Sponsor:	BIOTRONIK SE & Co. KG
Study name / EAC code:	BIO|Sync-HUTT / BA117
Version and date of the Statistical Analysis Plan:	1-0, dated 15-Sept-2023
Version and date of the underlying Clinical Investigation Plan:	2-0, dated 20-Apr-2022

Print Name & Title	**Signature**	**Date of Signature** (DD MMM YYYY)
[redacted]	[redacted]	15 SEP 2023
[redacted]	[redacted]	15-SEP-2023

Table of Content

1 Change History

Version 1.0

Initial document.

2 Introduction

2.1 Aim

The aim of this document is to provide detailed instructions on statistical analyses for the Clinical Investigation Report (CIR).

2.2 Data for which quality control is required

A quality control is needed for analyses of all data of interest as defined in the clinical investigation plan (CIP).

2.3 Unblinding

Not applicable.

2.4 General information

This SAP may contain verbatim excerpts from the version of the CIP specified at the cover sheet. Such excerpts are *italicized with light blue background*.

The main aspects and the design of the clinical investigation are presented in chapters 3-4.

General statistical procedures are summarized in chapter 5. Those methods are used in case there is no other specification within this document.

Analysis set(s) and other global variables are defined in detail in chapter 6.

Descriptive and inferential statistical analyses for endpoint(s) are handled in following chapters. Thereby the following statistical considerations are specified:

- Analysis set: Definition of the analysis population (e.g. Intention-to-Treat or Per-Protocol for controlled clinical investigations or all patients with valid informed consent for single-arm clinical investigations)
- Variable characteristics: Description of all relevant variables (directly addressable from validated tools, e.g. CDMS or CDW, and derived variables) such as variable name, variable label, variable values, and data type.
- Derived variables, if applicable: For variables, which are not directly addressable from validated tools but are derived from other variables, pseudo-code or other instructions for the variable construction shall be provided.
- Missing, unused or spurious data: Specification of all data to be excluded from the specific analysis, e.g. data measured after a pre-specified point in time or implantation date after pre-hospital discharge date; specification whether and –if applicable- how to impute missing data.
- Data analysis: Description of descriptive, exploratory, and confirmatory analyses in text, tables, or pseudo-code shall be provided for unambiguous data analysis.

All variables are defined in tables using the following columns:

Data file: Name of a data file exported from the CDMS and unique identifier, if applicable (e.g. patient-specific "patient_display_ID_full" or event-specific record_ID); new data files ("data_SAR") may be generated by merging all relevant data from the original CDMS data files and generating derived variables;

Notes: Information whether data shall be presented with "descriptive" methods as defined in this SAP, data for "case listings" of original data for each patient specified, or "no report" for data needed for generating derived variables only;

Variable name: Original name of CDMS data or new name of a derived variables (indicated with a prefix "SAR_" or a suffix "_SAR");

Variable label: Original labels of CDMS data will be used for generating the SAR unless a new label is defined in this document ("NEW");

Variable level: Nominal, ordinal, scale (synonymous for metric, continuous, interval scale and/or ratio scale), or date;

Nominal values: Original values of CDMS of nominal or ordinal data will be used unless new values are defined in this document ("NEW").

Data file, identifier patient_display_id_full	Notes	Variable name	Variable label	Variable level	Nominal values

3 Clinical Investigation

3.1 Objective(s)

CIP chapter 7.1

The purpose of this study is to add knowledge to better understand the hemodynamic mechanisms underlying recurrent syncopal events and optimal pacing programming.

CIP chapter 7.2

This study will provide standardized, complete and quality controlled data sets with parameters that describe hemodynamic changes and their timing with respect to CLS pacing activation during reflex syncope induced by HUTT.

3.2 Investigational device

CIP chapter 4 Device(s) used in the study

The following devices, tools and accessories will be used during the study:

• the CLS algorithm (as investigational device in this investigation according to, ISO14155) implemented in current dual-chamber pacemakers manufactured by:

BIOTRONIK SE & Co. KG
Woermannkehre 1
12359 Berlin
Germany
www.biotronik.com

• RENAMIC programmers or later models;
• Any external monitor capable of measuring continuously patient's hemodynamics (e.g. Task Force Monitor);
• Standard equipment needed for the HUTT execution.

Such devices must be available at the investigational sites before study participation and will not be provided by the Sponsor.

