Boston Scientific
Advancing science for life™

HeartLogic™ Heart Failure Diagnostic

In-Service

HeartLogic™
Heart Failure Diagnostic

Heart failure is a major clinical concern that impacts patients' quality of life and healthcare economics

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Overview | HeartLogic™ | MultiSENSE Study | Case Studies

Heart failure hospitalizations are associated with an **8-fold increase in mortality** and a **9-fold increase in recurrent hospitalizations**[1]

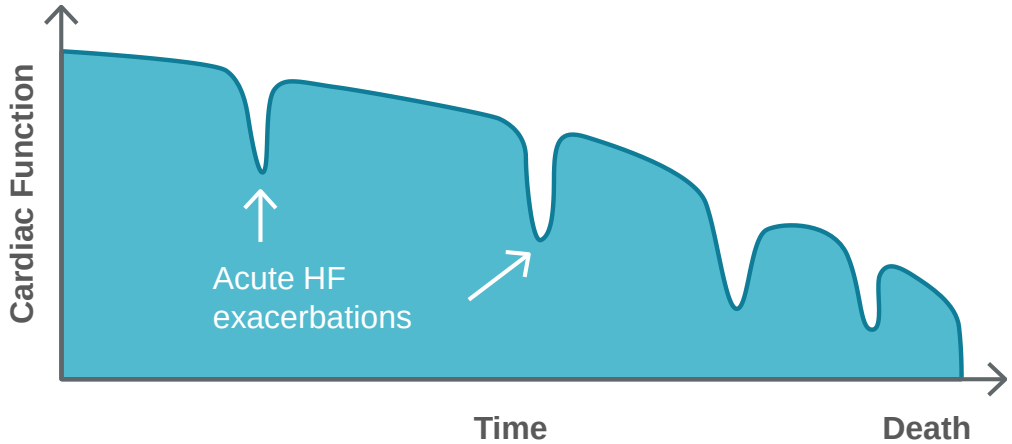

Figure adapted from Goodlin[1]

HF hospitalizations are the **biggest outflow** of **money**

- Accounting ≈ 60% of healthcare expenditure[2]

HeartLogic™
Heart Failure Diagnostic

1. March 18, 2010 Circulatory System Devices Panel - Boston Scientific, Inc: Sponsor Presentation 3 After Hospitalization: A Dartmouth Atlas Report on Post-Acute Care for Medicare Beneficiaries, Sept 28th, 2011

Heart failure symptoms of decompensation are possible to identify

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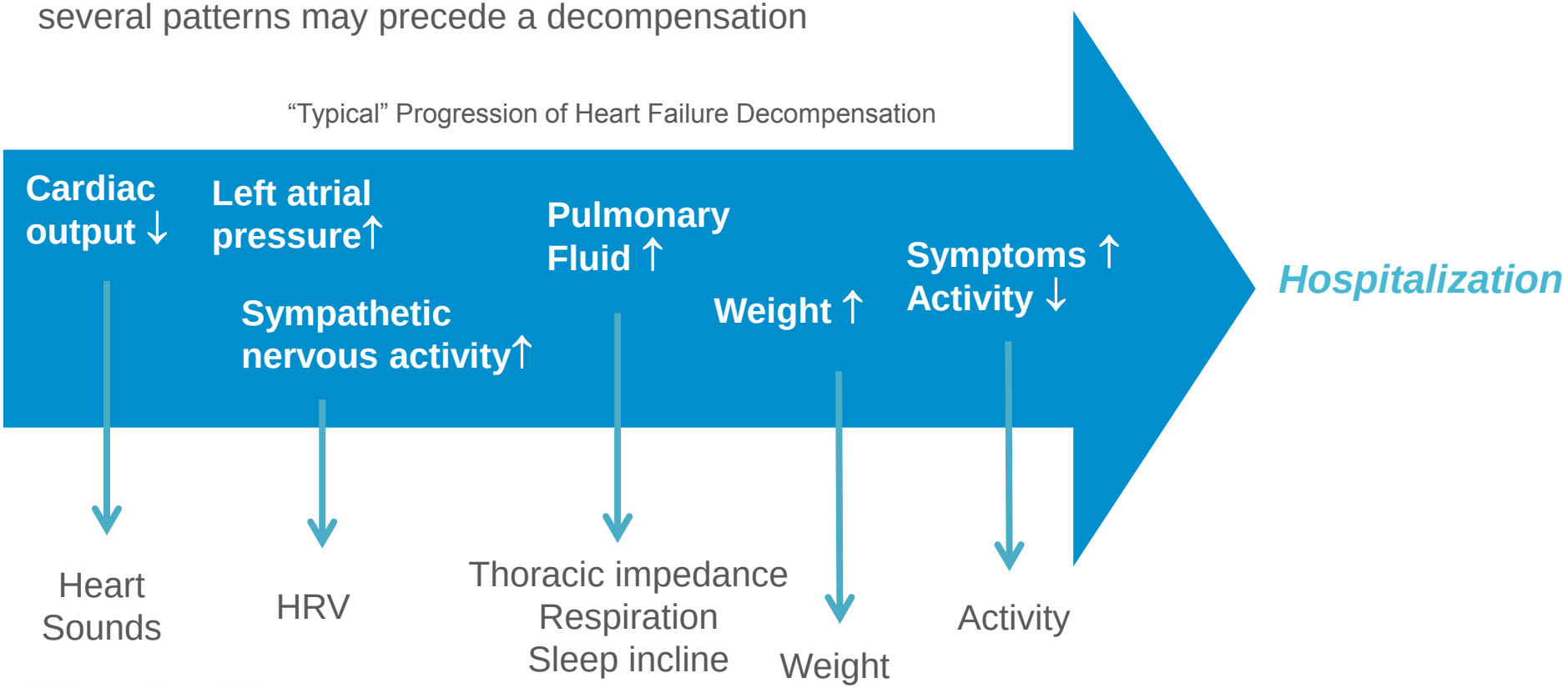
Overview | HeartLogic™ | MultiSENSE Study | Case Studies

Symptoms can vary in presentation and time course, nevertheless, several patterns may precede a decompensation



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Heart Failure Diagnostic

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Boston Scientific sensors enable the early detection of heart failure decompensation symptoms

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Sensors are intended to represent typical in-office tests and questions

Our sensors:	What Clinicians ask/do during a physical exam
Heart Sounds	Listen to the heart S3 heart sound
Heart Sounds	Listen to the heart S1 heart sound
Thoracic Impedance	Take chest X-ray for signs of pulmonary edema
Respiratory Rate	"Are you out of breath? Have difficulty breathing?"
Activity Level	"Are you able to get your mail/go upstairs?"
Weight	"Have you gained weight?" (check leg or abdominal swelling)
Night Heart Rate	Is resting heart rate elevated?

Key:
New to Resonate Platform
Legacy Trends
Unique to BSC

HeartLogic™
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Introducing HeartLogic™ Heart Failure Diagnostic

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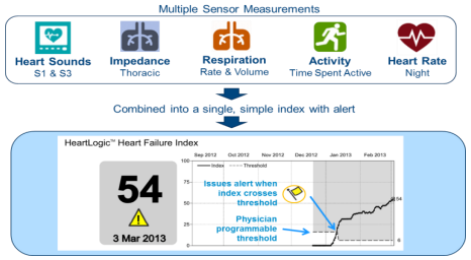
Overview | HeartLogic™ | MultiSENSE Study | Case Studies

HeartLogic™ enables **proactive care** of heart failure patient management **with a multifactorial approach**

Incorporates Multiple Sensors with a Single Composite Alert



Available on LATITUDE NXT for patients with **Resonate™** family of ICDs & CRT-Ds

The MultiSENSE study results[1] demonstrated:

High sensitivity of 70 % for detecting heart failure events

Weeks of advance notice of a potential heart failure event

Low burden of less than 2 alerts per patient per year.

HeartLogic™
Heart Failure Diagnostic

1) Boehmer, J et al., JACC-HF, 2017;5(3),2 1 6 – 2 5.

Benefit of Multifactorial Approach

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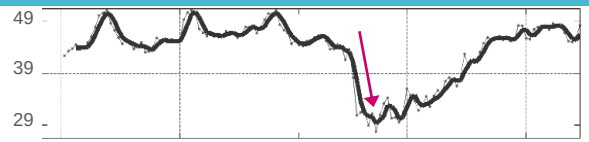
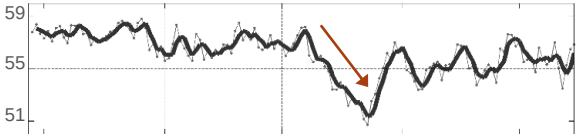
Overview | HeartLogic™ | MultiSENSE Study | Case Studies

Patient A — *Two Observed Cases* — **Patient B**

Which patient had a Heart Failure Event?



