EXCOR® Pediatric VAD

Ventricular Assist Device with Stationary Driving Unit Ikus Rev. 2.1

Instructions for Use 1000721x10 Revision 9

For products in USA:

Humanitarian Device. Authorized by Federal law for use in the treatment of pediatric patients with severe isolated left ventricular or biventricular dysfunction who are candidates for cardiac transplant and require circulatory support. The effectiveness of this device for this use has not been demonstrated.

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HOTLINE

Call Service Hotline! 866.249.0128

This IFU corresponds to the following product versions:

- Ikus software from V 3.41 forward
- Laptop software from V 3.50 forward
- Laptop from CF30 forward

Imprint
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2 Introduction

This IFU is intended for medical personnel involved in caring for any patient who is being supported by EXCOR® Pediatric VAD in conjunction with the Stationary Driving Unit Ikus (together referred to herein as EXCOR) .

It provides information on the structure, operation and application of EXCOR® . To ensure patient safety and comfort, please read these instructions carefully.

A Physicians Manual and the EXCOR Pediatric training are available as additional resource for medical personnel caring for patients who are being supported by EXCOR®

Medical personnel who have not been specifically trained in the use of EXCOR should not treat patients who are supported by EXCOR.

The information contained in this manual concerns the safe operation of EXCOR only. All decision related to patient care, including but not limited to implantation and component selection remain in the sole province of the treating physician.

Explanation of safety information and signal words

DANGER	Indicates a hazardous situation which, if not avoided, **will** result in death or serious injury.
WARNING	Indicates a hazardous situation which, if not avoided, **could** result in death or serious injury.
CAUTION	Indicates a hazardous situation which, if not avoided, could result in minor or moderate injury and/ or damage to the device.
NOTICE	Notes are practices not related to personal injury. Possible damage to the device.
ADVICE	This symbol identifies measures and procedures which have proved useful and successful in conjunction with EXCOR and which we therefore recommend.
HOTLINE	**Call Service Hotline! 866.249.0128**

Term definitions

Term	Definition
EXCOR®	EXCOR® Pediatric VAD in conjunction with the Stationary Driving Unit Ikus
EXCOR® Pediatric VAD	Paracorporeal VAD System for pediatric patients, consisting of the sterile components: blood pumps, cannulae, cannula extension sets / connecting sets, driving tubes, de-airing set, de-airing hammer, tube connecting set, and membrane set.
Ikus / Stationary Driving Unit Ikus	Pneumatic pump supply system for pulsatile blood flow, referred to herein as Ikus
Service Hotline / Customer Service / Service	Urgent clinical and technical assistance is available via the Berlin Heart Service Hotline. You can reach us 24 hours/day. This number is intended for use by medical personnel and should be used in cases of emergency only. HOTLINE **Call Service Hotline! 866.249.0128**
Product Life	Product life indicates the full duration of time during which the product can be used and after which maintenance and repairs should not be performed. For unsterile components, the product life begins on the day of (initial) shipment; for sterile components, the product life begins on the date of implantation. Sterile components are intended for single use only.
Expiration Date	Indicates the date by which the sterility is ensured for sterile components, and after which sterile components should not be used.
Maintenance Interval	The regular interval at which the product should be serviced.
Replacement Equipment	Appropriate components in case of an exchange e. g. blood pump, driving tube

Tab. 2-1 Term definitions

INSTRUCTION

1. Individual steps of the instructions are numbered in sequential order.

Definition of Fonts Used

Description	Meaning
bold, blue	Software texts (messages and menus) except in headings and lists
"text"	Quotation
<key>	Key on the laptop keyboard
<<filler text>>	E.g. if texts in error messages are various
[dimension unit]	Dimension units in tables; e.g. [mmHg]

Tab. 2-2 Fonts used

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3 General Information

3.1 Device Description

EXCOR is an extracorporeal, pneumatically driven Ventricular Assist Device (VAD). It is designed to support the right and/or left ventricles when the native heart is unable to maintain normal blood flows and pressures even with help of drug therapy and intra-aortic balloon counterpulsation. The device is designed for mid to long term mechanical support.

EXCOR consists of one or two extracorporeal, pneumatically driven blood pumps and cannulae which connect the blood pump(s) to the atrium or ventricle and to the great arteries. The Ikus provides alternating air pressure to the blood pumps through driving tubes.

The blood pump is divided into an air chamber and a blood chamber by a multi-layer flexible polyurethane membrane. The alternating air pressure provided by the *Ikus* moves the membrane, thus filling and emptying the blood pump. Both the blood chamber and the polyurethane connectors are transparent to allow for visual detection of deposits and for monitoring the filling and emptying of the blood pump.

Valves (three-leaflet polyurethane valves) are located at the inlet and outlet positions of the blood pump connector stubs, thus ensuring appropriate unidirectional blood flow.

Pulse rate, systolic drive pressure, diastolic suction pressure and the relative systolic duration can all be monitored and adjusted on the Ikus.

3.2 Indications for Use

EXCOR is intended to provide mechanical circulatory support as a bridge to cardiac transplantation for pediatric patients. Pediatric patients with severe isolated left ventricular or biventricular dysfunction who are candidates for cardiac transplant and require circulatory support may be treated using EXCOR.

3.3 Intended Operation Environment

Ikus is intended for use in a clinical setting. It can be used in any kind of hospital unit, e.g. OR, ICU, intermediate care unit or general care unit. It may be moved between clinical units using the built-in wheels, however a patient must always be accompanied by a person trained in the use of the manual pump and emergency procedures during transport in the event of an emergency.

The Ikus should not be transported by vehicle during operation.

During movement of the device in operation within the clinic all electromagnetic compatibility precautions (EMC precautions) must be observed. See chapter 19: EMC Tables, page 241.

3.4 Contraindications

Patients unable to tolerate systemic anticoagulation therapy should not be implanted with EXCOR components.

Magnetic Resonance Imaging (MRI) is contraindicated in patients after being implanted with EXCOR.

Patients with aortic valve regurgitation that is more than moderate that cannot be repaired at the time of implantation should not be implanted with EXCOR. If repair of the aortic valve regurgitation requires surgical closure of the aortic valve, EXCOR should not be implanted. EXCOR is not intended to be used as a total artificial heart and should not be used in this configuration.

3.5 Potential Adverse Events

Potential Adverse Events may include but are not limited to the following:

- Major Bleeding
- Cardiac Arrhythmia
- Pericardia Fluid Collection
- Hemolysis
- Hepatic Dysfunction
- Hypertension
- Infection
- Psychiatric Episode
- Neurological Dysfunction
- Renal Dysfunction
- Respiratory Failure
- Right Heart Failure
- Arterial Non-CNS thromboembolism
- Venous Thromboembolism Event
- Wound Dehiscence
- Device Malfunction

It is possible that these potential adverse events could result in disability or serious injury or death

3.6 Storage and Durability

WARNING

The sterile components of EXCOR should not be used after their expiration date and should never be re-sterilized. The expiration date can be found on the product labels on both the outer and inner packaging.

To ensure sterility, the long-term storage conditions for all sterile products should be observed as follows: temperature +15°C to +25°C, relative humidity: 35 % to 50 %. Store in a dry place!

EXCOR blood pumps and the driving tubes should be replaced with a new blood pump respectively new driving tube after one year of use.

IMPORTANT: If the Ikus is not in use, run it once a month for 24 hours in order to ensure that all batteries are adequately charged. Refer to section 7.5.1: Routine Start-Test when not in Operation, page 60.

3.7 Manufacturer's Warranty

According to the General Terms and Conditions of Berlin Heart GmbH the warranty is valid for 1 year.

All warranties apply only under the prescribed conditions of storage of the system, use in accordance with the instructions (intended use) and when the packaging is intact, including but not limited to the sterile packaging and to the aluminum-coated outer packaging of the blood pump(s).

The warranty is null and void, if the Ikus has been opened and/ or serviced by persons who are not members of the Berlin Heart GmbH/ Berlin Heart, Inc. or distributor´s service staff and/ or who have not been authorized by the Berlin Heart GmbH service department to do so.

Components	**Product life** (in sterile products starting from implantation)	**Maintenance interval**	**Expiration date** (from date of manufacture)	**Warranty**
Unsterile				
Ikus	Max. 8 years	6 months or 2000 operating hours (whichever occurs earlier)	x	1 year
Battery	Exchange as needed	6 months or 2000 operating hours (whichever occurs earlier)	x	6 months
Manual pump	Max. 6 years	Yearly	x	1 year
Sterile				
Driving tube	1 year (single-use product)	x	3 years	1 year
Blood pumps	1 year (single-use product)	x	4 years	1 year

Tab. 3-1 Product life, maintenance interval, expiration date, warranty

Components	Product life (in sterile products starting from implantation)	Maintenance interval	Expiration date (from date of manufacture)	Warranty
Cannulae	single-use product	x	3 years	1 year
Accessories: • Tank unit • T00L-002 see section 4.4: EXCOR Accessories, page 24	Single-use product	x	3 years	First use

Tab. 3-1 Product life, maintenance interval, expiration date, warranty

Please dispose components according to local regulations and site policies.

3.8 Battery Replacement and Disposal

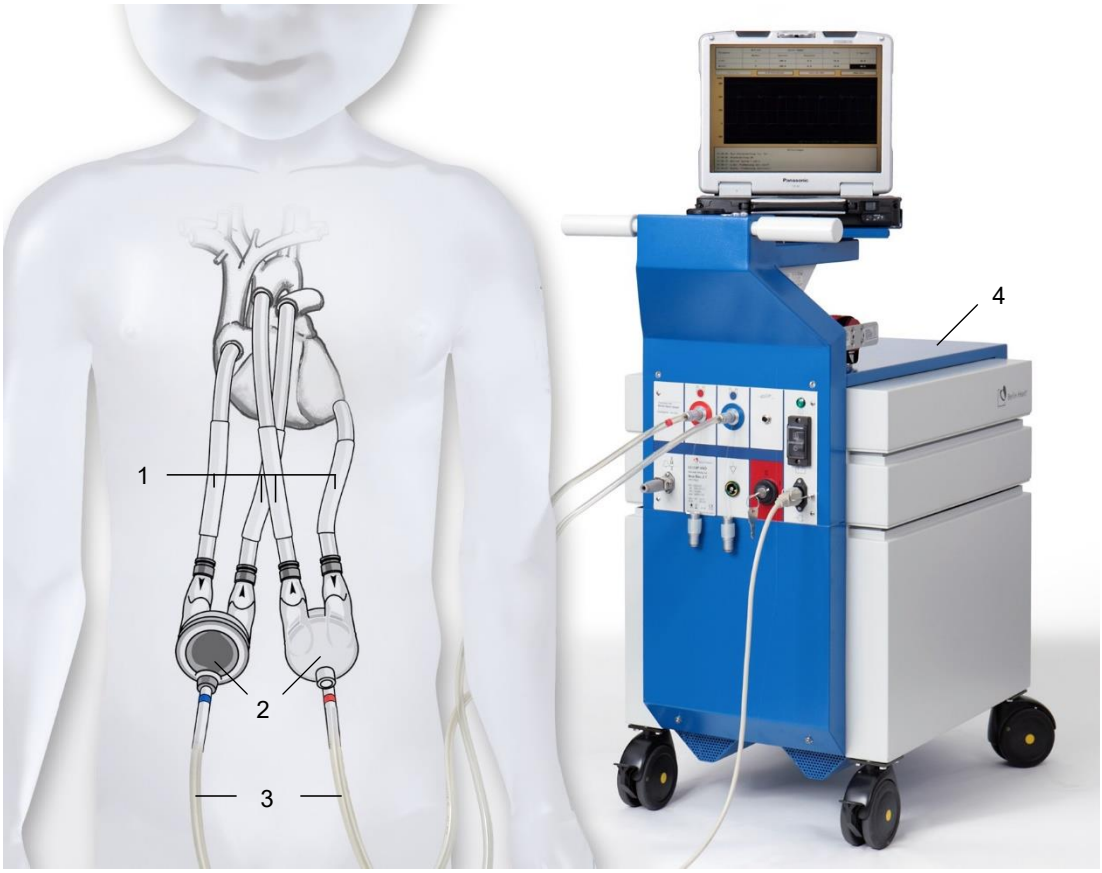
CAUTION

Only service staff of the distributor/ manufacturer or persons authorized by them may replace the batteries and dispose of them in accordance with the respective regulations.

4 Description: Blood Pump, Cannulae and Accessories

EXCOR is an extracorporeal electro pneumatically driven Ventricular Assist Device. It can be used for either univentricular or biventricular support. EXCOR is comprised of the following permanently active components:

- extracorporeal blood pump(s)
- inflow and outflow cannula(e)
- 1 driving tube for each blood pump
- Ikus



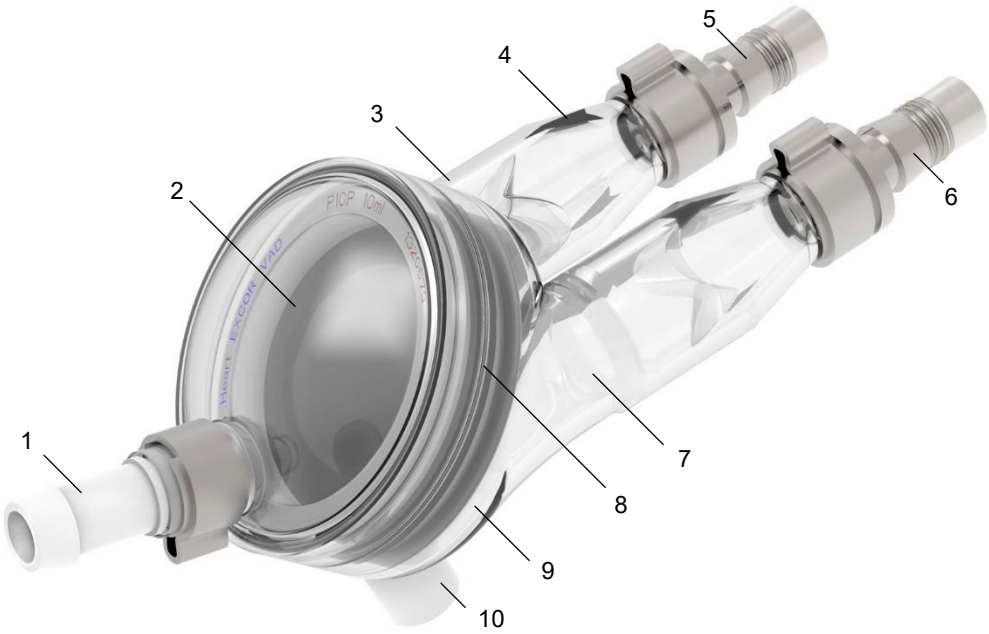
1 cannulae
2 blood pumps
3 driving tubes
4 Ikus

Fig. 4-1 EXCOR shown in situ as a biventricular assist device in pediatric application

Overview

Blood flows from the atrium or the ventricle through the inflow cannula into the blood chamber of the blood pump and then from this blood chamber through the outflow cannula into the aorta or into the pulmonary artery. A driving tube is used to connect the air chamber of the blood pump to the electro pneumatic Stationary Driving Unit Ikus. Ikus generates the suction and driving pressures required to move the triplelayer membrane separating the blood chamber from the air chamber.

4.1 EXCOR Blood Pumps



1 driving tube connector
2 air chamber
3 inflow stub
4 arrow mark: indicates blood flow direction
5 titanium connector: inflow stub – inflow cannula
6 titanium connector: outflow stub – outflow cannula
7 outflow stub
8 triple-layer membrane
9 blood chamber
10 de-airing nipple

Fig. 4-2 10 ml blood pump

EXCOR blood pumps have a transparent polyurethane (PU) housing which is divided into an air chamber and a blood chamber by a triple-layer membrane.

The blood chamber has an inflow and an outflow stub to which the inflow and outflow cannulae are connected respectively. The pump stubs themselves are made of polyurethane, the end of each stub is fitted with a titanium connector to which the cannula is connected. The valves located in the pump stubs keep blood flowing in one direction. EXCOR blood pumps are available with three-leaflet valves made of polyurethane (10 - 60 ml stroke volume).

All surfaces of the blood pump coming into contact with the blood are coated with a Carmeda® BioActive Surface (CBAS) coating. The transparent casing of the blood pump allows easy visual monitoring of the filling and emptying of the blood chamber.

The blood pump is equipped with a de-airing nipple which is used for de-airing the blood chamber when the blood pump is being commissioned.

The air chamber of the blood pump is equipped with a driving tube connector. This connector is used to connect the blood pump to the driving tube through which air is pumped from the Ikus. Ikus generates the suction and driving pressures required to move the blood pump's triple-layer membrane. A graphite powder layer is located between the membrane layers to minimize friction.

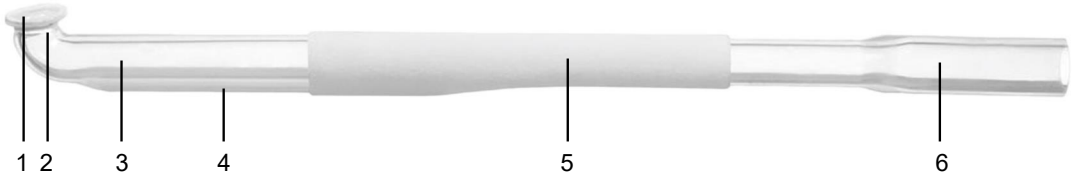
4.2 EXCOR Cannulae

Three different types of cannulae are available for EXCOR in various sizes:

- atrial cannulae (as inflow cannulae)
- apex cannulae (as inflow cannulae)
- arterial cannulae (as outflow cannulae)

The cannulae are made of tissue-friendly silicone. Polyester-velour suture rings enable convenient and safe anastomosis of the cannulae. The mid section of all cannulae are covered with polyester-velour to promote good ingrowth of the cannulae where they pass through the skin.

Some arterial cannulae have a flexible metal reinforcement which allows the cannulae to be adapted to an individual patient's anatomy.



1 Suture ring
2 Cannula head
3 Cannula body
4 Flexible metal reinforcement
5 Velour
6 Stage

Fig. 4-3 Cannula

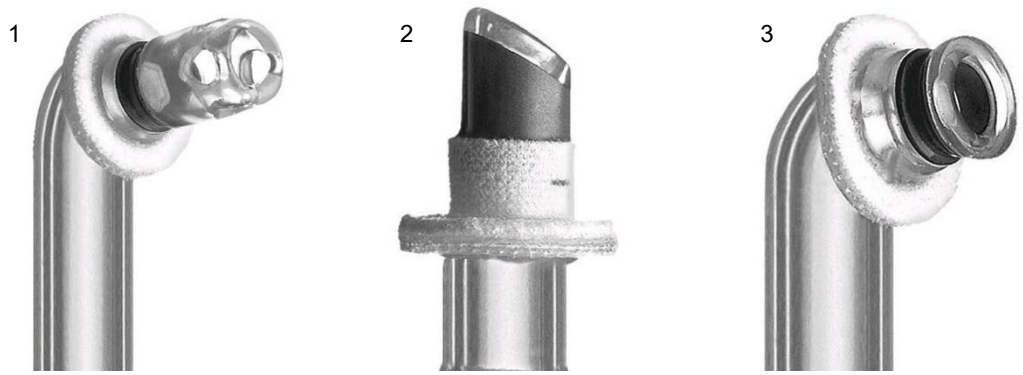


Fig. 4-4 Cannula heads: 1) atrial cannula, 2) apex cannula, 3) arterial cannula

4.3 Cannula Extension Set and Connecting Set

4.3.1 Cannula Extension Set

Application

For extending a shortened cannula. May be necessary when:

- replacing a blood pump
- the cannula has been shortened

The cannula extension set guarantees that the cannulae and titanium connectors on the blood pump can be visually inspected.

Assembly

1 Double-sided titanium connector
2 Tube section

Fig. 4-5 Cannula extension (2 per cannula extension set)

4.3.2 Connecting Set

Application

The connecting set is used to join blood pumps and cannulae of different sizes. This allows for greater flexibility when combining blood pumps and cannulae. The connecting set may be used during implantation or during the further course of therapy.

Assembly

1 Double-sided titanium connector
2 Tube section

Fig. 4-6 Connector (2 x per connecting set)

Depends on the cannula extension set, yet with two different diameters on the titanium connector (tube section: for the larger diameter).

4.4 EXCOR Accessories

The following EXCOR accessories are required in order to use EXCOR:

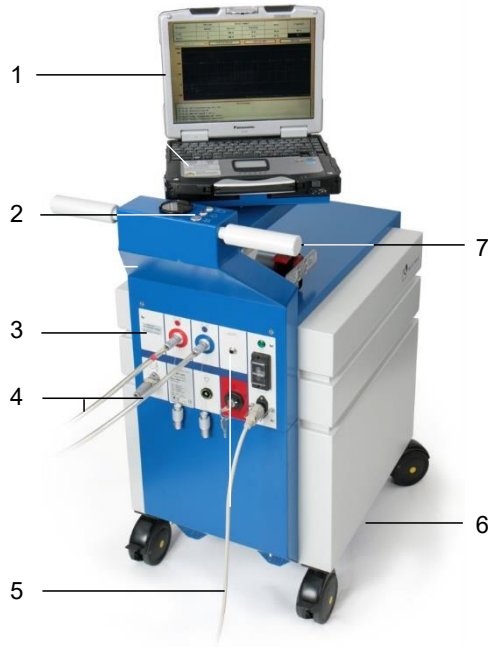
- 1 driving tube (PVC) for each blood pump
- 2 tank units
- 1 accessory set (T00L-002) which includes:
  - membrane set
  - de-airing set (2 x trocar, 2 x de-airing tube)
  - de-airing hammer
  - tube connecting set (cable ties, cable-tie gun)

There is enough material in one accessory set (T00L-002) to accommodate two EXCOR blood pumps.

5 Description: Ikus

5.1 Overview

The electro pneumatic Ikus generates the suction and driving pressures required to drive the blood pump(s). The driving unit contains the pneumatic and electronic components as well as a laptop computer that serves as an interface to the operator.



1 laptop computer with monitor program
2 display and operating panel
3 connection panel
4 driving tubes
5 mains cable
6 lifting bar
7 handle

Fig. 5-1 Ikus

Pneumatic systems

The Ikus has three pneumatic systems that operate independently of each other. One pneumatic system is required for each blood pump, while the third serves as an emergency backup. Each pneumatic system includes:

- a compressor;
- pressure and suction limiters;
- pressure and vacuum cylinders;
- control electronic; and
- control valves

The compressor and pressure and suction limiters deliver constant pressure conditions in the pressure and vacuum cylinders. The control valves at the outlet of each cylinder allow optimal adjustment of the positive and negative (suction) pressure values.

Control computer

The Ikus system has two control computers operate independentlyof each other: the active (main) control computer and the backup control computer.

Laptop with monitor program

Messages and pressure graphs in the monitor program inform the user of the current status and working condition of the system. In addition, the laptop computer is used for setting the system into operation and adjusting driving parameters. LOG files

containing information on the system's operating status are recorded on the laptop's hard drive.

Manual pump

If there is no working Ikus available, the manual pump mounted on the Ikus can be used temporarily to drive the blood pump(s).

USB stick to store LOG files

A USB stick is provided to be used for reading out and storing LOG files.

Do not use the USB stick for purposes other than reading out and storing the LOG files on the Ikus.

If the USB stick is no longer available, contact Berlin Heart, Inc. immediately and request a replacement stick.

5.2 Displays and Operating Elements

5.2.1 Connection Panel

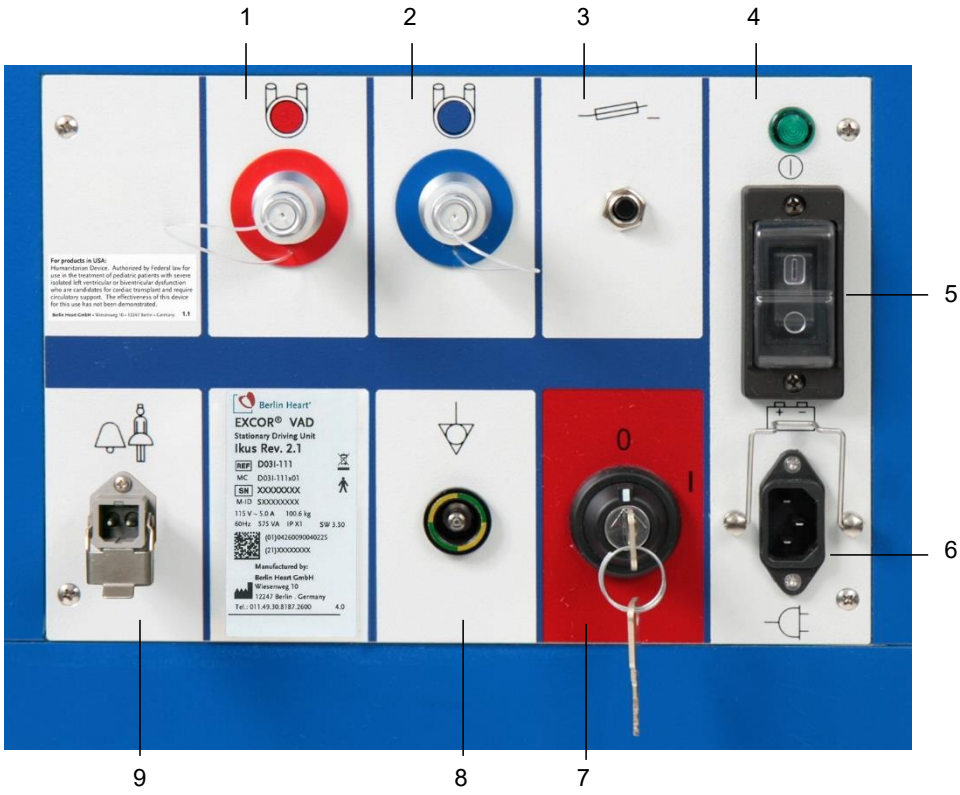
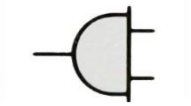


Fig. 5-2 Connection panel

	**1 Driving tube connector, left blood pump, red** The plug for the driving tube with the red marking is to be used with this connector.
	**2 Driving tube connector, right blood pump, blue** The plug for the driving tube with the blue marking is to be used with this connector.
	**3 Button *Circuit breaker*** The Ikus is protected against overcurrent. The circuit breaker is resettable (see section 16.8: Circuit Breaker and Battery Fuse, page 176).
	**4 Main operation indicator** Illuminated when using main power supply (default situation).
	5 Power switch (toggle switch)
	In [I] position, the drive is operated through the main power supply. The Ikus batteries are continuosly charged at the same time. In this switch position the Ikus changes between the main power supply and battery operation e. g. in case of a temporally interruption of the main power supply.
	In [0] position, the main power supply is interrupted. Ikus works in battery operation.
	**6 Main power connector (with plug clip)** The Ikus is connected to the main power supply with the aid of the main power cable. The plug clip prevents an accidental loosening of the connection.
	7 Main switch (key switch; 0/ I)
	Drive switched on

Tab. 5-1 User controls and according symbols on the connection panel

	Drive switched off
	**8 Connector *Potential equalization*** When several electric devices are positioned in the vicinity of the patient, they must be connected to a central grounding point. Use the connector labeled *Potential equalization* on the Ikus.
	**9 Connector *External alarm* (Nurse call)** This connector operates as a link to the clinic's internal alarm system. Technical Background: A relay connects the internal alarm circuit with the connector *External alarm*. In the default configuration, the relay opens a pair of contacts whenever an alarm occurs, to set off an external alarm (via a 2-pin plug with a protective ground). Depending on the specifications of a specific hospital, the configuration of the connector *External alarm* can be modified so that the contact closes in case of an alarm. This setting modification is to be made by the Berlin Heart, Inc. service department. Technical specifications: see section 18.2: Technical Specifications, page 226.

Tab. 5-1 User controls and according symbols on the connection panel

Connection of the blood pumps in univentricular / biventricular operation

1 red connector
2 red driving tube
3 seal plug

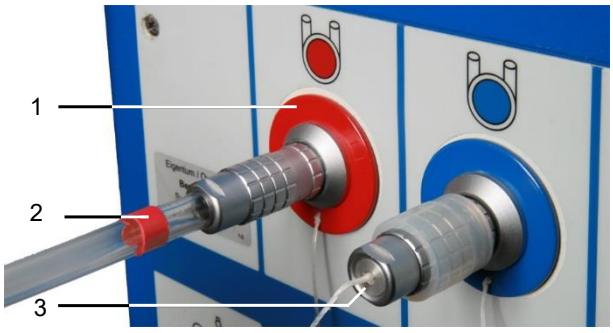


Fig. 5-3 Connection in univentricular mode

WARNING

To avoid risk of lung edema be sure the coloured markings on the driving tubes match the connectors of the Ikus (red to red and blue to blue).

1 red connector
2 red driving tube
3 blue connector
4 blue driving tube

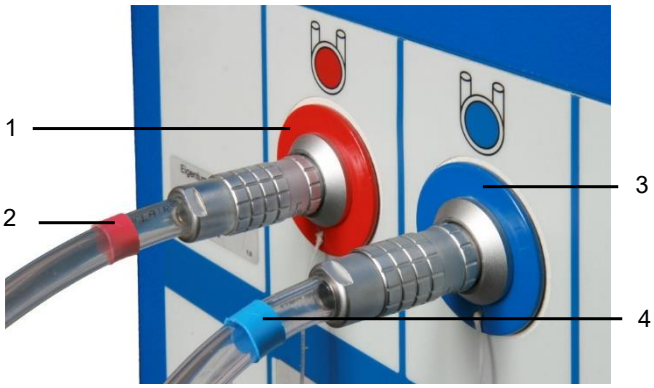


Fig. 5-4 Connection in biventricular mode

Main switch (key switch 0/ I) and power switch (toggle switch)

WARNING

After turning on the Ikus, pull the key out of the main switch (key switch) and store it in a safe place.

The Ikus power switch (toggle switch) must be turned on during the first use and remain set to [I] position, in order to ensure that the batteries remain fully charged.

While the Ikus is being operated, keep it connected to the stationary protective ground via the connector labeled „Potential equalization“.

The main switch (key switch) is used to turn the driving unit on and off. The main switch (key switch) can be operated only with the key.

However, a connection to the main power supply is not established until the power switch (toggle switch) is set to *[I]* position as well.

5.2.2 Display and Operating Panel

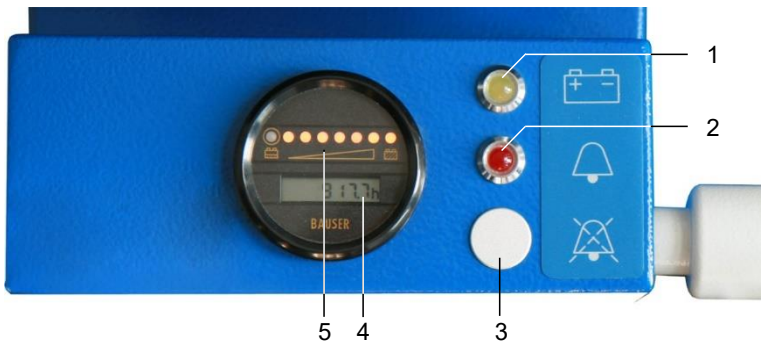
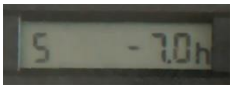


Fig. 5-5 Display and operating panel

1 **Battery operation** The yellow LED indicator lights up when the Ikus is running in battery operation
2 **Alarm** The red LED indicator lights up or flashes (design dependent) when there is an alarm message that has not been acknowledged by the monitor program
3 **Mute alarm (Audio paused**) temporarily mutes an alarm message. The message remains displayed on the laptop.
4 **Operating hour counter**
5 **Battery charge indicator**

The number of all operating hours is displayed. A maintenance sticker (on the right side under the laptop holder) notifies the user when maintenance is due.

When the Ikus has been in operation for 2000 operating hours (maintenance interval) after the last maintenance interval the display starts blinking and shows S -0.0 h.



The number of hours (i.e. S -7.0 h) exceeding the maintenance interval will be displayed.

Fig. 5-6 Operation hour counter

1 battery charge indicator

100 % to 50 %

less than 50 %

less than 10 min

less than 5 min

blinking - less than 2 min

batteries completely discharged

Fig. 5-7 Battery charge indicator

The LEDs of the battery charge indicator correspond to the maximum possible battery running time. The maximum permitted off-mains (battery) operating time is thirty minutes.

There are acoustic signals every ten minutes to remind you of battery operation. After thirty minutes of battery operation, a warning message **Batteries discharged - use power supply!** is displayed. Switch the Ikus over to mains operation. There will be acoustic signals two times per minute when you have to connect the Ikus to main power supply immediately (see table 7-4 on page 58). Failure to do so may result in failure of the device and damage to the battery system.

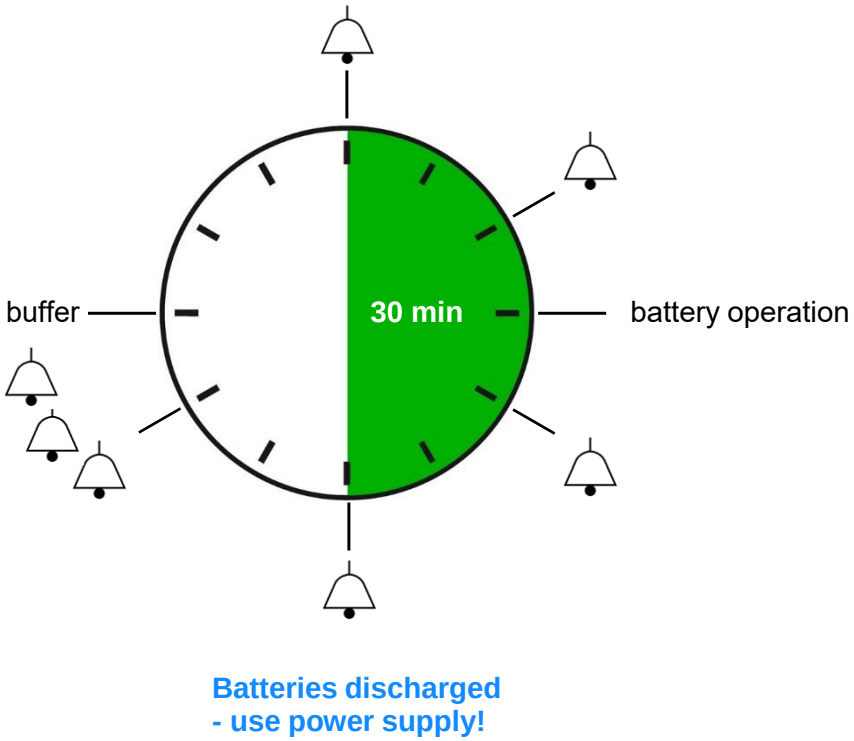


Fig. 5-8 Battery operation

Fresh, charged batteries have a buffer of about thirty minutes. This is valid for BVAD mode. The buffer may be larger in LVAD mode.

