Boston Scientific

CLINICAL SUMMARY

SAMURAI 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 SAMURAI CLINICAL STUDY

The SAMURAI Clinical study was designed to collect data to confirm the safety, performance, and effectiveness of the ImageReady™ MR Conditional[1] Pacing System (hereafter referred to as the ImageReady System) when used in the MRI environment under the labeled Conditions of Use. The ImageReady System consists of specific Boston Scientific model components including pulse generators (the Ingenio™ MRI pulse generator family), leads (INGEVITY™ MRI pace/sense leads), accessories, the Programmer/Recorder/Monitor (PRM), and the PRM Software Application.

STUDY DESIGN

The SAMURAI study is a prospective, open-label, two-group randomized clinical study continuing through 2019 with parallel groups at multiple centers globally. The overall study design included randomization of enrolled subjects at pre-discharge in a 2:1 ratio into the MRI Group or Control Group. An MRI/Control visit occurred 6-9 weeks after implant or lead revision or surgical modification of the ImageReady System. At this visit, MR scans were performed on subjects in the MRI Group. The MR scans were conducted in First-level Controlled Operating Mode (up to 4 W/kg whole body Specific Absorption Rate [SAR]), without requiring an anatomical isocenter exclusion zone (i.e., full body). Subsequent follow-up visits occurred at MRI/Control visit + 1 week and at MRI/Control visit + 1 Month. Safety and Effectiveness Endpoints were analyzed with these data. Additionally, subjects will be followed at the 1, 2, 3, 4, and 5 year post-implant clinic visits to continue evaluation of the ImageReady System after MR scans.

METHODS

Subject Selection

The study enrolled patients from an investigator's general population with a Class I or II indication for a single or dual chamber pacemaker. Test pulse generators consisted of the VITALIO™ MRI pacemakers, which are part of the Ingenio MRI pulse generator family. The specific models of VITALIO MRI pacemakers included in the study contain a superset of the therapy features available in the Ingenio MRI pulse generator family. The test leads consisted of the INGEVITY MRI pace/sense leads, both active and passive fixation. Subjects who met all of the SAMURAI study inclusion criteria, and none of the exclusion criteria, were randomized in a 2:1 (MRI:Control) ratio and included in the endpoint analysis.

Inclusion and Exclusion Criteria

Inclusion Criteria

- Subject must have the ImageReady System as their initial (de novo) pacing system implant
- Subject has a Class I or II indication for implantation of a single or dual chamber pacemaker according to the American College of Cardiology (ACC)/American Heart Association (AHA)/Hearth Rhythm Society (HRS), or European Society of Cardiology (ESC) guidelines, as appropriate per geography
- Subject is able and willing to undergo an MR Scan without intravenous sedation (oral sedation may be used, if necessary, based on medical discretion)
- Subject is willing and capable of providing informed consent (which can include the use of a legally authorized representative [LAR] for documentation of informed consent) and 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

1 As described in American Society for Testing and Materials (ASTM) F2503:2008, "Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment" ASTM International, West Conshohocken, PA, 2008, DOI: 10.1520/F2503-08, www.astm.org.

Exclusion Criteria

- Subject has or has had any pacing or ICD system implants
- Subject has any MR Unsafe implants or devices with an unknown MR status, including MR Unsafe sternal wires, neurostimulators, biostimulator, metals or alloys, per labeling of each implant
- Subject has any MR Conditional implants or devices that impact the ability to conduct this protocol
- Subject needs or will need another MR scan within 14 weeks of system implant, other than that required by the SAMURAI Study
- 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)[2] where the physician intends to implant a dual chamber pulse generator [single chamber VVI(R) pulse generators are acceptable]
- Subject is currently on the active heart transplant list
- 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 ImageReady System implant (method of assessment upon physician's discretion)
- Subjects currently requiring dialysis

SAMURAI Study Endpoints

Safety Endpoints

- Primary Safety Endpoint: MR Scan-related ImageReady System Complication-Free Rate from MR Scan through the MRI visit + 1 Month (MRI Group only)
- Secondary Safety Endpoint: System-related Complication-Free Rate from Implant through 3 Months Post-Implant (MRI Group and Control Group)

Effectiveness Endpoints

The following endpoints were analyzed at the MRI/Control visit + 1 Month follow-up to establish effectiveness of the ImageReady System.

- Primary Effectiveness Endpoint 1: Change in Pacing Threshold (at 0.5 ms pulse width) Pre- and 1 Month post-MR Scan or Control Group visit compared between the MRI and Control Groups
- Primary Effectiveness Endpoint 2: Change in Sensed Amplitude Pre- and 1 Month Post-MR Scan or Control Group visit compared between MRI and Control Groups

RESULTS

Results included in this SAMURAI Clinical study summary were collected through February 17, 2016. A summary of the subject disposition is shown in Figure 1 on page 3. A total of 363 subjects were enrolled at 41 centers in the study. Of those enrolled, 348 subjects were successfully implanted with the ImageReady System, and 347 subjects were randomized in a 2:1 ratio into the MRI Group or the Control Group.

