The new leadless pacemakers- when will they be feasible in children ?

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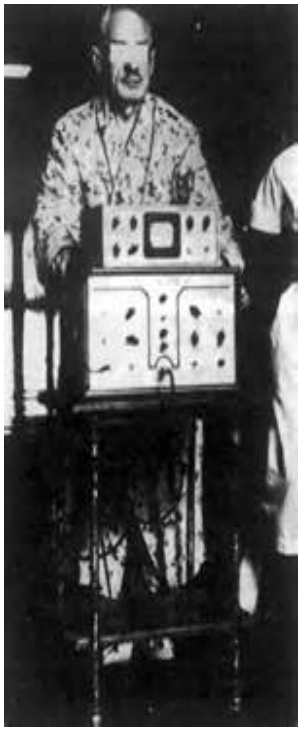
Pedirhythm VII,
Thessaloniki, 6th February 2017

Pacemaker Therapy

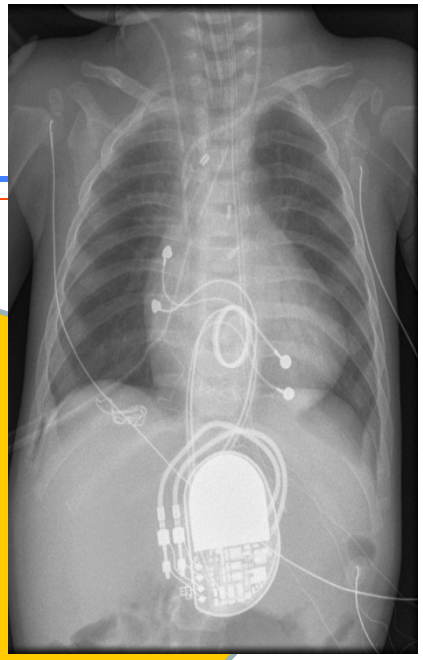


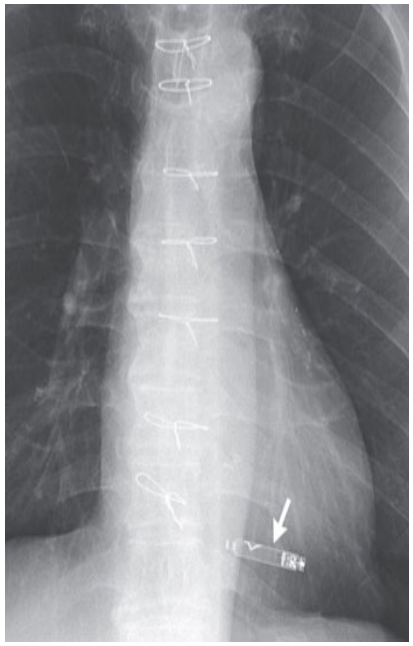
1956

2013

Each year nearly **1 million persons** worldwide receive transvenous cardiac pacemakers.
Still no pacemakers or leads are designed specifically for children

Why Leadless pacing?





Lead-associated complications

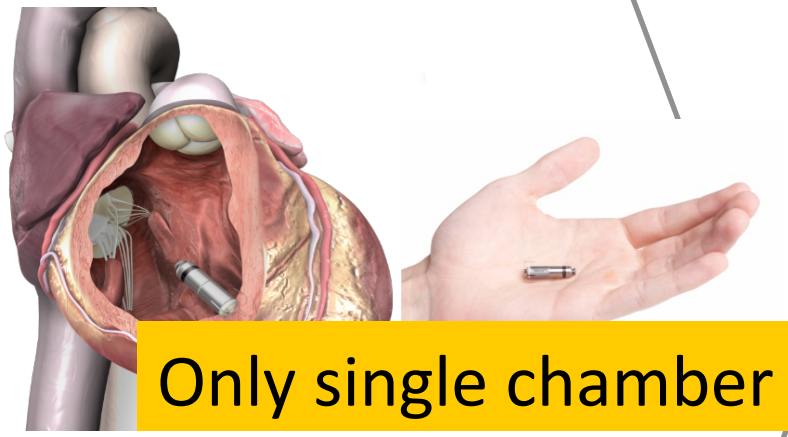
- Pneumothorax
- Cardiac perforation
- Dislodgement
- Venous occlusion
- Fracture, insulation failure