The buffer is getting smaller when:

- the batteries are not fresh e. g. to the end of the maintenance intervall,
- you often switch to battery operation without charging the batteries for six hours afterwards.
- the Ikus is used by a temperature higher than 30 °C / 86 °F.

5.2.3 Power Supply

WARNING

The Ikus is designed for stationary operation and to be run on main power supply. Do not run the Ikus on battery power unless it is for the temporary transport of the patient or in the event of an emergency.

To prevent rapid and premature aging of the batteries, the Ikus should be connected to a main power supply for at least six hours after battery operation.

Failure to follow these instructions will severely reduce the capacity of the batteries and will greatly shorten the maximum battery operating time! Always monitor the charging level display (see Fig. 5-5, page 29).

Mains operation with integral battery charging function (main power operation)

During normal operation the Ikus should be powered by a main power supply. During this time the batteries will be automatically charged. When the batteries are in the

process of being charged, the LED charge indicator change its status only when the batteries have been fully charged.

Battery operation

The Ikus has a rechargeable battery module (with 2 rechargeable batteries of 12V each) which can supply the system with power independently of the main power supply.

5.3 Operating Modes

5.3.1 Univentricular Operation

In univentricular operation, the driving tube of the blood pump should always be connected to the red marked connector.

5.3.2 Biventricular Operation

Synchronous mode

The systole cycles of the left and right blood pumps start simultaneously. Both blood pumps run at the same rate, and the rate can be adjusted only via the left blood pump. The systolic pressure, diastolic pressure and the relative systolic duration can be set individually for each blood pump.

Asynchronous mode

The systole cycle of the right blood pump is started when the left blood pump switches to the diastole cycle. Both blood pumps run at the same rate, and as (above) the rate can be adjusted only via the left blood pump. The systolic pressure, diastolic pressure and the relative systolic duration can be set individually for each blood pump.

Separate mode

The left and right blood pump operate independent of one another. All parameters can be adjusted as desired. IMPORTANT: The rate of the right blood pump may not exceed that of the left blood pump.

5.4 Laptop Computer with Monitor Program

NOTICE

If the laptop is switched off while the Ikus is in operation, the Ikus will continue to operate using the last set parameters.

The laptop computer is integrated into the Ikus equipment. The laptop contains software that can be used to start, set up and monitor the system.

The monitor program, when running, provides the user with a continuous stream of data on the system’s condition, as well as information on events and function faults. Simultaneously, relevant data is stored on the computer´s hard drive for subsequent evaluation. A detailed description of the monitor program is given in chapter 7: Instructions for Use: Ikus, page 45.

Fig. 5-9 Laptop

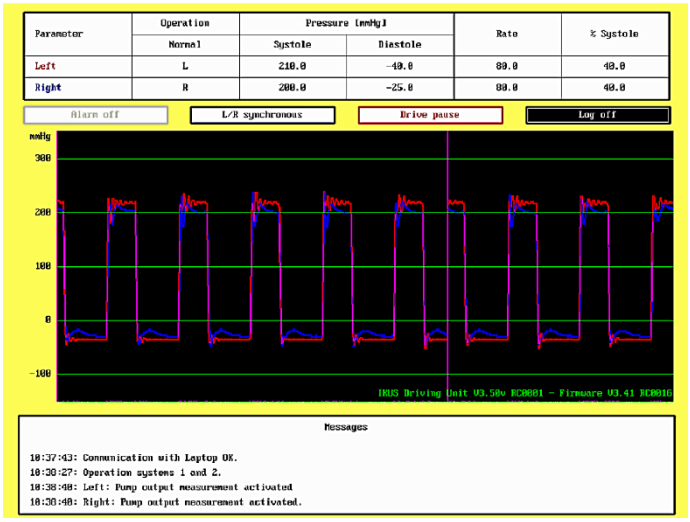


Fig. 5-10 Monitoring program

5.5 Safety

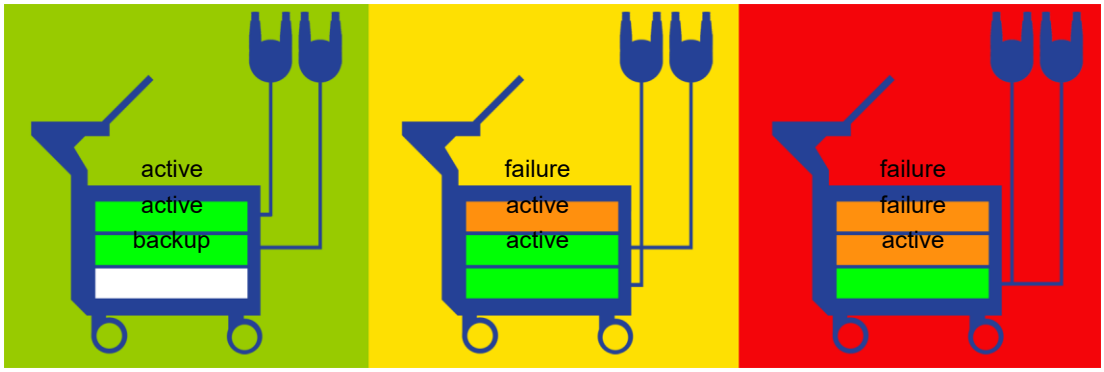
5.5.1 Redundant Design of Pneumatic Systems

Each blood pump is powered by one pneumatic systems. If one of the active pneumatic systems fails, the backup pneumatic system drives the corresponding blood pump. The performance of the Ikus will not be interrupted. If two systems should fail, the remaining pneumatic system will drive the blood pump(s) and the Ikus will run in emergency operating mode.

Emergency operating mode

If two pneumatic systems fail while in biventricular operation, the remaining system will drive both blood pumps. In this case, the *Ikus* will operate in synchronous mode with a 250 mmHg systolic pressure, -100 mmHg diastolic pressure, 70 bpm and a relative systolic duration period of 40 %.

If two pneumatic systems fail while in univentricular operation, the remaining system will drive the blood pump with the set parameters. The parameters can be changed.



Normal operation		Failure of 1 system		Failure of 2 systems	
System 1	left pump	System 1	failure	System 1	failure
System 2	right pump	System 2	right pump	System 2	failure
System 3	backup	System 3	left pump	System 3	left and right pump
		Message **Backup operation left. Contact customer service.** is displayed.		Message **Emergency operation System 3. Contact service now!** is displayed.	

Fig. 5-11 Pneumatic system redundancy in biventricular operation

5.5.2 Control Computer with Redundancy Design

The control computers are also designed to provide backup redundancy. The Ikus system has two independently operating control computers. The main computer controls the pneumatic systems and transmits important function-specific data to the laptop computer. The backup computer continuously compares its calculation results with those of the main computer. If the program detects a difference, an error message is generated. The control computers are located inside the Ikus casing and operate fully independently of the laptop.

Emergency pulse mode

The final safety system of the drive's electronic system is the emergency pulse circuit board. Should both control computers fail, this hardware takes over control of the system. In order to preclude all possible sources of faults, the emergency pulse circuit board runs autonomously and cannot be influenced by the two control computers nor by the laptop.

Independently from the settings used (univentricular, biventricular), in emergency pulse mode, the system will use system 1 for the left blood pump, system 2 for the right blood pump and operate with the following settings:

Synchronous mode (biventricular)				
	Systol. pressure [mmHg]	**Diastol. pressure [mmHg]**	**Rate [bpm]**	**Relat. systole duration [%]**
Left	210	-40	70	40
Right	150	-40	70	40

Tab. 5-2 Settings in emergency pulse mode

5.5.3 Battery Operation

If the main power supply fails, the batteries will supply power to the system.

5.5.4 Manual Pump

If a working Ikus is no longer available, the blood pump(s) can also be temporarily operated (even in BVAD mode) by the manual pump supplied with the system (see section 16.5: Driving Blood Pump(s) with the Manual Pump, page 173).

5.5.5 Password Protected User Profiles (Access Passwords)

Only a user who has logged into the monitor program with appropriate credentials can change settings within the monitor program. When the system is delivered, a single default user profile is configured. Up to nine additional user profiles can be added. All system setting changes are logged specifically for the user operating the Ikus.

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6 Important Safety Information

6.1 Warnings

⚠ WARNING

Before using EXCOR, read the IFU carefully. Be sure to follow the numbered instructions exactly in their sequential order.

EXCOR is available only upon the prescription of an attending physician.

Only qualified medical personnel trained to use EXCOR should work with EXCOR. To arrange a training course, please contact the distributor (see 1).

EXCOR should be used only with compatible components manufactured by Berlin Heart. Components from different manufacturers or implant systems should not be used together.

Do not modify the components of EXCOR.

Do not use damaged or defective EXCOR components. Replace any damaged or defective EXCOR component immediately.

To ensure patient safety, before using the Ikus, ensure that a replacement Ikus is available at the hospital. At least one replacement Ikus should be available for every 2 systems in use. For example:
1 replacement Ikus if 1 or 2 systems are in use,
2 replacement Ikus if 3 or 4 systems are in use,
3 replacement Ikus if 5 or 6 systems are in use.
If more than 6 systems are in use the number of replacement Ikus has to be 1/2 of the active systems.

6.1.1 Procedural Techniques - Ikus

⚠ WARNING

To avoid contamination keep all driving tube connectors covered at all times when not in use.

Place the Ikus on a firm and even surface.

Do not place objects on top of the Ikus.

When turning on the Ikus, be sure it is connected to a main power supply. This is the only way to ensure that the start test is completed and that any possible issues are detected (see section 7.2.1: Starting the Monitor Program, page 49). The user needs to ensure the Toggle Switch in in the ON position prior to running the Ikus on.

To avoid risk of electrical shock and/ or damage to the Ikus, the main power cable of the Ikus should be connected to a grounded power outlet with compatible supply voltage to the voltage requirements indicated on the Ikus identification plate.

Connect the Ikus to a grounding point. Use for all electrical equipment near the patient including the Ikus one and the same grounding point.

Turn on the Ikus two hours before use in order to run the start test (see chapter 8.1.2: Switching on the Ikus, page 70). During this time, be sure both tank units are connected to the Ikus (see section 8.1.1: Connecting the Tank Unit, page 70)!

To prevent the Ikus from overheating and to allow for proper ventilation, do not cover or obstruct the air vents during operation.

To avoid risk of a short circuit, do not use water or fluids to cool the Ikus!

Ensure that the acoustic alarm of the Ikus can be noticed by medical personnel at any time. The external alarm (Nurse call) can only be used in addition to the acoustic alarm.

Visual messages are displayed only when the monitor program is running. If the monitor program is not in use, the only indication of a potential error will be the acoustic signal and the alarm indicator on the Ikus operating panel lights up.

Rates < 60 bpm are intended to be used only for implantation and explantation. Never use the Ikus with a rate < 60 bpm without constant supervision.

If a backup system is in use, immediatly provide the patient with a replacement Ikus.

6.1.2 Packaging and Sterilization

WARNING

The following items are delivered in a sterile condition: blood pumps, cannulae, cannula extension sets / connecting sets, driving tubes, de-airing set, de-airing hammer, tube connecting set, and membrane set.

All sterile EXCOR components are intended for single-use only.

Sterile components are sterilized using ethylene oxide (ETO) and are packaged in a double-layer sterile package. Be sure that the various layers of the sterile packaging are not damaged in any way before they are opened. Do not use the components if either of the sterile packages is damaged or if the components have exceeded the expiration date printed on the label.

An aluminum-coated external packaging protects the Carmeda® BioActive Surface (CBAS) of the blood pump and its sterile packaging against fluctuations in relative humidity. Do not use blood pumps with damaged external packaging.

The external packaging and the outer surface of the outer sterile packaging are not sterile. These two packaging layers must be removed before the inner sterile packaging containing the components are passed into the sterile field.

6.1.3 Procedural Techniques of Sterile EXCOR Components

⚠ WARNING

To avoid infection, use strict aseptic techniques during implantation and exercise extreme caution throughout the period of EXCOR cardiac support.

Ensure proper placement of the cannulae, especially with respect to orientation of the LV apex cannula, to prevent suction of the myocardial wall or interventricular septum.

When connecting the blood pump(s) to the cannulae, be sure that the titanium connectors are connected appropriately to the inflow and outflow stubs by observing the indicated arrows that show the blood flow direction.

To avoid risk of damage to the sterile EXCOR components, do not touch or manipulate them with pointed or sharp-edged objects (such as surgical instruments, wire brushes, etc.).

Tunnel the cannulae transcutaneously using the cannula tunneling tip provided to advance the cannula through the prepared transcutaneous tunnel. (see section 10.2: Use of the Cannula Tunneling Tip, page 91) Never use a sharp surgical instrument directly on the cannula.

The distal end of the cannulae can be trimmed. At least 5 cm (2 inches) of material without polyester velour covering must remain to avoid damage to the cannulae stubs and allow visual inspection of the cannulae/ titanium-connector junctions.

Before connecting the blood pumps, cannulae, cannulae extensions set and connecting set make sure that the stubs of each connection is not damaged.

The cannula diameter may be adapted only once (either by using a staged cannula or a connector set). Multiple staging can result in limited blood pump performance and insufficient blood supply to the patient.

Take care not to manipulate or distort the blood pumps, cannulae, cannula extension set and connecting set during the removal of the cable tie(s) to prevent damage and mobilization of deposits.

To avoid damage to the membrane and ensure that the patient receives sufficient support, ensure that particles and/ or liquids do not enter the air chamber of the blood pump.

To avoid loose connections and insufficient blood supply to the patient, potentially resulting in injury or death, secure each connection between blood pumps, driving tubes, cannulae, extension sets and/or connection sets with at least one cable tie as soon as the proper function of EXCOR is established (see section 10.11: Securing the Connections, page 103).

To avoid risk of damage and obstructions of air and blood flow ensure that blood pumps, cannulae, cannula extension sets, connecting sets and driving tubes are not subject to external forces, like compression, traction or torsion forces, and are free of knots or sharp bends. Prevent the cannulae and connectors from being exposed to tensile forces. Otherwise there is a risk of damage and obstruction of the air and blood flow.

Take care to ensure that the cannulae do not become kinked directly at the connector to the blood pump or at the transition area between velour and silicone.

Take care to ensure that the patient, family and caregiver avoid pulling, kinking or engaging in any activity that could put stress on the blood pumps, cannulae, cannula extension sets, cannula connecting sets and driving tubes. Do not allow patient to pull or stretch the blood pumps, cannulae, cannula extension sets, cannula connecting sets and driving tubes, as this may lead to damage of the components, resulting in injury or death to the patient.

If air or blood collects between any of the layers of the membrane, replace the blood pump immediately.

When positioning the driving tubes mitigate the risk of adverse tubing and line incidents by routing the driving tubes in a clear pattern toward the feet and to the side.

Do not initiate cardiac support with EXCOR blood pumps until the blood pumps have been completely de-aired. After connecting the cannulae, ensure removal of all air that is still in the atria or ventricle by performing single steps (**Step left**, **Step right**) with subsequent removal of the bubbles inside the blood pump via the de-airing needle.

6.1.4 Maintenance

WARNING

The Ikus requires maintenance every six month when not in operation. When the Ikus is in operation it requires maintenance every 2000 operating hours.

The Ikus shall be serviced only by the manufacturer or the distributor or those authorized by them. For this reason, this document does not contain any circuit or wiring diagrams. The maintenance is performed based upon the *Maintenance Instructions*. This document also includes a technical description of the Ikus.

Any replacement parts used on the Ikus must be approved by the manufacturer.

6.1.5 Errors and Corrective Measures

WARNING

In case of an error message visually check that the EXCOR components show no sign of damage and the blood pump(s) is (are) filling and ejecting completely over a period of several pump cycles, before taking corrective action (chapter 15: Error Messages and Corrective Measures, page 143).

Check all the information and messages in the message window of the monitor program at least every four hours. Address messages as they occur and contact the service hotline for assistance if needed.

If a message with the content **... Contact (customer) service (now)!** is displayed in the message field on the laptop, replace the Ikus immediately (see chapter 15: Error Messages and Corrective Measures, page 143).

6.1.6 Ambient Conditions

WARNING

Do not store or operate the Ikus in a damp environment (e.g. bathroom, etc.) and ensure that no fluids enter into the Ikus.

Avoid exposure to strong electromagnetic radiation (as generated by mobile/cell phones and cordless phones when switched on, electromagnetic security systems etc.), see chapter 19: EMC Tables, page 241.

Use of the Ikus adjacent to or stacked with other equipment should be avoided because it could result in improper operation. If such use is necessary, the Ikus and the other equipment should be observed to verify that they are operating normally.

Take care to ensure that there is always a minimum distance between a cell phone and the Ikus of 30 inches. For further information please refer to chapter 19: EMC Tables, page 241.

When using an RFID device in the immediate environment of an Ikus in operation please make sure to keep a distance of at least 40 inches. For further information please refer to chapter 19: EMC Tables, page 241.

Protect the Ikus against temperatures below +10°C and above +35°C; this includes extreme temperature changes and overheating (e.g. direct sunlight or from heaters). Otherwise there is a risk of functional limitation and/or Ikus malfunction.

If an ambient temperature of +30°C is continuously exceeded during operation, the lifetime of the batteries is reduced.

Use the Ikus as far away as possible from environments containing flammable gases and use extreme caution. Otherwise there is a risk of explosion or gas ignition. The Ikus would be severely limited in function or malfunction altogether as a result of this damage.

Also see section 18.2: Technical Specifications, page 226.

6.1.7 Interaction with other Procedures and Therapies

WARNING

Magnetic Resonance Imaging cannot be performed while EXCOR is in use.

EXCOR patients with prosthetic aortic valves may have increased risk of thromboembolism.

The provision of other procedures or therapies during the use of EXCOR may result in complications and is not recommended, except as described below.

When exposing Ikus to the procedures and therapies listed below please observe EMC regulations given in chapter 19: EMC Tables, page 241.

The following procedures and therapies, can be performed safely with the Ikus, and in consultation with a treating physician. (see chapter 19: EMC Tables, page 241).
- Radiotherapy
- Nuclear diagnostics / nuclear therapy
- Electro stimulation therapy
- Therapeutic ultrasonic treatment (e.g. lithotripsy)
- External defibrillation

The following procedures and therapies have been tested in regard to their interaction with the Ikus and no harmful effects were found, however, these procedures and therapies must only be applied after consultation with the treating physician. Additionally the manufacturer does not guarantee that equivalent devices will not interfere.
- Diathermy
- X-rays
- Computed tomography

6.2 Precautions

6.2.1 VAD Placement Technique

CAUTION

Implantation - anesthesia: during implantation there should always be an adequate supply of prematched stored blood, fresh frozen plasma and platelet concentrates available for immediate transfusion if required.

The titanium connectors of the blood pumps have sharp edges designed to minimize the risk of clot formation at the junction. Be careful to avoid cutting yourself while connecting the blood pump and the cannulae.

6.2.2 Ambient Conditions

CAUTION

The Ikus is intended solely for use in a hospital setting.

Before putting the Ikus into operation, check that the ambient conditions are suitable (see section 18.2: Technical Specifications, page 226).

6.2.3 Transport Outside the Clinic

CAUTION

The crate may only be transported as described in section 7.7: Transportation and Packaging, page 61.

Also refer to section 7.7: Transportation and Packaging, page 61.

6.3 Obligations of the Operator

CAUTION

The operator (i.e. the hospital using EXCOR) is responsible for instruction and care of the patient. The patient must be instructed on safety risks and cautionary measures (e.g. forces that might damage the EXCOR components, moisture, temperature, electromagnetic fields, etc.).

The operator is also responsible for adherence to the prescribed maintenance and service intervals (see section 3.8: Battery Replacement and Disposal, page 20 and Tab. 3-1, page 19).

Replacement equipment must always be available in the hospital.

If any of the components are damaged call the service hotline.

7 Instructions for Use: Ikus

WARNING

Do not install any other software on this laptop.

Make sure that the **<NumLk>** and the **<Caps Lock>** key of the Ikus laptop are deactivated and that the status LED on the laptop marked with a lock and/or a number (e.g. 1) are not lit. (see Fig. 7-1, page 45 to Fig. 7-3, page 46)

Do not connect USB devices (i. e. wireless technology) to the USB port of the Ikus laptop other than those delivered.

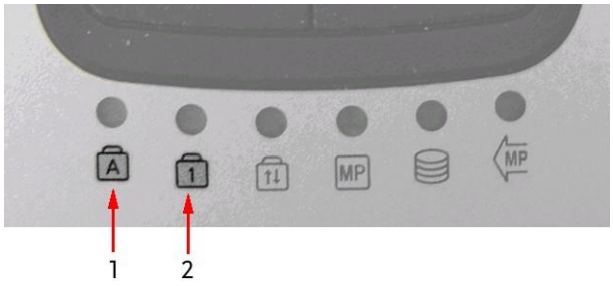
Check all the information and messages in the message window of the monitor program at least every four hours. If there is a message that indicates action must be taken, take the appropriate action and, if necessary, contact the service hotline.

Always turn the Ikus on before turning on the laptop. Turning on the equipment in the reverse order could generate false error messages.

NOTICE

For details on commissioning the system see chapter 8: First Use of Ikus and Setting Parameters, page 69.

The Ikus is controlled and monitored using the monitor program, which is permanently installed on the laptop. Only users who are properly logged in can use the monitor program to change system settings.

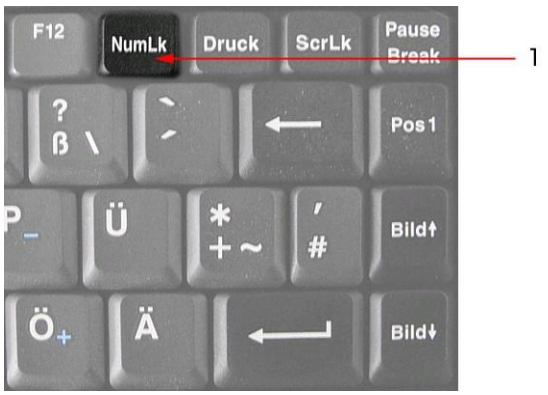


1 LED for **<Caps Lock>**
2 LED for **<NumLk>**

Fig. 7-1 LEDs below the mouse pad

1 **<Caps Lock>**
2 Press **<Shift>**

Fig. 7-2 De-activate the Caps Lock



1 Press **<NumLk>**

Fig. 7-3 De-activate the Numeric Lock

7.1 Start Menu

After the laptop is started, it will display the menu *Select language*.

Fig. 7-4 Select language

Then the start menu will open up and offer the following options:

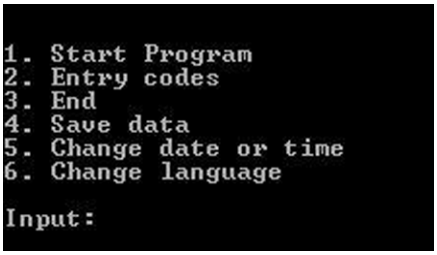


Fig. 7-5 Start menu

1. Start program	Select this option to start the monitor program.
2. Entry codes	With this option password-protected user profiles for the monitor program can be edited. (user no.: 1 digit; password: combination of max. 32 digits)
3. End	This option will shut down the operating system before switching off the laptop. The Ikus will continue to operate using the current parameter settings.
4. Save data	This option allows the LOG files to be saved on a USB stick. This should only be done after having consulted the service hotline.
5. Change date or time	This option enables the user to change the system date and time on the laptop.
6. Change language	This option enables the user to choose a different language for the monitor program interface.

7.1.1 Selecting an Option in the Start Menu

After starting the monitor program (**<1>**, **1. Start program** in the start menu) the user must log in with a user ID and password.

IMPORTANT: Before user profiles can be entered, the initial user must first log in with user ID and password of the default user profile. (**<2>**, **2. Entry codes**)

IMPORTANT: The default user profile is enclosed in the password envelope provided with the equipment in the accessory box delivered with the Ikus.

Fig. 7-6 User ID

Fig. 7-7 Password

INSTRUCTION

1. Type in the number of the menu item (e. g. **<1>** for **1. Start program**). The option is activated immediately.

ADVICE

Keep the envelope containing the password in a safe place.

7.1.2 Configuring User Passwords

A user profile (entry-code) is required to perform standard operating actions in the monitor program.

IMPORTANT: The default user profile (user ID and password in password envelope) is required in order to be able to manage user profiles.

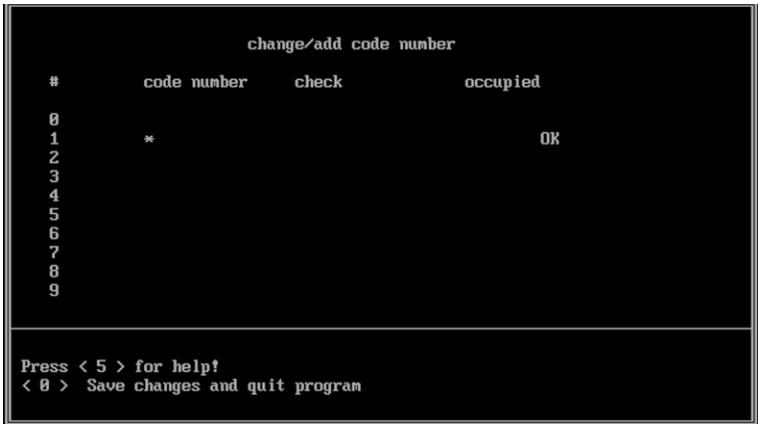


Fig. 7-8 Entry codes

INSTRUCTION

1. If the monitor program is running: press **<F10>** to exit the monitor program. Confirm by pressing **<X>** or **<1>**.
2. From the start menu, select **2. Entry-codes** (**<2>**).
3. Enter the default user profile code and confirm the input by pressing **<Enter>**. Now the password configuration program is started.
4. Use the arrow keys **<↓>/<↑>** to move the cursor to the desired user ID, then press **<Enter>** to confirm selection.
5. Enter the password (combination of max. 32 digits) and press **<Enter>** to confirm.
6. Repeat the entry and confirm with **<Enter>**.
7. If it is necessary, repeat steps 3 to 5 in order to configure additional user profiles.
8. To conclude and confirm all entries, press the **<0>** key. The passwords have now been assigned to the respective user IDs. The start menu is shown again.
9. In the start menu, select option **1. Start program** (**<1>**) to return to the monitor program.
10. Enter user ID and password, confirm by pressing **<Enter>**.

Other password configuration options

Key	Function
<ESC>	Discard all entries not yet confirmed with **<0>** and exit **2. Entry codes.**
<DEL>	Delete the selected user (press **<Enter>** to confirm)
<5>	Call up help text

Tab. 7-1 Other password configuration options

7.1.3 Saving Data on USB Stick

NOTICE

Consult the service hotline before proceeding with this option (refer to section 16.7: Reading out the LOG Files, page 175).

7.1.4 Changing Date or Time

Fig. 7-9 Change date or time

INSTRUCTION

1. If the monitor program is running: press **<F10>** to exit the monitor program and confirm by pressing **<X>** or **<1>**.
2. From the start menu, select **5. Change date or time** (**<5>**).
3. Move the cursor to the desired values using the **<←>** / **<→>** keys. Adjust the value with **<↓>**/**<↑>** (+/-1) and confirm with **<Enter>**.

Additional options changing date or time

Key	Function
<F6>	Switch between input field date and time fields
<F10>	Save settings and exit
<ESC>	Cancel and return to start menu

Tab. 7-2 Options changing date or time

7.2 Basic Instructions for Monitor Program

7.2.1 Starting the Monitor Program

INSTRUCTION

1. The start menu is displayed on the screen. Select **1. Start program** (**<1>**).
2. Enter the user ID, then the password. Confirm the password with **<Enter>**.

7.2.2 Shutting Down the Monitor Program

WARNING

Do not shut down the monitor program while EXCOR is in use unless absolutely necessary (e. g. to set up a new user profile). Restart the monitor program as soon as possible.

INSTRUCTION

1. Press **<F10>** and confirm by pressing **<X>** or **<1>**. The start menu is displayed on the laptop. The monitor program has now been shut down.

When the monitor program has been shut down:

- the system continues running with the currently set parameters
- no data on current events are recorded, and the LOG files will be incomplete
- an acoustic signal and the indicator light on the handle control panel will alert the user of new messages. However visual messages will not be displayed.

7.2.3 Logging in and out of the Monitor Program

To select options in the monitor program, to change parameters or scroll through the message window a user has to be logged into the monitor program. If no entries are made for several minutes, the monitor program will log the user out automatically. The Ikus continues to operate using the current parameter settings and the standard view is displayed.

IMPORTANT: The automatic forced logout does not occur after the first login after turning on the Ikus with the key switch.

The Ikus performs a self-test of the alarm circuit during each login procedure. If the self-test is completed successfully, the message **Acoustic alarm: OK** appears.The self-test does not occur if, at the time of login, an alarm is pending that was muted with the button *Mute alarm* (see section 5.2.2: Display and Operating Panel, page 29).

If a problem arises during the self-test of the alarm circuit, the acoustic signal continues for about ten seconds and cannot be muted. Acknowledgment is possible when one of the following messages appear: **Alarm circuit test failed - buzzer remains off!** or **Acoustic alarm is not properly recognized**.

7.2.4 Logging in

Fig. 7-10 User ID

Fig. 7-11 Password

INSTRUCTION

1. The monitor program is running. It now displays the field **User ID**. Enter user ID. The monitor program now displays the field **Password**.
2. Enter the password and confirm the password with **<Enter>**. The monitor program will now display the field **Log off**. The user now is logged into the monitor program.
   The alarm circuit test follows.

Logging out

INSTRUCTION

1. Select the menu item **Log off**, then press **<Enter>** to confirm. The monitor program now displays the field **User ID**. The user now is logged out of the monitor program. No further entries are possible until next login.

Cautionary measure

To ensure patient's safety, the user should log out of the monitor program before leaving the vicinity of the system.

7.2.5 Standard View – Monitor Program

WARNING

The displayed pressure graphs refer to the pneumatic pressures generated internally by the system and are shown in millimeters of mercury [mmHg]. They do not display the patient's blood pressure and cannot replace diagnostic measures by the medical personnel.

IMPORTANT: The monitor program also has two other views that are displayed only when the Ikus is turned on or is called up by using the command **Drive pause**.

- view *Select operating mode*, see Fig. 8-2, page 72
- view *Pump size and single-step mode*, see Fig. 8-6, page 76

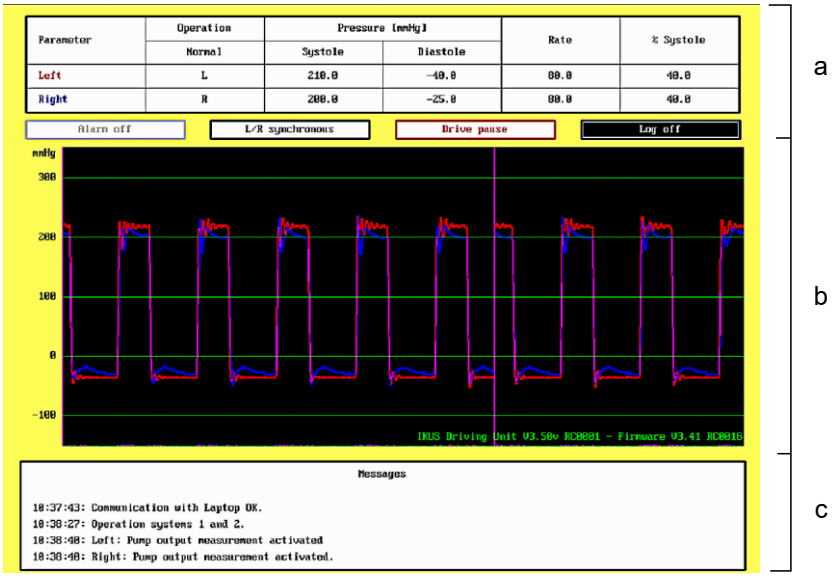


Fig. 7-12 Standard view of monitor program during start-test

A	Parameter table	current parameters are displayed and can be changed here
B	Pressure graphs	graphic display of the current pressure values in the respective pneumatic systems
C	Message window	information on the system status (e. g. **test operation**) and messages (error messages and messages confirming error correction; see chapter 15: Error Messages and Corrective Measures, page 143).

IMPORTANT: If the operator leaves the monitoring program or there is a failure of the monitoring program when there is an active alarm, the messages that had been displayed at that time will not be displayed again when the program is restarted. The messages can be recalled by Berlin Heart's service department.

Monitor program functions

Monitor and control system:

- If required, parameter adjustments can be made for the following:
  - systolic pressure
  - diastolic pressure
  - rate
  - biventricular: operating mode (synchronous mode; asynchronous mode; separate mode)
- View messages
- Acknowledge messages
- Pause drive
- Switch drive off

7.2.6 Selecting Monitor Program Options

INSTRUCTION

1. Use the <←>/<→> keys to move the cursor to the desired field. A pop-up menu will be displayed. To move to the next line up or down, the <←> /<→> keys have to be pressed repeatedly.

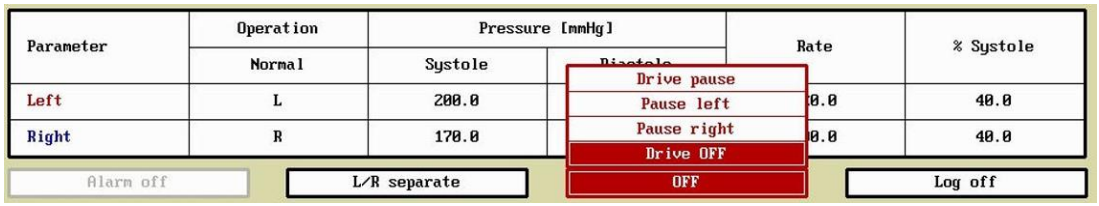


Fig. 7-13 Selecting monitor program options

with grey frame	field is not activated
black/ red frame	field is activated
colored background	field is selected

Selecting pump size(s) and cannula sizes

INSTRUCTION

1. Use the **<↓>/<↑>** keys to move the cursor to the desired field. All options that can be selected for this field are displayed.
2. Pop-up menus in the parameter table: press **<Enter>** to confirm the selection.
3. Pop-up menus Pump size Cannula size: after selecting the size, exit the field with **><←>/<→>.** The pop-up menu will close and the selected option will be displayed.