2 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

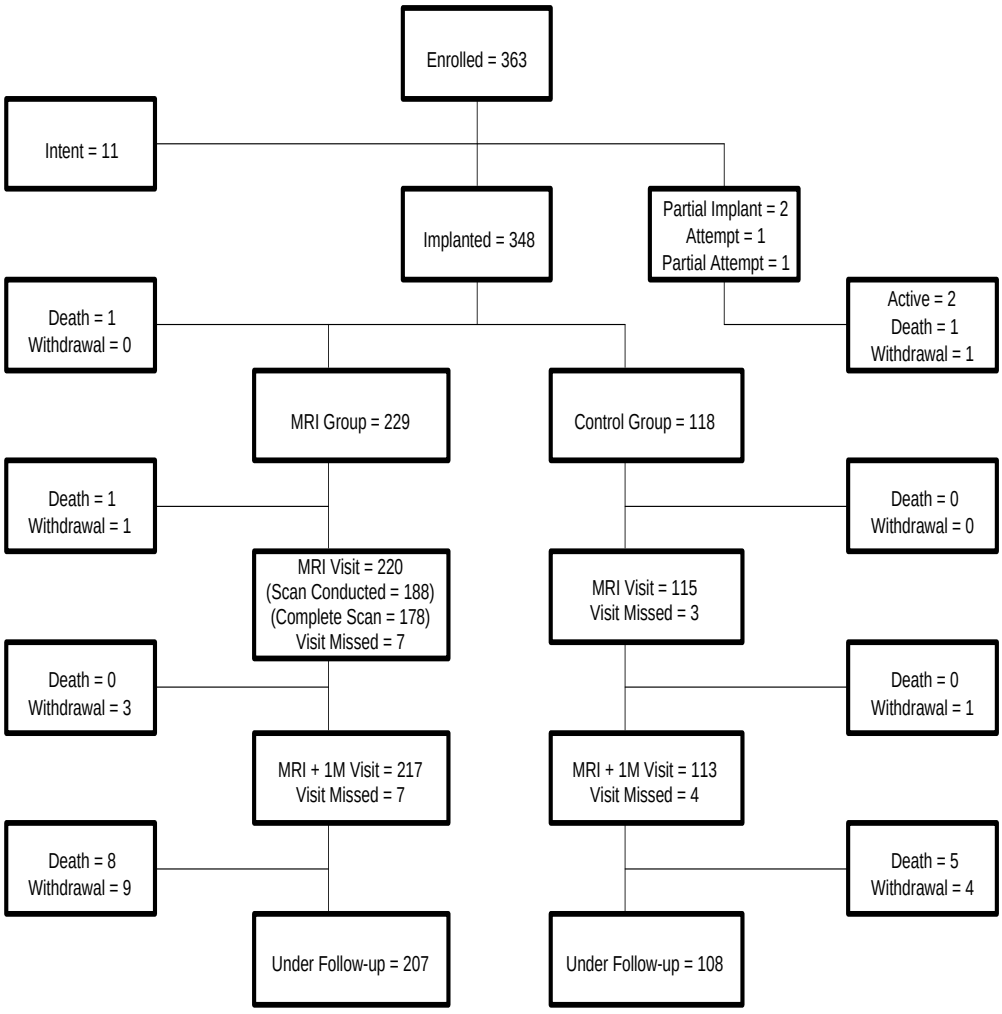


Figure 1. Subject Disposition

Subject Demographics

Overall, the average age of the subjects at implant was 69.4 ± 12.8 years, with an overall gender ratio of 46.6% females to 53.4% males (see Table 1 on page 3). Specifically in the MRI Group, the average age of the subjects at implant was 69.0 ± 13.0 years, with a gender ratio of 44.5% females to 55.5% males. In the Control Group, the average age of the subjects at implant was 70.4 ± 11.9 years, with a gender ratio of 53.4% females to 46.6% males.

Table 1. Implanted Component Information and Subject Demographics

Characteristic	Measurement	All Subjects	Randomized Groups	
			MRI Group	Control Group
Pulse Generator [N (%)]	Dual chamber	313 (89.4)	202 (88.2)	109 (92.4)
	Single chamber	37 (10.6)	27 (11.8)	9 (7.6)
Leads Implanted [N (%)]	Both RA and RV Leads	311 (88.9)	202 (88.2)	109 (92.4)
	RA only	3 (0.9)	3 (1.3)	0 (0.0)
	RV only	36 (10.3)	24 (10.5)	9 (7.6)

RESULTS

Characteristic	Measurement	All Subjects	Randomized Groups	
			MRI Group	Control Group
RA Fixation Type [N (%)]	Active	274 (87.3)	179 (87.3)	95 (87.2)
	Passive	40 (12.7)	26 (12.7)	14 (12.8)
RV Fixation Type [N (%)]	Active	284 (81.8)	184 (81.4)	98 (83.1)
	Passive	63 (18.2)	42 (18.6)	20 (16.9)
Age at Implant (years)	N	363	229	118
	Mean ± SD	69.4 ± 12.8	69.0 ± 13.0	70.4 ± 11.9
	Range	25.0-90.0	29.0-90.0	25.0-90.0
Gender [N (%)]	Female	169 (46.6)	102 (44.5)	63 (53.4)
	Male	194 (53.4)	127 (55.5)	55 (46.6)
Body Mass Index (kg/m^2)	N	363	229	118
	Mean ± SD	28.4 ± 5.6	27.9 ± 5.2	29.3 ± 6.0
	Range	16.4-52.3	16.4-44.1	18.9-47.6

Study Endpoint Results

Safety and Effectiveness Endpoint results are summarized below. All adverse events reported by the investigators were reviewed and classified by an internal committee. All reported complications were further adjudicated by the Independent Clinical Events Committee (CEC) for a relationship to the MR scan and for a relationship to the ImageReady System.

Safety Endpoint Results

A summary of the Safety Endpoints results is shown in Table 2 on page 4, with details provided in the following sections.

Table 2. Summary of Safety Endpoints Results

Safety Endpoint	Measurement	Performance Goal	Result (Confidence Limit)	Conclusion
Primary	MR Scan-Related ImageReady System Complication-Free Rate (MRI Group)	> 95%	100% (95% One-sided Lower Confidence Limit = 100%)	Endpoint Met
Secondary	System-Related Complication-Free Rate (all implanted and attempted subjects)	> 80%	94.5% (95% One-sided Lower Confidence Limit = 91.9%)	Endpoint Met

Primary Safety Endpoint: MR Scan-related ImageReady System Complication-Free Rate from MR Scan through the MRI Visit + 1 Month (MRI Group only)

The Primary Safety Endpoint for the SAMURAI study was assessed for all subjects randomized to the MRI Group who underwent any portion of the study protocol MR scan sequences, and did not have a medically necessary scan performed prior to the MRI visit + 1 Month follow-up. Safety was evaluated by the MR scan-related Complication-Free Rate (CFR) between the MR Scan and the MRI visit + 1 Month follow-up. For the purpose of this endpoint, a complication was defined as a detectable adverse event that could only be resolved by invasive intervention or that caused significant loss of device function. Complications that were determined to be associated with both MR scan and the ImageReady system were considered as MR scan-related complications and counted against this endpoint.

The MR Scan Related Complication-Free Rate from the time of the MR scan to the follow-up at MRI + 1 Month in the reporting sample was 100% with a 95% one-sided lower confidence limit of 100% (see Figure 2 on page 5).

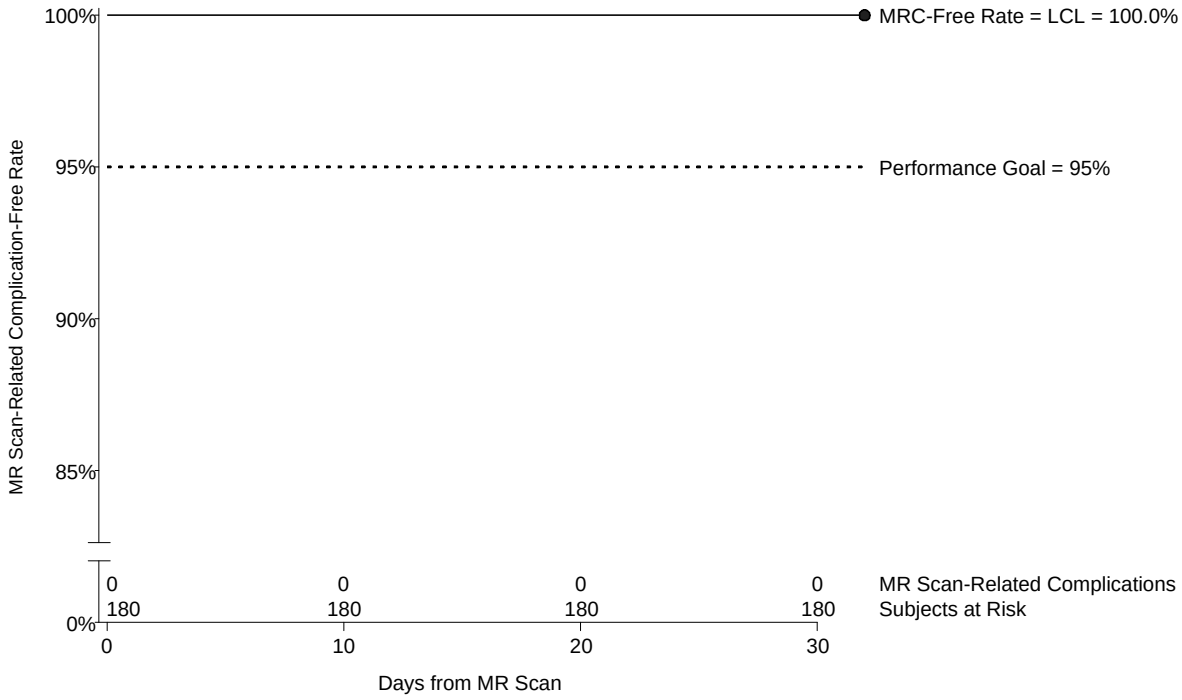


Figure 2. Primary Safety Endpoint Results. – MR Scan-Related Complication-Free Rate from MR Scan through MRI Visit + 1 Month

The data support the MRI safety of the ImageReady System when used in the MRI environment under the labeled Conditions of Use.