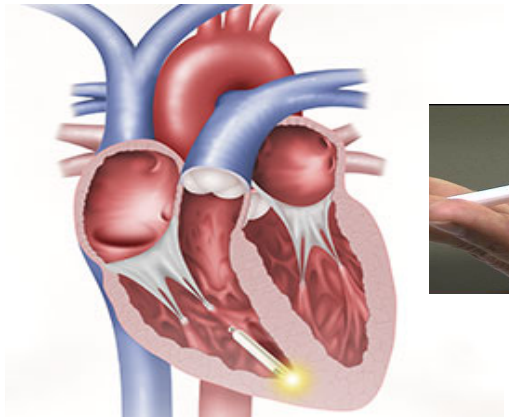
Pocket /Generator-related complications

- Hematoma
- Skin Erosion
- Infection
- Cosmetic concerns

Pacemaker related adverse events in ~ 1 of 10 patients

Potential benefits of leadless pacing





Only single chamber pacing (VVI/R) possible

1 **Less invasive**

Percutaneous, less hardware, no cosmetic issues

Reduction of acute and chronic complications

3 **Less costs**

Reduction of complications
Short in-hospital stay

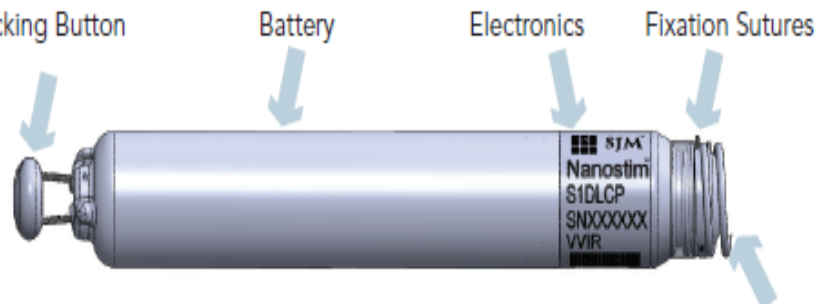
2 Systems

	St. Jude Medical Nanostim™	Medtronic Micra™
Size	41,4 mm, ø 5.9 mm	25.9 mm , ø 6.7 mm
Longevity	> 9,3 years	10 years
Access site	V. femoralis (18 Fr.)	V. femoralis (23 Fr.)
Fixation	Screw-in Helix (1,3 mm)	4 self-expand. Nitinol Tines
Retrieval option	Yes	Yes
CE Mark / FDA Approval	Oktober 2013/ No	April 2015/April 2016
MRI compatible	1.5 Tesla	1.5 and 3 Tesla