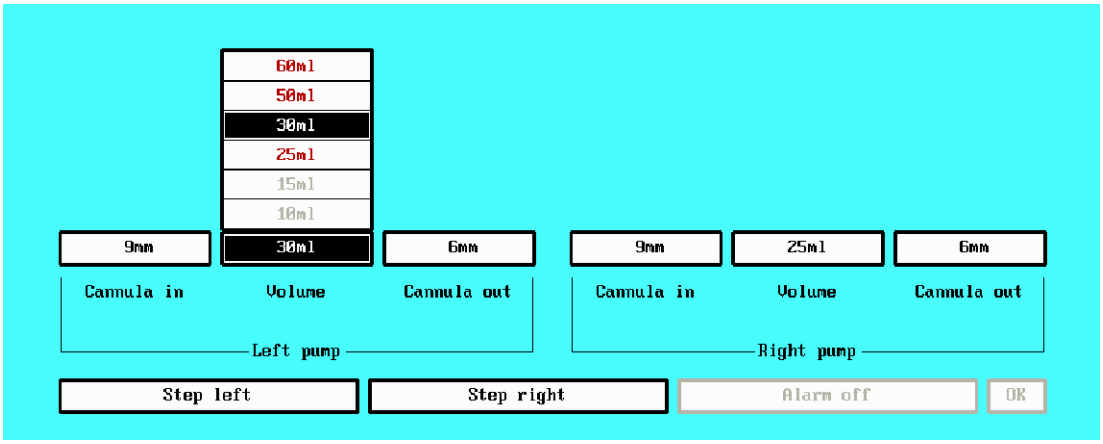


Fig. 7-14 Select pump size

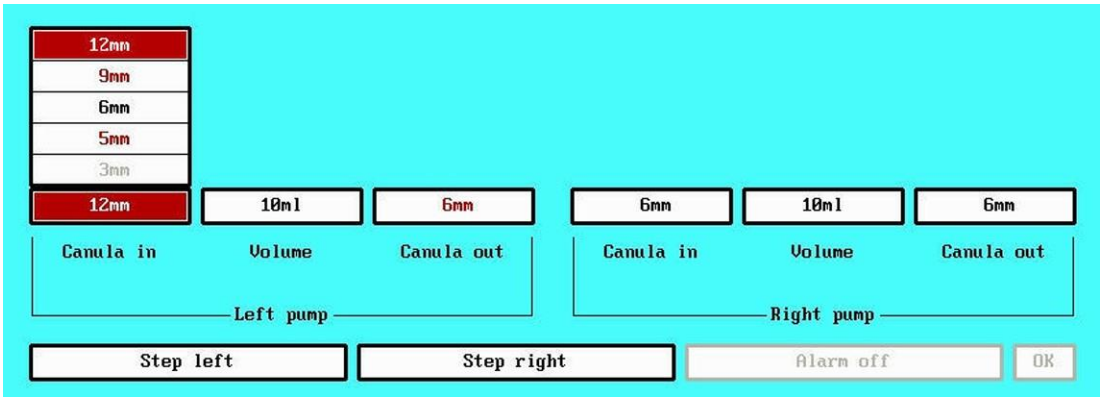


Fig. 7-15 Select cannulae size

The fields highlighted in red in the pop-up menus *(i.e.,Select pump size* and *Select cannulae size*) can be chosen. However, they are not the recommended option for each individual case (see section section 18.1.10: Maximum Rates for the Blood Pump - Cannula Combinations, page 224 and section 18.1.11: Blood Pump Combinations in Biventricular Mode, page 225).

The decision as to the appropriate combination of blood pumps and cannulae remains in the sole province of the implanting surgeon.

7.2.7 Adjusting the Parameter Values

NOTICE

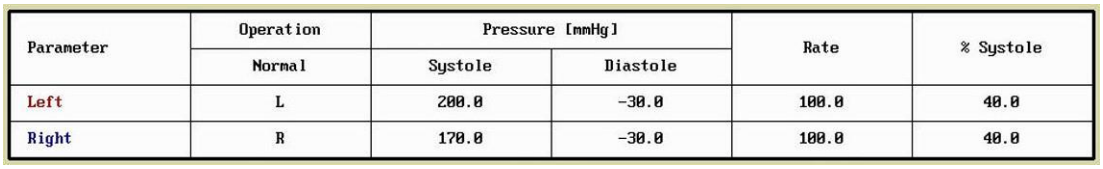
If the adjusted parameter was not confirmed with **<Enter>**, the parameter table will display the changed parameter until the automatic log off, but the Ikus will continue operating with the prior parameter.

The changed parameter display can be canceled with **<Esc>**. The original value continues to appear in the parameter table.

To confirm the change, press **<Enter>** and the new value will be displayed in the parameter table.

INSTRUCTION

1. Use the **<←>/<→>** keys to move the cursor to the desired field in the parameter table. The selected field is given a colored background.
2. Use the **<↓>,<↑>/ <Bild-↓>,<Bild-↑>** keys to adjust the value, then press **<Enter>** to confirm. The system will then operate using the new value.
3. Visually check that the blood pump(s) is (are) filling and ejecting completely over a period of several pump cycles!



Parameter	Operation	Pressure [mmHg]		Rate	% Systole
	Normal	Systole	Diastole		
Left	L	200.0	-30.0	100.0	40.0
Right	R	170.0	-30.0	100.0	40.0

Fig. 7-16 Parameter table

Parameter	**Range possible**	**<↓>/<↑> changes value by**	**<Bild-↓>/<Bild-↑> changes value by**
Systolic pressure [mmHg]	60 to 350	2.5	25
Diastolic pressure [mmHg]	0 to -100	2.5	25
Rate [bpm]	30 to 150	1	10
Relative systolic duration [%]	20 to 70	1	10

Tab. 7-3 Parameter adjustment

7.2.8 Browsing in the Message Window

INSTRUCTION

1. Press the **<7>** key to move the cursor in the message window.
2. Scroll through the messages: either 1 message at a time with <↓>/ <↑>; or 4 messages at a time with <Bild-↓>/ <Bild-↑>.
3. Exit the message window by pressing either **<Esc>**, **<Enter>** or **<←>/<→>**. The field **Log off** is automatically activated and appears with a black background.

7.3 Stopping the Blood Pump(s) and Switching off the Ikus

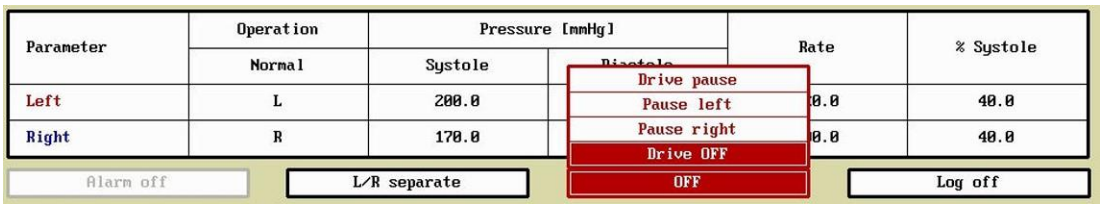


Fig. 7-17 Drive pause (with stop options)

The pop-up menu *Drive pause* offers the following options:

- **Drive pause**
- **Pause left**
- **Pause right** (only in biventricular operation)
- **Drive OFF**

7.3.1 Drive Pause: Stopping the Ikus Temporarily

INSTRUCTION

1. Select **Drive pause**, then press **<Enter>** to confirm. Respond to the prompt in the dialog window by pressing the **<X>** key or the **<1>** key. The Ikus will stop. The view *Select operating mode* is displayed.

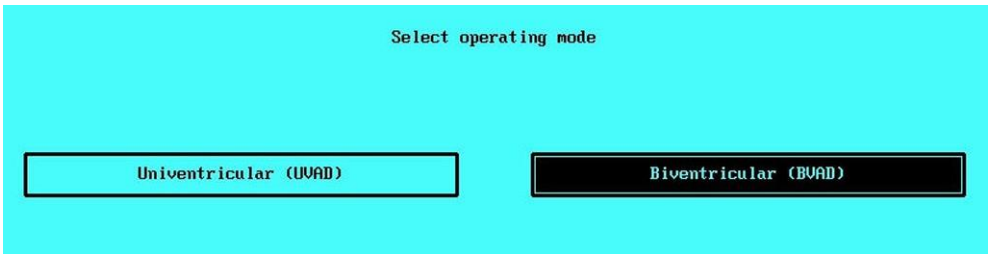


Fig. 7-18 Select operating mode

2. Select **Univentricular (UVAD)** or **Biventricular (BVAD)**, then confirm the selected operating mode with **<Enter>**. In biventricular mode the view *Pump size and single-step mode* appears. In univentricular mode, the seal test is performed first and then the view *Pump size and single-step mode* appears.

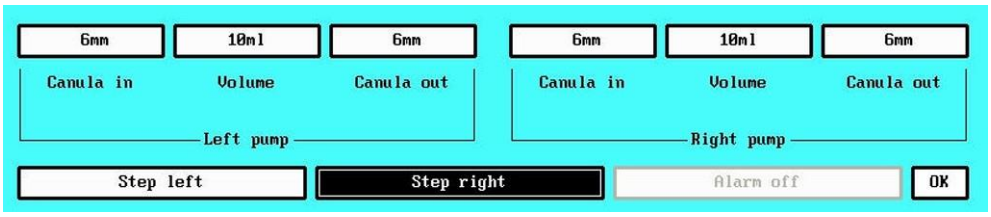


Fig. 7-19 Pump size and single-step mode

3. The cursor is located on the **OK** field. To restart the driving unit with the current settings, press the **<Enter>** key. IMPORTANT: If the user leaves the **OK** field before pressing **<Enter>**, **Step left** or **Step right**, respectively has to be performed again. Only then will the **OK** field be highlighted again and it is possible to confirm **OK** by pressing **<Enter>** (see section 8.2.3: Select the Blood Pump Size, page 73).

7.3.2 Pause Left / Pause Right: Stopping an Individual Blood Pump

IMPORTANT: The option **Pause right** is available only in biventricular mode. The option is displayed in univentricular mode, but it is not activated. It is only possible to select **Pause left**.

INSTRUCTION

1. Select **Pause left** or **Pause right**, as required, then press **<Enter>** to confirm. Respond to the prompt in the dialog window by pressing the **<X>** key or the **<1>** key. The selected pump will stop and the *Pump size and single-step mode* will be displayed.
2. To restart the pump, at least once **Step left** or **Step right**, respectively has to be performed (see section 8.2.3: Select the Blood Pump Size, page 73).

7.3.3 Drive OFF: Switching the Ikus off

CAUTION

Do not turn the Ikus off unless the batteries are fully charged (i.e. all yellow charge indicator LEDs are on).

INSTRUCTION

1. Do not turn the Ikus off until the batteries are fully charged. Once all of the yellow indicator lights are lit, proceed with the remaining instructions.
2. In the monitor program, select the **Drive OFF** option and press **<Enter>** to confirm.
3. Respond to the prompt in the dialog window by pressing the **<X>** key or the **<1>** key. The driving unit stops operation immediately and writes an operating LOG file.
4. Wait until the LOG file has been completed. When the message **Switch drive off with main switch**! appears, press **<F10>** to shut down the monitor program. Confirm by pressing **<X>** or **<1>**.
5. Select option **3. End** (**<3>**) in the start menu and switch off the laptop.
6. Turn the main switch (key switch) to *[0]* position.

IMPORTANT: Always use the main switch (key switch) to turn off the Ikus.

7.4 Battery Operation

WARNING

The Ikus is designed for stationary operation and should be connected to a main power supply. Do not run the Ikus on battery power unless it is for the temporary transport of the patient or in the event of an emergency.

Whenever the Ikus is running on battery power, the patient must always be accompanied by a person trained to use the manual pump.

Do not disconnect the Ikus from the main power supply unless the battery charge indicator shows that the batteries are full charged (all yellow LEDs light up).

If the charge level indicator lights are blinking or the message **Batteries discharged - use power supply!** appears, immediately connect the Ikus to the main power supply. Continuing to run the Ikus on battery supply in this condition may result in damage to the battery and the potential that the Ikus will not restart after being reconnected to a main power supply.

If the batteries are discharged completely (red LED of the charge indicator lights up), there is a danger of a total malfunction of the Ikus if battery operation is continued, and that the batteries will be damaged. If this happens, it cannot be guaranteed that the Ikus will restart after connecting it to the mains.

When the battery charge is low, the acoustic signal sounds two times a minute. The Ikus must be connected to the mains operation immediately.

ADVICE

Always take along the mains cable when operating the Ikus in battery operation. In this way the system can be connected briefly to the mains again if it becomes necessary.
If the patient has to be transported within the clinic choose a route as close to the power sockets as possible. Thus at any time the Ikus can be connected to the mains.

Switching over to battery operation

INSTRUCTION

1. Disconnect the Ikus from the main power supply by pulling the plug from the socket. Do not pull the cable from the Ikus.
2. Battery operation indicator light up to indicate that the Ikus is running on battery power.
3. Observe all acoustic signals, indicators and messages while the Ikus is running on battery power (see Tab. 7-4, page 58).

Behavior of the Ikus during charging and when running on battery power:

What?	When?	Meaning
The charge indicator shows the battery charge status	In battery operation: always When connected to the main power supply: all yellow LED indicators light up **after** the batteries have been completely recharged	Charge status
Battery charge indicator lights up	During battery operation	The Ikus is running on battery operation
Message: **Battery operation**, signal tone	Every 10 minutes	Reminder that the Ikus is running on battery operation. The Message and the signal can be either acknowledged on the laptop or muted by pressing the button *Mute alarm* on the operating panel
Message: **Batteries discharged - use power supply!**	After 30 minutes of operation, then at 10 minute intervals	The permissible runtime of 30 minutes on battery operation has been reached. The Ikus should be connected to a main power supply.
Message: **Batteries discharged - use power supply!**	Batteries have reached low charge state, 2-times per minute repeatedly	Maximum possible runtime: only a few minutes. Switch to main power supply immediately!
Yellow LED blinks (left)	Batteries are about to reach maximum possible runtime	Prewarning! Switch to main power supply immediately!

Tab. 7-4 Displays and messages during battery operation mode

What?	When?	Meaning
Message: **n - use power supply!** …together with message (1-time): **Fault:** **0000 0011 1101 1000 (fault in power supply)** red LED of the charge indicator also lights up	Batteries are no longer charged. (Batteries are completely dead) 2-times per minute repeatedly	Batteries are completely dead! Residual runtime: 0 minutes! Immediately switch to mains operation! Danger of total malfunction of the Ikus!
Blood pump stands still - no further pump function; acoustic alarm is still audible	Batteries are complete emptied or there is a serious fault in the batteries	Immediately connect the Ikus to the main power supply. Until that time use the manual pump.
Acoustic alarm is audible; the displays are off and it is not possible to perform any action on the laptop	Batteries are defective or mains failure	Immediately connect the Ikus to the main power supply. Until that time use the manual pump.

Tab. 7-4 Displays and messages during battery operation mode

Switching over to main power supply

INSTRUCTION

1. Connect the Ikus to the main power supply.
2. The indicator *Mains operation* lights up. The indicator *Battery operation* in the handle goes out. The batteries are now being charged.

7.5 Changing over from Univentricular to Biventricular Operation

CAUTION

When changing to biventricular operation patient-customized parameters will be set to the default settings and should be readjusted. The Ikus is operating in **separate mode**.

INSTRUCTION

1. De-air appropriate blood pump and connect to cannulae.
2. In the monitor program, select the option **Drive pause** (see Fig. 7-17, page 55) and press **<Enter>** to confirm. Confirm the selection in the dialog window by pressing **<X>** or **<1>**. The active blood pump will stop. The view *Select operating mode* appears.
3. Open the driving tube connector identified by a blue marking.
4. When changing from univentricular support to BVAD: ensure the LVAD blood pump is attached to the red connector and RVAD pump is attached to the blue connector. To do so, take hold of the plug's release sleeve and pull the plug out of the socket.

5. Plug the driving tube of the de-aired new blood pump into the free driving tube connector. The sound of the plug snapping into place is clearly audible. Check that the plug is securely connected by gripping the release sleeve above the grooved section and pull on it. Be sure not to pull from the release sleeve, and never from the tube!
6. Select **Biventricular (BVAD)** and confirm with **<Enter>**. All following steps are the same as required for the start-up procedure. See chapter 8: First Use of Ikus and Setting Parameters, page 69.

7.5.1 Routine Start-Test when not in Operation

IMPORTANT: If the Ikus is not in use, run it once a month for 24 hours in order to ensure that all batteries are adequately charged.

INSTRUCTION

1. Follow the procedure as described in section 8.1.1: Connecting the Tank Unit, page 70 and section 8.1.2: Switching on the Ikus, page 70.
2. Wait 24 hours.
3. Follow the procedure as described in section 7.2.1: Starting the Monitor Program, page 49 and section 8.1.4: Setting the Test Parameters, page 71.
4. Observe and evaluate the curve representation.
5. Select the option **Drive OFF**, then confirm with **<Enter>**.
6. Confirm the selection in the dialog window by pressing **<X>** or **<1>**. The system immediately stops the operation and writes an operating LOG file.
7. Wait until the LOG file is complete (message: **Switch off drive with main key switch**).
8. End the monitor program and turn off the laptop.
9. All of the yellow battery LEDs are lighted: Switch off the Ikus. To do so, set the main switch (key switch) to *[0]* position.
   Not all yellow LEDs are lit up: leave the Ikus on the power supply until all of the yellow LEDs light up. Then set the main switch (key switch) to *[0]* position.
10. Disconnect both tank units from the Ikus.
11. Seal the driving tube connection sockets with seal plugs.

If the system detects an error during the start-up test

INSTRUCTION

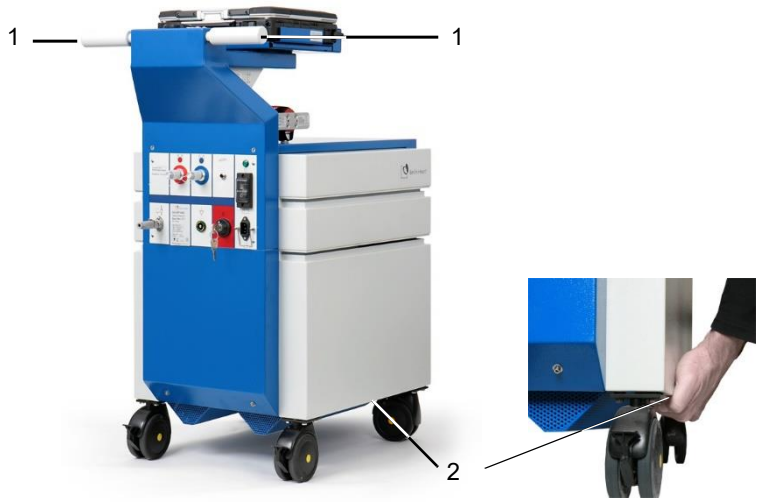
1. End the monitor program according to the instructions in the dialog.
2. Turn the Ikus off with the main switch (key switch).
   IMPORTANT: The power switch (toggle switch) remains on *[I]* position!
3. IMPORTANT: Wait 10 minutes.
4. Repeat the start-up procedure (see above).

If the system again detects an error in the start-up test or not all of the battery LEDs are illuminated after 24 hours, notify Berlin Heart:

HOTLINE

Call Service Hotline! 866.249.0128

7.6 Moving the Ikus



1 handle: push or pull the Ikus
2 lifting bar: the Ikus can be lifted here

Fig. 7-20 Handle and lifting bar

WARNING

To push or pull the Ikus: use the handle provided. Avoid any sudden motions. Exercise extreme caution when passing over smaller obstructions, pulling the Ikus backwards across the obstructions.

At least two to four people are required to lift the Ikus by using the lifting bars at the lower edge at each side of the Ikus. Do not attempt to lift the Ikus by its handle.

Rolling the Ikus over sloping surfaces: ensure that the person pushing it is strong enough to move the Ikus in a controlled manner. The slope of the surface may not be steeper than 10°.

7.7 Transportation and Packaging

CAUTION

To transport the Ikus, only the supplied original transport crate must be used.

Make sure that the Ikus is standing firmly and securely in the crate and that the crate is closed and sealed properly.

The crate must always be transported as marked. Do not tip the Ikus stored in the transport crate or turn it upside down.

Ikus Accessories and documents

- 1 IFU (supplied separately)
- 2 Tank units (supplied separately)
- 2 Keys
- 1 Power cable
- 1 Alarm connector
- 1 Envelope with password

Also see section 18.4: Sample Copy: Ikus Incoming Checklist, page 230.

7.7.1 Unloading the Ikus from the Shipping Crate

NOTICE Do not discard the shipping crate!

INSTRUCTION

1. Follow inspection steps per *Ikus Incoming Checklist*.
2. Place the crate with its back against a wall and/ or lock the brakes to prevent the crate from moving during unloading.
3. Open the door latches. Flip open the secure latch and turn counter clockwise to disengage latch from front door.
4. Swing front door open to the left.
5. Unlatch the ramp safety retainer.
6. Open the ramp while holding the black securing plate behind the ramp.
7. Open the front securing plate (is connected to the crate with a rope) and place the plate to the right of the crate.
8. Remove the white accessory box.
9. Disengage the Ikus front wheel brake (pulling the lever upwards).
10. Stand on the ramp and carefully pull out the *Ikus* by the handle bar.

For assistance please:

HOTLINE **Call Service Hotline! 866.249.0128**

7.7.2 Loading the Ikus into the Shipping Crate

During transport, the key remains in the main switch (key switch) in the *[0]* position.

Dimensions of the *Ikus* (W x H x D): 46 x 95 x 73 cm (approx. 18.5 x 37.5 x 29 inches) with laptop cover down

Weight of the *Ikus*: approx. 100.6 kg (approx. 219 lbs)

INSTRUCTION

1. Place the crate with its back against a wall and/ or lock the brakes to prevent the crate from moving during loading.
2. Open the door latches and swing front door open to the left. Unlatch the ramp safety retainer and open the ramp while holding the black door panel behind the ramp.

Fig. 7-21 Empty shipping crate

3. Make sure the laptop is closed and rotated in as shown in Fig. 7-22.

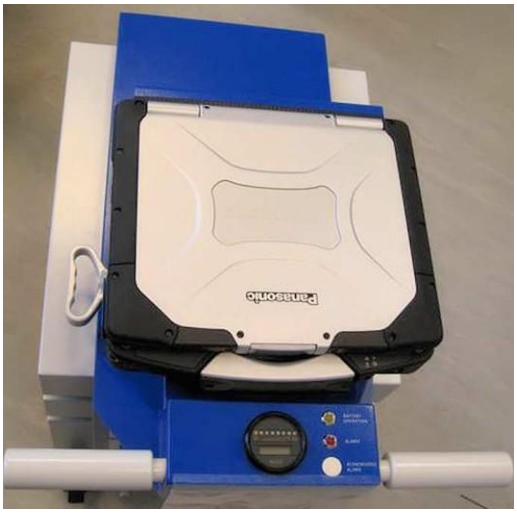


Fig. 7-22 Prepare the laptop

4. Line up the Ikus with the ramp. Push it upward on the handle bars all the way into the crate.

Fig. 7-23 Line up the Ikus

5. Engage the Ikus front wheel brake (pushing the lever down).

6. Place the accessory box in front of the Ikus top of the bottom.

Fig. 7-24 Place the accessory box

7. Reattach the securing plate.

Fig. 7-25 Reattach the securing plate

8. Lift up the ramp.

Fig. 7-26 Lift up the ramp

9. Fix the ramp with the safety retainer.

Fig. 7-27 Fix the ramp

10. Close the front door and apply the latches.

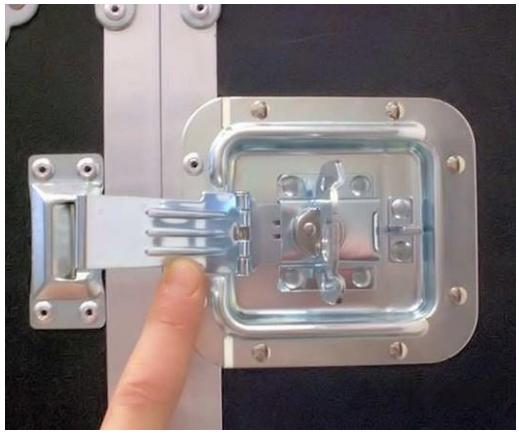


Fig. 7-28 Close the door

11. Lock the crate with a cable tie.

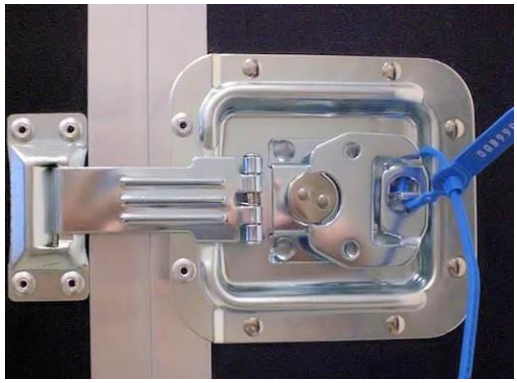


Fig. 7-29 Lock the crate

12. The crate is now ready for storage/ shipping.

Fig. 7-30 Crate ready for storage/ shipping

7.8 Cleaning and Disinfecting the Ikus

WARNING

Prevent liquids from spilling into the Ikus. Otherwise there is a risk of an electric shock and of a malfunction of the Ikus.

NOTICE

Do not use any corrosive or colored solutions or organic solvents to clean the Ikus as they may alter the surface of the product.
Ikus can be cleaned by wiping disinfection with an alcohol containing solution. Omit the air vents.

INSTRUCTION

1. Clean Ikus by wiping disinfection with an alcohol containing solution (e.g. Bacillol® plus).
   IMPORTANT: Do not expose display and keyboard to direct spray jet, but use a cloth that is moistened with disinfecting agent.

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8 First Use of Ikus and Setting Parameters

WARNING

Prior to initial operation of the blood pump(s) minimal initial start parameters have to be set on the Ikus laptop to ensure smooth transition from CPB to VAD support.

CAUTION

The Ikus should not be turned on for at least six hours after it is transported to allow the equipment to reach room temperature before being used on a patient.

Before putting the *Ikus* into operation, check that the ambient conditions are suitable (see section 18.2: Technical Specifications, page 226).

NOTICE

This chapter describes the technical aspects of commissioning the system as well as perioperative and postoperative drive management. When commissioning the system, it is vital to observe the instructions given in chapter 9: Implantation - Preparations in the Operating Room, page 85.

The drive management procedures described here are intended as recommendations only. There is no substitute for careful patient observation and evaluation by the appropriate medical personnel.

IMPORTANT: Make sure that the position of the Ikus always allows easy access to the main power sources´s plug.

8.1 Preparatory Steps Outside of the Operating Room

WARNING

Switch the Ikus on two hours before its intended use in order to adequately charge the batteries and so that a start-test can be performed to detect any possible faults in the device. During this period, always connect both tank units to the *Ikus* (see section 8.1.1: Connecting the Tank Unit, page 70)!

8.1.1 Connecting the Tank Unit

Fig. 8-1 Tank unit

IMPORTANT: Two separate tank units are used, each equipped with a driving tube.

IMPORTANT: The tank unit simulates the blood pumps during the warming-up period. If the test parameters have been set correctly the tank units prevent the Ikus from generating false error messages (see section 8.1.4: Setting the Test Parameters, page 71).

INSTRUCTION

1. Remove the seal plugs from the driving tube connection socket.
2. Connect the plug of the two tank units to the driving tube connection sockets.

8.1.2 Switching on the Ikus

WARNING

The *Ikus* must always be connected to the power supply when it is switched on. This is the only way to ensure that the start-up test (see section 8.1.3: Starting the Monitor Program, page 71) is performed completely and possible malfunctions can be detected.

INSTRUCTION

1. Connect the Ikus to the main power supply. Secure the main power cable with the plug clip. Ensure that the main power switch (toggle switch) is set to *[I]* position.
2. Turn the main switch (key switch) to the *[I]* position. The battery charge indicator will light up and the number of hours the Ikus has been operated will be displayed. The main operation indicator lights up.
3. The menu *Select language* appears after the laptop is switched on.
4. Select the desired language by pressing the corresponding number key. It is not necessary to press **<Enter>** to confirm this selection.
5. The start menu is displayed on the laptop.

8.1.3 Starting the Monitor Program

INSTRUCTION

1. Select the **1. Start program** option (**<1>**) in the start menu.
2. Enter user ID and password, confirm with **<Enter>**. The *Ikus* will carry out a start-test.
3. Wait for the start-test to finish (it takes several minutes). Do not mute the acoustic signal by pressing the *Mute button*. Exception: an error message is displayed. The messages in the message window will provide information on the status of the test. If the *Ikus* is found to be operating correctly, the view *Select operating mode* will be displayed next.

8.1.4 Setting the Test Parameters

NOTICE

When delivered, the Ikus employs standard default parameters following the start-up process (see section 7.5.1: Routine Start-Test when not in Operation, page 60 and section 16.3.2: Ikus Start-Test Following Emergency Pulse Mode, page 170). During the warm-up period with the tank unit, it is necessary to set the test parameters.

Systole [mmHg] left/right	**Diastole [mmHg] left/ right**	**Rate [bpm]**	**Rel. systole duration [%] left/right**	**Operating type/mode**
200	0	70	40	Biventricular, synchronous mode

Tab. 8-1 Test parameters

INSTRUCTION

1. Even with planned univentricular operation: navigate the cursor to **Biventricular (BVAD)**, confirm with **<Enter>**. The view *Pump size and single-step mode* appears.
2. Place the cursor with **<↑>** in the parameter table and navigate with **<←>/<→>** to the desired field in the parameter table. Adjust the value with **<↓>**,**<↑>** / **<Bild-↓>**, **<Bild-↑>**, then confirm with **<Enter>**.
3. Check that the batteries are sufficiently charged.
4. Disconnect the plug from the power supply and bring the Ikus immediately into operating room. Either acknowledge the message (**Battery operation**) on the laptop or mute it by pressing the button *Mute alarm* on the operating panel.
5. In operating room: Reconnect the *Ikus* to the power supply.

If Ikus has detected a fault

NOTICE

An overview of the messages that might occur during the start-test is given in section 15.24: Error Messages During the Start-up Test, page 158.

The display **FAULT** in the parameter table indicates that the start-test has detected a fault. Such faults may be caused, for instance, by operating errors when the system was last shut down or during the start-up procedure.

INSTRUCTION

1. Shut down the monitor program as instructed in the dialog window.
2. Use the main switch (key switch) to switch off the Ikus. IMPORTANT: The mains power switch (toggle switch) remains set to *[I]* position.
3. Wait for at least 10 minutes.
4. Commence the start procedure again (see section 8.1.3: Starting the Monitor Program, page 71).

If Ikus detects a fault again:

Do not use this Ikus.

HOTLINE **Call Service Hotline! 866.249.0128**

8.2 Intraoperative Drive Management

8.2.1 Disconnecting the Tank Unit from the Ikus

INSTRUCTION

1. Select **Drive pause** then press **<Enter>** to confirm. Confirm the decision in the dialog window by pressing the **<X>** key or the **<1>** key. The Ikus will stop. The view *Select operating mode* is displayed.
2. Disconnect both tank units from the *Ikus*.
3. Seal the driving tube connection sockets with seal plugs.

8.2.2 Selecting the Operating Mode (View Select Operating Mode)

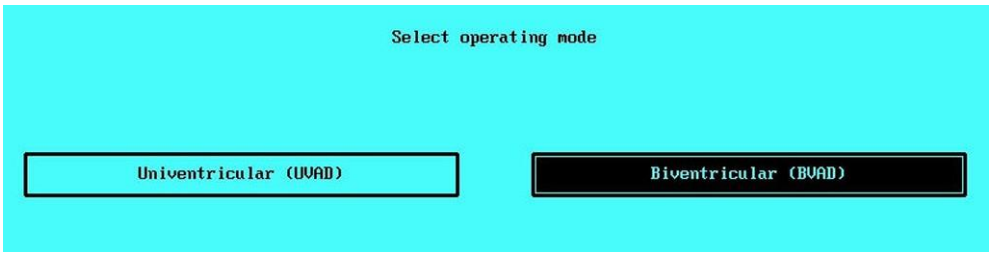


Fig. 8-2 Select operating mode

INSTRUCTION

1. In the operating room the *Ikus* should be reconnected to the mains immediately.
2. Select **Univentricular (UVAD)** or **Biventricular (BVAD)** with cursor, then confirm the selected operating mode with **<Enter>**.
3. In biventricular mode: the view *Pump size and single-step mode* appears (see Fig. 8-6, page 76).
   In univentricular mode, a connector seal test is first performed: the Ikus checks whether the driving tube connector socket with the blue marking has been sealed.

Univentricular operation: connector seal test

NOTICE

The Ikus will repeat the connector seal test up to three times. If the test is still not successful, the system will switch itself off. Please contact the service hotline.

HOTLINE

Call Service Hotline! 866.249.0128

INSTRUCTION

1. The message **Please close right outlet** is shown. Check the driving tube connector identified by a blue marking. If the connector is open: use the seal plug to close it.
2. Move the cursor to **OK** and press **<Enter>** to confirm. The *Ikus* will test whether the connector is properly sealed. If it is, the view *Pump size and single-step mode* is displayed. If not, the *Ikus* will repeat the connector seal test.

8.2.3 Select the Blood Pump Size

NOTICE

It is not possible to select a larger blood pump and/or a higher rate for the right blood pump than for the left one. The range of pump sizes available for the right blood pump is limited.

The available sizes are shown in black and red in the pop-up menu: *Select pump size*. The decision as to the appropriate combination of blood pumps and cannulae remains in the sole province of the implanting surgeon.

