Boston Scientific

CLINICAL SUMMARY

INGEVITY™ STUDY

CAUTION: Federal law restricts this device to sale by or on the order of a physician trained or experienced in device implant and follow-up procedures.

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CLINICAL STUDY - SUMMARY OF INGEVITY™ ACTIVE FIXATION AND PASSIVE FIXATION PACE/SENSE LEAD CLINICAL STUDY

The INGEVITY Active Fixation and Passive Fixation Pace/Sense Lead Clinical Study (hereafter referred to as the INGEVITY study) was designed to collect data to establish the safety, performance, and effectiveness of INGEVITY active fixation and passive fixation pace/sense leads.

STUDY DESIGN

The INGEVITY study is a prospective, non-randomized, multi-center, global clinical study continuing through 2018. Follow-up visits were scheduled for pre-discharge, 1 month, 3 months, and 12 months post implant, then annually for 5 years post-implant, to study the Safety and Effectiveness Endpoints. This summary includes data collected through the post-implant follow-up period date referenced in Results on page 3 .

METHODS

Subject Selection

The study enrolled patients with approved indications for a pacemaker or cardiac resynchronization therapy-pacemaker (CRT-P) implantable pulse generator who were implanted with an INGEVITY lead(s) and a Boston Scientific pulse generator as their initial (de novo) pacing system implant. Only patients who met all of the inclusion criteria, and none of the exclusion criteria, were enrolled.

Inclusion and Exclusion Criteria

Inclusion Criteria

- Subject is willing and capable of providing informed consent
- Subject must have the INGEVITY lead(s) and a Boston Scientific pulse generator as their initial (de novo) pacing system implants
- Subject has a Class I or II indication for implantation of a single [VVI(R) only] or dual chamber pacemaker or a CRT-P system according to the American College of Cardiology (ACC)/American Heart Association (AHA)/Hearth Rhythm Society (HRS), or European Society of Cardiology (ESC) guidelines
- Subject is willing and capable of participating in all testing/visits associated with this clinical study at an approved clinical study center and at the intervals defined by this protocol
- Subject is age 18 or above, or of legal age to give informed consent specific to state and national law

Exclusion Criteria

- Subject has or has had any pacing or Intra Cardiac Device (ICD) system implants
- Subjects who are intended to receive an AAI(R) pulse generator
- Subject has a known or suspected sensitivity to dexamethasone acetate (DXA)
- Subject has a mechanical tricuspid heart valve
- Subject is enrolled in any other concurrent study, with the exception of local mandatory governmental registries and observational studies/registries that are not in conflict
- Subjects with documented permanent or persistent atrial fibrillation (AF)[1] where the physician intends to implant dual chamber pulse generator [single chamber VVI(R) pulse generators in these subjects is acceptable]
- Subject is currently on the active heart transplant list

1. Calkins H, et al. HRS/EHRA/ECAS expert Consensus Statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures and follow-up. *Heart Rhythm* 4:816-861, 2007

- Subject has documented life expectancy of less than 12 months
- Women of childbearing potential who are or might be pregnant at the time of study enrollment or INGEVITY lead implant (method of assessment upon physician's discretion)
- Subjects currently requiring dialysis

INGEVITY Study Endpoints

Safety Endpoints

The following endpoints were evaluated to establish safety of the INGEVITY lead.

- Safety Endpoint 1: Lead-related Complication-Free Rate from Implant through Three Months Post-Implant
- Safety Endpoint 2: Lead-related Complication-Free Rate from Three Months Post-Implant through Twelve Months Post-Implant
- Safety Endpoint 3: Hazard of Lead-Related Complications over Time
- Ancillary Safety Endpoint (Long-term Safety evaluated upon study completion): Lead-related Complication-Free Rate from 3 Months through 60 Months Post Implant

Lead-related complications were defined as lead-related adverse events that resulted in death, serious injury, correction using invasive intervention, or permanent loss of device functions. Lead-related adverse events included, but were not limited to, the following based on the AdvaMed Industry Guidance for Uniform Reporting of Clinical Performance of Cardiac Rhythm Management Pulse Generators and Leads, and in accordance with the FDA Guidance:

- Cardiac perforation requiring surgical intervention
- Cardiac perforation not requiring surgical intervention
- Conductor fracture/helix damage
- Lead dislodgement
- Failure to capture
- Oversensing
- Failure to sense (undersensing)
- Insulation breach
- Abnormal pacing impedance
- Extracardiac stimulation

Lead-related complications associated with attempted INGEVITY lead implants counted toward the Safety Endpoints. Lead-related adverse events that were not a complication counted as a complication if intravenous (IV) drug therapy was necessary to treat the event. IV drug therapy that occurred concomitantly but unrelated to the lead-related adverse event did not count as a lead-related complication. Complications involving an INGEVITY lead that occurred as a result of a procedure unrelated to that INGEVITY lead did not count toward this Safety Endpoint.

Effectiveness Endpoints

The following endpoints were evaluated to establish effectiveness of the INGEVITY lead. These endpoints were analyzed separately by lead fixation type (active, passive) and chamber (RA, RV).

- Effectiveness Endpoint 1: Pacing Threshold at 0.5 ms pulse width at Three Months Post-Implant
- Effectiveness Endpoint 2: Sensed Amplitude at Three Months Post-Implant
- Effectiveness Endpoint 3: Pacing Impedance at Three Months Post-Implant

RESULTS

Results included in this INGEVITY study summary were collected through February 17, 2016. Some subjects contributed data for both a right atrial lead and a right ventricular lead. If a follow-up visit was missed, the subject remained eligible to contribute data at subsequent follow-up visits. A summary of the subject disposition is shown in Figure 1 on page 3.