3.3 Design & time course

CIP chapter 8.1.1

The study is designed as a prospective, non-randomized, multi-center, observational acute study without additional follow-ups after HUTT execution.

CIP chapter 8.2.4 Point of enrollment

A subject is considered enrolled in the BIO|Sync-HUTT Study upon the signature of the Informed Consent Form after confirmation of the elegibility criteria by the investigator.

CIP chapter 8.2.6 Expected duration of each subject's participation

Subjects participate from consent to HUTT execution with not further follow-up.

CIP chapter 9.1 Overview (study procedures)

This section describes all the study-related procedures as listed in Table 1 which will be performed during a routine scheduled patient follow-up. Prior to obtaining informed consent, the patient's background and medical history will be reviewed in order to ensure he/she is an appropriate candidate for the study. Patient who undergo HUTT during ordinary follow-up visits irrespective of study participation, is eligible. After the patient has been determined to be eligible for the study, written informed consent will be obtained and demographic and medication data will be collected. Syncope and presyncope questionnaires will be self-administered. Prior to the HUTT, pacemaker interrogation will be performed in order to check programming settings and to collect device diagnostics. The HUTT may be performed and also recorded by a high-definition camera if available. Full hemodynamic parameters and ECG traces will be acquired during the HUTT. Any collected data and adverse events will be documented in an electronic CRF.

Investigations	Enrollment/study visit
Verification of in- and exclusion criteria	X
Patient informed consent	X
Demographic data	X
Medical history	X
Co-morbidities	X
Medication therapy	X
Patient self-administered syncope and pre-syncope questionnaires	X
ECG	X
Device programming settings and diagnostics	X
Head-up tilt test (including video recording if available)	X
Collection of primary and secondary endpoint-related measurements	X
(S)AE, (S)ADE, DD monitoring	X

4 Data source

All the following datasets are exported from the CDMS:

- Enrollment
- Baseline
- Medical History
- Device Log
- Device Interrogation
- HUTT
- Study Termination
- Adverse Event
- Device Deficiency
- Deviation (patient related)

All datasets except "adverse_event" and "device_log_details" are patient-specific, i.e. one data row per patient.

5 General statistical procedures

CIP chapter 12 Statistical Design and Analysis

12.2 Descriptive statistics

Standard descriptive statistical methods are used depending on the type of the available data. For continuous variables, mean value, standard deviation, median, minimum, maximum and quartiles are calculated. For nominal variables, absolute and relative frequencies are calculated based on non-missing data. For ordinal variables, median, minimum, maximum and quartiles or absolute and relative frequencies are calculated for each category based on non-missing data. Shapiro-wilk test for normality for each variable is used.

12.3 Analytical procedures

Standard inferential statistical methods may be used depending on the type of the available data. For mean values, confidence intervals are calculated based on a t-distribution. For relative frequencies, confidence intervals are calculated based on a binomial distribution. Thereby, the significance value specified in the following sub-chapter is considered.

12.4 Significance level, statistical power, and statistical testing

Because there are no pre-specified hypotheses, all analyses are exploratory. However, a result of a two-sided statistical test with a p-value less than 5% or a one-sided statistical test with a p-value less than 2.5% is considered statistically significant.

For any inferential analyses, the result of a two-sided statistical test with a p-value less than 5% or a one-sided statistical test with a p-value less than 2.5% is considered statistically significant.

12.6 Interim analyses

There are no pre-planned interim analyses.

12.7 Bias

In case of a clear evidence of bias, which was not considered before, the Statistical Analysis Plan (SAP) is updated to avoid any bias.

12.10 Confounding factors (CIP chapter 8.1.2 Measures taken to minimize or avoid bias)

Accurate patient selection as described in section 8.2 and precise conduction of HUTT according to the procedures described in section 9 will allow to minimize potential confounding factors.

12.9 Missing, unused, and spurious data

All data needed to be analyzed are pre-documented in a Statistical Analysis Plan (SAP).

During a blind review process before any pre-planned analysis, missing and spurious data, which are relevant at least for the endpoints, are identified. In case such data can't be clarified via a query management process, the Statistical Analysis Plan (SAP) is updated to avoid any bias. If appropriate, analyses will be performed both with/without spurious data. Number of missing data are reported for each descriptive and inferential analysis in the Statistical Analysis Report (SAR) and Clinical Investigation Report (CIR), if applicable. Spurious data are commented in the Clinical Investigation Report (CIR), if applicable. Drop-outs are reported in the Statistical Analysis Report (SAR) and Clinical Investigation Report (CIR), if applicable. Missing data will not be replaced.

