

LEADLESS PACEMAKER

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Paradigm Shifts in Cardiac Pacemakers

1950s
AC-powered
pacemakers
tethered to an
extension cord
(Furman)



1950s
Battery-powered
transistorized
"wearable"
pacemakers
(Lillehei/Bakken)



1958
First fully
implantable
pacemaker
(Elmqvist/
Senning)



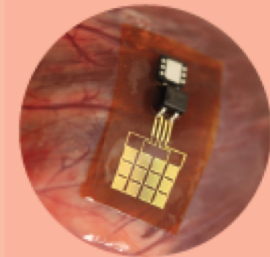
2015
Implantable
pacemaker—
basic system
had not evolved
significantly



2016
Leadless
pacemaker—the
entire device is
placed within
cardiac chambers



Future
Batteryless
devices, which
harvest cardiac
motion to power
pacing circuits

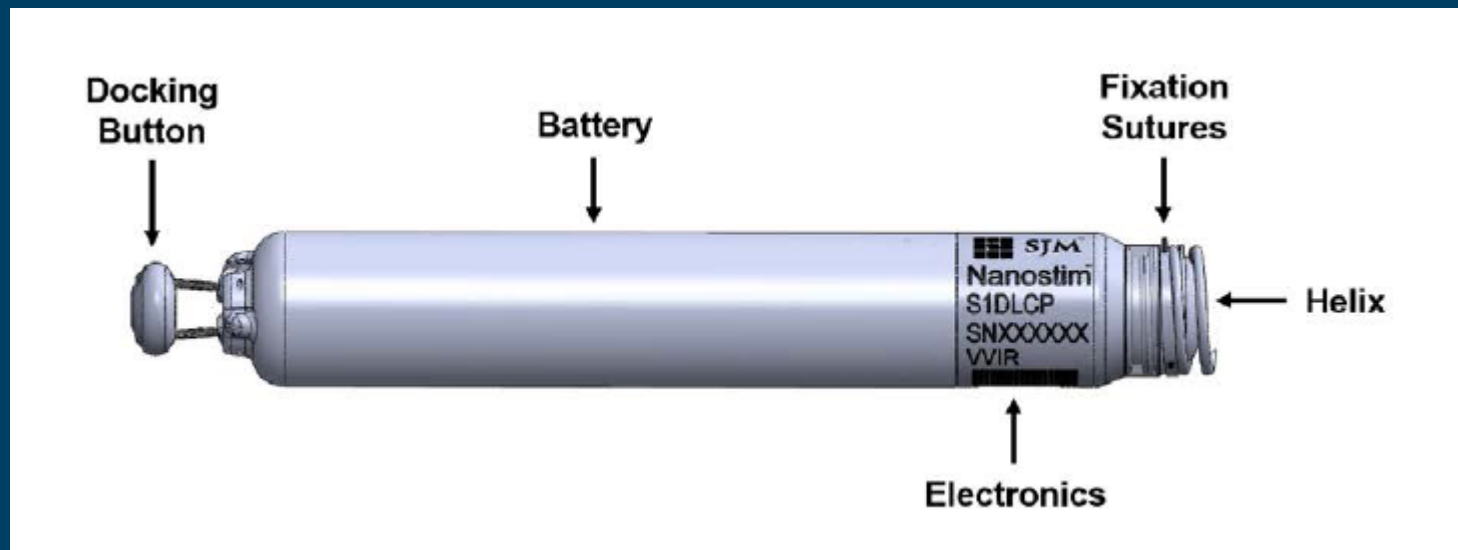


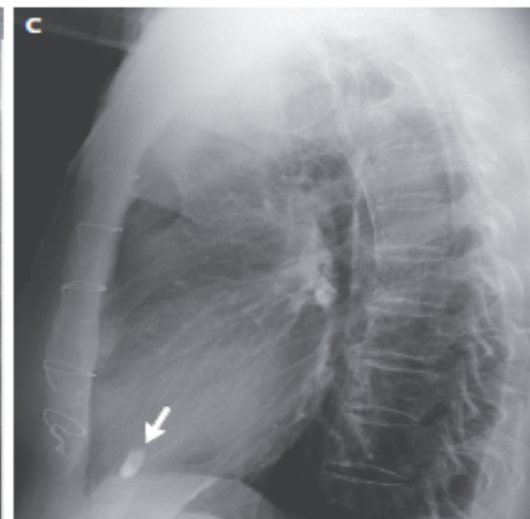
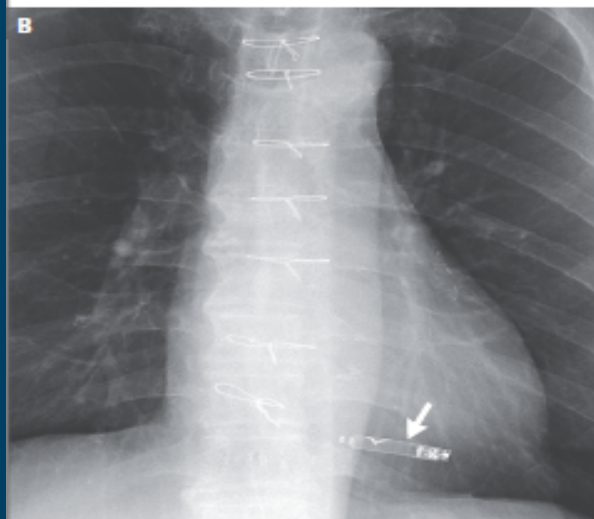
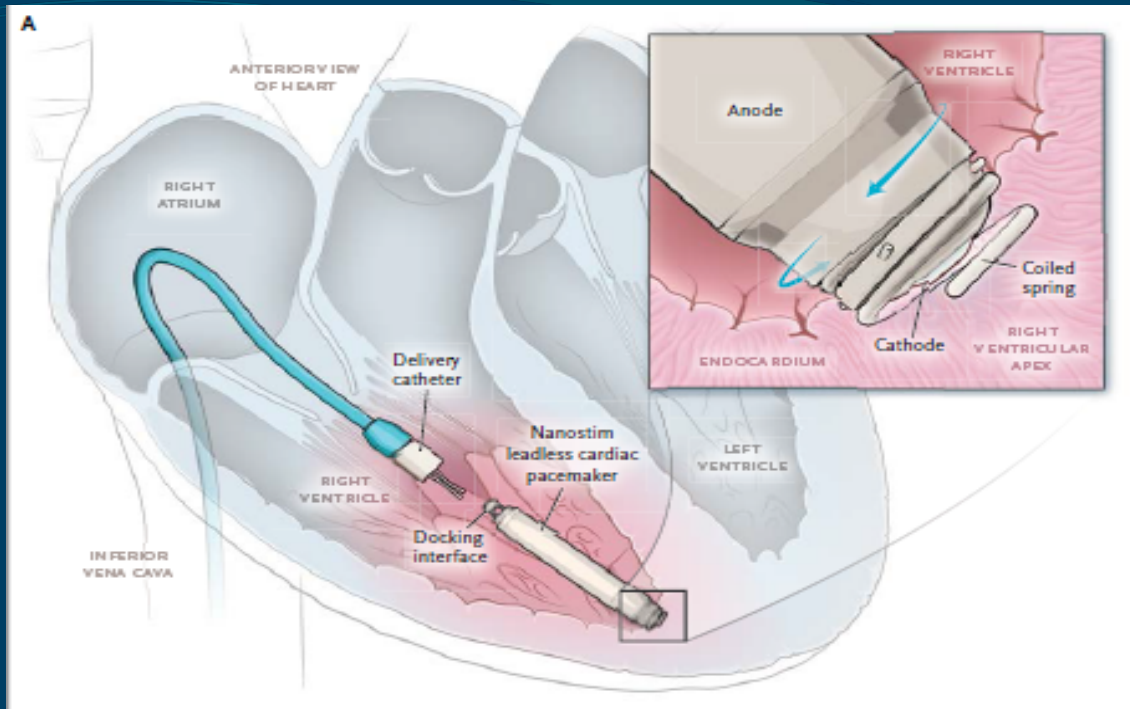
Mulpuru, S.K. et al. *J Am Coll Cardiol*. 2017;69(2):189-210.