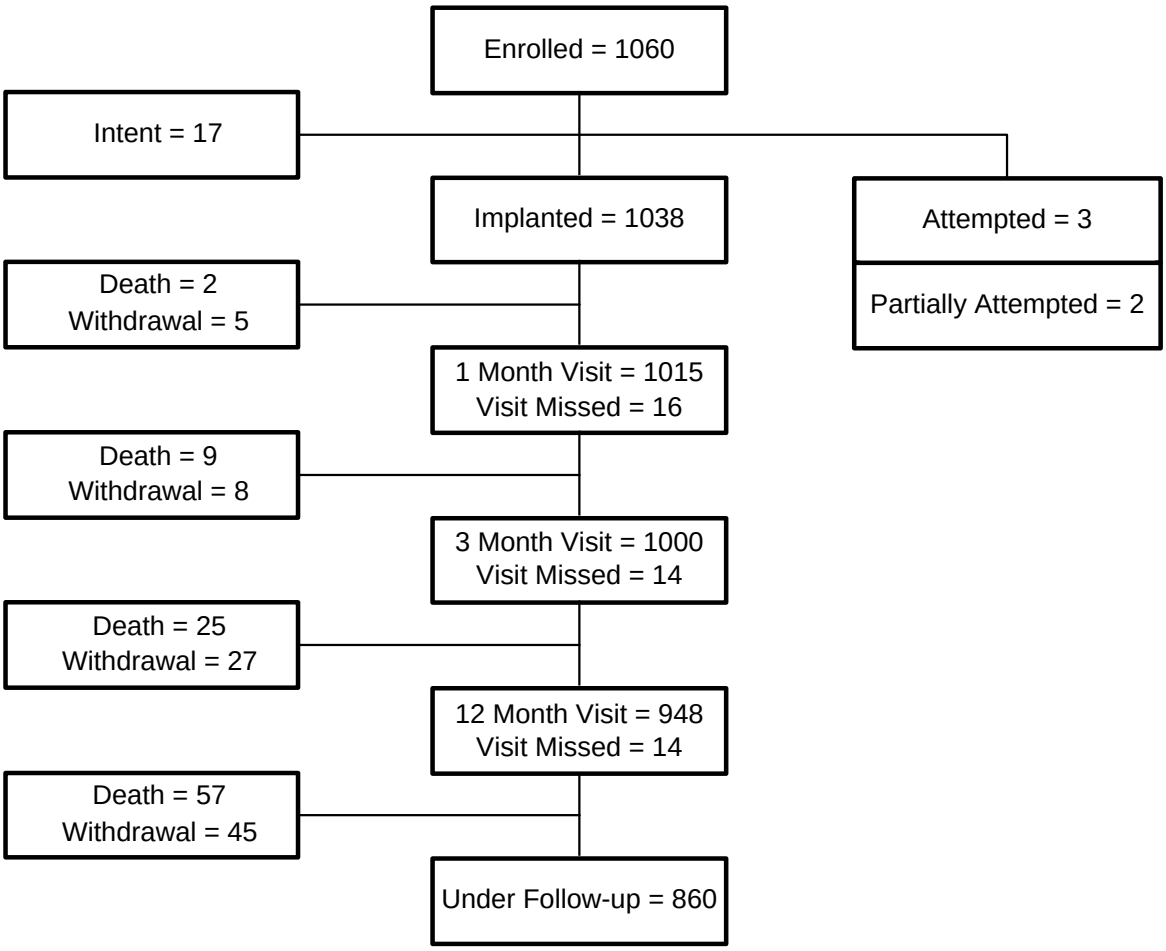


Figure 1. Subject Disposition

Subject Demographics

A total of 1060 subjects were enrolled at 77 centers in the study. See Table 1 on page 4 for a summary of the subject demographics. Overall, the average age of the subjects at implant was 74.3 ± 10.6 years, with an overall gender ratio of 55% males to 45% females. In total, 1270 active fixation and 329 passive fixation leads were implanted or implant was attempted, with 563 leads placed in the right atrium and 1036 leads placed in the right ventricle.

Table 1. Subject Demographics

Characteristic	Measurement	All Enrolled Subjects (N=1060)	Implanted or Attempted Subjects	
			Pacemaker (N=1006)	CRT-P (N=35)
Pulse Generator [N (%)]	Single Chamber Pacemaker	176 (17)	176 (17)	0 (0)
	Dual Chamber Pacemaker	830 (78)	830 (83)	0 (0)
	CRT-P	35 (3)	0 (0)	35 (100)
	No Device	19 (2)	0 (0)	0 (0)
Age at Implant (years)	N	1060	1006	35
	Mean ± SD	74.3 ± 10.6	74.3 ± 10.5	74.5 ± 13.4
	Range	23.0 - 98.0	23.0 - 98.0	24.0 - 88.0
Gender [N (%)]	Male	582 (55)	554 (55)	20 (57)
	Female	478 (45)	452 (45)	15 (43)
NYHA Class [N (%)]	I	138 (37)	136 (40)	1 (3)
	II	149 (40)	137 (41)	12 (39)
	III	44 (12)	27 (8)	16 (52)
	IV	3 (1)	1 (0)	2 (6)
	No-HF Subject	39 (10)	36 (11)	0 (0)
LVEF (%)	N	812	765	34
	Mean ± SD	57.4 ± 10.4	58.6 ± 8.9	31.8 ± 10.2
	Range	15.0 - 85.0	20.0 - 85.0	15.0 - 55.0
QRS Duration (ms)	N	957	908	34
	Mean ± SD	111 ± 28	110 ± 28	140 ± 29
	Range	55 - 261	55 - 261	85 - 202
Body Mass Index (kg/m^2)	N	1052	1000	35
	Mean ± SD	28.5 ± 6.5	28.5 ± 6.4	29.2 ± 5.4
	Range	10.7 - 105.3	10.7 - 105.3	19.4 - 43.9

Study Endpoint Results

Safety and Effectiveness Endpoint results are summarized below.

Safety Endpoint Results

A summary of the Safety Endpoints results is shown in the Table 2 on page 5, with details provided in the following sections.

Table 2. Summary of Safety Endpoints Results

Safety Endpoint	Measurement	Performance Goal	Result (Confidence Limit)	Conclusion
1	0-3 month Lead-related Complication Free Rate	> 91.4%	98.4% (95% One-Sided Lower Confidence Limit = 97.7%)	Endpoint Met
2	3-12 month Lead-related Complication Free Rate	> 94%	99.7% (95% One-Sided Lower Confidence Limit = 99.4%)	Endpoint Met
3	0-12+ month Lead Hazard Stability (Weibull shape parameter*)	< 1	0.23 (95% One-Sided Upper Confidence Limit = 0.30)	Endpoint Met

* A shape parameter < 1 obtained from a Weibull survival model describes a lead with a decelerating hazard of lead-related complications over time.

Safety Endpoint 1: Lead-related Complication-free Rate from Implant through Three Months Post-implant.

Safety of the INGEVITY lead was first evaluated by the lead-related complication-free rate (CFR) from lead implant through the three month post implant follow-ups, with a performance goal of > 91.4%. The CFR from 0 through 3 months for all INGEVITY leads was 98.4%, with a one-sided 95% lower confidence limit of 97.7% (see Figure 2 on page 5 and Table 3 on page 5).

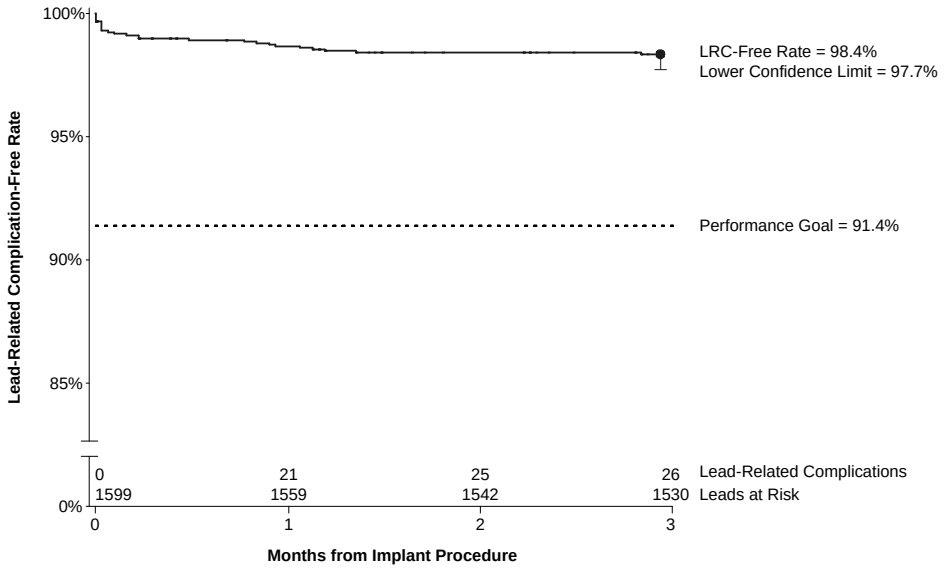


Figure 2. Safety Endpoint 1 Complication-free Rate from 0-3 months post-implant. Results for all leads.