12.14 Exploratory analysis and sensitivity analysis

Not applicable.

12.15 Deviations from the original statistical plan

A Statistical Analysis Plan (SAP) is provided after go-life of the Clinical Data Management System (CDMS). The SAP can be updated before CDMS-freeze or closure based on a review of the data, whereby the new version is containing a change history. Any deviation from the valid SAP version with respect to inferential analyses are indicated in the Clinical Investigation Report (CIR), if applicable.

6 Analysis set(s) and other global variables

6.1 Analysis set of enrolled patients

CIP chapter 12 Statistical Design and Analysis
13.1 Analysis population

All patients with valid patient informed consent (ICF) are included in the analysis set.

7 Analyses: Baseline

7.1 Analysis set

All analyses are performed for the analysis set with valid informed consent.

7.2 Variables

Baseline / Demographics

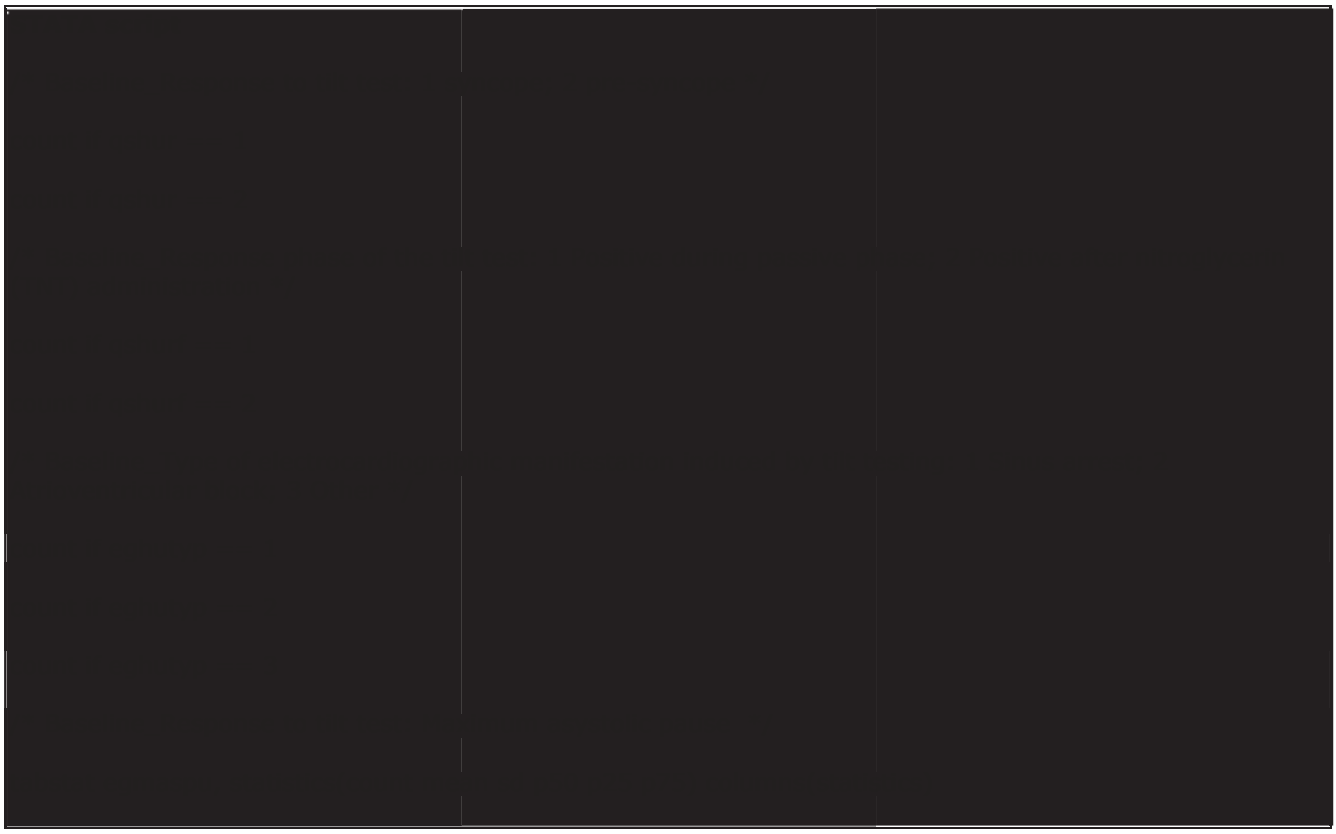
Data file, identifier patient_ display_id_full	Notes	Variable name	Variable label	Variable level	Nominal values
baseline	descriptive	dmsex	Gender	nominal	○ Yes ○ No
	descriptive	dmage	Age [Years]	scale	n.a.

