Boston Scientific

Advancing science for life™

Leadless Pacing Perspective
FDA Circulatory System Devices Panel

February 18, 2016

Agenda

- Unmet Clinical Need
  - VVI(R) pacemaker
  - Leadless pacemaker / S-ICD coordination
- Boston Scientific's Leadless Pacing System
- Safety Considerations
  - Performance criteria: contemporary pacemaker data
  - Encapsulation and device replacement
  - Implanter training
- Benefit-risk Considerations

Unmet Clinical Need

The unmet need for bradycardia therapy:

- Although contemporary VVI pacemakers have been shown to be safe and effective, the combination of a PG + endovascular lead may be associated with risks of:
  - Infection
  - Venous occlusion
  - Tricuspid regurgitation
  - Remedial actions that require lead extraction
- Avoiding the need for a lead directly connecting the subcutaneous space with the endovasculature may help mitigate risks

Unmet Clinical Need (cont.)

The unmet need for patients at risk of sudden death:

- For patients at-risk of SCD without an indication for pacing, an S-ICD may help avoid complications associated with a transvenous (TV) ICD lead
- S-ICD patients[1,2,3] may develop a need for:
  - Pacing support (0.06%-2.4% per year)[4]
  - ATP for recurrent monomorphic VT (0.4%-1.8% per year)[4,5]
- Today, patients requiring ATP or pacing support have only TV options
- A leadless pacing system that could coordinate with an S-ICD offers an alternative to a TV system, while also avoiding the known risks of ICD leads

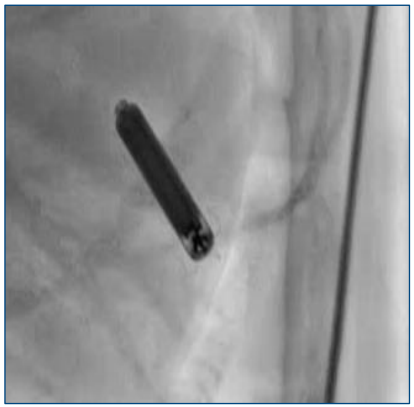
1. Theuns DAMJ, Crozier IG, Barr GS, et al. Longevity of the subcutaneous implantable defibrillator: Long-term follow-up of the European regulatory trial cohort. *Circ Arrhythmia Electrophysiol*. 2015:CIRCEP.115.002953; 06 July 2015 online.
2. Bardy GH, Lee KL, Mark DB, et al. Amiodarone or an implantable cardioverter–defibrillator for congestive heart failure. *N Engl J Med*. 2005;352(3):225-237.
3. Wilkoff BL, Cook JR, Epstein AE, et al. Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator. The Dual Chamber and VVI Implantable Defibrillator (DAVID) Trial. *JAMA.* 2002;288(24):3115-3123.
4. N=882 S-ICD Patients; mean follow-up 22 months. Burke MC, Gold MR, Knight BP, et al. Safety and efficacy of the totally subcutaneous implantable defibrillator: 2-year results from a Pooled Analysis of the IDE Study and EFFORTLESS Registry. *J Am Coll Cardiol*. 2015; 65(16):1605–1615.
5. N=811; mean follow-up 45.5 months. Poole JE, Gold MR. Who should receive the subcutaneous implanted defibrillator? The subcutaneous implantable cardioverter defibrillator (ICD) should be considered in all ICD patients who do not require pacing. *Circ Arrhythm Electrophysiol*. 2013;6:1236-1245.

