ALIZEA DR/ ALIZEA SR

IMPLANT MANUAL

Rate responsive dual-chamber pacemaker /
Rate responsive single-chamber pacemaker

MicroPort™
CRM

Intended audience

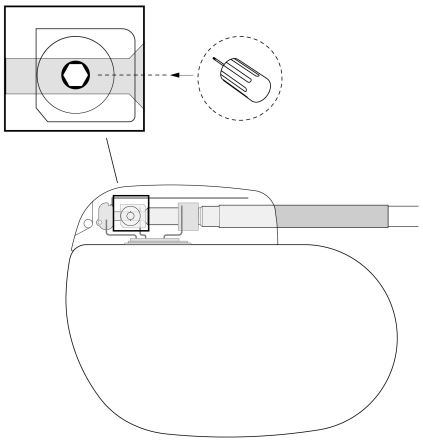
This manual is intended for use by professionals trained or experienced in device implant and/or follow-up procedures.

ALIZEA

Reminder

Leads connection

SR



DR

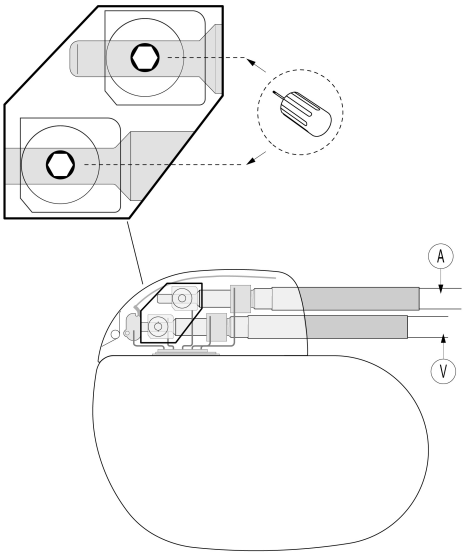


TABLE OF CONTENTS

1. GENERAL DESCRIPTION

ALIZEA DR is a DDDR-type dual-chamber rate-responsive pacemaker.

ALIZEA SR is a single-chamber rate-responsive pacemaker.

Both are equipped with a physiological sensor (minute ventilation) and an accelerometer to allow adaptation of pacing to suit the patient's activity.

ALIZEA DR and SR models can be programmed and interrogated via bi-directional telemetry using a MicroPort dedicated programmer connected to a MicroPort dedicated programming head.

ALIZEA DR and SR models are also equipped with the Bluetooth®[(1)] Low Energy wireless technology, which enables remote monitoring of patients who have the MicroPort SMARTVIEW CONNECT Monitor.

ALIZEA DR and SR models provide a range of highly effective therapeutic and monitoring functions.

The following table details which functions are available according to the pacemaker model:

Features	**DR model**	**SR model**
Automatic implant detection	x	x[(2)]
Protection of ventricles from atrial arrhythmias (Fallback Mode Switch)	x	
Preservation of atrioventricular conduction (SafeR mode and Dplus mode)	x	
Preservation of circadian cardiac rhythm (Rest rate)	x	x
Prevention of vasovagal syncope (Acceleration)	x	
Automatic adjustment of amplitude of atrial and ventricular pacing (Autothreshold)	x	x[(2)]
Automatic adjustment of atrial and ventricular sensitivity (Autosensing)	x	x[(2)]
Automatic atrial and ventricular Lead Polarity Switch	x	x[(2)]
Protection against Pacemaker-Mediated Tachycardia (Anti-PMT)	x	
Rate Response[(3)]	x	x
Auto MRI	x	x

[(1)]*The Bluetooth® word mark is a registered trademark of Bluetooth SIG, Inc. Any use of the word mark by MicroPort CRM is under license.*

[(2)]*Applicable only in the ventricular chamber for the SR model.*

[(3)]*Two sensors : minute ventilation (MV) and accelerometer (G)*

2. INTENDED USE AND TARGETED POPULATION

2.1. INTENDED USE

The ALIZEA pacemakers are intended to stimulate the bradycardic patient's heart with electrical impulses as indicated in the guidelines on cardiac pacing[(1)] in order to maintain or restore a normal heartbeat. SR devices are implantable single chamber pacemakers that must be used with one lead (right atrial or ventricular lead). DR devices are implantable dual chamber pacemakers that must be used with two leads (right atrial and ventricular leads).

[(1)]*Guidelines on cardiac pacing are provided by the European Society of Cardiology, the American College of Cardiology and the American Heart Association ("2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy". Eur Heart J 2013;34:2281–2329, "2012 ACCF/AHA/HRS Focused Update of the 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities". J Am Coll Cardiol. 2013; 61(3):e6-75).*

2.2. INDICATIONS AND TARGETED POPULATION

SR and DR pacemakers treat all types of bradycardia and are respectively indicated for atrial or ventricular pacing and synchronous atrio-Ventricular pacing as described below.

According to the guidelines, ALIZEA DR pacemakers are mainly indicated for the following conditions:

- Accepted patient conditions warranting chronic cardiac pacing which include:
  - symptomatic paroxysmal or permanent second- or third-degree AV block;
  - symptomatic bilateral bundle branch block;
  - symptomatic paroxysmal or transient sinus node dysfunctions with or without associated AV conduction disorders;
  - bradycardia-tachycardia syndrome to prevent symptomatic Bradycardia or some forms of symptomatic tachyarrhythmias;
  - vasovagal syndromes or hypersensitive carotid sinus syndromes.
- Rate adaptive pacing in patients who may benefit from increased pacing rates concurrent with increases in minute ventilation and/or activity.
- The ALIZEA DR are also indicated for dual-chamber and atrial tracking modes in patients who may benefit from maintenance of AV synchrony. Dual-chamber modes are specifically indicated for treatment of conduction disorders that require restoration of both rate and AV synchrony which include:
  - various degrees of AV block to maintain the atrial contribution to cardiac output;
  - VVI intolerance (e.g. pacemaker syndrome) in the presence of persistent sinus rhythm.

According to the guidelines, ALIZEA SR pacemakers are mainly indicated for the following conditions:

- Accepted patient conditions warranting chronic cardiac pacing which include:
  - symptomatic paroxysmal or permanent second- or third-degree AV block;
  - symptomatic bilateral bundle branch block;

- symptomatic paroxysmal or transient sinus node dysfunctions with or without associated AV conduction disorders;
- bradycardia-tachycardia syndrome to prevent symptomatic Bradycardia or some forms of symptomatic tachyarrhythmias;
- vasovagal syndromes or hypersensitive carotid sinus syndromes.

— Rate adaptive pacing in patients who may benefit from increased pacing rates concurrent with increases in minute ventilation and/or activity.

Guidelines on cardiac pacing are provided by the European Society of Cardiology, the American College of Cardiology and the American Heart Association ("2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy". Eur Heart J 2013;34:2281–2329, “2012 ACCF/AHA/HRS Focused Update of the 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities”. J Am Coll Cardiol. 2013; 61(3):e6-75).

3. CONTRAINDICATIONS AND ADVERSE EVENTS

3.1. GENERAL CONSIDERATIONS

For the DR model, the use of dual chamber pacing mode is contraindicated in patients with chronic atrial fibrillation. In general, the patient's medical and physical condition, as well as age, should always be taken into consideration when choosing the pacemaker and leads.

Furthermore, the benefits of pacing to pediatric subjects have not been evaluated. Adverse interactions may occur between the patient's spontaneous rate and pacemaker functions.

3.2. ADVERSE EVENTS, RISKS AND SIDE EFFECTS

Based on the literature and on pulse generator and/or lead implant experience, the following list includes the possible adverse events associated with implantation of pacing systems:

Events	Possible adverse effects
Procedure related	
Clotting disorder	Pocket hematoma, bleeding, formation of clots, may necessitate reintervention
Contamination, inflammation	Pocket infection, endocarditis, septicaemia, may become necessary to perform surgical intervention, to remove the device and/or the lead
Fibrotic tissue formation	Pain, risk of hematoma and infection at the time of replacement
Introduction of air (with subclavian approach)	Air embolism
Poor lead/pacemaker connection	Intermittent or continuous loss of pacing and/or sensing
Others	Adverse reaction to the procedure
	Pneumothorax linked to subclavian access
	Thrombosis
	Thrombic embolism
	Venous occlusion
	Venous trauma (e.g., perforation, dissection, erosion, rupture)
	Tissue necrosis
Pocket related	
Clotting disorder	Pocket hematoma, bleeding, formation of clots, may necessitate re-intervention
Contamination, inflammation	Pocket infection, endocarditis, septicaemia may become necessary to perform surgical intervention, to remove the device and/or the lead
Fibrotic tissue formation	Risk of hematoma and infection at the time of replacement
Skin erosion by the pacemaker with possible protrusion/extrusion of the casing	Generally linked to infection and/or hematoma, necessitates reintervention and to change the site of implantation

Events	Possible adverse effects
Others	Venous trauma (e.g., perforation, dissection, erosion, rupture)
	Tissue necrosis
Device related	
Casing migration	Pain, discomfort
Component failure	Complications and mortality due to inability to deliver appropriate and intended therapy, surgical intervention to remove/replace the device
Myopotential sensing	Oversensing
Sensing circuit inhibition, reversion to backup mode, or other failures due to electromagnetic interference	Inappropriate functioning
Early battery depletion	Complications and mortality due to inability to deliver appropriate and intended therapy, surgical intervention to remove/replace the device
Leads related	
Arrhythmia at implantation	Extrasystoles, tachycardia, ventricular/atrial fibrillation
Cardiac perforation	Intermittent or continuous loss of pacing and/or sensing
	Muscle or phrenic stimulation
	Cardiac tamponade, fluid accumulation
Contamination, inflammation	Pocket infection, endocarditis, septicaemia may become necessary to perform surgical intervention, to remove the device and/or the lead
Lead displacement, migration, conductor fracture or incorrect lead implantation	Intermittent or continuous loss of pacing and/or sensing
Lead insulation rupture or abrasion	Pectoral and other muscular stimulation, sudden fall in impedance, loss of efficacy of pacing, early battery depletion
Lead tip perforation and/or breakage by overtorquing	Intermittent or continuous loss of pacing and/or sensing
Myocardial trauma	Chest pain, cardiac wall perforation, arrhythmias, formation of clot at injury site, bleeding, embolism, pericardial effusion or rub, endocarditis
Threshold elevation	Loss of capture
Phrenic elevation	Pain, discomfort
Others	Heart block
	Valvular damage (particularly in fragile hearts)
	Tachyarrhythmias, which include acceleration of arrhythmias (caused by the device) and early, recurrent atrial fibrillation
General	
Others	Death
	Electrolyte imbalance/dehydration
	Pain, inaesthetic scar
	Vasovagal syncope

Events	Possible adverse effects
	Stroke
	Worsening heart failure
Long term	
Prolonged exposure to fluoroscopic radiation	*No data available*

NOTE: Any serious incident in relation to the device should be reported to MicroPort CRM and the local Competent Authority.

4. WARNINGS

4.1. PACEMAKER DEPENDENT PATIENTS

Electrograms of the patient's intrinsic activity should be obtained with care since the patient is without pacing support.

Automated threshold testing should be terminated, either by pressing any key or by removing the programming head when capture ceases in order to restore the preprogrammed pulse amplitude and ensure capture. Otherwise, the pacemaker will continue the threshold test for the remainder of the test period without pacing the patient (i.e. without capture of the heart).

4.2. WARNINGS TO PATIENTS

The patient should be warned of the potential risks of pacemaker malfunction if he/she is exposed to external magnetic, electrical, or electromagnetic signals.

Electrical equipment:

Household electrical appliances do not affect the functioning of the pacemaker, providing they are insulated according to current standards. However, patients should avoid using induction ovens and cookers.

Electronic Article Surveillance (EAS) and RadioFrequency IDentification equipment (RFID):

Patients should be advised to walk directly through and not lean against or linger near Electronic Article Surveillance (EAS) systems such as retail theft prevention systems, security gates, entry control systems, or tag readers including Radio Frequency IDentification equipment (RFID). These systems may be found at the entrances and exits of stores, libraries, banks, etc...and may interact with pulse generators. It is unlikely that these systems affect cardiac function when the patient walks through them at a normal pace. If patients do experience symptoms near these systems, they should promptly move away and inform their doctor.

Work environment:

The patient's work environment may be an important source of interference; as a result, specific recommendations may be required.

Cellular phones:

The devices are protected against high-frequency signals emitted by cellular telephones. Nevertheless it is recommended not to keep the cellular telephone too close to the pacemaker.

4.3. RISKS RELATED TO MEDICAL ENVIRONMENT

Pacemaker operation should be carefully monitored prior to and after any medical treatment during which an electrical current from an external source passes through the patient's body.

Magnetic Resonance Imaging:

When implanted in combination with MR Conditional lead(s), the pacing system constitutes an MR conditional system under specific conditions.

When these conditions are not met, MRI is contraindicated.

NOTE: Refer to the MRI Solutions manual for the complete instructions for use available at www.microportmanuals.com.

Mechanical ventilators:

Mechanical ventilators may cause pacing rate changes. Program the pacemaker to a non-rate responsive mode during ventilation.

Radiofrequency ablation:

A radiofrequency ablation procedure in a patient with a generator may cause device malfunction or damage. RF ablation risks may be minimized by:

1. Avoiding direct contact between the ablation catheter and the implanted lead or generator.
2. Positioning the ground, placing it so that the current pathway does not pass through or near the device, i.e. place the ground plate under the patient's buttocks or legs.
3. Having external defibrillation equipment available.

Electrocautery or diathermy device:

Diathermy and electrocautery equipment should not be used. If such devices must be used:

1. Keep the current path and ground plate as far away from the device and the leads as possible (a minimum of 15 cm [six inches]).
2. During the procedure, keep the electrocautery device as far as possible from the pacemaker. Set it at minimum intensity.
3. Use it briefly.
4. After the procedure, check for proper implant function. The device should never be exposed directly to the diathermy source.

External defibrillation:

If the patient must be defibrillated, it is recommended to avoid placing the defibrillating paddles directly over the casing or over the leads. The defibrillating paddles should preferably be placed in an anteroposterior position.

Any direct contact between the defibrillation paddles and the conductive parts of the implanted leads or casing of the implanted device may damage the pacing system.

After external defibrillation, check for proper device function.

Internal defibrillator:

Use of the pacemaker is contraindicated in patients implanted with defibrillator.

Radiation therapy:

Avoid exposure to ionizing radiation. Betatrons are contraindicated. If high doses of radiotherapy cannot be avoided, the pacemaker should be protected from direct exposure with a protection shield, and pacemaker operation should be monitored continuously.

Resulting damage may be immediately undetectable. If irradiation of tissues close to the implantation site is necessary, it is recommended that the pacemaker be moved. As a safety measure, temporary pacemaker back-up should be immediately available.

Lithotripsy

The risks associated with lithotripsy are limited unless the cardiac pacemaker is implanted in the abdominal position. However, in order to avoid all risk of ventricular or atrial fibrillation, shocks should be administered synchronously with pacing.

Therapeutic ultrasound:

The pacemaker should not be exposed to therapeutic levels of ultrasound.

Transcutaneous Electrical Nerve Stimulation (TENS):

TENS may interfere with pacemaker function. If necessary, the following measures may reduce interference:

1. Place the TENS electrodes as close together as possible and as far as possible from the pulse generator and leads.
2. Monitor cardiac activity during TENS use.