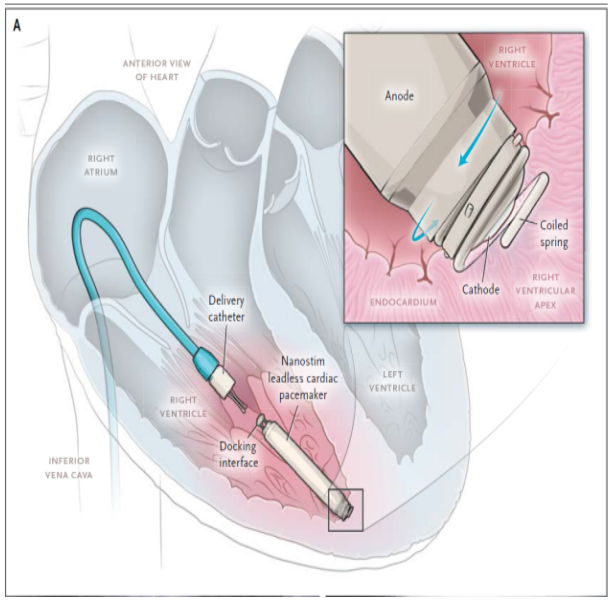
Source: Medtronic Inc, St. Jude Inc

2 Systems

Figure 2: Design of the Leadless Pacemaker



Nanostim™



Micra™

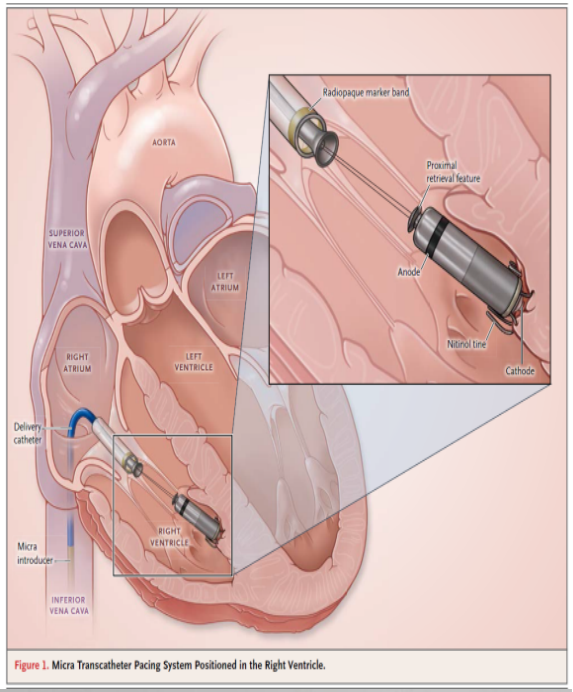
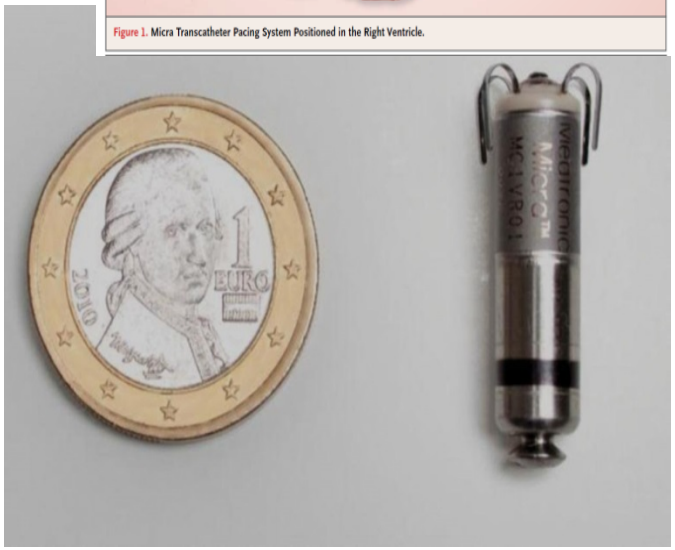


Figure 1. Micra Transcatheter Pacing System Positioned in the Right Ventricle.