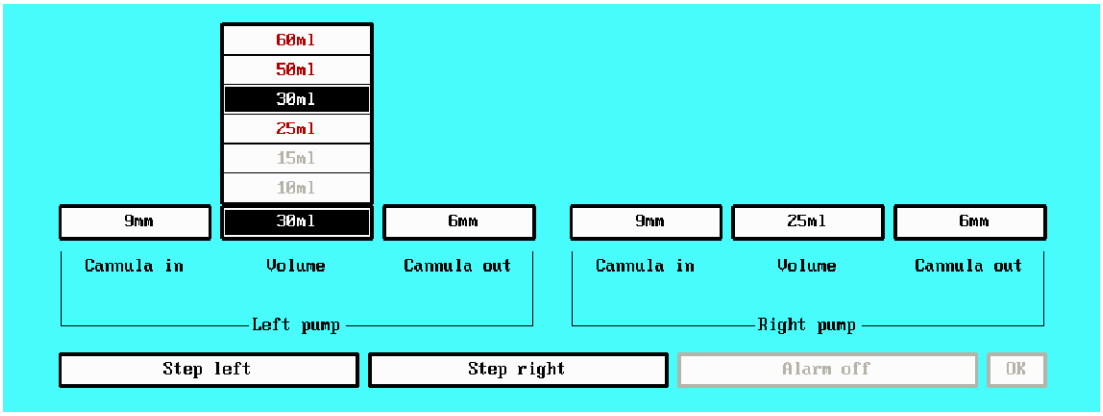
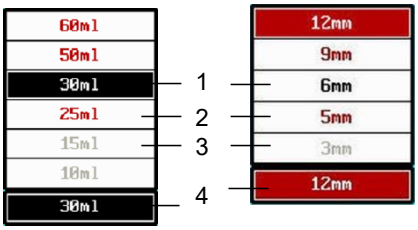


Fig. 8-3 Select the pump size



1 black/ white on black - recommended
2 red/ white on red - not recommended
3 grey - not available
4 coloured background - selected

Tab. 8-1 Meaning of colours

INSTRUCTION

1. In the pop-up menu, select the desired pump size with <↓>/ <↑>.
2. In biventricular mode: Using the cursor keys <←>/<→>, move to the field marked right pump, select the desired pump size with the cursor keys <↓>/<↑>.

8.2.4 Select the Cannula Size

NOTICE

The available sizes are shown in black and red in the pop-up menu: *Select the inflow and outflow cannula sizes* The decision as to the appropriate combination of blood pumps and cannulae remains in the sole province of the implanting surgeon.

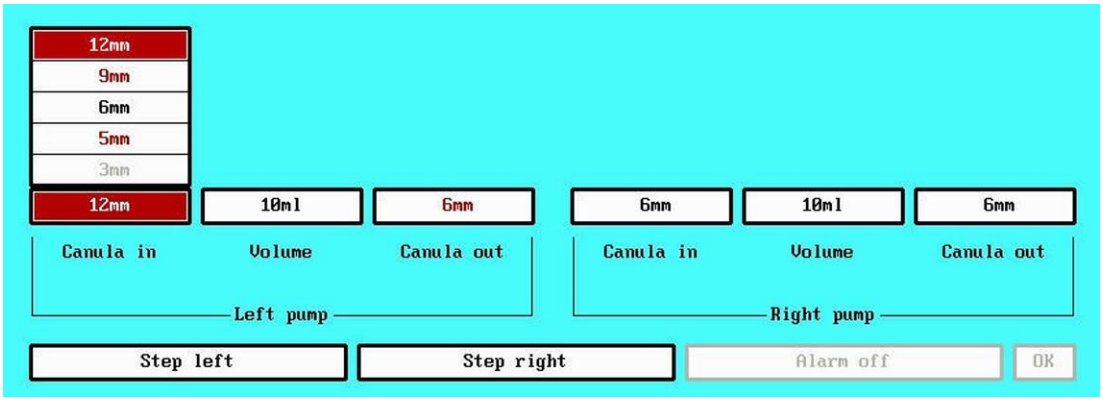


Fig. 8-4 Cannula in for the left pump

INSTRUCTION

1. From the pop-up menu **Cannula in** for the left pump, select the inflow cannula size for the left pump with <↓>/<↑>.
2. Move cursor with <←>/<→> to the pop-up menu **Cannula out** for the left pump. With <↓>/<↑> select the outflow cannula size for the left pump.
3. In biventricular mode: move the cursor with <←>/<→> to the pop-up menu **Cannula in** for the right pump, select cannula size with <↓>,<↑>.
4. Move cursor with <←>/<→> to the pop-up menu **Cannula out** for the right pump. With <↓>/<↑> select the outflow cannula size for the right pump.

8.2.5 Display Blood Pump and Cannula Sizes

It's possible to display the selected pump and cannula sizes on the laptop screen.

INSTRUCTION

1. Press **<F10>** to shut down the monitor program. Confirm the decision in the dialog window by pressing the **<X>** key or the **<1>** key.
2. The start menu is displayed.
3. In the start menu, select the option **1. Start program** (**<1>**).
4. Enter user ID and password, confirm by pressing **<Enter>**.
5. In the message window the selected pump and cannula sizes are displayed.

Fig. 8-5 Display pump and cannula sizes

8.2.6 Setting the Start-up Parameters

WARNING

To connect the blood pump(s), always set the start-up parameters!

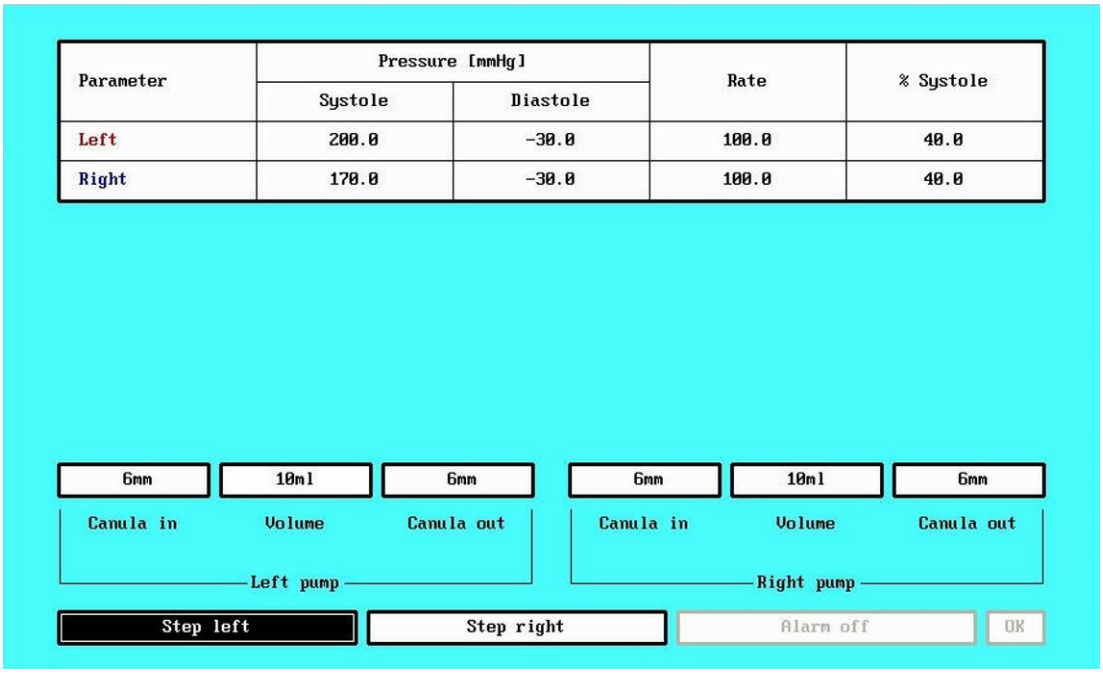


Fig. 8-6 Pump size and single-step mode

INSTRUCTION

1. Place the cursor with **<↑>** in the parameter table and navigate with **<←>/ <→>** to the desired field in the parameter table. Adjust with **<↓>**, **<↑>** /**<Bild-↓>**, **<Bild-↑>** then confirm with **<Enter>**.
2. Set the start-up parameters:

Systole [mmHg] left/ right	**Diastole [mmHg] left/ right**	**Rate [bpm]**	**Rel. systol. duration [%] left/ right**
100/ 80	-5/-5	30	40/40

Tab. 8-2 Start-up parameters

8.2.7 Connecting the Blood Pump(s) to the Ikus

WARNING

Do not kink either the driving tubes or the cannulae.

NOTICE

State of the blood pumps when they are initially connected: filled with sterile injectable saline, de-airing needle in place.

INSTRUCTION

1. Open the red driving tube connector (univentricular) or both connectors (biventricular). To do so, pull the seal plugs out of the connector(s).
2. Connect the driving tube to the Ikus by pushing the plug of the driving tube into the connector. The sound of the plug snapping into place is clearly audible. Check that the plug is securely connected. To do so, grip the plug body above the release sleeve and pull on it. Do not pull from the release sleeve, and never from the tube!
3. In biventricular mode: observe the color of the markings.
4. In biventricular mode: repeat the procedure for the second pump.

Operating mode	Ikus connector
Biventricular	LVAD: connector marked red RVAD: connector marked blue
Univentricular	Connector marked red

Tab. 8-3 Assignment: operating mode, blood pump, connector

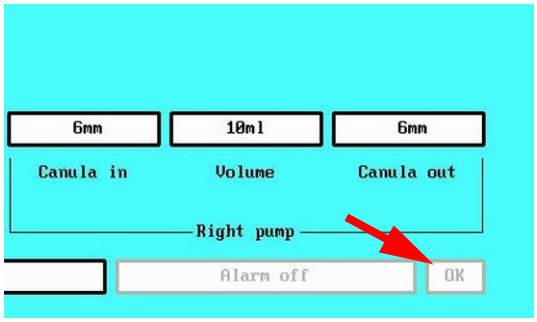
8.2.8 De-airing the Blood Pumps in Single-step Mode

NOTICE

Each de-airing step (**Step left**/ **Step right**) carries out half a pump cycle (systole or diastole), with the first step being a diastole. Normally, several de-airing steps are required for each pump. In single-step mode, the pumps will operate using the pressures shown in the parameter table. It is not possible to switch to the standard view unless at least one de-airing step has been completed for each connected pump.

INSTRUCTION

1. Put the patient into the Trendelenburg position.
2. Move the cursor to the field marked **Step left**.
3. Lift the blood pump. By doing so, infiltrated air will accumulate around the de-airing nippel.
4. To trigger a single step, press the **<Enter>** key. If necessary, use the de-airing needle to vent the air from the pump (see section 9.4: De-airing the Blood Pump, page 86). After consulting the surgeon: if necessary, press **<Enter>** repeatedly to trigger further single steps until all air has been removed from the blood pump(s). If the blood pump is not filling sufficiently, ensure there is sufficient preload and if necessary, increase the diastolic pressure.
5. In biventricular mode: move the cursor to the field **Step right**. Repeat the procedure for the second blood pump.



Transition to continuous pumping mode is not yet possible because **OK** field is still inactive.

Fig. 8-7 Single-step mode

8.2.9 Starting the Blood Pump (Changing to Standard View)

WARNING

Do not start the blood pump(s) until all air has been removed.

INSTRUCTION

1. Move cursor to the **OK** field and press **<Enter>** to confirm. The system now starts with the parameter values visible in the parameter table.

8.2.10 Checking the Parameters when the Blood Pump Is Started and Adjusting them

WARNING

In order to avoid air being sucked into the blood pump through the cannula anastomosis, adjust the parameters gradually. If air does enter the system, disconnect the driving tubes from the Ikus and de-air the system using the de-airing needle.

Continuously monitor all settings.

NOTICE

If the blood pump is not filling adequately at this stage, increase the preload by adding volume from the CPB circuit. After adding volume, adjust the parameters on the laptop of the *Ikus* as described in the following table.

INSTRUCTION

1. Observe the left blood pump. Is the blood pump ejecting completely? If not: increase the left driving pressure if necessary.
2. Observe the right blood pump. Is the blood pump ejecting completely? If not: increase the right driving pressure if necessary.

Observe	Action / measure
Left blood pump does not fill up completely	Check the central venous pressure (CVP) • CVP low: substitute the volume • CVP normal: increase the suction pressure **If there is no improvement**: perform echocardiography to check the cannula position • Under LVAD: an increase in suction pressure does not produce improvement: check the function of the right ventricle. If RV is OK, then check the cannula position. If RV function is reduced, then right ventricular support is required. • Under BVAD: check the function of the right blood pump.
Left blood pump does not empty completely	Monitor the mean arterial pressure (MAP) (guideline value 60 mmHg - 80 mmHg) • MAP normal: check the function of the blood pump, • MAP too high: reduce to guideline value
Right blood pump does not fill up completely.	Check the central venous pressure (CVP) • CVP low: substitute the volume • CVP normal: increase the suction pressure **If there is no improvement**: perform echocardiography to check the cannula position
Right blood pump does not empty completely	Check the PAP • PAP too high: reduce with medication • PAP normal: increase driving pressure

Tab. 8-4 Pump filling criteria

Keep the following points in mind with regard to filling of the right blood pump:

The aim is to reduce the right ventricle's load to a large extent but not completely. Signs that the RV load has been reduced completely are:

- filling of the blood pump depends largely on the respiratory cycle
- ventricle is empty/limp
- membrane stops abruptly during filling

IMPORTANT: If the three above-mentioned phenomena are observed, do one of the following:

- reduce the diastolic pressure
- substitute volume

Adjusting parameters

INSTRUCTION

1. Use the **<←>/<→>** keys to move the cursor to the desired field in the parameter table. The selected field is given a colored background.
2. Use the **<↓>,<↑>** or **<Bild-↓>**, **<Bild-↑>** keys to adjust the value, then press **<Enter>** to confirm the input.

Parameter	**Range possible**	**<↓>/<↑> changes value by**	**<Bild-↓>/<Bild-↑> changes value by**
Systolic pressure [mmHg]; driving pressure	60 to 350	2.5	25
Diastolic pressure [mmHg]; suction pressure	0 to -100	2.5	25
Rate [bpm]	30 to 150	1	10
Relative systolic duration [%]	20 to 70	1	10

Tab. 8-5 Parameter's possible adjustments

In biventricular operation: adjusting the operating mode

To run the blood pumps in the asynchronous mode or separate mode instead of the synchronous mode the appropriate mode must be selected.

- asynchronous mode is recommended for patients who have a small thorax volume in comparison to the pump volume. In asynchronous mode, the intrathoracic blood volume remains unchanged.
- separate mode is useful, under some circumstances, for patients with intracardiac shunts or when using on left and right blood pumps with the equal size.

INSTRUCTION

1. Use the **<←>/<→>** keys to move the cursor to the field showing the current operating mode. A pop-up menu showing the available operating modes is opened (see Tab. 8-3, page 77).
2. Select the desired operating mode with **<↓>,<↑>** and confirm with **<Enter>**. The system will now work in the selected mode.

Guideline values

The most important criterion when selecting the drive parameters is that filling and emptying of the blood pump is consistently good while employing the lowest possible systolic and diastolic pressures; the settings must be geared to achieving this goal. Monitor the filling behavior of the blood pump over several pump cycles.

NOTICE

The systolic driving pressure must be higher than the patient's physical systolic pressure. IMPORTANT: If the systolic duration (% systole) is reduced or if very small cannulae are used, it may be necessary in some cases to select a higher value than recommended here.

The actual driving pressures achieved are influenced by the diameter of the cannulae used.

8.2.11 Switching from CPB Support to VAD Support

The aim here is to reduce the CPB flow and in doing so to shift the blood volume from the CPB to the patient (i.e. to the VAD)

INSTRUCTION

1. When the blood pump(s) starts to fill, reduce the CPB flow and gradually increase the EXCOR rate from an initial 30 bpm until CPB has been terminated and the required flow is achieved. IMPORTANT: In doing so, make sure that the pump fills adequately, and if necessary regulate the driving pressure.
2. If necessary, adjust the systolic pressure, diastolic pressure and the systolic percent.

8.2.12 Possible Complications

Decreased filling after stable filling conditions

If good filling behavior is achieved at first (filling pressures LA/CVP < 10 mmHg and diastolic pulmonary artery pressure < 15 mmHg) with good drainage and nominal rate (normally 80 bpm), but the filling has deteriorated over time, it usually will not help to increase the diastolic pressure.

Deterioration in the filling behavior despite stable inflow conditions may indicate hypovolemia or obstruction of the inflow cannula. The cause of deterioration in filling behavior must be identified and addressed.

NOTICE

Manipulations during implantation can severely influence the inflow temporarily – wait for the situation to stabilize before adjusting the values.

INSTRUCTION

1. Evaluate volume status and transfuse if necessary. Evaluate and if necessary correct the cannula position.

Pump filling deteriorates when thorax is closed

If atrial cannulation is used, a slight decrease in the filling may be observed in some cases when the thorax is closed. This may be caused by compression of the atria or a slight shift in the position of the cannulae.

INSTRUCTION

1. Evaluate volume status and transfuse if necessary. IMPORTANT: Observe the effect volume replacement on the pump filling!
2. Increase suction pressure.

Distinct decrease in filling or generally poor inflow conditions on right side

INSTRUCTION

1. Make sure that there is no inflow obstruction.
2. If a suction pressure of less than -50 mmHg is necessary, increase the relative diastolic duration as an additional measure. At the same time, the systolic duration is reduced accordingly. IMPORTANT: Increase the driving pressure accordingly!

Incomplete ejection right/left

INSTRUCTION

1. Observe the arterial blood pressure, and at the same time observe the ejection movement of the blood pump membrane.
2. If complete emptying of the blood pump is no longer achieved, adjust the driving pressure accordingly. IMPORTANT: Do not respond to extreme – temporary – increases in the arterial blood pressure (due to manipulation, catecholamine, etc.).

8.3 Postoperative Drive Management

8.3.1 After Transfer to the Ward

If a good filling and stable ejection of the blood pump(s) is observed in the immediate post-operative period, it is normally not necessary to adjust the driving and suction pressures.

- Good filling means that the suction pressure is adequate.
- Stable ejection (at normal arterial blood pressure) means that the driving pressure is adequate.

NOTICE

For further details on regular monitoring of pump(s) and cannulae, see section 12.5: Regular Checks of Blood Pump(s) and Cannulae, page 113.

8.3.2 Follow-up Treatment

Guideline values and criteria for adjusting the parameter settings: see, page 81.

It is only necessary to adjust the left driving pressure when

- the arterial blood pressure increases (e. g. after lifting sedation, when the patient wakes up)
- when the patient is mobilized (moving to an upright position, sitting, standing – in order to compensate for the additional hydrostatic pressure component).

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9 Implantation - Preparations in the Operating Room

9.1 Preparing the Components and Materials Required

NOTICE

Selection of blood pump(s): see section 18.1: Overview: Product Range and Possible Combinations, page 219.

General (all sterile)

- 500 ml sterile injectable saline
- 2 small sterile basins
- 50 ml disposable syringe with luer lock connector
- suture (to secure the trocar to the de-airing nipple and the de-airing tube to the trocar)
- heavy scissors
- tube clamp
- other instruments and equipment as required for open-heart surgery

EXCOR components and accessories

- blood pump(s), each with a pump seal
- 1 driving tube for each blood pump
  - univentricular: red driving tube
  - biventricular: 1 red driving tube and 1 blue driving tube
- inflow cannula(e) (atrial or apex cannula)
- outflow cannula(e)
- accessory set (T00L-002) for blood pumps with PU valves
  - membrane set
  - de-airing set (2 x trocar, 2 x de-airing tube)
  - de-airing hammer
  - tube connecting set (cable ties, cable-tie gun)

9.2 Unpacking the Sterile Components

WARNING

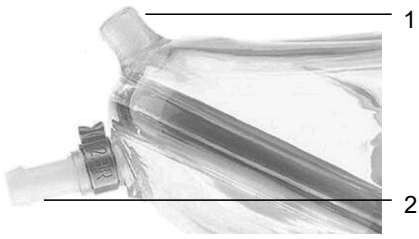
Only use sterile components which have been delivered in undamaged sterile condition (sterile packaging intact, expiration date not expired).

Only use blood pumps which have an undamaged aluminum-coated outer packaging.

INSTRUCTION

1. Blood pump: non-sterile operating room personnel opens the aluminum-coated package and removes the pump in its double sterile packaging.
2. The non-sterile person opens the outer sterile package and offers it to medical personnel in the sterile field.
3. A sterile person takes out the inner sterile package, opens it and places the components on the prepared sterile field.

9.3 Moving the Membrane to the End-of-Diastole Position



1 de-airing nipple (blood chamber)
2 driving tube connector (air chamber)

Fig. 9-1 De-airing nipple and driving tube connector

INSTRUCTION

1. Pick up adapter tube, disposable syringe (membrane set) and the blood pump.
2. Connect the adapter tube to the disposable syringe.
3. Connect the free end of the adapter tube to the driving tube connector of the blood pump.
4. Remove all air from the air chamber of the blood pump. The blood pump membrane is now in the end-of-diastole position.
5. Seal the adapter tube with a tube clamp in order to keep the membrane in this position.

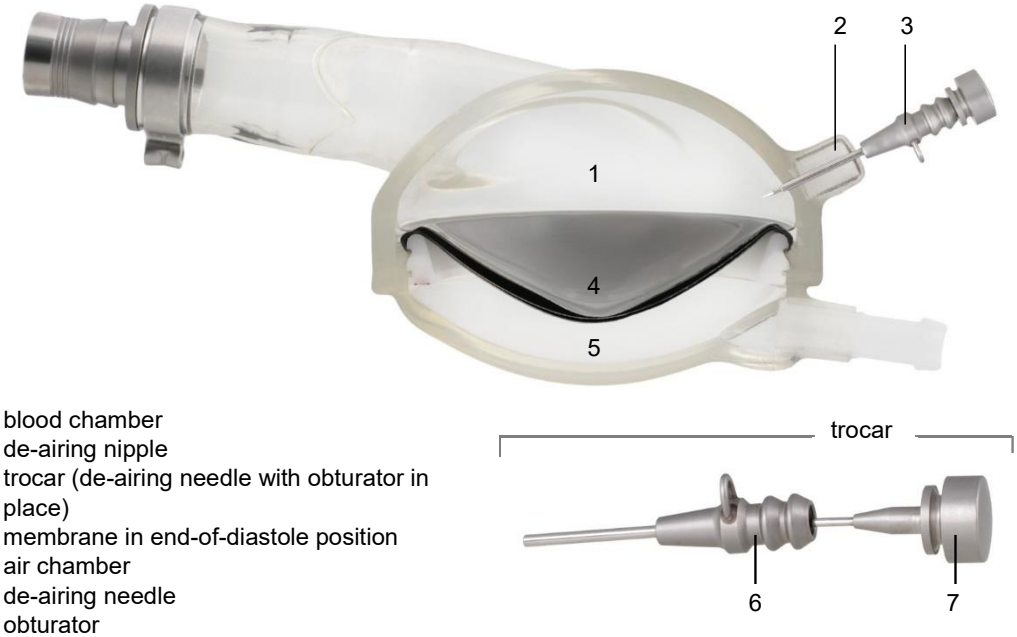
9.4 De-airing the Blood Pump

WARNING

Make sure that no particles or liquids enter the air chamber of the blood pump.

Prepare and place the following ready for use:

- blood pump(s) with pump seal(s)
- 1 de-airing set (trocar and a de-airing tube) for each blood pump
- 50 ml disposable syringe for each blood pump



1 blood chamber
2 de-airing nipple
3 trocar (de-airing needle with obturator in place)
4 membrane in end-of-diastole position
5 air chamber
6 de-airing needle
7 obturator

Fig. 9-2 Blood pump with trocar in place (de-airing needle with inserted obturator)

9.4.1 Inserting the De-airing Needle

WARNING

The membrane must be kept in the end-of-diastole position. Keep the clamped membrane set connected to the blood pump.

INSTRUCTION

1. Take hold of the trocar (de-airing needle with obturator) and remove the protective silicone cap.
2. Push the trocar as pictured above as far as it will go through the center of the blood pump's de-airing nipple. Never turn the trocar when inserting it, as this increases the risk of removing a large piece of the silicone material in the de-airing nipple.
3. Remove the obturator.
4. Use the ligature to secure the de-airing needle to the de-airing port.
5. Push the free end of the de-airing tube onto the de-airing needle as far as it will go.
6. Use the ligature to secure the de-airing tube to the trocar.
7. Withdraw the de-airing needle by approx. 2 mm. IMPORTANT: The tip of the cannula should still be visible in the blood chamber.

9.4.2 Rinsing and Filling the Blood Pump

Fill and empty the pump once or twice with sterile injectable saline:

INSTRUCTION

8. Fill the syringe with sterile injectable saline.

9. Connect the syringe to the stopcock end of the de-airing tube.
10. Slowly fill the blood chamber of the blood pump with sterile saline solution. Inspect the blood chamber for particles. If present, flush out the particles.
11. Using the de-airing hammer, tap lightly against the casing of the blood pump to dislodge any air bubbles. Expel all the air from the blood pump through the de-airing needle and outflow stub.
12. Fill the blood pump with sterile injectable saline. Rock the pump back and forth to move any bubbles to the outflow stub.
13. Close the stopcock on the de-airing tube.
14. Tap the blood pump body gently in order to free all remaining bubbles. Remove all air from the pump through the outflow connector.
15. Use the seal caps to close the titanium cannula connectors.
16. Remove the adapter tube from the pump.
17. Place the pump ready for connection with the connectors pointing up.

9.4.3 Connecting the Driving Tube to the Blood Pump

Select the driving tubes as follows:

- BVAD: Systemic circulation red, pulmonary circulation blue
- LVAD: red

INSTRUCTION

1. Connect the driving tube to the driving tube connector on the blood pump by pushing it onto the driving tube connector as far as it will go.
2. Lay out the prepared blood pump with the titanium connectors pointing upwards.

10 Implantation - Surgical Procedure

This chapter describes the product-specific measures to be observed when implanting an EXCOR blood pump. The setting of the Ikus parameters during and after implantation is described in chapter 8: First Use of Ikus and Setting Parameters, page 69. If the *Ikus* is brought into the OR, it should be prepared as described in section 8.1: Preparatory Steps Outside of the Operating Room, page 69.

Implantation is accomplished using a CPB with bicaval cannulation. Implantation can be achieved with induced ventricular fibrillation or on a beating heart Hypothermia is usually not required.

WARNING

After implantation inspect the cannulae and connections to ensure they are tight.

Do not start pump operation until the blood pump is completely free of air!

To avoid risk of damage to the steril EXCOR components, do not touch or manipulate them with pointed or sharp-edged objects (such as surgical instruments, wire brushes, etc.).

If a cannula is bent with flexible metal reinforcement to adjust it to the anatomical conditions: determine by visual inspection that the blood flow in the cannula is not restricted.

When positioning the driving tubes mitigate the risk of adverse tubing and line incidents by routing the driving tubes in a clear pattern toward the feet and to the side.

To avoid pulmonary edema when using blood pumps of equal size on the left and right, verify that the pulmonary circulation is not being overloaded.

NOTICE

For the suture use an appropriate suture material. It should be a nonabsorbable monofilament, not traumatizing material.

ADVICE

For BVAD, carry out anastomosis of the cannulae in the following order:
apical cannulation:
1. LV apex
2. right atrium
3. pulmonary artery
4. aorta

atrial cannulation:
1. left atrium
2. right atrium
3. pulmonary artery
4. aorta

ADVICE

Before surgery begins, mark on the patient the points for the exit sites of the cannulae. The aim is to achieve a stable final position of the cannulae without exerting any tension on the skin. Caution: with biventricular support, two of the four cannulae will cross each other. This crossing point should be outside of the thorax as far as possible.

10.1 Cannula Exit Sites

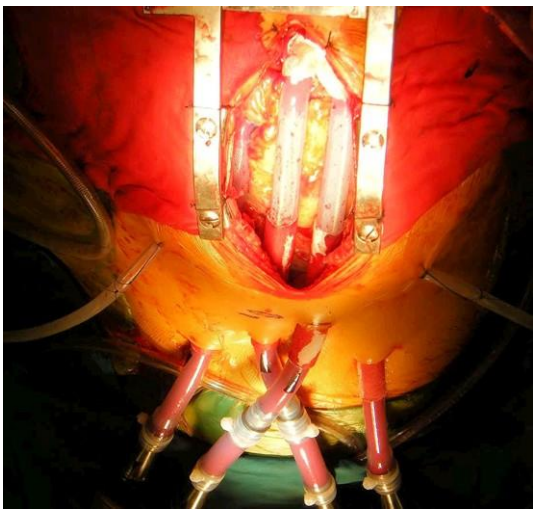
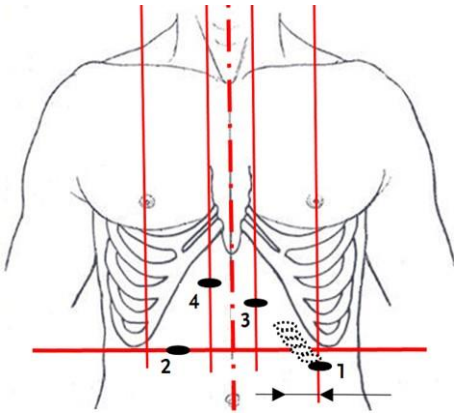


Fig. 10-1 Cannula position following implantation



1 LV apex cannula
2 RA cannula
3 PA cannula
4 Aortic cannula

Possible exit site for LV apex cannulation (depending on the size of the patient's heart)

Fig. 10-2 Suggested cannulae exit sites (Example: BVAD with LV apex cannulation)

10.2 Use of the Cannula Tunneling Tip

The cannula tunneling tip is a sterile disposable product supplied with each cannula. Sizes available: see section Fig. 10-3: Available sizes of cannula tunneling tips, page 91. Staged cannulae are supplied with 2 different tunneling tips.

INSTRUCTION

1. Push the cannula tunneling tip firmly into the distal end of the cannula.
2. Advance the forceps through the subcostal incision and the cannula tunnel into the mediastinum, so that the cannula tunneling tip can be gripped.
3. Use the forceps to firmly grip the flat end piece, pull it through the cannula tunnel and the skin incision and position it.
4. Carefully remove the tunneling tip from the cannula by bending it back and forth.

Refer to the respective cannula type as described in section 10.3: Cannulae, Cannula Extension Set and Connecting Set, page 91 to section 10.7: Arterial Cannula(e), page 99 of the IFU to determine the sequence of cannulae anastomosis and tunneling.

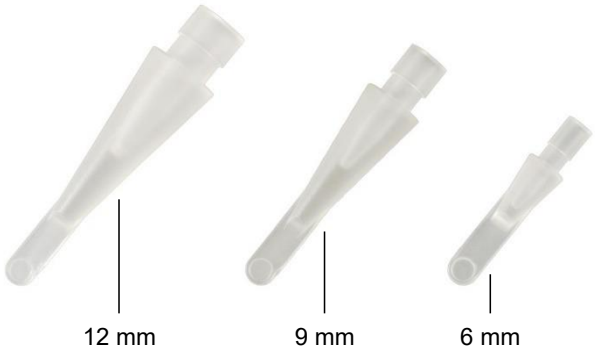
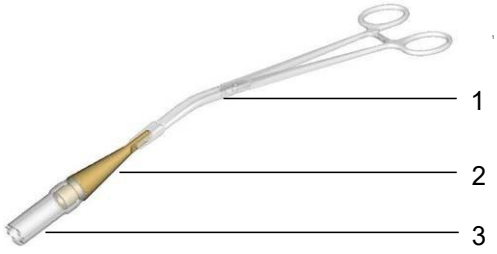


Fig. 10-3 Available sizes of cannula tunneling tips



1 Dressing forceps
2 Cannula tunnelling tip
3 Cannula

Fig. 10-4 Use of cannula tunneling tip

10.3 Cannulae, Cannula Extension Set and Connecting Set

To avoid damaging the cannulae careful attention should be paid to the following safety precautions.

The use of the cannula extension set / of the connecting set involves further safety precautions. See section 10.3.2: Instructions for Use: Cannula Extension Set and Connecting Set, page 93.

WARNING

The cannula tunneling tip (provided with each cannula) should be used during implantation of the EXCOR system.

If it is necessary to apply a clamp directly to the cannula in order to pull the cannula through the skin, the following procedures should be observed:
- Position the clamp at the distal end of the cannula
- After the cannula has been pulled through the skin, cut off and discard the part of the cannula where the clamp was applied.

If it is necessary to clamp any part of the cannula (cannula extension set / connecting set resp.) that is not covered with velour, cover the part that will be clamped with a gauze sponge.

If replacement of an EXCOR blood pump is required, the following procedures should be observed:
- The cable tie covering the EXCOR cannula on the stub of the blood pump should be removed carefully. Use an appropriate blunt tool. Never use a sharp instrument, such as scalpel or scissors, to remove the cable tie as this may damage the cannula.
- If a cannula extension set/ connecting set needs to be cut for a blood pump replacement, ensure that there will be sufficient length of the tube part remaining to meet the minimum length recommendations. See Tab. 10-1, page 94.

To ensure sufficient output, do not kink the driving tubes or cannulae needlessly.

10.3.1 Description: Cannula Extension and Connecting Sets

Berlin Heart supplies connecting sets to bridge different connector diameters in the blood pump and cannula (6/9, 9/12). This allows for greater flexibility when combining blood pumps and cannulae. The connecting set may be used during implantation or during the further course of therapy.

Berlin Heart supplies cannula extension sets for blood pumps / cannula combinations with diameters of 6 / 6, 9 / 9 and 12 / 12.

The cannula extension set is used to lengthen the piece of cannula which remains after the cannula has been shortened.

These sets could be necessary in the following contexts:

- during implantation
- when replacing a blood pump
- when cutting off a piece of cannula (due to visible deposits or damaged cannula)

The cannula extension set / connecting sets thus guarantee that the blood pump and cannulae can still be safely connected with one another and that the cannulae and titanium connectors on the blood pump can still be visually inspected.

Each cannula extension set / connecting set consists of two cannula extensions / connectors. Each cannula extension / connector comprises a double-sided titanium connector to which a piece of tube is connected on one side.

Fig. 10-5 Cannula extension: titanium connector with tube section

10.3.2 Instructions for Use: Cannula Extension Set and Connecting Set

Cannula extension set

WARNING

If, on shortening of the cannula, visual inspection of the titanium connector on the blood pump is no longer possible: use the cannula extension set. Take into account that there might be the need to shorten the cannula during a blood pump replacement.

Cannula extension set and connecting set

WARNING

There is an increased risk of thrombogenesis and deposits each time the cannula is extended. Use the cannula extension set only when absolutely necessary.

To avoid loose connections and insufficient blood supply to the patient, potentially resulting in injury or death, secure each connection between blood pumps, driving tubes, cannulae, extension sets and/or connection sets with at least one cable tie as soon as the proper function of EXCOR is established (see section 10.11: Securing the Connections, page 103).

All efforts shall be made to minimize the manipulation and distortion of the blood pumps, cannulae, cannula extension set and connecting set during the removal of the cable ties to prevent damage and mobilization of deposits.

When using a cannula extension set / a connecting set it may be necessary to shorten the respective connecting tube, however, take care to ensure that the minimum length of the cannulae maintained. . See Tab. 10-1, page 94.