Secondary Safety Endpoint: System-related Complication-Free Rate from Implant through 3 Months Post-Implant (MRI Group and Control Group)

Overall safety of the ImageReady System was assessed by evaluation of system-related complications for both the MRI Group and the Control Group. A complication was defined as an adverse event that resulted in death, serious injury, correction using invasive intervention, or permanent loss of device functions. A system-related complication was a complication caused by either the implanted VITALIO MRI pacemaker or the INGEVITY MRI lead (collectively, the system). Any adverse events that occurred within 91 days of initial ImageReady System implant and adjudicated as a system-related complication counted against this endpoint. The performance goal for this safety endpoint was greater than 80%.

The system-related Complication-Free Rate from 0 to 3 months for all SAMURAI study subjects who underwent an implant procedure was 94.5% with a one-sided 95% lower confidence limit of 91.9% (see Figure 3 on page 6).

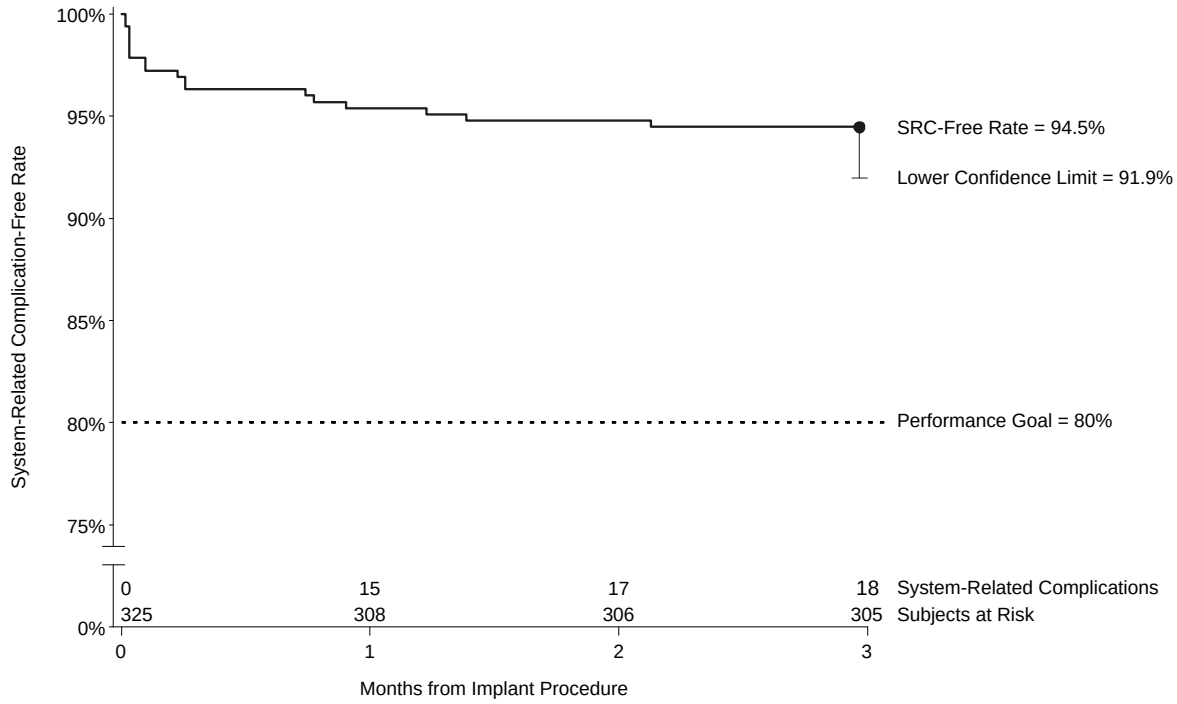


Figure 3. Secondary Safety Endpoint Results. – System-Related Complication-Free Rate from Implant through 3 Months Post-implant

The data support the overall safety of the ImageReady System.

Effectiveness Endpoint Results

The MR scan can result in damage to cardiac tissue surrounding lead electrodes due to RF field-induced heating, which in turn may cause elevated pacing thresholds. The Effectiveness Endpoints were set up to evaluate any chronic effects from lead heating that would be seen through increased pacing threshold or decreased sensed amplitude at the MRI/Control visit + 1 Month follow-up.

Primary Effectiveness Endpoints 1 and 2 were each analyzed by both an intention-to-treat (ITT) and per-protocol (PP) analysis. The ITT analysis analyzed subjects according to their assigned randomization group for all subjects who had pacing threshold or sensed amplitude measurements at both the MRI visit and the MRI/Control visit + 1 Month follow-up. The per-protocol analysis only included subjects who received their assigned randomization, and did not include subjects who met any of the following exclusions:

- Had a medically necessary scan between implant and the MRI/Control visit + 1 Month follow-up
- Failed to meet the labeled MRI Conditions of Use
- Experienced a lead-related complication between MRI/Control visit and the MRI/Control visit + 1 Month follow-up
- Had an incomplete scan based on the SAMURAI MR Scan Sequences protocol.

The difference in the success rate between the two randomization groups was compared to 10% using a one-sided Farrington-Manning score test for non-inferiority at a significance level of 0.05. A summary of the Effectiveness Endpoints results is shown in Table 3 on page 7, with details provided in the following sections.

Table 3. Summary of Effectiveness Endpoint results.

Effectiveness Endpoint	Measurement	Analysis Subgroup*	Difference Control-MRI (Upper One-sided 95% CI)	Conclusion
Primary 1	Pacing Threshold (difference in success rates between MRI and Control Groups)	ITT	-0.5% (3.3%)	Endpoint Met
		PP	-0.3% (3.9%)	Endpoint Met
Primary 2	Sensed Amplitude (difference in success rates between MRI and Control Groups)	ITT - Right Atrium	-0.0% (4.6%)	Endpoint Met
		ITT - Right Ventricle	0.7% (5.1%)	Endpoint Met
		PP - Right Atrium	-0.1% (5.0%)	Endpoint Met
		PP - Right Ventricle	-0.0% (4.7%)	Endpoint Met

* ITT (Intention to Treat), PP (Per Protocol)

Primary Effectiveness Endpoint 1 - Pre- vs. 1 Month Post-MR Scan/Control Group Visit Pacing Threshold at 0.5 ms

Changes in pacing threshold (at 0.5 ms) pre- and 1 Month post-MR Scan or Control Group visit were compared between the MRI and Control Groups. Three pacing threshold measurements taken at each of the two visits (pre-MR Scan/Control Group visit and the MRI/Control visit + 1 Month follow-up) were averaged to determine the average pacing threshold at each visit for each subject. The lead fixation type and lead chamber data were pooled for this endpoint since the passive and active fixation INGEVITY MRI leads, as well as the RA and RV leads, were expected to perform similarly regarding any effect of MRI on pacing threshold.

Subjects with an increase in pacing thresholds ≤ 0.5V (at 0.5 ms) from pre-MR Scan/Control Group visit to MRI/Control visit + 1 Month follow-up were considered a success. A success rate was calculated for both the MRI and the Control Groups. Subjects with more than one investigational lead were counted as a failure if either lead failed to meet the success criteria.