Source: , St. Jude Medical, Medtronic

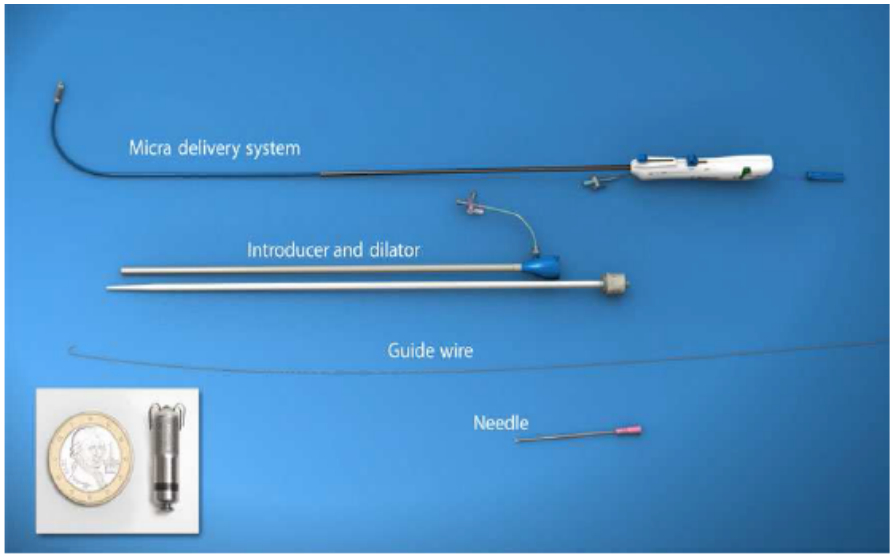
St. Jude Medical

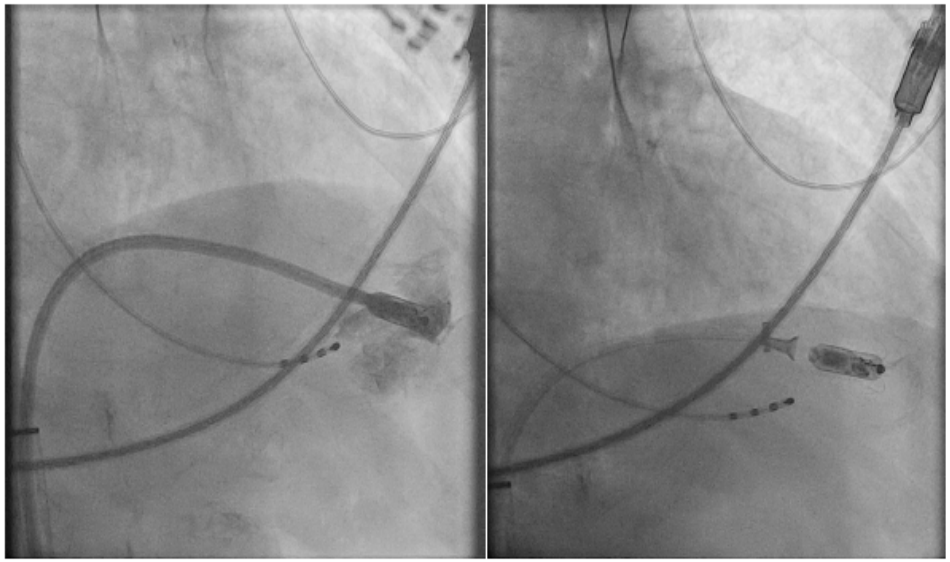
28 th October 2016

St. Jude Medical has pressed **pause on all implants of its Nanostim leadless cardiac pacemakers** due to a battery problem that has resulted in loss of pacing and telemetry in a few devices. The issue has been observed in seven devices (29-37 months after implant) out of approximately 1400 implants around the world—a 0.5% rate.

1.5 Tesla

Leadless pacing- Implantation

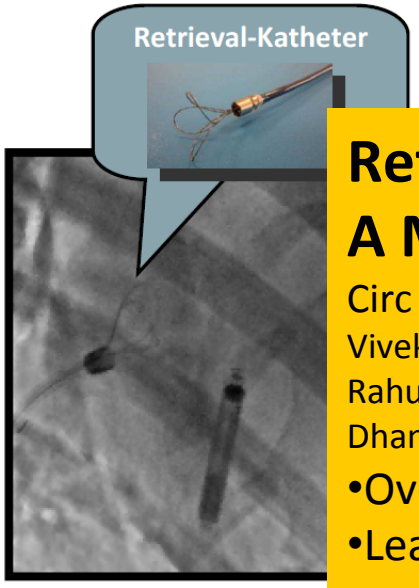




Catheter based delivery in the lower right ventricular septum

Sources.: DHM, Medtronic

Removal seems possible



Quelle: DHM, St. Jude Medical

Retrieval of the Leadless Cardiac Pacemaker
A Multicenter Experience

Circ Arrhythm Electrophysiol 2016, December; 9 (12)

