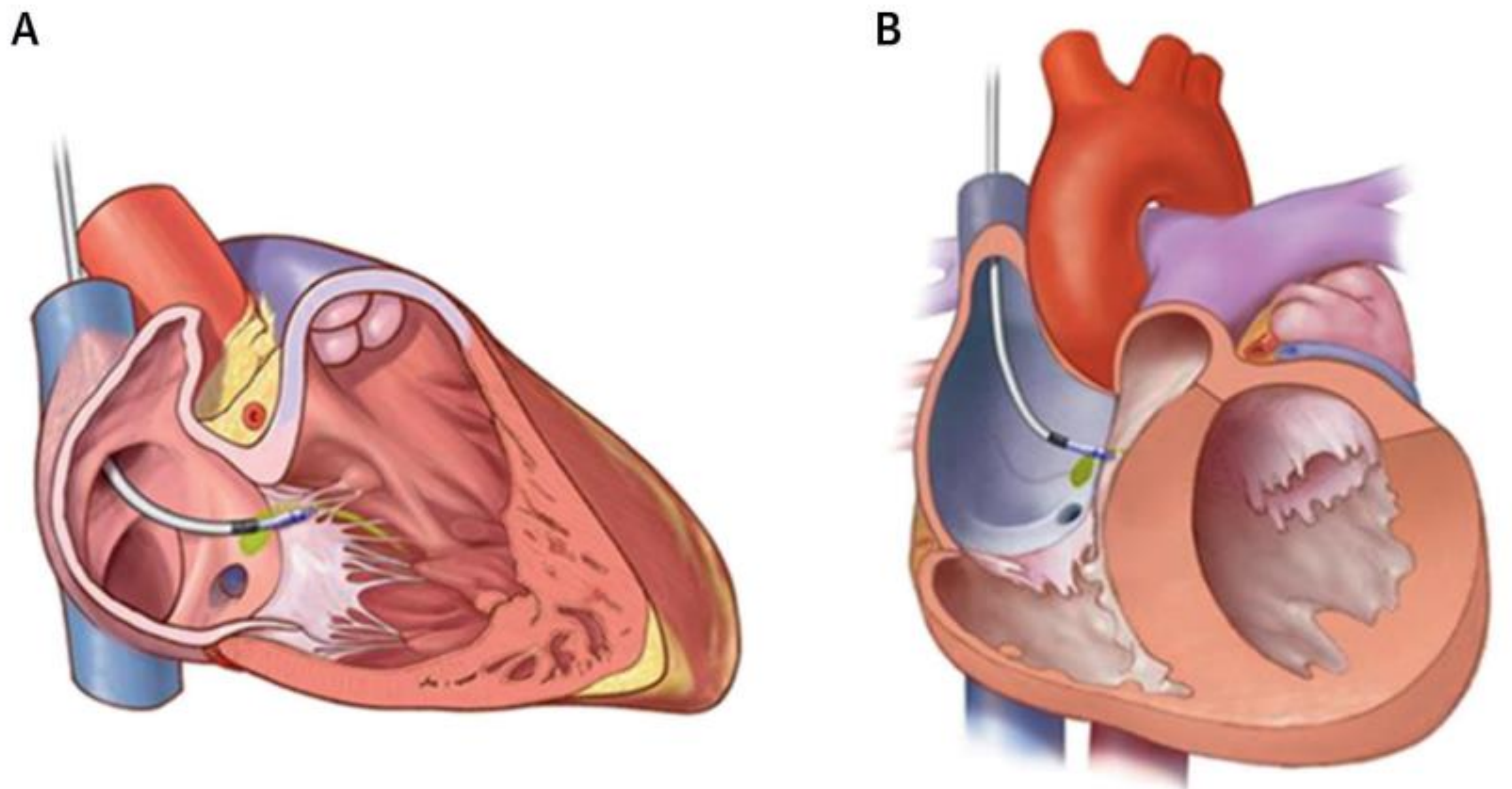
	Austria	Belgium & Lux	Czech Republic	Denmark	Finland	France	Germany	Greece	Hungary	Ireland	Italy	Netherlands	Norway	Poland	Portugal	Spain	Sweden	Switzerland	United Kingdom	Europe*
2017	44	59	45	81	53	67	53	9	40	40	42	63	52	20	36	26	76	65	87	52
2018	51	71	57	70	50	71	58	12	35	44	44	61	60	23	36	28	85	70	85	55
2019	47	74	46	75	61	71	68	16	32	55	47	70	79	23	42	32	91	73	91	59
2020	43	70	57	85	67	72	70	11	N/A	51	44	68	86	24	38	31	84	82	80	57
2021	54	74	59	81	72	78	78	12	N/A	50	51	69	82	29	48	32	85	92	94	64

CRT-D - Units per million inhabitants



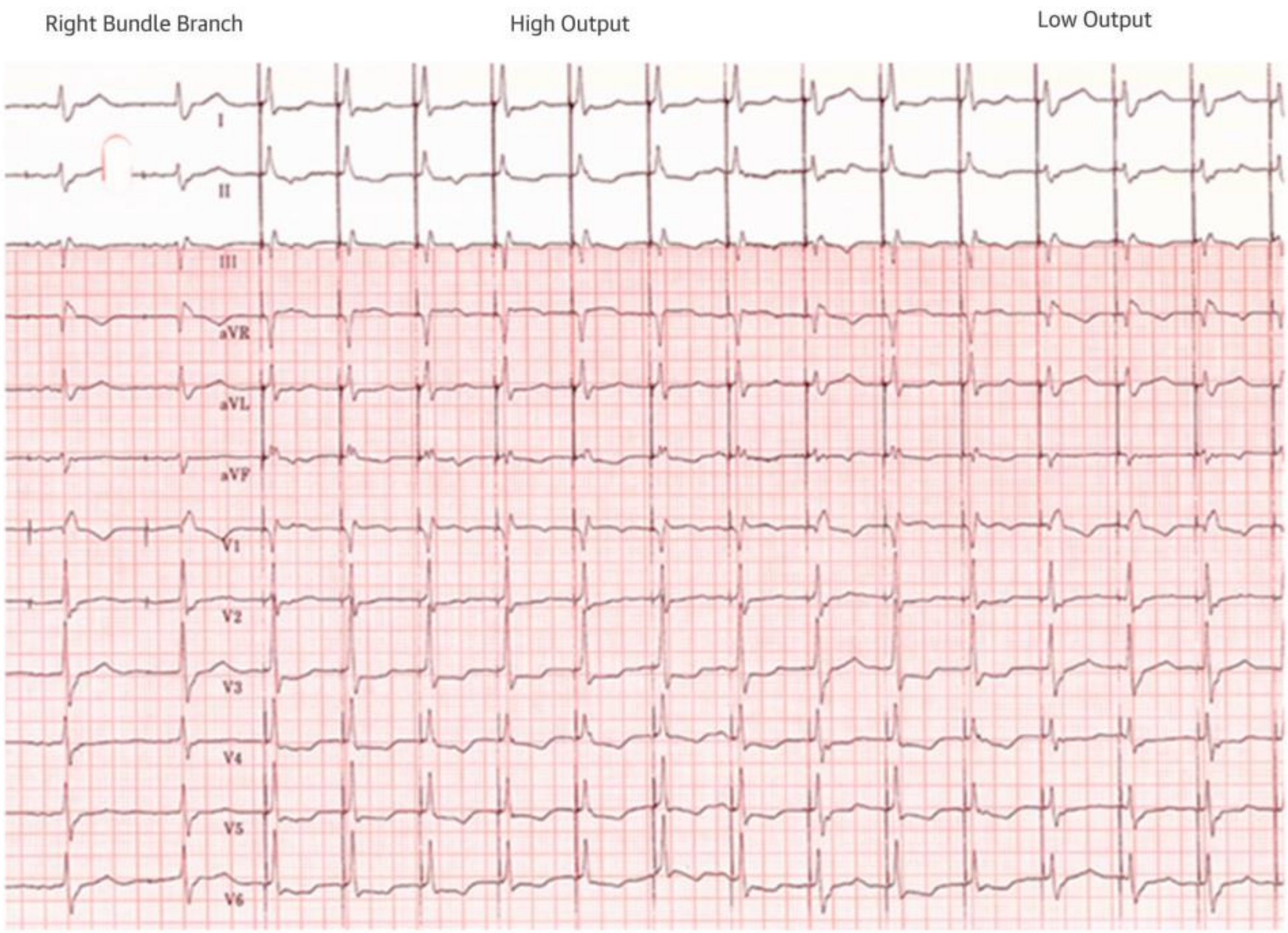
	Austria	Belgium & Lux	Czech Republic	Denmark	Finland	France	Germany	Greece	Hungary	Ireland	Italy	Netherlands	Norway	Poland	Portugal	Spain	Sweden	Switzerland	United Kingdom	Europe*
2017	93	87	192	110	84	95	204	60	51	82	174	142	75	102	85	49	100	89	103	122
2018	96	90	177	102	80	94	195	59	43	84	166	148	74	110	84	50	92	79	86	117
2019	99	90	204	108	98	96	188	71	71	74	171	137	86	109	90	53	99	83	85	119
2020	98	93	212	121	88	96	189	58	N/A	68	163	126	92	98	85	52	95	94	78	114
2021	103	105	216	126	79	96	189	75	N/A	82	190	128	92	112	98	59	101	101	87	122