4.4. STORAGE

The pacemaker is packaged in a sterile pack contained within a cardboard storage package. It is recommended that the pacemaker be stored at a temperature ranging from 0°C to 50°C.

The cardboard package protects the pacemaker from impact during shipping.

Devices subjected to excessive impact, such as those that have been dropped on a hard floor, should not be implanted. Any device subjected to such an impact should be returned to your MicroPort representative for examination.

Devices MUST NOT be interrogated and programmed within the vicinity of other devices.

4.5. PACKAGING

4.5.1. Characteristics of the sterile package

The pacemaker and its ratchet screwdriver are sterilized with ethylene oxide.

Once sterilized, the contents are hermetically sealed in a transparent dual package in accordance with international standards.

4.5.2. Characteristics of the non-sterile package

— Identification stickers
— Patient booklet & patient implant card
— Implant registration form and USA return envelope
— Website leaflet

5. CLINICAL STUDIES

ALIZEA SR is limited to single chamber features, but is otherwise the same as ALIZEA DR.

ALIZEA DR and SR offer features which have been evaluated during clinical study of Reply DR, whose results are presented in the following paragraph:

5.1. METHODS

All patients were implanted with a REPLY DR rate-responsive dual-chamber pacemaker. A variety of marketed atrial and ventricular pacing and sensing leads were used. The pacemaker was programmed and interrogated via bi-directional telemetry using a programmer and a CPR3 programming head.

The study's routine evaluation consisted of pre-implant screening, implant, pre-discharge evaluation, and scheduled follow-up visit at one month. During hospitalization, a 24-hour Holter recording was performed and pacemaker memory was read. At one month, pacemaker memory was read. Investigators also documented adverse events.

5.2. PATIENTS STUDIED

A total of 71 patients from 15 centers were implanted with REPLY DR pacemakers. Of these, 38 (54%) were female and 33 (46%) were male. Patient age ranged from 46 to 96 with a mean age (±SD) of 74 ± 10 years.

Primary indications for implant were: sinus dysfunction (39%), AV block and/or branch block (38%), sinus dysfunction and AV block and/or branch block (20%) or other (3%).

5.3. SAFETY RESULTS

To determine the safety of the REPLY DR system (REPLY DR pacemaker, RA lead, RV lead and programming system), procedure and system complication-free rate was reported at one month.

The following table presents the complication-free rate estimate and its bilateral 95% confidence interval at one month.

Number of patients included	Number of patients with complications	Complication free-rate estimate (bilateral 95% confidence interval)
71	1 [1]	98.57 % (92.29 %, 99.96 %)

The incidence and nature of adverse events are described in "Contraindications and adverse events" section.

5.4. EFFECTIVENESS RESULTS

To determine the effectiveness of system performances, a 24-hour Holter recording was performed and pacemaker memory was read during hospitalization. A 24-hour Holter recording or pacemaker memory was defined as a success if it presented both of the following conditions:

— absence of unexpected ventricular cycle longer than programmed maximal ventricular pause in SafeR mode or twice of the current escape interval in other modes

1. The complication reported is linked to the system (lead dislodgment).

— absence of unexpected short ventricular cycle

The following table presents the percentage of success and its unilateral 95% confidence interval.

Number of patients included	Number of failures observed	% of successes (unilateral 95% confidence interval)
60	0	100% (95.12%)

To determine the effectiveness of automatic implantation detection function, the function was activated in all implanted patients.

The following table presents the percentage of success and its unilateral 95% confidence interval.

Number of patients included	Number of failures observed	% of successes (unilateral 95% confidence interval)
70	0	100% (95.80%)

To determine the effectiveness of automatic lead impedance measurement function, pacemaker memory was read at one month. A success was defined by at least 5 daily measures of lead impedance available on one week in authorized conditions by the function at one month.

The following table presents the percentage of success and its unilateral 95% confidence interval for atrial lead and ventricular lead at one month.

Lead	Number of patients included	Number of failures observed	% of successes (unilateral 95% confidence interval)
Atrial	61	0	100% (95.20%)
Ventricular	61	0	100% (95.20%)

6. PATIENT SELECTION AND TREATMENT

6.1. SPECIFIC PATIENT POPULATIONS

- Pregnancy: If there is a need to image the device, care should be taken to minimize the radiation exposure to the fetus and the mother.
- Labor and delivery: If minute ventilation mode is enabled breathing patterns associated with birthing may drive the pacing rate to the programmed maximum sensor rate.
- Nursing mothers: Although appropriate biocompatibility testing has been conducted for this implant device, there has been no quantitative assessment of the presence of leachables in breast milk.
- Pediatric patients: This device has not been studied in patients younger than 25 years of age. Breathing rates, particularly in neonates, are typically higher than in adults and care should be taken in selection of parameter values associated with minute ventilation (see Warnings and Precautions).
- Geriatric patients: Most of the patients receiving this device in clinical studies were over the age of 60 years (see Clinical Studies).
- Handicapped and disabled patients: Special care is needed in using this device for patients using electrical wheel chair or other external or implanted electrical devices.

7. PATIENT COUNSELING INFORMATION

Physicians should consider the following points in counseling the patient about this device:

- Provide patient with (temporary) pacemaker ID card – inform them that a permanent ID card will be issued by the pacemaker manufacturer.
- Need to notify other health care providers (e.g., dentist, physical therapist, anesthesiologist, surgeon, etc.) of the presence and type of pacemaker.
- Symptoms of pacemaker syndrome.
- Twiddler’s syndrome and its consequences.

8. DECLARATION OF CONFORMITY

MicroPort declares that this device is in conformity with the essential requirements of Radio Equipment Directive 2014/53/EU, with the mutual recognition of their conformity (RED).

Federal Communication Commission Interference Statement 47 CFR Section 15.19 and 15.105(b)

The FCC product ID is :

- **ALIZEA DR: YSG1614**
- **ALIZEA SR: YSG1311**

ALIZEA pacemaker is featuring Bluetooth Low Energy communication capability. Using a standard Bluetooth Low Energy component not initially intended for use in life support applications, MicroPort CRM has fully qualified that Bluetooth Low Energy communication to comply with implantable medical devices intended use and safety requirements.

This equipment has been tested and found to comply with the limits for a Class B digital device, pursuant to Part 15 of the FCC Rules. These limits are designed to provide reasonable protection against harmful interference in a residential installation. This equipment generates, uses and can radiate radio frequency energy and, if not installed and used in accordance with the instructions, may cause harmful interference to radio communications. However, there is no guarantee that interference will not occur in a particular installation.

This device complies with Part 15 of the FCC Rules. Operation is subject to the following two conditions: (1) This device may not cause harmful interference, and (2) this device must accept any interference received, including interference that may cause undesired operation.

FCC Interference Statement 47 CFR Section 15.21 - No Unauthorized Modifications

CAUTION:
This equipment may not be modified, altered, or changed in any way without signed written permission from MicroPort. Unauthorized modification may void the equipment authorization from the FCC and will void the MicroPort warranty.

Identification of the equipment according to Section 95.1217(a)

This transmitter is authorized by rule under the Medical Device Radiocommunication Service (in part 95 of the FCC Rules) and must not cause harmful interference to stations operating in the 400.150-406.00 MHz band in the Meteorological Aids (i.e., transmitters and receivers used to communicate weather data), the Meteorological Satellite, or the Earth Exploration Satellite Services and must accept interference that may be caused by such stations, including interference that may cause undesired operation. This transmitter shall be used only in accordance with the FCC Rules governing the Medical Device Radiocommunication Service. Analog and digital voice communications are prohibited. Although this transmitter has been approved by the Federal Communications Commission, there is no guarantee that it will not receive interference or that any particular transmission from this transmitter will be free from interference.

9. PHYSICIAN GUIDELINES

9.1. PHYSICIAN TRAINING

Physicians should be familiar with sterile pulse generator. They must apply these procedures according to professional medical training and experience.

Physicians should be familiar with follow-up evaluation and management of patients with a pacemaker (or referral to such a physician).

This training guideline for implantation and follow-up of pacemakers comes from the Heart Rhythm Society to provide standards for hospital credentialing bodies to help ensure appropriate patient care and lead to improved patient outcomes. The following is a summary of requirements for an alternate training pathway for pacemaker implantations[(1)]:

- Documentation of current experience: 35 pacemaker implantations per year and 100 implantations over the prior 3 years
- Completion of didactic course and/or IBRHE exam
- Monitoring of patient outcomes and complication rates
- Established patient follow-up

[(1)]*Please consult full text of both publications for details. 2004 Heart Rhythm Society Clinical Competency Statement and the 2005 Addendum on Training Pathways for Implantation of Cardioverter Defibrillators and Cardiac Resynchronization Devices. Heart Rhythm (2004) 3.*

9.2. DIRECTIONS FOR USE

Pacemaker operating characteristics should be verified at the time of implantation and recorded in the patient file. Complete the Patient Registration Form and return it to MicroPort, as it provides necessary information for warranty purposes and patient tracking.

Additional programming instructions can be found by accessing Programming Guide on the MicroPort dedicated website www.microportmanuals.com. Paper copies of Programming Guide can be obtained by contacting your MicroPort representative.

9.3. MAINTAINING DEVICE QUALITY

This device is **FOR SINGLE USE ONLY**. Do not resterilize and reimplant explanted pacemakers.

Do not implant the device when:

- It has been dropped on a hard surface because this could have damaged pulse generator components.
- Its storage package has been pierced or altered, because this could have rendered it non-sterile.
- It has been stored or transported outside the environmental temperature limits: 32 °F (0 °C) to 122 °F (50 °C)
- "Use by" date has expired, because this can adversely affect pulse generator longevity or sterility.

9.4. IMPLANTATION AND DEVICE PROGRAMMING

Use only a MicroPort programmer to communicate with the device.

Replace the device when the RRT (Recommended Replacement Time*) point (defined by a battery voltage of 2.63 V if Remote monitoring activated or 2.70 V if Remote monitoring deactivated) is reached.

Lead System

Do not use a lead system other than those with demonstrated compatibility because undersensing cardiac activity and failure to deliver necessary therapy may result.

Failure to properly insert the torque screwdriver into the perforation at an angle perpendicular to the connector receptacle may result in damage to the sealing system and its self-sealing properties.

**corresponds to ERI (Elective Replacement Indicator) previously used.*

9.5. LEAD EVALUATION AND LEAD CONNECTION

ALIZEA DR has two IS-1 BI connector ports.

ALIZEA SR has one IS-1 connector port.

IS-1 refers to the international standard whereby leads and generators from different manufacturers are assured a basic fit (ISO 5841-3:2013).

Do not use any lead with this pulse generator without first verifying IS-1 compatibility, because use with other leads can damage the connector or result in a leaking or intermittent connection. ALIZEA pacemakers are not compatible with 3.2 mm low profile leads.

Do not use a unipolar lead with ALIZEA SR if minute ventilation rate response is required because the device's minute ventilation rate response function will only operate with a bipolar lead.

For MRI compatibility with ALIZEA SR, the lead shall be bipolar.

Do not use a unipolar atrial lead with ALIZEA DR / ALIZEA SR if atrial autosensing is required, because atrial autosensing does not operate with a unipolar lead. For MRI compatibility with ALIZEA DR, both leads shall be bipolar.

Do not enable Ventricular Auto-threshold when using high polarization leads because the polarization could prevent the pacemaker from assessing ventricular pacing threshold accurately.

Consider lead maturation in choice of pacing amplitude and sensitivity, because:

— Acute pacing thresholds > 1 V or 2 mA or chronic pacing thresholds > 3 V or 6 mA can result in loss of capture because thresholds may increase after implantation;

— R wave amplitude < 5 mV or P wave amplitude < 2 mV can result in undersensing because sensed amplitude may decrease after implantation.

If a unipolar lead is used, program the lead configuration to unipolar prior to implantation. If the lead configuration is programmed to bipolar with a unipolar lead, pacing will not be provided.

Do not tie a ligature directly to the lead body, tie it too tightly, or otherwise create excessive strain at the insertion site as this may damage the lead. Use the lead stabilizer to secure the lead lateral to the venous entry site.

Do not immerse the leads in mineral oil, silicone oil, or any other liquid.

Do not grip the lead with surgical instruments.

Do not use excessive force or surgical instruments to insert a stylet into a lead.

Use ventricular transvenous leads with caution in patients with either a mechanical or bioprosthetic tricuspid valvular prosthesis.

Use the correct suture sleeve (when needed) for each lead, to immobilize the lead and protect it against damage from ligatures.

Do not kink leads. Kinking leads may cause additional stress on the leads, possibly resulting in lead fracture.

Do not insert a lead connector pin into the connector block without first visually verifying that the setscrew is sufficiently retracted. Do not tighten the setscrew unless a lead connector pin is inserted because it could damage the connector block.

If a pacing lead is abandoned rather than removed, it must be capped to ensure that it is not a pathway for currents to or from the heart.

If a header port is unused on the generator, the port must be plugged to protect the generator.

9.6. PROGRAMMING AND PACEMAKER OPERATION

Rate adaptive pacing should be used with care in patients unable to tolerate increased pacing rates.

Minute ventilation rate responsive pacing may be inappropriate for patients who can achieve respiratory cycles shorter than 1.25 seconds (greater than 48 breaths per minute). Higher respiratory rates attenuate the impedance signal, which diminishes the MV rate response, i.e., the pacing rate will drop toward the programmed basic rate.

Do not use the as shipped generator values for pacing amplitude and sensitivity without verifying that they are appropriate for the patient, because this may result in shortened battery longevity, improper sensing or loss of capture.

Single chamber ventricular pacing should be used with care in patients who may develop pacemaker syndrome or who may have a need for maximal atrial contribution.

Abdominal implantation: Do not use combined sensor or minute ventilation sensor-driven pacing when the pacemaker is implanted abdominally. Accurate measurement of minute ventilation has not been demonstrated for abdominal placements.

Epicardial leads: Do not use epicardial leads for combined sensor minute ventilation sensor-driven pacing. Epicardial leads have not been demonstrated to measure minute ventilation.

Rate response should not be enabled before implantation because the sensor will sense noise resulting in inappropriate rates.

For ALIZEA DR model:

Crosstalk results in atrioventricular (AV) pacing with a 95 ms AV delay. This may be avoided by appropriate choice of sensitivities.

Slow retrograde conduction, especially with conduction time > 469 ms, may induce pacemaker-mediated tachycardia.

9.7. RATE INCREASES

Twiddler’s syndrome, i.e., patient manipulation of the device after implant, may cause pacing rate to increase temporarily if the pacemaker is programmed to combined sensor or accelerometer-only sensor mode.

9.8. GENERATOR EXPLANT AND DISPOSAL

Interrogate the device prior to explanting.

Return all explanted generators and leads to the manufacturer.

Never incinerate the device due to the potential for explosion. The device must be explanted before cremation.

10. PATIENT INFORMATION

Information for the patient is available in the patient booklet, contained in the outer storage package. Additional copies can be obtained by contacting your MicroPort representative.

This information should be given to each patient with his or her first pacemaker and offered to the pacemaker patient on each return visit or as deemed appropriate.

11. HOW SUPPLIED

11.1. STERILITY

The ALIZEA pacemakers are supplied one per package in a sterile package.

11.2. WARRANTY AND REPLACEMENT POLICY

MicroPort warrants its pacemakers. Refer to the "Warranty" section for additional information.