Boston Scientific - Key Components of Leadless Pacemaker System*

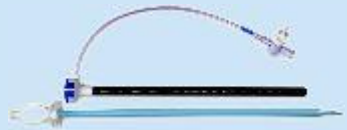
Boston Scientific

Pulse Generator

Delivery



Accessories



Programmer

Retrieval

**Concept device or technology . Not available for sale.*

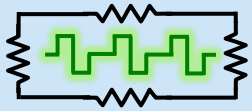
Boston Scientific - Key Components of Leadless Pacemaker / S-ICD Coordinated System*

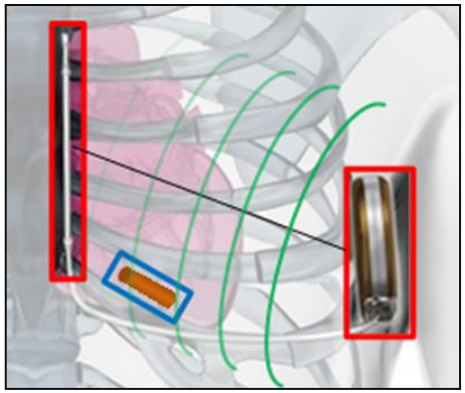
Boston Scientific

Pulse Generator

Delivery

Communication Link





Accessories

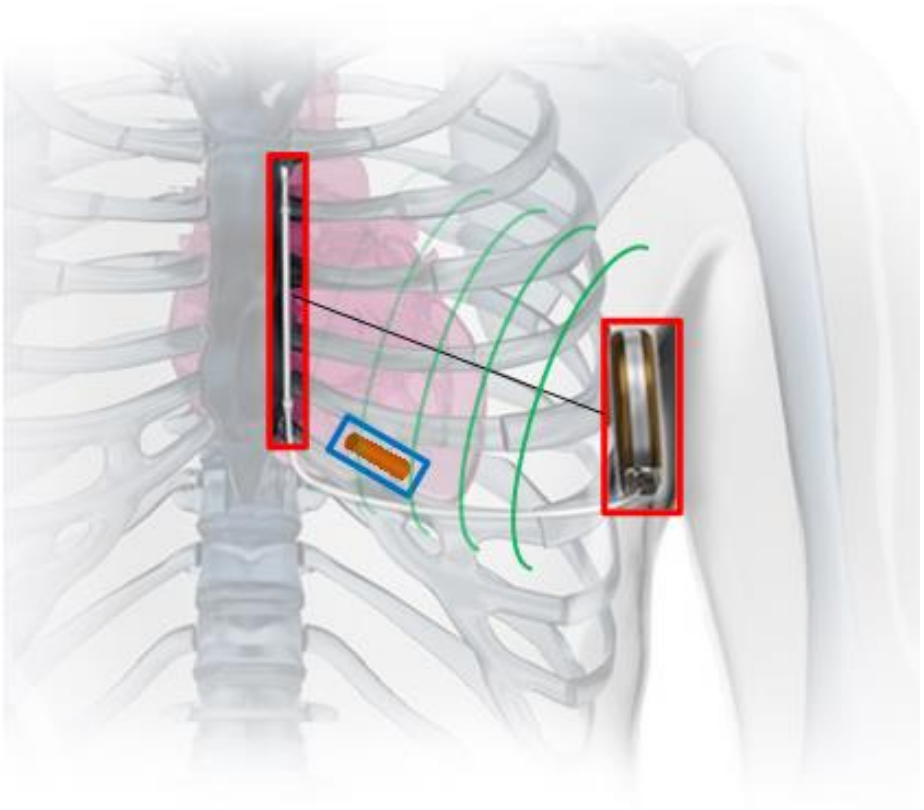
S-ICD

Programmers

Retrieval

*Concept device or technology . Not available for sale.