Thoracic Impedance



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Benefit of Multifactorial Approach

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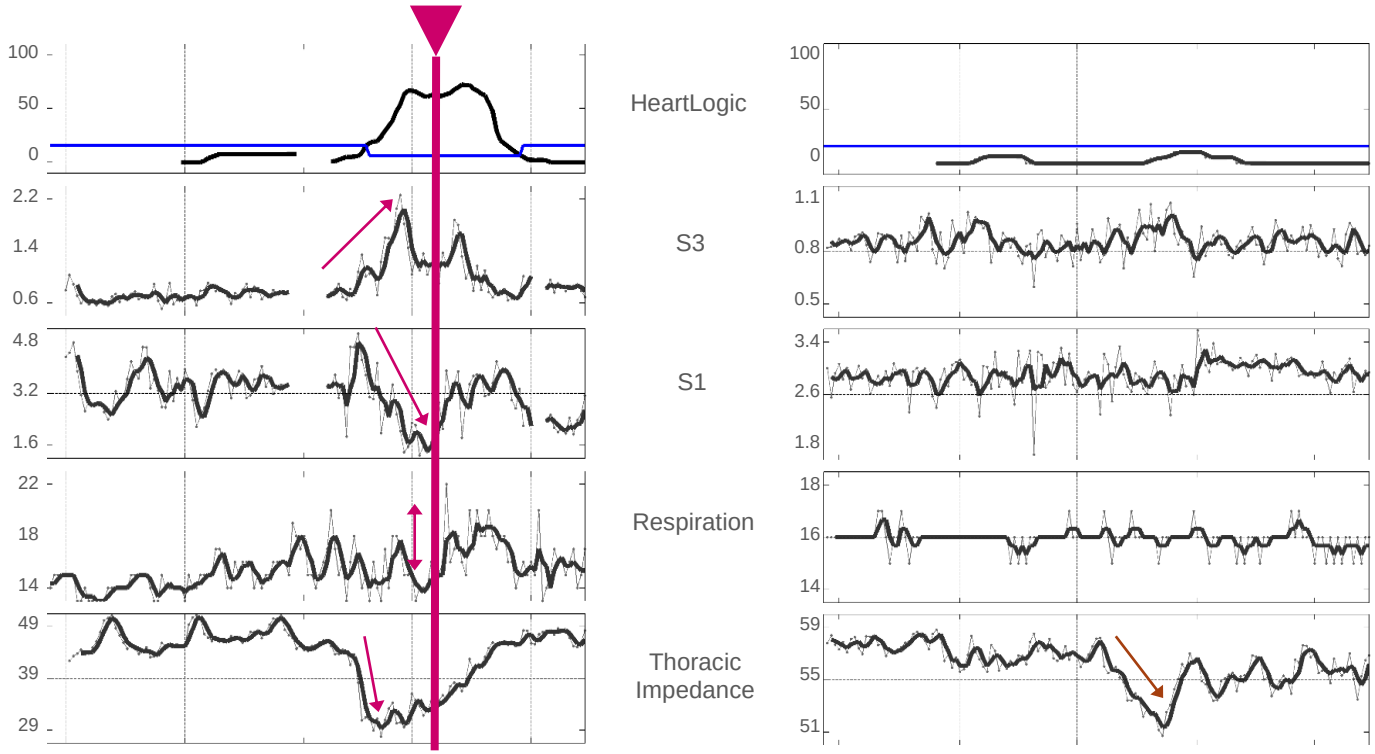
Overview | HeartLogic™ | MultiSENSE Study | Case Studies

Patient A — *Two Observed Cases* — Patient B

Multi-sensor Changes before a **HF Event**

Impedance-only Change with **NO** Event



HeartLogic Uses Multiple Sensors

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HeartLogic™ Heart Failure Diagnostic

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Overview | HeartLogic™ | MultiSENSE Study | Case Studies

HeartLogic was validated[1] to detect the early warning signs of worsening heart failure by combining data from **5 sensors** into a single composite index.

Multiple Sensor Measurements

Heart Sounds S1 & S3

Impedance Thoracic

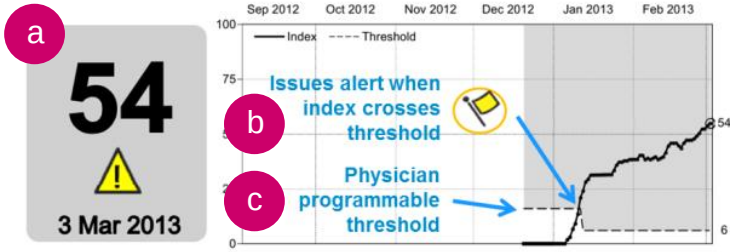
Respiration Rate & Volume

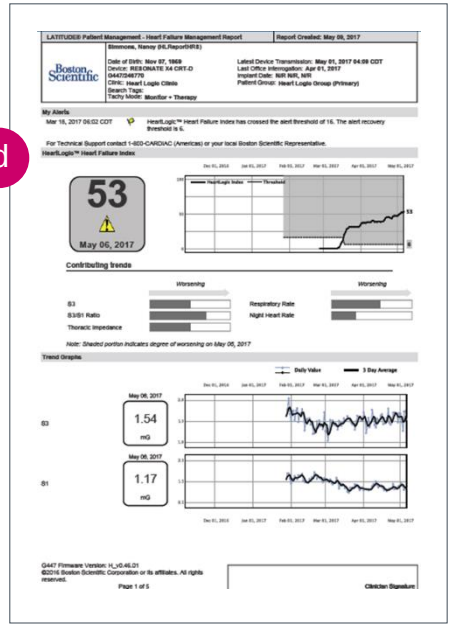
Activity Time Spent Active

Heart Rate Night

Combined into a single, simple index with alert

HeartLogic™ Heart Failure Index





HeartLogic™ Includes:

- **a** Composite HeartLogic™ Index trend
- **b** Actionable HeartLogic™ Alert
- **c** Configurable HeartLogic™ Threshold
- **d** Heart Failure Management Report with HeartLogic™ Data

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Heart Failure Diagnostic

1) Boehmer, J et al., JACC-HF, 2017;5(3),2 1 6 – 2 5.

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Heart Sounds; new to Resonate Platform, **Unique to Boston Scientific**

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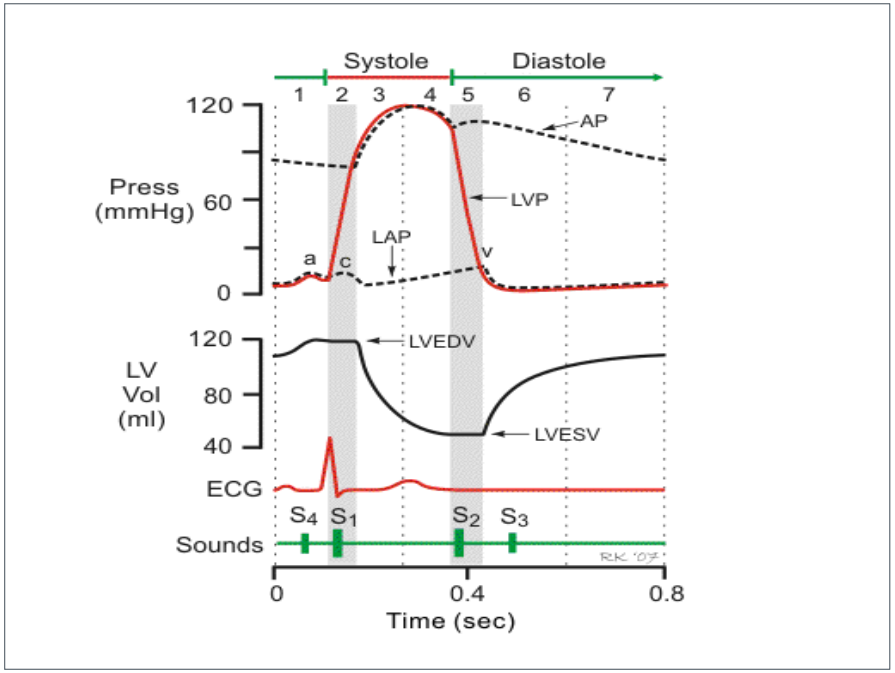
Overview | HeartLogic™ | MultiSENSE Study | Case Studies

Heart Sounds | Respiration | Night Heart Rate | Activity | Thoracic Impedance | Report

Heart Sounds were traditionally evaluated based on physician audibility using a stethoscope



- In a normal subject, the first heart sound S1 happens shortly after the Q-wave in an EKG, produced by the closing of atrioventricular valves.
- S3 is caused by rapid filling of blood against a stiffer ventricular wall during passing filling. It may not be audible in normal subject