Please see the following labeling sections for information concerning the performance of this device: Indications, Contraindications, Warnings and Precautions, and Adverse Events.

12. IMPLANT PROCEDURE

12.1. NECESSARY EQUIPMENT

Implantation of ALIZEA DR / SR requires the following equipment:

- MicroPort dedicated programmer, equipped with the SMARTVIEW software interface and inductive telemetry head,
- pacing system analyzer, as well as its sterile connecting cables, to evaluate the pacing and sensing thresholds,
- a complete set of leads with corresponding introducers,
- physiological signal monitor capable of displaying simultaneously the surface ECG and arterial pressure,
- an external defibrillator with sterile external paddles,
- sterile cover for the telemetry head.

12.2. PACKAGING CONTENTS

ALIZEA DR / SR and its accessories are ethylene oxide sterilized and hermetically sealed in two-ply clear packaging meeting international requirements.

The sterile packaging contains:

- the pacemaker,
- a ratcheting screwdriver.

As delivered, ALIZEA DR / SR is programmed to as-shipped values that are different from nominal values (see “Programmable Parameters” section for details).

12.3. OPTIONAL EQUIPMENT

The following equipment may be required during implantation of ALIZEA DR / SR:

- an IS-1 insulating plug to close the atrial port (only for ALIZEA DR),
- sterile water to clean traces of blood. Any parts cleaned with sterile water must be thoroughly dried,
- mineral oil to lubricate if necessary,
- a lead cap to isolate a lead which is not used.

12.4. OPENING THE PACKAGE

Before opening the package:

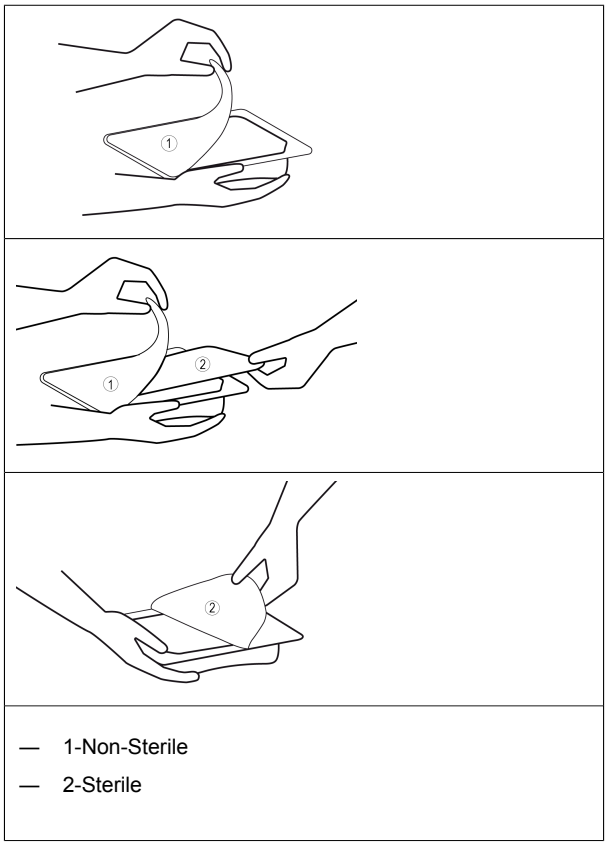
- Check the "Use by" date printed on the labels on the box and on the sterile package. Pacemakers not implanted before the “Use by” date should be returned to your MicroPort representative.
- Interrogate the device before activating the remote monitoring: if a warning is displayed or if battery voltage is too low (< 3.04V), do not implant the device and contact your MicroPort representative.

NOTE:The battery voltage can decrease before the expiration date is reached. However, the battery voltage should be equal to or higher than 3.04V at the time of implant.

Devices MUST NOT be interrogated and programmed within the vicinity of other devices.

Also check the integrity of the sterile package. The sterility of the contents is no longer guaranteed if the package has been pierced or altered. If the pacemaker is no longer sterile, it should be returned in its packaging to your MicroPort representative. Any re-sterilization of the unit is at the discretion of MicroPort.

Open the sterile package within the sterile field and carefully remove the device (see *Figure - Opening the sterile package*).



— 1-Non-Sterile
— 2-Sterile

Figure - Opening the sterile package

Handling - Do not drop. If an unpackaged pacemaker is dropped onto a hard surface, return it to MicroPort .

WARNING:
Inadequate therapy due to defective device If an unpacked device is dropped on a hard surface during handling, electronic parts could be damaged.

— Use a replacement device
— Return the damaged device to MicroPort

12.5. PREPARING THE POCKET

Because of the orientation of the pacemaker connector, it is advisable to create the pocket in a left pectoral position.

In its final position, the pacemaker should be no more than 4 - 5 cm below the skin surface.

12.6. CHOOSING THE TYPE OF LEAD

For the DR model, for optimal use of pacemaker functions, the atrial lead should be bipolar. If a unipolar atrial lead is used, the Autosensing function will not be available. For MRI compatibility, both leads should be bipolar.

For the SR model, for optimal use of pacemaker functions, the lead used should be bipolar. If a unipolar lead is used, the following function will not be available: the rate-response function based on minute ventilation. For MRI compatibility, the lead should be bipolar.

Use of a high polarization ventricular lead interferes with normal operation of the Ventricular Autothreshold function.

Connections:

The pacing/sensing connectors are IS-1 compatible. Other lead configurations are not compatible.

12.7. MEASUREMENT OF THRESHOLDS AT IMPLANT

Pacing and sensing thresholds should be measured at implant.

Pacing thresholds:

Acute thresholds should be lower than 1 V for a 0.5 ms pulse width, both in the ventricle and in the atrium.

Chronic thresholds should be less than 3 V for a 0.5 ms pulse width.

Sensing thresholds:

For proper ventricular sensing, the amplitude of the R-wave should be greater than 5 mV. For proper atrial sensing, the amplitude of the P-wave should be greater than 2 mV.

12.8. LEAD CONNECTIONS

It is imperative that each lead be properly connected to the corresponding pacemaker connector (the position of each connector is indicated on the casing).

CAUTION:

For the SR model, only one lead will be connected (ventricular or atrial). For the **DR model**, two leads will be connected: ventricular and atrial.

For each lead, only distal inserts must be tightened. To connect each lead, proceed as follows:

1. **For the SR model**, insert the ventricular or atrial lead pin all the way into the pacemaker port.

   For the DR model, insert the ventricular lead pin all the way into the appropriate pacemaker port (marked V) of the pacemaker.
2. Insert the screwdriver in the centre of the prominent screwdriver slot contour on the distal insert, then into the pre-inserted screw.
3. Tighten the screw until the screwdriver clicks. Check the fixation by pulling the lead (the lead should remain in the pacemaker when pulling to check the tightness).

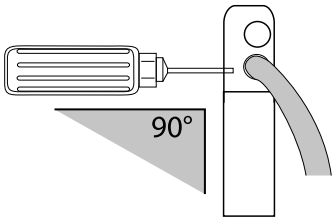
4. **For the DR model**, insert the atrial lead pin all the way into the appropriate port (marked A) of the pacemaker and proceed as in steps 2 and 3.

CAUTION:

— Do not tighten the pre-inserted screw when there is no lead connector inserted (this could damage the connector block).

— Do not loosen the screw before inserting the lead into the connector (subsequent risk of being unable to reinsert the screw).

— Use only the screwdriver provided with the pacemaker. Maintain the screwdriver's shaft perpendicular to the plane of the pacemaker (see figure below).



WARNING: Ensure that the screwdriver's tip is fully inserted in the setscrew; otherwise, the screwdriver might damage the setscrew and prevent connection with or disconnection from the lead.

To ensure full insertion, push the screwdriver's hex tip smoothly into the setscrew until it reaches the bottom of the hex chamber in the screw, which can be felt as a solid metallic contact. Do not implant the pacemaker if there is no feeling of solid metallic contact. Do not implant the pacemaker if the screwdriver does not click when attempting to tighten the setscrew on the lead pin.

12.9. IMPLANT CONSIDERATIONS

After placing the device in its pocket, check the pacemaker functioning using an ECG.

Suture the device to the muscle in order to avoid potential migration of the device into the pectoral muscle.

13. PACEMAKER INTERROGATION AND UPGRADE

The pacemaker can be interrogated and programmed via telemetry using a suitable programming head connected to a MicroPort dedicated programmer. Refer to the programmer manual supplied with the programmer for details concerning its use.

Implant software upgrade: in case new implant software is downloaded in the device memory through the programmer, a warning message may be displayed by the programmer to inform the user and give the proper instructions to follow.

14. SPECIAL MODES

14.1. NOMINAL MODE (SAFETY MODE)

Safety settings may be rapidly restored by pressing the Emergency button below: via the MicroPort dedicated programmer screen, the programming head or the MicroPort dedicated programmer keyboard.

In nominal mode, the pacemaker operates with the parameters from the table of programmable parameters.

14.2. STANDBY MODE

In the event of self-test failure, the pacemaker switches **automatically** to a safe mode of operation known as standby mode. In most cases, normal pacemaker operation may be re-established (if the pacemaker is at a stabilized temperature of approximately 37°C) by confirming the reinitialization function suggested by the MicroPort dedicated programmer. If this is not the case, contact your MicroPort representative.

In standby mode, the pacemaker operates with the following parameters: VVI, 70 ppm, 5 V, 0.5 ms, sensitivity 2.2 mV, unipolar for the **DR model and the SR model** when implanted in the ventricle or AAI for the **SR model** when implanted in the atrium.

Programming is then impossible and test modes, including magnet mode, are ineffective.

14.3. MAGNET MODE

When a magnet is applied, the pacemaker terminates the cycle in progress and operates using the following parameters:

Mode	DOO (if mode programmed: Dxx or SafeR for the **DR model only**) VOO (if mode programmed: Vxx) AOO (if mode programmed: Axx)
Rate	Magnet rate
Pulse amplitude	5 V (or greater if the programmed amplitude value is greater)
Pulse width	0.5 ms (or greater if the programmed pulse width value is greater)
AV delay (for the **DR model only**)	Rest AV delay

On exiting magnet mode, the device operates:

— for 6 cycles by pacing at the magnet rate, with an AV delay of 95 ms (if applicable and for the **DR model only)**, with the programmed amplitude and pulse width in asynchronous mode,

— then for 2 cycles with the programmed parameters in asynchronous mode.

14.4. RESPONSE IN THE PRESENCE OF INTERFERENCE

If the pacemaker senses electrical noise at a frequency above 20 Hz, it switches to an asynchronous mode at the basic rate. The programmed mode is restored as soon as the

noise is no longer detected.

15. FUNCTIONS AND PARAMETERS

15.1. PACING MODES

The pacing mode determines pacemaker operation when pacing and sensing. The meanings of the codes (e.g., DDD, VVI, AOO) are provided in Standards EN 45502-2-1 and ISO 14708-2.

For the DR model, the SafeR and DPlus modes are described in the section "Therapeutic improvements".

Contraindications to the use of specific modes for the both SR and DR models:

1. AAI(R) pacing is contraindicated where AV conduction is impaired.
2. Asynchronous pacing is contraindicated when there is competition between the patient's intrinsic rhythm and the pacemaker.

Contraindications for the DR model: DDD pacing is contraindicated in patients with chronic atrial fibrillation or flutter, or in those with slow retrograde conduction, which may induce Pacemaker-Mediated Tachycardia

15.1.1. MRI Mode

The MRI mode is an asynchronous mode (VOO/AOO or OOO for the **SR model**; DOO, VOO, AOO or OOO for the **DR model**) which is triggered either manually or upon detection of a strong magnetic field.

The MRI Mode is intended to be applied during MRI examination. When MRI Mode is activated (Auto or Manual), the magnet mode is ineffective.

NOTE: Refer to the MRI Solutions manual for the complete instructions for use available at www.microportmanuals.com.

15.2. RATES

15.2.1. Basic rate

The basic rate is the pacing rate in the absence of sensed events. If the patient’s spontaneous rate falls below this limit, the pacemaker takes over.

Special case:

If rest rate or hysteresis is programmed, the lower limit of the intrinsic rate may reach a value below the basic rate.

Programming requirement:

If the rate-responsive pacing function is ON, the lower limit of the basic rate is 50 ppm.

15.2.2. Maximum tracking rate

The maximum tracking rate determines the upper limit of the pacing rate.

Special case:

In triggered mode (single or dual chamber), the device may exceed the maximum tracking rate and pace to the rate limit value.

15.2.3. Rate hysteresis

Rate hysteresis determines the ability of the patient's natural sinus rhythm to decrease below the escape rate. After sensing, the pacemaker operates with an escape rate reduced by the programmed percentage of hysteresis.

Programming requirements:

1. If the Rate Response function is programmed, the escape rate cannot be below 50 ppm.
2. When the basic rate is less than or equal to 45 ppm, rate hysteresis is programmed to 0% and is not accessible.

NOTE: **For the DR model**: When Dplus mode is selected, the suggested percentage of hysteresis is 20%.

15.3. PACING AND SENSING PARAMETERS

15.3.1. Pulse amplitude

The pulse amplitude determines the voltage applied to the heart during pacing.

Recommendation:

Use the "as shipped" value (or a higher value if required) immediately after implant to avoid loss of capture due to the early rise in threshold. After threshold stabilization, a setting that provides a suitable safety margin (twice the chronic threshold) and saves the pacemaker battery can be found.

For the DR model, pulse amplitude is programmed independently for atrial pacing and ventricular pacing.

15.3.2. Pulse width

The pulse width determines the duration for which the pulse amplitude is applied to the heart during pacing.

Pulse width can be used to adjust pacemaker output.

For the DR model, pulse width is programmed independently for atrial pacing and ventricular pacing.

Programming requirements:

When the Ventricular Autothreshold function is programmed to "Monitor" or "Auto", the programmable ventricular pulse width is less than or equal to 0.5 ms.

For the DR model, when the Atrial Autothreshold function is programmed to "Monitor" or "Auto", the programmable atrial pulse width is less than or equal to 0.5 ms.

15.3.3. Sensitivity

The sensitivity determines the minimum signal sensing threshold. For example, a sensitivity of 1 mV will allow sensing of only signals with amplitude greater than 1 mV. In order to detect a low-amplitude cardiac signal, a higher sensitivity (lower value) must be programmed. However, if the pacemaker detects extracardiac signals, a lower sensitivity (higher value) must be programmed.

Recommendations:

1. The sensitivity should be prorammed 25% to 30% of the measured amplitude to ensure proper detection.
2. Programming a high atrial sensitivity (value less than or equal to 0.6 mV) should be reserved for P-waves of very low amplitude, since this increases sensitivity to external interference.

   For the DR model, these values may also be programmed for patients likely to present paroxysmal episodes of atrial fibrillation.

Programming requirements:

1. **For the DR model**, in unipolar mode, atrial sensitivity values below 0.4 mV are not available.
2. When the ventricular (or atrial) Autosensing is programmed to Auto, the ventricular (or atrial) sensitivity is no longer programmable.

15.3.4. Pacing and sensing polarities

Although mechanically configured as a bipolar pulse generator, the pacemaker may be programmed either to unipolar or bipolar configuration.

Pacing and sensing polarity configuration can be programmed independently.

For the DR model, pacing and sensing polarities can be programmed independently for the atrial and ventricular channels.

The pacemaker is shipped with bipolar sensing and pacing configuration.