Article	Diameter	Minimum length
Cannula extension set		
A06-006	6 mm	55 mm
A09-009	9 mm	60 mm
A12-012	12 mm	75 mm
Connecting set		
A06-009	From 6 mm to 9 mm (blood pump connector)	60 mm
A09-012	From 9 mm to 12 mm (blood pump connector)	75 mm

Tab. 10-1 Cannula extension set / connecting set: minimum length of tube section

Ensure that the cannulae are no longer than necessary for the purposes of therapy. Shorten the cannulae, if necessary, since they may otherwise be prone to kinking. Avoid shortening the cannula too much so as to prevent an overlap of the connector end and velour, and to ensure that visual inspection of the cannula and connector, respectively, is still possible. Pay attention also to Tab. 10-1, page 94.

Preparation

INSTRUCTION

1. Take hold of the cannula extension set (the connecting set respectively).
2. If necessary: cut the section of tube to the desired length. Cut perpendicular to the axis of the tube section and ensure a straight cut. Ensure that the required minimum length is maintained. See Tab. 10-1, page 94. Ensure that the end position of the tube sections, cannulae and blood pump are free of tension.
3. Make sure that the cannulae are free of deposits.

During implantation / when replacing a blood pump

INSTRUCTION

1. Connect the cannula extensions (the connectors respectively) with the blood pump. To do so, push the section of the cannula extension (the connector resp.) onto the titanium connector of the blood pump. Prime the blood pump with the cannula extensions (with connectors resp.).
2. Connect the cannula extensions (the connectors respectively) to the cannulae. To do so, push each cannula onto the titanium connectors of the cannula extension (of the connectors respectively) while flushing with sterile injectable saline solution.
3. Proceed according to context. See section 9.3: Moving the Membrane to the End-of-Diastole Position, page 86 and section 16.1: Replacing the Blood Pump(s), page 165.

Without replacing a blood pump

INSTRUCTION

1. Push the free end of the cannula onto the titanium connector of the cannula extension (of the connector respectively).
2. Flush the tube sections with sterile injectable saline solution.
3. Push the sections of tube, which are free of air, onto the titanium connectors of the blood pump.
4. Proceed according to context. Act according to 16.1.2, page 166 and 16.1.3, page 167 respectively but without replacing the blood pump.

Securing the connections

INSTRUCTION

1. Secure each connection between silicone tube and titanium connector with at least 1 cable tie. See section 10.11: Securing the Connections, page 103.

10.4 Access

INSTRUCTION

1. Median sternotomy. Make sure that there is absolutely no bleeding.
2. Insert standard cardiopulmonary bypass cannulae (bicaval cannulation).
3. Initiate extracorporeal circulation.
4. Place a vent in the left atrium, if necessary.

10.5 Apex Cannula

Refer to section 10.2: Use of the Cannula Tunneling Tip, page 91.

10.5.1 Anastomosis of Inflow Cannula with LV Apex

WARNING

During anastomosis of the LV apex cannula, make sure that the cannula head is facing in the right direction: the long side of the head should be parallel to the lateral wall. This prevents the ventricular lateral wall from being sucked into the tip of the cannula. After the cannula head has been placed, its position can be checked by means of the flow direction arrow on the cannula body (except apex cannulae C14A-040, C18A-020). The arrow is aligned with the long side of the cannula head (see Fig. 10-8, page 96).

INSTRUCTION

1. If indicated, initiate ventricular fibrillation as needed.
2. Apical excision of the LV: The ideal implant position of the LV cannula is slightly off-center of the LV apex toward the lateral wall. The distance from LAD/ septum to the center of the excised muscle core is about 2 cm for children (see 1 in Fig. 10-8, page 96).
3. We recommend that a circular apical core with a diameter slightly smaller than the size of the cannula head be excised.
4. Start with muscle core incision on the side away from the septum/ LAD (see 2 in Fig. 10-8, page 96) to avoid septal injury.
5. Check left ventricle for thrombi and excise the excess trabeculae.

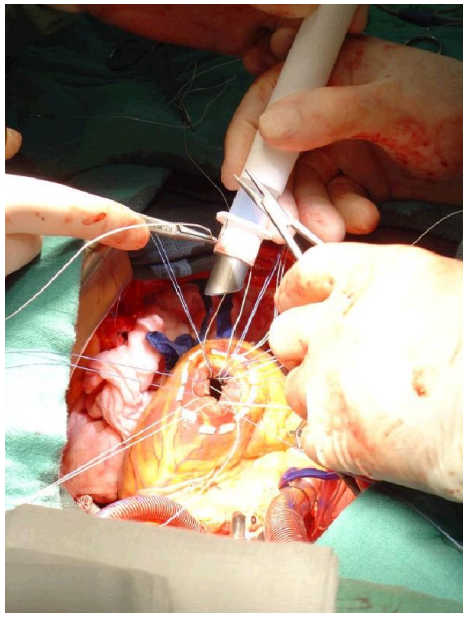


Fig. 10-7 Anastomosis of LV apex cannula

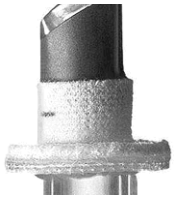


Fig. 10-6 Head of LV apex cannula

1 Long side of LV apex cannula head

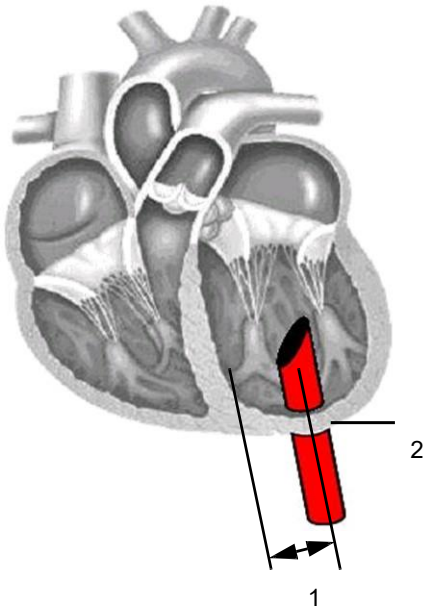


Fig. 10-8 Ideal position of the LV apex cannula

1 ca. 2 cm
2 see point 4 of instructions

10.5.2 Creating a Transcutaneous Tunnel for the LV Apex Cannula

WARNING

Make sure that cannulae come to rest in a stable position without tension.

The incision must be slightly smaller than the cannula diameter (to ensure good ingrowth) but large enough to prevent necrosis.

Plan the cannula exit sites appropriately. Leave an adequate bridge of skin and subcutaneous tissue between the cannula exit incisions to prevent breakdown and necrosis of the skin and tissue. If possible, the cannula exit sites should be on different planes (see Fig. 10-2, page 90).

INSTRUCTION

1. Prepare the transcutaneous tunnel. Ensure that the incision is large enough.
2. Incise the pericardium widely in a lateral direction. Prepare the cannula tunnel by blunt dissection. IMPORTANT: Do not tunnel transperitoneally.
3. Tunnel the LV apex cannula through the transcutaneous passage by using a pair of forceps to firmly grip the flat end piece of the tunneling tip and pull it through the cannula tunnel and the skin incision.
   IMPORTANT: Do not rotate the cannula while pulling it through the tunnel. At the end of this procedure, the apex of the heart should be in its native position without torsion.
4. De-air the cannula in a retrograde direction. Clamp the cannula outside of the body.
5. Terminate ventricular fibrillation if necessary.

10.6 Atrial Cannula(e)

Refer to section 10.2: Use of the Cannula Tunneling Tip, page 91.

ADVICE

For atrial cannulae supplied with a flexible reinforcement, the transcutaneous tunnel should be created and the cannula advanced through the tunnel and skin incision prior to the anastomosis.
For all other atrial cannulae, the sequence is arbitrary.

10.6.1 Creating a Transcutaneous Tunnel for Atrial Cannula(e)

WARNING

Make sure that cannulae come to rest in a stable position without tension.

Using a pair of forceps, firmly grip the flat end piece of the tunneling tip and pull it through the cannula tunnel and the skin incision.
IMPORTANT: Do not rotate the cannula while pulling it through the tunnel.

The incision must be slightly smaller than the cannula diameter (to ensure good ingrowth) but large enough to prevent necrosis.

Plan the cannula exit sites appropriately. Leave an adequate bridge of skin and subcutaneous tissue between the cannula exit incisions to prevent breakdown and necrosis of the skin and tissue. If possible the cannula exit sites should be on different planes.

INSTRUCTION

1. Prepare the transcutaneous tunnel. Ensure that the incision is large enough.
2. Prepare the cannula tunnel by blunt dissection. IMPORTANT: Do not tunnel transperitoneally.
3. Using a pair of dressing forceps, tunnel the cannula through the transcutaneous tunnel. IMPORTANT: Do not rotate the cannula while pulling it through the tunnel.

10.6.2 Anastomosis of Atrial Cannulae

Right atrium

ADVICE

Create the anastomosis laterally, directly above the tricuspid valve.

a) Closed technique

INSTRUCTION

1. Make a running (purse-string) suture with monofilament, secured with pledgets at 4 positions.
2. Place 4 single U-sutures secured with pledgets on each side of the purse string suture.
3. Make a sufficiently long incision inside of the suture circle and extend it as required.
4. Push the cannula down on the sutures, at the same time slightly reduce the venous inflow to the CPB while inflating the lung in order to prevent negative pressure in the left atrium.
5. Remove all air by flushing the cannula and use a tube clamp to clamp the cannula below the exit sites.

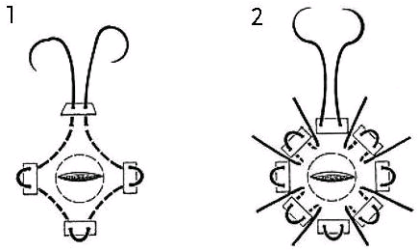


Fig. 10-9 Suture technique, right atrium

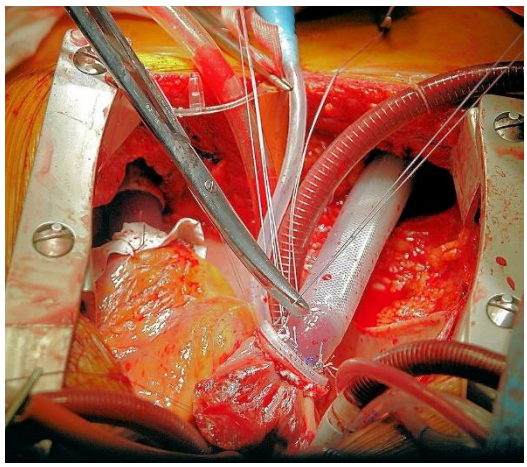


Fig. 10-10 Cannulation of right atrium

b) Open technique with bicaval cannulation

With bicaval cannulation, the right atrial cannula can be inserted in an open technique.

Left atrium

The procedure for anastomosis of the left atrium corresponds to the procedure applied to the right atrium.

ADVICE

Place anastomosis at the junction of the right upper pulmonary vein and the left atrium. The atrial wall is the recommended implantation location. The pulmonary vein should be left intact.

10.7 Arterial Cannula(e)

Refer to section 10.2: Use of the Cannula Tunneling Tip, page 91.

ADVICE

For cannulae supplied with a flexible reinforcement, the transcutaneous tunnel should be created and the cannula advanced through the tunnel and skin incision prior to the anastomosis.

10.7.1 Creating a Transcutaneous Tunnel for Arterial Cannula

WARNING

Make sure that cannulae come to rest in a stable position without tension.

Using a pair of forceps, firmly grip the flat end piece of the tunneling tip and pull it through the cannula tunnel and the skin incision. IMPORTANT: Do not rotate the cannula while pulling it through the tunnel.

The incision must be slightly smaller than the cannula diameter (to ensure good ingrowth) but large enough to prevent necrosis.

Plan the cannula exit sites appropriately. Leave an adequate bridge of skin and subcutaneous tissue between the cannula exit incisions to prevent breakdown and necrosis of the skin and tissue. If possible the cannula exit incisions should be on different planes (see Fig. 10-2, page 90).

INSTRUCTION

1. Prepare the transcutaneous tunnel. Ensure that the incision is large enough.
2. Prepare cannula tunnel by blunt dissection. IMPORTANT: Do not tunnel trans-peritoneally.
3. Using a pair of forceps, firmly grip the flat end piece of the tunneling tip and pull it through the cannula tunnel and the skin incision. IMPORTANT: Do not rotate the cannula while pulling it through the tunnel.

10.7.2 Anastomosis of the Arterial Cannula

Aorta

INSTRUCTION

1. Tangentially clamp the ascending aorta and make a longitudinal opening of a length which is suitable for the cannula diameter. If necessary, offset the incision laterally to the right by up to 45°.
2. Anastomose the cannula using ten teflon-backed double-reinforced individual monofilament (e. g. 4-0 EB) U-sutures. (If simpler conditions are encountered, a running suture can be made instead.)
3. Remove all air from the cannula and use a tube clamp to clamp the cannula below the exit sites. If it is necessary to clamp any part of the cannula that is not covered with velour, cover the part of the cannula that will be clamped with a gauze sponge.

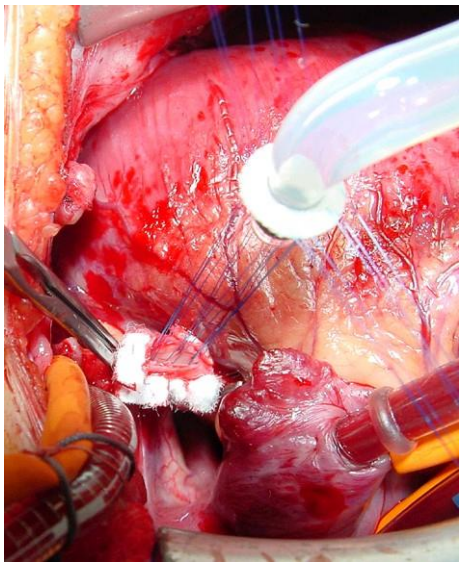


Fig. 10-11 Anastomosis of the aortic cannula

Pulmonary artery

INSTRUCTION

1. Make a longitudinal incision of a size suitable for the cannula diameter in the pulmonary artery.
2. Anastomose the cannula using 10 teflon-backed, double-reinforced individual monofilament (e. g. 4-0 EB) U-sutures. (If simpler conditions are encountered, a running suture can be made instead.)
3. Remove all air from the cannula and use a tube clamp to close it below the exit sites. If it is necessary to clamp any part of the cannula that is not covered with velour, cover the part of the cannula that will be clamped with a gauze sponge.

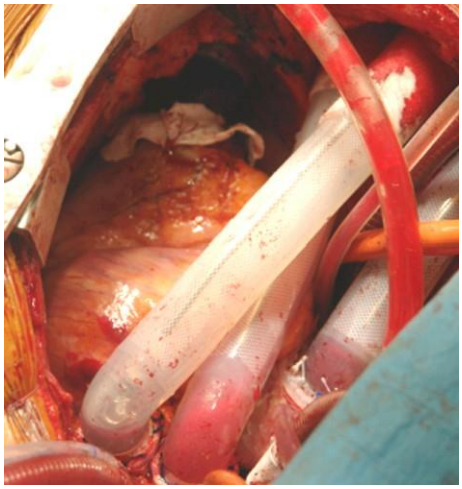


Fig. 10-12 Cannulation of the pulmonary artery

10.8 Shortening the Cannulae if Necessary

WARNING

If an EXCOR cannula extension set or connecting set is required for implantation and the length of the tube part needs to be reduced, the tube part should be cut but only to achieve the minimum lengths: see Tab. 10-1, page 94.

INSTRUCTION

1. Cut the cannulae to the required length. Make the cut perpendicular to the cannula axis and ensure that the cut is straight.
2. Make sure that the lengths of the 2 cannulae leading to the same pump match. It must be possible to connect the cannulae to the pump without having to exert any tension.

10.9 Connecting the Blood Pumps to the Cannulae

WARNING

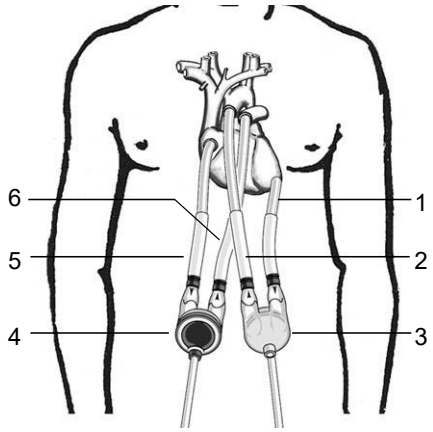
Ensure that cannulae, blood pump(s) and driving tubes are not subject to external forces and are free of kinks or sharp bends.

Type of support	Anastomosis of inflow cannula to	Points upwards ...
Univentricular		
LVAD	Apex	Blood chamber
LVAD	Atrium	Air chamber
Biventricular		
LVAD	Apex	Blood chamber
LVAD	Atrium	Air chamber
RVAD	Atrium	Air chamber

Tab. 10-2 Anastomosis and direction of the blood chambers

INSTRUCTION

1. Put the patient into the Trendelenburg position.
2. Release the tube clamps, flush the cannulae and then use tube clamps to clamp the cannulae below the exit sites. If it is necessary to clamp any part of the cannula that is not covered with velour, cover the part of the cannula that will be clamped with a gauze sponge.
3. First connect the inflow cannula to the pump, then connect the outflow cannula. When doing so, add sterile injectable saline with a bulb syringe in order to connect the pump air free. Be careful to avoid damaging the gloves, the inner cannula (lumen) and blood pump surfaces.
4. Release the tube clamps, de-air the blood pump(s) and the cannulae.



1 inflow cannula from LV apex
2 outflow cannula to ascending aorta
3 left pump (blood-chamber pointing upwards)
4 right pump (air-chamber pointing upwards)
5 inflow cannula from right atrium
6 outflow cannula to pulmonary artery

Fig. 10-13 Final position of the blood pumps, for example: BVAD with LV apex cannulation

10.10 Removing the De-airing Needle

WARNING

Before removing the de-airing needle, be sure that the de-airing tube is secured to the de-airing needle.

When removing the de-airing needle, do not pull on the de-airing tube, but on the de-airing needle itself. see also Fig. 9-2, page 87)

Once the de-airing needle has been removed it should not be re-inserted.

Do not remove the de-airing needle until all air is removed, the blood pump is running, all parameters have been adjusted and the chest has been closed. (see section 8.2.10: Checking the Parameters when the Blood Pump Is Started and Adjusting them, page 78).

INSTRUCTION

1. Cut the suture material between the de-airing needle and the de-airing nipple (see image 1 in Fig. 10-14, page 102). IMPORTANT: Leave the ligature around the de-airing nipple (see image 2 in Fig. 10-14, page 102).
2. Pull the de-airing needle out of the de-airing nipple.

Fig. 10-14 Removing the de-airing needle

After the patient has been weaned from the CPB and the proper function of EXCOR is established, the connections of the driving tubes and cannulae to the blood pump(s) have to be secured.

10.11 Securing the Connections

10.11.1 Using the Cable Tie Gun

The cable tie gun contained in the accessory set (T00L-002) is preset for appropriate tension. The setting must not be changed.

1 Tie entry
2 Trigger

Fig. 10-15 Cable tie gun

INSTRUCTION

1. Loop the cable tie around the cannula. Tighten the cable tie by hand. Pay attention to the proper position of the cable tie. See section 10.11.2: Positioning of the Cable Ties, page 104

2. Position the cable tie gun at the head of the cable tie

3. Operate the trigger until the cable tie is automatically cut off.

10.11.2 Positioning of the Cable Ties

WARNING

All connections have to be secured by at least one cable tie. Two cable ties may be used. Exception: connection between driving tube and driving tube connector of the blood pump: one cable tie only!

INSTRUCTION

1. Secure the following connections:
   - inflow cannula on the connector of the blood pump / cannula extension set / connecting set
   - outflow cannula on the connector of the blood pump / cannula extension set / connecting set
   - cannula extension set / connecting set on the connector of the blood pump
   - driving tube on the driving tube connector
2. The first cable tie must be positioned exactly on the groove profile of the connector (*1*). IMPORTANT: The heads of the cable ties have to be directed away from the patient‘s body.
3. Fasten the cable ties by the cable tie gun.

Fig. 10-16 Cable tie, exactly positioned

4. A second cable tie can be used optionally. If a second cable tie shall be used (*2*) it has to be positioned next to the first cable tie. IMPORTANT: the heads of the cable tie straps should both be staggered and directed away from the patient‘s body.

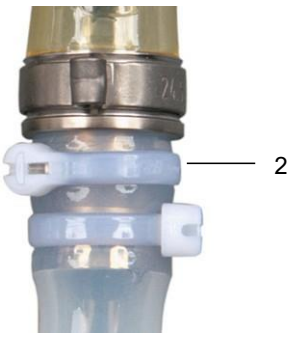


Fig. 10-17 Second cable tie (optional)

11 Implantation - Anesthesia

The following risk factors should be closely monitored for anesthetic and hemodynamic management:

- right heart function during LVAD implantation
- coagulopathy
- renal insufficiency
- abnormal reactions to inotrope administration
- pulmonary hypertension

CAUTION

Ensure that an adequate supply of pre-matched stored blood, fresh frozen plasma and platelet concentrates is available for immediate transfusion if required.

Keep blood product transfusions to a minimum. Blood transfusions may lead to the development of antibodies, which are known to promote coagulation and inflammatory response.

ADVICE

Medication for right ventricular afterload reduction should be available for use in the operating room (nitric oxide NO, phosphodiesterase inhibitor, prostaglandin, etc)

Auto-transfusion equipment (e. g. Cellsaver) should be available for use in the operating room.

For patients with an LVAD, start ventilation with nitric oxide or administer the appropriate medication to treat pulmonary hypertension and reduce afterload for right ventricle 15 minutes before weaning from the CPB. This can help to prevent or lower the risk of right ventricular failure.

Monitoring procedure

Intraoperative monitoring should include the same monitoring procedures applied during major cardiothoracic surgery:

- central venous line
- Swan-Ganz catheter (if appropriate)
- arterial line
- ECG
- pulse oximetry
- central temperature monitor
- urine catheter

Additional recommended monitoring procedures

- cardiac output calculation (if appropriate)
- intraoperative transesophageal echocardiogram (inflow cannula position, heart valve function, intracardial shunts, volume status
- right heart function in case of LVAD

Any other monitoring processes can be used (e. g. neurological monitoring) at the anesthesiologist's discretion.

12 Wound Care and Treatment

Cannula exit sites should be treated like open wounds. The patient's wounds should always be attended to by a small group of nurses in the inpatient area.

The only way to ensure a minimum risk of infection is to provide good wound care.

WARNING

Before cleaning the wound (see section 12.3: Cleaning of the Wound, page 109), put on sterile disposable gloves, cap and mask.

Cleaning the blood pump, extension set, connecting set and the driving tube: do not use any acetone or petroleum based products near the blood pump or driving tube.
Use only water or alcohol to clean the blood pump and the driving tube.
IMPORTANT: Do not use any corrosive or colored solutions or organic solvents to clean the blood pump or the driving tube as they may alter the surface of the product.

Cleaning the cannulae and transcutaneous exit sites: do not use any acetone or petroleum based products near the cannulae and the transcutaneous exit site.
Use chlorhexidine to clean the cannulae and transcutaneous exit site.
IMPORTANT: Do not use any corrosive or colored solutions or organic solvents to clean the cannulae and the transcutaneous exit site as they may alter the surface of the product.

NOTICE

Do not stick bandages to the cannulae. Over time, remnants of adhesive contaminate the cannulae and increase the risk of infection.

Do not use any adhesive on the velour coating of the cannula as it is difficult to remove and may adversely manipulate the cannula.

Do not use organic solvents near EXCOR such as petroleum, ether or turpentine oil, as they could damage the cannulae and the blood pumps. The plastic parts should not be in contact with chlorinated hydrocarbon (e.g. chloroform), thinners (e.g. acetone, naphtha, toluol, xylene, heptane) or similar compounds.

Do not mark or write on the plastic parts.

Material required (with biventricular access)

- sterile dressing tray
- disinfectant i.e. 2 % chlorhexidine solution
- clean gloves
- mask
- sterile gloves and towel
- *Metalline*® drain compress
- 2X2 gauze, 4X4 gauze
- adhesive dressing (i.e. *Mepore*®)
- adhesive remover
- non sting barrier film sticks
- abdominal pads
- tape
- tubular bandage (i.e. *Burnnet*)

How often to change the dressing

If the wound is dry and not infected:

- POD 1- once a day
- POD 11-28 every second day, if the wound is dry and not infected
- POD > 28 twice a week, if the wound is dry and not infected

If the wound shows signs of infection: clean wound and change dressing twice a day

12.1 Removing the Old Dressings

INSTRUCTION

1. Unpack all the material required to dress the wound and place this within reach on a sterile sheet.
2. Put on disposable gloves, remove old dressings.
3. Take off the disposable gloves, put on the sterile gloves.
4. Remove old dressing using no-touch technique.
5. Examine the places where the cannulae pass through the skin and if changes are apparent take appropriate measures if necessary.
6. Use adhesive remover to remove any adhesive dressing.
   IMPORTANT: Adhesive remover (depending on contents) might damage cannula and the pump, use only on skin.

12.2 Cleaning the Blood Pump

INSTRUCTION

1. Cleanse the exposed cannula and the pump head with disinfectant (i.e. 2 % chlorhexidine solution) then place on sterile towel.
2. Examine cannulae and cannulae exit sites.
3. Remove gloves.

Fig. 12-1 Cleaning the blood pump

Fig. 12-2 Examining the cannulae

12.3 Cleaning of the Wound

INSTRUCTION

1. Observe hand hygiene, prepare sterile dressing tray, put on sterile gloves. If assistance is necessary notify Berlin Heart.
2. Clean each cannula exit site using 4X4 gauze soaked in 2 % chlorhexidine in a circular motion outward to a radius of approximately 10 cm (4 inch).
3. Using a new soaked 4X4 repeat two more times beginning at the exit site and clean in larger circles each time.
4. Wrap 4X4 gauze soaked in 2 % chlorhexidine around cannula and gently cleanse with back/forth motion.
5. Repeat with each cannula exit site.

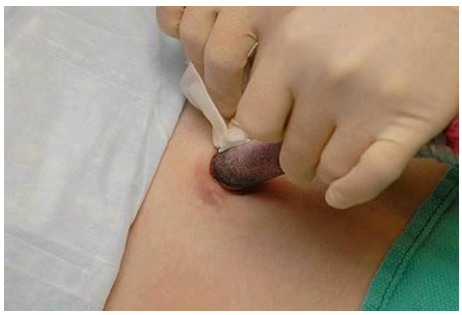


Fig. 12-3 Cleanse each cannula exit site

Fig. 12-4 Cleanse with back/forth motion

6. Cleanse entire cannula (upper and bottom side).
7. 4 X4 gauze soaked in 2 % chlorhexidine solution.
8. Starting at the exit site moving down cannula approximately 10 cm (4 inch) from exit site.
9. Repeat for each cannula exit site.
10. Allow chlorhexidine to dry completely.

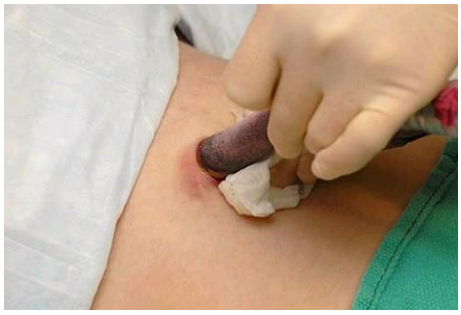


Fig. 12-5 Cleanse entire cannula

12.4 The New Dressing

12.4.1 Preparing a New Dressing

INSTRUCTION

1. Apply non sting barrier film to skin around cannulae. Non sting barrier prevents skin maceration around cannula exit sites.

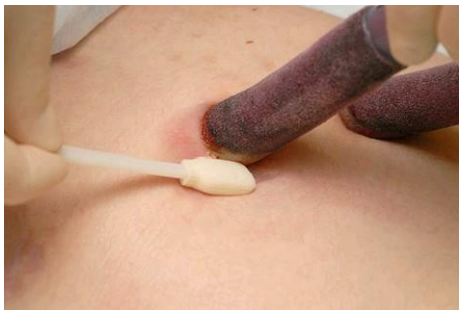


Fig. 12-6 Non sting barrier film

12.4.2 Applying a New Dressing

INSTRUCTION

1. Wrap a *Metalline* drain compress around each cannula (from right to left, slit always facing upwards).

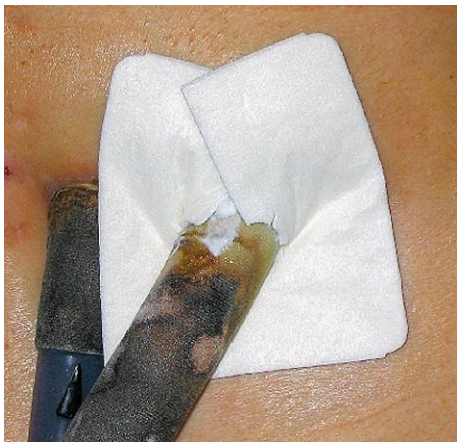


Fig. 12-7 Metalline drain compress

2. Attach the *Metalline* drain compresses above the cannulae using sterile bandages. First secure the outer compresses, then the inner compresses.

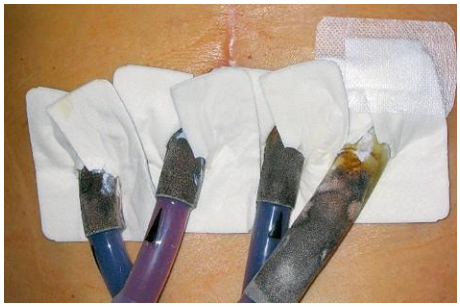


Fig. 12-8 Secure with a sterile bandage

3. Pass a gauze compress folded lengthwise beneath the two left cannulae. The open end of the folded compress should point in the direction of the wound. Pull the cannulae into place by tugging the compress slightly.

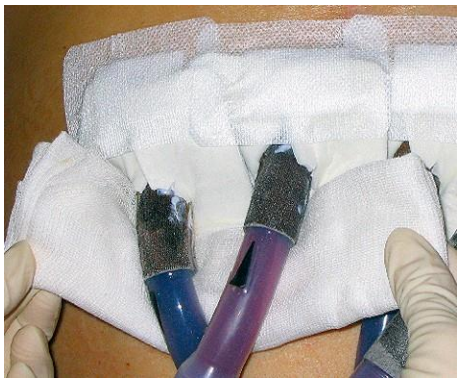


Fig. 12-9 Gauze compress under the cannulae

4. Fold the left end of the compress upwards, diagonally to the right and secure with a sterile bandage.

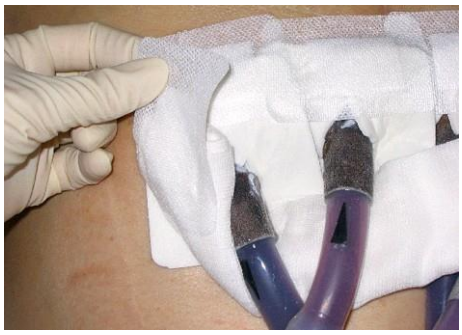


Fig. 12-10 Fold the left end of compress and secure

5. Fold the right end of the compress upwards, diagonally to the left and secure with a sterile bandage.

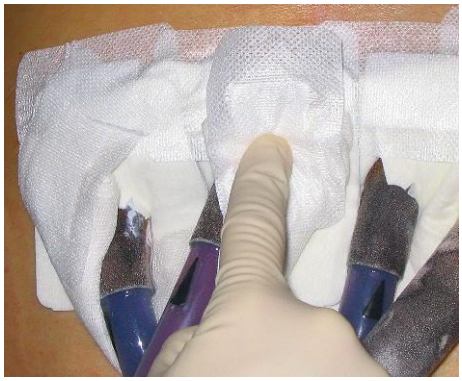


Fig. 12-11 Fold the right end of compress and secure

6. Repeat this procedure for the two right cannulae. In this way, the four cannulae are padded so that they do not press on the skin or wound.

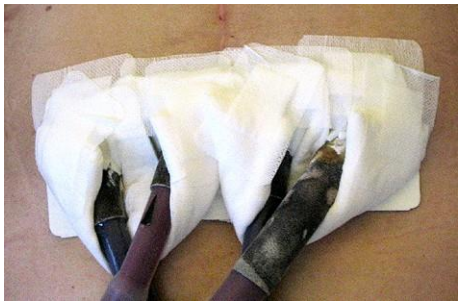


Fig. 12-12 Cannulae are padded

7. Cover the entire wound broadly with gauze compresses.

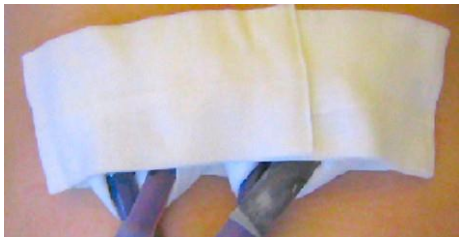


Fig. 12-13 Cover with sterile gauze compresses

8. Secure the upper part of the dressing with a sterile bandage.

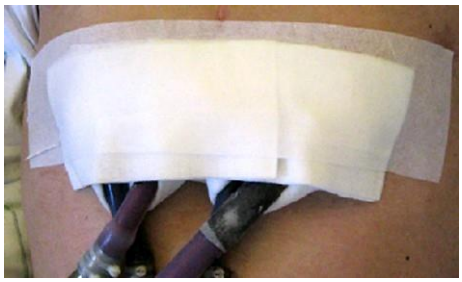


Fig. 12-14 Secure with a sterile bandage

9. Finally, seal the dressing at the left and right side, below the cannulae and between the individual cannulae with strips of adhesive bandage (e. g. Leukoplast).

Fig. 12-15 Seal with strips of adhesive bandage

10. Place tubular bandage (i.e. *Burnnet*) around patient.
11. Tie in front to secure dressing.

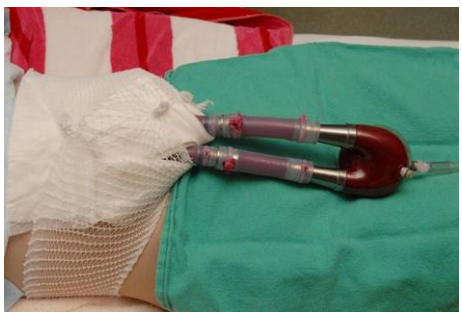


Fig. 12-16 Tubular bandage

12.5 Regular Checks of Blood Pump(s) and Cannulae

Frequency of inspection: every four hours

WARNING

Medical personnel caring for an EXCOR patient must be trained to carry out a visual check, to evaluate the filling behavior of the blood pump(s) and to detect deposits.