[redacted]

Baseline / Previous Tilt test

Data file, identifier patient_ display_id_full	Notes	Variable name	Variable label	Variable level	Nominal values
Baseline	descriptive	QSHUR	Response to tilt test	nominal	○Syncope ○Pre-syncope
Baseline	descriptive	QSHURF	Response phase of the tilt test	nominal	○Positive during passive phase ○Positive after nitroglycerin (TNT) administration
baseline	descriptive	EGHUTYP	Type of electrocardiographic manifestation induced by tilt testing	nominal	○Sinus arrest ○Atrioventricular block ○Other

baseline	Case listing for EGHUTYP = Other	COHUTYP	Specification of other type of electrocardiographic manifestation induced by tilt testing	text	○n.a.
Baseline	Descriptive	EGMASPU	Maximum asystolic pause [s]	scale	○n.a.



Baseline / ECG diagnostics

Data file, identifier patient_ display_id_full	Notes	Variable name	Variable label	Variable level	Nominal values
baseline	descriptive	CVEGARH	Atrial rhythm during ECG recording	nominal	○ Sinus rhythm ○ Atrial fibrillation ○ Atrial flutter/other SVT ○ Atrial paced rhythm ○ Other
baseline	Case listing for CVEGARH = Other	COEGARH	Specification of other atrial rhythm during ECG recording	Text	n.a.
baseline	descriptive	CVEGVRH	Ventricular rhythm during ECG recording	nominal	o Intrinsic - atrial conducted o Intrinsic - escape rhythm o Ventricular paced rhythm o Other

baseline	Case listing for CVEGVRH = Other	COEGVRH	Specification of other ventricular rhythm during ECG recording	Text	n.a.
baseline	descriptive	EGHRTR	Resting HR [bpm]	scale	n.a.
baseline	descriptive	EGPRI	PR interval [ms]	scale	n.a.
baseline	descriptive	QSEGABN	Any relevant findings in resting ECG?	nominal	○ Yes ○ No
baseline	Case listing for QSEGABN = Yes	COEGABN	Specification of relevant findings	Text	n.a.

Baseline / Echocardiography diagnostics

Data file, identifier patient_ display_id_full	Notes	Variable name	Variable label	Variable level	Nominal values
baseline	descriptive	EHLVEF	Left ventricular ejection fraction [%]	Scale	n.a.

[redacted]

Baseline / Syncope and pre-syncope questionnaires

Data file, identifier patient_ display_id_full	Notes	Variable name	Variable label	Variable level	Nominal values
baseline	descriptive	CESNC	Have you experienced episodes of syncope and/or pre-syncope after the pacemaker implantation?	nominal	○ Yes ○ No
baseline	Descriptive for CESNC = Yes	CESNCTOT	Total number of syncope/s	Scale	n.a.
baseline	Descriptive for CESNC = Yes	CEPSNCTO	Total number of pre-syncope/s	Scale	n.a.

[redacted]

Medical history / Known Cardiac History - Heart Diseases

Data file, identifier patient_ display_ id_full	Notes	Variable name	Variable label	Variable level	Nominal values
medical_ history	descriptive	MHHF	History of heart failure	nominal	○ Yes ○ No
		MHCAD	History of coronary artery disease	nominal	○ Yes ○ No
		MHHHD	Hypertensive heart disease	nominal	○ Yes ○ No
		MHVHD	Valvular heart disease	nominal	○ Yes ○ No
		MHHCM	Hypertrophic cardiomyopathy	nominal	○ Yes ○ No
		MHRCM	Restrictive cardiomyopathy	nominal	○ Yes ○ No
		MHDCM	Dilated cardiomyopathy	nominal	○ Yes ○ No
		MHHDOTH	Other heart diseases	nominal	○ Yes ○ No
medical_ history	Case listing for MHHDOTH = Yes	COHDOTH	Specification of other heart diseases	Text	n.a.