The results were further analyzed by lead fixation type and heart chamber (see Table 3 on page 5).

Table 3. Safety Endpoint 1 Complication-free Rate from 0-3 months post-implant. Results for all groups of leads.

Group	N	Lead-Related Complication Free Rate 0-3 months	95% One-Sided Lower Confidence Limit
All Leads	1599	98.4%	97.7%
- RV Active Fixation	828	98.5%	97.7%

Group	N	Lead-Related Complication Free Rate 0-3 months	95% One-Sided Lower Confidence Limit
- RA Active Fixation	442	98.4%	97.0%
- RA/RV Passive Fixation	329	97.9%	96.1%

Since the lower confidence limit was greater than the performance goal of 91.4% for all groups, the data support the safety of the INGEVITY lead through the 3 month post-implant period.

Safety Endpoint 2: Lead-related Complication-free Rate from Three Months Post-implant through Twelve Months Post-implant.

Safety of the INGEVITY lead was next evaluated by the lead-related complication-free rate (CFR) from 3 months post-implant through 12 months post-implant, with a performance goal of > 94%. The CFR from 3 through 12 months for all INGEVITY leads was 99.7%, with a one-sided 95% lower confidence limit of 99.4% (see Figure 3 on page 6 and Table 4 on page 6).

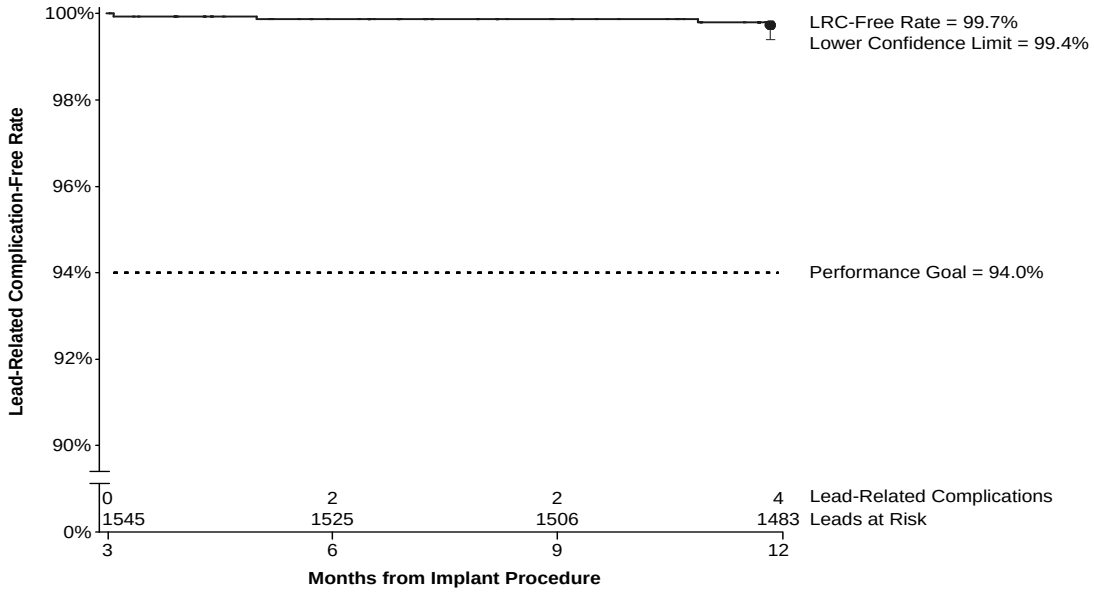


Figure 3. Safety Endpoint 2 Complication-free Rate from 3-12 months post-implant. Results for all leads.

The results were further analyzed by lead fixation type and heart chamber (see Table 4 on page 6).

Table 4. Safety Endpoint 2 Complication-free Rate from 3-12 months post-implant. Results for all groups of leads.

Group	N	Lead-Related Complication Free Rate 3-12 months	95% One-Sided Lower Confidence Limit
All Leads	1545	99.7%	99.4%
- RV Active Fixation	804	99.5%	98.8%
- RA Active Fixation	424	100.0%	100.0%
- RA/RV Passive Fixation	317	100.0%	100.0%

Since the lower confidence limit was greater than the performance goal of 94% for all groups, the data support the safety of the INGEVITY lead through the 12 month post-implant period.

Safety Endpoint 3: Hazard of Lead-related Complications over Time

The hazard of lead-related complications over time was analyzed by Weibull regression analysis of all Safety Endpoint data collected through the post-implant follow-up period date referenced in Results on page 3 (median follow-up time = 32 months). The exact follow-up time in the post-implant period for each lead was included in the analysis. A Weibull shape greater than one (>1), equal to one (=1) and less than one (<1) indicated accelerating, constant, and decelerating hazard over time, respectively.

A Weibull shape parameter of 0.23 derived from analysis of lead-related complications over the post-implant follow-up period indicated a decelerating hazard rate over time (see Figure 4 on page 7). The figure presents the smooth modeled Weibull hazard resulting from the Weibull regression analysis overlayed on top of the raw observed lead-related complication hazard data. The corresponding one-sided 95% upper confidence limit was 0.30.