At least every four hours, check to be sure that the blood pumps, visible part of cannulae, cannula extension set and connecting set for deposit formation, that they show no signs of damage and that the blood pump(s) are filling and ejecting completely over a period of several pump cycles. If a blood pump is not filling and/or ejecting completely institute the appropriate corrective action (Tab. 16-1, “Possible problems,” on page 183). Verify that the blood pump is not damaged, which can result in injury or death to the patient.

When changing the wound dressings, the covered part of the cannulae shall be inspected for signs of wear or damage. (for interval see “Wound Care and Treatment” on page 107)

In case of floating deposits the blood pump must be replaced.

To avoid kinking of the cannulae and insufficient blood pump output, use a mirror for inspection of the bottom of the blood pump.

12.5.1 Visual Inspection: Pump Filling and Ejection

The filling and ejection behavior of a blood pump is optimal when the membrane surface is completely smooth at the end-of-systole and end-of-diastole positions. Check visually that the pump(s) is (are) filling and ejecting completely over a period of several pump cycles. If a blood pump is not filling and/ or ejecting completely, take the appropriate corrective action.

Cautionary measures

For all blood pumps: check the position and condition of the driving tube and the cannulae (inflow deterioration due to kinks in cannulae/driving tubes is rather rare).

For all blood pumps: check the membrane movement.

Medical examination of patient

Check CVP, mean arterial pressure and adjust therapy if necessary.

Check the volume status:

- amount of bleeding
- increased urine output (use of diuretics?)
- tamponade
- IMPORTANT: Increasing the suction pressure will not bring about any distinct improvement if there is not sufficient volume available.

LVAD: observe the functions of the right ventricle.

Adjusting the parameter values

Only adjust the parameters if the measures listed above have no effect or in case of:

- Mobilization of patient: adjust the systolic pressure, both left and right. When pressures have increased, do not reduce these again, even when the patient is lying down.
- Signs of low cardiac output: the membrane is moving properly while at the same time a decrease in urine output, lactate increase and dyspnea (shortage of breath) can be observed. In this case, increase the rate and adjust other settings as required.

INSTRUCTION

1. Use the **<←>/<→>** keys to move the cursor to the desired field in the parameter table. The selected field is given a colored background.
2. Use the **<↓>**,**<↑>** and **<Bild-↓>**, **<Bild-↑>** keys to adjust the value, then press **<Enter>** to confirm the input. The system will now operate using the new settings.

Cautionary measure

Confirm each changed parameter value by pressing **<Enter>**. The system does not take over the new, changed value until it has been confirmed with **<Enter>**.

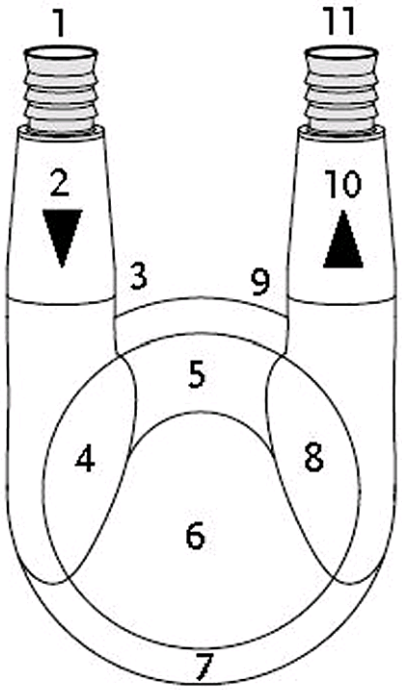
ADVICE

Enter all the changes to the parameter values into the parameter log. (see section 18.7: Pump Performance Flow Sheet, page 239).

12.5.2 Visual Inspection: Deposits

Check the blood pump(s) and the visible part of the cannulae (cannula extension set / connecting set respectively) for visible deposits (fibrin, clots) every four hours. If deposits develop, check the pump(s) every hour.

Checking the pump areas which come in contact with blood



1 transition inflow cannula – inflow connector
2 inflow stub in front of inflow valve
3 inflow valve
4 inflow stub behind inflow valve
5 area between inflow and outflow stubs
6 remaining area of blood chamber
7 transition blood chamber - membrane (directly above the reinforcement ring)
8 outflow stub in front of outflow valve
9 outflow valve
10 outflow stub behind outflow valve
11 transition outflow connector – outflow cannula

Fig. 12-17 Diagram of EXCOR blood pump (top view of blood chamber)

ADVICE

During the visual check, first clean the blood pump. Then illuminate the blood chamber with a flashlight. This makes it easier to detect deposits. Enter all of the findings into the blood pump log. (see section 18.6: Sample Copy: EXCOR Pump Log, page 236).

Cautionary measures

Initial signs of deposits: check anticoagulation therapy and adjust therapy if necessary.

Floating deposits inside the pump: replace the pump!

12.5.3 Checks Using the Monitor Program

Record all drive parameters and adjust if necessary.

Objective: the blood pump(s) must fill and eject completely in each pumping cycle, the diastolic pressure should be as low as possible.

ADVICE

Record the parameter values once a day.

To record the parameters use the sample copy in section 18.7: Pump Performance Flow Sheet, page 239.

12.5.4 Replacing the Blood Pump Due to Growth of the Patient

CAUTION

Replacing the blood pump due to growth of the patient: in children, the blood pump(s) need to be replaced with larger blood pump(s) periodically, to sufficient support and discharge rate.

The pump selected at the time of transplantation may not be adequate for the entire period of cardiac support. Growth and/or weight gain can result in the patient not receiving adequate support. Use the chart in section 18.1.2: Overview: Relationship: Body Weight – Pump Size, page 219, to plan, in good time, which pump(s) the patient may need to change over to. This chart is a guideline only and is not intended to replace the surgical judgement of the attending physician.

HOTLINE

Call Service Hotline! 866.249.0128

The blood pump(s) must be replaced as described in section 16.1: Replacing the Blood Pump(s), page 165.

13 Anticoagulation Therapy

13.1 Before Implantation of EXCOR

13.1.1 General Considerations

Patients with an EXCOR system must be maintained on anticoagulation therapy.

Anti-Xa levels should be specific to the drug being used, either unfractionated heparin or enoxaparin.

The TEG® may be useful in managing unfractionated heparin and antiplatelet therapy. Please contact Berlin Heart, Clinical Affairs for further information.

13.1.2 Pre Implantation

The following laboratory tests should be considered prior to implantation.

- Platelet Function Studies, INR, PTT, fibrinogen, antithrombin III, and platelet count to establish a baseline. Assessment for thrombophilia by measuring Protein C, S, Factor V Leiden, Prothrombin 20210 defect, as well as Heparin Induced Thrombocytopenia (HIT) is recommended.

13.2 During Implantation - Cardiopulmonary Bypass

13.2.1 Cardiopulmonary Bypass (CPB)

Use unfractionated heparin as per institutional protocol for cardiopulmonary bypass.

13.2.2 Post CPB

Completely reverse heparin with protamine sulphate as per institutional protocol.

The goal post-CPB is to achieve normal (institution specific) coagulation parameters (INR, PTT, fibrinogen, platelet count).

In the early post-operative period, the possibility of surgical bleeding, GI bleeding, internal bleeding in the retro-peritoneum or other bleeding diathesis is possible and must be monitored.

If the patient is bleeding despite normal coagulation parameters consider:

- Von Willebrand's
- Surgical bleeding

13.3 Postoperative Anticoagulation Therapy

13.3.1 General Considerations

Primary tests used to evaluate anticoagulation in the patient include antifactor Xa levels and/or PTT.

13.3.2 Starting Anticoagulation Therapy

During the first 24 hours following implantation, no anticoagulants should be administered.

Approximately 24 - 48 hours after implantation, commence unfractionated heparin therapy (i.v.) if the following criteria are met:

- platelet count >20,000/µl
- normal platelet function studies
- minimal bleeding in infants and young children

13.3.3 Unfractionated Heparin Therapy (i.v.) Patient < 12 Months

- initial dose 15 IU/kg/hour.
- do not use a bolus
- After 6 hours if the patient does not have increased bleeding, increase the heparin infusion to 28 IU/kg/hour (therapeutic dose).

6 hours after increasing the heparin to the therapeutic dose, obtain a PTT and an antifactor Xa level.

If the anti factor Xa level is in the desired range (0.35-0.5 U/ml) and the PTT is in the therapeutic range (institution dependent), then either the PTT or anti factor Xa level may be used to follow the heparin therapy.

If the anti factor Xa level is <0.35 U/ml or >0.5 U/ml, increase or decrease the heparin infusion, respectively until the anti factor Xa level is in the therapeutic range (see Tab. 13-1, page 122).

Anti factor Xa levels should be obtained daily. IMPORTANT: Hyperbilirubinemia may result in falsely low anti factor Xa levels. If anti Xa levels do not correlate with the PTT in this setting, consider using the PTT to monitor heparin therapy.

Antithrombin should be >70 %. If the antithrombin is <70 %, treat according to institutional protocol.

13.3.4 Unfractionated Heparin Therapy (i.v.) Patient ≥ 12 Months

Initial dose 10 IU/kg/hour.

Do not use a bolus.

After 6 hours if the patient does not have increased bleeding, increase the heparin infusion to 20 IU/kg/hour (therapeutic dose).

6 hours after increasing the heparin to the therapeutic dose, obtain a PTT and an anti factor Xa level.

If the anti factor Xa level is in the desired range (0.35-0.5 U/ml) and the PTT is in the therapeutic range (institution dependent), then either the PTT or anti factor Xa level may be used to follow the heparin therapy.

If the anti factor Xa level is < 0.35 U/ml or > 0.5 U/ml, increase or decrease the heparin infusion, respectively until the anti factor Xa level is the therapeutic range (see Tab. 13-1, page 122).

Anti factor Xa levels should be obtained daily. IMPORTANT: Hyperbilirubinemia may result in falsely low anti factor Xa levels. If anti Xa levels do not correlate with PTT in this setting, consider using the PTT to monitor heparin therapy.

Antithrombin should be >70 %. If the antithrombin is <70 %, treat according to institutional protocol.

NOTICE

If during standard unfractionated heparin therapy:
1. Platelet count is < 40,000/µl revert to the Stage I heparin dose for continuous infusion (see Tab. 13-1, page 122)
2. Platelets <20,000/ul discontinue heparin and consider evaluation for heparin induced thrombocytopenia (HIT).

If the anti factor Xa or PTT is too low or too high during heparin therapy, never use a bolus of heparin or protamine. Instead, increase or decrease the heparin dose, IU/hour, as required (see Tab. 13-1, page 122).

13.3.5 Thromboelastography (TEG®)

TEG® analysis may be useful in managing the anticoagulation and anti-platelet therapy. Please contact Berlin Heart Inc., Clinical Affairs for further information.

13.4 Low Molecular Weight Heparin

At 48 hours following surgery if all bleeding has stopped, the creatinine is within normal limits, and the patient is hemodynamically stable, switching from unfractionated heparin to low molecular weight heparin (LMWH) is recommended.

- Patient < 3 months start administration of Enoxaparin at 1.8 mg/kg subcutaneously every 12 hours.
- Patient > 3 - 12 months start administration of Enoxaparin at 1.4 mg/kg subcutaneously every 12 hours.
- Patient > 1 – 5 years start administration of Enoxaparin at 1.2 mg/kg subcutaneously every 12 hours.
- Patient > 5 – 16 years start administration of Enoxaparin at 1.1 mg/kg subcutaneously every 12 hours.
- Stop heparin infusion and administer LMWH (subcutaneously) simultaneously.
- Obtain the first anti factor Xa level at four hours after the 2nd LMWH dose is administered. See Tab. 13-2, page 122 for monitoring and dosing.
- Anti factor Xa therapeutic range: 0.6 to 1.0 U/ml.
- Anti factor Xa should be monitored along with platelet count, and creatinine
- When using LMWH, monitor Anti factor Xa daily. Once the Anti Factor Xa level is in the therapeutic range at a stable dose, monitor twice a week for 2 weeks, and then weekly.

13.5 Oral Anticoagulation Therapy (only for patients ≥ 12 months of age who are taking a full oral diet)

ADVICE

This section only applies to patients ≥ 12 months. Oral anticoagulation in children < 12 months of age is not recommended due to difficulty monitoring the effects of warfarin.

When the patient's condition has been fully stabilized (e.g. hemodynamically stable, no evidence of bleeding, etc), switch to oral anti-coagulation therapy with a vitamin K antagonist (target INR: 2.7 to 3.5), with an initial loading dose of 0.2 mg/kg/day. Do not exceed maximum loading dose of 5mg/day. The INR must be checked daily in the first

4 weeks, twice a week for the next 4 weeks (if INR is stable), and once a week thereafter (see Tab. 13-3, page 123 and Tab. 13-4, page 123.

Until the target INR is achieved, simultaneous administration of warfarin and heparin is necessary (approximately 4 days). Once the target INR is achieved, heparin therapy can be discontinued. If the INR decreases to < 2.7, administer LMW heparin immediately and then q12h until an INR of > 2.7 is achieved (see Tab. 13-5, page 123). If INR is 2.0- 2.7 use an enoxaparin dose of 0.5 mg/kg targeting an anti factor Xa level of 0.3-0.5, if INR is <2.0 use an enoxaparin dose of 1 mg/kg targeting an anti factor Xa level of 0.5 - 1.0.

When unable to achieve a stable INR with warfarin, LMWH should be used instead. Discontinue the warfarin and administer LMWH as per previously discussed age related dosing (see Tab. 13-2, page 122).

13.6 Monitoring of Blood Count and Anticoagulation Status

Monitoring the anticoagulation status as well as infection risk, and renal and hepatic function is important and should be monitored with the following frequency:

- Daily while on UFH, twice a week while on enoxaparin/coumadin for 4 weeks then once week: Fibrinogen, D-dimer, aPTT, PT/INR, Platelet Count, TEG®, Antithrombin, WBC, HgB, HCT, BUN/SCr, AST/ALT, bilirubin T/D, prealbumin, CRP.
- While on UFH obtain anti factor Xa level daily.
- While on enoxaparin obtain anti factor Xa daily until in therapeutic range and on a stable dose, then twice a week for two weeks and then weekly.

If infection is suspected, appropriate measures must be taken immediately (antibiotic therapy, adjustment of the anticoagulation and platelet inhibition therapy) including increased monitoring of the coagulation system. In addition, in the setting of hemodynamic instability, organ dysfunction, and inadequate anticoagulation daily monitoring should be performed until any of these issues are resolved.

13.7 Postoperative Platelet Inhibition Therapy

As individual patient responses vary to the anti-platelet agents, the optimum dosage for each patient will be that which minimizes both the risk of thromboembolic complications when the dose is too low and the risk of hemorrhagic complications when the dose is too high. Acetylsalicylic acid (ASA) and dipyridamole are the anti-platelet agents recommended.

13.7.1 Start of Therapy

Dipyridamole

At 48 hours after surgery, start dipyridamole, 4mg/kg/day p.o. divided into 4 doses (1 mg/kg Q6) (maximum dose 15mg/kg/day). If the following are present:

- All bleeding has stopped, AND
- The patient is hemodynamically stable AND,
- Platelet studies do not show significantly decreased function,
- Platelet count is > 40,000/µl

Acetylsalicylic Acid

At 4 days post implantation, following the removal of all drainage tubes, start acetylsalicylic acid (ASA) 1mg/kg/day p.o., divided into 2 doses (0.5 mg/kg Q 12), if the following are present:

- Platelet studies show platelet inhibition in the presence of ASA < 70 %

The ASA dose should split and be administered two times daily (0.5 mg/kg Q 12) due to the short half life and the high turnover of the platelets (approximately 10 % new platelets per day).

13.8 Adjunctive Medication

The inflammation parameters (tissue factor pathway inhibitor, prothrombin fragment 1-2, fibrinogen, Factor VIII) for patients on Ventricular Assist Device support are often elevated above normal. Accordingly, the physician may choose to administer the following medications at his/her discretion to facilitate the overall anticoagulation/anti-platelet management of the patient:

- Omega-3 fatty acids (e.g. DHA/EPA), have been shown to have an anti-inflammatory effect and also decrease premature activation of platelet membrane. Omega-3-fatty acids are composed of long chain polyunsaturated long chain carbons. Only alpha-linolenic acid (ALA) of the omega-3 family is truly essential.

Antioxidants (vitamin C and E) also have been shown to have an anti-inflammatory effect, and may be considered.

13.9 Anticoagulation Therapy

13.9.1 Therapeutic Heparin Administration and Adjustment

NOTICE

This table assumes the site therapeutic PTT is 60 to 85 seconds (Monagle, P, et al.). Each site should use their hospital calculated therapeutic range.

Stage	Description	Anti factor Xa [u/ml]/PTT	Infusion	Hold heparin	Rate change [%]	Repeat PTT
I	Initial Dose (first 6 hours)					
	Infant < 12 mo		15 IU/kg/h			
	Child ≥12mo		10 IU/kg/h			
II	Therapeutic Dose					
	Infant < 12 mo		28 IU/kg/h			after 6h
	Child ≥12mo		20 IU/kg/h			after 6h
III	Adjustment					
		<0.1/<50	0	0	+15 %	4h
		0.1-0.34/ 50-60	0	0	+10 %	6h
		0.35-0.50/ 60-85	0	0	0	next day
		0.51-0.70/ 86-95			-10 %	6h
		0.71-0.89/ 96-120		30 min.	-10 %	4h
		= 0.90/ >120		60 min.	-15 %	4h

Tab. 13-1 Unfractionated Heparin adjusted to maintain an anti factor Xa level of 0.35 to 0.50 U/ml.

Anti Factor Xa level U/ml?	Hold Next Dose?	Dose Change?	Repeat Anti Factor Xa?
< 0.35	no	increase dose by 25 %	4 h after next dose
0.36 - 0.45	no	increase dose by 15 %	4 h after next dose
0.46 - 0.59	no	increase dose by 10 %	4 h after next dose
0.6 - 1.0	no	no	4 h after next dose
1.1 - 1.25	no	decrease dose by 20 %	4 h after next dose
1.26 - 1.5	no	decrease dose by 30 %	4 h after next dose

Tab. 13-2 Enoxaparin, low molecular weight heparin dosing (Monagle, P, et al.)

Anti Factor Xa level U/ml?	Hold Next Dose?	Dose Change?	Repeat Anti Factor Xa?
1.6 - 2.0	yes for 3h	decrease dose by 40 %	Before next dose then 4h after next dose
> 2.0	yes, until anti factor Xa level is <0.5 U/ml	decrease dose by 50 %	Before next dose is administered, if >0.5 U/ml (therapeutic level), do not give next enoxaparin dose & repeat anti factor Xa level in 12 h. When level <0.5 U/ml, administer 50 % original dose.

Tab. 13-2 Enoxaparin, low molecular weight heparin dosing (Monagle, P, et al.)

Stage	INR	Action
Day 1	1.0 - 1.8	0.2 mg/kg orally
Day 2-4	1.1 - 1.3	repeat day 1 loading dose
	1.4 - 1.9	50 % of day 1 loading dose
	2.0 - 3.0	50 % of day 1 loading dose
	3.1 - 3.5	25 % of day 1 loading dose
	> 3.5	hold dosing until INR is < 3.5

Tab. 13-3 Warfarin loading dose to maintain an INR of 2.7 - 3.5 (Monagle, P, et al.)

Stage	INR	Action
Maintenance : = Day 5 and long term	1.1 - 1.9	increase dose by 40 -50 %
	2.0 - 2.4	increase dose by 10 %
	2.7 - 3.5	no change
	3.6 - 4.0	administer next dose at 50 % then restart at 20 % less maintenance dose
	4.1- 5.0	hold one dose then 20 % less maintenance dose

Tab. 13-4 Warfarin Maintenance Dosing for Day 5 and longer to maintain INR 2.7-3.5

INR 2.7 to 3.5	use only warfarin p.o.
INR < 2.7	use warfarin plus enoxaparin as outlined in section 5 until INR ≥ 2.7

Tab. 13-5 Drugs and Dose for specific INR range

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14 Weaning and Explantation for BTR and BTT

14.1 Weaning Procedure

14.1.1 Introduction

This document summarizes the clinical guideline for weaning and explantation of EXCOR. The decision to wean EXCOR should be made cautiously after careful review of all available clinical and laboratory data. This document should be considered a guideline only. As always treatment must be individualized to each patient based on his/her unique clinical circumstances.

It is important to recognize that prolonged pump stoppage and operation of the device at lower beat rates is not recommended due to the risks of blood stagnation and thrombus formation. This risk increases with the smaller blood pumps (e.g. 10, 15, 25 and 30 ml devices) where the luminal sizes and flow rates are the lowest. Therefore, a size-based guideline has been developed to test the adequacy of the native circulation without a prolonged pump stoppage using a combination of gradual weaning, brief pump stoppages, careful anticoagulation monitoring, invasive hemodynamic testing, and a brief afterload challenge. It is not recommended that weaning proceed unless all parameters especially those pertaining to anti-coagulation have been fully optimized. This protocol reflects the most recent understanding of the safest possible weaning strategy based on the collective US and European experience to date.

14.1.2 Indication

Weaning may be considered in children supported with EXCOR judged to have sufficient evidence of myocardial recovery to provide adequate systemic perfusion independent of VAD support.

14.1.3 Eligibility Criteria

⚠ WARNING

Continuous reassessment of eligibility criteria is critical to reducing the risks associated with weaning of VAD support. Weaning criteria must be satisfied at all times in order to proceed with the weaning protocol.

Special attention must be taken to ensure the patient's anticoagulation status remains within the targeted range.

Weaning of EXCOR may be considered in subjects who meet the following eligibility criteria:

- LVEDD within normal limits (< 98th percentile, or Z-score of +2)
- EF = 45 % (i.e. no less than mild dysfunction)
- Lactate < 3 mmol/L
- No clinical evidence of thromboembolism or bleeding
- Anticoagulation markers within target parameters

14.1.4 Weaning Protocol

WARNING

If the patient does not meet the eligibility criteria at any time during the weaning process: resume pumping at rate prior to weaning (initial rate, IR).

The weaning protocol can be divided into five steps and generally takes one week to complete.

- Day 0 (and throughout the weaning process). Confirmation of eligibility criteria for weaning.
- Day 0. Acute weaning challenge
- Day 1-4. Graduated weaning challenge with non-invasive assessment (echo).
- Day 5. Pump stoppage with invasive hemodynamic assessment with afterload challenge.
- Day 6. Pump stoppage with invasive hemodynamic assessment in OR (full anticoagulation).

This size-based weaning protocol accounts for physiologic differences in heart rate and stroke volume observed in children of varying ages.

14.1.5 10 ml / 15 ml Blood Pump

The individual weaning progress is based upon the following parameters:

Parameter	Explanation	Abbr.	Value
Initial rate	Rate prior to any weaning	IR	Please enter: IR = _____bpm
Weaning rate	Lowest rate achieved during weaning process, depends on blood pump size	WR	50 bpm
Total weaning interval	Difference between initial rate and explantation rate: TWI = IR - WR	TWI	Please enter: IR ___bpm - WR 50 bpm = TWI ___ bpm
Reduced rate	Rate resumed at the end of day 1 to 3	RR_1 to RR_3	Please refer to Tab. 14-2, page 127.

Tab. 14-1 Important parameters for weaning progress

Reduced rate (RR_x)	Calculation
RR_1	Please enter: RR_1 = WR 50 bpm + 0.75 x TWI (___bpm) = _____bpm
RR_2	Please enter: RR_2 = WR 50 bpm + 0.50 x TWI (___bpm) = _____bpm
RR_3	Please enter: RR_3 = WR 50 bpm + 0.25 x TWI (___bpm) = _____bpm

Tab. 14-2 Reduced rate day 1 to day 3

10 ml / 15 ml blood pump weaning sequence

10 ml / 15 ml blood pump weaning sequence		
Day 0	**After confirmation of eligibility criteria, the following steps should be performed under echo guidance [1]:**	
	1. Administer unfractionated heparin (UFH) 75 units/kg x _____ kg = _____ mg IV x 1 [max 5000 units]. 2. After 5 minutes, reduce the pump rate stepwise from IR (_____ bpm) to 30 bpm in increments of 5 bpm q5 min. After 5 minutes at 30 bpm, reassess LV size and function. 3. After an additional 5 minutes (i.e. total time = **10 min** at 30 bpm), stop the pump for **3 min** and reassess LV size and function. During pump stoppage, use the manual pump to pump twice q30 seconds to minimize the risk of thrombus formation due to blood stagnation while Ikus is disconnected. 4. After 3-minute pump stop, reconnect pump to Ikus and resume pump speed at IR (___ bpm).	
	Did the patient satisfy all 5 eligibility criteria throughout the period of weaning and pump stoppage?	☐ **NO -STOP** ☐ **YES - Proceed** **MD_____**

Tab. 14-3 10 ml / 15 ml blood pump weaning sequence

10 ml / 15 ml blood pump weaning sequence		
Day 1	**After confirmation of eligibility criteria, the following steps should be performed sequentially under echo guidance** [1]:	
	1. Administer UFH 75 units/kg x _____kg = _____mg IV x 1 [max 5000 units]. 2. After 5 minutes, reduce the pump rate stepwise by from the IR (bpm) to 30 bpm in increments of 5 bpm q 5 min. After 5 minutes at 30 bpm, reassess LV size and function. 3. After a total time of **10 min** at 30 bpm, stop the pump for **3 min** and reassess LV size and function. During pump stoppage, use the manual pump to pump twice q30 seconds to minimize the risk of thrombus formation due to blood stagnation while Ikus is disconnected. 4. After 3-minute pump stop, reconnect pump to Ikus and resume pumping at rate RR1 (___ bpm).	
	Did the patient satisfy all 5 eligibility criteria throughout the period of weaning and pump stoppage?	☐ **NO -STOP** ☐ **YES - Proceed** **MD_____**
Day 2	**After confirmation of eligibility criteria, the following steps should be performed under echo guidance** [1]:	
	1. Administer UFH 75 units/kg x _____kg = _____mg IV x 1 [max 5000 units]. 2. After 5 minutes, reduce the pump rate stepwise from RR1 (_____ bpm) to 30 bpm in increments of 5 bpm q 5 min. After 5 minutes at 30 bpm, reassess LV size and function. 3. After a total time of **20 min** at 30 bpm, stop the pump for **3 min** and reassess LV size and function. During pump stoppage, use the manual pump to pump twice q30 seconds to minimize the risk of thrombus formation due to blood stagnation while Ikus is disconnected. 4. After 3-minute pump stop, reconnect pump to Ikus and resume pumping at RR2 (___bpm).	
	Did the patient satisfy all 5 eligibility criteria throughout the period of weaning and pump stoppage?	☐ **NO -STOP** ☐ **YES - Proceed** **MD_____**

Tab. 14-3 10 ml / 15 ml blood pump weaning sequence

10 ml / 15 ml blood pump weaning sequence		
Day 3	**After confirmation of eligibility criteria, the following steps should be performed under echo guidance** [1]:	
	1. Administer UFH 75 units/kg x _____ kg = _____ mg IV x 1 [max 5000 units]. 2. After 5 minutes, reduce the pump rate stepwise from RR2 (___ bpm) to 30 bpm in increments of 5 bpm q 5 min. After 5 minutes at 30 bpm, reassess LV size and function. 3. Initiate exercise with gentle age-appropriate play tasks (e.g. rattle, clapping) as clinically appropriate, where possible 4. After a total time of **30 min** at 30 bpm, stop the pump for **3 min** and reassess LV size and function. During pump stoppage, use the manual pump to pump twice q30 seconds to minimize the risk of thrombus formation due to blood stagnation while Ikus is disconnected. After 3-minute pump stop, reconnect pump to Ikus and resume pumping at RR3 (___ bpm).	
	Did the patient satisfy all 5 eligibility criteria throughout the period of weaning and pump stoppage?	**□ NO -STOP** **□ YES - Proceed** **MD_____**
Day 4	**After confirmation of eligibility criteria, the following steps should be performed under echo guidance** [1]:	
	1. Administer UFH 75 units/kg x _____kg = _____mg IV x 1 [max 5000 units]. 2. After 5 minutes, reduce pump rate stepwise from RR3 (___ bpm) to 30 bpm in increments of 5 bpm q 5 min. After 5 minutes at 30 bpm, reassess LV size and function. 3. Initiate exercise with gentle age-appropriate play tasks (e.g. rattle, clapping) as clinically appropriate, where possible. 4. After a total time of **30 min** at 30 bpm, stop the pump for **3 min** and reassess LV size and function. During pump stoppage, use the manual pump to pump twice q30 seconds to minimize the risk of thrombus formation due to blood stagnation while Ikus is disconnected. 5. After a 3-minute pump stop: if the patient meets all eligibility criteria, reconnect pump to Ikus and resume pumping at WR (50 bpm). If the patient does not meet all criteria, reconnect Ikus and resume pumping at IR.	
	Did the patient satisfy all 5 eligibility criteria throughout the period of weaning and pump stoppage?	**□ NO -STOP** **□ YES - Proceed** **MD_____**

Tab. 14-3 10 ml / 15 ml blood pump weaning sequence

10 ml / 15 ml blood pump weaning sequence		
Day 5	**After confirmation of eligibility criteria, the following steps should be performed in the cath lab under echo guidance** [1]:	
	1. Obtain standard access for RHC (if possible without sedation). 2. Administer UFH 75 units/kg x _____kg = _____mg IV x 1 [max 5000 units]. 3. After 5 minutes, reduce the pump rate stepwise from WR (50 bpm) to 30 bpm in increments of 5 bpm q5 min. After 5 minutes at 30 bpm, reassess LV size and function. 4. After a total time of **10 min** at 30 bpm, stop the pump for **3 min** and reassess LV size and function. During pump stoppage, use the manual pump to pump twice q30 seconds to minimize the risk of thrombus formation due to blood stagnation while Ikus is disconnected. 5. After 3 minutes, initiate norepinephrine infusion at 0.01 mcg/kg/min IV gtt titrated to MAP 20 % above baseline x 5 min. While doing so, proceed pumping manually twice q30 seconds. 6. If LV size and function acceptable, proceed pumping manually twice q30 seconds for **3 min**. While doing so, reassess LV size & function, and record RAP, PAP, PCWP and MVS. 7. After 6-minute pump stop: if the patient meets all eligibility criteria, reconnect pump to Ikus and resume pumping at 50 bpm until the actual surgical procedure of explantation takes place. If the patient does not meet all criteria, reconnect Ikus and resume pumping at IR.	
	Did the patient satisfy all 5 eligibility criteria throughout the period of weaning and pump stoppage?	**☐ NO -STOP** **☐ YES - Proceed** **MD_____**

Tab. 14-3 10 ml / 15 ml blood pump weaning sequence

[1] TEE unless echo windows insufficient. The last weaning increment may be less than 5 bpm if the wean interval is not a multiple of 5.

14.1.6 25 ml / 30 ml Blood Pump

The individual weaning progress is based upon the following parameters:

Parameter	Explanation	Abbr.	Value
initial rate	Rate prior to any weaning	IR	Please enter:
Weaning rate	Lowest rate achieved during weaning process, depends on pump size	WR	40 bpm

Tab. 14-4 Important parameters for weaning progress

Parameter	Explanation	Abbr.	Value
Total weaning interval	Difference between initial rate and explantation rate: TWI = IR - WR	TWI	Please enter: IR ___ bpm - WR 40 bpm = TWI ___ bpm
Reduced rate	Rate resumed at the end of day 1 to 3	RR_1 to RR_3	Please refer Tab. 14-5, page 131.