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.

- Nanostim (St Jude Medical)
- Micra (Medtronic)
- WISE CRT-LV lead (EBR Systems)
- Empower (Boston Scientific-Subkutan ICD ile kombine)

Nanostim Leadless Cardiac Pacemaker (St. Jude Medical)





LEADLESS çalışması

- Leadless pillerin ilk insan çalışması
- 33 hasta, 32'sinde başarılı implantasyon
- 1 hastada kardiyak perforasyon ve tamponad
- İşlem süresi ortalama 30 dak
- 1. yıl sonunda pilin elektriksel performansı stabil ve cihaz ilişkili komplikasyon yok.
- Ortalama eşik (0.4-ms pw), 6. ayda 0.40 ± 0.26 V, 12. ayda 0.43 ± 0.30 V

J Am Coll Cardiol 2015;65:1497–504

40. ay takip sonuçları: en uzun takip verisi

3 hastada cihaz ilişkili sorun, %10 komplikasyon oranı: 2 tanesi cihazın yerleştirilmesi sırasında, 1 tanesi 37. ayda batarya tükenmesi

Elektriksel performans stabil

Circulation. 2018;137:633–635

ORIGINAL ARTICLE

Percutaneous Implantation of an Entirely
Intracardiac Leadless Pacemaker

- LEADLESS II
- Çok merkezli
- Başarılı yerleştirme oranı: %95.8 (526 hastanın 504'ü)
- 6. ayın sonunda cihaz ilişkili olumsuz olay sıklığı %6.7
 - Cihazın yerinden oynaması nedeniyle perkutan çıkarılma: %1.7
 - Kardiyak perforasyon: %1.3
 - Eşik yükselmesi nedeniyle cihazın çıkarılması: %1.3
- Sonuç: Cihaz önceden belirlenen pace ve sense hedeflerine ulaştı. Cihaz ilişkili olumsuz olay 15 kişiden birinde görüldü.

Reddy et al, N Engl J Med 2015; 373:1125-1135



ST. JUDE MEDICAL

St. Jude Medical
15900 Valley View Court
Sylmar, CA 91342 USA
Main 818 362 6822
Fax 818 364 5814

October 28, 2016

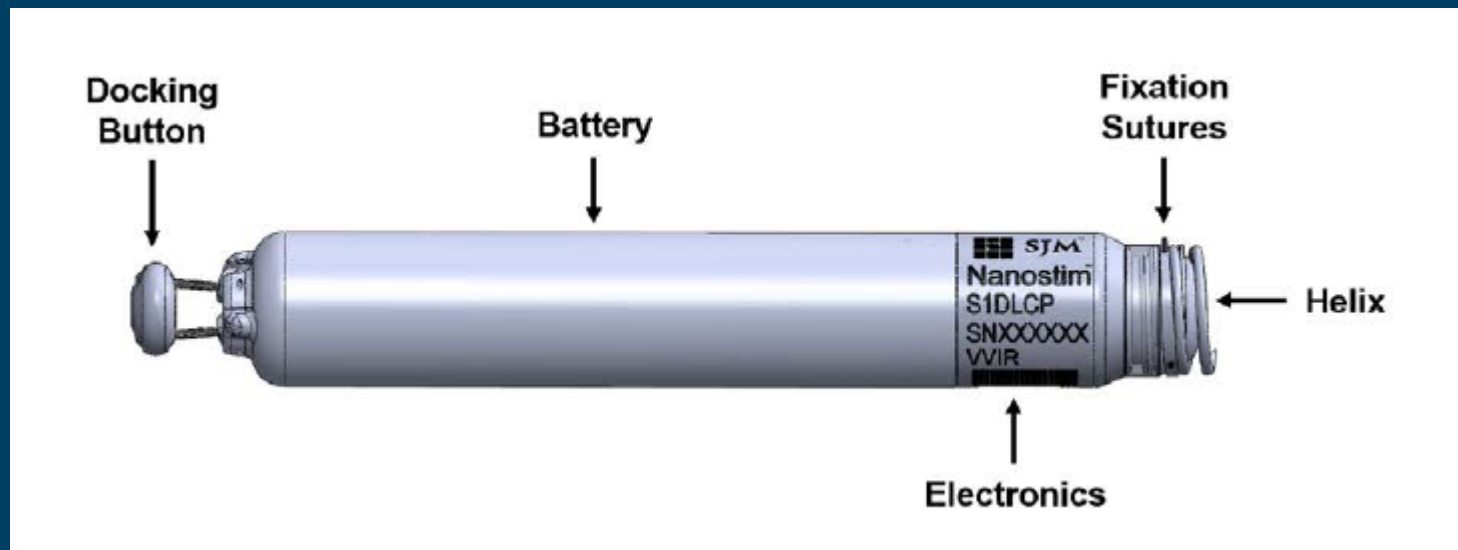
Study: Nanostim™ Leadless II IDE/CAP

Subject: Leadless II IDE/CAP Study Pause

Dear Leadless II Investigator,

St. Jude Medical (SJM) was made aware of seven (7) reports worldwide of lost telemetry and pacing output as a result of a battery malfunction associated with SJM Nanostim Leadless Cardiac Pacemaker (LCP) devices, Model Number **S1DLCP**. Due to these events, we have decided to pause Nanostim LCP implants in the Leadless II IDE/CAP study.

Nanostim Leadless Cardiac Pacemaker (St. Jude Medical)