A total of 101 Control Group subjects and 203 MRI Group subjects had paired threshold measurements and were included in the ITT endpoint analysis. The success rate in the Control group was 98.0%, and 98.5% in the MRI group, resulting in a difference of -0.5% and an upper one-sided 95% confidence interval of 3.3%. The Farrington-Manning score test resulted in a p-value < 0.0001.

For the per-protocol analysis, a total of 96 Control Group subjects and 167 MRI Group subjects had paired threshold measurements and met the inclusion criteria. The success rate in the Control group was 97.9%, and 98.2 % in the MRI group, resulting in a difference of -0.3% and an upper one-sided 95% confidence interval of 3.9%. The Farrington-Manning score test resulted in a p-value < 0.0001. Endpoint results are presented in Figure 4 on page 8.

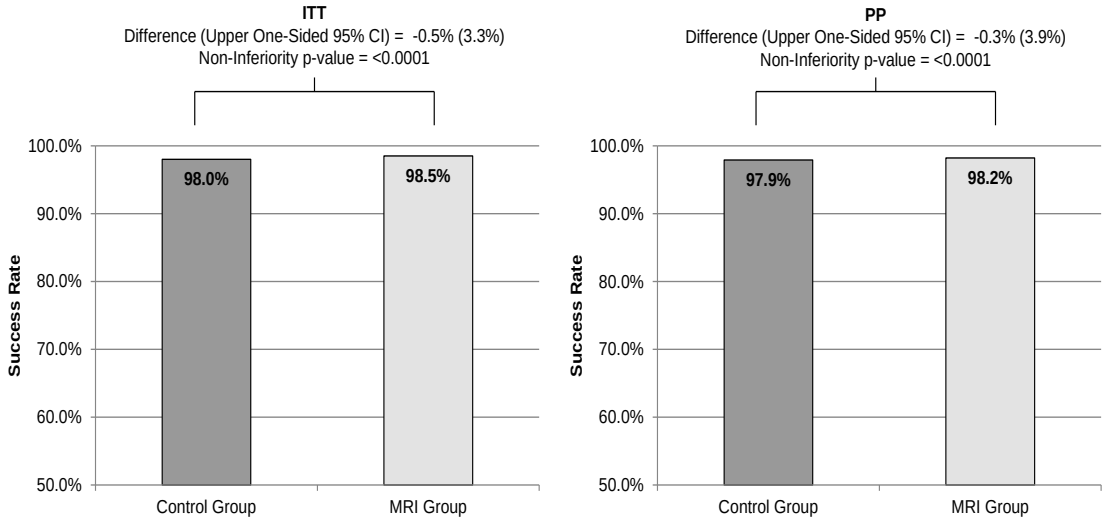


Figure 4. Primary Effectiveness Endpoint 1 Results – Success Rates of Changes in Pacing Threshold (at 0.5 ms pulse width) Pre- and 1 Month post-MR Scan or Control Group Visit compared between the MRI and Control Groups (ITT and PP analyses).

The success rates for the threshold measurement results observed for both the MRI Group and the Control Group were comparable, and the difference between the groups was lower than the non-inferiority margin of 10%. The data support the effectiveness of the ImageReady System with respect to stable pacing thresholds pre- and post-MR scan (a surrogate measurement for clinical effects of lead heating) when subjects were scanned according to the MRI Conditions of Use.

Primary Effectiveness Endpoint 2 - Pre- vs. 1 Month Post-MR Scan/Control Group Visit Sensed Amplitude

Changes in sensed amplitude pre- and 1 Month post-MR Scan or Control Group visit were compared between the MRI and Control Groups. Three sensed amplitude measurements taken at each of the two visits (pre-MR Scan/Control Group visit and the MRI/Control visit + 1 Month follow-up) were averaged to determine the average sensed amplitude at each visit for each subject. Data were analyzed separately by chamber for this endpoint, while the lead fixation type data were pooled since the passive and active fixation INGEVITY MRI leads were expected to perform similarly regarding any effect of MRI on sensed amplitude. A success rate was calculated for the MRI Group and for the Control Group. Subjects with more than one investigational lead were counted as a failure if either lead failed to meet the success criteria.

For atrial sensed amplitudes, a subject was considered a success if the sensed amplitude at the MRI/Control visit + 1 Month follow-up remained ≥ 1.0 mV and above 50% of the pre-MR scan/Control Group visit value. There were 250 subjects (83 Control and 167 MRI) included in the ITT endpoint analysis, and 213 subjects (78 Control and 135 MRI) included in the per protocol endpoint analysis of the right atrial sensed amplitude. For the ITT analysis, the success rate in the Control Group was 96.4%, and 96.4% in the MRI Group, resulting in a difference of -0.0% and an upper one-sided 95% confidence interval of 4.6%. For the per protocol analysis, the success rate in the Control Group was 96.2%, and 96.3% in the MRI group, resulting in a difference of -0.1% and an upper one-sided 95% confidence interval of 5.0%. The p-values were 0.0002 and 0.0006 respectively for the ITT and the per protocol endpoint analyses of the right atrial sensed amplitude as shown in Figure 5 on page 9.

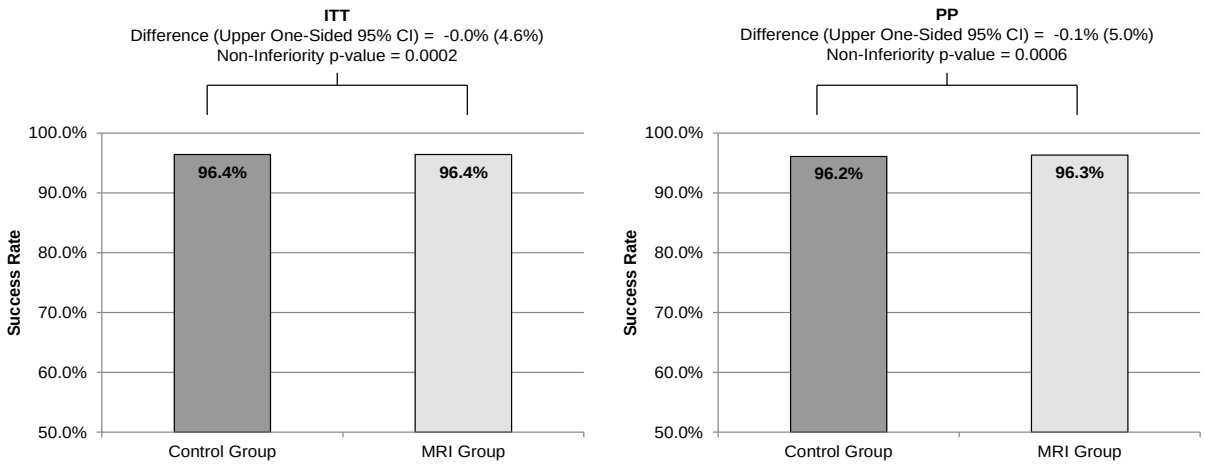


Figure 5. Primary Effectiveness Endpoint 2 RA Results – Success Rates of Changes in Sensed Amplitude Pre- and 1 Month post-MR Scan or Control Group Visit compared between the MRI and Control Groups (ITT and PP analyses).