Vivek Y. Reddy, Marc A. Miller, Reinoud E. Knops, Petr Neuzil, Pascal Defaye, Werner Jung, Rahul Doshi, Mark Castellani, Adam Strickberger, R. Hardwin Mead, Harish Doppalapudi, Dhanunjaya Lakkireddy, Matthew Bennett, Johannes Sperzel

- Overall leadless pacemaker retrieval success rate was 94%:
- Leadless cardiac pacemaker implanted <6 weeks, complete retrieval in 100% (n=5/5)
- For those implanted for ≥ 6 weeks, retrieval achieved in 91% (n=10/11)
- Mean duration of time from implant to retrieval attempt 346 days (range, 88–1188 days); nearly two thirds (n=7; 63%) implanted for >6 months
- No procedure-related adverse events at 30 days post retrieval procedure.

Indications

Patients with Indication for VVI (R) Pacing

- Chronic atrial fibrillation with 2 or 3° AV Block

- Sinus rhythm with 2 or 3° AV or BBB block, low level of physical activity or patients with a lifespan < 10 years

- Sinus Bradycardia with infrequent pauses or unexplained syncope

Potential indications

? Physically very active patients (avoid pocket)

? Venous access problems

? S/p pocket infection

? Patients at increased risk for lead failure or infection

? Neurocardiogenic syncope cardioinhibitory type

Data

Nanostim n= 526

Table 1. Patient Characteristics at Baseline and Procedural Characteristics.*

Characteristic	Primary Cohort (N=300)	Total Cohort (N=526)
Patient characteristics		
Age — yr		
Mean	75.7±11.6	75.8±12.1
Range	30–96	19–96
Body-mass index†		
Mean	29.2±7.3	28.7±6.8
Range	15.8–60.3	15.2–60.3
Sex — no. (%)		
Male	193 (64.3)	325 (61.8)
Female	107 (35.7)	201 (38.2)
Race or ethnic group — no. (%)‡		
White	269 (89.7)	478 (90.9)
Black	21 (7.0)	35 (6.7)
American Indian or Alaska Native	1 (0.3)	1 (0.2)
Asian	7 (2.3)	10 (1.9)
Other	2 (0.7)	2 (0.4)
Hispanic or Latino ethnic group — no. (%)‡		
Hispanic or Latino	13 (4.3)	17 (3.2)
Non-Hispanic or non-Latino	287 (95.7)	508 (96.6)
Unknown	0	1 (0.2)