FIGURE 8 **His Bundle Pacing**



(A) Right anterior oblique and **(B)** left anterior oblique views of the heart showing placement of the lead on the proximal conduction system.

FIGURE 9 ECG Demonstrating Effects of His Bundle Pacing



Graphical Abstract

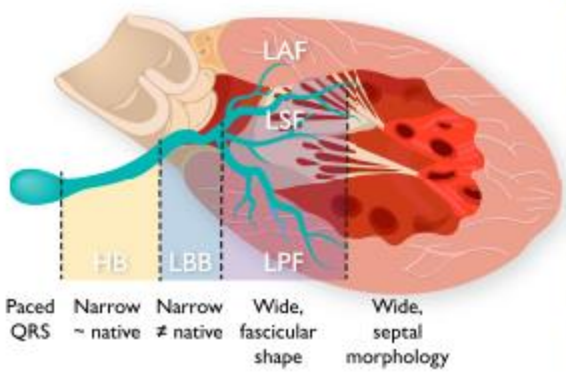
Milestones during 6 decades of pacing development

	1960–1970	1970–1980	1980–1990	1990–2000	2000–2010	2010–2020
Mode	VOO	VVI	VVIR/VDD	DDDR	BiV pacing Avoid apical RVP	CSP (HBP/LBBAP)
Evidence	No trials	No trials	VVIR>VVI	DDDR>VVIR	BiV>apical RV Avoid RVP>DDD	CSP>apical RV
Complications	Very high	High	VVI low VDD high	Low	BiV high	High

Selecting the best pacing mode:
Practical instructions (while awaiting for RCTs)

Setting	CSP (HBP/LBBAP)	Goal of pacing mode
SSS	Not needed	DDDR with minimization of unnecessary VP
AVB, pacing <20%	Not needed	DDD with minimization of unnecessary VP
AVB narrow QRS pacing >20%	CSP	DDD narrow QRS (~ native)
AVB, wide QRS	CSP	DDD QRS width < RVP
HF (CRT indications)	•HOT-CRT or LOT-CRT •CSP alone if narrow QRS is achieved	QRS width < BiV CRT

Left bundle area pacing in perspective



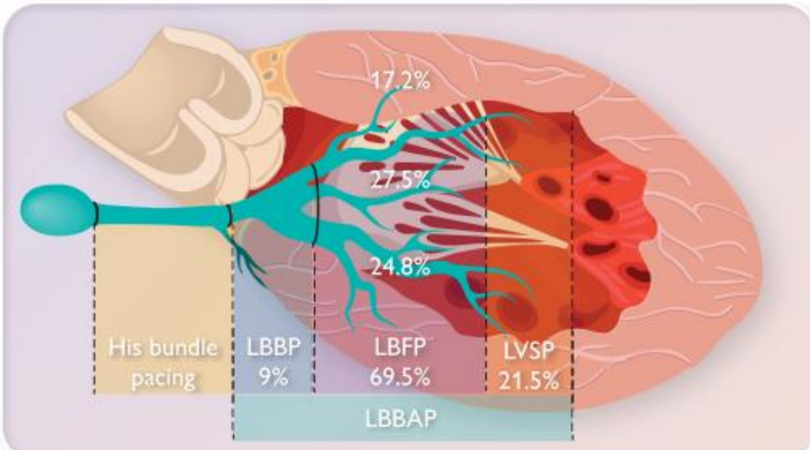
Conduction system pacing in perspective. Abbreviations: RVP = right ventricular pacing; BiV = biventricular pacing; CSP = conduction system pacing; HBP = His bundle pacing; LBBAP = left bundle branch area pacing; CRT = cardiac resynchronization therapy; HOT-CRT = His-optimized CRT; LOT-CRT = left bundle branch optimized CRT; SSS = sick sinus syndrome; AVB = atrioventricular block.

MELOS — MULTICENTER EUROPEAN LEFT BUNDLE BRANCH AREA PACING OUTCOMES STUDY

Prospective, multicenter, registry-based observational study

2533 Participants

14 European centres



Independent predictors of LBBAP lead implantation failure

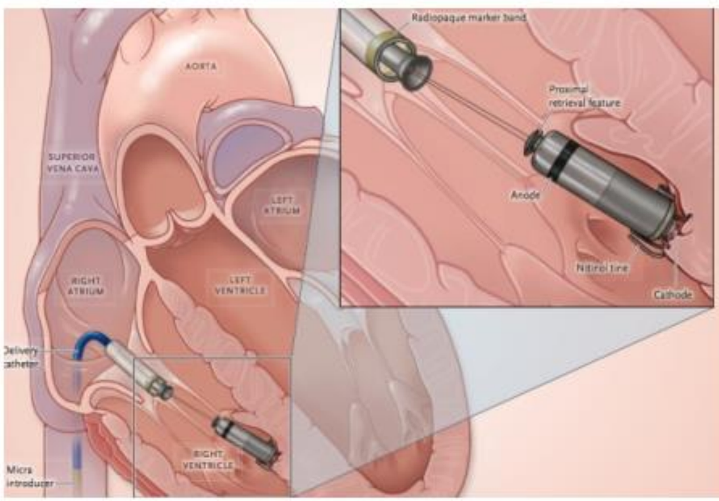
Heart failure indication	**OR 1.49**, 95% CI 1.01–2.21
Baseline QRS duration, per 10 ms	**OR 1.08**, 95% CI 1.03–1.14
LVEDD, per 10 mm increase	**OR 1.53**, 95% CI 1.26–1.86