For ventricular sensed amplitudes, a subject was considered a success if the sensed amplitude at the MRI/ Control visit + 1 Month follow-up remained ≥ 5.0 mV and above 50% of the pre-MR scan/Control Group visit value. There were 277 subjects (96 Control and 181 MRI) included in the ITT endpoint analysis, and 243 subjects (91 Control and 152 MRI) included in the per protocol endpoint analysis of the right ventricular sensed amplitude. For the ITT analysis, the success rate in the Control Group was 96.9%, and 96.1% in the MRI Group, resulting in a difference of 0.7% (rounded) and an upper one-sided 95% confidence interval of 5.1%. For the per protocol analysis, the success rate in the Control Group was 96.7%, and 96.7% in the MRI group, resulting in a difference of -0.0% and an upper one-sided 95% confidence interval of 4.7%. The p-values were 0.0002 and 0.0002 respectively for the ITT and the per protocol endpoint analyses of the right ventricular sensed amplitude as shown in Figure 6 on page 9.

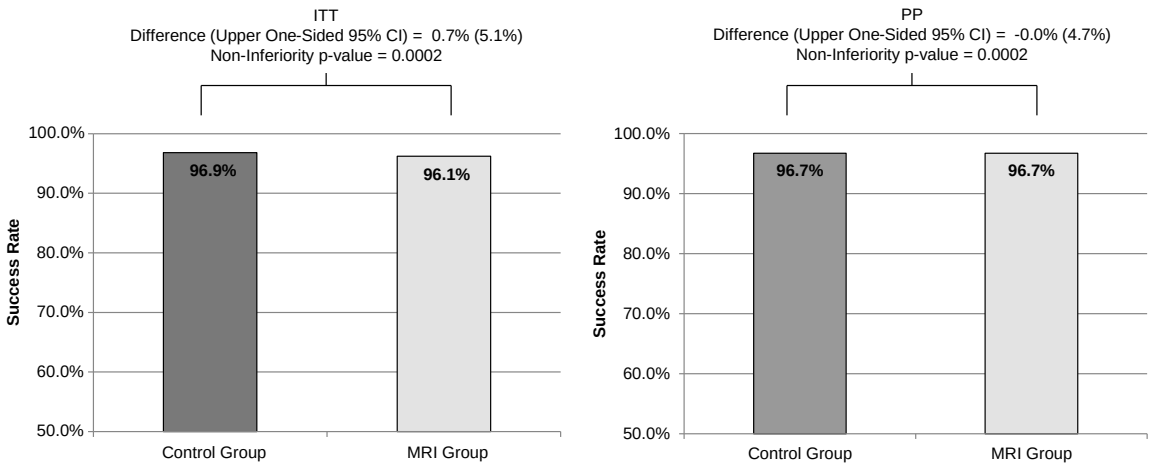


Figure 6. Primary Effectiveness Endpoint 2 RV Results – Success Rates of Changes in Sensed Amplitude Pre- and 1 Month post-MR Scan or Control Group Visit compared between the MRI and Control Groups (ITT and PP analyses).

The success rates for the sensed amplitude results observed for both for the MRI Group and the Control Group were comparable for each lead implant location, and the differences between the groups were lower than the non-inferiority margin of 10%. The data support the effectiveness of the ImageReady System with respect to stable sensed amplitudes pre- and post-MR scan (a surrogate measurement for clinical effects of lead heating) when subjects were scanned according to the MRI Conditions of Use.

ADVERSE EVENTS SUMMARY

SAMURAI Study

A summary of Adverse Events by Complication and Observation is shown in Table 4 on page 10. As of February 17, 2016, of the 351 implanted or partial/attempted subjects, there were no reported MRI-related complications. Further, of this group, 94.3% were free from adverse events related to the pacemaker, 89.7% were free from adverse events related to the implant procedure, and 94.3% and 95.7% were free from adverse events related to the INGEVITY MRI RA and RV leads, respectively.

All adverse events were reviewed by an independent committee, the SAMURAI Data Monitoring Committee (DMC). During the course of the SAMURAI study, the DMC did not identify any serious risks to subjects.

Table 4. Adverse Events Summary: Clinical Complications and Observations

Relationship	Total		Classification			
			Complication		Observation	
	Events	N (%)	Events	N (%)	Events	N (%)
Total (N at risk = 351)	964	275 (78.3%)	294	146 (41.6%)	664	237 (67.5%)
PG (N at risk = 351)	23	20 (5.7%)	1	1 (0.3%)	22	19 (5.4%)
RA Lead (N at risk = 314)	18	18 (5.7%)	8	8 (2.5%)	10	10 (3.2%)
RV Lead (N at risk = 347)	16	15 (4.3%)	9	9 (2.6%)	7	7 (2.0%)
Procedure (N at risk = 351)	46	36 (10.3%)	12	11 (3.1%)	34	28 (8.0%)
Protocol Testing (N at risk = 351)	5	5 (1.4%)	0	0 (0.0%)	5	5 (1.4%)
Cardiovascular - HF (N at risk = 351)	41	29 (8.3%)	30	22 (6.3%)	11	10 (2.8%)
Cardiovascular - Non-HF (N at risk = 351)	325	177 (50.4%)	72	61 (17.4%)	253	147 (41.9%)
Non-cardiovascular (N at risk = 351)	450	174 (49.6%)	149	77 (21.9%)	301	140 (39.9%)
Other (N at risk = 351)	34	23 (6.6%)	13	10 (2.8%)	21	14 (4.0%)
Unclassified (N at risk = 351	6	6 (1.7%)	0	0 (0.0%)	0	0 (0.0%)

Lead-related Safety Data from INGEVITY and SAMURAI Studies

Data collected in the SAMURAI study provided additional evidence to support the safety of INGEVITY pace/sense leads as analyzed in another Boston Scientific clinical study, the INGEVITY Active Fixation and Passive Fixation Pace/Sense Lead Clinical Study (hereafter referred to as the INGEVITY study). The INGEVITY study was designed to establish the safety, performance, and effectiveness of INGEVITY active and passive fixation pace/sense leads. INGEVITY MRI pace/sense leads are a component of the ImageReady System examined in the SAMURAI study, 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. Table 5 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 5. 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.

Table 6 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 6. 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

As of February 17, 2016, sixteen SAMURAI study subjects had died (4.4% of all enrolled subjects). Table 7 on page 13 provides an overview of all subject deaths that occurred in the SAMURAI study. Death information was provided per the case report forms (site information and an external Clinical Events Committee [CEC] adjudication). No deaths were attributed to an MR scan.

Table 7. Summary of Study Deaths (N = 363 Enrolled Subjects)

Cause of Death	Classification N (%)	MRI Related		System Related	
		Yes N (%)	Unknown N (%)	Yes N (%)	Unknown N (%)
Non Cardiac	7 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiac: Arrhythmic	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiac: Ischemic	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiac: Pump Failure	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiac: Unknown	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
Unknown	5 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Total	**16 (4.4%)**	**0 (0.0%)**	**0 (0.0%)**	**0 (0.0%)**	**1 (0.3%)**

CONCLUSION

The results from this SAMURAI clinical study performed with the ImageReady MR Conditional Pacing System indicate that all the Safety Endpoints and all the Effectiveness Endpoints were met. Safety was assessed by determination of the MR scan-related and the overall ImageReady System-related complication-free rates. Effectiveness was analyzed by comparison of the differences in the success rates for pacing threshold and for sensed amplitude between the MRI Group and the Control Group. All performance goals were met for all Endpoints. Therefore, this study demonstrated the overall safety and effectiveness of the ImageReady MR Conditional Pacing System, with clinical performance similar to approved devices.