[redacted]

Medical history / Known Cardiac History - Brady- and Tachyarrhythmias

Data file, identifier patient_ display_id_full	Notes	Variable name	Variable label	Variable level	Nominal values
medical_ history	descriptive	MHAVB	History of AV block	Nominal	o Yes o No
medical_ history	Descriptive for MHBBBTYP = Yes	MHAVBTYP	Type of AV block	Nominal	o AV block I° o AV block II° o AV block III°
medical_ history	descriptive	MHBBB	History of bundle branch block	nominal	o Yes o No
medical_ history	Descriptive for MHBBB = Yes	MHBBBTYP	Type of bundle branch block	nominal	o LBBB o RBBB o Other
medical_ history	Case listing for MHBBBTYP = Other	COBBBTYP	Specification of other type of bundle branch block	Text	n.a.
medical_ history	descriptive	MHCNDDOT	History of other type of conduction disease	nominal	o Yes o No

medical_ history	Case listing for MHCNDDOT = Yes	COCNDDOT	Specification of other type of conduction disease	Text	n.a.
medical_ history	descriptive	MHAFB	History of atrial fibrillation	nominal	o Yes o No
medical_ history	Descriptive for MHAFB = Yes	CVAFBTYP	Type of atrial fibrillation	nominal	o Paroxysmal o Persistent o Long-standing persistent o Permanent
medical_ history	descriptive	MHAVA	History of other atrial/supraventricular arrhythmias	nominal	o Yes o No
medical_ history	Descriptive for MHAVA = Yes	MHAFL	History of atrial flutter	nominal	o Yes o No
medical_ history	Descriptive for MHAVA = Yes	MHAT	History of atrial tachycardia	nominal	o Yes o No
medical_ history	Descriptive for MHAVA = Yes	MHSVT	History of supraventricular tachycardia	nominal	o Yes o No
medical_ history	Descriptive for MHAVA = Yes	MHAVAOTH	History of other type of atrial/ supraventricular arrhythmias	nominal	o Yes o No
medical_ history	Case listing for MHAVAOTH = Yes	COAVAOTH	Specification of other type of atrial/ supraventricular arrhythmias	Text	n.a.
medical_ history	descriptive	MHVA	History of ventricular arrhythmias	nominal	o Yes o No
medical_ history	Case listing for MHVA = Yes	COVA	Specification of ventricular arrhythmias	Text	n.a.

[redacted]

Medical history / Known Co-morbidities

Data file, identifier patient_ display_id_full	Notes	Variable name	Variable label	Variable level	Nominal values
medical_ history	descriptive	MHHP	Hypertension (including well-controlled)	nominal	o Yes o No
medical_ history	descriptive	MHASTH	Asthma or other chronic lung disease (except COPD)	nominal	o Yes o No
medical_ history	descriptive	MHCOPD	Chronic obstructive pulmonary disease (COPD)	nominal	o Yes o No
medical_ history	descriptive	MHCKD	Chronic renal insufficiency / chronic kidney disease (CKD) (i.e. eGFR < 60 ml/min/1.73 m²)	nominal	o Yes o No
medical_ history	descriptive	MHDIAM	Diabetes mellitus	nominal	o Yes o No
medical_ history	descriptive	MHNEUD	Neurological disease	nominal	o Yes o No
medical_ history	descriptive	MHCNCR	Cancer	nominal	o Yes o No
medical_ history	descriptive	MHHPLP	Hyperlipidemia	nominal	o Yes o No
medical_ history	descriptive	MHCMBOTH	Other co-morbidities	nominal	o Yes o No
medical_ history	Case listing for MHCMBOTH = Yes	COCMBOTH	Specification of other co-morbidities	Text	n.a.