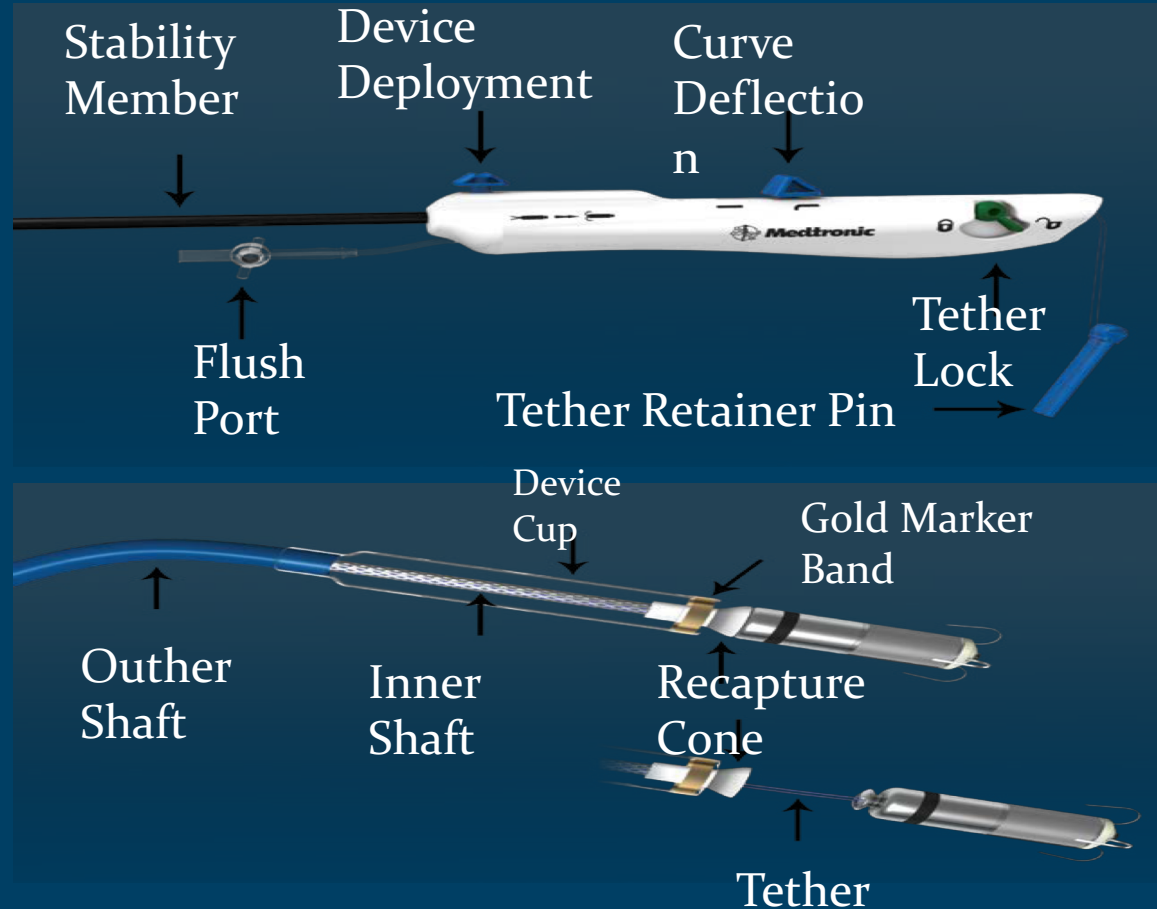
Nanostim vs Micra



Nanostim vs Micra

Özellikler	Nanostim	Micra
Uzunluk, mm	41.4	25.9
Hacim, cm ³	1	0.8
Ağırlık, gr	2	2
Sabitlenme mekanizması	Aktif, vidalanan helix	Pasif, nitinol kancalar
Pace modu	VVI/R	VVI/R
Sensör	Isı	Akselerometre
Batarya ömrü, yıl	9.8(2.5 V-0.4msn) 14.7(1.5V-0.24msn)	4.7(2.5V-0.4msn) 10(1.5V-0.24msn)

Micra Yerleştirme Sistemi



Protective Sleeve Being
Withdrawn -
Tines Extending

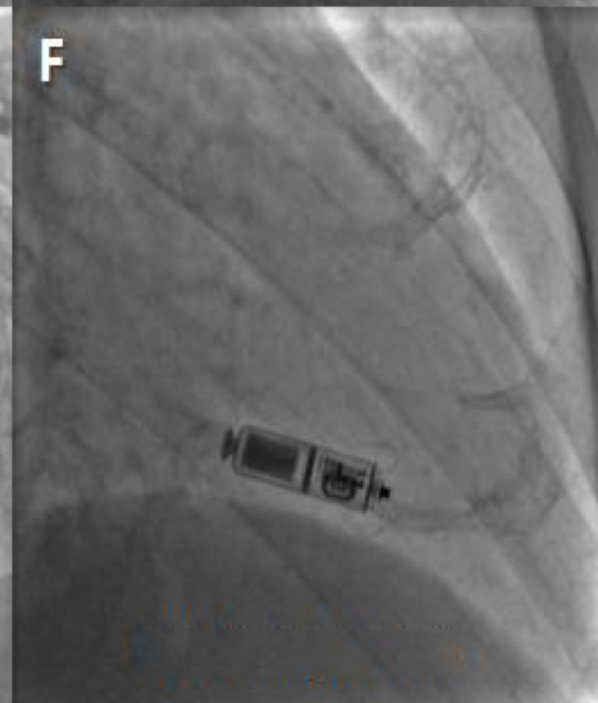
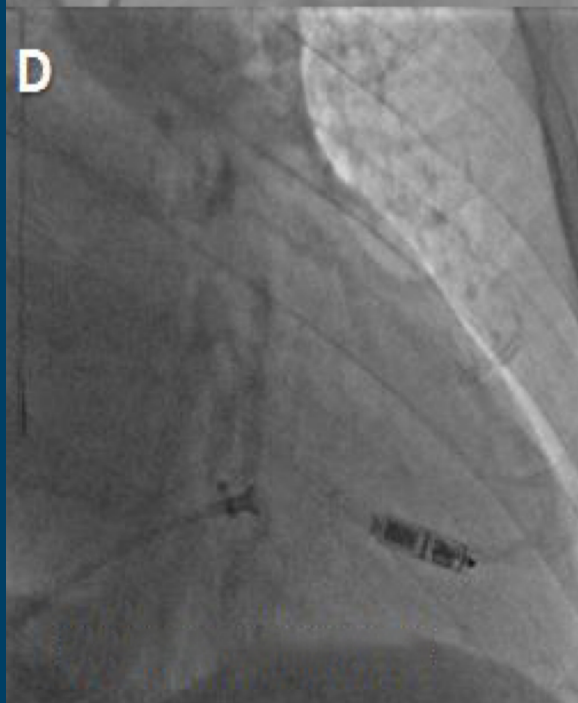
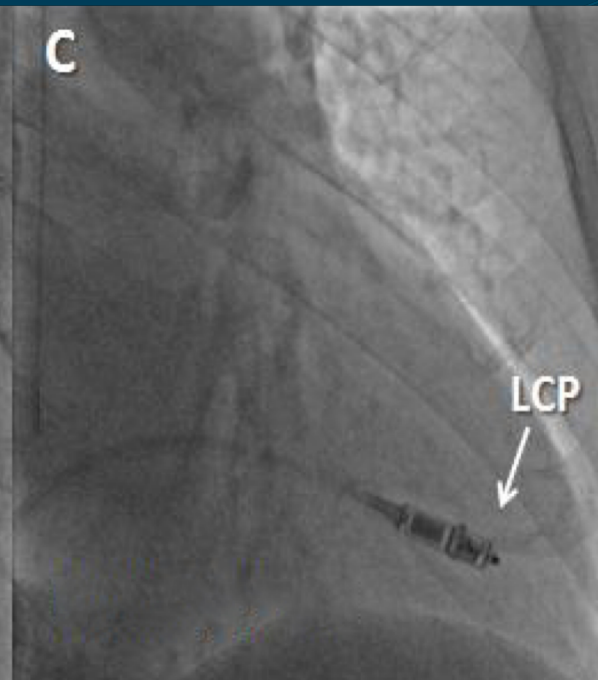


Tines Completely Retroflexed -
Micra Still In Sheath



Sleeve Withdrawn -
Micra Remains Tethered at
Delivery Tool Interface





Micra Transcatheter Pacing Study

- Prospektif, çok merkezli
- 725 hasta, %99.2 başarılı yerleştirme (719 hasta)
- 6 aylık izlem
- 28 majör komplikasyon
- Veriler post hoc olarak 2667 hastanın olduğu, 6 farklı transvenöz pil çalışma verileri ile karşılaştırılmış
- Micra vs kontrol grubu majör komplikasyon oranları: %4 vs %7.6 (%48 daha az komplikasyon)
- 6 ay sonunda hastaların %96'sında komplikasyon yok.