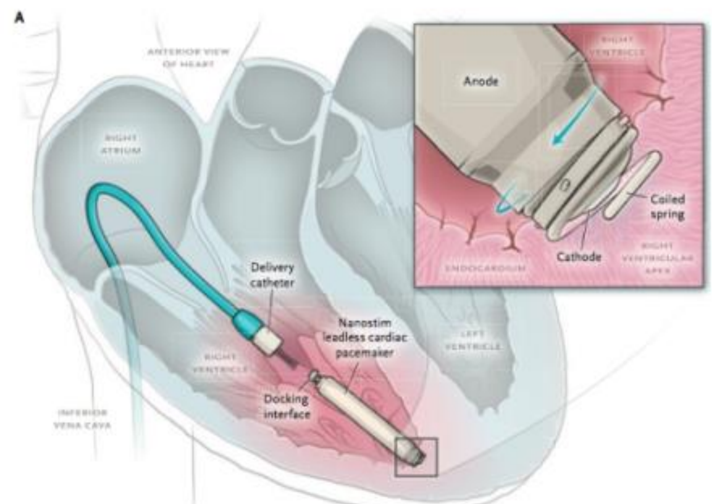
LBBAP implantation success

Bradycardia indication success	**92.4%**
Heart failure indication success	**82.2%**

LBBAP lead complications	**8.3%**
• Acute perforation to LV	3.7%
• Lead dislodgement	1.5%
• Acute chest pain	1.0%
• Capture threshold rise	0.7%
• Acute coronary syndrome	0.4%
• Trapped/damaged helix	0.4%
• Delayed perforation to LV	0.1%
• Other	0.7%


EVOLUTION OF PACEMAKER TECHNOLOGY
1958
Weight: 73.4g
Size: 35cc
1981
Weight: 55g
Size: 25cc
1995
Weight: 14g
Size: 6cc
2009
Weight: 23g
Size: 12.8cc
2013
Weight: 2g
Size: 1cc

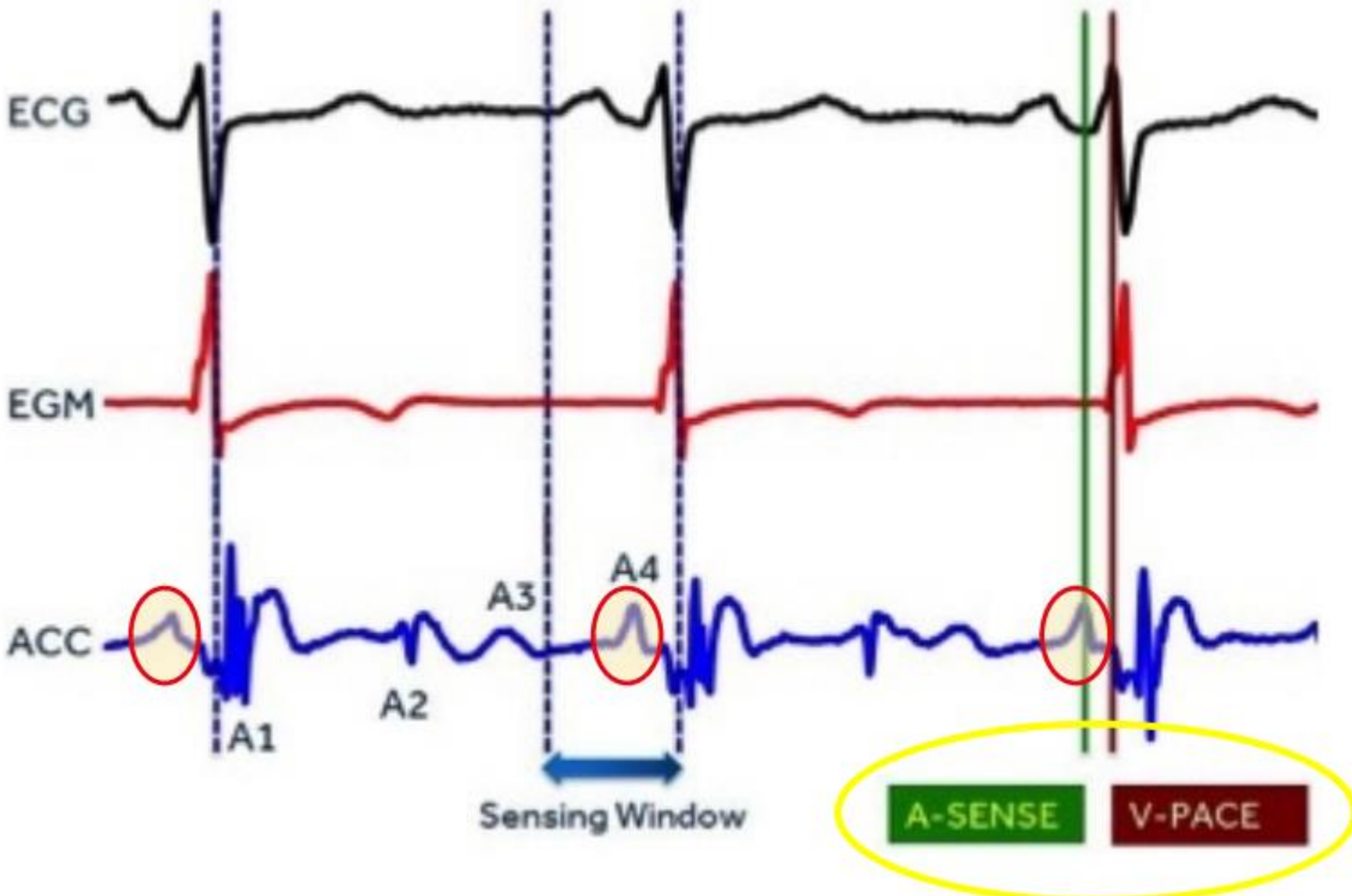




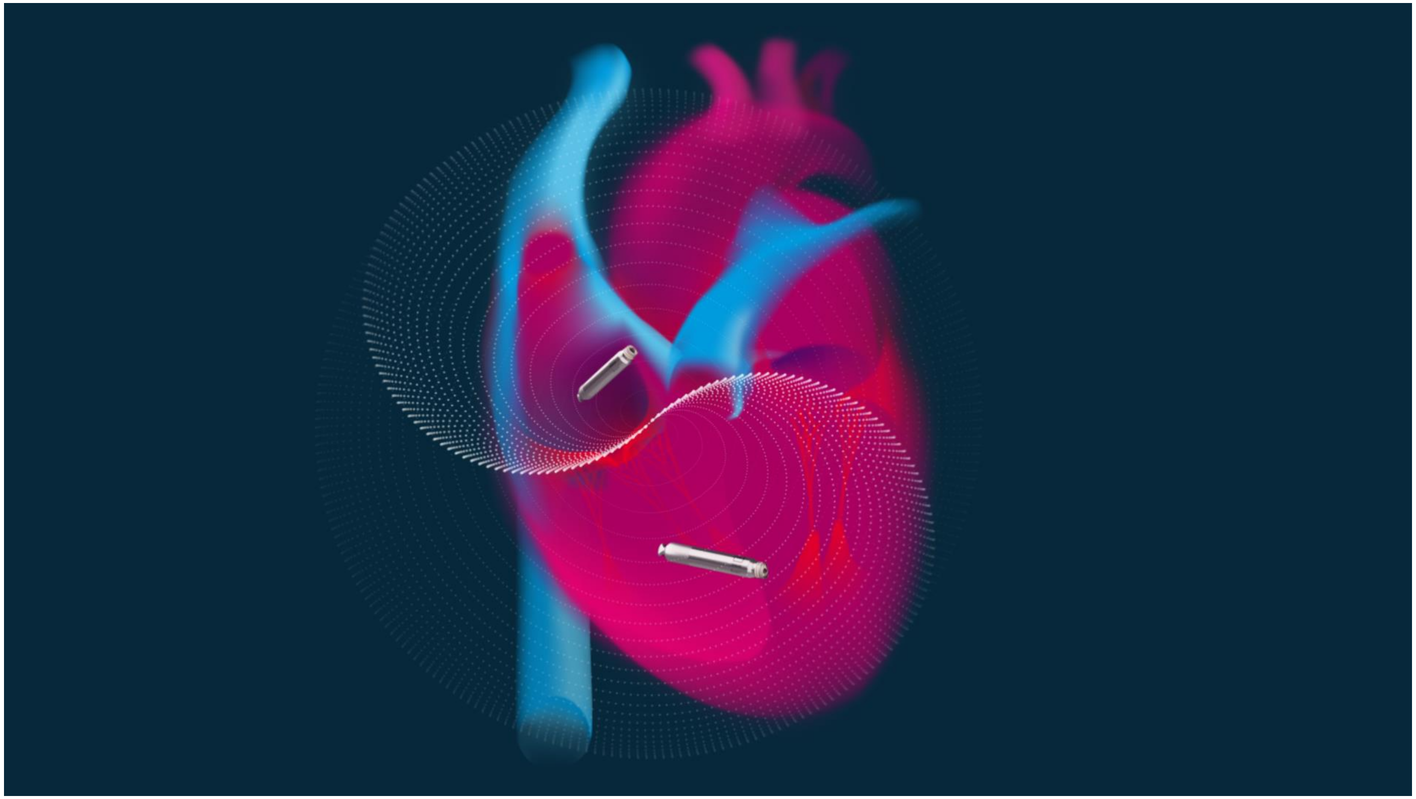
Reynolds D et al., N Engl J Med. 2016;374(6):533-41.