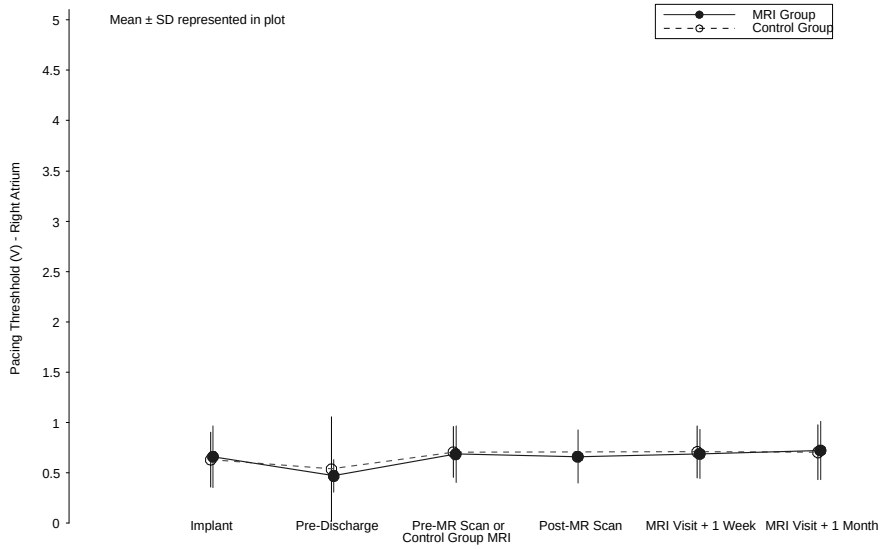
APPENDIX 1 LEAD MEASUREMENTS FROM IMPLANT THROUGH FOLLOW-UP

The following figures present data for leads over the course of the SAMURAI study follow-up:

- Pacing Threshold (Appendix Figure 1 on page 14 and Appendix Figure 2 on page 15)
- Sensed Amplitude (Appendix Figure 3 on page 15 and Appendix Figure 4 on page 16)
- Pacing Impedance (Appendix Figure 5 on page 16 and Appendix Figure 6 on page 17)

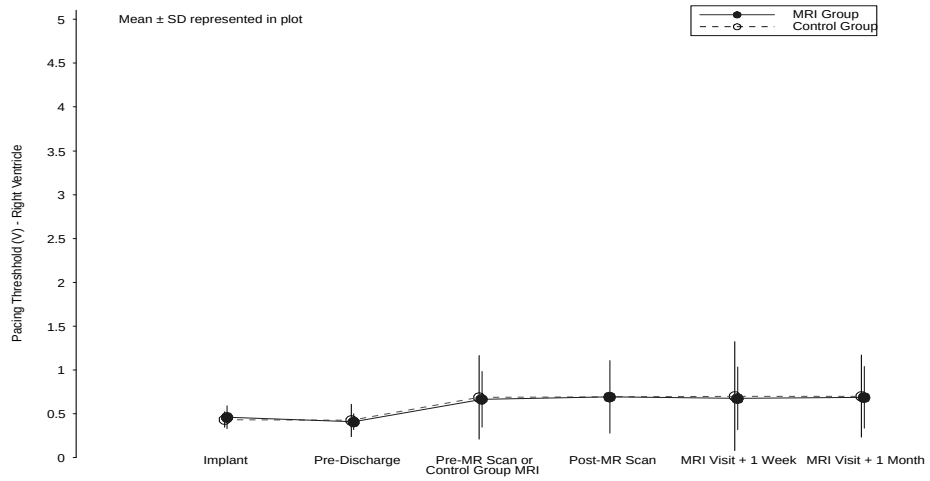
There were no significant changes for lead measurements throughout this period, and also no statistical differences between the MRI Group and the Control Group data.

Pacing Threshold Data



		Implant	Pre-Discharge	Pre-MR Scan or Control Group MRI	Post-MR Scan	MRI Visit + 1 Week	MRI Visit + 1 Month
MRI Group	N	184	186	187	159	185	183
	Mean ± SD	0.66 ± 0.31	0.47 ± 0.16	0.69 ± 0.28	0.66 ± 0.27	0.69 ± 0.24	0.72 ± 0.29
	(Min - Max)	(0.30 - 2.40)	(0.20 - 1.70)	(0.30 - 2.87)	(0.30 - 2.73)	(0.30 - 1.90)	(0.33 - 2.57)
Control Group	N	100	99	98	Not Applicable	96	98
	Mean ± SD	0.63 ± 0.27	0.54 ± 0.52	0.71 ± 0.25		0.71 ± 0.26	0.70 ± 0.27
	(Min - Max)	(0.30 - 2.13)	(0.30 - 5.00)	(0.37 - 1.50)		(0.35 - 1.80)	(0.40 - 2.10)

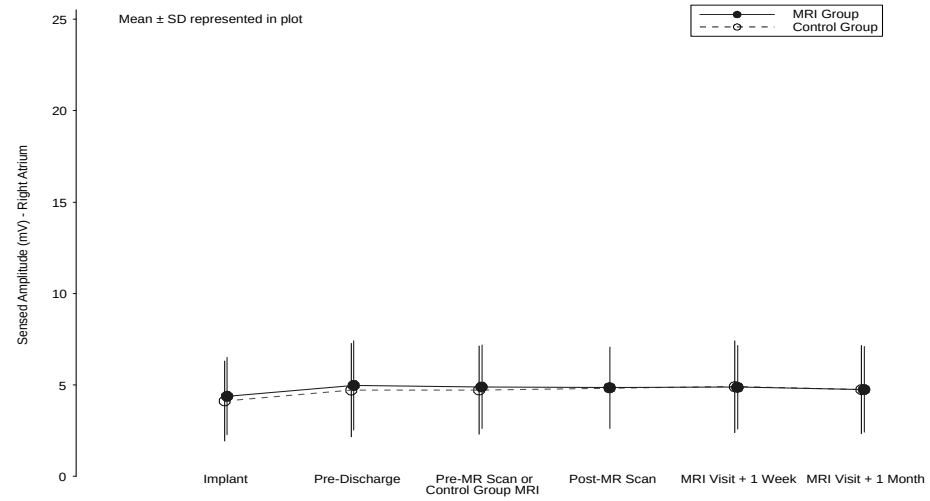
Appendix Figure 1. RA Pacing Threshold Measurements throughout Follow-up



		Implant	Pre-Discharge	Pre-MR Scan or Control Group MRI	Post-MR Scan	MRI Visit + 1 Week	MRI Visit + 1 Month
MRI Group	N	226	225	217	186	214	213
	Mean ± SD	0.46 ± 0.13	0.41 ± 0.09	0.67 ± 0.32	0.69 ± 0.41	0.67 ± 0.36	0.69 ± 0.35
	(Min - Max)	(0.27 - 0.97)	(0.23 - 0.80)	(0.30 - 3.10)	(0.37 - 3.53)	(0.33 - 3.47)	(0.30 - 3.50)
Control Group	N	117	117	114	Not Applicable	112	113
	Mean ± SD	0.44 ± 0.09	0.43 ± 0.19	0.69 ± 0.48		0.70 ± 0.62	0.70 ± 0.47
	(Min - Max)	(0.30 - 0.73)	(0.27 - 2.17)	(0.27 - 5.17)		(0.30 - 6.83)	(0.27 - 5.00)