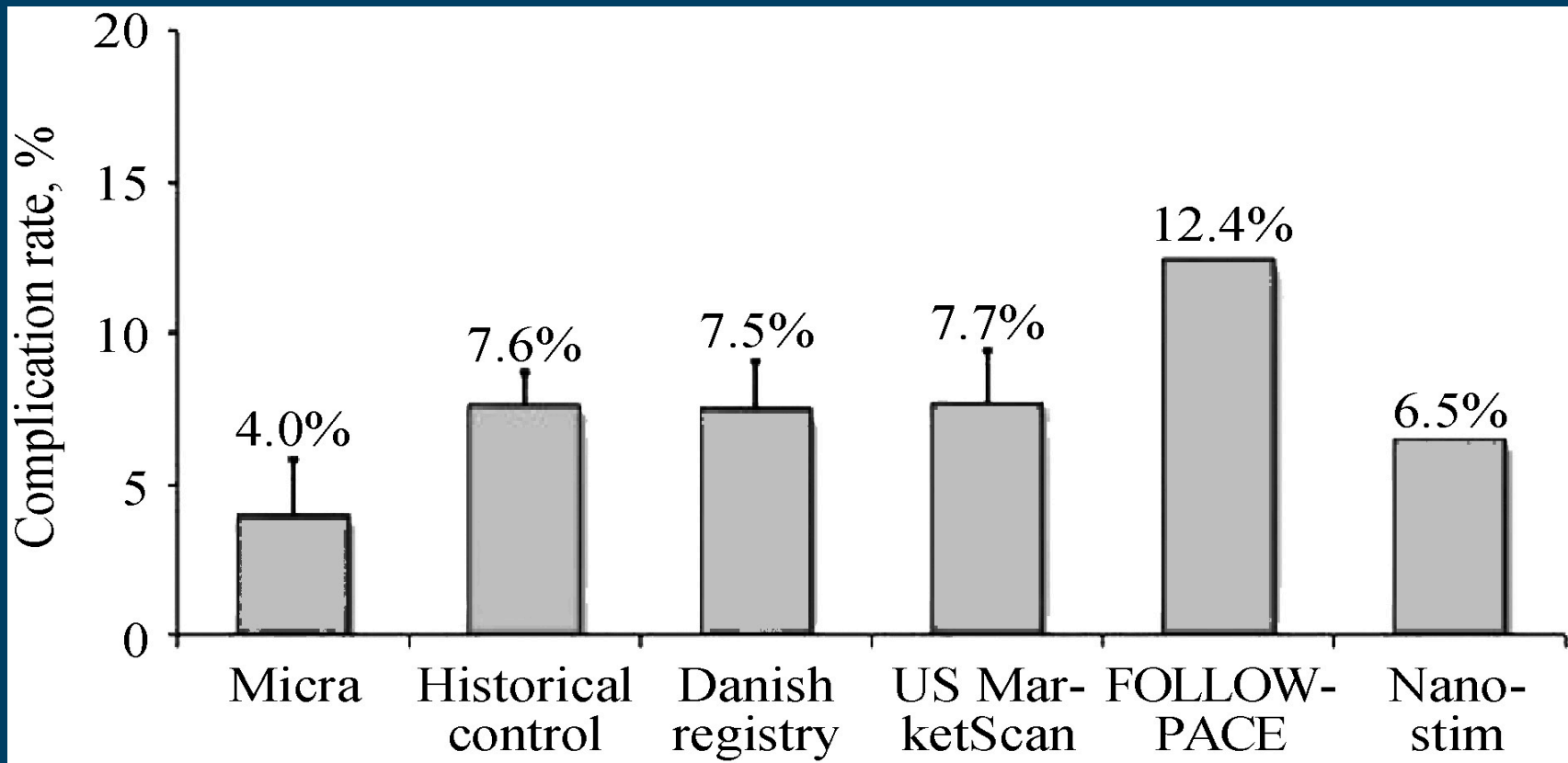
N Engl J Med 2016;374:533-41

Bütün Micra çalışmaları göz önüne alındığında, 1521 hastada 1 adet makrodislodgement olmuş, bunda da emboli izlenmemiş.

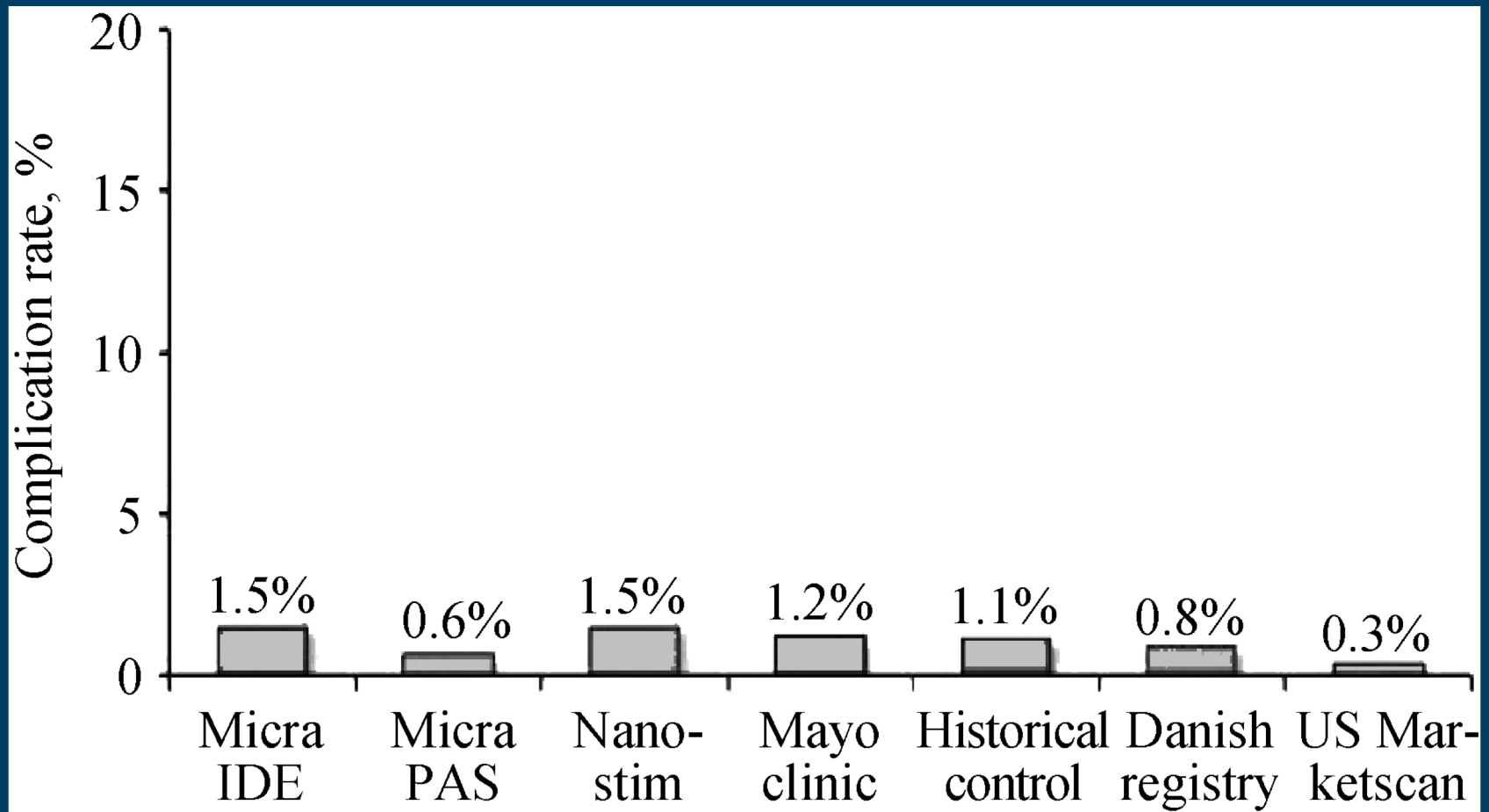
Table 2. Major Complications in 725 Patients Who Underwent a Transcatheter Pacemaker Implantation Attempt.

Adverse Event	No. of Events Associated with Major Complication Criterion*						No. of Patients (%)†
	Death	Loss of Device Function	Hospitalization	Prolonged Hospitalization‡	System Revision	Total Events	
Embolism and thrombosis	0	0	1	1	0	2	2 (0.3)
Deep vein thrombosis	0	0	0	1	0	1	1 (0.1)
Pulmonary thromboembolism	0	0	1	0	0	1	1 (0.1)
Events at groin puncture site: atrioventricular fistula or pseudoaneurysm	0	0	2	3	0	5	5 (0.7)
Traumatic cardiac injury: cardiac perforation or effusion	0	0	3	9	0	11	11 (1.6)
Pacing issues: elevated thresholds	0	1	2	1	2	2	2 (0.3)
Other events	1	0	5	4	1	8	8 (1.7)
Acute myocardial infarction	0	0	0	1	0	1	1 (0.1)
Cardiac failure	0	0	3	2	0	3	3 (0.9)
Metabolic acidosis	1	0	0	0	0	1	1 (0.1)
Pacemaker syndrome	0	0	1	0	1	1	1 (0.2)
Presyncope	0	0	0	1	0	1	1 (0.1)
Syncope	0	0	1	0	0	1	1 (0.1)
Total	1	1	13	18	3	28	25 (4.0)