Boston Scientific
Leadless Pacemaker / S-ICD Coordinated System*

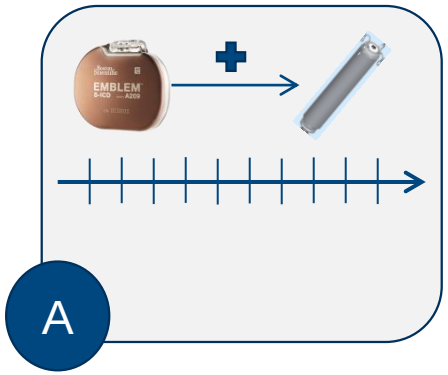


1. Leadless pacemaker will sense and treat bradycardia independently from the S-ICD
2. ATP schemes are built into the leadless pacemaker, but can be activated only by the S-ICD or the programmer
3. S-ICD will continue to sense tachycardia, then command ATP in the leadless pacemaker prior to a shock

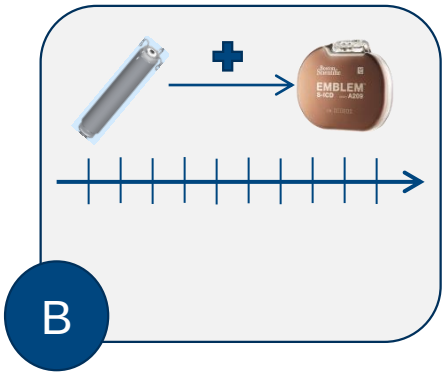
**Concept device or technology . Not available for sale.*

Leadless Pacemaker / S-ICD Coordinated System* Provides Clinical Options

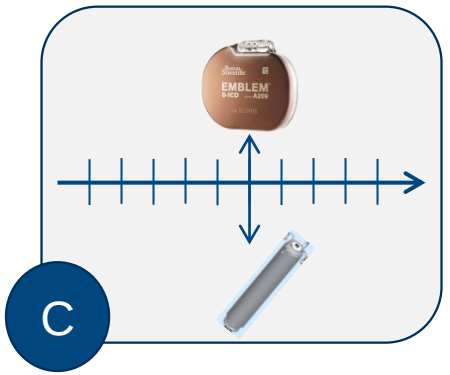
Use cases for a leadless pacemaker with the S-ICD:



- **S-ICD implanted first**
- **Leadless pacemaker implanted later**



- **Leadless pacemaker implanted first**
- **S-ICD implanted later**



- **Leadless pacemaker + S-ICD implanted together**

**Concept device or technology . Not available for sale.*

Leadless Technology Safety Considerations

Boston Scientific

Leadless technology safety considerations include:

- Requirement for TV leads to:
  - Pass an overall freedom from adverse event endpoint
  - Show adequate performance with respect to individual adverse events
- Nature and severity of complications in TV pacing systems vs leadless pacemaker
- Physician and patient information to ensure appropriate risk awareness and avoidance
- Risk of adverse events with leadless pacemaker should be, at worst, comparable to TV pacemaker

Leadless Technology Safety Considerations (cont.)

- Perform a safety endpoint evaluation - compared aggregated rate of all device-related complications vs pre-defined performance goal
- Separately evaluate the components of this aggregated rate to ensure that each one is within the bounds of acceptability

Boston Scientific envisions that a similar approach will be taken for leadless pacemakers as TV pacemakers

Event-specific Performance Goals

Boston Scientific

Data collected from a recently completed large, long-duration TV brady lead trial* can serve as a comparative, contemporary dataset for traditional pacemakers

Major System Complication[1]	Observed Complication Rate through 24 Months[2]		
	Single-chamber PM (N = 213)	Dual-chamber PM with RA Lead Excluded (N = 1143)	Total (N = 1356)
Perforation	0.0%	0.5%	0.4%
Pericardial Effusion	0.6%	0.2%	0.2%
Dislodgment	1.4%	1.1%	1.1%
Embolization	0.0%	0.0%	0.0%
Other (e.g., infection, arrhythmia)	3.8%	5.1%	4.9%

[1]*Definition matches what was used in Micra Trial*
[2]*24-month (BSC) versus 6-month observational period (Micra)*

**Caution: Investigational Device. Limited by US law to investigational use only. Not available for sale.*

Event-specific Performance Goals

Boston Scientific

Data collected from a recently completed large, long-duration TV brady lead trial* can serve as a comparative, contemporary dataset for traditional pacemakers