Reddy VY et al., N Engl J Med. 2015;373:1125-35

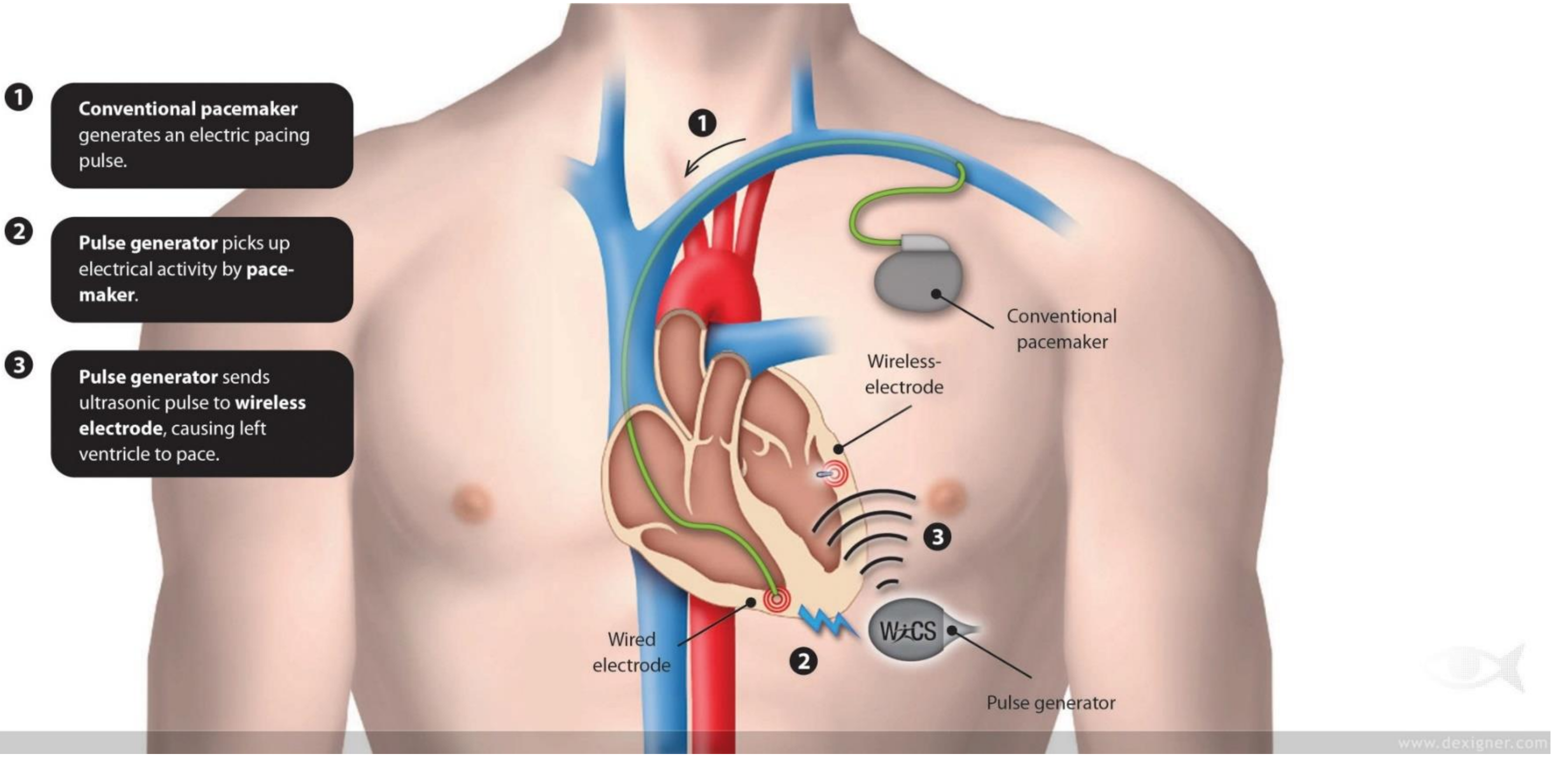
VDDR: accelerometer derived atrial signals