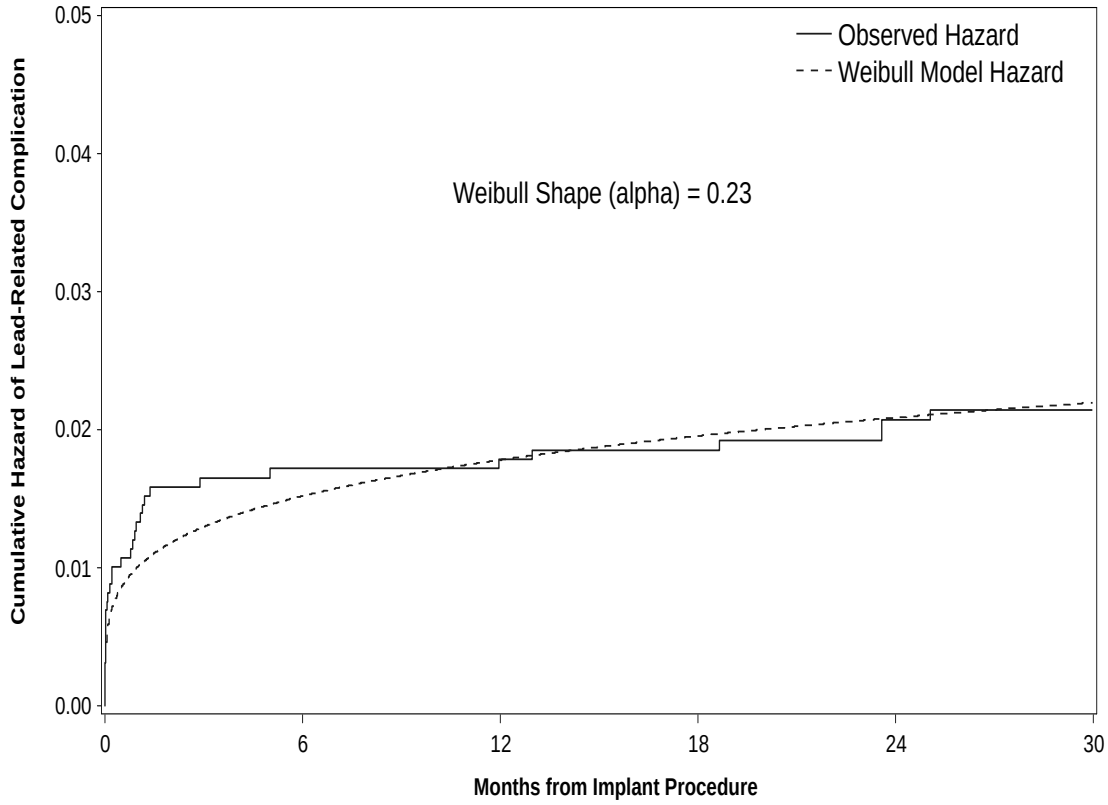


Figure 4. Safety Endpoint 3 Hazard of Lead-related Complications over Time. Results for all leads.

The results were further analyzed by lead fixation type and heart chamber (see Table 5 on page 7).

Table 5. Safety Endpoint 3 Hazard of Lead-related Complications over Time. Results for all groups of leads.

Group	Weibull Shape Parameter (Alpha)	95% One-Sided Upper Confidence Limit
All Leads	0.23	0.30
- RV Active Fixation	0.24	0.35
- RA Active Fixation	0.32	0.54

Group	Weibull Shape Parameter (Alpha)	95% One-Sided Upper Confidence Limit
- RA/RV Passive Fixation	0.15	0.28

Since the hazard of lead-related complications decelerated over the course of the follow-up period, the data support the safety of the INGEVITY lead.

Effectiveness Endpoint Results

A summary of the Effectiveness Endpoints results is shown in the table below (Table 6 on page 8), with details, including results for lead fixation type and heart chamber, provided in the following sections.

Table 6. Summary of Effectiveness Endpoints Results

Effectiveness Endpoint	Measurement	Performance Goal	Result ± SD (Confidence Limit)	Conclusion
1	3 month Pacing Threshold	< 1.5 V	0.67 V ± 0.33 V (Upper One-sided 95% Confidence limit = 0.69)	Endpoint Met
2	RA 3 month Sensed Amplitude	> 1.5 mV	4.8 mV ± 2.6 mV (Lower One-sided 95% Confidence limit = 4.6)	RA Endpoint Met
	RV 3 month Sensed Amplitude	> 5.0 mV	16.5 mV ± 6.5 mV (Lower One-sided 95% Confidence limit = 16.2)	RV Endpoint Met
3	3 month Pacing Impedance	300 - 1300 Ω	773 Ω ± 155 Ω (90% Confidence Interval = 766, 779)	Endpoint Met

Effectiveness Endpoint 1: Pacing Threshold at 0.5 ms Pulse Width at Three Months Post-implant

The first aspect of effectiveness of the INGEVITY lead was determined by evaluation of bipolar pacing thresholds at a 0.5 ms pulse width at 3 months post-implant. Only leads with a measurement taken at the 3 month follow-up were included in the analysis.

The mean pacing threshold for a total of 1482 threshold measurements collected at the 3 month follow-up was 0.67 V with an upper one-sided 95% confidence limit of 0.69 V, resulting in a p-value < 0.001 (see Table 7 on page 8). A total of 98.5% of threshold measurements were at or below the performance goal value of 1.5 V.

The results were further analyzed by lead fixation type (active, passive) and chamber (RA, RV) (see Table 7 on page 8).

Table 7. Effectiveness Endpoint 1 Pacing Threshold at 0.5 ms pulse width at 3 months post-implant. Results for all groups of leads.

Group	N	Mean Pacing Threshold V ± SD	Upper One-sided 95% Confidence Limit
All Leads	1482	0.67 ± 0.33	0.69
- RV Active Fixation	782	0.68 ± 0.33	0.69
- RA Active Fixation	394	0.75 ± 0.39	0.78
- RA/RV Passive Fixation	306	0.57 ± 0.19	0.59

Since for all cases the mean pacing threshold obtained at 3 months post-implant was significantly lower than the performance goal, the data from analysis of all leads, and from analyses of lead fixation type and chamber, support the effectiveness of the INGEVITY lead at 3 months post-implant.

Effectiveness Endpoint 2: Sensed Amplitude at Three Months Post-implant

The second aspect of effectiveness of the INGEVITY lead was determined by examination of sensed amplitudes at 3 months post-implant. Analysis was performed separately for each heart chamber. Leads that did not have P- or R-wave sensed amplitude data collected at the 3 month follow-up were not included in the analysis of P- and R-waves, respectively.

A total of 1435 sensed amplitude measurements (521 in the right atrium and 914 in the right ventricle) were taken at the 3 month follow-up visit and included in the endpoint analysis. The mean sensed amplitude in the right atrium was 4.8 mV with a lower one-sided 95% confidence limit of 4.6 mV, resulting in a p-value < 0.001 (see Table 8 on page 9). The mean sensed amplitude in the right ventricle was 16.5 mV with a lower one-sided 95% confidence limit of 16.2 mV, resulting in a p-value < 0.001 (see Table 8 on page 9). A total of 91.6 % of measurements in the atrium and 96.4 % of measurements in the ventricle were at or above the performance goals of 1.5 mV and 5.0 mV, respectively.

Table 8. Effectiveness Endpoint 2 Sensed Amplitude at 3 months post-implant. Results for all groups of leads.

Group	N	Mean Sensed Amplitude mV ± SD	Lower One-sided 95% Confidence Limit
All Right Atrial Leads	521	4.8 ± 2.6	4.6
- RA Active fixation	409	4.8 ± 2.7	4.6
- RA Passive fixation	112	4.7 ± 2.5	4.3
All Right Ventricular Leads	914	16.5 ± 6.5	16.2
- RV Active fixation	738	16.7 ± 6.5	16.3
- RV Passive fixation	176	16.0 ± 6.5	15.2

Since the mean sensed amplitude obtained in both the right atrium and the right ventricle at 3 months post-implant was significantly greater than the respective performance goals, these data also support the effectiveness of the INGEVITY lead at 3 months post-implant.

Effectiveness Endpoint 3: Pacing Impedance at Three Months Post-implant

The third aspect of effectiveness of the INGEVITY lead was determined by analysis of pacing impedance at 3 months post-implant. Leads that did not have pacing impedance values collected at 3 months post-implant were not included in this analysis.

A total of 1526 pacing impedance measurements were taken at the 3 month follow-up visit and included in the endpoint analysis. The mean pacing impedance was 773 Ω with a confidence interval of 776 to 779 Ω, between the performance goals of 300 and 1300 Ω, resulting in a p-value < 0.001 (see Table 9 on page 9). A total of 98.6% of measurements were observed to be between the performance goals of 300 and 1300 Ω. The results were further analyzed by lead fixation type (active, passive) and chamber (RA, RV) (see Table 9 on page 9).