Heart Sounds; new to Resonate Platform, **Unique to Boston Scientific**

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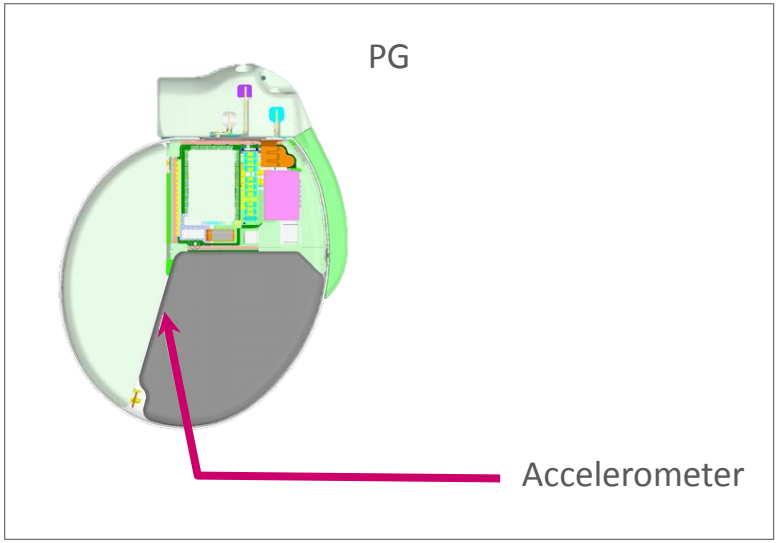
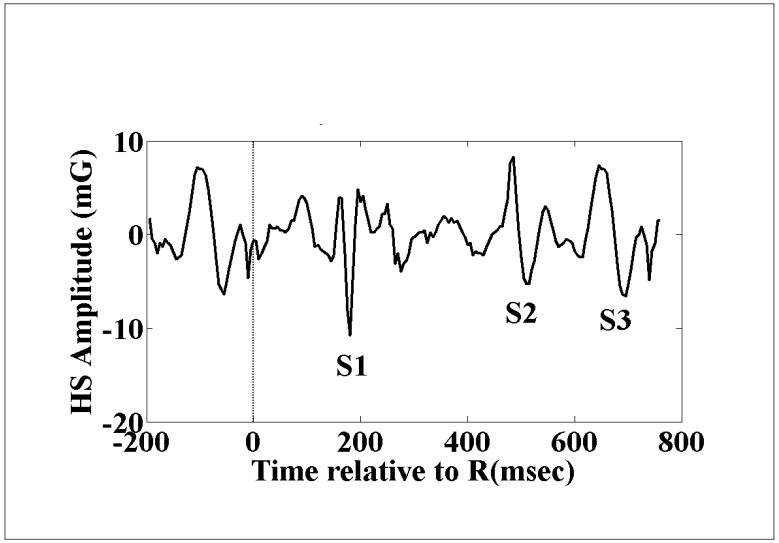
Overview | HeartLogic™ | MultiSENSE Study | Case Studies

Heart Sounds · Respiration · Night Heart Rate · Activity · Thoracic Impedance · Report

Heart sounds are measured from the accelerometer and reveals signs of elevated filling pressure and weakened ventricular contraction via S3 and S1 heart sounds.





Worsening heart failure may be associated with an increase in S3 or a decrease in S1, or both

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Device-measured S3 more efficient than auscultation

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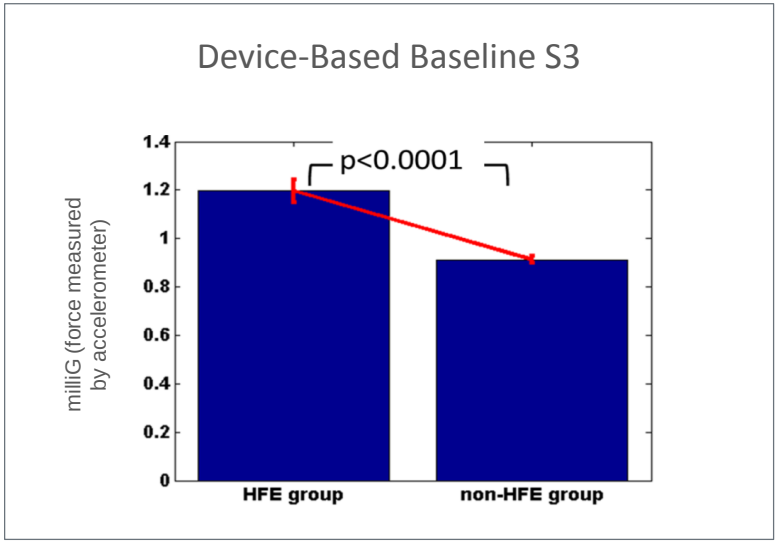
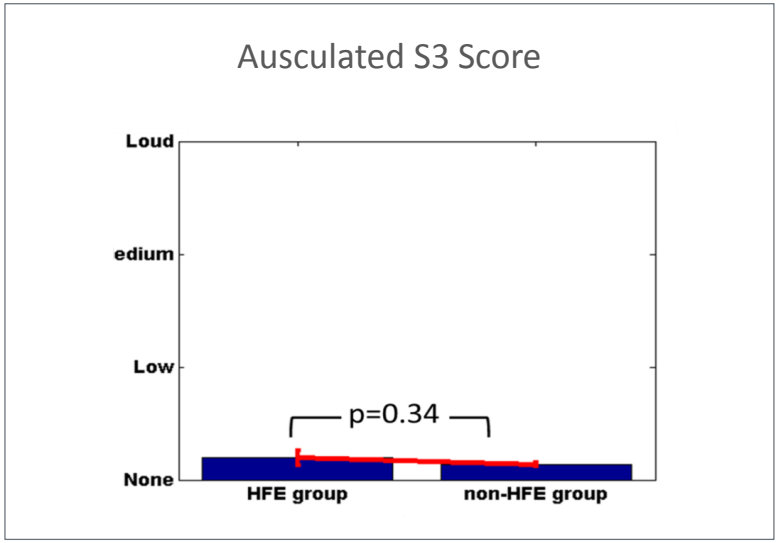
Overview | HeartLogic™ | MultiSENSE Study | Case Studies

Heart Sounds · Respiration · Night Heart Rate · Activity · Thoracic Impedance · Report

Device-based **S3** includes audible and sub-audible frequencies and therefore can **pick up vibrations that cannot be detected by the human ear**





- Device-based S3 was significantly louder in patients with HF events
- Auscultated S3 was mostly absent and no different between groups

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Presented at HRS 2015 Nair D. et al. "Baseline S3 Measured using Implanted Accelerometer is more Prominent in Patients with Heart Failure Decompensations", Heart Rhythm, 2015; Volume 12, Issue 5 , Supplement: S372-424.

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Device-based S1 and S3 measured during clinically stable periods

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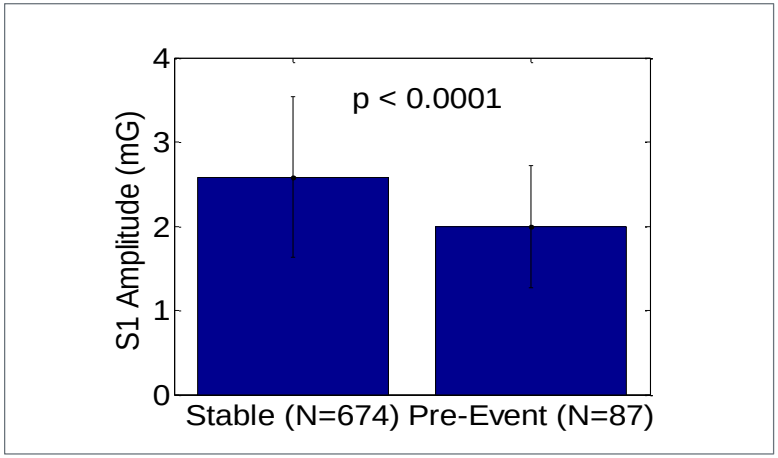
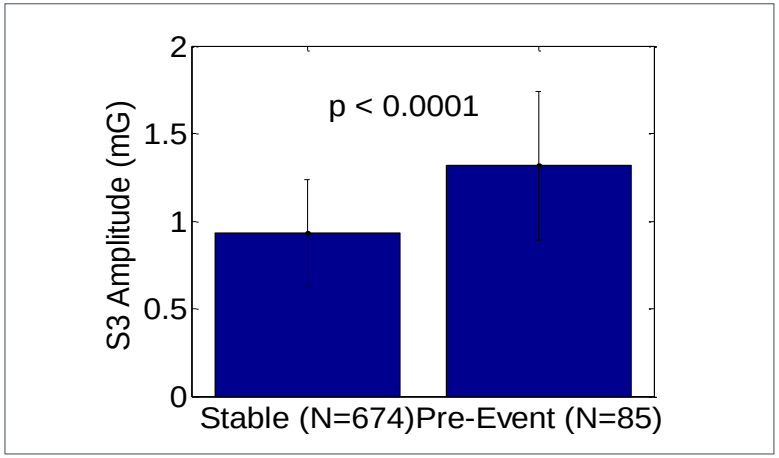
Overview | HeartLogic™ | MultiSENSE Study | Case Studies