Leadless pillerin transvenöz piller ile karşılaştırılması

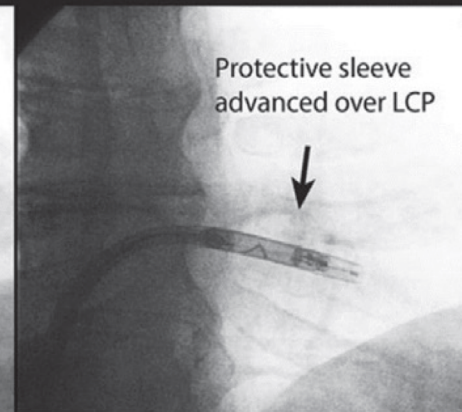
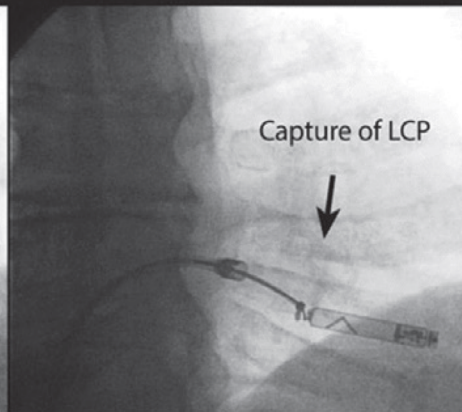
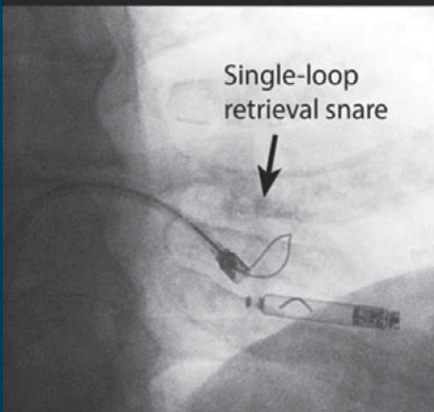


Perikardiyal efüzyon oranları

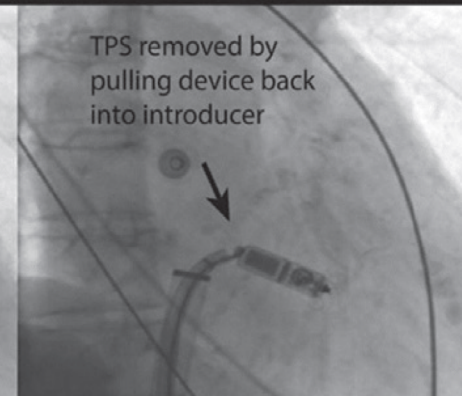
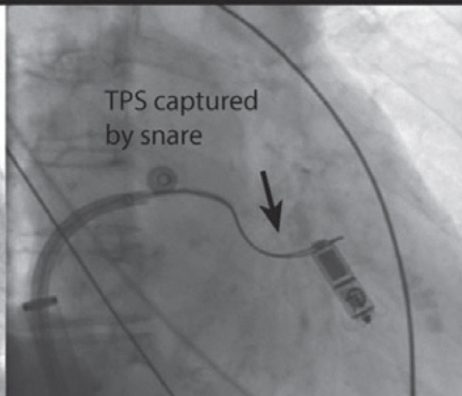
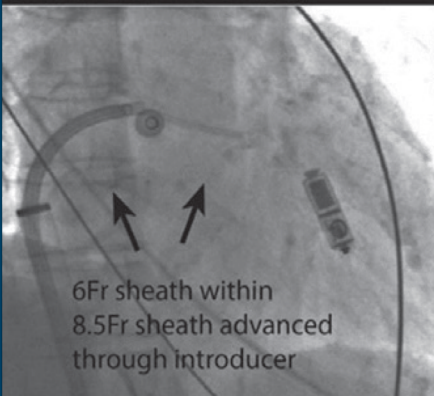


Leadless pacemakerların çıkarılması

Retrieval of LCP



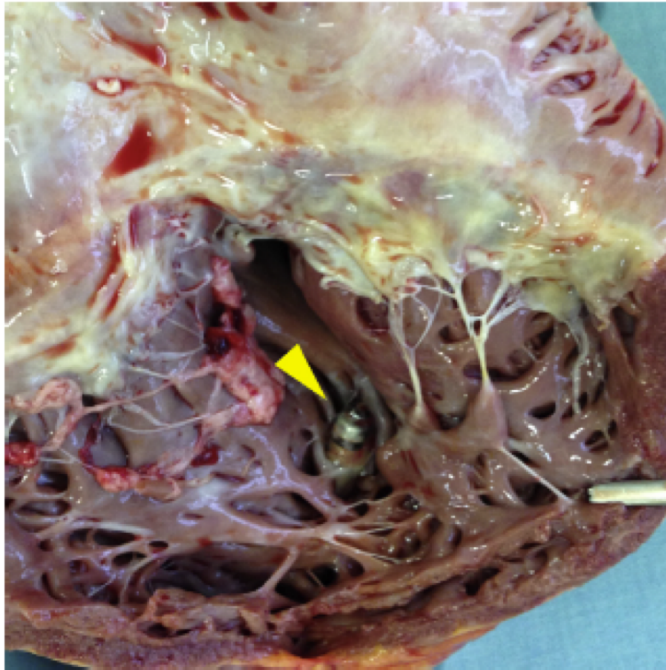
Retrieval of TPS



Study Type	Leadless Pacemaker	Year of Publication	First Author	Number	Time LP <i>in situ</i> (mean)	Extraction Success Rate	Reason Unsuccessful Extraction
Pre-clinical	Nanostim	2014	Koruth	10	160 days	100 %	N/A
				8	2.3 years	100 %	N/A
	Micra TPS	2014	Bonner	4	28 months	75 % (3)	Complete encapsulation of device
Clinical	Nanostim	2016	Jung	1	506 days	100 %	N/A
	Nanostim	2016	Reddy	5	<6 weeks	100 %	The docking feature could not be reached.
				11	>6 weeks	91 % (10)	
	Nanostim	2017	Lakkireddy	73	1.7 years	90.4 % (66)	The docking button could not be reached in six cases. In one case, the docking button detached.
	Micra TPS	2017	Tjong and Reddy	10	229 and 259 days*	80 % (8)	Unable to be removed due to fluoroscopy malfunction
	Micra TPS	2016	Karim	1	3 weeks	100 %	N/A
	Micra TPS	2016**	Giocondo	1	228 days	0 %	Unknown
	Micra TPS	2016	Koay	1	1 month	100 %	N/A
	Micra TPS	2016	Gerdes	1	Intraprocedural	100 %	N/A

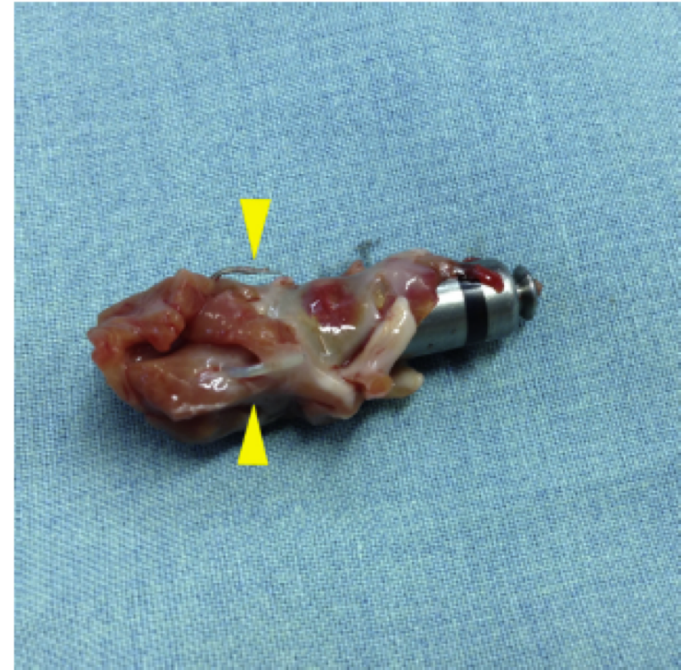
LP = leadless pacemaker; N/A = not applicable; TPS = transcatheter pacing system. *In unsuccessful attempt cases used source: Micra Transcatheter Pacing System, 2016.” **Heart Rhythm Society, 2016.”