Tab. 14-4 Important parameters for weaning progress

Reduced rate (RR_x)	Calculation
RR_1	Please enter: RR_1 = WR 40 bpm + 0.75 x TWI (___ bpm) = ____bpm
RR_2	Please enter: RR_2 = WR 40 bpm + 0.50 x TWI (___ bpm) = ____bpm
RR_3	Please enter: RR_3 = WR 40 bpm + 0.25 x TWI (___ bpm) = ____bpm

Tab. 14-5 Reduced rate day 1 to day 3

25 ml / 30 ml blood pump weaning sequence

25 ml / 30 ml blood pump weaning sequence		
Day 0	**After confirmation of eligibility criteria, the following steps should be performed under echo guidance:**[1]	
	1. Administer unfractionated heparin (UFH) 75 units/kg x _____ kg = _____mg IV x 1 [max 5000 units]. **2.** After 5 minutes, reduce the pump rate stepwise from IR (_____ bpm) to 30 bpm in increments of 5 bpm q5 min. After 5 minutes at 30 bpm, reassess LV size and function. **3.** After an additional 5 minutes (i.e. total time = 10 min at 30 bpm), stop the pump for 5 min and reassess LV size and function. During pump stoppage, use the manual pump to pump twice q30 seconds to minimize the risk of thrombus formation due to blood stagnation while Ikus is disconnected. **4.** After 5-minute pump stop, reconnect pump to Ikus and resume pump speed at IR(___ bpm).	
	Did the patient satisfy all 5 eligibility criteria throughout the period of weaning and pump stoppage?	☐ **NO - STOP** ☐ **YES - Proceed** **MD_____**

Tab. 14-6 25 ml / 30 ml blood pump weaning sequence

25 ml / 30 ml blood pump weaning sequence		
Day 1	**After confirmation of eligibility criteria, the following steps should be performed sequentially under echo guidance:**[1]	
	1. Administer UFH 75 units/kg x _____kg = _____mg IV x 1 [max 5000 units]. **2.** After 5 minutes, reduce the pump rate stepwise by from the IR (_____bpm) to 30 bpm in increments of 5 bpm q 5 min. After 5 minutes at 30 bpm, reassess LV size and function. **3.** After a total time of **10 min** at 30 bpm, stop the pump for **5 min** and reassess LV size and function. During pump stoppage, use the manual pump to pump twice q30 seconds to minimize the risk of thrombus formation due to blood stagnation while Ikus is disconnected. **4.** After 5-minute pump stop, reconnect pump to Ikus and resume pumping at rate RR1 (_ __ bpm).	
	Did the patient satisfy all 5 eligibility criteria throughout the period of weaning and pump stoppage?	☐ **NO - STOP** ☐ **YES - Proceed** **MD**_____
Day 2	**After confirmation of eligibility criteria, the following steps should be performed under echo guidance:**[1]	
	1. Administer UFH 75 units/kg x _____kg = _____mg IV x 1 [max 5000 units]. **2.** After 5 minutes, reduce the pump rate stepwise from RR1 (_____ bpm) to 30 bpm in increments of 5 bpm q 5 min. After 5 minutes at 30 bpm, reassess LV size and function. **3.** After a total time of **20 min** at 30 bpm, stop the pump for **10 min** and reassess LV size and function. During pump stoppage, use the manual pump to pump twice q30 seconds to minimize the risk of thrombus formation due to blood stagnation while Ikus is disconnected. **4.** After 10-minute pump stop, reconnect pump to Ikus and resume pumping at RR2 (___ bpm).	
	Did the patient satisfy all 5 eligibility criteria throughout the period of weaning and pump stoppage?	☐ **NO - STOP** ☐ **YES - Proceed** **MD**_____

Tab. 14-6 25 ml / 30 ml blood pump weaning sequence

25 ml / 30 ml blood pump weaning sequence		
Day 3	**After confirmation of eligibility criteria, the following steps should be performed under echo guidance:**[1]	
	1. Administer UFH 75 units/kg x _____kg = _____mg IV x 1 [max 5000 units]. **2.** After 5 minutes, reduce the pump rate stepwise from RR2 (___bpm) to 30 bpm in increments of 5 bpm q 5 min. After 5 minutes at 30 bpm, reassess LV size and function. **3.** Initiate exercise with gentle age-appropriate play tasks (e.g. patty cake) as clinically appropriate, where possible **4.** After a total time of **30 min** at 30 bpm, stop the pump for **10 min** and reassess LV size and function. During pump stoppage, use the manual pump to pump twice q30 seconds to minimize the risk of thrombus formation due to blood stagnation while Ikus is disconnected. **5.** After 10-minute pump stop, reconnect pump to Ikus and resume pumping at RR3 (___ bpm).	
	Did the patient satisfy all 5 eligibility criteria throughout the period of weaning and pump stoppage?	☐ **NO - STOP** ☐ **YES - Proceed** **MD_____**
Day 4	**After confirmation of eligibility criteria, the following steps should be performed under echo guidance:**[1]	
	1. Administer UFH 75 units/kg x _____kg = _____mg IV x 1 [max 5000 units]. **2.** After 5 minutes, reduce pump rate stepwise from RR_3 (___ bpm) to 30 bpm in increments of 5 bpm q 5 min. After 5 minutes at 30 bpm, reassess LV size and function. **3.** Initiate exercise with gentle age-appropriate play tasks (e.g. patty cake) as clinically appropriate, where possible. **4.** After a total time of **30 min** at 30 bpm, stop the pump for **15 min** and reassess LV size and function. During pump stoppage, use the manual pump to pump twice q30 seconds to minimize the risk of thrombus formation due to blood stagnation while Ikus is disconnected. **5.** After a 15-minute pump stop: if the patient meets all eligibility criteria, reconnect pump to Ikus and resume pumping at WR (40 bpm). If the patient does not meet all criteria, reconnect Ikus and resume pumping at IR.	
	Did the patient satisfy all 5 eligibility criteria throughout the period of weaning and pump stoppage?	☐ **NO - STOP** ☐ **YES - Proceed** **MD_____**

Tab. 14-6 25 ml / 30 ml blood pump weaning sequence

25 ml / 30 ml blood pump weaning sequence		
Day 5	**After confirmation of eligibility criteria, the following steps should be performed in the cath lab under echo guidance:**[1]	
	1. Obtain standard access for RHC (if possible with out sedation). **2.** Administer UFH 75 units/kg x _____kg = _____mg IV x 1 [max 5000 units]. **3.** After 5 minutes, reduce the pump rate stepwise from WR (50 bpm) to 30 bpm in increments of 5 bpm q5 min. After 5 minutes at 30 bpm, reassess LV size and function. **4.** After a total time of **30 min** at 30 bpm, stop the pump for **15 min** and reassess LV size and function. During pump stoppage, use the manual pump to pump twice q30 seconds to minimize the risk of thrombus formation due to blood stagnation while Ikus is disconnected. **5.** After 15 minutes, initiate norepinephrine infusion at 0.01 mcg/kg/min IV gtt titrated to MAP 20 % above baseline x 5 min. While doing so, proceed pumping manually twice q30 seconds. **6.** If LV size and function acceptable, proceed pumping manually twice q30 seconds for **5 min**. While doing so, reassess LV size & function, and record RAP, PAP, PCWP and MVS. **7.** After 20-minute pump stop: if the patient meets all eligibility criteria, reconnect pump to Ikus and resume pumping at 50 bpm until the actual surgical procedure of explantation takes place. If the patient does not meet all criteria, reconnect Ikus and resume pumping at IR.	
	Did the patient satisfy all 5 eligibility criteria throughout the period of weaning and pump stoppage?	☐ **NO - STOP** ☐ **YES - Proceed** **MD_____**

Tab. 14-6 25 ml / 30 ml blood pump weaning sequence

[1] TEE unless echo windows insufficient. The last weaning increment may be less than 5 bpm if the wean interval is not a multiple of five.

14.1.7 50 ml / 60 ml Blood Pump

The individual weaning progress is based upon the following parameters:

Parameter	Explanation	Abbr.	Value
Initial rate	Rate prior to any weaning	IR	Please enter: IR = _____ bpm
Weaning rate	Lowest rate achieved during weaning process, depends on pump size	WR	30 bpm

Tab. 14-7 Important parameters for weaning progress

Parameter	Explanation	Abbr.	Value
Total weaning interval	Difference between initial rate and explantation rate: TWI = IR - WR	TWI	Please enter: IR ___ bpm - WR 30 bpm = TWI ___ bpm
Reduced rate	Rate resumed at the end of day 1 to 3	RR_1 to RR_3	Please refer to Tab. 14-8, page 135.

Tab. 14-7 Important parameters for weaning progress

Reduced rate (RR_x)	Calculation
RR_1	Please enter: RR_1 = WR 30 bpm + 0.75 x TWI (___ bpm) = ____bpm
RR_2	Please enter: RR_2 = WR 30 bpm + 0.50 x TWI (___ bpm) = ____bpm
RR_3	Please enter: RR_3 = WR 30 bpm + 0.25 x TWI (___ bpm) = ____bpm

Tab. 14-8 Reduced rate day 1 to day 3

50 ml / 60 ml blood pump weaning sequence

50 ml / 60 ml blood pump weaning sequence		
Day 0	**After confirmation of eligibility criteria, the following steps should be performed under echo guidance:**[1]	
	1. Administer unfractionated heparin (UFH) 75 units/kg x _____ kg = _____mg IV x 1 [max 5000 units]. **2.** After 5 minutes, reduce the pump rate stepwise from IR (_____ bpm) to 30 bpm in increments of 5 bpm q5 min. After 5 minutes at 30 bpm, reassess LV size and function. **3.** After an additional 5 minutes (i.e. total time = 10 min at 30 bpm), stop the pump for 5 min and reassess LV size and function. During pump stoppage, use the manual pump to pump twice q30 seconds to minimize the risk of thrombus formation due to blood stagnation while Ikus is disconnected. **4.** After 5-minute pump stop, reconnect pump to Ikus and resume pump speed at IR(___ bpm).	
	Did the patient satisfy all 5 eligibility criteria throughout the period of weaning and pump stoppage?	☐ **NO - STOP** ☐ **YES - Proceed** **MD_____**

Tab. 14-9 50 ml / 60 ml blood pump weaning sequence

50 ml / 60 ml blood pump weaning sequence		
Day 1	**After confirmation of eligibility criteria, the following steps should be performed sequentially under echo guidance:**[1]	
	1. Administer UFH 75 units/kg x _____kg = _____mg IV x 1 [max 5000 units]. **2.** After 5 minutes, reduce the pump rate stepwise by from the IR (_____bpm) to 30 bpm in increments of 5 bpm q 5 min. After 5 minutes at 30 bpm, reassess LV size and function. **3.** After a total time of **10 min** at 30 bpm, stop the pump for **10 min** and reassess LV size and function. During pump stoppage, use the manual pump to pump twice q30 seconds to minimize the risk of thrombus formation due to blood stagnation while Ikus is disconnected. **4.** After 10-minute pump stop, reconnect pump to Ikus and resume pumping at rate RR1 (_ __ bpm).	
	Did the patient satisfy all 5 eligibility criteria throughout the period of weaning and pump stoppage?	☐ **NO - STOP** ☐ **YES - Proceed** **MD**_____
Day 2	**After confirmation of eligibility criteria, the following steps should be performed under echo guidance:**[1]	
	1. Administer UFH 75 units/kg x _____kg = _____mg IV x 1 [max 5000 units]. **2.** After 5 minutes, reduce the pump rate stepwise from RR1 (_____ bpm) to 30 bpm in increments of 5 bpm q 5 min. After 5 minutes at 30 bpm, reassess LV size and function. **3.** After a total time of **15 min** at 30 bpm, stop the pump for **15 min** and reassess LV size and function. During pump stoppage, use the manual pump to pump twice q30 seconds to minimize the risk of thrombus formation due to blood stagnation while Ikus is disconnected. **4.** After 15-minute pump stop, reconnect pump to Ikus and resume pumping at RR2 (___ bpm).	
	Did the patient satisfy all 5 eligibility criteria throughout the period of weaning and pump stoppage?	☐ **NO - STOP** ☐ **YES - Proceed** **MD**_____

Tab. 14-9 50 ml / 60 ml blood pump weaning sequence

50 ml / 60 ml blood pump weaning sequence		
Day 3	**After confirmation of eligibility criteria, the following steps should be performed under echo guidance:**[1]	
	1. Administer UFH 75 units/kg x _____kg = _____mg IV x 1 [max 5000 units]. **2.** After 5 minutes, reduce the pump rate stepwise from RR2 (___bpm) to 30 bpm in increments of 5 bpm q 5 min. After 5 minutes at 30 bpm, reassess LV size and function. **3.** Initiate exercise with gentle age-appropriate play tasks (e.g. ambulate) as clinically appropriate, where possible **4.** After a total time of **30 min** at 30 bpm, stop the pump for **20 min** and reassess LV size and function. During pump stoppage, use the manual pump to pump twice q30 seconds to minimize the risk of thrombus formation due to blood stagnation while Ikus is disconnected. **5.** After 20-minute pump stop, reconnect pump to Ikus and resume pumping at RR3 (___ bpm).	
	Did the patient satisfy all 5 eligibility criteria throughout the period of weaning and pump stoppage?	☐ **NO - STOP** ☐ **YES - Proceed** **MD_____**
Day 4	**After confirmation of eligibility criteria, the following steps should be performed under echo guidance:**[1]	
	1. Administer UFH 75 units/kg x _____kg = _____mg IV x 1 [max 5000 units]. **2.** After 5 minutes, reduce pump rate stepwise from RR_3 (___ bpm) to 30 bpm in increments of 5 bpm q 5 min. After 5 minutes at 30 bpm, reassess LV size and function. **3.** Initiate exercise with gentle age-appropriate play tasks (e.g. ambulate) as clinically appropriate, where possible. **4.** After a total time of **30 min** at 30 bpm, stop the pump for **30 min** and reassess LV size and function. During pump stoppage, use the manual pump to pump twice q30 seconds to minimize the risk of thrombus formation due to blood stagnation while Ikus is disconnected. **5.** After a 15-minute pump stop: if the patient meets all eligibility criteria, reconnect pump to Ikus and resume pumping at WR (40 bpm). If the patient does not meet all criteria, reconnect Ikus and resume pumping at IR.	
	Did the patient satisfy all 5 eligibility criteria throughout the period of weaning and pump stoppage?	☐ **NO - STOP** ☐ **YES - Proceed** **MD_____**

Tab. 14-9 50 ml / 60 ml blood pump weaning sequence

50 ml / 60 ml blood pump weaning sequence		
Day 5	**After confirmation of eligibility criteria, the following steps should be performed in the cath lab under echo guidance**[1] **1.** Obtain standard access for RHC (if possible with out sedation). **2.** Administer UFH 75 units/kg x _____kg = _____mg IV x 1 [max 5000 units]. **3.** Assess LV size and function to obtain data for comparison. **4.** Stop the pump for **15 min** and reassess LV size and function. During pump stoppage, use the manual pump to pump twice q30 seconds to minimize the risk of thrombus formation due to blood stagnation while Ikus is disconnected. **5.** After 15 minutes, initiate norepinephrine infusion at 0.01 mcg/kg/min IV gtt titrated to MAP 20 % above baseline x 5 min. While doing so, proceed pumping manually twice q30 seconds. **6.** If LV size and function acceptable, proceed pumping manually twice q30 seconds for **15 min**. While doing so, reassess LV size & function, and record RAP, PAP, PCWP and MVS. **7.** After 30-minute pump stop: if the patient meets all eligibility criteria, reconnect pump to Ikus and resume pumping at 50 bpm until the actual surgical procedure of explantation takes place. If the patient does not meet all criteria, reconnect Ikus and resume pumping at IR.	
	Did the patient satisfy all 5 eligibility criteria throughout the period of weaning and pump stoppage?	☐ **NO - STOP** ☐ **YES - Proceed** **MD**_____

Tab. 14-9 50 ml / 60 ml blood pump weaning sequence

[1] TEE unless echo windows insufficient. The last weaning increment may be less than 5 bpm if the wean interval is not a multiple of five.

14.1.8 Explantation Criteria

NOTICE

ASA and dipyridamole should be discontinued 24 hours prior to device explantation; coumadin / enoxaparin should be transitioned back to unfractionated heparin (titrated to therapeutic levels).

Milrinone 0.75 µg/kg/min should be started 12 hours prior explantation. ACE inhibitor, ß-Blocker and Spirinolactone should be not stopped.

In the operating room, explantation should be considered if the following criteria are met with the pump stopped for 20 minutes (after anticoagulation has been established in the target range for cardiopulmonary bypass):

- LVEDD less than 98th percentile (Z-score less than +2)
- EF ≥ 45 % (i.e. no more than mild ventricular dysfunction)
- Normotensive on only Milrinone (no other inotropes)
- Lactate < 3 mmol/L
- LVEDP < 12 mmHg
- Resting CI of > 2.8 L/min/m^2

Surgery should be performed without cardiopulmonary bypass. Control all bleeding immediately during and post implantation.

14.2 Explantation for BTR

14.2.1 Explantation With Univentricular Support

The procedure is analogous to that used after BTT (see section 14.3: Explantation for BTT, page 140). Sew over all anastomosis areas where cannulae were placed.

14.2.2 Explantation After Biventricular Support

Stopping the right pump

INSTRUCTION

1. Select **Pause right** (see Fig. 14-1, page 139), then press **<Enter>** to confirm. Respond to the prompt in the dialog window by pressing the **<X>** key or the **<1>** key. The right pump will stop. The view **Pump size and single-step mode** is shown (see Fig. 8-6, page 76). The cursor is located on the **OK** field.
2. Unplug the driving tube of the right pump from the connector on the Ikus. Use the seal plug to seal the connector.
3. To confirm the **OK** selection, press **<Enter>**. The Ikus continues running. The screen shows the standard view.

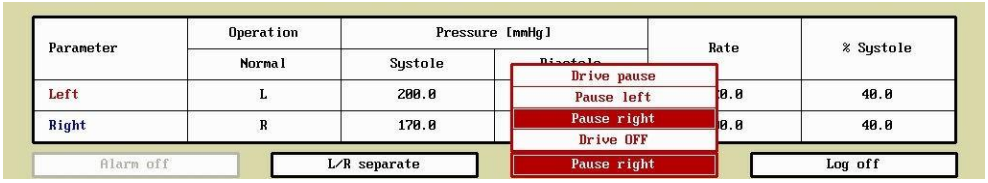

Fig. 14-1 Pause right

Switching the Ikus off

WARNING

Always use the key switch to switch off the Ikus.

INSTRUCTION

1. Put the patient on cardiopulmonary bypass (CPB).
2. Disconnect the driving tubes and connect both tank units to the Ikus.
3. Leave the Ikus running with the tank units until the patient is stable on CPB and the blood pumps have been explanted.
4. In the monitor program, select the option **Drive OFF** (see Fig. 14-2, page 141) and press **<Enter>** to confirm.
5. Respond to the prompt in the dialog window by pressing the **<X>** key or the **<1>** key. The system stops operation immediately and writes an operating log.
6. Disconnect the driving tube(s) from the connector(s). To do so, take hold of the plug's release sleeve and pull the plug out of the connector.
7. Use the seal plugs to seal the driving tube connector sockets.
8. Wait until the log has been completed. When the message **Switch drive off with main switch!** appears, press **<F10>** to shut down the monitor program. Confirm by pressing the **<X>** key or the **<1>** key.
9. Select **3. End** (**<3>**, see Fig. 14-3, page 141) in the start menu and switch off the laptop.
10. Switch the Ikus off, provided that the batteries are fully charged. To do so, turn the key switch to *[0]* position.

14.3 Explantation for BTT

NOTICE

When planning and timing the transplantation, be aware that massive adhesions may exist in the transplant recipient.

Preparing the donor organ

ADVICE

Leave adequate lengths of the aorta and the pulmonary artery attached to the donor organ in order to be able to continue using those parts of the original vessels used for anastomosis of the VAD cannulae.

Leave the Ikus running with the tank units until the patient is stable on CPB and the blood pumps have been explanted.

Switching the Ikus off

CAUTION

Always use the key switch to switch off the Ikus.

INSTRUCTION

1. Put the patient on cardiopulmonary bypass.
2. Disconnect the driving tubes and connect both tank units to the Ikus.
3. Leave the Ikus running with the tank units until the patient is stable on CPB and the blood pumps have been explanted.
4. Next in the monitor program, select the Drive OFF option and press **<Enter>** to confirm (see Fig. 14-2, page 141).
5. Respond to the prompt in the dialog window by pressing the **<X>** key or the **<1>** key. The system stops operation immediately and writes an operating log.
6. Disconnect the driving tube(s) from the connector(s). To do so, take hold of the release sleeve and pull this out of the connector.
7. Use the seal plugs to seal the driving tube connectors.
8. Wait until the log has been completed. When the message Switch drive off with main switch! appears, press **<F10>** to shut down the monitor program. Confirm by pressing the **<X>** key or the **<1>** key.
9. Select 3. End (<3>, see Fig. 14-3, page 141) in the start menu and switch off the laptop.
10. Switch the Ikus off, provided that the batteries are fully charged. To do so, turn the key switch to [0] position.

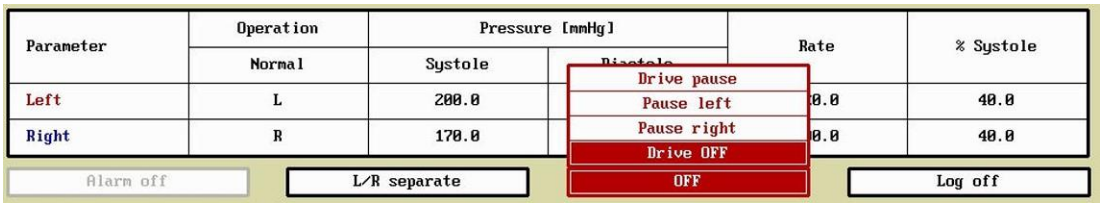

Fig. 14-2 Drive OFF

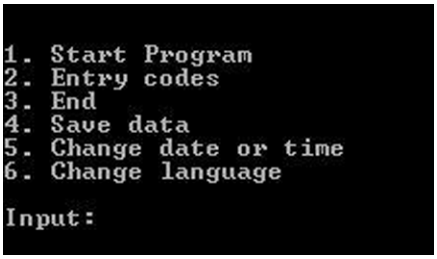

Fig. 14-3 Start menu

Removing the VAD cannulae

INSTRUCTION

1. Clamp off the cannulae.
2. Disconnect the pump from the cannulae.
3. Remove the cannulae. Sew over the anastomosis areas of the atrium.

The remaining procedure is the same as for any primary orthotopic heart transplantation.

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15 Error Messages and Corrective Measures

This chapter describes all Ikus error messages and explains what measures should be taken if an error does occur.

Keep calm!

Ikus treats all error messages with the same priority.

HOTLINE

Call Service Hotline! 866.249.0128

NOTICE

Even after being acknowledged on the laptop, some errors retrigger an alarm as long as they are still active. In such case mute the alarm on the handle. Before acknowledging the alarm wait for the error message and then take appropriate action.

When an error message occurs, the following happens:

- An acoustic signal (two different beep sounds) sounds.
- The indicator light on the control panel of the handle lights up.
- A red border is shown around the field **Alarm off** in the monitor program display.
- In the message window of the monitor program, a warning is displayed informing about the time of occurrence, the type of fault and the corrective measures which must be taken. IMPORTANT: Always observe the instructions! In addition, some of the more complex error messages contain an 8- or 16-digit binary code which enables the service department to identify the exact cause of the fault.

What to do when an error message is shown

INSTRUCTION

1. Check the status of the patient.
2. Observe the filling and ejection behavior of the blood pump (visual check) over several pump cycles!
3. Carry out the appropriate measures and acknowledge the message.

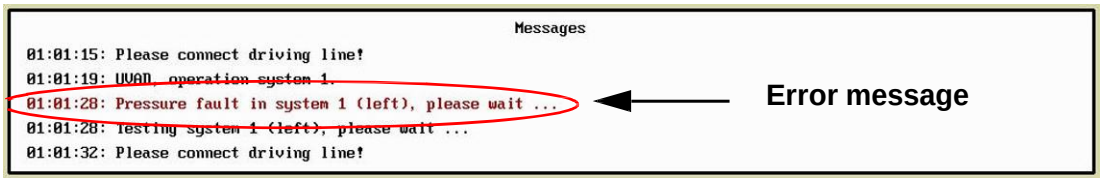


Fig. 15-1 Example of an error message in the message window

Acknowledging an error message

If the monitor program has been shut down, no data on current events are recorded and the LOG files will be incomplete. Accordingly do not shut down the monitor program unless absolutely necessary (e. g. if it is necessary to set up new user profiles)! Restart the monitor program as soon as possible!

The monitor program shows some of the error messages with an additional reference to system 1, 2 or 3. The system descriptions left and right refer to the internal arrangement of the pneumatic systems and not to the left or right pump.

This refers to the following connections specifically:

- system 1 (left): the system connected to the red connector
- system 2 (right): the system connected to the blue connector
- system 3 (backup): backup system

All messages, together with their time of occurrence, are recorded in the log file. In the case of some messages, the cause of the fault may correct itself automatically after a short time. In this case, a corresponding message is shown (e. g. **Please check left driving tube and pump or Left: driving tube/ pump OK**).

INSTRUCTION

1. Press the *mute button* on the control panel of the handle to mute the error message. This switches off the acoustic signal temporarily. The **Alarm off** field lights up red in the monitor program.
2. Read the displayed message(s) carefully. Observe the instructions provided in the message text.
3. Take corrective measures immediately!
4. Acknowledge the message in the monitor program. To do so, move the cursor to the **Alarm off** field and then press **<Enter>** to confirm. Otherwise the acoustic alarm will sound again after 10 minutes at the latest. Exceptional cases: section 15.4: Please Check Left / Right Pump and Driving Tube, page 146 and section 15.14: Temperature Sensors: <<8-digit binary code>>, page 153.

Message	Duration of muting:
Please connect driving tube!	10 s + 8 cycle s (systole + diastole)
Please check left / right pump and driving tube!	1 min
Batteries discharged - use power supply!	max. 1 min
Any other message	10 min

Tab. 15-1 Duration of muting

15.1 Pressure Error / Time Error in System 1 (or in system 2 or 3)

- **Pressure fault in system 1 (left), please wait ...**
- **Pressure fault in system 2 (right), please wait ...**
- **Pressure fault in system 3 (backup), please wait ...**
- **Time error system 1 (left), please wait ...**
- **Time error system 2 (right), please wait ...**
- **Time error system 3 (backup), please wait ...**

The air volume pumped per cycle by the Ikus or the pressure required to pump it has changed. The Ikus checks whether there is an internal system fault (e. g. a compressor has broken down) or whether there is an external error (e. g. driving tube not connected or driving tube leak).

WARNING

The blood pump of the corresponding system is stopped for the duration of this test (for approx. 10 seconds).

If the Ikus has detected a pneumatic system fault…

the Ikus switches to backup operation and the message Backup operation left/right appears. **Contact customer service** is shown together with a request to inform the service department (see section 15.5: Backup Operation Left/Right, page 147).

HOTLINE

Call Service Hotline! 866.249.0128

If the Ikus has detected an external fault …

it displays the message **Please connect driving tube!** (see section 15.3: Please Connect Driving Tube, page 145). Provide the patient immediately with a replacement Ikus.

If the main computer and the backup computer arrive at different results in the test phase …

the backup computer generates the message **Backup computer reports faulty test** (see section 15.11.4: ... Reports Faulty Test, page 151).

Follow the instructions exactly as described in each section.

15.2 Throttle Valve Error in System 1 (or system 2 or 3)

- **Throttle fault in system 1 (left), please wait ...**
- **Throttle fault in system 2 (right), please wait ...**
- **Throttle fault in system 3 (backup), please wait ..**.

HOTLINE

Call Service Hotline! 866.249.0128

In an active system, the Ikus has detected a throttle valve error (throttle: internal module for pneumatics test) and switches to backup operation (see section 15.5: Backup Operation Left/Right, page 147). Provide the patient immediately with a replacement Ikus. A throttle is an internal assembly for the pneumatic test.

15.3 Please Connect Driving Tube

Please connect driving tube!

INSTRUCTION

1. Inspect the driving tube and the connectors.
2. If a plug is not seated correctly: re-insert it by gripping the release sleeve and pulling it out of the connector. Then plug it back in. Check that the plug is securely connected. To do so, grip the plug body above the release sleeve and pull on it. Do not pull from the release sleeve or tube!

15.3.1 Replacing a Driving Tube

The driving tubes (red/blue) must be replaced after one year.(see Tab. 3-1, page 19)

WARNING

To replace a driving tube, the blood pump must be stopped temporarily. If the left driving tube is being replaced in a driving unit providing biventricular support, the right blood pump must also be stopped while the driving tube is being replaced in order to avoid overloading of the pulmonary circulation and a risk of pulmonary edema.

Material

- 1 driving tube, red or blue
- 1 tube connecting set (cable tie, cable-tie gun), from accessory set

INSTRUCTION

1. Log into the monitor program by entering user ID and password and confirm with **<Enter>**.
2. Select the option **Drive pause** and press **<Enter>** to confirm. Respond to the prompt in the dialog window by pressing the **<X>** key or the **<1>** key. The Ikus will stop.
3. Carefully cut the cable tie on the defective driving tube.
4. As soon as the pump has stopped, remove the driving tube from the pump.
5. Connect the new driving tube to the blood pump. To do so, carefully push the end of the driving tube onto the driving tube connector.
6. Remove the driving tube from the Ikus connector socket. To do so, take hold of the release sleeve and pull this out of the connector.
7. Connect the new driving tube to the connector. The sound of the plug snapping into place should be clearly audible. Check that the plug is securely connected by gripping the plug body above the release sleeve and pulling on it. Do not pull from the release sleeve or tube!
8. The view *Select operating mode* appears on the monitor. Select **Univentricular (UVAD)** or **Biventricular (BVAD)**, then confirm the selected operating mode with **<Enter>**. In biventricular mode the view *Pump size and single-step mode* appears. In univentricular mode, the connector seal test is performed first and then the view *Pump size and single-step mode* appears.
9. To confirm the **OK** selection, press **<Enter>**.
10. The system starts up again using the defined parameters.
11. Check whether the pump is filling correctly and, if necessary, adjust the Ikus parameters.
12. Secure the pump end of the driving tube with a cable tie strap. Important: Only the cable ties and cable tie guns provided should be used. See section 10.11: Securing the Connections, page 103.

15.4 Please Check Left / Right Pump and Driving Tube

- **Please check left pump and driving tube!**
- **Please check right pump and driving tube!**

The Ikus has detected an excessively deviating flow: The mean values of the last 16 cycles and of the last 1024 cycles deviate by more than 10 % from each other. Depending on the components, the parameters and the cause of the message, the message will be displayed usually within 5 s to 1 min.

IMPORTANT: To avoid alarms sounding in error, first mute the message on the drive unit. When muted, the alarm will be audible again in an 1-minute interval.

INSTRUCTION

1. Mute the message on the drive unit.
2. Inspect the driving tube and the cannulae: are kinks blocking the flow? Correct the positions to ensure an unimpaired flow.
3. Inspect the driving tube and the plugs. If a plug is not positioned correctly: re-insert it correctly. If the driving tube is defective: replace it (see section 15.3.1: Replacing a Driving Tube, page 145).
4. If necessary, adjust the parameters. Wait until the message **Left: Pump output measurement activated** or **Right: Pump output measurement activated** appears.
5. If necessary, correct the position of the cannulae.
6. Assess the hemodynamic status of the patient (volumes, MAP, PAP, CVP, etc.).

If the message appears again:

INSTRUCTION

1. Mute the message on the drive.
2. Confirm the parameter values. Position the cursor in the parameter table.
3. Assess the patient's hemodynamic status (volume, MAP, PAP, CVP,)
4. Monitor the membrane movement and make sure that the pump(s) are filling and ejecting completely. If this is quite correct, confirm the message in the monitor program.
5. If the message appears again, then the parameters can be modified slightly to normalize the flow.
6. Assess the hemodynamic status of the patient (volumes, MAP, PAP, CVP, etc.).
7. Monitor the membrane movement and make sure that the pump(s) are filling and ejecting completely. If this is functioning properly, then acknowledge the message in the monitor program.
8. If the message appears again, check if it is necessary to adjust the cannulae.

If the message appears again:

HOTLINE **Call Service Hotline! 866.249.0128**

15.5 Backup Operation Left/Right

- **Backup operation (right). Contact costumer service**
- **Backup operation (left). Contact costumer service**

The left (or right) pneumatic system has failed. The respective pump is now being powered by the backup system.

INSTRUCTION

1. Provide the patient immediately with a replacement Ikus.

HOTLINE

Call Service Hotline! 866.249.0128

15.6 Error Messages in Emergency Operating Mode

15.6.1 UVAD, Emergency Operation!. Contact Service Immediately!

UVAD, emergency operation! Contact service immediately!

Appears in univentricular mode.

WARNING

No more system is available as a redundancy. If the only remaining intact pneumatic system fails, there is a risk that the Ikus will shut down.

The blood pump is being driven by the last intact pneumatic system.

The pneumatic system continues running with the currently set parameters. The parameters can still be adjusted if necessary. However, it is not possible to switch over to biventricular operation.

INSTRUCTION

1. Provide the patient immediately with a replacement Ikus.

HOTLINE

Call Service Hotline! 866.249.0128

15.6.2 Emergency Operation System 1 (or System 2 or 3). Contact Service Now!

- **Emergency operation System 1. Contact service now!**
- **Emergency operation System 2. Contact service now!**
- **Emergency operation System 3. Contact service now!**

WARNING

There is no longer a redundant backup system. If the only remaining intact system fails, there is a risk that the Ikus will stop running altogether.

Appears in biventricular mode

Both blood pumps are being driven by the last intact pneumatic system.

The pneumatic system will now operate with fixed parameters (synchronous mode, systolic pressure 250 mmHg, diastolic pressure -100 mmHg, 70 bpm, relative systolic duration 40 %). It is not possible to change these settings.

Possible causes:

- 2 of the 3 pneumatic systems have developed faults.
- The Ikus has been running on battery power for too long and could no longer generate reliable values (Error message: **Emergency operation due to empty batteries: Risk of total failure!**). The Ikus has switched to the backup system and backup control computer. The message **Backup computer started! Contact customer service.** is displayed.

INSTRUCTION

1. Provide the patient immediately with a replacement Ikus.

HOTLINE **Call Service Hotline! 866.249.0128**

15.7 System 1 (or System 2) Is Defective!

- **System 1 (left) is defective!**
- **System 2 (right) is defective!**

The respective pneumatic system has developed a fault and a backup system (system 3) has been activated. If this error occurs during backup operation, Ikus will be running in emergency operating mode. In this case, Ikus has no more redundancy.

INSTRUCTION

1. Provide the patient immediately with a replacement Ikus.

HOTLINE **Call Service Hotline! 866.249.0128**

15.8 System 3 (Backup) Is Defective!

System 3 is defective!

The backup pneumatic system is detected as a fault during backup operation.

The Ikus runs in emergency operating mode. Provide the patient immediately with a replacement Ikus.

INSTRUCTION

1. Provide the patient immediately with a replacement Ikus.

HOTLINE **Call Service Hotline! 866.249.0128**

15.9 Alarm Circuit Fault: Buzzer Remains Off (or On)

- **Alarm circuit test failed - buzzer remains off!**
- **Alarm circuit test failed - buzzer remains on!**

WARNING The Ikus will not generate an acoustic signal in an alarm situation, or it will generate a wrong signal. Observe the messages displayed in the message window carefully and look for the visual alarm signal in the display and operating panel. As long as the patient is not provided with a replacement Ikus, the patient and the Ikus must be permanently monitored by medical personnel.

A fault in the alarm circuit is discovered during the self-test for the alarm circuit or when an alarm situation occurs. Depending on the type of fault, the message appears:

- **Alarm circuit test failed - buzzer remains off!**
- **Alarm circuit test failed - buzzer remains on!**
- **Acoustic alarm is not properly recognized**

INSTRUCTION

1. Provide the patient immediately with a replacement Ikus.

HOTLINE **Call Service Hotline! 866.249.0128**

15.10 Backup Computer Faulty! Contact Customer Service.

Backup computer faulty! Contact customer service.

NOTICE

Depending on when the fault occurs, the error message **Processor down. Inform service!** may not appear due to unfavorable resynchronization time response. In such case the drive will provide a visual and acoustic signal, however, no error message will be displayed.

One of the processors has failed. If the main computer fails, the message **Backup computer started! Contact costumer service.** also appears.

INSTRUCTION

1. Provide the patient immediately with a replacement Ikus.

HOTLINE **Call Service Hotline! 866.249.0128**

15.11 Backup Computer

15.11.1 ... Reports Discrepancy in Left/Right Pump Output Measurements!

- **Backup computer: discrepancy in left pump output measurement**
- **Backup computer: discrepancy in right pump output measurement**

The main computer has detected a flow error. This message appears only in conjunction with the message in section 15.4: Please Check Left / Right Pump and Driving Tube, page 146. Immediately take the measures described there

HOTLINE **Call Service Hotline! 866.249.0128**

15.11.2 ... Reports Faulty Measurements on the Left (or Right)

- **Backup computer: reports faulty measurement left!**
- **Backup computer: reports faulty measurement right!**

The main and backup computers show different results.

If this message appears only once:

no further measures are necessary.

If the message appears again:

INSTRUCTION

1. Check the status of the patient.
2. Check the filling and emptying of the blood pump(s), and monitor the function of the Ikus. As long as the patient is not provided with a replacement Ikus, the patient and the Ikus must be permanently monitored by medical personnel.
3. Provide the patient immediately with a replacement Ikus and switch off the malfunctioning Ikus. (see section 16.4: Connecting the Patient to a Replacement Ikus, page 171). If no replacement Ikus is available: Support the patient, if necessary using a manual pump! (see section 16.5: Driving Blood Pump(s) with the Manual Pump, page 173).