Reddy et al NEJM 2015; 373:1125

Micra n= 725

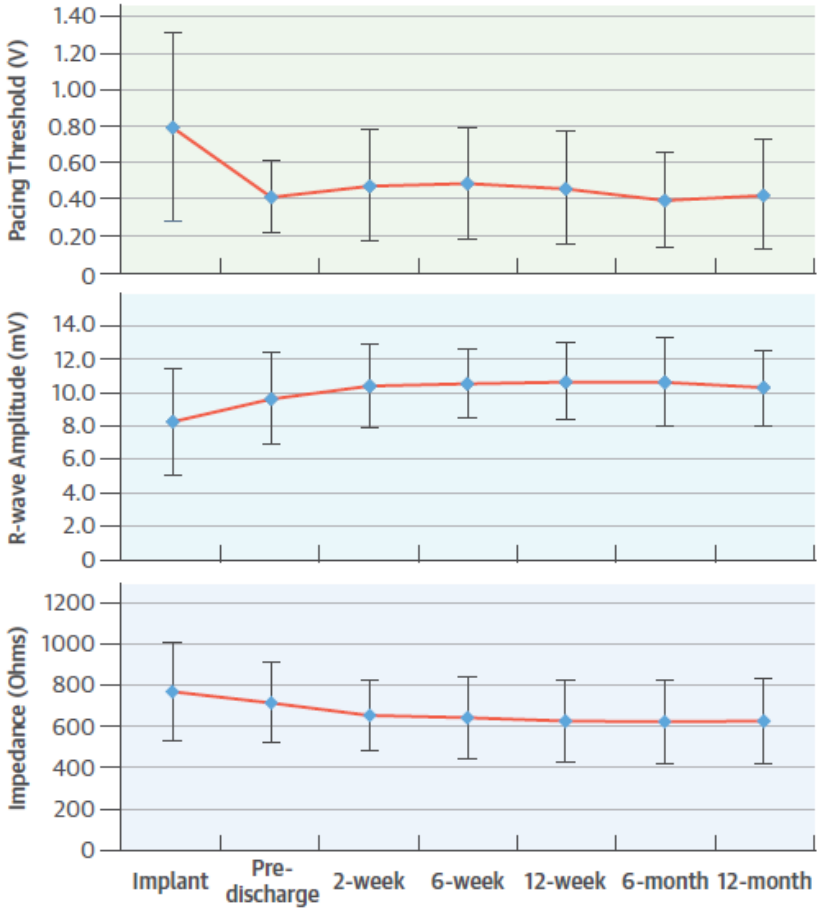
Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Patients Who Underwent Attempted Implantation (N=725)
Age — yr	
Mean	75.9±10.9
Range	19.0–94.0
Sex — no. (%)	
Male	426 (58.8)
Female	299 (41.2)
Left ventricular ejection fraction — %†	
Mean	58.8±8.8
Range	25.0–91.0
Coexisting conditions — no. (%)	
Diabetes	207 (28.6)
Chronic obstructive pulmonary disease	90 (12.4)
Renal dysfunction	145 (20.0)
Left bundle-branch block	98 (13.5)
Vascular disease	53 (7.3)
Coronary artery disease	203 (28.0)
Atrial fibrillation	526 (72.6)
Congestive heart failure	123 (17.0)
Hypertension	570 (78.6)
Valvular disease	306 (42.2)