Table 9. Effectiveness Endpoint 3 Pacing Impedance at 3 Months Post-implant. Results for all groups of leads.

Group	N	Mean Pacing Impedance Ω ± SD	90% Confidence Interval
All Leads	1526	773 ± 155	(766, 779)
- RV Active Fixation	795	824 ± 158	(815, 834)
- RA Active Fixation	420	711 ± 139	(700, 722)
- RA/RV Passive Fixation	311	724 ± 116	(713, 734)

The overall mean pacing impedance obtained at 3 months post-implant for all groups of leads was within the performance goal range, and supports the effectiveness of the INGEVITY lead at 3 months post-implant.

ADVERSE EVENTS SUMMARY

INGEVITY Study

As of February 17, 2016, of the 1041 implanted or attempted subjects, 92.2% were free from adverse events related to the implant procedure, and 95.4% and 97.7% were free from adverse events related to the INGEVITY RA and RV leads, respectively. A summary of Adverse Events by Complication and Observation is shown in Table 10 on page 10. A complication was defined as an adverse event that resulted in death, serious injury, correction using invasive intervention, or permanent loss of device functions.

Table 10. Adverse Events Summary

Relationship	Total		Classification			
			Complication		Observation	
	Events	Subjects (%)	Events	Subjects (%)	Events	Subjects (%)
Total (N at risk = 1041)	3464	789 (75.8%)	1150	497 (47.7%)	2293	673 (64.6%)
PG (N at risk = 1041)	47	41 (3.9%)	9	8 (0.8%)	38	33 (3.2%)
RA Lead - INGEVITY-related (N at risk = 564)	27	26 (4.6%)	14	14 (2.5%)	13	12 (2.1%)
RA Lead - Other (N at risk = 858)	16	15 (1.7%)	10	10 (1.2%)	6	6 (0.7%)
RV Lead - INGEVITY-related (N at risk = 1041)	31	24 (2.3%)	23	16 (1.5%)	8	8 (0.8%)
RV Lead - Other (N at risk = 1041)	1	1 (0.1%)	1	1 (0.1%)	0	0 (0.0%)
LV Lead (N at risk = 47)	9	8 (17.0%)	1	1 (2.1%)	8	7 (14.9%)
Procedure (N at risk = 1041)	92	81 (7.8%)	28	27 (2.6%)	64	57 (5.5%)
Cardiovascular - HF (N at risk = 1041)	237	140 (13.4%)	148	95 (9.1%)	89	72 (6.9%)
Cardiovascular - Non-HF (N at risk = 1041)	1046	528 (50.7%)	217	166 (15.9%)	829	462 (44.4%)
Non-cardiovascular (N at risk = 1041)	1783	542 (52.1%)	666	342 (32.9%)	1114	418 (40.2%)
Other (N at risk = 1041)	157	129 (12.4%)	33	32 (3.1%)	124	103 (9.9%)
Unclassified (N at risk = 1041)	18	17 (1.6%)	0	0 (0.0%)	0	0 (0.0%)

Lead-related Safety Data from INGEVITY and SAMURAI Studies

Additional data applicable to the INGEVITY lead were collected from another Boston Scientific clinical study, the SAMURAI Clinical study, which was designed to confirm the safety, performance, and effectiveness of the ImageReady™ MR Conditional Pacing System (hereafter referred to as the ImageReady System). INGEVITY MRI pace/sense leads are a component of the ImageReady System, and are identical in design to INGEVITY pace/sense leads, with the exception of the product-specific markings. Therefore, lead-related safety data collected in the SAMURAI study are applicable to INGEVITY pace/sense leads.

The table below (Table 11 on page 11) is a summary of comparable safety data across the two studies. Data are presented as the “number of leads with events/total number of leads eligible for safety analysis (%

of total)". The median follow-up time for the INGEVITY study was 32 months, and the median follow-up time for the SAMURAI study was 23 months.

Table 11. Summary of Safety Data for the INGEVITY study and the SAMURAI study

Adverse Event	Leads Included	INGEVITY	SAMURAI	Total of both
Lead-Related Adverse Event	All Leads	67/1599 (4.19%)	33/665 (4.96%)	100/2264 (4.42%)
- Lead-Related Complication	All Leads	34/1599 (2.13%)	20/665 (3.01%)	54/2264 (2.39%)
Dislodgement	All Leads	21/1599 (1.31%)	8/665 (1.20%)	29/2264 (1.28%)
Perforation/Pericardial Effusion	Active Fixation Leads	4/1270 (0.31%)	7/563 (1.24%)	11/1833 (0.60%)
- Perforation	Active Fixation Leads	0/1270 (0.00%)	7/563 (1.24%)	7/1833 (0.38%)
- Pericardial Effusion	Active Fixation Leads	4/1270 (0.31%)	0/563 (0.00%)	4/1833 (0.22%)
Conductor Coil Fracture	All Leads	2*/1599 (0.13%)	0/665 (0.00%)	2/2264 (0.09%)

*Two conductor coil fractures occurred in the INGEVITY study, and were classified as ventricular lead fractures at the costoclavicular junction, consistent with subclavian crush.
Note: The leads eligible for safety analysis include a maximum of one lead per subject per chamber.

Similar lead-related adverse events results were obtained in both the INGEVITY study and the SAMURAI study. Therefore, the data from the SAMURAI study further support the safety of the INGEVITY lead.

DEVICE DEFICIENCIES SUMMARY

The INGEVITY study and the SAMURAI study each collected device deficiencies. Per ISO 14155, a device deficiency was defined as any inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. Device deficiencies include malfunctions, misuse or use errors, and inadequate labeling. Per ISO 14155, device deficiencies and adverse events have unique definitions. Therefore, device deficiencies were separately reported from adverse events (see adverse events definition in "Safety Endpoints" on page 2).

Table 12 on page 12 is a summary of device deficiencies reported in the INGEVITY study, the SAMURAI study, and the two studies combined. Data are presented as the "number of leads with deficiencies/total number of leads implanted and attempted (% of total)". The rate of occurrence of device deficiencies across both studies was 6.5%. Some examples of device deficiencies include poor visibility of suture sleeve, inability to place the lead, and difficulty with helix extension/retraction. The most common device deficiency observed was difficulty with helix extension/retraction, 3.9% for the INGEVITY study, 7.2% for the SAMURAI study, and 4.9% across both studies.

Some of these helix extension/retraction device deficiencies resulted in lead conductor coil breaks, which were consistent with acute overload and not flex fatigue fracture. The rate of occurrence of lead conductor coil breaks was 1.6% for the INGEVITY study, 3.7% for the SAMURAI study, and 2.2% across both studies. In each case of conductor coil break, inadequate functionality of the lead was identified prior to pocket closure and the lead was removed from service. The leads were subsequently determined to have broken coils based on return product analysis. Implant of a lead with a broken coil during the study was prevented by physician attention to two procedural indicators: a) inability to extend or retract the helix per labeling instructions and/or b) unacceptable electrical measurements as determined by testing per labeling, which includes tests using the pacing system analyzer (PSA) and pulse generator.

Analysis of study data did not show an elevated safety risk of death, adverse events, serious adverse events, or complication for subjects with a helix extension/retraction device deficiency or a lead conductor

coil break when compared to those who did not experience a helix extension/retraction device deficiency or lead conductor coil break.