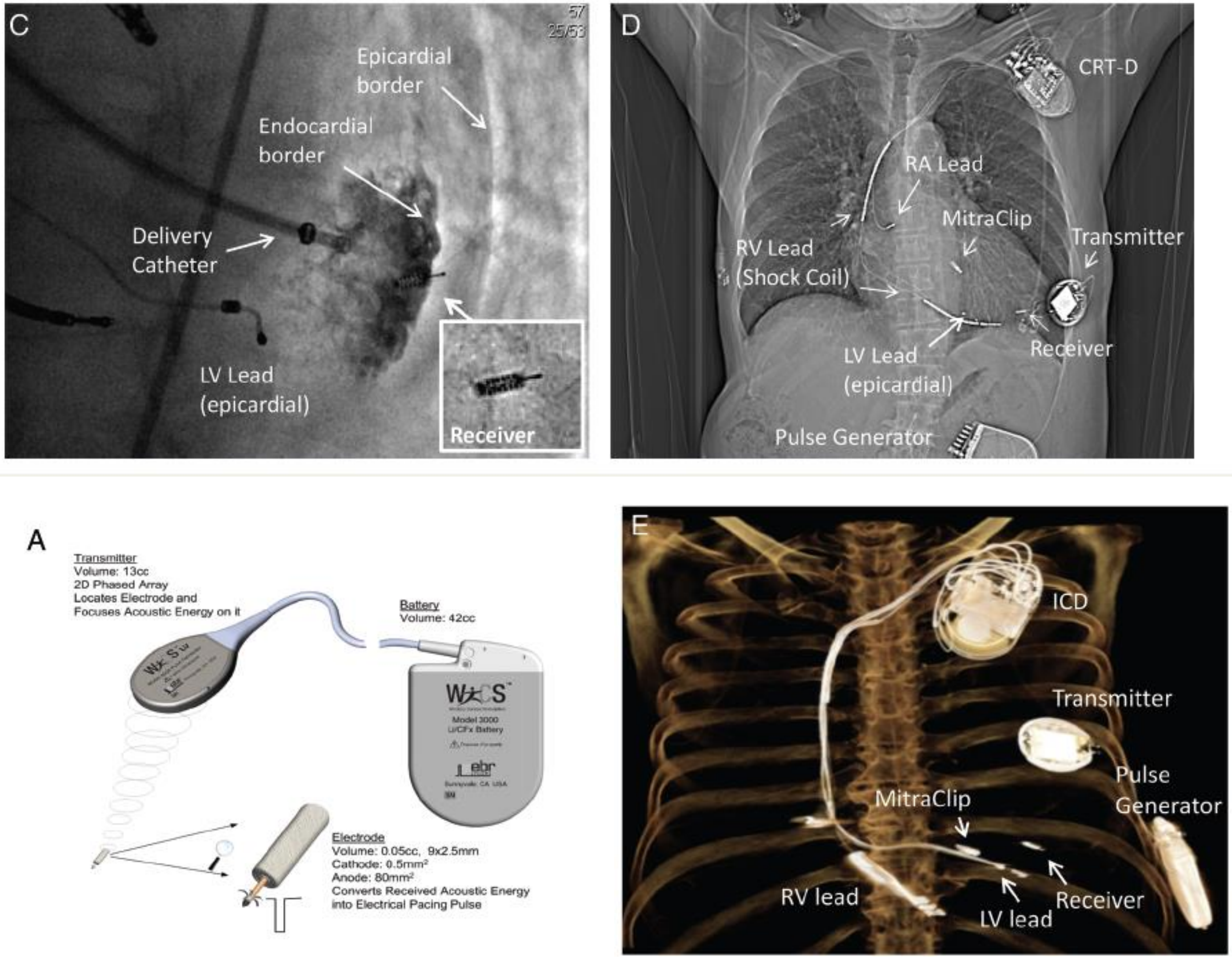


AVEIR DR



CRT leadless using ultrasound technology





C
57
25/53
Epicardial border
Endocardial border
Delivery Catheter
LV Lead (epicardial)
Receiver
D
CRT-D
RA Lead
MitraClip
Transmitter
RV Lead (Shock Coil)
LV Lead (epicardial)
Receiver
Pulse Generator
A
Transmitter
Volume: 13cc
2D Phased Array
Locates Electrode and
Focuses Acoustic Energy on it
Battery
Volume: 42cc
WiCS
Model 3000
Li/CFx Battery
ebr
Sunnyvale CA USA
Electrode
Volume: 0.05cc, 9x2.5mm
Cathode: 0.5mm²
Anode: 80mm²
Converts Received Acoustic Energy
into Electrical Pacing Pulse
E
ICD
Transmitter
Pulse Generator
MitraClip
RV lead
LV lead
Receiver

CENTRAL ILLUSTRATION **An Overview of the History of Cardiac Pacing**

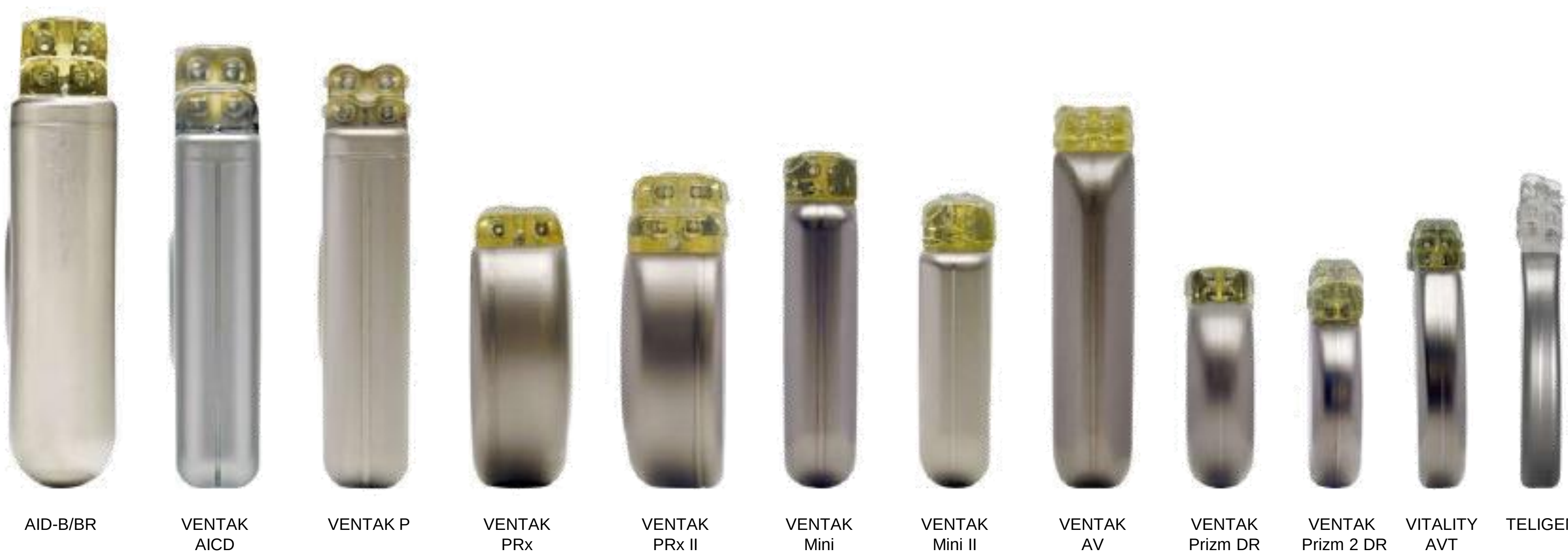
Paradigm Shifts in Cardiac Pacemakers

1950s	1950s	1958	2015	2016	Future
AC-powered pacemakers tethered to an extension cord (Furman)	Battery-powered transistorized "wearable" pacemakers (Lillehei/Bakken)	First fully implantable pacemaker (Elmqvist/ Senning)	Implantable pacemaker— basic system had not evolved significantly	Leadless pacemaker—the entire device is placed within cardiac chambers	Batteryless devices, which harvest cardiac motion to power pacing circuits

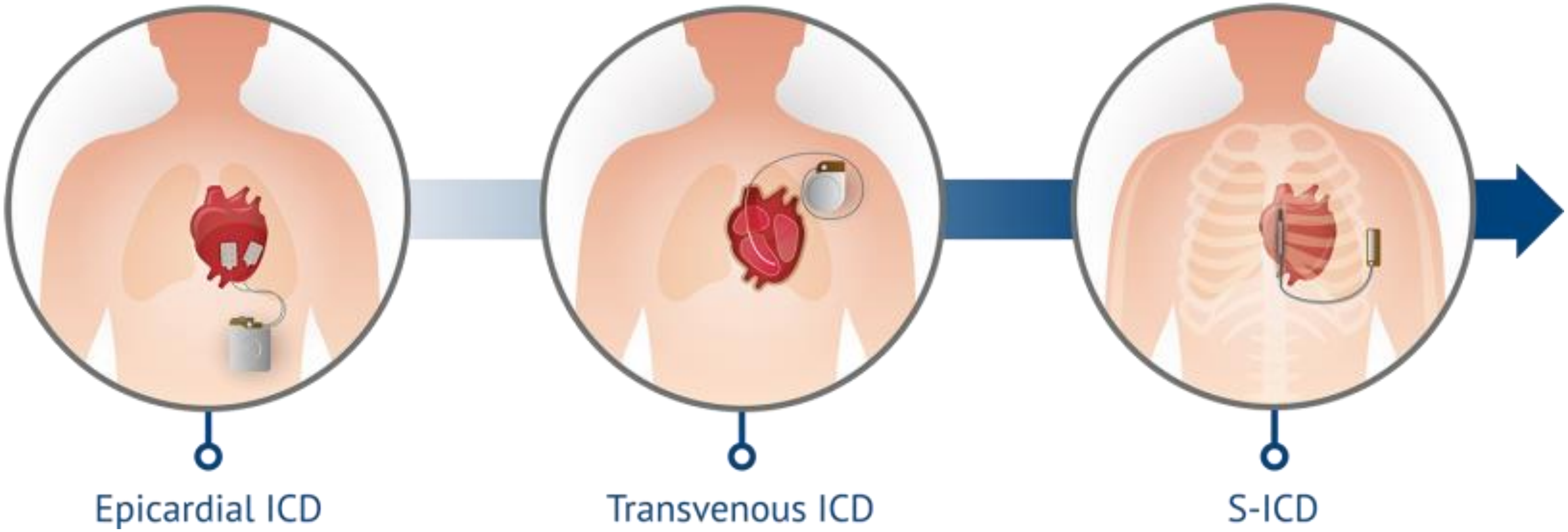
Mulpuru, S.K. et al. J Am Coll Cardiol. 2017;69(2):189-210.