FIGURE 1 MICRA Pacemaker in the Apical Region of the Right Ventricle



The **yellow arrowhead** indicates the MICRA pacemaker.

FIGURE 2 Nitinol Fixation Tines Totally Embedded in Myocardial Tissue



The **yellow arrowheads** indicates the nitinol fixation tines.

Çözüm bekleyen sorunlar

- Vasküler girişim yeri ile ilgili problemler
- Yerleştirme sistemi ile ilgili problemler
- Pilin sabitleme mekanizmasıyla ilgili problemler
- Batarya tükenmesi
- Pilin çıkarılması ile ilgili problemler
- Sadece VVI pace yapılabilmesi

WISE-CRT

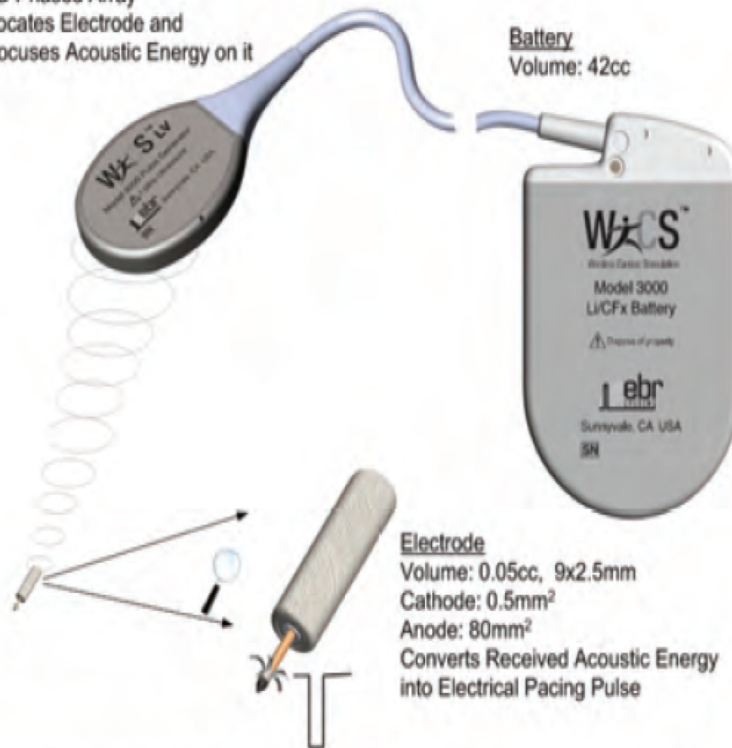
A

Transmitter

Volume: 13cc
2D Phased Array
Locates Electrode and
Focuses Acoustic Energy on it

Battery

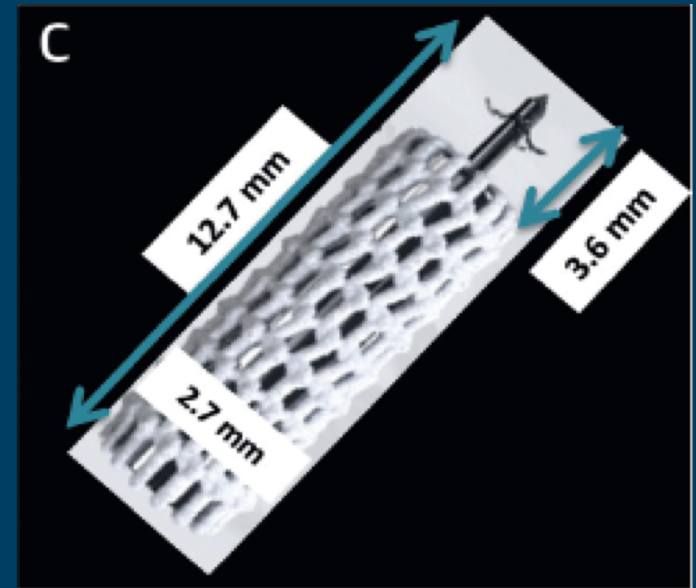
Volume: 42cc



Electrode

Volume: 0.05cc, 9x2.5mm
Cathode: 0.5mm²
Anode: 80mm²
Converts Received Acoustic Energy
into Electrical Pacing Pulse