Heart Sounds · Respiration · Night Heart Rate · Activity · Thoracic Impedance · Report

S3 and **S1** amplitudes were **significantly different** in **pre-event windows** from those during clinically stable periods in ambulatory heart failure patients





A clinically stable period is defined as a period between office visits when: a) NYHA classification was unchanged, b) Weight change ≤ 5 lbs (2.27kg), c) No adverse events were reported between the visits

- Presented at HFSA 2013; data from PRE-SENSE study, E. Klodas, et. al. Journal of Cardiac Failure, 2013, 19(8): S67
- Gardner RS, Nair DG, Eldadah Z, Stancak B, Thakur P, Wariar R, Zhang Y, An Q, Averina V, Sweeney R, Boehmer JP. Heart failure diagnostic sensor measurements during clinically stable epochs in ambulatory heart failurepatients. Eur J of Heart Failure 2017;19(Suppl. S1):277(P1132). Cao M, Schulze C, Gardner R, An Q, Thakur P, Thompson J, Boehmer J. Device-measured third heart sound predicts heart failure events better than auscultatedthird heart sound. Europace 2017; 19 (suppl_3): iii332-iii333.
- Sriratanasathavorn C, Fisher J, Bransford P, Chan R, Sweeney R, Ahmed R, Averina V, An Q, Thakur P, Zhang Y, Boehmer J. Heart Failure Diagnostic Sensor Measurements Change Prior to Heart Failure Decompensation Events.Accepted at APHRS 2017
- TSUGUYA SAKAMOTO, REIZO KUSUKAWA, DONALD M. MACCANON, ALDO A. LUISADA and Ivan Harvey. Hemodynamic Determinants of the Amplitude of the First Heart Sound. Circulation Research. 1965;16:45-57, originallypublished January 1, 1965. https://doi.org/10.1161/01.RES.16.1.45. Thakur, P. H., An, Q., Swanson, L., Zhang, Y., and Gardner, R. S. (2017)Haemodynamic monitoring of cardiac status using heart sounds from an implantedcardiac device. ESC Heart Failure, doi: 10.1002/ehf2.12171.

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Device-measured 3S HFE prediction Vs. auscultated third heart sound

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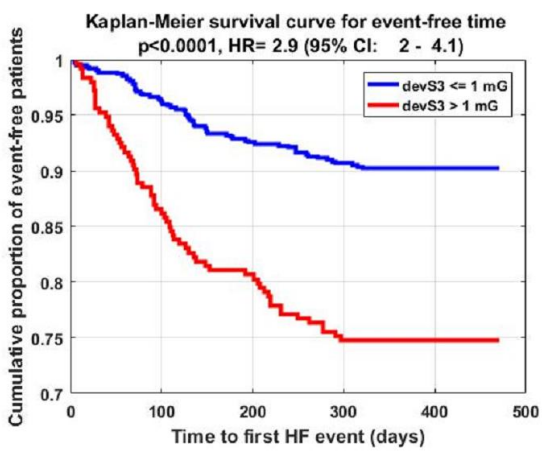
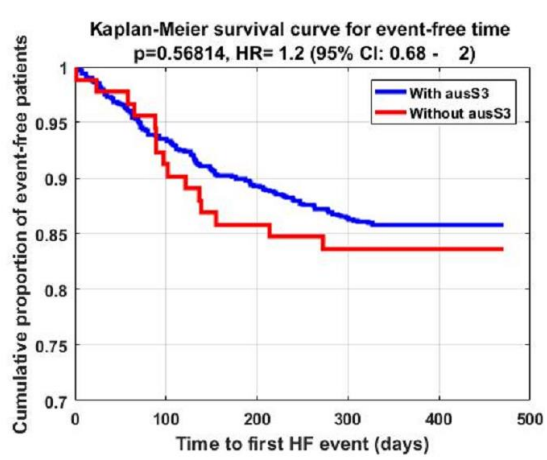
Device-measured **S3** has better correlation with the **risk of heart failure** events over one year than auscultated S3





This superiority may be attributable to the subjective nature of auscultation, limitations of the frequency range of human hearing, as well as limitations of a single snap-shot auscultation assessment.

Device-measured S3 significantly correlated to echo parameters

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Overview | HeartLogic™ | MultiSENSE Study | Case Studies

Heart Sounds · Respiration · Night Heart Rate · Activity · Thoracic Impedance · Report

In PRE-SENSE, a related feasibility study conducted on CRT-D patients:

- S3 amplitude was significantly correlated with EDT, EDR, E/A ratio and E/E' ratio, which are often used to assess LV diastolic function
- There was significant separation across almost all echo parameters between the low and high S3 groups (high = top quartile).

Measures		Low S3 (n=48)	High S3 (n=14)	p-value
LVEF (%)		41.5	28.4	**0.004**
LV Volume	LVEDD (cm)	5.57	6.71	**<0.001**
	LVEDV (mL)	134.8	182.6	**0.005**
	LVESD (cm)	4.35	5.81	**<0.001**
	LVESV (mL)	83.5	134.6	**0.003**
LA volume	LAEDV (mL)	72.1	101.1	**0.006**
Diastolic Filling (E and A waves)	E (cm/s)	62.8	89.0	**0.006**
	EDT (ms)	279.5	193.3	**<0.001**
	EDR (m/s^2)	2.63	5.02	**<0.001**
	E/A ratio	0.89	1.49	**0.020**
	E/E' septal ratio	13.2	19.4	**0.003**
	E' septal (cm/s)	5.31	4.29	0.162

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Presented at HFSA 2013; data from PRE-SENSE study E. Klodas, et. al. Journal of Cardiac Failure, 2013, 19(8): S67.

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HeartLogic Sensors

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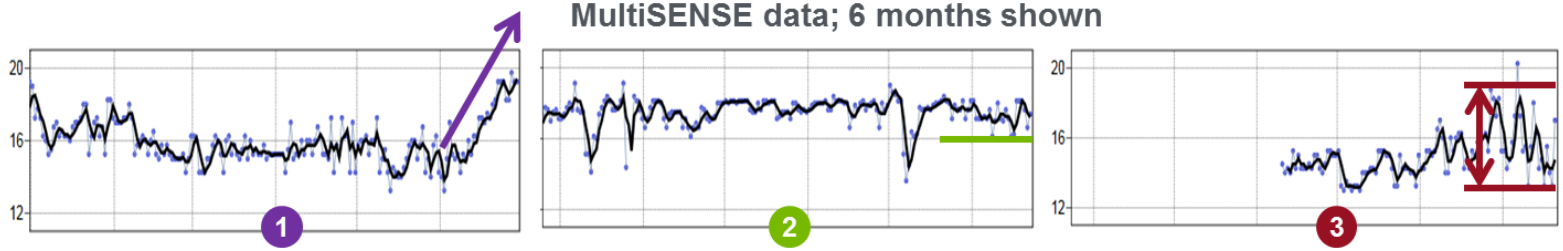
Overview | **HeartLogic™** | MultiSENSE Study | Case Studies

Heart Sounds | **Respiration** | Night Heart Rate | Activity | Thoracic Impedance | Report

- The Respiratory Sensor uses transthoracic impedance measurements to collect respiration-related data, specifically respiration rate and tidal volume.
- Respiration rate and tidal volume are combined to produce additional respiration metrics.
- **Worsening heart failure may be associated with an elevated RR, an increase in RR, or an increase in day-to-day RR variability**.

MultiSENSE data; 6 months shown



Respiratory rate **increases** prior to heart failure events.[1]

Respiratory rate **above 20 breaths/min** on average over 30 days has **3.5-fold increased risk** of HF hospitalisation within the following 30 days.[2]

Respiratory rate with a **higher range** over 30 days has **4.9-fold increased risk** of HF hospitalisation within the following 30 days.[3]

HeartLogic™
Heart Failure Diagnostic

1. Presented at ESC 2014. A. Capucci, et al., EHJ, 2014; Vol. 35, Suppl 1, pp. 678. 2Presented at HRS 2016. M. Atkas, et al., Heart Rhythm, 2016 3Presented at HRS 2013 and AAHFN 2014. J. P. Boehmer, et al., Heart Rhythm, 2013;10(5):S66.