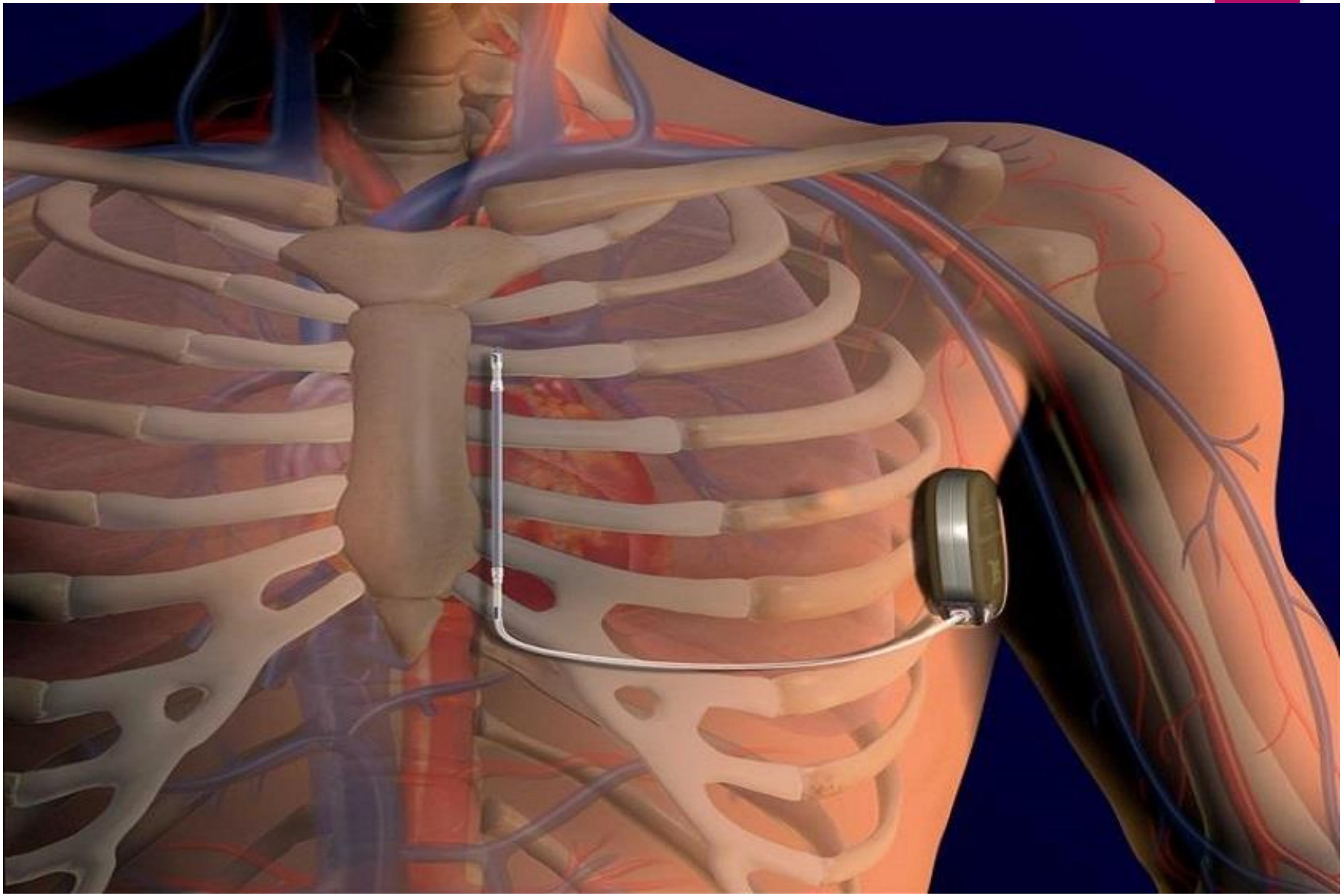
Historically, pacing developed using large, external, alternating current (AC)-powered devices, which subsequently evolved to "wearable" transistorized battery powered pacemakers—both comprise the era of external devices. A paradigm shift occurred with the introduction of the entirely implantable pacemaker, composed of an extravascular pulse generator connected to a transvenous lead in contact with the myocardium. This paradigm continues to this day. An emerging and rapidly developing new paradigm is that of leadless pacemakers, which are available for clinical use. Batteryless pacemakers that harvest cardiac mechanical motion to generate current, or that modify or add cells to introduce biological pacing activity, are under active investigation.