Pacing polarity

In unipolar pacing configuration, the anode (positive pole) is the pacemaker’s titanium case and the distal electrode is the cathode (negative pole). In bipolar pacing configuration, the proximal electrode is the anode (positive pole) and the distal electrode is the cathode (negative pole).

One advantage of bipolar pacing is avoidance of nerve and muscle stimulation. However, unipolar pacing pulses are larger and therefore more visible on a surface ECG.

Sensing polarity

In unipolar sensing configuration, the potential difference is measured between the pacemaker titanium case and the distal tip of the lead. In bipolar sensing configuration, the potential difference is measured between the proximal ring and the distal tip of the lead.

One advantage to bipolar sensing is a lower susceptibility to detection of myopotentials and electromagnetic interference. In a given patient, unipolar or bipolar configuration may provide better sensing.

The risk of pectoral stimulation is lower with bipolar pacing. With bipolar sensing, the pacemaker is less sensitive to myopotentials and to external electromagnetic noise.

Programming requirement:

The pacemaker cannot be programmed to bipolar configuration if a bipolar lead is not connected (measurement of the impedance determines the type of lead present when programming to bipolar configuration).

15.4. REFRACTORY PERIODS

Post R and Post V Atrial Blanking, committed period, automatic AV delay and AVD paced/sensed offset are not available for the **SR model**.

15.4.1. Absolute refractory periods: post R and post V Atrial Blanking

Absolute atrial and ventricular refractory periods are initiated by any sensed or paced ventricular or atrial event. These periods are composed of an absolute Refractory Period and a retriggerable Refractory Period.

The duration of the refractory periods lengthens automatically as needed.

Post R and Post V Atrial Blanking special case:

For the DR model: Post R and Post V Atrial Blanking are absolute refractory periods that are programmable.

15.4.2. Committed period **(for the DR model only)**

In dual-chamber pacing modes, atrial pacing may be sensed by the ventricular sensing circuits, and may inhibit ventricular pacing. The pacemaker is protected against this phenomenon (called Crosstalk) by the committed period.

15.4.3. Automatic AV delay **(for the DR model only)**

The AV delay is the programmable time interval between atrial sensing or pacing and ventricular pacing.

In DOO and DDI mode, only the rest AV delay is programmable. In DDD mode, rest and exercise AV delays are programmable.

The rest AV delay is used at the programmed basic rate. The exercise AV delay is used at the programmed maximum rate. Between basic rate and maximum rate, the AV delay is calculated at each cycle by the pacemaker on the basis of a linear relationship between the AV delay and the atrial rate.

A fixed AV delay may be obtained by programming the rest AV delay equal to the exercise AV delay.

NOTES:

The Rest AV delay and the Exercise AV delay are automatically programmed and calculated when Dplus mode is selected.

If the basic rate is equal to 30 ppm, the effective AV delay may be shorter than the programmed value.

If the basic rate is less than 60 ppm, the rest AV delay is used for all rates between the basic rate and 60 ppm.

The effective AV delay following atrial pacing may be longer than the programmed AV delay if an AVD Paced/Sensed Offset is programmed.

The effective AV delay following atrial sensing may be longer than the value programmed (Wenckebach mode).

An AV delay of 30 ms is applied if atrial sensing occurs outside refractory periods in Wenckebach response mode.

The AV delay can be shorter than the programmed AV delay if pacing is delivered at the end of the committed period.

During periods of suspected atrial arrhythmia, an AV delay of 30 ms is applied if atrial sensing occurs. An AV delay of less than or equal to 110 ms is used if there is atrial pacing (the exercise AV delay is used if it is less than 110 ms).

If rest rate or rate hysteresis is programmed, the rest AV delay is applied for rates below the basic rate.

The anti-PMT algorithm may modify the AV delay during the confirmation phase (see "Protection from Retrograde P Waves" section).

15.4.4. AVD Paced/Sensed Offset **(for the DR model only)**

In DDD mode, the programmed value of the AVD Paced/Sensed Offset is added to the AV delay after atrial pacing. The difference between AV and PV intervals compensates for the lag between the atrial stimulus and atrial contraction. This helps to maintain a consistent interval between ventricular and atrial contractions whether AV sequential or P synchronous pacing occurs.

Programming requirement:

In Dplus mode, the AV delay plus the AVD paced/sensed offset between atrial and ventricular pacing cannot exceed 350 ms. In the other pacing modes, the AV delay plus the AVD paced/sensed offset between atrial and ventricular pacing cannot exceed 300 ms.

15.5. RATE RESPONSE

The Rate Response function makes it possible to adjust the pacing rate based on the patient's physical activity.

Sensors used:

The pacemaker is equipped with two sensors that prevent rate increases due to artifact through cross-checking of information:

1. Minute ventilation (MV): this is calculated based on the measurement of transthoracic impedance by standard (unipolar or bipolar for the **DR model**, bipolar for the **SR model**) intracardiac leads. It is used to obtain a physiological response proportional to the degree of exertion during periods in which the patient is active.
2. An accelerometer (G), which measures changes in the patient's anteroposterior acceleration: a rapid response may thus be obtained at the start of exertion and the end of exertion can be detected immediately.

The combination of these two sensors also prevents rate increases due to artifacts through continuous cross-checking of information from each sensor. Any rate increase not confirmed by the second sensor results in a return to the basic escape rate.

In dual sensor mode (Twin Trace), the MV sensor is dominant and solely determines the rate response when both sensors detect exercise.

The rate-responsive mode, the sensor choice and the physical activity are the only parameters to be programmed.

As long as the patient is at rest, the sensor-driven rate is equal to the basic rate. When the patient reaches his maximum exercise capacity, the sensor-driven rate is equal to the maximum rate. During exercise, the rate variation is proportional to the measured sensor level. The programmed physical activity determines the relationship between the measured sensor level and the sensor-driven rate.

Rate response can be programmed:

For the SR model: only if the pacing mode is programmed to AAIR or VVIR.

For the DR model: only if the pacing mode is programmed to SafeR-R, SafeR/DDIR, Dplus-R, Dplus/DDIR, AAIR, DDDR, DDD/DDIR, DDIR, VVIR.

Examples:

1. Automatic rate response ("RR Auto" option). The pacing rate is constantly adapted to the patient's physical activity.
2. Manual rate response ("RR Fixed" option). In that case, manual programming of the patient's physical activity determines the pacing rate applied, based on the sensor signal.The physical activity parameter should be programmed according to the patient's activity level, to which ALIZEA associates the maximum rate. It is recommended to program very low or low values for sedentary patients and high or very high values for active patients.
3. **For the DR model**, rate response during fallback mode switching (SafeR/DDIR, DDD/DDIR and Dplus/DDIR modes). Rate response is inactive if the patient is in sinus rhythm. It becomes active during atrial arrhythmia.

WARNINGS: Use the Rate Response function with caution in cases of:
1. Severe coronary insufficiency.
2. Severe aortic stenosis.
3. Myocardial function compromised by undue accelerations of the pacing rate.

Programming at implant:

"Learn" and "RR Auto" should not be programmed prior to implant so as not to distort autocalibration.

Surgical procedure:

For safety reasons, it is preferable to deprogram the Rate Response function before any surgical procedure on the pacemaker patient.

Programming requirement:

For the DR model: The SafeR/DDIR, DDD/DDIR and Dplus/DDIR modes (Rate response during fallback mode switching) are accessible only if Fallback mode switching is programmed.

15.6. THERAPEUTIC IMPROVEMENTS

Features	DR model	SR model
SafeR	x	
Dplus	x	
Rate acceleration	x	
Rest rate	x	x
Smoothing	x	x
Mode switching	x	

15.6.1. SafeR mode

The SafeR mode is intended to minimize unnecessary ventricular pacing and to promote spontaneous atrioventricular conduction. It gives priority to pacemaker operation in AAI(R) mode: the sensed P wave does not trigger the AV delay and recycles an atrial escape interval.

Indication:

SafeR is designed for patients requiring AAI(R) pacing (sinus node dysfunction) and/or who are at risk for AV conduction disorders (paroxysmal AV block, permanent first degree AV block, or exercise-induced AV block).

Operation:

The pacemaker functions in AAI(R) mode and temporarily converts to DDD(R) mode in the following cases:

— AVB III: Two consecutive atrial events (paced or sensed) occur without subsequent ventricular beats.

— AVB II: Three atrial events in twelve consecutive atrial cycles without subsequent ventricular beats.

— AVB I: Six consecutive atrial events occur without subsequent ventricular beats within a programmed PR interval (Long PR min and Long PR max parameters). This AVB I criterion can be activated continuously or only during exercise phase depending on the AVB I switch parameter.

— PAUSE: No ventricular beat occurs within a programmed interval (Max pause parameter, programmable to 2, 3 or 4 seconds).

The device regularly switches back to AAI(R) mode (at least once a day):

— after sensing 12 consecutive spontaneous ventricular events

— automatically every 100 paced ventricular cycles.

After an automatic switch to AAI(R) mode, if the intrinsic AV conduction has not resumed, the device switches back to DDD(R) mode according to the criteria listed above (third degree AVB, second degree AVB, first degree AVB or the pause).

The **SafeR-R mode** is a SafeR mode with Rate Response.

The SafeR/DDIR mode activates a switch from SafeR to DDIR mode when the pacemaker enters Fallback Mode Switching. Rate responsive pacing is only functional when the patient is in Fallback Mode Switching. The physical activity used during the Fallback Mode Switching phase is equal to the programmed parameter.

Adaptation to nocturnal AV blocks:

The device switches to DDD(R) mode and remains in DDD(R) mode when it has:

— 45 episodes of AV block or more during the last 24 hours

— 15 episodes of AV block or more per 24 hours during 3 consecutive days

— 50% DDD(R) pacing or more during one hour.

In these cases the automatic switch to AAI(R) following every 100 ventricular paced cycles is suspended. It remains in DDD(R) mode until 8:00 am the next morning.

Adaptation to conduction disorders during exercise:

When an AV block occurs during an exercise, after 3 switches the device remains in DDD(R) mode until the end of the exercise in order to avoid patient symptoms during exercise.

NOTE:

Physicians may alternatively program AAI(R), or DDD(R) with a long AV delay, to minimize ventricular pacing. However, AAI(R) will not provide ***any*** ventricular pacing in case of AV block. DDD(R) mode will ***always*** provide ventricular pacing after every normal atrial beat at the programmed AV delay; consequently in the circumstances listed above, DDD(R) will provide more ventricular pacing than SafeR(R).

15.6.2. Dplus mode

The Dplus pacing mode preserves spontaneous atrioventricular conduction.

Operation:

An AV monitoring period allows for small variations in the spontaneous atrioventricular delay. If no ventricular sensing occurs during that period, the pacemaker converts to DDD mode until atrioventricular conductions return to normal. In DDD mode, the pacemaker uses the AV delays calculated from the averaged PR intervals.

The Dplus-R mode is a Dplus mode with Rate Response.

The Dplus/DDIR mode activates a switch from Dplus to DDIR mode when the pacemaker enters Fallback Mode Switching. Rate responsive pacing is only functional when the patient is in Fallback Mode Switching. The physical activity used during the Fallback Mode Switching phase is equal to the programmed parameter.

15.6.3. Rate acceleration

The Acceleration function is used to suppress the cardiac pause and to reduce the vasodepressive response that accompanies it.

Indication:

Acceleration should be used only for patients presenting sinocarotid hypersensitivity with vasodepressive response.

Operation:

1. The pacing rate is gradually increased (up to the programmed percentage) when an abrupt drop in sinus rate is sensed.
2. The rate is then gradually reduced in accordance with the principle of rate smoothing.

Limitation:

The pacing rate induced by rate acceleration is limited to 120 ppm (or to the maximum rate if the latter is lower).

Programming constraints:

1. This function is available when Dplus or DDD mode is programmed.
2. If any of the AA prevention functions is activated, acceleration is forced to 0% and is not programmable.

AV delay shortening

The Acceleration function (only) may be accompanied by a shortening of the AV delay, intended to increase hemodynamic response.

Indication:

Shortening of the AV delay should be used only for patients presenting sinocarotid hypersensitivity with vasodepressive response.

Programming constraint:

This function is available when rate acceleration is programmed.

15.6.4. Rest rate

The rest rate is the pacing rate to which the pacemaker adjusts when it senses that the patient is sleeping or resting.

Sensing principle:

Sleep or rest phases are determined by reduced respiratory and cardiac activity and a low occurrence of premature complexes.

Programming requirements:

1. To be taken into consideration by the pacemaker, the rest rate must be below the basic rate.
2. This function is programmable when the Rate Response mode is programmed to “RR Auto”, “RR Fixed” or “Learn” and if sensor is "MV" or "MV + G".

15.6.5. Rate smoothing

The Smoothing function is designed to prevent a sharp rate drop to the programmed basic rate in patients presenting with episodes of paroxysmal bradycardia.

Operation:

1. If the patient’s spontaneous rate drops, the pacemaker takes over at a rate slightly lower than the spontaneous rate immediately prior to the pause.
2. The pacing rate is then gradually reduced until the basic rate is reached or the spontaneous rhythm is restored.

Programming at implant:

It is not advisable to program the Smoothing function before implantation, since the pacemaker may detect noise and pace at a rate higher than the programmed basic rate.

Recommendation:

Concomitant use of the Hysteresis function is highly advisable to avoid triggering of pacing for slight variations in the patient's spontaneous cycle (unless one of the AA prevention functions is activated, for the **DR model only**).

15.6.6. Protecting the ventricles against AA: Mode switching

The Mode switching function is designed to avoid prolonged ventricular pacing at a high rate for the entire duration of sustained atrial arrhythmia, by conversion to DDI(R) mode.

Operation:

1. Arrhythmia is identified by detection of abrupt acceleration of atrial rhythm. During the phase of identification of an atrial arrhythmia, the ventricular pacing rate cannot exceed 120 ppm (or the maximum rate if the latter is lower) unless the patient has an exercise induced SVT (rates above 120 ppm can be reached). The AV delay is 30 ms following atrial sensing and 110 ms (or the exercise AV delay if the latter is lower) following atrial pacing.
2. When atrial arrhythmia is confirmed, the pacemaker converts to DDI(R) mode at a pacing rate that decreases gradually until it reaches the sensor-driven rate or the basic rate or the rest rate.
3. As soon as the arrhythmia ceases, the pacing rate is gradually increased up to the atrial rate (or sensor-driven rate). The pacemaker then converts to DDD mode: the atrium and ventricle are resynchronized.

Limitation:

Mode switching occurs only if atrial arrhythmia is greater than 120 ppm.

NOTE: In SafeR mode, the Pause is automatically and temporarily set to 2 seconds in the event of atrial arrhythmia (as-shipped value is 3 seconds).
If a retrograde P wave falls within the refractory period, the pacemaker does not start an AV delay, thus preventing induction of PMT.

15.7. OPTIMIZING OPERATION

The following table details which functions are available according to the pacemaker model:

Features	DR model	SR model
Automatic implant detection	x	x*
Autosensing	x	x*
Ventricular Autothreshold	x	x*
Atrial Autothreshold	x	
PMT protection	x	
Lead Polarity Switch	x	x*

**except if the SR is implanted for the atrium*

15.7.1. Automatic detection of implantation

Operation:

At implantation, once the ventricular lead has been connected to the pacemaker and the case is in contact with the tissue, the device starts the detection of implantation. After five minutes, the device automatically checks if the ventricular lead is still connected to the pacemaker and the case still in contact with the tissue:

1. If yes, the detection of implantation is automatically confirmed.
2. If no, a new check is done by the device every five minutes, until the ventricular lead connection and the contact between the pacemaker and the tissue are confirmed.