To mitigate the extension/retraction device deficiencies, manufacturing improvements were made and the instructions for use were clarified. For marketed INGEVITY lead performance data including occurrence of conductor coil breaks, see the Boston Scientific Rhythm Management Product Performance Report at **www.bostonscientific.com/ppr**.

Table 12. Summary of Device Deficiencies for the INGEVITY study and the SAMURAI study

Device Deficiency	Leads Included	INGEVITY	SAMURAI	Total of both
All Reported	All	98/1659 (5.9%)	55/705 (7.8%)	153/2364 (6.5%)
- Active Fixation	Active Fixation	91/1325 (6.9%)	55/601 (9.2%)	146/1926 (7.6%)
- Passive Fixation	Passive Fixation	7/334 (2.1%)	0/104 (0.0%)	7/438 (1.6%)
Helix Extension/ Retraction	Active Fixation	52/1325 (3.9%)	43/601 (7.2%)	95/1926 (4.9%)
- Right Atrium	RA Active Fixation	36/478 (7.5%)	24/299 (8.0%)	60/777 (7.7%)
- Right Ventricle	RV Active Fixation	16/847 (1.9%)	19/302 (6.3%)	35/1149 (3.0%)
Coil Breaks*	Active Fixation	21/1325 (1.6%)	22/601 (3.7%)	43/1926 (2.2%)
- Right Atrium	RA Active Fixation	14/478 (2.9%)	12/299 (4.0%)	26/777 (3.3%)
- Right Ventricle	RV Active Fixation	7/847 (0.8%)	10/302 (3.3%)	17/1149 (1.5%)

*Coil Breaks are a subset of Helix Extension/Retraction device deficiencies.
Note: All implanted and attempted leads are included.

DEATH SUMMARY

Table 13 on page 13 provides an overview of the 93 subject deaths (8.8% of enrolled subjects) that occurred during the INGEVITY study. Classification of the deaths was provided by the independent Clinical Events Committee (CEC). The four “Unclassified” deaths are pending classification, upon review of further source information.

Table 13. Summary of Study Deaths (N = 1060 Enrolled Subjects)

CEC Adjudicated Primary Organ Cause	Number (%) of Subjects	Lead-Related Number (%) of total deaths	
		Yes	Unknown
Non Cardiac	46 (4.3%)	0 (0%)	0 (0%)
Cardiac: Pump Failure	6 (0.6%)	0 (0%)	0 (0%)
Cardiac: Arrhythmic	1 (0.1%)	0 (0%)	0 (0%)
Cardiac: Ischemic	1 (0.1%)	0 (0%)	0 (0%)
Cardiac: Other Cardiac	1 (0.1%)	0 (0%)	1 (0.1%)
Cardiac: Unknown	1 (0.1%)	0 (0%)	0 (0%)
Unknown	33 (3.1%)	0 (0%)	7 (0.7%)
Unclassified	4 (0.4%)	Not applicable	Not applicable

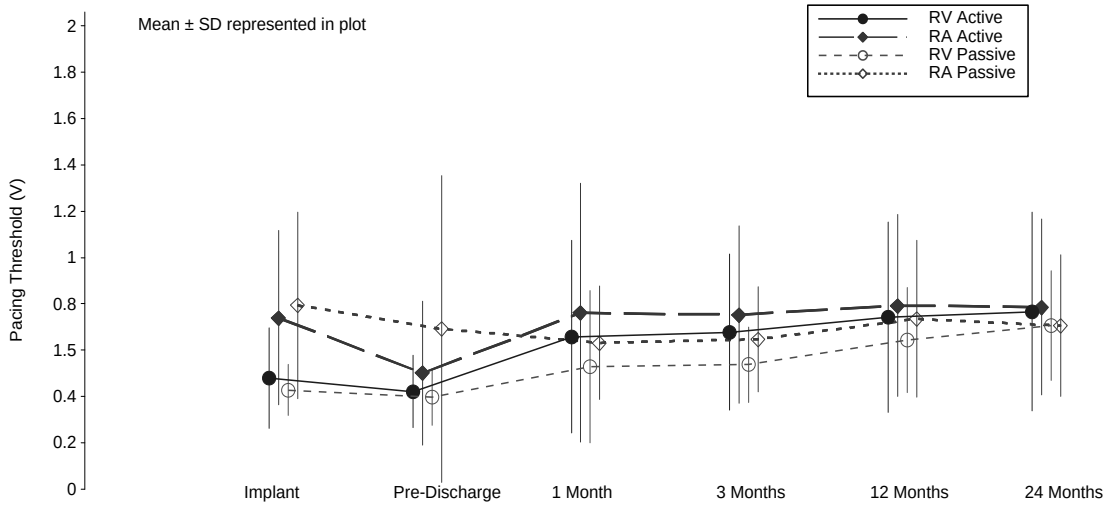
The CEC did not attribute any deaths to be related to the INGEVITY lead. Due to insufficient source information on some deaths, the CEC was unable to classify the relationship of the death to the INGEVITY lead in seven of the 33 deaths where the primary organ cause was unknown. In addition, there was one death due to other cardiac reasons for which the CEC was unable to classify the relationship of the death to the INGEVITY lead.

CONCLUSIONS

The results from this clinical study performed with INGEVITY active fixation and passive fixation pace/sense leads indicate that all Safety Endpoints and all Effectiveness Endpoints were met. The Safety Endpoints analyzed the lead-related complications-free rate through the post-implant follow-up period included in this summary, and, therefore, demonstrate safety for long-term implant. Effective performance of the lead was exhibited by evaluation of pacing thresholds, sensed amplitude, and pacing impedance through 3 months of follow-up post-implant. The results indicate clinically acceptable values for all categories. In conclusion, this clinical study demonstrated the safety and effectiveness of INGEVITY active fixation and passive fixation pace/sense leads.

APPENDIX 1 LEAD MEASUREMENTS FROM IMPLANT THROUGH FOLLOW-UP

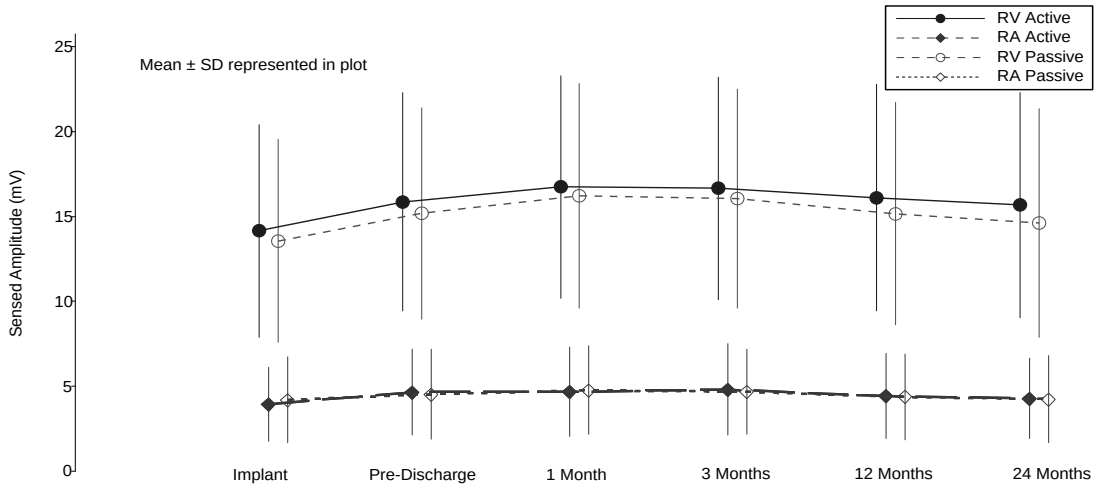
The following figures present pacing threshold, sensed amplitude and pacing impedance data for INGEVITY leads over the course of follow-up. Refer to Appendix Figure 1 on page 14, Appendix Figure 2 on page 15, and Appendix Figure 3 on page 16.