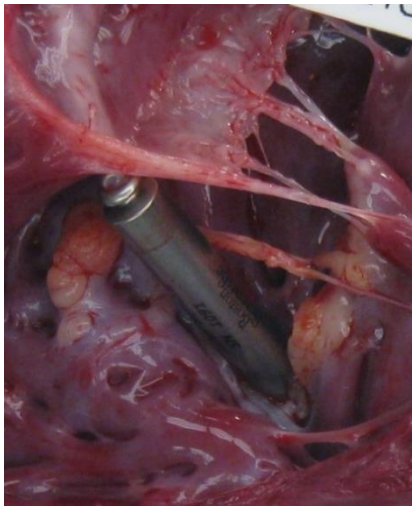
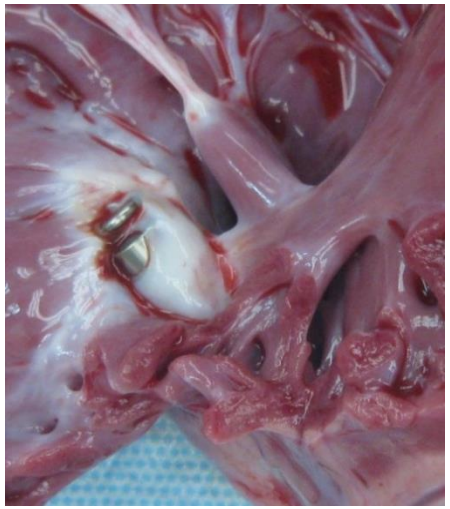
Major System Complication[1]	Observed Complication Rate through 24 Months[2]		
	Single-chamber PM (N = 213)	Dual-chamber PM with RA Lead Excluded (N = 1143)	Total (N = 1356)
Perforation	0.0%	0.5%	0.4%
Pericardial Effusion	0.6%	0.2%	0.2%
Dislodgment	1.4%	1.1%	1.1%
Embolization	0.0%	0.0%	0.0%
Other (e.g., infection, arrhythmia)	3.8%	5.1%	4.9%

[1]*Definition matches what was used in Micra Trial*
[2]*24-month (BSC) versus 6-month observational period (Micra)*

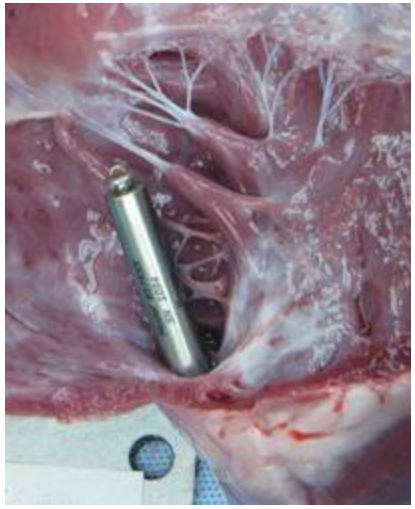
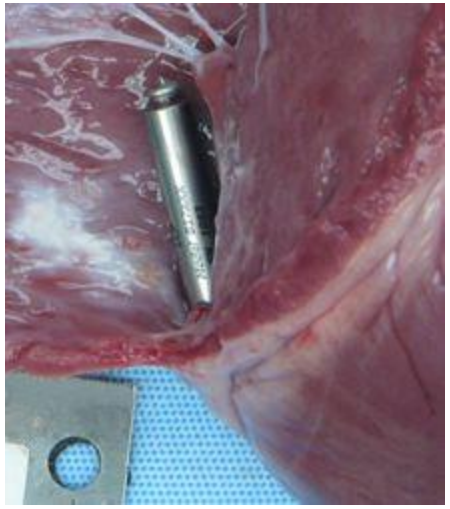
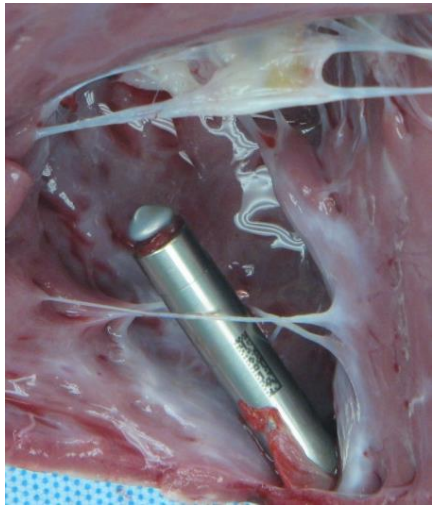
**Caution: Investigational Device. Limited by US law to investigational use only. Not available for sale.*