C

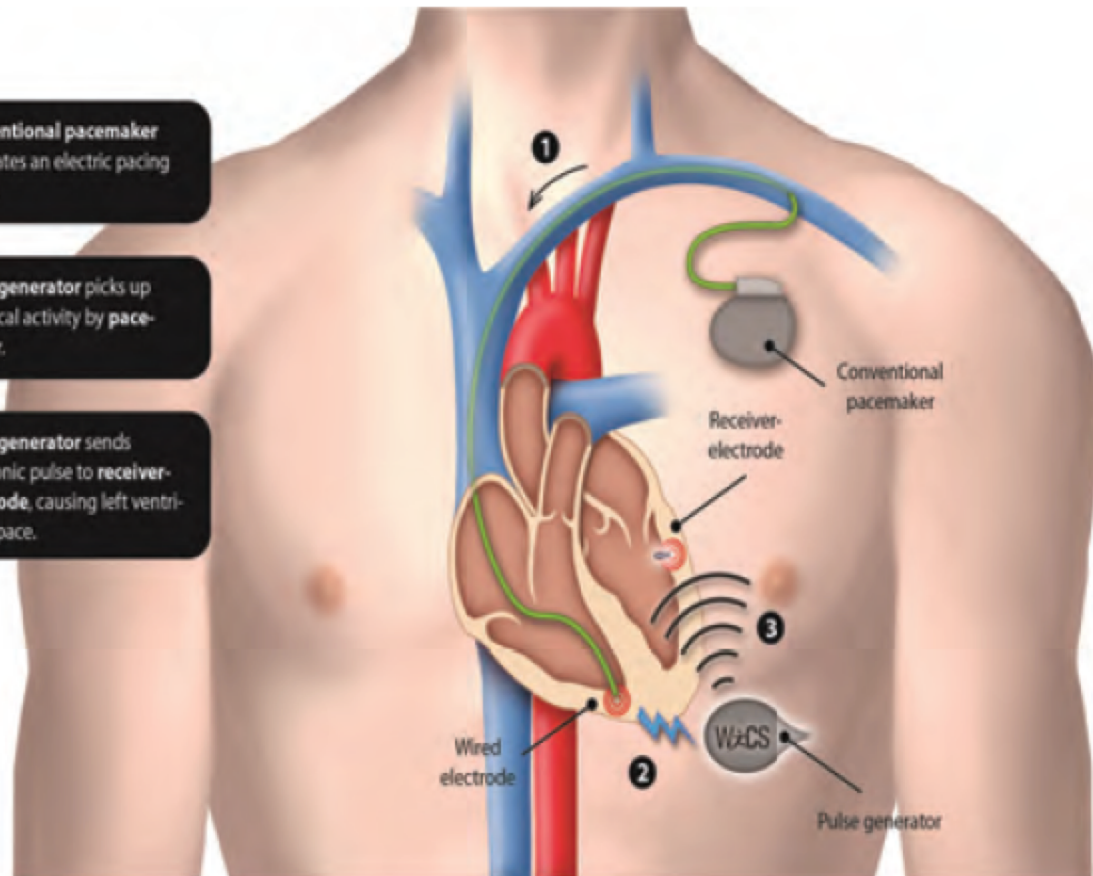


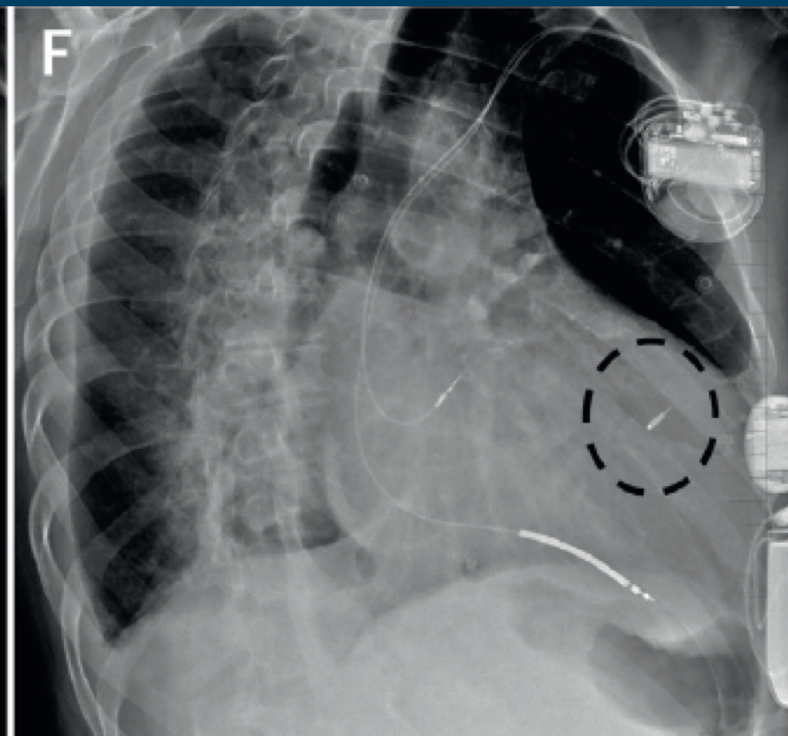
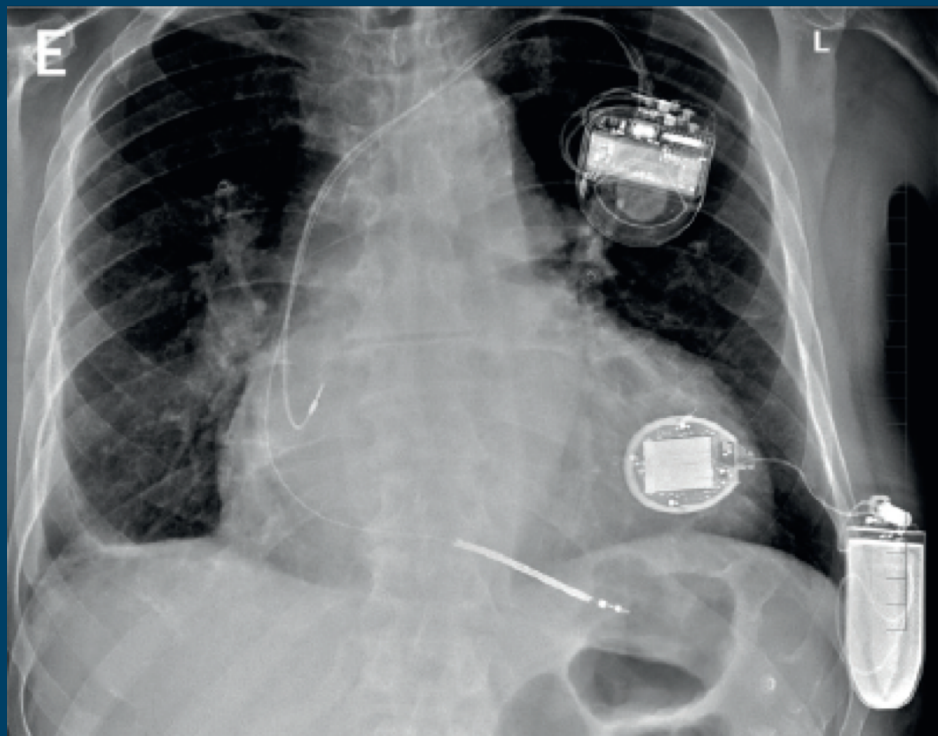
B

① Conventional pacemaker generates an electric pacing pulse.

② Pulse generator picks up electrical activity by **pace-maker**.

③ Pulse generator sends ultrasonic pulse to **receiver-electrode**, causing left ventricle to pace.





WISE CRT çalışması

- 17 hastada durduruldu
- Cihaz implant başarısı % 76.5, 4 hastada takılamamış-ciddi perikardiyal efüzyon(3), uygun eşik bulunamaması(1).
- Takipte:
 - Hastaneden çıkış öncesi 2 hastada pace etmeme- 1'i düzeltilebilmiş
 - 6. ayda 1 hastada erken batarya tükenmesi
- Cihaz ilişkili sorun sıklığı %35

SELECT-LV

- Çok merkezli, prospektif, 35 hasta
- Primer son nokta: 1 ay sonunda EKG’de biventriküler pace bulgusu olması, %97.1; 6. ayda %93.9

J Am Coll Cardiol 2017;69:2119–29

SELECT-LV

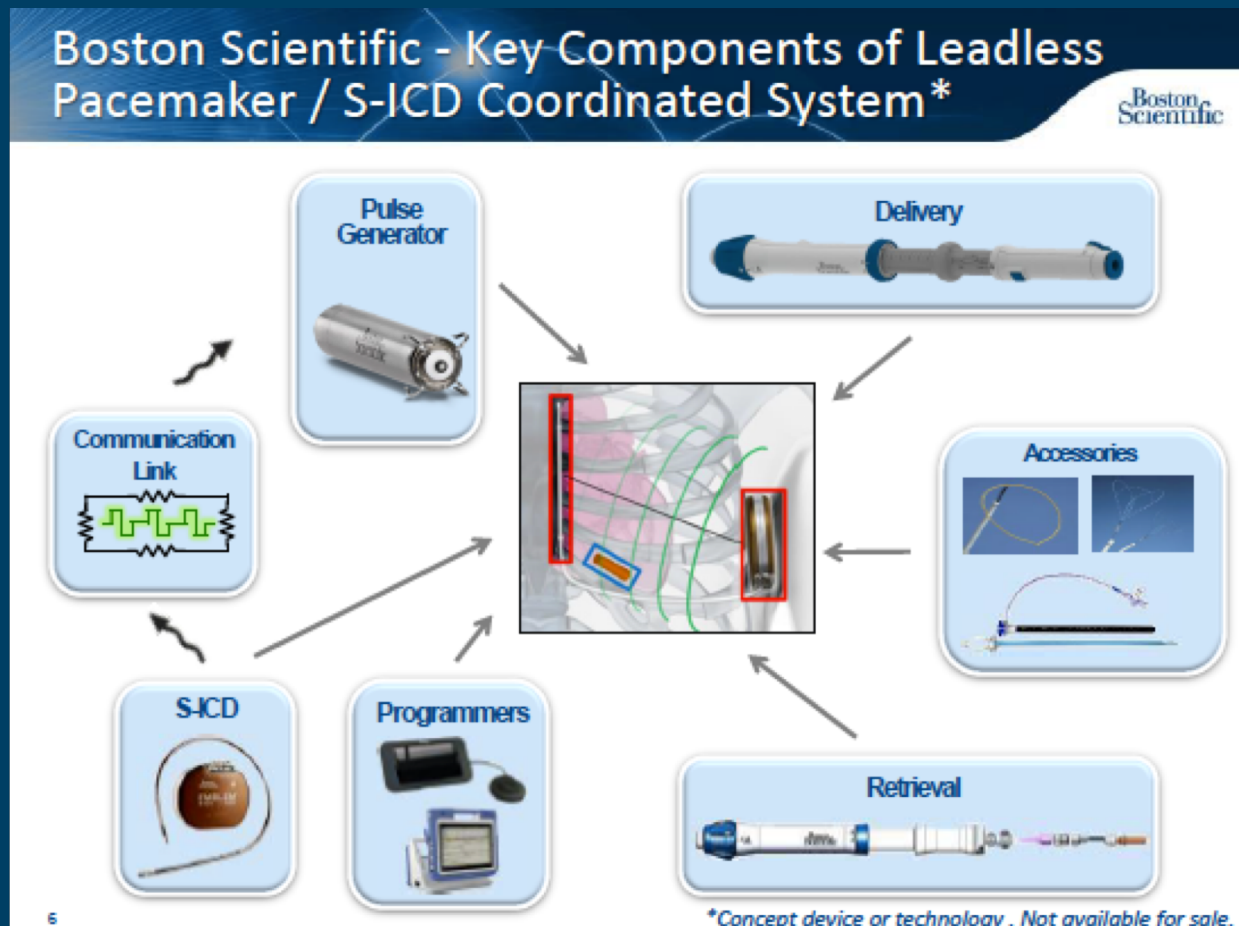
TABLE 3 Device- or Procedure-Related Adverse Events (n = 35)