The automatic detection of implantation can be deactivated via the programmer. In such case none of the automatic configuration steps described below will be done automatically; they shall be done manually as appropriate.

Measurements of lead impedances:

Twenty minutes after the detection of implantation has been confirmed, the device starts measuring the lead impedance(s) every 6 (six) hours and data is stored for each chamber.

Automatic launch of parameters:

Twenty minutes after the detection of implantation:

1. Memories are initiated.
2. Sensor is programmed to "Learn".
3. Statistics are reset to zero.
4. Remote monitoring is activated if programmed
5. Ventricular Autothreshold is activated if programmed
6. For the **DR model**, Atrial Autothreshold is activated if programmed
7. Lead polarity Switch is activated if programmed
8. For the **DR model**, the device switches from DDD to SafeR mode if programmed.

15.7.2. Autosensing

The Autosensing function allows automatic adjustment of the sensitivity for the **SR model** and for both atrial and ventricular sensitivities for the **DR model**.

Operation:

1. If the ventricular (or atrial) Autosensing function is programmed to Auto, the ventricular (or atrial) sensitivity is constantly adjusted to 37.5% of the mean amplitude of the ventricular (or atrial) signals.
2. When the atrium is paced, the sensitivity tends toward 0.4 mV. **For the DR model**, for the duration of an atrial arrhythmia, the atrial sensitivity tends toward 0.4 mV.
3. When the ventricle is paced, the ventricular sensitivity tends toward 1.5 mV in bipolar configuration and toward 2.5 mV in unipolar configuration.

Programming constraints:

1. The atrial Autosensing function (Auto mode) is available only when the atrial sensing polarity is bipolar.

2. **For the DR model**, when the Overdrive function is activated, the atrial Autosensing function is not programmable.

15.7.3. Ventricular Autothreshold (automatic adjustment of ventricular pacing amplitude)

The Ventricular Autothreshold function allows automatic adjustment of the amplitude of ventricular pacing, according to a threshold test performed by the device at regular intervals.

Description:

ALIZEA searches for the ventricular threshold daily at 0am, 6am, 12am and 6pm. This search is done only if the rhythm is below 95 bpm in dual chamber modes out of fallback mode switch and below 80 bpm for single chamber modes or in case of Fallback Mode Switch.

It is based on the measurement of negative sensing signal deflection during the 65 ms following ventricular pacing. In order to avoid the risks of ventricular fusion, in dual chamber modes, the AV delay is forced to 39 ms after a P wave or 63 ms after an atrial pacing pulse. In single chamber modes or Fallback mode switch, the escape interval is decreased by 109 ms while searching for the threshold. Following the AV delay or escape interval reduction, the calibration phase is starting only if 4 consecutive cycles are paced.

Calibration phase, consisting of 3 ventricular pacing pulses at 4 V and 3 ventricular pacing pulses at 2 V (followed, after 65 ms, by a back-up safety pulse at 4 V and 1 ms) and 2 ventricular pacing at 0 V (followed, after 65 ms, by a back-up safety pulse at 4 V and 1 ms), determines the capture criterion.

Searching for the ventricular threshold consists of a series of ventricular pacing pulses decreasing from 1.75V to 0.25 V by step of 0.25V.

This search stops as soon as a pacing pulse is ineffective (then followed, after 65 ms, by back-up pacing at 2.5 V and 1 ms). The ventricular pacing threshold corresponds to the amplitude of the last effective pacing pulse.

If the Ventricular Auto-threshold function is programmed to Auto, the ventricular pacing amplitude is programmed to twice* the pacing threshold limited to a programmed minimal value (2.5V**). This value is set until the next threshold search.

**as-shipped, programmable “RV amplitude safety margin”*

***as-shipped, programmable “RV min amplitude”*

If the threshold search is not successful, the ventricular pacing amplitude is forced to a safe amplitude (either the programmable “Maximum Amplitude” or “Safety Amplitude”).

Whenever Ventricular Auto-threshold is programmed to Monitor, the programmed ventricular pacing amplitude is maintained

When Ventricular Auto-threshold is programmed to Monitor or Auto, the programmable pulse widths are limited to values between 0.12 ms and 0.50 ms

NOTE: : For optimal operation of the Ventricular Auto-threshold function, it is advisable to avoid using high polarization leads.

WARNING: Certain drugs can greatly increase the pacing threshold. The Ventricular Autothreshold function should be used with caution, properly adjusting the minimal ventricular pacing amplitude.

Programming constraint:

The Ventricular Autothreshold function is not programmable when the basic rate is above 85 ppm.

15.7.4. Atrial Autothreshold **(for the DR model only)**

The Atrial Autothreshold function allows automatic adjustment of the amplitude of atrial pacing, according to a threshold test performed by the device at regular intervals.

Description:

Once a day (at 2 am by default), ALIZEA searches for the atrial threshold. This search is done either if the atrium is paced or not. The Atrial autothreshold test is starting only if the rhythm is not too fast so the cardiac interval must be longer than programmed the atrial autothreshold max rate interval + 200 ms.

2 types of test are possible: P test in case of stable intrinsic rhythm or AR test in case of stable AV conduction. A first phase of selection determines the appropriate test. The pacemaker is pacing at 50 min-1 to search for intrinsic atrial rhythm. If 8 stable P-P intervals are detected, the P test will be launched. If not, the pacemaker overdrives the atrial rhythm and prolongs the AV delay to 450ms to promote AV conduction. If 8 stable A-R intervals are detected, the AR test will be launched. Else, the atrial autothreshold will not start.

Then, a calibration phase, consisting of one pacing pulse at 2 V, determines the starting amplitude.

When P test is selected, the basic rate is forced to 50 min-1 to promote intrinsic atrial rhythm and searching for the atrial threshold consists of a series of atrial pacing pulses increasing from either 2.25 V (if the initial calibration 2V pacing pulse was ineffective) or 0.25V to 4V, so increasing from ineffective atrial pulse amplitude to effective pulse amplitude. The P test principle is pacing the atrium 200ms before the expected next P wave on one cardiac cycle out of three. If the next P wave occurs, it indicates that atrial pacing was not effective and so atrial amplitude is increased. As soon as next P wave does not occur, it means that atrial pacing is effective. The threshold search stops and the atrial pacing threshold corresponds to this atrial pulse amplitude.

When AR test is selected, searching for the atrial threshold consists of a series of atrial pacing pulses decreasing from either 4V (if the initial calibration 2V pacing pulse was ineffective) or 1.75V to 0.25 V, so decreasing from effective atrial pulse amplitude to ineffective pulse amplitude. The AR test principle is looking at a ventricular sensed event after the atrial pacing on one cardiac cycle out of two. If a ventricular event is sensed, it means that atrial pacing is effective and so atrial amplitude is decreased. As soon as no ventricular event is sensed, it means that atrial pacing is ineffective and a atrial back-up is applied. The threshold search stops and the atrial pacing threshold corresponds to the amplitude of the last effective atrial pacing pulse.

1. If the Atrial Autothreshold function is programmed to "Auto”, the atrial pacing amplitude is programmed to twice* the pacing threshold (but not below the programmable “Minimum Amplitude”).

   **as-shipped, programmable “A amplitude safety margin”*

   If the threshold search is not successful at 4V (the max tested amplitude), the atrial pacing amplitude is forced to 5V.

   If the threshold search is not successful, the atrial pacing amplitude is unchanged, but after 7 consecutive days with no success, the pacing amplitude is forced to the programmed Safety amplitude (or the last programmed amplitude if higher) until a new

test is successful.

2. When the Atrial Autothreshold function is programmed to "Monitor," the programmed atrial pacing amplitude value is preserved.

Programming constraint:

The Atrial Autothreshold function is not programmable when the basic rate is above:

— 85 ppm with an atrial autothreshold max rate at 120 ppm,

— 80 ppm with an atrial autothreshold max rate at 110 ppm,

— 70 ppm with an atrial autothreshold max rate at 100 ppm.

WARNING: Certain drugs can greatly increase the pacing threshold. In case the patient has a complete AV block, the test is not launched and is considered not successful. The Atrial Autothreshold function should be used with caution, properly adjusting the minimal atrial amplitude.

15.7.5. PMT protection **(for the DR model only)**

Protection against Pacemaker-Mediated Tachycardia (PMT) can be provided for all patients with retrograde ventriculoatrial conduction without reducing atrial sensing capability.

Description:

Since most PMTs are initiated by AV dissociations (PVCs) or by asynchronous to synchronous switching (magnet mode, threshold test, noise sensing, and reassociation after Fallback Mode Switching), the pacemaker automatically extends a post ventricular atrial refractory period to 500 ms for one cycle following detection of any such event.

The pacemaker does not trigger an AV delay on a P wave likely to be retrograde, thus PMT is prevented.

Other events such as isolated artifacts or loss of capture can induce PMTs. The pacemaker can identify these PMTs by means of an algorithm based on the stability of the VP interval (from ventricular paced beat to retrograde P wave). Once a PMT has been confirmed, the pacemaker initiates a post-ventricular atrial refractory period of 500 ms in order to terminate the PMT. Termination occurs within 12 cardiac cycles.

NOTE:AV delay is modified for 1 or 2 cardiac cycles.

Example: Palliative protection (permanently applicable). The pacemaker does not trigger an AV delay on a P wave detected within 500 ms following an asynchronous ventricular event.

15.7.6. Lead Polarity Switch

The Lead Polarity Switch feature measures lead impedances over the long-term operation of the device and enables the device to switch bipolar pacing and sensing to unipolar when bipolar lead integrity is in doubt. When a bipolar lead impedance is less than 200 Ω or more than 3000 Ω, the lead could be considered defective. Lead impedance measurements are performed every 6 hours. If 2 out of the last 4 measurements of a bipolar lead are out of range, the Lead Polarity Switch operates.

CAUTION: If the Lead Polarity Switch detects out-of-range lead impedance, investigate possible lead system failures. Lead system failures can prevent adequate sensing or full pacing support.

NOTE for the DR model: When operating on the atrial lead, the lead polarity switch changes the pacing mode to VVI(R). For optimal use of pacemaker functions, the atrial lead should be bipolar.

Programming constraints:

1. **For both SR and DR models**, Ventricular Lead Polarity Switch can be turned ON for leads programmed in bipolar pacing modes only.
2. **For the DR model**, in order to turn ON Atrial Lead Polarity Switch, the pacing mode must be programmed to a dual chamber pacing mode.

15.8. FOLLOW-UP FUNCTION

Storage of memory data:

AIDA (Automatic Interpretation for Diagnosis Assistance) software provides access up to 6 months of patient follow-up with day by day data collection, or up to 24 hours with hourly data collection.

Episodes of Right atrial autothreshold and Right ventricular autothrehsold are recorded with 3 EGM channels (EGM A, EGM V and RV Ring-CAN).

Episodes of SafeR (AV conduction), Fallback Mode Switch, A burst and V burst are recorded with 2 EGM channels (EGM A and EGM V).

Alerts/Warnings:

The device routinely performs security self-checks and technical measurements to ensure system integrity. When system integrity is found to be at risk outside a follow-up, alerts are stored in the device memory. When system integrity is found to be at risk during a follow-up, the information is managed by a warning (pop-up message) to immediately notify the user.

15.9. REMOTE MONITORING FUNCTION

Remote monitoring enables the automatic remote transmission of implant data to the physician thanks to the wireless Bluetooth Low Energy communication ability of the implant in order to provide the physician with a comprehensive report about device functioning and patient cardiac status without having the patient physically in the clinic.

The data are transmitted from the implant to the SMARTVIEW CONNECT monitor, a small transmitter placed in the patient's home.

Implant data are first transmitted to the SMARTVIEW CONNECT monitor via Bluetooth Low Energy. Data are then routed through the mobile network to a protected remote server. This server is responsible for transforming the implant data into a comprehensive report that can be consulted by the physician on a dedicated website. The server also sends notifications to the physician via SMS, email or fax when a new transmission report is available.

15.9.1. SMARTVIEW CONNECT monitor

The SMARTVIEW CONNECT monitor is a small device equipped with a Bluetooth Low Energy transmission module to communicate with the implant and a modem to export data

through the Internet.

The SMARTVIEW CONNECT monitor is delivered to the patient who has to install it at home. Preferably, the SMARTVIEW CONNECT monitor will be placed on the nightstand of the patient, as close as possible to the side of the bed where the patient usually sleeps. The SMARTVIEW CONNECT monitor needs to be connected to the power plug. The scheduled transmissions, as well as alert transmissions (see below) are done during the night when the patient is asleep next to the SMARTVIEW CONNECT monitor without any intervention from the patient.

15.9.2. Transmission trigger

There are 3 different triggers for a remote transmission:

- The **remote follow-up transmission** is scheduled by the physician to occur regularly (according to the programming).
- The **alert transmission** will take place when the implant has recorded an abnormal event. The list of abnormal events is available in a following paragraph. Alert conditions are checked daily.
- The **on-demand follow-up transmission** is triggered by the patient himself, using a specific software button on the SMARTVIEW CONNECT monitor's user interface.

15.9.3. Data transmitted

The data transmitted are identical to the data available during a standard interrogation with the dedicated programmer. All counters, histograms, IEGMs and diagnosis available in the device are transmitted containing (not an exhaustive list):

- Programmed parameters;
- Information on patient and system implanted;
- Battery status;
- Lead status;
- Pacing counters and mean heart rate;
- Atrial and ventricular arrhythmia counters and episodes.

Data are presented in the form of two reports to the physician: the first one contains a summary of major counters, histograms, warnings and diagnosis. The second one presents the most important IEGM episodes automatically selected based on the degree of severity for the patient.

15.9.4. User website

On the website, the physician is able to:

- Consult and schedule the remote follow-ups of patients;
- Configure additional ways of being notified of alerts (for instance by SMS, fax or e-mail);
- Consult, print and export patient reports.

15.9.5. Alert system

The following set of alert triggers can be independently programmed ON/OFF by the physician using the dedicated programmer and can trigger an alert transmission:

- Low or high lead impedance (A,V);

- High pacing threshold (A,V);
- Lead Polarity Switch (A,V);
- AF occurrence with 3 thresholds (for DR only);
- Fast V rate during AF (for DR only);
- Asynchronous mode;
- MRI notifications.

The following set of alert triggers (system alerts) cannot be deactivated when the Alerts are programmed “On” and can trigger an alert transmission:

- Battery depletion – RRT;
- System integrity;
- Reset.

WARNING: The use of remote monitoring does not replace regular follow-up. Therefore, when using remote monitoring, the time period between follow-up visits should not be extended.

The pacemaker uses BLE technology with authenticated pairing with the Smartview Connect monitor, and data encryption for secure communication.

An excessive BLE usage is an indicator for a possible cyberattack. In this case, the BLE communication may be automatically forced to off. In such event, a warning will appear on the programmer during a follow-up visit to acknowledge the physician.

16. PATIENT FOLLOW-UP

16.1. RECOMMENDED REPLACEMENT TIME (RRT)

The Recommended Replacement Time (RRT), previously known as Elective Replacement Indicator (ERI) is controlled by:

- a battery voltage:
  - of 2.63 V if Remote monitoring activated;
  - of 2.70 V if Remote monitoring deactivated.