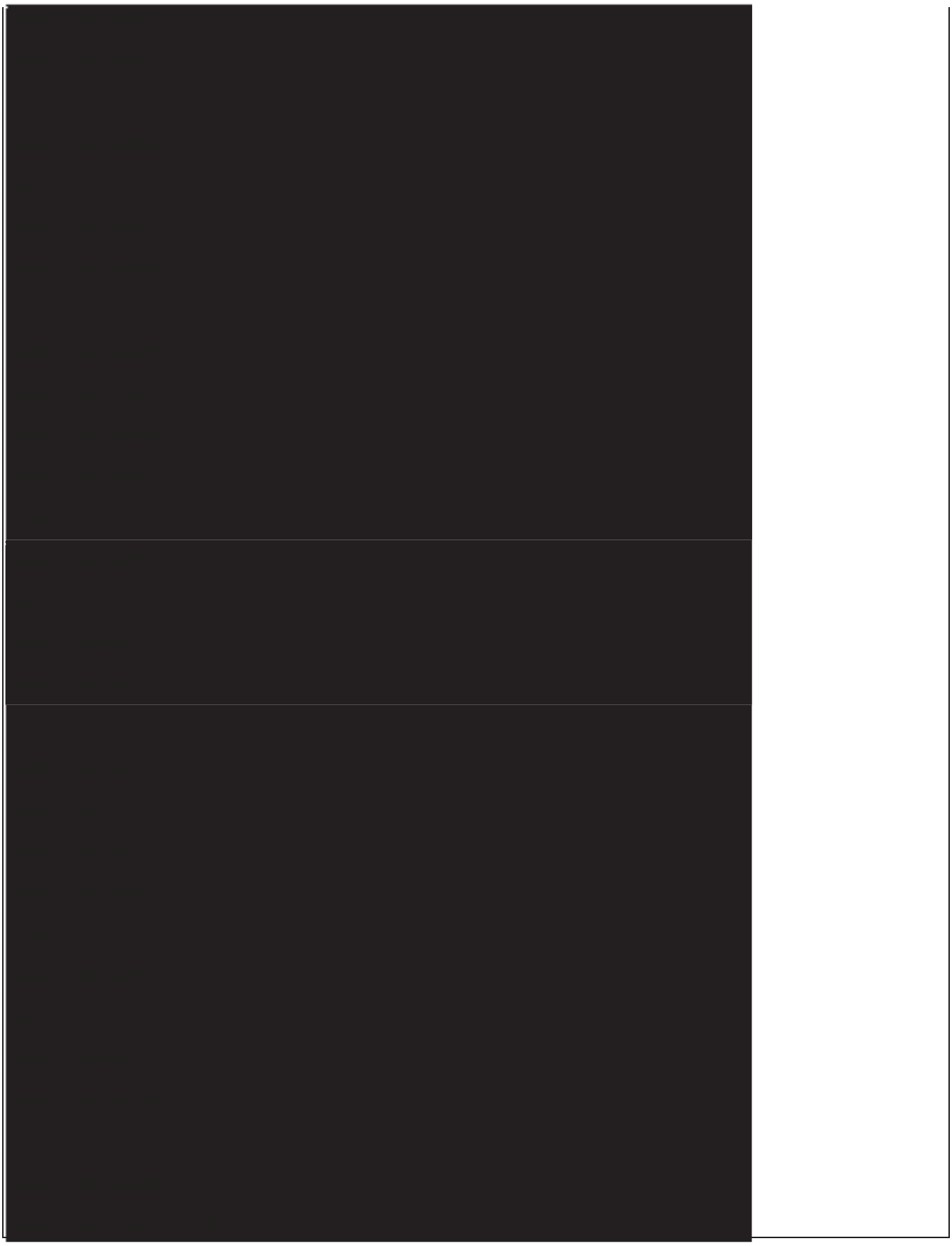
[redacted]

Medical history / Medication therapy

Data file, identifier patient_ display_id_full	Notes	Variable name	Variable label	Variable level	Nominal values
medical_ history	descriptive	CMCVM01	ACE inhibitors	nominal	o Yes o No
	descriptive	CMCVM02	Angiotensin II receptor blocker	nominal	o Yes o No
	descriptive	CMCVM03	Ca2 antagonist	nominal	o Yes o No
	descriptive	CMCVM04	Alpha – Antagonist	nominal	o Yes o No
	descriptive	CMCVM05	Beta blocker	nominal	o Yes o No
	descriptive	CMCVM06	Diuretics including aldosterone blocker	nominal	o Yes o No
	descriptive	CMCVM07	Antiarrhythmic drugs	nominal	o Yes o No
	Descriptive for CMCVM07 = Yes	CMCVM08	Sotalol	nominal	o Yes o No