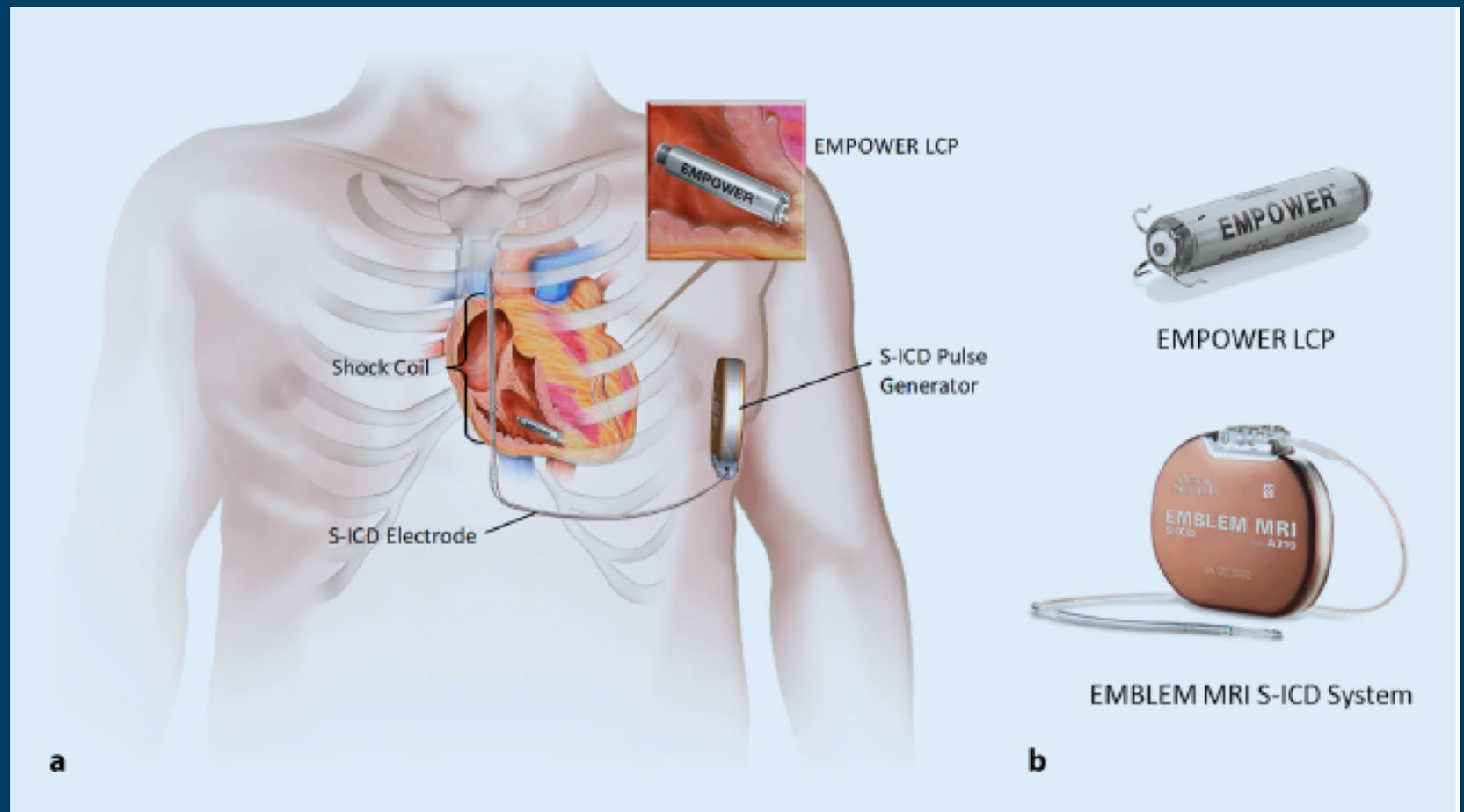
<24 h	3 (8.6%)
VF during catheter contact with LV endocardium	1
Electrode embolization to lower extremity	1
Femoral artery fistula (required surgical repair)	1
24 h to 1 month	8 (22.3)
Acute CVA (AF noncompliant with anticoagulation)	1
Femoral pseudoaneurysm	2
Pocket hematoma (generator)	1
Suspected infection (generator site)	3
Death (following VF during initial implant procedure)	1
1 to 6 months	3 (8.6)
Defective transmitter circuitry	3

Values are n (%) or n.

AF = atrial fibrillation; CVA = cerebrovascular accident; LV = left ventricular; VF = ventricular fibrillation.

EMPOWER Sistemi: S-ICD+Leadless pacemaker





Empower sistemi

- Deney hayvanlarında yapılan çalışmalar umut verici
- 2019'da insan klinik çalışmalarının sonuçları bekleniyor.

The first batteryless, solar-powered cardiac pacemaker



Heart Rhythm 2015;12:1317–1323



Figure 2 The sunlight-driven pacemaker prototype 2 (2 devices are shown). **Top**, A conventional bipolar active pacemaker lead (Safio S60, Biotronik) is attached via an IS-1 header. **Bottom**, The back side of the device reveals a small lithium-polymer accumulator (visible as silver part of the device on the right). The energy source for the device, a solar module, can be seen in the frontal view (device on the left). The dimensions of the device are 30 × 35 × 6 mm.

The Swiss approach for a heartbeat-driven lead- and batteryless pacemaker

Heart Rhythm. 2017 Feb;14(2):294-299



REVIEWS

Next-generation pacemakers: from small devices to biological pacemakers

Eugenio Cingolani, Joshua I. Goldhaber and Eduardo Marbán

Nat Rev Cardiol. 2018 Mar;15(3):139-150

Study	Model (animal; location)	Biological construct	Biological pacemaker activity	Delivery system	Monitoring	Immunosuppression	Refs
Qu et al. (2003)	Dog; atrial appendage	Ad-HCN2	++	Open chest	ECG Holter	No	84
Plotnikov et al. (2004)	Dog; left bundle	Ad-HCN2	++	Arterial catheter	ECG Holter	No	85
Kehat et al. (2004)	Pig; left ventricle	hESCs	+/-	Open chest	ECG	Yes	90
Tse et al. (2006)	Pig; left atrium	Ad-HCN1Delta	++	Open chest	ECG Holter	No	100
Bocchi et al. (2006)	Dog; left bundle	Ad-HCN2 versus Ad-HCN2-E324A	++	Arterial catheter	ECG Holter	No	96
Plotnikov et al. (2007)	Dog; left ventricle	HCN2-expressing hMSCs	++	Open chest	ECG Holter	No	93
Plotnikov et al. (2008)	Dog; left bundle	Ad-HCN2-1-2	++	Arterial catheter	ECG Holter	No	113
Shlapakova et al. (2010)	Dog; left bundle	Ad-HCN2	++	Arterial catheter	ECG Holter	No	114
Cingolani et al. (2012)	Pig; AV junction	Ad-HCN2+KIR2.1AAA	+++	Venous catheter	ECG Holter	No	101
Boink et al. (2013)	Dog; left bundle	Ad-HCN2+SKM1	+++	Arterial catheter	ECG Holter	No	115
Hu et al. (2014)	Pig; AV junction	Ad-TBX18	++++	Venous catheter	Continuous ECG telemetry	No	98
Chauveau et al. (2017)	Dog; left ventricle	iPSC-derived cardiomyocytes	+/-	Open chest	ECG Holter	Yes	92