When RRT is reached, a magnet rate of 80 ± 1 ppm is applied by the device. As the EOS (End Of Service) approaches, the magnet rate decreases to 70 ± 1 ppm.

CAUTION:
The pacemaker should be replaced as soon as the Recommended Replacement Time (RRT or ERI) point is reached.

When the RRT (or ERI) point is reached, the following parameters are switched to the settings specified below until the end of the device's service:

- Mode: VVI
- Basic rate: 70 ppm
- Rate hysteresis : off
- Rate response mode: off
- Smoothing: off

Other parameters remain as programmed.

If activated, the remote monitoring function is deactivated after RRT once the RRT alerts have been sent.

After having reached the RRT (or ERI), the Prolonged Service Period (PSP) of the device is:

- at least 3 months under the following conditions: VVI, 70 ppm, 5V, 0.35ms, 500 Ω, 100% pacing (Nominal parameters).
- at least 6 months under the following conditions: VVI, 60 ppm, 2.5V, 0.35ms, 600 Ω, 100% pacing according to ISO14708 section 19.2.

Time to RRT (residual longevity): estimated remaining service time of the device. This estimate is calculated using battery voltage, leads measurements, statistics and programmed parameters. This value is refreshed automatically after each programming impacting device longevity.

16.2. FOLLOW-UP RECOMMENDATIONS

Standard follow-up

Annual standard follow up is recommended. Before the patient’s discharge, and at each follow-up visit, it is advisable to:

1. Check the battery status.

2. Check for proper sensing (sensitivity for the **both SR and DR models**, crosstalk for the **DR model**) and pacing; set the pacing amplitude to twice the pacing threshold.
3. Interrogate the device memories (AIDA)
4. Keep a printout of programmed parameters, test results, and memory data.

Frequent follow-up

When the minimum estimated residual longevity displayed by the MicroPort dedicated programmer is less than or equal to 12 months:

— It is recommended to conduct patient follow-up visit at an interval that is between the minimal and the typical residual longevities displayed by the MicroPort dedicated programmer, without exceeding 12 months (i.e. the annual standard follow-up).

— For pacemaker-dependent patients, it is recommended to conduct patient follow-up visit at an interval equal to the minimal residual longevity displayed by the MicroPort dedicated programmer.

NOTES:
“Time to RRT = N/A” is displayed by the MicroPort dedicated programmer

— If less than 5 minutes statistics are available (i.e. first interrogation at implant, device reset),

— If any lead impedance related to each currently pacing chamber does not have a valid value (range between 200 and 3000 Ω).

If “Time to RRT” is still N/A (outside of the two cases listed here above), contact your MicroPort Representative.

Replacement

The pacemaker should be replaced as soon as the Recommended Replacement Time (RRT) point is reached.

Implant software upgrade

In case new implant software is downloaded in the device memory through the MicroPort dedicated programmer, a warning message may be displayed by the MicroPort dedicated programmer to inform the user and give the proper instructions to follow.

16.3. EXPLANTATION

The pacemaker should be explanted in the following cases:

— End of service;

— Confirmed malfunction;

— Cremation of the patient (the pacemaker may explode if placed in an incinerator);

— Patient death: for environmental reasons, the local regulation may require the explantation of the devices containing a battery supply.

WARNING:
The pacemaker is a single use impantable device. The explanted pacemaker should not be reused in another patient. It could lead to inflammation, intoxication or infection of the patient.

All explanted pacemakers should be returned to your MicroPort representative carefully cleaned of all traces of contamination. Cleaning can be achieved by immersing the pacemaker in an aqueous sodium hypochlorite containing at least 1% chlorine, followed by rinsing copiously with water.

The pacemaker should be packaged so as to protect against the mechanical impact and temperature variations that may occur during shipping.

16.4. PROGRAMMER TESTS

The MicroPort dedicated programmer is designed to:

- perform impedance tests on the lead for the **SR model** and on both atrial and ventricular leads for the **DR model**,
- perform pacing threshold tests on the paced cavity(ies) in asynchronous mode, in the ventricle this test can be performed manually or automatically,
- determine the amplitude of sensed waves for the **SR model** and atrial and ventricular waves for the **DR model**,
- display the patient's ECG with temporarily modified programming parameters (e.g., to observe the patient's subjacent rhythm),
- perform electrophysiologic studies (bursts and extrastimulus sequences).

16.5. INTERROGATING THE DIAGNOSTIC DATA (AIDA)

Interrogating the diagnostic data provides:

- statistics since the last follow-up,
- 6-month curves and histograms for evaluating device operation if AIDA programmed on 6 months,
- recorded episodes (fallback mode switching for the **DR model**, atrial and/or ventricular bursts, switches from AAI to DDD for the **DR model**, atrial and/or ventricular autothreshold episodes) including intracardiac ECGs and continuous heart rate recording over the last 7 days,
- diagnostic messages about events detected by the device.

16.5.1. SafeR (Preservation of AV conduction)

The following AV conduction graphs are presented:

1. Monitoring of the evolution of patient’s AV conduction
2. Overview of all switches due to various types of AV blocks, classified by day/night and by exercise/rest.
3. Histograms showing the day to day distribution of blocked atrial events and the number of pacemaker switches from AAI to DDD(R)
4. EGM strips associated to AV block switches and pauses.

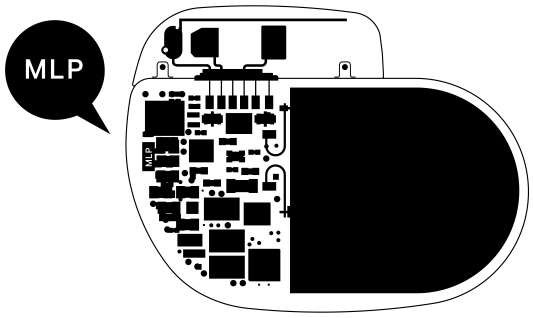
16.6. PACEMAKER IDENTIFICATION

The pacemaker can be interrogated and programmed via telemetry, using the programming head interfaced with the MicroPort dedicated programmer.

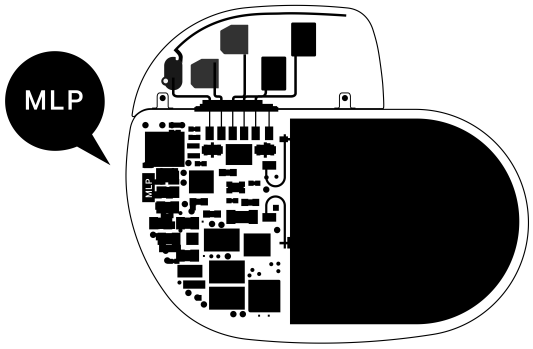
The device can be non-invasively identified as follows:

1. Take an X-ray to identify the name of the manufacturer printed on the device (MLP = MRI Conditional MicroPort Pacemaker model).

   For the SR model:



   For the DR model:



2. Interrogate the device using the MicroPort dedicated programmer. The model and serial number of the device are automatically displayed.

17. STANDBY MODE

Standby is a safety mode of operation that the pacemaker enters in response to a failure of one of the self-tests that are performed periodically. The programmer has the ability to examine the pacemaker by telemetry and restart or, if possible, re-initialize the pacemaker. Test modes, including magnet mode, are disabled and statistics are not incremented. In standby mode, programming is not possible and the device functions as follows:

Mode	VVI*
Basic rate	70 ppm
Rate hysteresis	0%
Pulse amplitude	5 V
Pulse width	0.50 ms
Sensitivity	2.2 mV
Polarity (pacing and sensing)	Unipolar
Rate smoothing	OFF
Rate-responsive mode	OFF
Remote monitoring	OFF

**VVI mode for the DR model and the SR model when implanted in the ventricle or AAI for the SR model when implanted in the atrium*

NOTE:

Pacing thresholds do not vary significantly for pulse widths ranging from 0.5 ms to 1 ms, so a 0.50 ms pulse width has been selected to save energy.

18. MEDICAL FOLLOW-UP

18.1. MAGNET TEST

The magnet test gives an indication of the cell capacity, atrial and/or ventricular capture, amplitude and basic rate programmed without using the programmer. Application of a magnet over the pacemaker makes the pulse generator operate in a simple safety mode.

18.1.1. Magnet On

When a magnet is applied over the pacemaker, the pulse generator finishes the cycle in progress and then switches to the magnet test mode described below:

Mode	DOO (if mode programmed: Dxx or SafeR **for the DR model only**) VOO (if mode programmed: Vxx) AOO (if mode programmed: Axx)
Rate	Magnet rate
Pulse amplitude	5 V (or greater if the programmed amplitude value is greater)
Pulse width	0.5ms (or greater if the programmed pulse width value is greater)
AV delay **(for the DR model only)**	Rest AV delay

18.1.2. Magnet Off

On exiting magnet mode, the device operates:

— for 6 cycles by pacing at the magnet rate, with an AV delay of 95ms (if applicable and for the DR model only) and with the programmed amplitude and pulse width in asynchronous mode,

— then for 2 cycles with the programmed parameters, in asynchronous mode.

18.2. CAPTURE TEST MODE:

The purpose of this test is to demonstrate that the programmed voltage and pulse width are sufficient to capture. During the capture test, the pacemaker operates as follows:

Mode	DOO (if mode programmed: Dxx or SafeR **for the DR model only**) VOO (if mode programmed: Vxx) AOO (if mode programmed: Axx)
Rate	Magnet rate
Pulse amplitude and width	As programmed
AV delay **(for the DR model only)**	94ms

18.3. RATE TEST MODE:

The purpose of this mode is to measure the programmed amplitude and rate and, in dual chamber pacing, the programmed AV delay.

During the rate test, the pacemaker operates as follows:

Mode	DOO (if mode programmed: Dxx or SafeR **for the DR model only**) VOO (if mode programmed: Vxx) AOO (if mode programmed: Axx)
Rate	Basic rate
Pulse amplitude and width	As programmed
AV delay **(for the DR model only)**	94ms

NOTES:

— If the magnet is reapplied during the capture test or the rate test, the pacemaker reverts to the magnet test.

— The programmer is not effective during either magnet, capture, or rate test.

— **For the DR model only**: AVD Paced/Sensed Offset is not applied

18.4. THRESHOLD TESTS

Non-invasive threshold measurements can be performed in both chambers through the pacemaker. Intracardiac ECG and markers are automatically transmitted for the paced chamber during the threshold test.

18.4.1. Ventricular threshold test

The ventricular threshold test can be used when the pacemaker is programmed to

— VOO, VVI and VVT mode **for the SR model**

— VOO, VVI, VVT, DOO, DDI, DDD, Dplus and SafeR mode **for the DR model**

The test begins at user demand in the programmed mode, at the programmed start amplitude (in volts) with the programmed number of spike(s) per amplitude. During the test, ventricular pacing (and atrial if programmed **for DR model**) is (are) asynchronous. The pacing rate, the pulse width and the polarity are respectively the programmed threshold rate, programmed threshold pulse width and programmed threshold polarity.

The ventricular amplitude (in volts) sequence is 6V, 5V, 4.5V, 4V, 3.5V, 3V, 2.75V and then decreases by steps of 0.25 V.

For the DR model, the AV delay is fixed to 95ms. If a magnet is applied, if the programming head is removed, or if any key of the programmer is pressed, the test is immediately stopped.

18.4.2. Atrial threshold test

The atrial threshold test can be used when the pacemaker is programmed to

— AOO, AAI and AAT mode **for the SR model**

— AOO, AAI, AAT, DOO, DDI, DDD, Dplus and SafeR mode **for the DR model**

The test begins at user demand in the programmed mode, at the programmed start amplitude (in volts) with the programmed number of spike(s) per amplitude. During the test, atrial pacing (and ventricular if programmed **for DR model**) is (are) asynchronous. The pacing rate, the pulse width and the polarity are respectively the programmed threshold rate, programmed threshold pulse width and programmed threshold polarity.

The atrial amplitude (in volts) sequence is 6V, 5V, 4.5V, 4V, 3.5V, 3V, 2.75V and then decreases by steps of 0.25 V.

For the DR model, the AV delay is fixed to 250ms. If a magnet is applied, if the programming head is removed, or if any key of the programmer is pressed, the test is immediately stopped.

18.5. LEAD MEASUREMENTS

The lead measurement test mode allows non-invasive measurements of atrial and/or ventricular lead characteristics. The lead measurement test mode begins when programmed and lasts one cycle.

The pacing rate is programmable (80, 90, 100, 110, 120 ppm) and the pulse width is greater than or equal to 0.5 ms in the paced chamber(s).

The programmer displays the measured averages for voltage current and impedance.

MEASURABLE RANGE		
Parameters	**Min.**	**Max.**
Voltage (V)	1.4	7.5
Current (mA)	0.5	28.0
Impedance (kΩ)	0.2	3.0

18.6. STATISTICS

The pacemaker automatically stores data via diagnostic counters that can be reset at any time. These counters can be used to check the function of the pacemaker, to optimize programmable values and to evaluate the need for special features.

18.7. MARKERS AND INTRACARDIAC ECG

The atrial or ventricular EGM and the markers can be obtained simultaneously on the programmer screen.

18.7.1. Markers

Event markers are particularly useful in the interpretation of dual chamber pacemaker ECGs.

Positive markers: atrial events	
Ar marker Small marker	Atrial sensing during a relative refractory period and in DDI mode
As marker Intermediate marker	Atrial sensing outside the refractory periods
Ap marker Large marker	Atrial pacing (including pacing initiated in the SST mode)
An marker Large marker	Atrial pacing inside absolute refractory periods

Negative markers: ventricular events	
Vr marker Small marker	Ventricular sensing during a relative refractory period
Vs marker Intermediate marker	Ventricular sensing outside the refractory periods
Vp marker Large marker	Ventricular pacing (including pacing initiated in the SST mode)
Vn marker Large marker	Ventricular pacing inside absolute refractory periods

The pacemaker starts transmitting markers when commanded by the programmer (see programmer manual). Transmission is ended when the programmer head is removed, a magnet is applied, or any key of the programmer is pressed.

18.7.2. Intracardiac ECG

The pacemaker provides noninvasive atrial and ventricular intracardiac ECGs, as well as, atrial + ventricular intracardiac ECGs, which are essential to evaluate the pacing system. The intracardiac ECG can be used to select pacing and sensing polarities, to reveal possible myopotentials that are not visible on the surface ECG or to measure the retrograde conduction time. The pacemaker stops transmitting intracardiac ECGs when the programmer head is removed, a magnet is applied, or any key of the programmer is pressed.

NOTE:
The programmed sensed polarity determines the intracardiac ECG polarity displayed on the programmer screen.

18.8. TEMPORARY PROGRAMMING

Temporary programming parameters:

- Mode
- Basic rate
- Maximum rate
- Sensing and pacing polarities
- Atrial and/or ventricular sensitivity
- Atrial and/or ventricular amplitude and pulse width
- Rest and exercise AV delays **for DR model only**
- AVD Paced/Sensed Offset **for DR model only**

Temporary parameters can be batch programmed. When temporary programming is used, rate hysteresis is fixed to 0 % and rate response and smoothing are permanently disabled.

18.9. MEMORY FUNCTIONS

Memory functions are useful for assessing the performance of the pacemaker during the patient's daily life. They can be used in conjunction with the statistics function. The large memory capacity of the pacemaker allows the beat-to-beat monitoring of many events for a long period of time. Types of events and periods of time are listed in the descriptions that follow.