Appendix Figure 2. RV Pacing Threshold Measurements throughout Follow-up

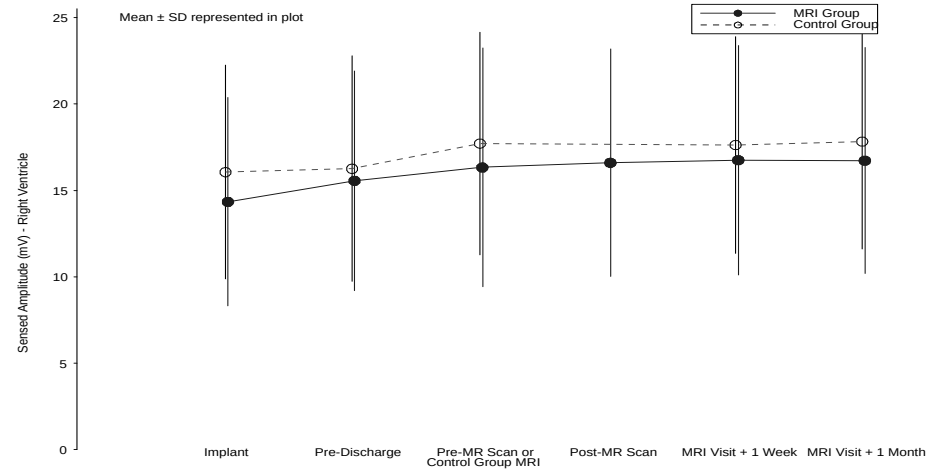
Sensed Amplitude Data



		Implant	Pre-Discharge	Pre-MR Scan or Control Group MRI	Post-MR Scan	MRI Visit + 1 Week	MRI Visit + 1 Month
MRI Group	N	182	184	182	157	180	179
	Mean ± SD	4.4 ± 2.1	5.0 ± 2.4	4.9 ± 2.3	4.9 ± 2.2	4.9 ± 2.3	4.8 ± 2.3
	(Min - Max)	(0.9 - 11.1)	(0.9 - 13.0)	(0.7 - 11.5)	(0.6 - 11.3)	(0.6 - 10.7)	(0.8 - 10.8)
Control Group	N	101	98	98	Not Applicable	94	97
	Mean ± SD	4.1 ± 2.2	4.7 ± 2.6	4.7 ± 2.4		4.9 ± 2.5	4.8 ± 2.4
	(Min - Max)	(0.9 - 11.7)	(0.7 - 12.3)	(0.4 - 12.7)		(0.8 - 12.3)	(0.8 - 11.9)

Appendix Figure 3. RA Sensed Amplitude Measurements throughout Follow-up

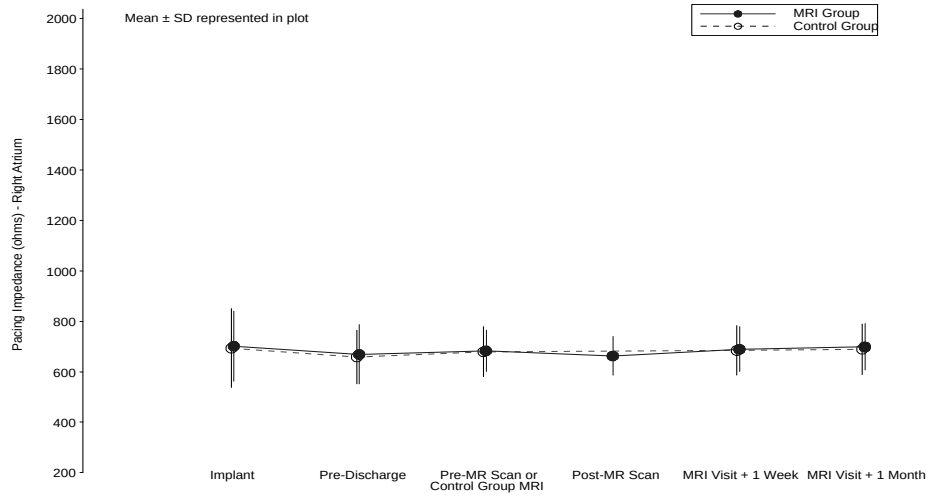
APPENDIX 1 Lead Measurements from Implant through Follow-Up



		Implant	Pre-Discharge	Pre-MR Scan or Control Group MRI	Post-MR Scan	MRI Visit + 1 Week	MRI Visit + 1 Month
MRI Group	N	215	218	200	180	195	200
	Mean ± SD	14.3 ± 6.0	15.6 ± 6.4	16.3 ± 6.9	16.6 ± 6.6	16.8 ± 6.6	16.7 ± 6.5
	(Min - Max)	(0.0 - 25.0)	(0.0 - 25.0)	(2.0 - 25.0)	(2.8 - 25.0)	(2.9 - 25.0)	(2.5 - 25.0)
Control Group	N	109	109	109	Not Applicable	105	110
	Mean ± SD	16.1 ± 6.2	16.3 ± 6.5	17.7 ± 6.4		17.6 ± 6.3	17.9 ± 6.2
	(Min - Max)	(4.3 - 25.0)	(2.6 - 25.0)	(0.0 - 25.0)		(2.3 - 25.0)	(2.2 - 25.0)

Appendix Figure 4. RV Sensed Amplitude Measurements throughout Follow-up

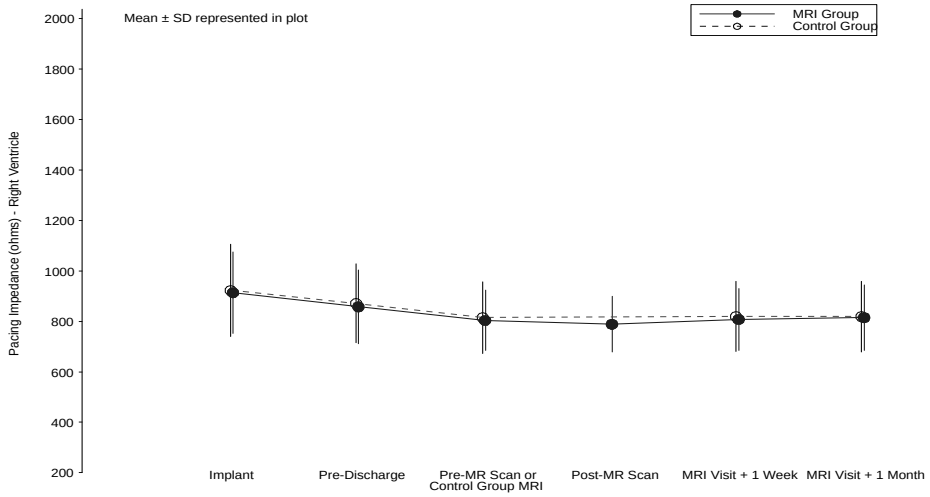
Pacing Impedance Data



		Implant	Pre-Discharge	Pre-MR Scan or Control Group MRI	Post-MR Scan	MRI Visit + 1 Week	MRI Visit + 1 Month
MRI Group	N	205	205	199	173	197	196
	Mean ± SD	702 ± 139	669 ± 117	683 ± 83	663 ± 77	689 ± 89	699 ± 92
	(Min - Max)	(534 - 1794)	(492 - 1747)	(481 - 943)	(491 - 1095)	(497 - 1091)	(507 - 1023)
Control Group	N	109	109	106	Not Applicable	103	104
	Mean ± SD	694 ± 156	659 ± 106	680 ± 98		685 ± 98	691 ± 100
	(Min - Max)	(527 - 1655)	(499 - 1316)	(511 - 905)		(511 - 939)	(522 - 944)

Appendix Figure 5. RA Pacing Impedance Measurements throughout Follow-up

APPENDIX 1 Lead Measurements from Implant through Follow-Up



		Implant	Pre-Discharge	Pre-MR Scan or Control Group MRI	Post-MR Scan	MRI Visit + 1 Week	MRI Visit + 1 Month
MRI Group	N	226	226	217	187	214	213
	Mean ± SD	914 ± 161	858 ± 146	804 ± 119	789 ± 110	808 ± 123	815 ± 130
	(Min - Max)	(592 - 1531)	(591 - 1389)	(598 - 1266)	(597 - 1237)	(598 - 1285)	(597 - 1334)
Control Group	N	118	118	115	Not Applicable	112	113
	Mean ± SD	923 ± 182	870 ± 157	815 ± 142		819 ± 139	820 ± 140
	(Min - Max)	(614 - 1690)	(622 - 1447)	(537 - 1338)		(540 - 1363)	(541 - 1277)

Appendix Figure 6. RV 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 18. Overall, implanting physicians were satisfied with the handling of the lead.