		Implant	Pre-Discharge	1 Month	3 Months	12 Months	24 Months
RV Active	N	828	826	806	797	757	639
	Mean ± SD	0.48 ± 0.22	0.42 ± 0.16	0.66 ± 0.42	0.68 ± 0.34	0.74 ± 0.41	0.77 ± 0.43
	(Min - Max)	(0.10 - 3.50)	(0.10 - 2.60)	(0.10 - 7.50)	(0.10 - 4.00)	(0.10 - 6.50)	(0.10 - 7.50)
RA Active	N	411	417	403	403	376	329
	Mean ± SD	0.74 ± 0.38	0.50 ± 0.31	0.76 ± 0.56	0.75 ± 0.38	0.79 ± 0.39	0.79 ± 0.38
	(Min - Max)	(0.10 - 3.00)	(0.10 - 3.40)	(0.10 - 5.00)	(0.00 - 4.50)	(0.10 - 4.50)	(0.30 - 5.00)
RV Passive	N	208	207	201	197	184	164
	Mean ± SD	0.43 ± 0.11	0.40 ± 0.12	0.53 ± 0.33	0.54 ± 0.16	0.64 ± 0.23	0.71 ± 0.24
	(Min - Max)	(0.10 - 1.10)	(0.20 - 1.10)	(0.20 - 3.50)	(0.10 - 1.40)	(0.10 - 2.00)	(0.30 - 1.90)
RA Passive	N	119	116	110	113	109	88
	Mean ± SD	0.79 ± 0.40	0.69 ± 0.66	0.63 ± 0.25	0.65 ± 0.23	0.73 ± 0.34	0.71 ± 0.30
	(Min - Max)	(0.40 - 3.50)	(0.10 - 5.00)	(0.30 - 1.80)	(0.20 - 1.60)	(0.40 - 3.30)	(0.30 - 2.60)

Appendix Figure 1. INGEVITY Pacing Threshold Measurements throughout Follow-Up

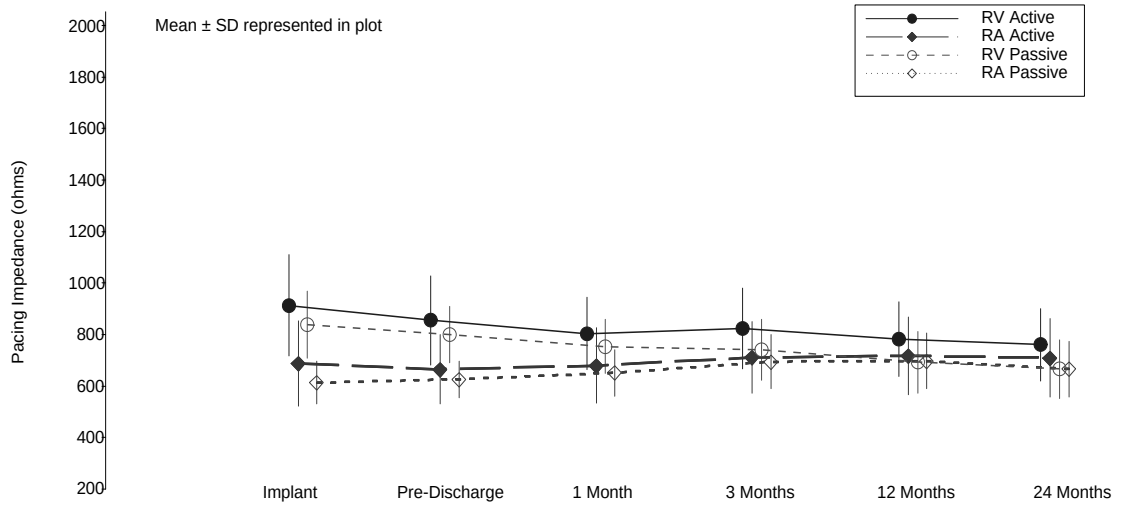
APPENDIX 1 Lead Measurements from Implant through Follow-Up



		Implant	Pre-Discharge	1 Month	3 Months	12 Months	24 Months
RV Active	N	789	776	757	742	673	541
	Mean ± SD	14.2 ± 6.3	15.9 ± 6.4	16.7 ± 6.5	16.7 ± 6.5	16.1 ± 6.7	15.7 ± 6.6
	(Min - Max)	(1.9 - 25.0)	(1.3 - 35.0)	(2.2 - 25.0)	(2.2 - 25.0)	(0.0 - 25.0)	(2.3 - 25.0)
RA Active	N	433	427	415	412	390	349
	Mean ± SD	3.9 ± 2.2	4.7 ± 2.5	4.7 ± 2.6	4.8 ± 2.7	4.4 ± 2.5	4.3 ± 2.4
	(Min - Max)	(0.3 - 14.8)	(0.4 - 13.8)	(0.1 - 16.5)	(0.3 - 16.1)	(0.3 - 19.0)	(0.3 - 14.9)
RV Passive	N	201	194	182	176	159	144
	Mean ± SD	13.6 ± 6.0	15.2 ± 6.2	16.2 ± 6.6	16.1 ± 6.5	15.2 ± 6.6	14.6 ± 6.7
	(Min - Max)	(3.4 - 25.0)	(3.0 - 25.0)	(3.0 - 25.0)	(1.6 - 25.0)	(1.9 - 25.0)	(0.0 - 25.0)
RA Passive	N	120	117	115	114	111	93
	Mean ± SD	4.2 ± 2.5	4.5 ± 2.7	4.8 ± 2.6	4.7 ± 2.5	4.4 ± 2.5	4.2 ± 2.6
	(Min - Max)	(0.7 - 13.6)	(0.7 - 14.3)	(0.7 - 13.1)	(0.3 - 11.5)	(0.6 - 12.3)	(0.3 - 12.2)