18.9.1. EGM storage

For the SR model

Intracardiac ECGs A and V of 24 seconds each are stored by the following trigger:

— Ventricular arrhythmias
— Ventricular autothreshold

For the DR model

Intracardiac ECGs A and V of 28 seconds each are stored by the following triggers:

— Sustained PAC runs
— FMS

Intracardiac ECGs A and V of 24 seconds each are stored by the following triggers:

— Ventricular arrhythmias
— Switches from AAI to DDD (SafeR(R) mode)

Ventricular arrhythmias Intracardiac ECGs A, V and RV Ring-CAN of 24 seconds each are stored by the following triggers:

— Atrial autothreshold
— Ventricular autothreshold

NOTE:
The EGM duration may slightly change depending on the signal variations which results in more or less signal compression.

18.9.2. Mean Heart Rate Curve

Description: The pacemaker automatically records heart rate variations over one week period. The pacemaker averages the heart rate every 8.5 minutes and calculates the percentage numbers of spontaneous and paced cycles. These results are displayed as a curve that differentiates spontaneous from paced cardiac activity.

Use: When programmed to dual chamber **for DR model** or ventricular single chamber modes **for SR and DR model**, a ventricular rate curve is recorded. When programmed to atrial single chamber modes, an atrial rate curve is recorded.

18.9.3. Ventricular Autothreshold curve

If Ventricular Autothreshold is programmed to Monitor or Auto, measured ventricular capture thresholds are stored for one month and are displayed in the Ventricular Autothreshold curve.

18.9.4. Atrial Autothreshold curve

If Atrial Autothreshold is programmed to Monitor or Auto, measured atrial capture thresholds are stored for one month and are displayed in the Atrial Autothreshold curve.

18.9.5. Autosensing histograms and curves

If autosensing is programmed in Monitor or Auto mode, P and R waves are continuously recorded and can be displayed through the autosensing histograms.

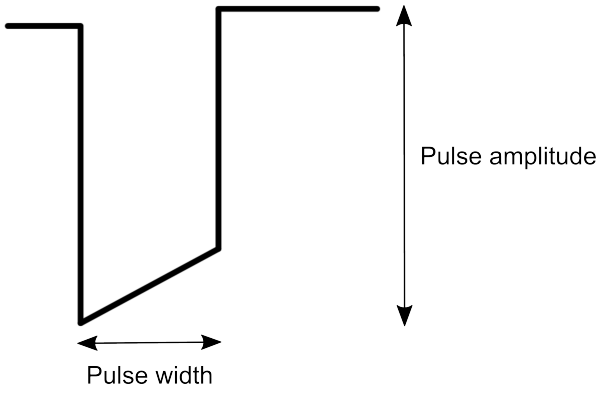
When programmed to Auto mode, curves of the target thresholds determined by the algorithm in each chamber, stored every 8.5 minutes, are also available.

19. PHYSICAL CHARACTERISTICS

	DR model	SR model
Dimensions	45.5 x 54.3 x 6.1 mm	41.4 x 54.3 x 6.1 mm
Weight	24.2 g	23.3 g
Volume	11 cm^3	10.50 cm^3
Connector	IS-1 (2x)	IS-1
Active surface area of casing	34.2 cm^2	34.2 cm^2
Guaranteed connector holding power	14N	14N
Materials used	Active surface area of casing: 99% pure titanium Connectors: polyurethane* and silicone* Pin : Titanium pin (99% pure Titanium) or Stainless Steel (Iron, Chromium, Nickel, Molybdenum, Manganese)	Active surface area of casing: 99% pure titanium Connectors: polyurethane* and silicone* Pin : Titanium pin (99% pure Titanium) or Stainless Steel (Iron, Chromium, Nickel, Molybdenum, Manganese)

*Medical-grade materials that have undergone "in vitro" and "in vivo" qualifications.

20. ELECTRICAL CHARACTERISTICS

Input impedance	Unipolar ≥ 40 kΩ Bipolar ≥ 40 kΩ
Pulse form	

20.1. CURRENT DRAIN AT BEGINNING OF SERVICE

Battery condition BOS=3.20 V without Remote monitoring

Battery condition BOS=3.10 V with Remote monitoring

For the DR model, the current drain at the beginning of service is as follows:

Shipment conditions(1)	SafeR mode(3)	Inhibited: 6.0 µA With pacing: 8.0 µA
Shipment conditions(1)	DDD mode	Inhibited: 6.0 µA 100% pacing: 13.4 µA
Cenelec conditions(2)	SafeR mode(3)	Inhibited: 6.1 µA With pacing: 7.8 µA
Cenelec conditions(2)	DDD mode	Inhibited: 6.1 µA 100% pacing: 12.2 µA

(1) 60 ppm, 3.5 V, 0.35 ms, 500 Ω, Holter ON, sensors ON.

(2) 70 ppm, 2.5 V, 0.5 ms, 500 Ω, Holter ON, sensors ON.

(3) Twenty minutes after the detection of implantation, the device switches automatically from DDD to SafeR mode, assuming 5% ventricular pacing and 50% atrial pacing.

For the SR model, the current drain at the beginning of service is as follows:

Shipment conditions(1)	VVI mode	Inhibited: 5.8 µA 100% pacing: 10.1 µA
Cenelec conditions(2)	VVI mode	Inhibited: 5.8 µA 100% pacing: 8.8 µA

(1) 70 ppm, 3.5 V, 0.35 ms, 500 Ω, Holter ON, sensors ON.

(2) 70 ppm, 2.5 V, 0.5 ms, 500 Ω, Holter ON, sensors ON.

20.2. CORRESPONDENCE BETWEEN MAGNET RATE AND BATTERY LIFE

Table of magnet rate:

Battery life	BOS	RRT	EOS
Magnet Rate (bpm)	96	80	70

20.3. BATTERY

Manufacturer	LITRONIK GmbH
Type	Lithium manganese dioxide (LiMnO2)
Model	LiS 3150 MP
Total capacity	1.2 Ah
Usable capacity	Without Remote monitoring, between BOS and RRT = 1.123 Ah, between RRT et EOS = 0.053 Ah. With Remote monitoring, between BOS and RRT = 1.040 Ah, between RRT and EOS = 0.136 Ah.
Voltage	BOS: 3.20 V without Remote monitoring BOS: 3.10 V with Remote monitoring RRT: 2.70 V without Remote monitoring RRT: 2.63 V with Remote monitoring EOS: 2.50 V

20.4. LONGEVITY

For the DR model:

The longevities are calculated by taking into account 6 months storage.

Longevity projection at 60 min^{-1}, 2.50 V, 0.35 ms, Holter ON, Remote OFF

Mode	%A pacing	% V pacing	Impedance (Ω)	Sensors	Longevity (years)
SafeR	50	5	750	OFF	16.2
SafeR	50	5	750	ON	14.7
SafeR	50	5	500	OFF	15.5
SafeR	50	5	500	ON	14.1
DDD	100	100	750	OFF	12.7
DDD	100	100	750	ON	11.8
DDD	100	100	500	OFF	11.2
DDD	100	100	500	ON	10.5

8.7 years	Cenelec conditions and DDD mode, assuming 100% pacing 70 min^{-1}, 2.5 V, 0.5 ms, 500 Ω, Holter ON, sensors ON, Remote OFF
11.1 years	ISO14708-2 conditions and DDD mode, assuming 100% pacing 60 min^{-1}, 2.5 V, 0.35 ms, 600 Ω, Holter ON, sensors ON, Remote OFF
12.7 years	Shipment conditions and SafeR mode, assuming 5% V pacing & 50% A pacing 60 min^{-1}, 3.5 V, 0.35 ms, 500 Ω, Holter ON, sensors ON, Remote OFF
12.8 years	SafeR mode, assuming 50% A pacing and 5% V pacing 60 min^{-1}, 2.5 V , 0.35 ms, 750 ohms, sensors ON, Holter ON, Remote ON
13.0 years	Cenelec conditions and SafeR mode, assuming 5% V pacing & 50% A pacing 70 min^{-1}, 2.5 V, 0.5 ms, 500 Ω, Holter ON, sensors ON, Remote OFF

For the SR model:

The longevities are calculated by taking into account 6 months storage.

Longevity projection with VVI mode at 60 min^{-1}, 2.50 V, 0.35 ms, Holter ON, Remote OFF

% V pacing	Impedance (Ω)	Sensors	Longevity (years)
50	750	OFF	17.0
50	750	ON	15.4
50	500	OFF	16.2
50	500	ON	14.8
100	750	OFF	15.4
100	750	ON	14.1
100	500	OFF	14.3
100	500	ON	13.1

10.3 years	Shipment conditions and VVI mode, assuming 100% pacing 70 min^{-1}, 3.5 V, 0.35 ms, 500 Ω, Holter ON, sensors ON, Remote OFF
11.6 years	Cenelec conditions and VVI mode, assuming 100% pacing 70 min^{-1}, 2.5 V, 0.5 ms, 500 Ω, Holter ON, sensors ON, Remote OFF
13.6 years	ISO14708-2 conditions and VVI mode, assuming 100% pacing 60 min^{-1}, 2.5 V, 0.35 ms, 600 Ω, Holter ON, sensors ON, Remote OFF

An excessive number of remote follow-ups can have a non-negligible impact on device longevity.

20.5. RADIO EQUIPMENT EMISSION

Radio Equipment	Transmitter Frequency Bands Maximal Power	Receiver Frequency Bands
Inductive Telemetry	Slow mode: 8kHz, Fast mode: 16kHz Simulated Worst Case (16kHz) in continuous communication, -10.31 dBµA/m max at 10m	Slow mode: Frequency ~30kHz modulation pulsed, Fast mode: Frequency ~70 kHz modulation pulsed.
Bluetooth Low Energy™ ® RF telemetry (ISM Band)	Bluetooth Low Energy 4.2 2400-2483.5 MHz -17.9 dBm max	Bluetooth Low Energy 4.2 2400-2483.5 MHz

21. PROGRAMMABLE PARAMETERS

Measured at 37 °C under a 500 Ω load.

The programming of the following parameters can be performed through MicroPort programmer.

21.1. ANTIBRADYCARDIA PACING

Basic parameters	Models	Values	Nominal value	"As shipped" value
Chamber	**SR**	A-V	V	V
Pacing Mode [1][2]	**DR**	DDD-DDDR-DDD/DDIR-SafeR-SafeRR-SafeR/DDIR-Dplus-Dplus-R-Dplus/DDIR-DDI-DDIR-DOO-VVI-VVIR-VVT-VOO-AAI-AAIR-AAT-AOO-OOO	VVI	DDD
Pacing Mode [3][2]	**SR**	VVI-VVIR-VVT-VOO-AAI-AAIR-AAT-AOO-OOO	VVI	VVI
Basic rate (ppm) [4]	**DR**	30-35-40-45-50-55-60-65-70-75-80-85-90-95 (± 2 ppm)	70	60
Basic rate (ppm) [4]	**SR**	30-35-40-45-50-55-60-65-70-75-80-85-90-95 (± 2 ppm)	70	70
Rest rate (ppm)	**SR**	50-55-60-65-70-75-80-85-90-95 (± 2 ppm)	70	70
Rest rate (ppm)	**DR**	50-55-60-65-70-75-80-85-90-95 (± 2 ppm)	70	60
Maximum tracking rate (ppm)	**SR, DR**	100-110-120-130-140-155-165-175-185 (± 5 ppm)	130	130
Rate hysteresis (%)	**SR, DR**	0-5-10-20-35 (± 4 %)	0	0
Rest AV delay (ms)	**DR**	30-45-65-80-95-110-125-140-155-170-190-205-220-235-250 (± 10 ms)	155	155
Exercise AV delay (ms)	**DR**	30-45-65-80-95-110-125-140-155-170-190-205-220-235-250 (± 10 ms)	80	80
AVD Paced/Sensed Offset (ms)	**DR**	0-15-30-45-65-80-95-110-125 (± 5 ms)	65	65

(1) Twenty minutes after the automatic detection of implantation by the device, the as-shipped pacing mode (DDD) is automatically reprogrammed to SafeR.

(2) Do not program OOO mode in pacing-dependent patients.

(3) The nominal value depends on the chamber selected.

(4) The corresponding basic periods and escape intervals are as follows: 1961-1500-1333-1200-1091-1000-923-857-800-750-706-667-632 ms.

Pacing/Sensing	Models	Values	Nominal value	"As shipped" value
Atrial or ventricular pulse amplitude (V) (1)	**DR**	1-1.5-2-2.5-3-3.5-4-5-6 (± 20 %) 7.5 (± 30 %)	5.0	3.5
Pulse amplitude (V) (1)	**SR**	1-1.5-2-2.5-3-3.5-4-5-6 (± 20 %) 7.5 (± 30 %)	5.0	3.5
Atrial or ventricular pulse width (ms) (1)	**DR**	0.12-0.25-0.35-0.5-0.6-0.75-0.85 -1 (± 35 µs)	0.5	0.35
Pulse width (ms) (1)	**SR**	0.12-0.25-0.35-0.5-0.6-0.75-0.85 -1 (± 35 µs)	0.5	0.35
Atrial sensitivity (mV) (2)(3)(4)	**DR**	0.1* (± 0.025 mV ± 60 %) 0.2*-0.3*-0.4 (± 0.025 mV ± 40 %) 0.6-0.8-1-1.2-1.5-1.8-2-2.2-2.5-2.7-3-3.5-4-4.5-5-6 (± 20 %) *only available in bipolar mode	1.0	0.6
Ventricular sensitivity (mV) (2)(3)(4)	**DR**	0.4 (± 0.025 mV ± 40 %) 0.6-0.8-1-1.2-1.5-1.8-2-2.2-2.5-2.7-3-3.5-4-4.5-5-6-8-10-15 (± 20 %)	2.5	1.5
Sensitivity (mV) (2)(3)(4)	**SR**	0.4 (± 0.025 mV ± 40 %) 0.6-0.8-1-1.2-1.5-1.8-2-2.2-2.5-2.7-3-3.5-4-4.5-5-6-8-10-15 (± 20 %)	2.5	1.5
Atrial or ventricular sensing polarity (5)	**DR**	Unipolar-Bipolar	Unipolar	Bipolar
Sensing polarity (5)	**SR**	Unipolar-Bipolar	Unipolar	Bipolar
Atrial or ventricular pacing polarity (5)	**DR**	Unipolar-Bipolar	Unipolar	Bipolar
Pacing polarity (5)	**SR**	Unipolar-Bipolar	Unipolar	Bipolar
Atrial or ventricular lead polarity switch	**DR**	ON-OFF	OFF	OFF
Ventricular lead polarity switch	**SR**	ON-OFF	OFF	OFF

(1) If the programmed value is higher than the nominal value, the programmed value will be applied for the nominal settings.

(2) Values are measured using a positive and negative triangular signal of 2/13 ms.

(3) For sensitivity settings below 3 mV, the pacemaker may detect noise lower than the level specified in clause 27.5.1 of standard EN 45502-2-1 and clause 4.5.2.1 of standard ISO 14117:2019.

(4) For sensitivity settings below 1 mV, the pacemaker may detect noise lower than the level specified in clause 27.4 of standard EN 45502-2-1 and clause 4.4.1 of standard 14117:2019.

(5) As soon as the detection of implantation has been confirmed, the lead configuration is automatically programmed according to auto implantation pacing polarity.