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HeartLogic Sensors

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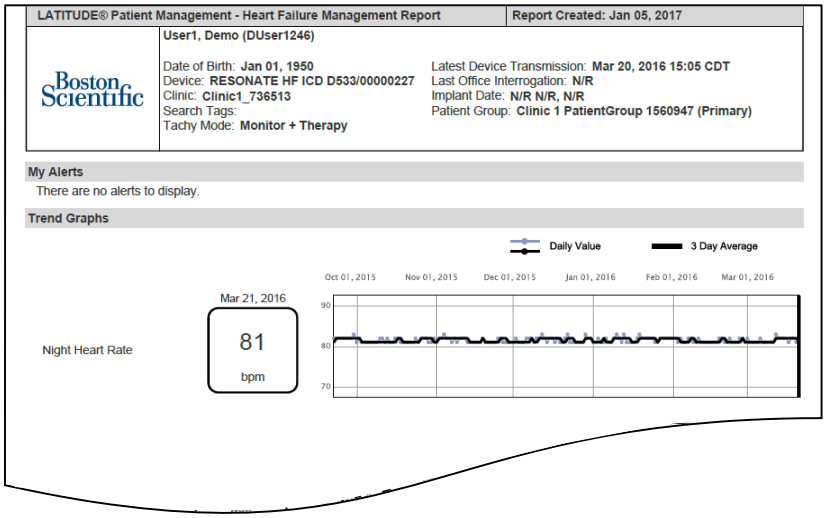
Overview | HeartLogic™ | MultiSENSE Study | Case Studies

Heart Sounds · Respiration · **Night Heart Rate** · Activity · Thoracic Impedance · Report

Worsening heart failure may be associated with **increases in Night Heart Rate**

Night Heart Rate

- Average Heart Rate from 12 am to 6 am
- Tends to capture close to resting heart rate for most patients
- Resting HR are known to be prognostic for cardiovascular outcomes
- Look for increases as a sign of heart failure worsening



HeartLogic™
Heart Failure Diagnostic

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HeartLogic Sensors

Worsening heart failure may be associated with a **decrease in a patients activity level**

Activity

- Numbers of hours per day a patient is active.
- Overall status and fatigue.

HeartLogic Sensors

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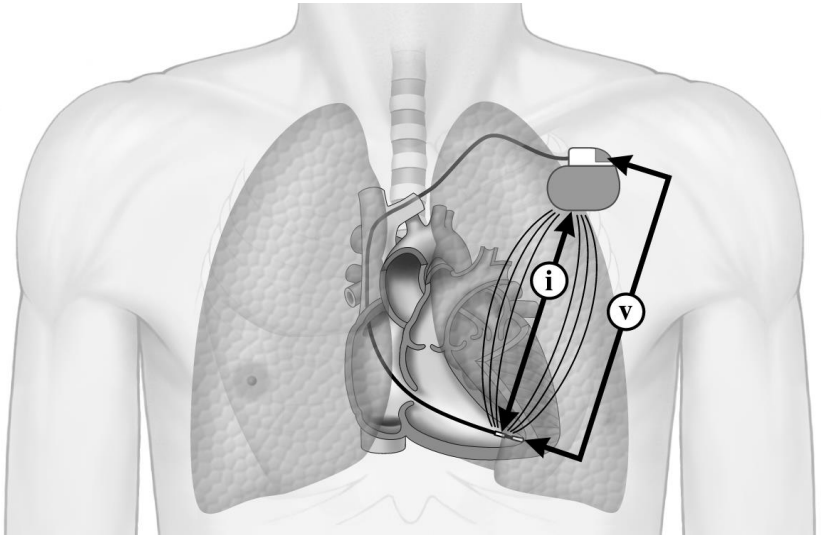
Overview | HeartLogic™ | MultiSENSE Study | Case Studies

Heart Sounds · Respiration · Night Heart Rate · Activity · **Thoracic Impedance** · Report

Thoracic Impedance[2]

- The Thoracic Impedance sensor measures impedance between electrodes on the RV lead and the pulse generator (PG) can.
- Thoracic Impedance may be associated with the fluid level in the patient's chest and may track fluid level changes.



Worsening heart failure may cause a patient's fluid level to increase, therefore, decrease in thoracic impedance. This information can be valuable when used in conjunction with a multifactorial approach to assess and treat HF patients[1]

- Wang L, Lahtinen S et al. Feasibility of using an implantable system to measure thoracic congestion in chronic heart failure. Pacing Clin Electrophysiol. 2005;28:404-411
- Sriratanasathavorn C, Fisher J, Bransford P, Chan R, Sweeney R, Ahmed R, Averina V, An Q, Thakur P, Zhang Y, Boehmer J. Heart Failure Diagnostic Sensor Measurements Change Prior to Heart Failure Decompensation Events.Accepted at APHRS 2017.
- Yu CM et al. Intrathoracic impedance monitoring in patients with heart failure: correlation with fluid status and feasibility of early warning preceding hospitalization. Circulation, 2005 Aug; 9; 112(6): p841-8.

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HeartLogic™
Heart Failure Diagnostic

HeartLogic™: Heart Failure Management Report

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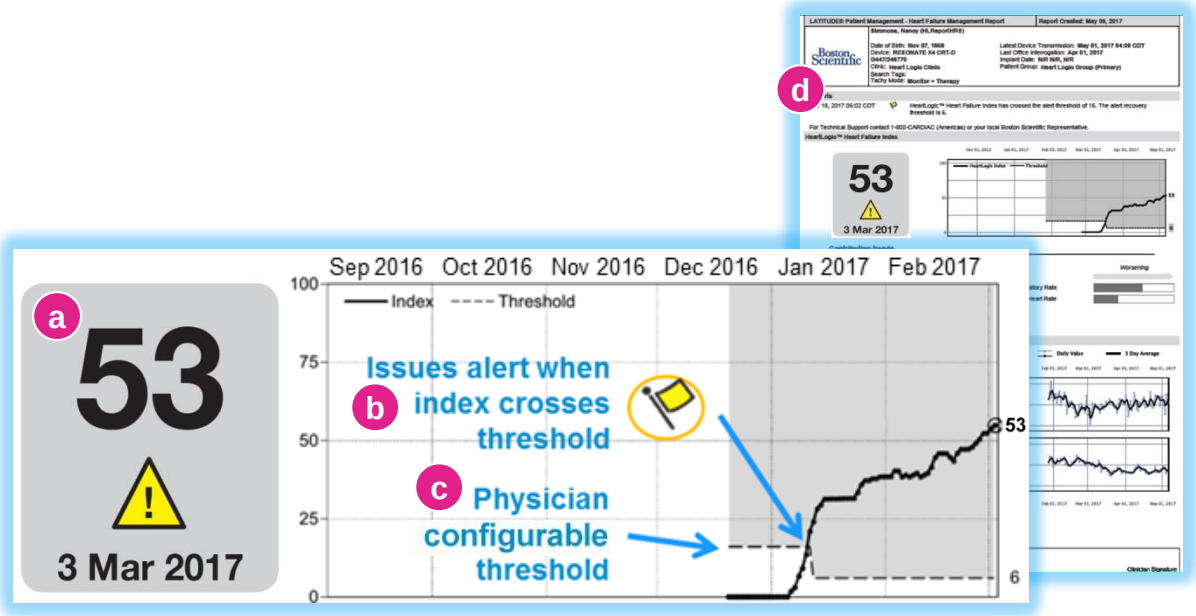
Overview | HeartLogic™ | MultiSENSE Study | Case Studies

Heart Sounds · Respiration · Night Heart Rate · Activity · Thoracic Impedance · **Report**

HeartLogic collects information through the implanted device **without patient involvement** and provides data via **LATITUDE NXT 24/7**

HeartLogic™ Includes:

- **a** Composite HeartLogic™ Index trend
- **b** Actionable HeartLogic™ Alert
- **c** Configurable HeartLogic™ Threshold
- **d** Heart Failure Management Report with HeartLogic™ Data



High performing composite indicator for detecting worsening of heart failure using multiple physiologic measurements

HeartLogic™
Heart Failure Diagnostic

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Boehmer, J et al., JACC-HF, 2017;5(3),2 1 6 – 2 5

Enabling HeartLogic™ : Quick review

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There are essentially two steps required to enable HeartLogic:

- Program the device to ensure that Heart Failure Sensor Suite is activated. Heart Failure Sensor Suite is on by default
- Ensure that the patient with the implanted device is added to the Latitude™ NXT system, provided with a Communicator, and that the Latitude™ NXT system is programmed appropriately.

It will take up to 37 days from the time of implant to the point where it begins compliling Index numbers, allowing potential transmission of HeartLogic™ Alerts over Latitude™ NXT, assuming it is programmed ON.