Appendix Table 1. Implant Questionnaire Results (N = 661 Implanted or Attempted Leads)

Item	Number of Responses (%)				
	RV Active Leads (N=284)	RA Active Leads (N=274)	RV Passive Leads (N=63)	RA Passive Leads (N=40)	All Leads (N=661)
Q1. Rate the radiopacity quality of the extendable/retractable helix markers					
(1) Exceeded Expectations	33 (11.8%)	34 (12.4%)	Not Applicable	Not Applicable	67 (12.1%)
(2) Very Good	135 (48.4%)	132 (48.2%)	Not Applicable	Not Applicable	267 (48.3%)
(3) Good	73 (26.2%)	68 (24.8%)	Not Applicable	Not Applicable	141 (25.5%)
(4) Met Expectations	32 (11.5%)	35 (12.8%)	Not Applicable	Not Applicable	67 (12.1%)
(5) Unacceptable	6 (2.2%)	5 (1.8%)	Not Applicable	Not Applicable	11 (2.0%)
Q2. Rate Handling and Maneuverability of the stylet and lead used					
(1) Exceeded Expectations	57 (20.4%)	55 (20.1%)	12 (19.0%)	7 (17.5%)	131 (20.0%)
(2) Very Good	136 (48.7%)	133 (48.5%)	40 (63.5%)	28 (70.0%)	337 (51.4%)
(3) Good	57 (20.4%)	54 (19.7%)	9 (14.3%)	4 (10.0%)	124 (18.9%)
(4) Met Expectations	29 (10.4%)	30 (10.9%)	2 (3.2%)	1 (2.5%)	62 (9.5%)
(5) Unacceptable	0 (0.0%)	2 (0.7%)	0 (0.0%)	0 (0.0%)	2 (0.3%)
Q3. Rate overall Handling Performance of the Lead					
(1) Exceeded Expectations	72 (25.8%)	66 (24.1%)	11 (17.5%)	7 (17.5%)	156 (23.8%)
(2) Very Good	131 (47.0%)	125 (45.6%)	42 (66.7%)	28 (70.0%)	326 (49.7%)
(3) Good	49 (17.6%)	50 (18.2%)	8 (12.7%)	4 (10.0%)	111 (16.9%)
(4) Met Expectations	27 (9.7%)	28 (10.2%)	2 (3.2%)	1 (2.5%)	58 (8.8%)
(5) Unacceptable	0 (0.0%)	4 (1.5%)	0 (0.0%)	0 (0.0%)	4 (0.6%)
(6) N/A or Rarely Used	0 (0.0%)	1 (0.4%)	0 (0.0%)	0 (0.0%)	1 (0.2%)
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	6 (15.0%)	6 (15.0%)
(2) Very Good	Not Applicable	Not Applicable	Not Applicable	30 (75.0%)	30 (75.0%)
(3) Good	Not Applicable	Not Applicable	Not Applicable	4 (10.0%)	4 (10.0%)
(4) Met Expectations	Not Applicable	Not Applicable	Not Applicable	0 (0%)	0 (0%)
(5) Unacceptable	Not Applicable	Not Applicable	Not Applicable	0 (0%)	0 (0%)

Item	Number of Responses (%)				
	RV Active Leads (N=284)	RA Active Leads (N=274)	RV Passive Leads (N=63)	RA Passive Leads (N=40)	All Leads (N=661)
Q5. (Single Chamber) - The Lead is easy to pass through small vessels					
(1) Strongly Agree	12 (4.6%)	Not Applicable	2 (3.5%)	Not Applicable	14 (4.4%)
(2) Agree	12 (4.6%)	Not Applicable	7 (12.3%)	Not Applicable	19 (6.0%)
(3) Somewhat Agree	0 (0%)	Not Applicable	0 (0%)	Not Applicable	0 (0%)
(4) Disagree	0 (0%)	Not Applicable	0 (0%)	Not Applicable	0 (0%)
(5) N/A	237 (90.8%)	Not Applicable	48 (84.2%)	Not Applicable	285 (89.6%)
Q6. (Dual Chamber) - The Lead is easy to pass through small vessels and/or vessels with multiple leads					
(1) Strongly Agree	58 (21.2%)	65 (24.4%)	19 (31.7%)	11 (28.9%)	153 (24.0%)
(2) Agree	155 (56.8%)	161 (60.5%)	33 (55.0%)	27 (71.1%)	376 (59.0%)
(3) Somewhat Agree	10 (3.7%)	10 (3.8%)	0 (0.0%)	0 (0.0%)	20 (3.1%)
(4) Disagree	0 (0.0%)	1 (0.4%)	0 (0.0%)	0 (0.0%)	1 (0.2%)
(5) N/A	50 (18.3%)	29 (10.9%)	8 (13.3%)	0 (0.0%)	87 (13.7%)
Q7. Rate the visibility of the radiopaque suture sleeve on x-ray during and after the implant procedure					
(1) Exceeded Expectations	39 (14.0%)	39 (14.2%)	15 (23.8%)	9 (22.5%)	102 (15.5%)
(2) Very Good	81 (29.0%)	79 (28.8%)	25 (39.7%)	18 (45.0%)	203 (30.9%)
(3) Good	91 (32.6%)	90 (32.8%)	14 (22.2%)	9 (22.5%)	204 (31.1%)
(4) Met Expectations	43 (15.4%)	40 (14.6%)	2 (3.2%)	1 (2.5%)	86 (13.1%)
(5) Unacceptable	4 (1.4%)	4 (1.5%)	0 (0.0%)	0 (0.0%)	8 (1.2%)
(6) N/A or Rarely Used	21 (7.5%)	22 (8.0%)	7 (11.1%)	3 (7.5%)	53 (8.1%)
Q8. The design of the low profile suture sleeve helps minimize bulk in the pocket					
(1) Strongly Agree	48 (17.2%)	45 (16.4%)	14 (22.2%)	10 (25.0%)	117 (17.8%)
(2) Agree	142 (50.9%)	140 (51.1%)	43 (68.3%)	25 (62.5%)	350 (53.4%)
(3) Somewhat Agree	61 (21.9%)	63 (23.0%)	5 (7.9%)	4 (10.0%)	133 (20.3%)
(4) Disagree	22 (7.9%)	22 (8.0%)	0 (0.0%)	1 (2.5%)	45 (6.9%)
(5) N/A	6 (2.2%)	4 (1.5%)	1 (1.6%)	0 (0.0%)	11 (1.7%)

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