Reynolds et al , NEJM 2016;374:533

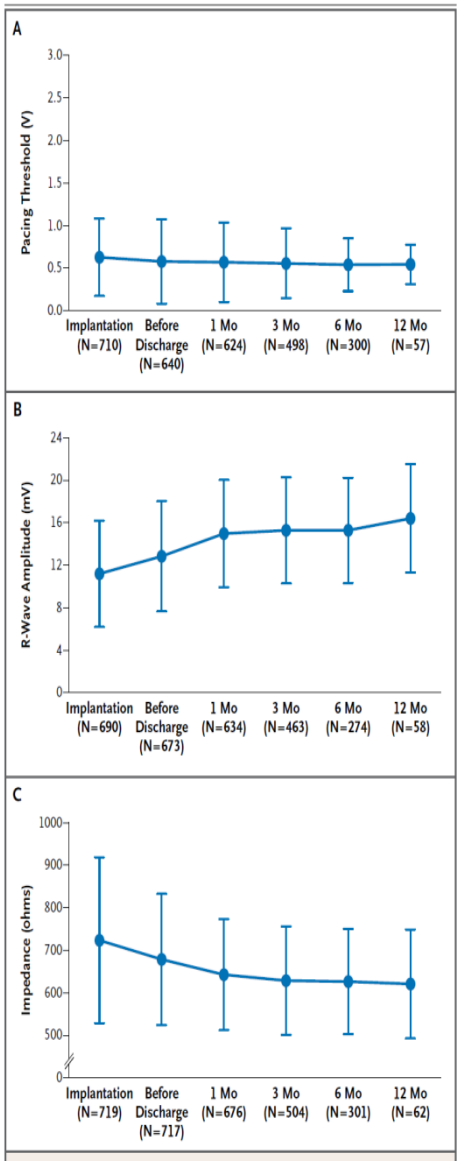
Efficacy

Nanostim



Efficacy endpoint reached in > 90%

Micra



Safety- Nanostim

Table 2. Device-Related Serious Adverse Events.*

Event	Primary Cohort (N=300)			Total Cohort (N=526)		
	No. of Events	No. of Patients	Event Rate %	No. of Events	No. of Patients	Event Rate %
Total	22	20	6.7	40	34	6.5
Cardiac perforation						
Cardiac tamponade with intervention	1	1	0.3	5	5	1.0
Cardiac perforation requiring intervention	1	1	0.3	1	1	0.2
Pericardial effusion with no intervention	2	2	0.7	2	2	0.4
Vascular complication						
Bleeding	2	2	0.7	2	2	0.4
Arteriovenous fistula	1	1	0.3	1	1	0.2
Pseudoaneurysm	1	1	0.3	2	2	0.4
Failure of vascular closure device requiring intervention	0	0	0	1	1	0.2
Arrhythmia during device implantation						
Asystole	1	1	0.3	1	1	0.2
Ventricular tachycardia or ventricular fibrillation	1	1	0.3	2	2	0.4
Cardiopulmonary arrest during implantation procedure	0	0	0	1	1	0.2
Device dislodgement	5	5	1.7	6	6	1.1
Device migration during implantation owing to inadequate fixation	0	0	0	2	2	0.4
Pacing threshold elevation with retrieval and implantation of new device	4	4	1.3	4	4	0.8
Other						
Hemothorax	0	0	0	1	1	0.2
Angina pectoris	0	0	0	1	1	0.2
Pericarditis	1	1	0.3	1	1	0.2
Acute confusion and expressive aphasia	0	0	0	1	1	0.2
Dysarthria and lethargy after implantation	0	0	0	1	1	0.2
Contrast-induced nephropathy	0	0	0	1	1	0.2
Orthostatic hypotension with weakness	1	1	0.3	1	1	0.2
Left-leg weakness during implantation	0	0	0	1	1	0.2
Probable pulmonary embolism	1	1	0.3	1	1	0.2
Ischemic stroke	0	0	0	1	1	0.2

At 6 months:

Device related serious events **in 6.7%;**

- Cardiac perforation in 1.3%
- Device dislodgement in 1.7%
- Threshold elevation in 1.3%
- Vascular complications 1.3%

Safety- Micra

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)

At 6 months

A total of 28 events in 25 patients **(4%)**

- Cardiac injury in 1.6%

Leadless pacing in children

- Safety and feasibility of using this leadless pacemaker in patients younger than 18 years of age **unknown**

- **Size** of the introducer sheath (18 French/23 French) may make its use in children more difficult (complications related to either the femoral access site or catheter manipulation within the right ventricle)

- Devices placed in the smaller right ventricles of children ⇨ **TV-problems** , **proarrhythmia** ?

- Further **miniaturization** required; shorter battery life ?
- **Extractability** (first data in humans about removal of chronically implanted systems; risk of fibrosis higher in children ?)

Leadless pacing in adults with CHD

- Safety and feasibility of using this leadless pacemaker in adult CHD patients **unknown**

- Indications based on adult population indications; single chamber pacing

Unsolved Issues

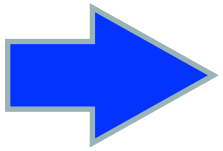
- Morphologically left ventricles (S/p atrial switch) without trabeculation ?

- Retrograde placement in a (single) ventricle ?

- Risk of Thrombosis - anticoagulation management ?

Summary

- Leadless pacing seems an exciting new development
- Electrical performance comparable with transvenous pacemakers
- Acute complications such as tamponade or perforation need to be addressed ⇨ safe(r) implantation techniques
- Long-term issues (thrombogenity, proarrhyhtmia, extractability) need to be addressed/solved



Systems applicable for children currently lacking

Summary

- Leadless pacing s… …velopment
- Ele…

What´s next ?

Smaller devices ?
Leadless atrial devices ?
Communication with ventricular device ?
Leadless pacer and subcutaneous ICD ?
Intravascular ICDs ?

- L… extr…

Systems applicable for children currently lacking

Thank you for your attention
and thank you Christof Kolb !

Conflicts of interest

Lecture fees and travel support

St. Jude Medical
Biosense Webster
Boston Scientific