In order to see HeartLogic data, remember that patients need to be on Latitude™ NXT and HeartLogic has to be activated for the patient.

Primary Results from the MultiSENSE Study

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A **Multi-Sensor Algorithm Predicts Heart Failure** Events in Patients with Implanted Devices

- International, multi-center, non-randomized, clinical study designed to **develop** and **prospectively evaluate** a multi-sensor index and alert for the **early detection of worsening heart failure**.
- **New sensors created** with enhanced components and **novel data collection** and **processing techniques**.

Key inclusion criteria	• HeartLogicAge 18 or above • Currently implanted with a COGNIS CRT-D system • NYHA Class II, III or IV within the last 6 months
Key exclusion critera	• Documented as pacemaker dependent • History of appropriate Tachy therapy 1 week prior to enrollment • Likely to undergo lead or PG revision • Subjects that have received a heart or lung transplant • Receiving mechanical circulatory transplant • A life expectancy of less than 12 months

Boehmer, J et al., JACC-HF, 2017;5(3),2 1 6 – 2 5.

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Primary Results from the MultiSENSE Study

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Independent clinical events committee (CEC) Adjudication:

Heart failure Events (HFE)	**Primary** cause of event was worsening heart failure and • Is **admitted** for HF and receives an augmented HF regimen with oral or intravenous medications, or • Receives unscheduled **intravenous** decongestive therapy that does not involve formal in-patient hospital admission, regardless of the setting
True Position Alerts	• Onset before a usable HFEs • Recovery no earlier than **30 days** before usable HFEs
HF Related Alerts	Same onset and recovery window but broader set of HF events: • hospitalizations with a **secondary** cause of HF, • outpatient visits with a primary cause of HF and augmented **oral** medication changes, • HFEs that did not meet sensor **data availability** criteria or occurred within 45 days of device conversion
Unexplained Alerts	• All other alerts

HeartLogic™
Heart Failure Diagnostic

Boehmer, J et al., JACC-HF, 2017;5(3),2 1 6 – 2 5.

Primary Results from the MultiSENSE Study

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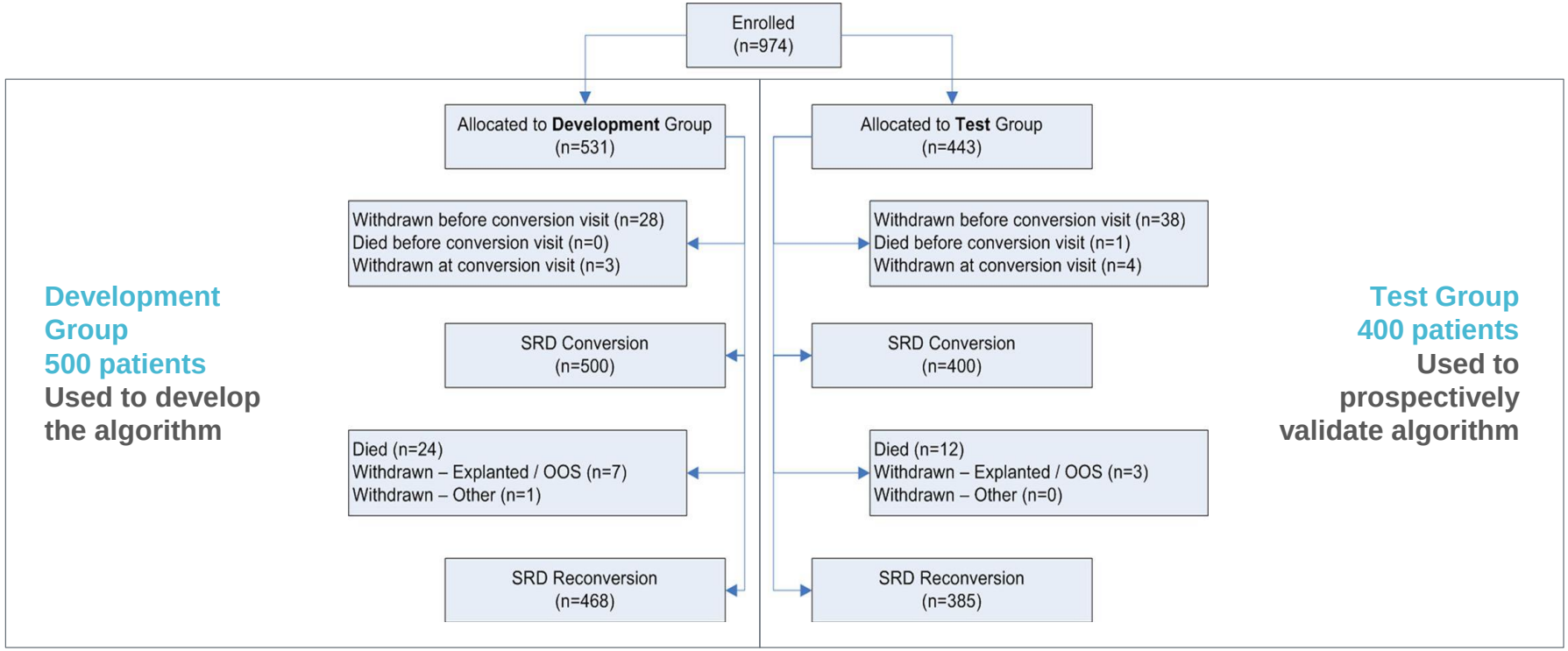
Overview | HeartLogic™ | MultiSENSE Study | Case Studies

Data was used to develop individual physiologic sensor trends and a **multi-sensor composite alert for worsening heart failure**



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Primary Results from the MultiSENSE Study

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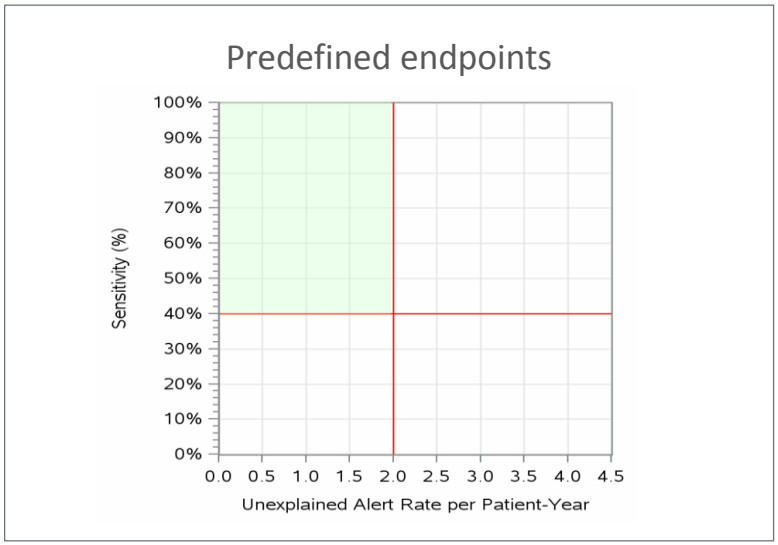
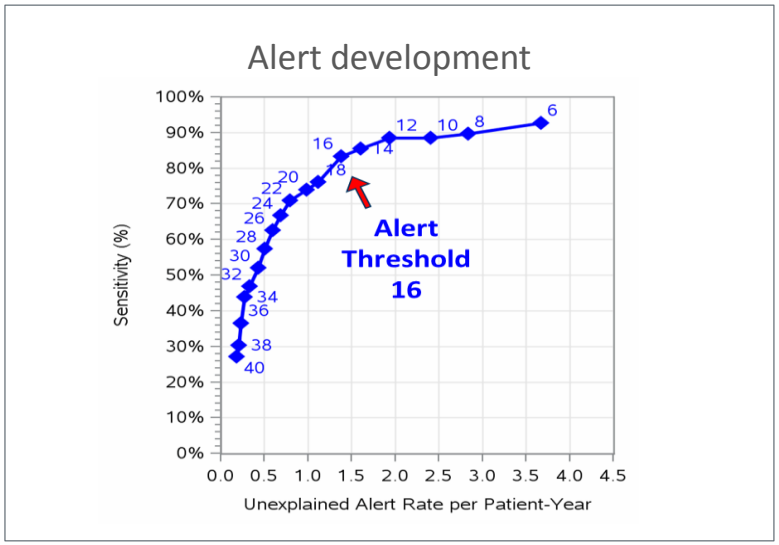




- Endpoint 1: **Sensitivity** for detecting usable heart failure events **>40 %**
- Endpoint 2: **Unexplained alert rate** (UAR) per patient year **<2.0**

- **HeartLogic threshold** is configurable to user's preference for sensitivity and specificity
- By increasing sensitivity the UAR decreases

HeartLogic™
Heart Failure Diagnostic

Boehmer, J et al., JACC-HF, 2017;5(3),2 1 6 – 2 5.