Appendix Figure 2. INGEVITY Sensed Amplitude Measurements throughout Follow-Up

APPENDIX 1 Lead Measurements from Implant through Follow-Up



		Implant	Pre-Discharge	1 Month	3 Months	12 Months	24 Months
RV Active	N	828	826	809	799	757	639
	Mean ± SD	913 ± 196	855 ± 173	804 ± 141	824 ± 158	782 ± 145	760 ± 142
	(Min - Max)	(417 - 2000)	(476 - 2000)	(424 - 1741)	(437 - 1747)	(400 - 1776)	(367 - 2000)
RA Active	N	439	438	429	423	403	360
	Mean ± SD	688 ± 165	665 ± 135	679 ± 147	711 ± 139	718 ± 151	709 ± 152
	(Min - Max)	(441 - 1826)	(352 - 1490)	(382 - 2000)	(407 - 2000)	(426 - 2000)	(374 - 2000)
RV Passive	N	208	207	200	197	185	164
	Mean ± SD	839 ± 131	799 ± 109	754 ± 105	741 ± 118	692 ± 119	667 ± 114
	(Min - Max)	(431 - 1400)	(501 - 1110)	(501 - 1244)	(469 - 1282)	(411 - 1210)	(421 - 1128)
RA Passive	N	121	121	115	116	113	98
	Mean ± SD	613 ± 84	626 ± 71	651 ± 91	695 ± 105	697 ± 108	665 ± 107
	(Min - Max)	(383 - 890)	(420 - 800)	(419 - 836)	(414 - 910)	(423 - 894)	(414 - 874)

Appendix Figure 3. INGEVITY Pacing Impedance Measurements throughout Follow-Up

APPENDIX 2 IMPLANTATION QUESTIONNAIRE

Investigators were asked to evaluate handling of the lead during the implantation procedure. The results of this lead handling questionnaire are provided in Appendix Table 1 on page 17. Overall, implanting physicians were satisfied with handling of the lead.

Appendix Table 1. Implant Questionnaire Results (N = 1653 Implanted or Attempted Leads)

Item	Number of Responses (%)				
	RV Active Leads (N=844)	**RA Active Leads (N=475)**	**RV Passive Leads (N=213)**	**RA Passive Leads (N=121)**	**All Leads (N=1653)**
Q1. Rate the radiopacity quality of the extendable/retractable helix markers					
(1) Exceeded Expectations	136 (16.6%)	41 (9.4%)	Not applicable	Not applicable	177 (14.1%)
(2) Very Good	408 (49.7%)	222 (50.7%)	Not applicable	Not applicable	630 (50.0%)
(3) Good	164 (20.0%)	94 (21.5%)	Not applicable	Not applicable	258 (20.5%)
(4) Met Expectations	104 (12.7%)	74 (16.9%)	Not applicable	Not applicable	178 (14.1%)
(5) Unacceptable	9 (1.1%)	7 (1.6%)	Not applicable	Not applicable	16 (1.3%)
Q2. Rate Handling and Maneuverability of the stylet and lead used					
(1) Exceeded Expectations	177 (21.4%)	69 (15.7%)	25 (11.8%)	22 (18.3%)	293 (18.3%)
(2) Very Good	459 (55.5%)	260 (59.2%)	122 (57.8%)	58 (48.3%)	899 (56.3%)
(3) Good	148 (17.9%)	81 (18.5%)	44 (20.9%)	25 (20.8%)	298 (18.7%)
(4) Met Expectations	41 (5.0%)	28 (6.4%)	19 (9.0%)	14 (11.7%)	102 (6.4%)
(5) Unacceptable	2 (0.2%)	1 (0.2%)	1 (0.5%)	1 (0.8%)	5 (0.3%)
Q3. Rate overall Handling Performance of the Lead					
(1) Exceeded Expectations	197 (23.8%)	75 (17.1%)	22 (10.5%)	17 (14.2%)	311 (19.5%)
(2) Very Good	441 (53.4%)	253 (57.6%)	122 (58.4%)	65 (54.2%)	881 (55.3%)
(3) Good	147 (17.8%)	81 (18.5%)	49 (23.4%)	27 (22.5%)	304 (19.1%)
(4) Met Expectations	37 (4.5%)	25 (5.7%)	15 (7.2%)	10 (8.3%)	87 (5.5%)
(5) Unacceptable	4 (0.5%)	5 (1.1%)	1 (0.5%)	1 (0.8%)	11 (0.7%)
Q4. Rate the overall handling and ease of implant using the Pre-formed Atrial J lead					
(1) Exceeded Expectations	Not applicable	Not applicable	Not applicable	20 (16.8%)	20 (16.8%)
(2) Very Good	Not applicable	Not applicable	Not applicable	57 (47.9%)	57 (47.9%)
(3) Good	Not applicable	Not applicable	Not applicable	29 (24.4%)	29 (24.4%)
(4) Met Expectations	Not applicable	Not applicable	Not applicable	13 (10.9%)	13 (10.9%)

APPENDIX 2 Implantation Questionnaire

Item	Number of Responses (%)				
	RV Active Leads (N=844)	RA Active Leads (N=475)	RV Passive Leads (N=213)	RA Passive Leads (N=121)	All Leads (N=1653)
(5) Unacceptable	Not applicable	Not applicable	Not applicable	0 (0%)	0 (0%)
Q5. (Single Chamber) - The Lead is easy to pass through small vessels					
(1) Strongly Agree	51 (38.9%)	Not applicable	18 (40.9%)	Not applicable	69 (39.4%)
(2) Agree	75 (57.3%)	Not applicable	24 (54.5%)	Not applicable	99 (56.6%)
(3) Somewhat Agree	5 (3.8%)	Not applicable	2 (4.5%)	Not applicable	7 (4.0%)
(4) Disagree	0 (0%)	Not applicable	0 (0%)	Not applicable	0 (0%)
Q6. (Dual Chamber) - The Lead is easy to pass through small vessels and/or vessels with multiple leads					
(1) Strongly Agree	191 (30.3%)	117 (29.6%)	47 (29.7%)	33 (28.0%)	388 (29.8%)
(2) Agree	398 (63.2%)	246 (62.3%)	100 (63.3%)	76 (64.4%)	820 (63.0%)
(3) Somewhat Agree	35 (5.6%)	30 (7.6%)	10 (6.3%)	7 (5.9%)	82 (6.3%)
(4) Disagree	6 (1.0%)	2 (0.5%)	1 (0.6%)	2 (1.7%)	11 (0.8%)
Q7. Rate the visibility of the radiopaque suture sleeve on x-ray during and after the implant procedure					
(1) Exceeded Expectations	94 (14.1%)	40 (11.6%)	21 (11.7%)	8 (7.4%)	163 (12.5%)
(2) Very Good	284 (42.6%)	143 (41.3%)	77 (43.0%)	53 (49.1%)	557 (42.9%)
(3) Good	186 (27.9%)	94 (27.2%)	58 (32.4%)	38 (35.2%)	376 (28.9%)
(4) Met Expectations	87 (13.1%)	55 (15.9%)	20 (11.2%)	9 (8.3%)	171 (13.2%)
(5) Unacceptable	15 (2.3%)	14 (4.0%)	3 (1.7%)	0 (0.0%)	32 (2.5%)
Q8. The design of the low profile suture sleeve helps minimize bulk in the pocket					
(1) Strongly Agree	155 (19.3%)	69 (16.0%)	36 (17.1%)	23 (19.0%)	283 (18.0%)
(2) Agree	439 (54.5%)	240 (55.7%)	127 (60.2%)	73 (60.3%)	879 (56.1%)
(3) Somewhat Agree	146 (18.1%)	83 (19.3%)	32 (15.2%)	19 (15.7%)	280 (17.9%)
(4) Disagree	65 (8.1%)	39 (9.0%)	16 (7.6%)	6 (5.0%)	126 (8.0%)

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