Retrieval / Extraction Challenges - Encapsulation

Canine Chronic Functional*
(90 days post implant)


Ovine Chronic Functional*
(90 days post implant)

**Concept device or technology . Not available for sale.*

Device Replacement Considerations

Clinician / Patient shared decision making related to options

Physician Training Considerations

Leadless delivery tools and techniques differ significantly

Boston Scientific has a long history of training physicians on novel technologies

- Endocardial ICD leads
- Cardiac Resynchronization Therapy
- S-ICD
- WATCHMAN

Phase I

Self-Study and Expectation Setting

Phase II

Professional Training Event

Phase III

Initial Cases and Building Confidence through Cadence

Phase IV

Transition to Independence

Benefit-risk Considerations

Boston Scientific

Benefit-risk considerations differ according to the clinical use:

- For VVI pacing, a well-established therapy already exists with excellent short- and long-term safety
- Intrinsic risks associated with endovascular leads connected to a subcutaneous pocket
- For appropriately selected patients at high risk of complications from endovascular leads, leadless pacing will offer a positive benefit-risk as long as the rate of life-threatening complications can be proven to be acceptably low

Benefit-risk Considerations (cont.)

For patients with an S-ICD who manifest a need for ATP or brady pacing, the benefit vs risk of a leadless pacemaker / S-ICD Coordinated System* needs to be evaluated against the alternative of device explant with implantation of a new TV-ICD

For both of these scenarios, a patient-centered approach to individualized benefit-risk assessment will be of paramount importance

**Concept device or technology . Not available for sale.*

Complication Rates from TV Studies

Data from 8 prospective pre-market pacemaker lead approval trials[1] (N=3761) were pooled to establish representative TV rates for various event types

	Weighted Mean	Range
Perforation	0.3%	0.0 – 1.7%
Pericardial Effusion	0.4%	0.0 – 1.1%
Dislodgment	1.5%	0.8 – 2.1%

[1]Data source:

- Boston Scientific INGEVITY™ Active Fixation and Passive Fixation Pace/Sense Lead Clinical Study. 12-month Follow-up Clinical Report.*
- Boston Scientific ImageReady™ MR Conditional Pacing System (SAMURAI) Clinical Study. MRI Visit +1-month Follow-up Clinical Report.*
- Medtronic CapSureFix® Novus 5076 Technical Manual.
- St. Jude Medical Tendril® SDX Model 1488T/TC/K User's Manual.
- Boston Scientific Clinical Report of the FLEXTEND™ Straight Bipolar Lead Models 4080/4081/4082.
- Medtronic SelectSecure® 3830 Technical Manual.
- Medtronic Revo MRI™ SureScan™ Pacing System Clinical Study. Summary of clinical results.
- Gimbel JR, Bello D, Schmitt M, et al. Randomized trial of pacemaker and lead system for safe scanning of 1.5 Tesla. *Heart Rhythm*. 2013;10:685-691.
- Wilkoff BL, Bello D, Taborsky M, et al. Magnetic resonance imaging in patients with a pacemaker system designed for the magnetic resonance environment. *Heart Rhythm*. 2011;8:65-73.

**Caution: Investigational Device. Limited by US law to investigational use only. Not available for sale.*