	Descriptive for CMCVM07 = Yes	CMCVM09	Amiodarone	nominal	o Yes o No
	Descriptive for CMCVM07 = Yes	CMCVM10	Other antiarrhythmics	nominal	o Yes o No
	Case listing for CMCVM10 = Yes	COCVM10	Specification of Other antiarrhythmics	Text	n.a.
	descriptive	CMCVM11	Anticoagulants	nominal	o Yes o No
	Case listing for CMCVM11 = Yes	COCVM11	Specification of anticoagulants	Text	n.a.
	descriptive	CMCVM12	Antiplatelet agents	nominal	o Yes o No
	descriptive	CMCVM13	NSAIDs (nonsteroidal anti-inflammatory drugs)	nominal	o Yes o No
	descriptive	CMCVM14	Vasodilator agents	nominal	o Yes o No
	descriptive	CMCVM15	Nitrates	nominal	o Yes o No
	descriptive	CMCVM16	Digitalis	nominal	o Yes o No
	descriptive	CMCVM17	Lipid lowering agents	nominal	o Yes o No
	Case listing for CMCVM17 = Yes	COCVM17	Specification of lipid lowering agents	Text	n.a.
	descriptive	CMCVM18	Psychiatric drugs	nominal	o Yes o No
	descriptive	CMCVMOTH	Other	nominal	o Yes o No
	Case listing for CMCVMOTH = Yes	COCVMOTH	Specification of other	text	n.a.

[redacted]



7.3 Missing, unused or spurious data

See chapter 5.

7.4 Hypotheses & statistical tests

There are no pre-defined statistical hypotheses.

8 Analyses: Data of interest

All analyses are performed for the enrollment analysis set with valid informed consent and DDD-CLS pacing mode activated according to the CIP.

10.1 Study-specific dates

Data file: Identifier patient_ display_id_full	Notes	Variable name	Variable label	Variable level	Nominal values
device_log_details	No report	PRIMSTDT	Implantation/Use date	date	n.a.
hutt	No report	SVHUSTDT	Date of visit	date	n.a.
Data_SAR	Descriptive	TIME_IMPL_HUTT_SAR	Days from implantation to HUTT examination [years]	Scale	n.a.

[redacted]

[redacted]

10.2 HUTT

Data file: Identifier patient_ display_id_full	Notes	Variable name	Variable label	Variable level	Nominal values
hutt	Case listing	CVMHRTTM	Time of maximum spontaneous heart rate (end of phase 1/beginning phase 2 of the reflex)	Scale	n.a.
	descriptive	QSHUPMPC	Did the pacemaker pace during HUTT?	nominal	o Yes o No
	Case listing	PRPCSTTM	Time of pacing onset/maximum pacing rate	scale	n.a.
	Case listing	PRHRPCTM	Time of recovery of basic pacing rate or spontaneous rhythm after pacing (end of recovery period)	Scale	n.a.
	Case listing	PRHRHRTM	Time of recovery of starting spontaneous heart rate	Scale	n.a.

		(for QSHUPMPC = No)			
	descriptive	QSHUSNC	Did syncope (i.e. loss of consciousness) occur during HUTT?	Nominal	n.a.
	Case listing	QSSNCTM	Time of syncope	Scale	n.a.
	Case listing	QSTDTM	Time of tilt-down (supine patient position just after tilt-down)	scale	n.a.
	descriptive	QSHRHRDU	Duration of the recovery phase (interval from maximum pacing rate to basic rate or spontaneous rhythm from the start of the HUTT) [sec]	Scale	n.a.
	descriptive	CVHRHUST	HR at HUTT start [bpm] (upright patient position just after tilt)	Scale	n.a.
	descriptive	CVMHRT	HR at time of maximum spontaneous heart rate (end of phase 1/beginning phase 2 of the reflex) [bpm]	Scale	n.a.
	descriptive	CVHRPC	HR at time of pacing onset/maximum pacing rate [bpm]	Scale	n.a.
	descriptive	CVHRAPC	HR at time of recovery of basic pacing rate or spontaneous rhythm after pacing (end of recovery period) [bpm]	Scale	n.a.
	descriptive	CVHRAPCN	HR at time of recovery of basic pacing rate or spontaneous rhythm after pacing not applicable	nominal	o True o False
	descriptive	CVHRHU	HR at time of syncope during HUTT [bpm]	Scale	n.a.
	descriptive	CVHRAHU	HR at time of tilt-down	Scale	n.a.
	descriptive	CVSBPHST	Systolic BP at HUTT start [mmHg]	Scale	n.a.
	descriptive	CVDBPHST	Diastolic BP at HUTT start [mmHg]	Scale	n.a.
	descriptive	CVSBPMHR	Systolic BP at time of maximum spontaneous heart rate (end of phase 1/beginning phase 2 of the reflex) [mmHg]	Scale	n.a.
	descriptive	CVDBPMHR	Diastolic BP at time of maximum spontaneous heart rate (end of phase 1/beginning phase 2 of the reflex) [mmHg]	Scale	n.a.
	descriptive	CVSBPPC	Systolic BP at time of pacing onset/maximum pacing rate [mmHg]	Scale	n.a.
	descriptive	CVDBPPC	Diastolic BP at time of pacing onset/maximum pacing rate [mmHg]	Scale	n.a.
	descriptive	CVSBPAPC	Systolic BP at time of recovery of basic pacing rate or spontaneous rhythm after pacing (end of recovery period) [mmHg]	Scale	n.a.
	descriptive	CVDBPAPC	Diastolic BP at time of recovery of basic pacing rate or spontaneous rhythm after pacing (end of recovery period) [mmHg]	Scale	n.a.
	descriptive	CVSBPHU	Systolic BP at time of syncope during HUTT [mmHg]	Scale	n.a.
	descriptive	CVDBPHU	Diastolic BP at time of syncope during HUTT [mmHg]	Scale	n.a.
	descriptive	CVSBPAHU	Systolic BP at time of tilt-down (supine patient position just after tilt-down) [mmHg]	Scale	n.a.
	descriptive	CVDBPAHU	Diastolic BP at time of tilt-down (supine patient position just after tilt-down) [mmHg]	Scale	n.a.