An unique evolution of ICD size



ICD Evolution

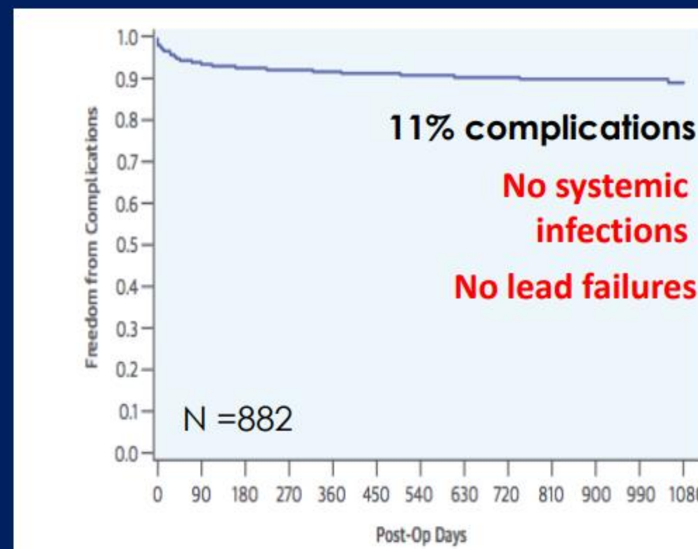




S-ICD introduced to reduce transvenous lead related complications

S-ICD Pooled data from EFFORTLESS and IDE Trial

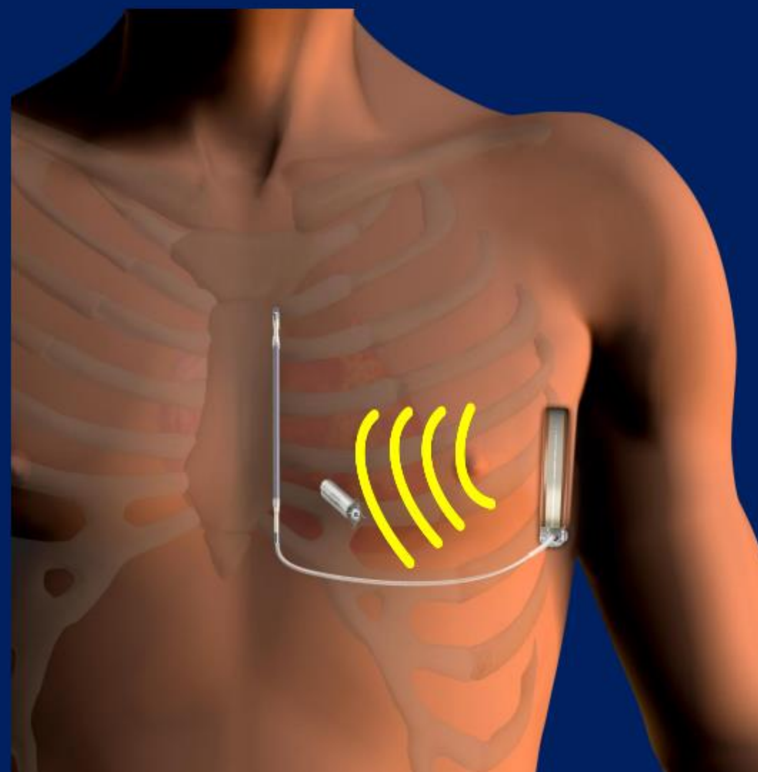
Bardy et al NEJM 2010



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

Burke et al JACC 2015

Combined implant of Communicating ATP-enabled Leadless Pacemaker and S-ICD



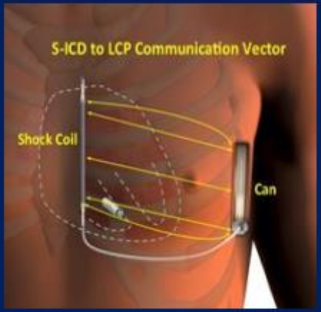
Results

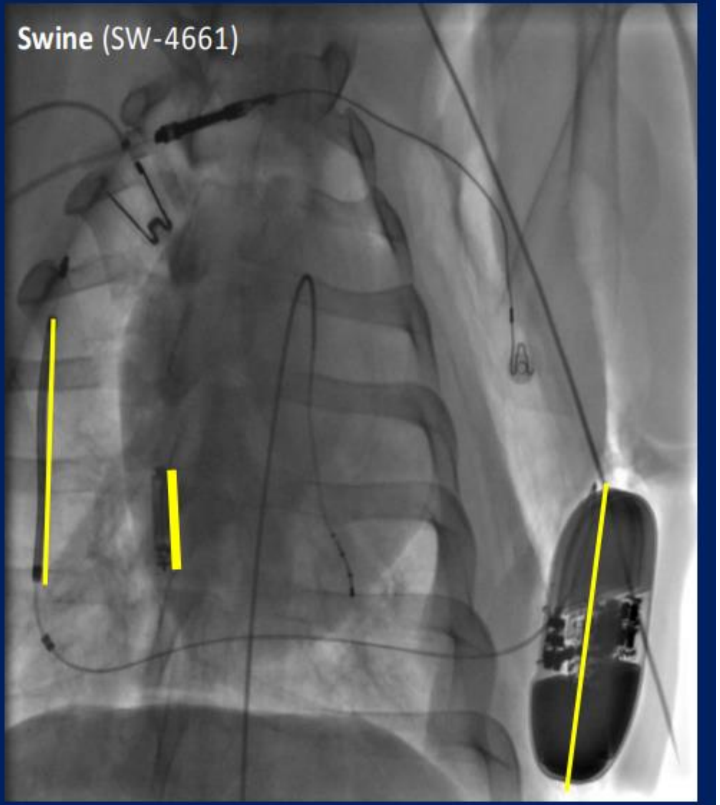
① LCP implant ② **Device-device communication** ③ Therapy

High success rate for device-device communication:

99% (306/309 attempts)

Challenging device orientation in animals

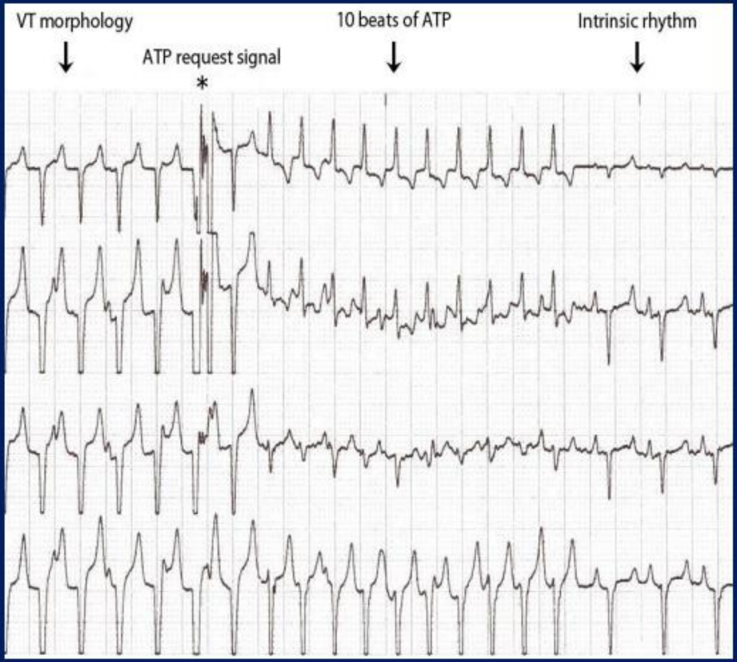




Results ① LCP implant ② Device-device communication ③ Therapy

High ATP-therapy delivery success rate of 99%

ATP Therapy success rates		
Total ATP requests	309	100%
Mean #ATP/animal	8	
Total ATP communication success	309	99%
Total ATP delivery success	**306**	**99%**