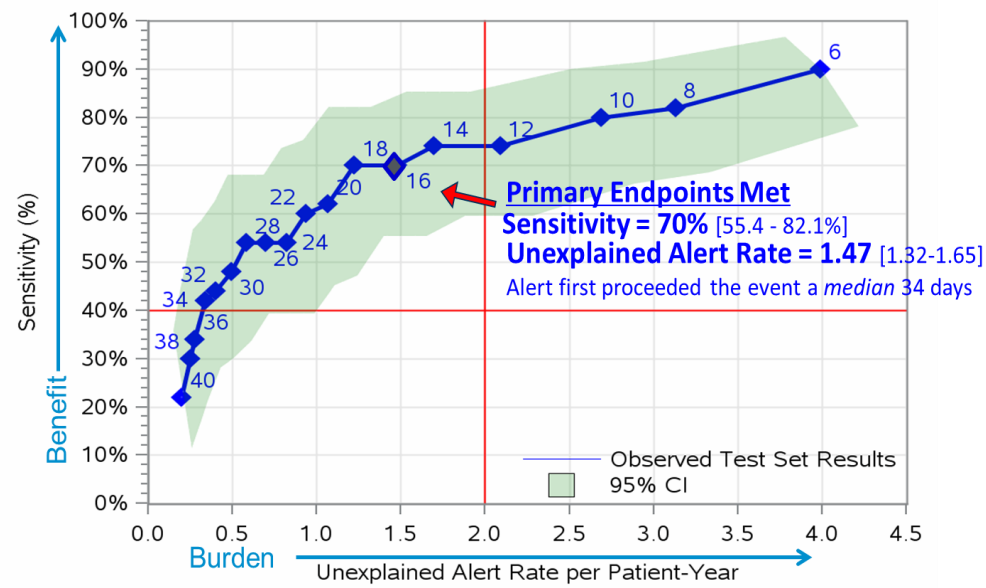
Primary Results from the MultiSENSE Study

Boston Scientific

Overview | HeartLogic™ | MultiSENSE Study | Case Studies

The MultiSENSE Study data validated that HeartLogic™:

- Had **high sensitivity** of 70 % in detecting heart failure events
- Had a very **low burden** of less than 2 alerts per patient per year
- May have allow several **weeks of advanced notice** to clinicians of a potential event



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Boehmer, J et al., JACC-HF, 2017;5(3),2 1 6 – 2 5.

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HeartLogic™ Index Trends

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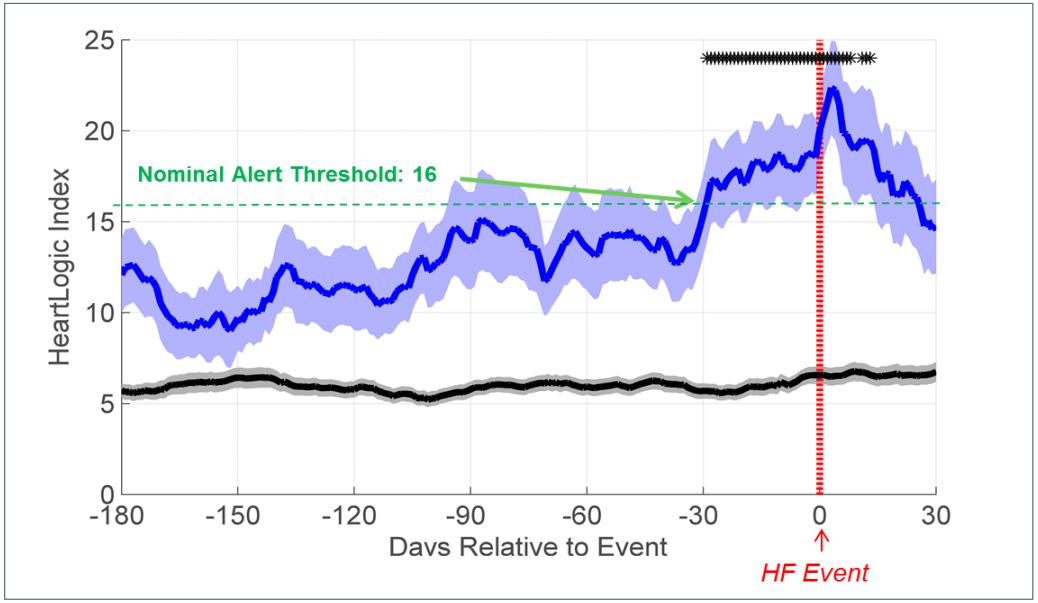
Overview | HeartLogic™ | MultiSENSE Study | Case Studies

MultiSENSE Study results showed that it could have allowed **weeks of advanced notice** to clinicians to a potential heart failure event.



HeartLogic™ Index in patients **with** Heart Failure Events

HeartLogic™ Index in patients **without** Heart Failure Events

Compared to 3 month baseline, HeartLogic Index was **statistically higher** beginning 29 days prior to event.

HeartLogic™
Heart Failure Diagnostic

Boehmer, J et al., JACC-HF, 2017;5(3),2 1 6 – 2 5.

CRM-495201-AB

Event Rate Ratio Presented as a LBCT at ESC-HF 2017

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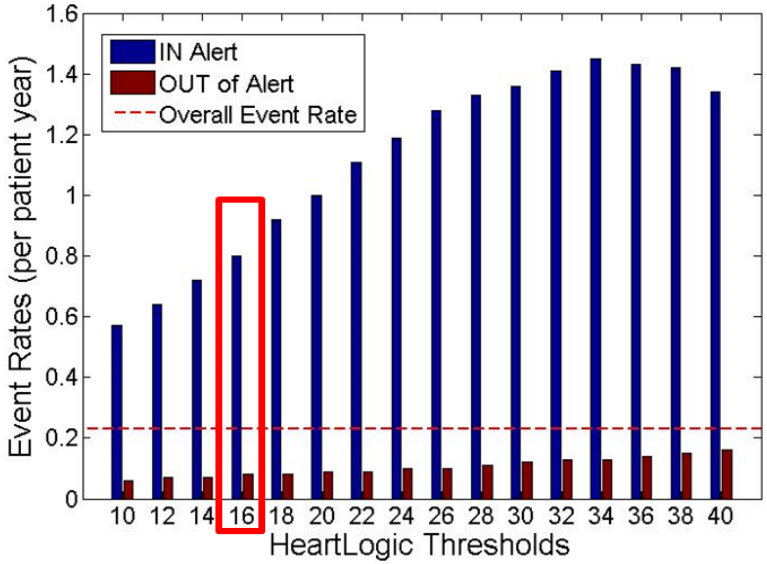

- At nominal HeartLogic Threshold = 16
  - HF Event Rate was **10x higher** when **IN a HeartLogic Alert** versus **NOT in an alert**
- 17 % of patient-days IN Alert State

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LBCT at ESC-HF 2017. NOTE: Event rate ratio calculation.

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HeartLogic was better pronosticator than a baseline NT-proBNP