Blanking	Models	Values	Nominal value	"As shipped" value
Post R Atrial Blanking (ms)	**DR**	95-110-125-140-155-170-185-200 (± 10 ms)	95	95
Post V Atrial Blanking (ms)	**DR**	150-170-185-200-215-230-245-260 (± 10 ms)	150	150

Special features	Models	Values	Nominal value	"As shipped" value
Rate smoothing	**SR, DR**	OFF-Very Slow-Slow-Medium-Fast	OFF	OFF
Acceleration (%)	**DR**	0-5-15-25-35-45	0	0
AVD shortening (ms)	**DR**	0-15-30-45-65-80-95-110	0	0
Mode Switch	**DR**	ON-OFF	ON	ON
Mode Switch rate (ppm)	**DR**	30-35-40-45-50-55-60-65-70-75-80-85-90-95	60	60
PMT protection	**DR**	Termin.-OFF	Termin.	Termin.
Atrial or ventricular Autosensing	**DR**	Auto-Monitor	Monitor	Monitor
Autosensing	**SR**	Auto-Monitor	Monitor	Monitor
Atrial or Ventricular Autothreshold	**DR**	Auto-Monitor-OFF	OFF	OFF
Ventricular Autothreshold	**SR**	Auto-Monitor-OFF	OFF	OFF
Ventricular amplitude safety margin	**SR, DR**	x1.5-x2-x2.5-x3	x2	x2
Minimum ventricular amplitude (V)	**SR, DR**	1.5-2-2.5-3-3.5 (± 20 %)	2.5	2.5
Ventricular safety amplitude (V)	**SR, DR**	2-2.5-3-3.5-4-4.5-5-6 (± 20 %)	3.5	3.5
Atrial amplitude safety margin	**DR**	x1.5-x2-x2.5-x3	x2	x2
Minimum atrial amplitude (V)	**DR**	1-1.5-2-2.5-3-3.5 (± 20 %)	1.5	1.5
Atrial safety amplitude (V)	**DR**	2-2.5-3-3.5-4-4.5-5 (± 20 %)	3.5	3.5
Atrial Autothreshold max rate (ppm)	**DR**	100-110-120 (± 2 ppm)	110	110
Atrial Autothreshold start time	**DR**	12am-01am-02am-12pm	02am	02am

Rate responsive parameters	Models	Values	Nominal value	"As shipped" value
Sensor choice	**SR, DR**	Twin Trace-MV-G	G	MV+G
Rate response mode (1)	**SR, DR**	Learn-RR auto-RR fixed-No	No	Learn
Physical activity	**SR, DR**	Very low-Low-Medium-High-Very high	Medium	Medium

(1) Twenty minutes after the automatic detection of implantation by the device, the as-shipped rate response mode (NO) is automatically reprogrammed to Learn.

SafeR parameters	Models	Values	Nominal value	"As shipped" value
Max Pause (s)	**DR**	2-3-4	3	3
Long PR at rest (ms)	**DR**	200-250-300-350-400-450-500	350	350
Long PR at exercise (ms)	**DR**	200-250-300-350-400-450-500	250	250
AVB I switch	**DR**	Rest+Exercise-Exercise	Rest+Exercise	Rest+Exercise

MRI Mode parameters	Models	Values	Nominal value	"As shipped" value
MRI Mode	**SR, DR**	Auto-Manual-OFF	OFF	OFF
MRI Pacing Mode	**DR**	DOO-VOO-AOO-OOO	DOO	DOO
MRI Pacing Mode (1)	**SR**	AOO/VOO-OOO	AOO/VOO	AOO/VOO
MRI Pacing Rate (ppm) (2)	**DR**	50-55-60-65-70-75-80-85-90-95-100-105-110-115-120 (± 2 ppm)	80	80
MRI Pacing Rate (ppm) (2)	**SR**	50-55-60-65-70-75-80-85-90-95-100-105-110-115-120 (± 2 ppm)	90	90
MRI Monitoring Period (h)	**SR, DR**	2h-4h-6h-12h-24h-48h-3 days-7 days-10 days	24h	24h

(1) The as-shipped and nominal values (AOO/VOO) depend on the chamber selected.

(2) Default pacing rate is 20 min^{-1} over programmed basic rate.

Automatic detection of implantation parameters	Models	Values	Nominal value	"As shipped" value
Auto implant detection	**SR, DR**	ON-OFF	OFF	ON
SafeR Auto launch	**DR**	ON-OFF	OFF	ON
Right Atrial Autothreshold	**DR**	Auto-Monitor-OFF	OFF	Monitor
Right Ventricular Autothreshold	**SR, DR**	Auto-Monitor-OFF	OFF	Monitor
Lead Polarity Switch	**SR, DR**	ON-OFF	OFF	OFF
Remote monitoring	**SR, DR**	ON-OFF	OFF	OFF

NOTE: The Automatic implant detection function is not available in a SR model when A chamber is selected.

21.2. REMOTE ALERTS AND WARNINGS

General parameters	Models	Values	Nominal value	"As shipped" value
RF communication (1)	**SR, DR**	ON-OFF	ON	OFF
Alerts	**SR, DR**	ON-OFF	ON	ON

(1) The nominal value depends on the state of the battery (residual capacity)

When Alerts are programmed "ON", the following System Alerts are automatically activated:

— “Battery depletion – RRT”

— “System integrity”

— Reset

Lead Alerts	Models	Values	Nominal value	"As shipped" value
Abnormal A lead impedance	**SR, DR**	ON-OFF	ON	ON
Abnormal A lead low limit (Ω)	**SR, DR**	200-250-300-350-400-450-500	300	300
Abnormal A lead high limit (Ω)	**SR, DR**	1500-1750-2000-2500-3000	2000	2000
Atrial autothreshold	**DR**	ON-OFF	ON	ON
Atrial high threshold limit (V)	**DR**	1-1.25-1.5-1.75-2-2.25-2.5-3-3.5-4	2.5	2.5
Atrial Lead Polarity Switch	**DR**	ON-OFF	ON	ON
Abnormal V lead impedance	**SR, DR**	ON-OFF	ON	ON
Abnormal V lead low limit (Ω)	**SR, DR**	200-250-300-350-400-450-500	300	300
Abnormal V lead high limit (Ω)	**SR, DR**	1500-1750-2000-2500-3000	2000	2000
Ventricular Autothreshold	**SR, DR**	ON-OFF	ON	ON
Ventricular high threshold limit (V)	**SR, DR**	1-1.25-1.5-1.75	1.75	1.75
Ventricular lead polarity switch	**SR, DR**	ON-OFF	ON	ON

Clinical alerts	Models	Values	Nominal value	"As shipped" value
AT/AF burden	**DR**	ON-OFF	OFF	OFF
Low AF burden daily limit (h)	**DR**	6 min-15 min-30 min-1h-3h-6h-12h-24h	6 min	6 min
Mid AF burden daily limit (h)	**DR**	OFF-6 min-15 min-30 min-1h-3h-6h-12h-24h	6h	6h
High AF burden daily limit (h)	**DR**	OFF-6 min-15 min-30 min-1h-3h-6h-12h-24h	24h	24h
Fast V Rate during AT/AF	**DR**	ON-OFF	OFF	OFF
Fast V Rate limit (ppm)	**DR**	80-90-100-110-120	100	100
Fast V Duration limit (h)	**DR**	0.5-1-3-6-12-24	1	1

Other alerts	Models	Values	Nominal value	"As shipped" value
MRI notifications	**SR, DR**	ON-OFF	OFF	OFF
Asynchronous mode	**SR, DR**	ON-OFF	ON	ON

22. NON-PROGRAMMABLE PARAMETERS

Parameters	Values
MV configuration	A Bipolar - V Bipolar - Double Monopolar
Committed period (ms) **for the DR model (only)**	95 (± 5 ms)
Rate limit (ppm)	195 (± 5 ppm)
Refractory periods	Automatic (see table below)

The minimum refractory period values are as follows:

For the DR model, the minimum refractory period values are as follows (except in AAI, AAT, DDTA and DDTAV modes):

Event	Minimum atrial refractory periods (ms)	Minimum ventricular refractory periods (ms)
Atrium sensed	80 ± 10 ms	–
Atrium paced	AV delay	30 ± 2 ms
Ventricle sensed	Programmable	95 ± 10 ms
Ventricle paced	Programmable	150 ± 10 ms

For the DR model, the minimum refractory period values are in AAI, AAT, DDTA and DDTAV modes as follows:

Mode	Event	Minimum atrial refractory periods (ms)
AAI, AAT	Atrium sensed or paced	345 ms ± 10 ms
DDTA, DDTAV	Atrium sensed	205 ms ± 10 ms
DDTA, DDTAV	Atrium paced	AV delay

For the SR model, the minimum refractory period values are as follows:

Mode	Type of event	Minimum refractory periods (ms)
VVI, VVT	Ventricle sensed	95 ms (V chamber)
VVI, VVT	Ventricle paced	150 ms (V chamber)
AAI, AAT	Atrium sensed or paced	345 ms ± 10 ms (A chamber)

23. WARRANTY

Warranty duration: 5 Years

The ALIZEA implantable cardiac pacemaker is the result of highly advanced research and all components have been selected after exhaustive testing.

MicroPort CRM S.r.l. (identified as “MicroPort” hereafter) guarantees the product ALIZEA against any damage caused by component failure or production defects during a period of five years after the implantation date, and warranty commits itself to replace all ALIZEA devices according to the terms described in articles 1 and 2.

MicroPort makes no claim that the human body will not react unsuitably to the implantation of a ALIZEA device, or that failure will never occur.

MicroPort does not guarantee the suitability of ALIZEA device in defined types of patients: selection of the device is a medical decision.

MicroPort shall not be held liable for any damage indirectly associated with the ALIZEA device, whether as part of normal or abnormal operation of the latter, nor damage from its explantation or replacement.

MicroPort does not authorize anyone to modify these warranty conditions.

23.1. ARTICLE 1: TERMS OF WARRANTY

1. The ALIZEA implantable cardiac pacemaker is only guaranteed for the first implantation.
2. The EURID/IAPM implant form must be sent to MicroPort within 30 days after implantation.
3. The ALIZEA cardiac pacemaker must be implanted by the end of the "use on or before" date indicated on the packaging.
4. The guarantee only applies to suspect devices returned to the manufacturer, carefully packed and accompanied by an explantation report duly completed by the hospital or the doctor and considered defective after analysis by MicroPort.
   - The device must be returned within the 30 days following explantation to MicroPort.
   - Any device returned and replaced under the terms of this warranty will become the exclusive property of MicroPort.
   - Any rights under the terms of this warranty will be forfeited if the ALIZEA device has been opened by anyone other than MicroPort.
   - These rights will also be forfeited if the device has been damaged by carelessness or accident.
   - This is the case especially if the device has been exposed to temperatures above 50°C, to electrical abuse or to mechanical shock, particularly as a result of being dropped. Consequently, any expert opinion offered by a third party after the device has been removed also nullifies the guarantee.
5. The warranty will be forfeited if it is proven that the device has been misused or inadequately implanted, against the physicians’ manual recommendations of ALIZEA device.
6. The warranty does not include leads and other accessories used for the implantation.
7. The replacement terms or conditions described in article 2 shall not apply to all devices that shall be replaced within the warranty period because of battery depletion, and which

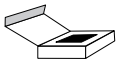
do not have any link to a component failure or a production hazard. The device battery longevity varies with the device settings and pacing operation over time.

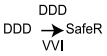
23.2. ARTICLE 2: TERMS OF REPLACEMENT

1. In case of ALIZEA device failure because of a component failure, a production defect, or a conception error, occurring within five-year period starting from the implantation date, MicroPort is committed to:
   - replacing free of charge the explanted device by a MicroPort device with equivalent features,
   - or issuing a replacement credit equal to the purchase price for the purchase of any other MicroPort replacement device.
2. In any case, the credit issued by the warranty terms cannot exceed the purchase price of a MicroPort replacement device.

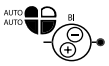
24. EXPLANATION OF SYMBOLS

The symbols on package labeling have the following meaning (where applicable):

General symbols	Explanation of symbols
	Use by
	Date of manufacture
	Manufacturer
	Catalogue number
	Serial number
	Implantable device Uncoated
	Medical Device
	Unique device identifier
	Double entry package with external single sterile barrier system
	Packaging contents
	Sterile package contents
	Open here
	Do not use if the package is damaged
	Do not reuse

General symbols	Explanation of symbols
	Do not resterilize
	Sterilized using ethylene oxide
	Sterilized using hydrogen peroxide
	Non sterile
	Temperature limitation
	Screwdriver
	Mode
	Maximum tracking rate and minimum rate
	Minimum rate
	Consult instructions for use
	Instructions for use on the website
	This icon is used to call your attention to a particularly important point.
	This icon alerts you to a hazard that may result in equipment damage or personal injury. Carefully read the instructions provided with this icon.

Pacemaker symbols	Explanation of symbols
	Cardiac resynchronization therapy pacemaker (RA, RV, LV)
	Pacemaker (dual chamber, RA, RV)
	Pacemaker (single chamber, RV)
	IS1 Connectors (CRT-P)
	IS1 connectors (dual chamber)
	IS1 connector (single chamber)
	Accelerometer
	Minute ventilation
	Sleep Apnea Monitoring (SAM)
	MR Conditional
	Full Body

Pacemaker symbols	Explanation of symbols
	A-V interval (paced/sensed)
	Amplitude and pulse width, RA, RV, LV
	Amplitude and pulse width, RA, RV
	Amplitude and pulse width, RV
	Amplitude and pulse width, RA
	Refractory periods, RA, RV
	Refractory periods, RV
	Pacing polarity, CRTP
	Pacing polarity, RA, RV
	Pacing polarity, RV
	Sensing polarity, RA, RV
	Sensing polarity, RV
	Sensitivity, RA
	Sensitivity, RV

The ALIZEA models are covered by the following US patents:

US 5 167 224, US 5 226 415, US 5 249 572, US 5 271 394, US 5 303 702, US 5 312 451, US 5 318 594, US 5 411 533, US 5 522 860, US 5 622 428, US 5 645 574, US 5 645 576, US 5 674 265, US 5 702 424, US 5 702 426, US 5 713 928, US 5 722 996, US 5 741 315, US 5 891 184, US 5 899 931, US 5 931 856, US 5 954 660, US 6 052 616, US 6 230 058, US 6 307 261, US 6 336 048, US 6 337 996, US 6 397 105, US 6 408 209, US 6 487 451, US 6 487 452, US 6 505 068, US 6 532 238, US 6 574 507, US 6 711 441, US 6 773 404, US 6 778 859, US 6 830 548, US 6 890 306, US 6 898 845, US 6 912 421, US 6 975 905, US 7 020 515, US 7 072 716, US 7 164 946, US 7 076 297, US 7 142 924, US 7 395 115, US 7 440 795, US 7 440 801, US 7 630 770, US 7 797 045, US 8 043 225, US 7 856 705, US 8 583 255, US 8 554 318.

MANUFACTURED IN ITALY

MicroPort CRM S.r.l.
Via Crescentino S.N.
13040 Saluggia (VC)
Italy
Tel: +39 0161 487095
US Phone: 877.663.7674

www.crm.microport.com

FOR US ONLY - CAUTION: FEDERAL LAW RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN

2020-06
UA10414A

MicroPort™ CRM