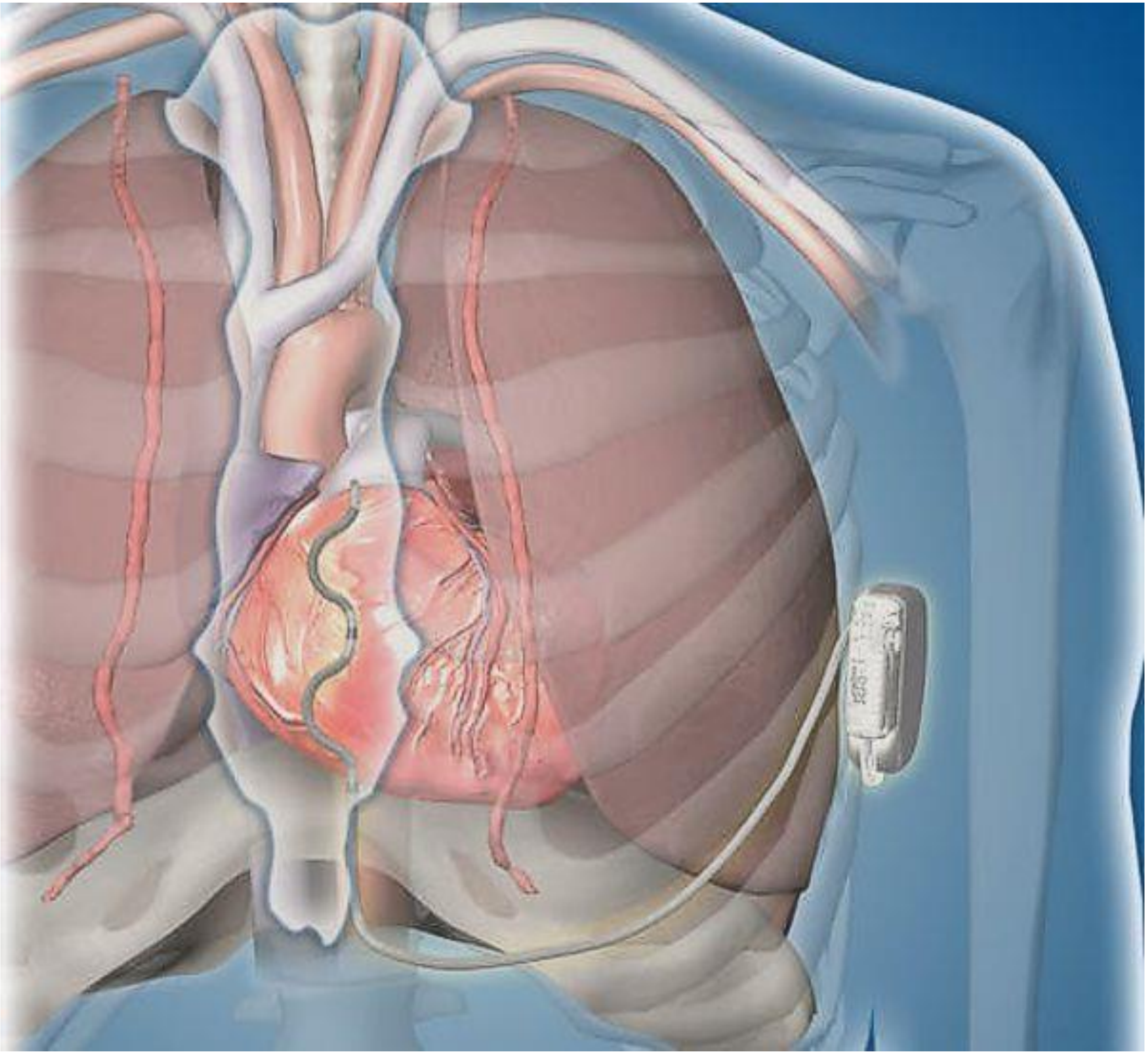
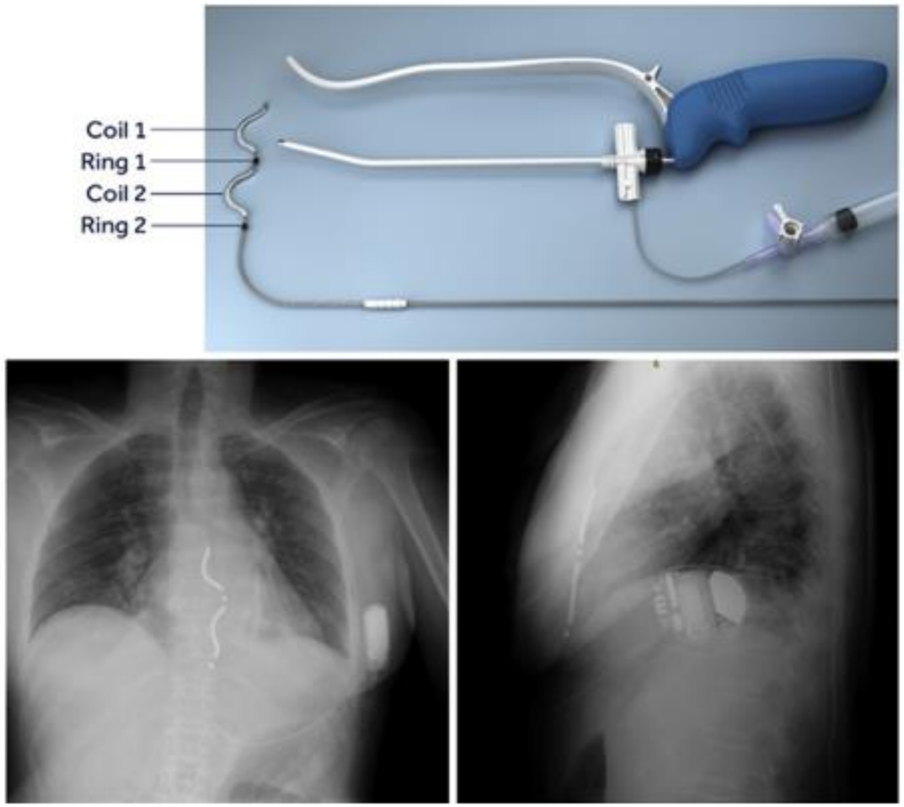
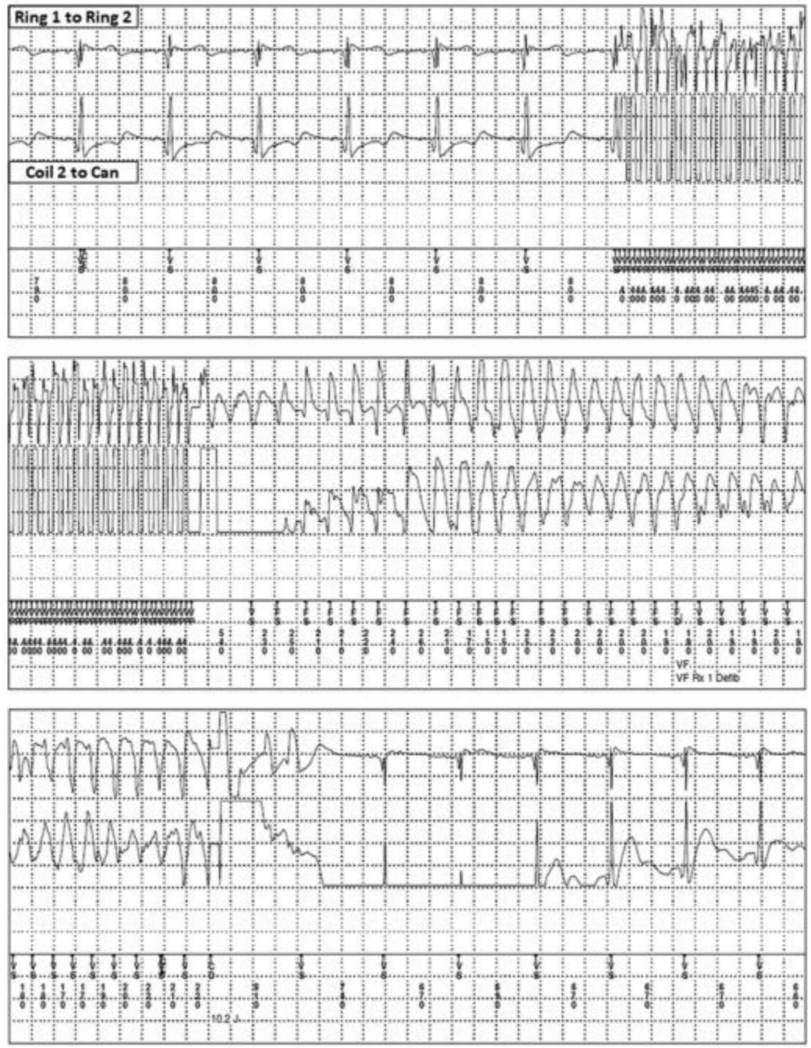


FIGURE 1 **Extravascular Implantable Cardioverter-Defibrillator System**



Extravascular implantable cardioverter-defibrillator lead and tunneling tool **(top)** with anteroposterior **(bottom Left)** and lateral **(bottom right)** fluoroscopic images of fully implanted system in situ.

FIGURE 6 Arrhythmia Induction and Therapy



Induction, detection, and shock termination of ventricular fibrillation by extravascular implantable cardioverter-defibrillator during implant testing.