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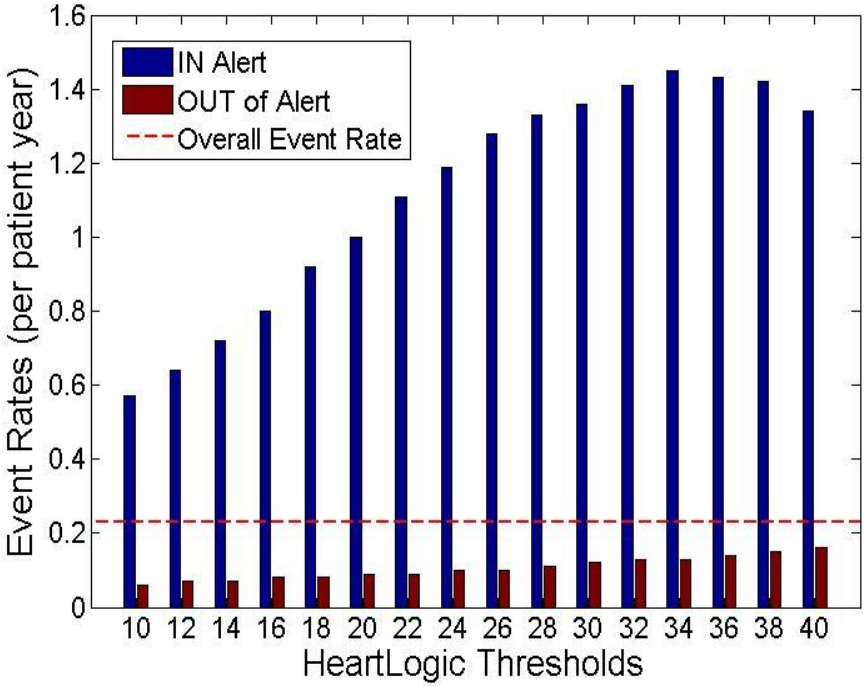
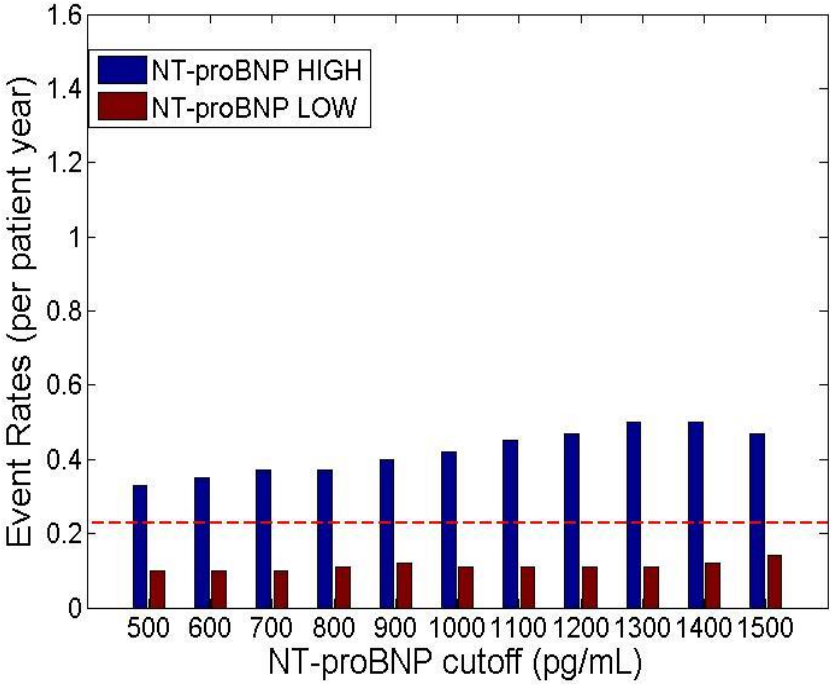
Event Rates as a Function of Daily HeartLogic Score



Event Rates as a Function of Baseline NT-proBNP



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LBCT at ESC-HF 2017. NOTE: Event rate ratio calculation.

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HeartLogic Significantly Augments The Prognostic Ability Of NT-proBNP Assessment

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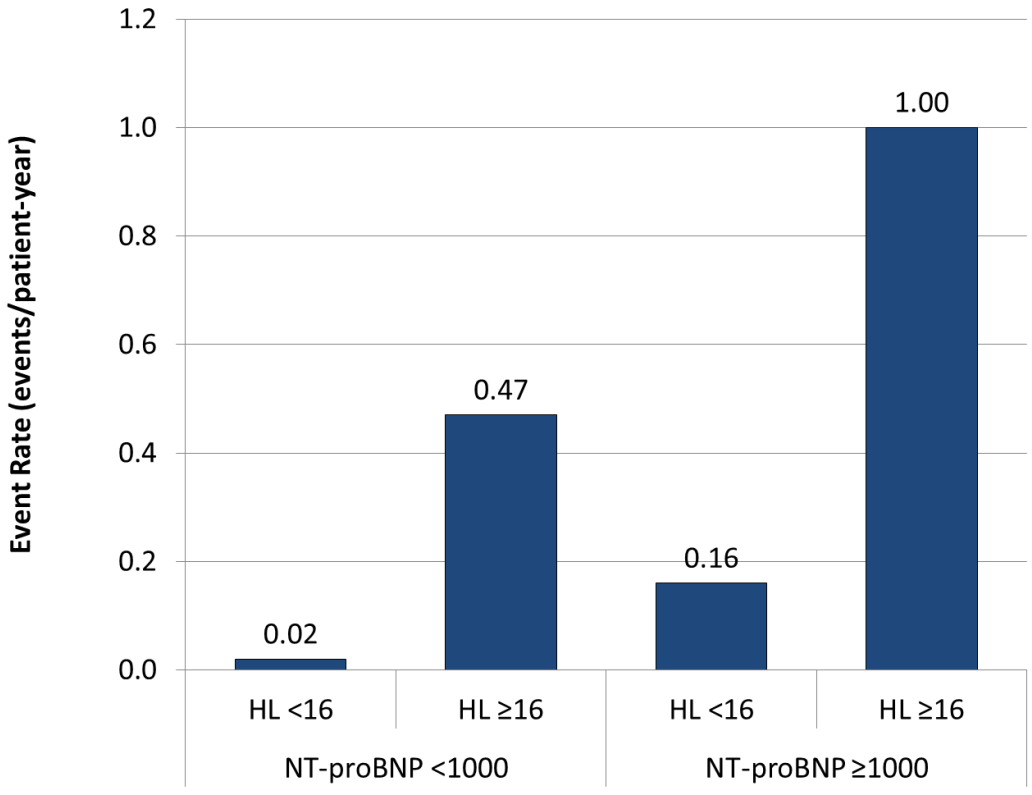

% of Follow-up	53%	7%	30%	10%

Half of patient follow-up in lowest risk group.

Event Rate Ratio compared to lowest risk group:

- LOW NT-proBNP, IN HL alert: **23.5**
- HIGH NT-proBNP, OUT HL alert: **8.0**
- HIGH NT-proBNP, IN HL alert: **50.0**

HeartLogic™
Heart Failure Diagnostic

2017 HFSA late breaker presentation

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Conclusions

- HeartLogic was established and validated in the MultiSENSE trial with a **sensitivity of 70% and UAR of 1.47 alerts / patient-year at the nominal value of 16**
  - Other HeartLogic values can be tailored to the user's preference for sensitivity and specificity.
- **HeartLogic predicted risk** of HF event independent of baseline variables.
- Using HeartLogic threshold at 16, the median of detection was **34 days prior to a HFE**.
  - 89 % of true positive alerts occurred at least 2-weeks prior to a HFE.
- **Event Rate** was **10 times higher** when HeartLogic was **IN alert state** compared to OUT of alert state.
- Healthcare resources may be diverted to those with greater need.
- HeartLogic was a **better prognosticator than a baseline NT-proBNP**.

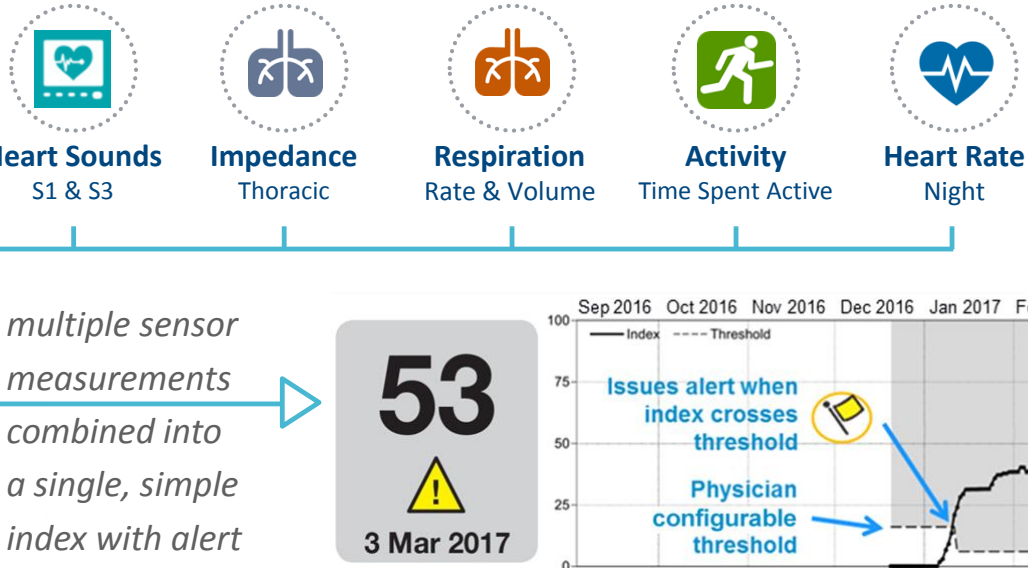
Thank You!

Boston Scientific

HeartLogic™ shifts heart failure patient management from reactive treatment to **proactive care** that is validated in the MultiSENSE Study to have:

- High sensitivity of 70% for detecting heart failure events
- Weeks of advance notice of a potential heart failure event
- Low burden of less than 2 alerts per patient per year

HeartLogic™ incorporates multiple sensors with a single composite alert



Available on **LATITUDE™ NXT** for patients with **Resonate™** family of ICDs & CRT-Ds

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