	descriptive	CVSVHUST	SV at HUTT start [ml]	Scale	n.a.
	descriptive	CVSVMHRT	SV at time of maximum spontaneous heart rate (end of phase 1/beginning phase 2 of the reflex) [ml]	Scale	n.a.
	descriptive	CVSVPC	SV at time of pacing onset/maximum pacing rate [ml]	Scale	n.a.
	descriptive	CVSVAPC	SV at time of recovery of basic pacing rate or spontaneous rhythm after pacing (end of recovery period) [ml]	Scale	n.a.
	descriptive	CVSVHU	SV at time of syncope during HUTT [ml]	Scale	n.a.
	descriptive	CVSVAHU	SV at time of tilt-down (supine patient position just after tilt-down) [ml]	Scale	n.a.
	descriptive	CVTPRHUS	TPR at HUTT start [dyn·s/cm5]	Scale	n.a.
	descriptive	CVTPRMHR	TPR at time of maximum spontaneous heart rate (end of phase 1/beginning phase 2 of the reflex) [dyn·s/cm5]	Scale	n.a.
	descriptive	CVTPRPC	TPR at time of pacing onset/maximum pacing rate [dyn·s/cm5]	Scale	n.a.
	descriptive	CVTPRAPC	TPR at time of recovery of basic pacing rate or spontaneous rhythm after pacing (end of recovery period) [dyn·s/cm5]	Scale	n.a.
	descriptive	CVTPRHU	TPR at time of syncope during HUTT [dyn·s/cm5]	Scale	n.a.
	descriptive	CVTPRAHU	TPR at time of tilt-down (supine patient position just after tilt-down) [dyn·s/cm5]	Scale	n.a.
Termination	Case listing	COSUM	General Comments	Text	n.a.
Data_SAR	descriptive	SLOPE_HR_HUTT_SAR	Slope in heart rate (bpm per sec) during the recovery phase	Scale	n.a.
Data_SAR	descriptive	SLOPE_SBP_HUTT_SAR	Slope in systolic blood pressure (mmHg per sec) during the recovery phase	Scale	n.a.

[redacted]

[redacted]

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9 Abbreviations

- BP Blood pressure
- CDMS Clinical Data Management System
- CI Confidence Interval
- CIP Clinical Investigation Plan
- CIR Clinical Investigation Report
- CLS Closed loop stimulation
- COPD Chronic obstructive pulmonary disease
- CRF Case Report Form
- CKD Chronic kidney disease
- ECG Electrocardiogram
- FU(P) Follow-up
- HR Heart Rate
- HUTT Head-up tilt test
- ICF Informed consent form
- SAP Statistical Analysis Plan
- SAR Statistical Analysis Report
- SOP Standard Operating Procedure
- SV Stroke volume
- TPR Total peripheral resistance