HOTLINE **Call Service Hotline! 866.249.0128**

15.11.3 ... Reports an Error in Output Measurement on the Left (or Right) Pump

- **Backup computer reports error: left pump output measurement**
- **Backup computer reports error: right pump output measurement**

The backup computer has detected a flow error, but the main computer has not.

INSTRUCTION

1. Check the filling and emptying of the blood pump(s).
2. Check the plausibility of the measured values.
3. Reset all of the parameter values. In addition, log out of the monitor program and then log back into it. Navigate the cursor with <←> / <→> to the desired field, adjust the value with <↓>/<↑>/ <Bild ↓>, <Bild ↑> , then confirm with <Enter>. The system works with the new value.

If the message appears again:

HOTLINE **Call Service Hotline! 866.249.0128**

15.11.4 ... Reports Faulty Test

Backup computer reports faulty test

The main computer cannot end the test phase to check the system after the error message... (See section 15.1: Pressure Error / Time Error in System 1 (or in system 2 or 3), page 144.)

- **Pressure fault in system 1 (left), please wait ...**
- **Pressure fault in system 2 (right), please wait ...**
- **Pressure fault in system 3 (backup), please wait ...**
- **Time error system 1 (left), please wait ...**
- **Time error system 2 (right), please wait ...**
- **Time error system 3 (backup), please wait ...**

IMPORTANT: The blood pump being driven by the tested system stops for approx. 10 seconds during the test phase.

INSTRUCTION

1. Check the status of the patient.
2. If the Ikus switches to backup operating mode or this message repeatedly appears, call the Service Hotline immediately.
3. Provide the patient immediately with a replacement Ikus. See section 16.4: Connecting the Patient to a Replacement Ikus, page 171.

HOTLINE **Call Service Hotline! 866.249.0128**

15.12 Measurement Discrepancy in Main Computer (Backup Computer)

- **Measurement discrepancy in main computer!**
- **Measurement discrepancy in backup computer!**

WARNING Between the error message **Measurement discrepancy in main computer!** and the 2nd (relevant) error message there can be a delay of several seconds. Wait for both error messages.

Only the active processor has detected an error. This message only appears in conjunction with an additional, relevant error message. Immediately take all of the necessary measures for this second message.

If the message appears only once:

no measures are necessary.

If the message appears several times:

INSTRUCTION

1. Provide the patient immediately with a replacement Ikus.

HOTLINE **Call Service Hotline! 866.249.0128**

15.13 Parameter Set Update Failure

- **Parameter set update failure**

The Ikus cannot store the changed parameter values in the internal system memory. The driving unit is operating with the changed values, but if a reset was to be performed, the old values would be valid again.

INSTRUCTION

1. Check the parameter values regularly. After a reset, if the Ikus continues to work with the old parameter values: re-adjust the parameter values.

If the message appears again:

INSTRUCTION

1. Provide the patient immediately with a replacement Ikus.

HOTLINE

Call Service Hotline! 866.249.0128

15.14 Temperature Sensors: <<8-digit binary code>>

- **Temperature sensors: <<8-digit binary code>>**

WARNING

Do not use water or other liquids to cool the Ikus!

IMPORTANT: An alarm was triggered by one of the sensors and an user muted it (mute interval: 10 min). During this mute interval now another sensor generates another alarm which is also muted by the user. This means that the remaining mute time of the first triggered alarm will be extended for another full mute interval.

INSTRUCTION

1. Determine whether internal or external influences have caused the driving unit to overheat. Is it exposed to direct heat from external sources? Is the ambient temperature too high?
2. If possible, remedy the situation (move the Ikus away from the heater, etc.). Provide adequate ventilation. Acknowledge the message. The Ikus takes a few minutes to cool down. Acknowledge the message repeatedly if necessary.

Usually, overheating of the Ikus is due to external factors such as direct thermal radiation (e. g. direct sunlight or from heaters). Overheating may also be caused by an internal fault, but this rarely occurs.

If external influences can be excluded as factors causing the message …

HOTLINE

Call Service Hotline! 866.249.0128

IMPORTANT: When passing on the error code to the service department directly (by telephone or fax): remember to state all 8 digits!

If necessary the service department will request to read out the LOG files and send a copy to Berlin Heart, Inc. (see section 16.7: Reading out the LOG Files, page 175).

15.15 Fault: <<16-digit binary code>> (<<type of fault>>)

- **Fault: <<16-digit binary code>>**
- **<<type of fault>>**

HOTLINE

Call Service Hotline! 866.249.0128

IMPORTANT: When passing on the error code to the service department directly (by telephone or fax): remember to state all 8 digits!

If necessary the service department will request to read out the LOG files and send a copy to Berlin Heart, Inc. (see section 16.7: Reading out the LOG Files, page 175).

15.16 Batteries Discharged; Battery Operation Not Possible

ABORT: Batteries discharged! No Battery operation possible!

The batteries have become discharged while connected to a main power supply by a battery malfunction.

WARNING Continue to operate the Ikus on main power supply!

INSTRUCTION

1. Check the status of the patient.
2. Check the filling and emptying of the blood pump(s), and monitor the function of the Ikus. As long as the patient is not provided with a replacement Ikus, the patient and the Ikus must be permanently monitored by medical personnel.
3. Provide the patient immediately with a replacement Ikus and switch off the malfunctioning Ikus. (see section 16.4: Connecting the Patient to a Replacement Ikus, page 171). If no replacement Ikus is available: support the patient, if necessary using a manual pump! (see section 16.5: Driving Blood Pump(s) with the Manual Pump, page 173)

HOTLINE **Call Service Hotline! 866.249.0128**

If this message appears during the start test

it is only an information message. Continue to operate the Ikus on main power supply! After sufficient charging time the message **Battery charge OK.** appears.

15.17 Batteries Recharged Insufficiently!

- **Batteries recharged insufficiently!**

WARNING Keep Ikus connected to main power supply! There is a danger of total shutdown after brief battery operation.

INSTRUCTION

1. Check the status of the patient.
2. Check the filling and emptying of the blood pump(s), and monitor the function of the Ikus.
3. The Ikus must be connected for six hours on the main power supply. If the batteries reach an adequate charge level, the message **Batteries recharged sufficiently!** will appear. The Ikus is fully functioning.
   As long as the batteries are not charged sufficiently the patient and the Ikus must be permanently monitored by medical personnel.
4. If the message **Batteries recharged sufficiently!** does not appear within 6 hours, use a replacement Ikus (see section 16.4: Connecting the Patient to a Replacement Ikus, page 171). If no replacement Ikus is available: support the patient, if necessary using a manual pump! (see section 16.5: Driving Blood Pump(s) with the Manual Pump, page 173)

HOTLINE **Call Service Hotline! 866.249.0128**

15.18 Error Messages - Circuit Breaker and Internal Battery Fuse

- **DANGER: Battery fuse test failed! - Check circuit breaker! No battery mode possible! Contact service.**
- **DANGER: Internal battery fuse test failed! No battery mode possible! Contact service.**

The following applies to both error messages:

WARNING

Ikus must be kept connected to the power supply! Danger of total shutdown in battery mode!

INSTRUCTION

1. Try to reset the circuit breaker on the connection panel (press button circuit breaker).
2. If the button circuit breaker can be pressed, the message **Battery fuse test OK** will appear within 10 minutes. After this the error has been eliminated and battery operation is possible again.
3. If the button circuit breaker cannot be pressed or triggers again, the internal battery fuse has failed. In this case the replacement Ikus must be connected immediately (see section 16.4: Connecting the Patient to a Replacement Ikus, page 171).

Also see section 16.8: Circuit Breaker and Battery Fuse, page 176.

15.19 Electronic Malfunction. Contact Customer Service!

This message appears if the internal power supply of the electronic equipment is faulty.

WARNING

Danger of total malfunction of the Ikus in the event of an additional error! Take immediate action!

INSTRUCTION

1. Provide the patient immediately with a replacement Ikus and switch off the malfunctioning Ikus. (see section 16.4: Connecting the Patient to a Replacement Ikus, page 171). If no replacement Ikus is available: support the patient, if necessary (in the event of malfunction of the defective Ikus), by means of the manual pump! (see section 16.5: Driving Blood Pump(s) with the Manual Pump, page 173)

HOTLINE

Call Service Hotline! 866.249.0128

15.20 Acoustic Alarm is Not Properly Recognized

If the message **Acoustic alarm: OK** appears within 8 seconds after the error message, the Ikus is working perfectly. No further measures are necessary.

If the message **Acoustic alarm: OK** does not appear within 8 seconds, the alarm circuit is defective. A possible error might not have been detected.

INSTRUCTION

1. Check the status of the patient.
2. Check the filling and emptying of the blood pump(s), and monitor the function of the Ikus. As long as the patient is not provided with a replacement Ikus, the patient and the Ikus must be permanently monitored by medical personnel.
3. Provide the patient immediately with a replacement Ikus and switch off the malfunctioning Ikus. (see section 16.4: Connecting the Patient to a Replacement Ikus, page 171). If no replacement Ikus is available: support the patient, if necessary (in the event of malfunction of the defective Ikus), by means of the manual pump! (see section 16.5: Driving Blood Pump(s) with the Manual Pump, page 173)

HOTLINE **Call Service Hotline! 866.249.0128**

15.21 Error: No Data / No Reaction from the Control Computer

- **Error: no data from Master.**
- **Error: no reaction from Master.**

In the event of the simultaneous malfunction of both control computers or the malfunction of the power supply, the Ikus cannot generate a specific error message in the message window.

INSTRUCTION

1. Check the status of the patient.
2. Evaluate the malfunction scenario:
   - **no alarm, but the Ikus continues to function:** no communication between the control computers and the laptop
   - **optical and acoustic alarm, and the Ikus is working in emergency mode:** both control computers are defective
   - **The Ikus is halted; acoustic alarm only:** defective power supply
3. Immediately provide the patient with a replacement Ikus and switch off the malfunctioning Ikus. (see section 16.4: Connecting the Patient to a Replacement Ikus, page 171).
   If no replacement Ikus is available and the Ikus is running: Check the filling and emptying of the blood pump(s), and monitor the function of the Ikus. Do not operate the Ikus without supervision!
   If no replacement Ikus is available and the defective Ikus is halted: Support the patient with the manual pump. (see section 16.5: Driving Blood Pump(s) with the Manual Pump, page 173).

HOTLINE **Call Service Hotline! 866.249.0128**

15.22 Left / Right Flow Sensor Defective. Notify Service!

- **Left flow sensor fault. Contact customer service.**
- **Right flow sensor fault. Contact customer service.**

The corresponding flow sensor is defective. Although the Ikus continues to run, the excessively low flow would not be detected - possibly due to a kink in a cannula or the driving tube.

WARNING

As long as the patient is not provided with a replacement Ikus, the patient and the Ikus must be permanently monitored by medical personnel.

NOTICE

When stopping and restarting a blood pump, a previous flow alarm will be deleted.

.

INSTRUCTION

1. Check the status of the patient.
2. Check the filling and emptying of the blood pump(s), and monitor the function of the Ikus. Do not operate the Ikus without supervision!
3. Provide the patient with a replacement Ikus and switch off the Ikus. (see section 16.4: Connecting the Patient to a Replacement Ikus, page 171). If no replacement Ikus is available: support the patient, if necessary (in the event of malfunction of the defective Ikus), by means of the manual pump! (see section 16.5: Driving Blood Pump(s) with the Manual Pump, page 173)

HOTLINE

Call Service Hotline! 866.249.0128

15.23 Self-test is not Completed by Passive Computer!

The passive processor was unable to end the self-test of the alarm circuit.

If, within 8 seconds, the message Alarm circuit test OK appears,

the Ikus is working perfectly. No further measures are necessary.

If the message Alarm circuit test OK does not appear within 8 seconds,

the alarm circuit is defective. A possible error might not have been detected.

INSTRUCTION

1. Check the status of the patient.
2. Check the filling and emptying of the blood pump(s), and monitor the function of the Ikus.
3. Provide the patient with a replacement Ikus and switch off the Ikus. (see section 16.4: Connecting the Patient to a Replacement Ikus, page 171). If no replacement Ikus is available: support the patient, if necessary (in the event of malfunction of the defective Ikus), by means of the manual pump! (see section 16.5: Driving Blood Pump(s) with the Manual Pump, page 173)

HOTLINE

Call Service Hotline! 866.249.0128

15.24 Error Messages During the Start-up Test

In addition to the error messages listed below there are additional messages possible that are described in chapter 12.

The error messages listed here occur during the start test. Wait until the end of the start test to take appropriate measures.

If one of the following messages occur outside the start-up test replace the Ikus.

15.24.1 Battery Test Skipped (Battery problem!)

- **Battery test skipped (Battery problem!)**

The charge level of the batteries is too low to permit battery operation.

INSTRUCTION

1. Operate the Ikus on main power supply. Battery operation is possible only when all of the yellow LEDs are illuminated.

15.24.2 Additional Messages During the Start-up Test

If the Ikus detects an error during the start-up test, one of the following messages appears in the message window depending on the nature of the error:

- **Problem: batteries have very different charges.**
- **Problem: battery controller: batteries are discharged**
- **Problem: charge unit fault. Contact customer service.**
- **Problem: laptop fault. Contact customer service.**
- **Problem: power relay. Contact customer service.**
- **Problem: mains sensor fault. Contact customer service.**
- **Problem: mains voltage. Check power and switch.**
- **Problem: power pack fault. Contact customer service.**
- **Problem: WR2 fault / relay board**
- **Problem: relay 1 faulty. Contact customer service**
- **Problem: relay 2 faulty. Contact customer service**
- **Problem: WR1 not switching. Contact customer service.**
- **Problem: 0000 0011 0011 0111(fault in power supply)** see section 15.15: Fault: <<16-digit binary code>> (<<type of fault>>), page 153.

Restart the Ikus after the start-up test if one of the above messages appears

INSTRUCTION

1. According to display: if necessary: enter **<7>** to read any messages; go back by pressing **<Enter>**. Important: enter **<1>** or **<x>** to exit the monitor program. A second window appears.
2. Second window: according to the display, select the option **End**. The monitor program writes a log file and is terminated. Wait until the message **Switch off drive with main switch!** appears.
3. Switch off the main switch (key switch) and then switch it back on again.

If the Ikus now ends the start-up test without a message:

Ikus is ready for use

If one of the above messages appears again:

INSTRUCTION

1. Do not use the Ikus.

HOTLINE

Call Service Hotline! 866.249.0128

15.25 Discrepancy in Pressure Measurement: System 1 (or System 2/3)

- **Discrepancy in pressure measurement: system 1 (left)**
- **Discrepancy in pressure measurement: system 2 (right)**
- **Discrepancy in pressure measurement: system 3 (backup)**

NOTICE

Avoid a further increase in the rate or, alternatively, the driving pressure for parameters set at high values. Otherwise the Ikus might perform a test phase, which means that the blood pump of the corresponding system is briefly stopped for the duration of this test

The information message **Discrepancy in pressure measurement: system 1 (2 or 3)** is not accompanied by an acoustic signal.

The message appears if the compressed air being produced at a constant rate by the compressor in the present pump cycle is unable to meet the levels required for achieving the defined parameters. The message can have the following causes:

- The set pressure values and rates are extremely high
- The performance capability of the pneumatics is limited (maintenance required)
- Malfunction in the system

INSTRUCTION

1. Check the status of the patient.
2. Check the filling and emptying of the blood pump(s), and monitor the function of the Ikus.
3. Compare the set target parameter values with the parameter values actually generated. In the event of deviation from high set values, reduce the rate and/ or vary the relative systolic duration, reduce the systolic driving pressure (e.g., from 210 mm Hg to 200 mm Hg) and/or the diastolic suction pressure (e.g., from -40 mm Hg to -45 mm Hg), as necessary.
   IMPORTANT: If the set parameter values are high, do not increase the rate or systolic driving pressure any further. Otherwise, Ikus may conduct a self-test. This would cause the blood pump(s) to be stopped temporarily.
4. Check to see whether the message occurs again.

If the message appears several times over the course of 24 hrs:

HOTLINE

Call Service Hotline! 866.249.0128

15.26 Communication with Laptop Failed

- **Communication with laptop failed**

This message informs the user that the communication between the control computers and the monitor program has been temporarily interrupted. This occurs if the monitor program is exited for any reason (i.e. administer user IDs and passwords). This message does not require user intervention.

16 Troubleshooting and Correcting Faults

HOTLINE **Call Service Hotline! 866.249.0128**

Problem	Cause of problem / action to be taken
Deposits in the pump	Initial deposits: check anticoagulation status and adjust therapy if necessary. If floating deposits are detected (may cause thromboembolic complication): replace the blood pump. See section 16.1: Replacing the Blood Pump(s), page 165.
Visible blood pump faults	Replace the blood pump. See section 16.1: Replacing the Blood Pump(s), page 165.
Pump membrane remains in the diastolic or systolic position despite vibration / movement of the pump indicating that the Ikus is attempting to provide diastolic or systolic pressure	**Possible causes:** • kinking of the cannula • clotting of the pump • partial malfunction of the Ikus **What to do?** Check for external forces on the cannula and whether it may be necessary to manipulate the cannula. See section 15.4: Please Check Left / Right Pump and Driving Tube, page 146. Check for clots in the pump or cannula that may be obstructing flow and replace the pump if necessary. See section 16.1: Replacing the Blood Pump(s), page 165. Initiate hand-pumping to try to eject the pump. See section 16.5: Driving Blood Pump(s) with the Manual Pump, page 173. Switch the patient to the back-up Ikus driving unit. See section 16.4: Connecting the Patient to a Replacement Ikus, page 171.
Pump membrane remains in one position despite the above manipulations	**Additional possible causes:** • high vascular resistance • defective blood pump There may be air leaking into the space between the first and second layer of the triple-layer pump membrane. This accumulated air may gradually create a “pillowing” effect between the membranes. The top (visible) membrane layer will appear to be continuously in diastole while the bottom two membrane layers are in fact continuously in systole.

Tab. 16-1 Possible problems

Problem	Cause of problem / action to be taken
	As the Ikus continues to provide filling and emptying pressure to the pump, the pump (and possibly the membrane layers) will flex slightly under the changing pressures but will not operate fully. **What to do?** If the patient has high vascular resistance, treat medically as appropriate to reduce the resistance. Adjust system parameters to encourage emptying of the pump. If the pump is defective, replace the pump, see section 16.1: Replacing the Blood Pump(s), page 165.
Blood is seen in front of or in the area around the stabilization ring in the blood pump.	**Possible causes:** The triple layer membrane is allowing blood to leak into the space between the layers in the area around the stabilization ring. **What to do?** Replace the pump. See section 16.1: Replacing the Blood Pump(s), page 165.
Condensation in area around the stabilization ring of the blood pump	Monitor the blood pump function more frequently for proper blood pump function. Clear fluid content if any in the driving tube and air chamber of the blood pump. Check if the condensate will leave in the next days. Call Service Hotline.
Flapping or fluttering of membrane during membrane movement of the pump	**Possible cause:** Partial rupture of one or two layers of the triple-layer membrane. Changes in air pressure during systole and diastole may cause the ruptured layer(s) to flutter. **What to do?** Replace the pump. See section 16.1: Replacing the Blood Pump(s), page 165.
Blood pump membrane rupture during pump priming (prior to patient support)	**Possible cause:** If the pump membrane is not moved completely to the diastolic position prior to insertion of the de-airing needle, a puncture of the membrane can occur. When the membrane is in the complete diastolic position, the needle will not puncture the membrane. **What to do?** Discard the damaged pump and do not use with the patient. Prime a new pump following the directions in section 9.3: Moving the Membrane to the End-of-Diastole Position, page 86.

Tab. 16-1 Possible problems

Problem	Cause of problem / action to be taken
Cannula rupture	**Possible cause:** Damage to cannula caused by excessive external forces or a sharp object. **What to do?** Immediately stop the support by disconnecting the driving tube from the Ikus. Clamp the cannula. Follow directions to replace the pump, see section 16.1: Replacing the Blood Pump(s), page 165. After removing the current pump, trim the cannula proximal to the damaged area.
Damaged driving tube(s) found through visible or audible inspection of the tube(s) or from Ikus alarm(s)	**Possible causes:** The driving tube has been damaged and the integrity of the tubing may be compromised. There may or may not be an audible sound from air escaping the tubing. This condition may be accompanied by the following error messages. • section 15.1: Pressure Error / Time Error in System 1 (or in system 2 or 3), page 144 followed by: • section 15.3: Please Connect Driving Tube, page 145 **What to do?** If the driving tube is damaged, replace it; see section 15.3.1: Replacing a Driving Tube, page 145. If a fault in the tubing is not apparent upon inspection, but the Ikus has the above error(s), then follow the directions associated with the error message on the Ikus; see chapter 15: Error Messages and Corrective Measures, page 143:
Visible Ikus faults	Call Service Hotline!

Tab. 16-1 Possible problems

Problem	Cause of problem / action to be taken
Ikus: the graph display stops moving, parameters cannot be adjusted	**Possible causes** • faulty communications between control computer and laptop • batteries not supplying enough current • the electronics (main and backup control computers) have failed **What to do?** Switch the laptop off and then back on again and wait for the start-up procedure to be completed. Then start the monitor program. IMPORTANT: The Ikus continues running with the currently set parameters. **The graphs remain frozen** The Ikus is operating in emergency pulse mode, see section 16.3: Emergency Pulse Mode, page 169. Call Service Hotline! Restart the Ikus after consulting the service department staff: See section 16.2: Restarting Ikus, page 168.
Acoustic and visual alarm from the Ikus, message **Error: no data from Master** or **Error: no reaction from Master**	**Possible causes** • simultaneous malfunction of both control computers • power supply malfunction **What to do?** Assess the condition of the patient and the hemodynamic values. Call Service Hotline immediately.
Pump stands still - no further pump function; acoustic alarm is still audible	**Possible causes** • complete failure of the Ikus • batteries are completely empty or serious fault in the batteries **What to do?** Immediately connect the Ikus to a main power supply. Until then, use the manual pump. See also section 7.4: Battery Operation, page 56 and section 16.5: Driving Blood Pump(s) with the Manual Pump, page 173. Notify Hotline immediately.

Tab. 16-1 Possible problems

16.1 Replacing the Blood Pump(s)

WARNING

The blood pump may be replaced only under sterile conditions!

While replacing a blood pump verify that all connections and cannulae stubs are intact.

All efforts shall be made to minimize the manipulation and distortion of the blood pumps, cannulae, cannula extension set and connecting set during the removal of the cable ties to prevent damage and mobilization of deposits.

Cable ties must be removed carefully. Use an appropriate blunt tool. Never use a sharp instrument such as scalpel or scissors, to remove the cable ties which can result in damage and leakage, resulting injury or death to the patient.

BVAD: if the left blood pump is being replaced, the right blood pump must also be stopped while the pump is being replaced to avoid the risk of pulmonary edema.

NOTICE

If the replacement blood pump has a larger volume than the one being replaced, the use of a connector set must be considered, the corresponding parameter in the view *Pump size and single-step mode* must be updated.

IMPORTANT: When two blood pumps need to be replaced, replace the right blood pump first followed by the left blood pump.

IMPORTANT: Sedate the patient if necessary and use appropriate anticoagulation protocol.

When using a cannula extension set / connecting set: See section 10.3: Cannulae, Cannula Extension Set and Connecting Set, page 91.

16.1.1 Preparing a Replacement Blood Pump

Material

- replacement blood pump of appropriate type and size
- driving tube, red or blue
- accessory set (for blood pumps with PU valves) with tube connecting set; IMPORTANT: Only the cable ties and the cable tie gun provided should be used.

INSTRUCTION

1. Bring membrane to the end-of-diastole position, position de-airing needle, rinse and fill pump with sterile injectable saline (see section 9.3: Moving the Membrane to the End-of-Diastole Position, page 86 and section 9.4: De-airing the Blood Pump, page 86).
2. Connect the driving tube to the respective driving tube connector of the pump.

3. Place the pump, ready for connection, with the titanium connectors pointing upwards.

16.1.2 Replacing the Right Blood Pump (BVAD)

Material

- prepared replacement blood pump (see section 16.1.1: Preparing a Replacement Blood Pump, page 165)
- tube connecting set (cable tie, cable-tie gun), included in the accessory set. Only the cable ties and cable tie guns provided should be used.

Stopping the right blood pump and detaching the blood pump from Ikus

INSTRUCTION

1. Put the patient in the Trendelenburg position.
2. Remove the cable tie covering the EXCOR cannula on the stub of the blood pump carefully using an appropriate blunt tool.
   Important: never use a sharp instrument, for example, a scalpel or scissors, to remove the cable tie. This may cause damage to the cannula. Check cannulae immediately to make sure they are not damaged.
3. If necessary log into the monitor program by entering user ID and password, confirming the password with **<Enter>**.
4. Reduce rate of left blood pump to 30 bpm. Use <←>/ <→> to navigate cursor to the respective field of the parameter table, then use <↓> to adapt value. Confirm with <Enter>.
5. In the monitor program, select the option **Pause right** and press **<Enter>** to confirm. Respond to the prompt in the dialog window by pressing the **<X>** key or the **<1>** key. The right blood pump will stop.
   The view *Pump size and single-step mode* for the right blood pump is displayed.
6. As soon as the right pump has stopped, clamp off the cannulae beneath the right pump to be replaced and slide the cannulae off the pump. If it is necessary to clamp any part of the cannula that is not covered with velour, cover the part of the cannula that will be clamped with a gauze sponge.
7. Check cannulae for visible deposits. If necessary, remove these deposits carefully.
8. Remove the driving tube of the right blood pump from the Ikus by taking hold of the release sleeve and pulling out of the connector.

Connect new right blood pump

INSTRUCTION

1. Fill the free ends of the cannulae with sterile saline solution. Make sure that all air has been removed. Connect the prepared replacement pump to the cannulae.
2. Plug the new driving tube into the blue connector. The plug snapping into place is clearly audible.
3. Check that the plug is securely connected by gripping the plug body above the release sleeve and pulling on it. Do not pull from the release sleeve or tube!
4. Release the tube clamps from the cannulae.

Starting the Ikus

INSTRUCTION

1. Move the cursor to the field **Step right**.
2. Confirm **Step right** with **<Enter>** to trigger a single step.
3. If any air bubbles are visible remove them via the de-airing needle.
4. Move cursor to the **OK** field and press **<Enter>** to confirm. The driving unit starts up again.
5. Increase the rate of left blood pump to required value. For asynchronous mode: set the rate for the right blood pump.
6. Check whether the blood pump is filling correctly and, if necessary, adjust the parameters.
7. Remove the de-airing needle from the right blood pump.
8. Secure all connections with cable ties. See section 10.11: Securing the Connections, page 103.

16.1.3 Replacing the Left Blood Pump (LVAD/ BVAD)

Material

- prepared replacement blood pump (see section 16.1.1: Preparing a Replacement Blood Pump, page 165)
- tube connecting set (cable tie, cable-tie gun), included in the accessory set. Only the cable ties and cable tie guns provided should be used.

Stopping the left blood pump and detaching the blood pump from Ikus

INSTRUCTION

1. Put the patient in the Trendelenburg position.
2. Remove the cable tie covering the EXCOR cannula on the stub of the blood pump carefully using an appropriate blunt tool. Important: never use a sharp instrument, for example, a scalpel or scissors, to remove the cable tie. This may cause damage to the cannula. Check cannulae immediately to make sure they are not damaged.
3. If necessary log into the monitor program by entering user ID and password, confirming the password with **<Enter>**.
4. In the monitor program, select the option **Pause left** (LVAD) respectively **Drive pause** (BVAD) and press **<Enter>** to confirm. Respond to the prompt in the dialog window by pressing the **<X>** key or the **<1>** key. The left respectively both blood pumps will stop.
   LVAD: **Pause left** the view *Pump size and single-step mode* is displayed.
   BVAD: **Drive pause** the view *Select operating mode* is displayed.
5. As soon as the blood pump(s) has/have stopped, clamp off the cannulae beneath the blood pump to be replaced and slide the cannulae off the blood pump. If it is necessary to clamp any part of the cannula that is not covered with velour, cover the part of the cannula that will be clamped with a gauze sponge.
6. Check cannulae for visible deposits. If necessary, remove these deposits carefully.
7. Remove the driving tube of the left blood pump from the Ikus by taking hold of the release sleeve and pulling it out of the connector.

Connect new left blood pump

INSTRUCTION

1. Fill the free ends of the cannulae with sterile saline solution. Make sure that all air has been removed. Connect the prepared replacement blood pump to the cannulae.
2. Plug the new driving tube into the red connector. The plug snaps into place clearly audible.
3. Check that the plug is securely connected by gripping the plug body above the release sleeve and pulling on it. Do not pull from the release sleeve or tube!
4. Release the tube clamps from the cannulae.

Starting the Ikus

INSTRUCTION

1. Move the cursor to the field **Step left**.
2. Confirm **Step left** with **<Enter>** to trigger a single step.
3. If any air bubbles are visible remove them via the de-airing needle.
4. Move cursor to the **OK** field and press **<Enter>** to confirm. The driving unit starts up again using the defined parameters.
5. Check whether the blood pump is filling correctly and, if necessary, adjust the parameters.
6. Remove the de-airing needle from the left blood pump.
7. Secure all connections with cable ties. See section 10.11: Securing the Connections, page 103.

16.2 Restarting Ikus

WARNING

Do not turn off and restart the Ikus unless requested by a service consultant.

If the graphs in the monitor program are frozen (not moving) and the parameters cannot be adjusted even after the laptop and the monitor program have been restarted, then the Ikus is operating in emergency pulse mode. In such case, proceed as described in section 16.3: Emergency Pulse Mode, page 169 instead.

INSTRUCTION

1. Support patient with a replacement *Ikus* (see section 16.4: Connecting the Patient to a Replacement Ikus, page 171) or manual pump (see section 16.5: Driving Blood Pump(s) with the Manual Pump, page 173).
2. Use the seal plugs to seal the driving tube connectors.
3. Switch off the *Ikus* . In the monitor program, select the **Drive OFF** option and press **<Enter>** to confirm. Respond to the prompt in the dialog window by pressing the **<X>** or the **<1>** key. IMPORTANT: If it is not possible to select the **Drive OFF** option, the Ikus is running in emergency pulse mode. In this case, proceed as explained in section 16.3: Emergency Pulse Mode, page 169.
4. Wait until the log has been completed. If the message **Switch off drive with main switch!** appears, turn the key switch to the *[0]* position.

5. Turn off the laptop.
6. Turn Ikus on again immediately. To do so, turn the key switch to the *[I]* position.
7. Turn the laptop on. Select the **1. Start program** option (**<1>**). Enter user ID and password, confirming the password with **<Enter>**.
8. Check all parameters and re-adjust them if necessary.
9. For univentricular operation, unplug the connector marked in red. For biventricular operation, unplug both connectors. To do so, pull the seal plug(s) out of the respective connector(s).
10. Disconnect the driving tube(s) from the replacement *Ikus* or the manual pump and connect it to the Ikus. IMPORTANT: Observe the colored markings. The sound of the plug snapping into place should be clearly audible.
11. Check that the plug is securely connected by gripping the plug body above the release sleeve and pulling on it. Do not pull from the release sleeve or the tube!
12. Move cursor to the **OK** field and press **<Enter>** to confirm. The standard view is shown. The system will operate with the current parameter settings.
13. Turn off the replacement *Ikus* driving unit (see section 7.3.3: Drive OFF: Switching the Ikus off, page 56).

16.3 Emergency Pulse Mode

WARNING

If the Ikus is operating in emergency pulse mode, visually check to be sure the blood pump(s) is (are) filling and ejecting completely. If one blood pump is not filling and/or ejecting completely, the patient must be supported immediately using the manual pump (see section 16.5: Driving blood pump(s) with the manual pump, page 196).

If the emergency pulse mode is activated while the backup system is already active, the Ikus is no longer able to drive both blood pumps. In this case the patient must immediately be supported using the manual pump (see section 16.5: Driving blood pump(s) with the manual pump, page 196).

IMPORTANT: In emergency pulse mode a controlled shut down is not possible.

IMPORTANT: In emergency pulse mode it is not possible to acknowledge the acoustic alarm.

If the graphs in the monitor program are not moving and the parameters cannot be adjusted even after the laptop and the monitor program have been restarted, then the *Ikus* is operating in emergency pulse mode. Both control computers have failed and are no longer communicating with each other. The emergency pulse board has taken over control of the left and the right pneumatic system.

Replace the Ikus with a replacement Ikus if possible. If no replacement Ikus is available, the Ikus will continue to support the patient in emergency pulse mode until a replacement Ikus is ready.

In emergency pulse mode the system operates with the following settings:

Synchronous mode (biventricular)

	Systolic pressure [mmHg]	Diastolic pressure [mmHg]	Rate [bpm]	Relative systole duration [%]
Left	210	-40	70	40
Right	150	-40	70	40

Tab. 16-2 Settings in emergency pulse mode

HOTLINE

Call Service Hotline! 866.249.0128

16.3.1 Emergency Pulse Mode - Turning off the Ikus

WARNING

Only proceed as described below if a replacement *Ikus* is available to support the patient.

INSTRUCTION

1. Support the patient by a replacement *Ikus* (see section 16.4: Connecting the Patient to a Replacement Ikus, page 171).
2. Use the seal plugs to seal the driving tube connectors on the *Ikus*.
3. Switch off the laptop.
4. Switch off the *Ikus*. To do so, turn the key switch to *[0]* position.

16.3.2 Ikus Start-Test Following Emergency Pulse Mode

WARNING

Do not reconnect the original Ikus to the patient until the Berlin Heart, Inc. service has evaluated the LOG files or has serviced the Ikus.

Wait for at least 5 minutes after switching the Ikus off while in emergency pulse mode. Otherwise, only the service staff will be able to restart it.

INSTRUCTION

1. **After 5 minutes**: insert the USB stick into the USB port of the laptop and switch on the *Ikus*. To do so, turn the key switch to the *[I]* position. The battery charge indicator will light up and the number of hours the Ikus has been used to date will be displayed. The main power supply indicator should light up.
2. Turn the laptop on. The menu *Select language* appears.
3. Select the desired language by pressing the corresponding number key. It is not necessary to press **<Enter>** to confirm this selection. The start menu will be displayed on the laptop.
4. Select the **1. Start program** option (**<1>**). Enter user ID and password, confirming the password with **<Enter>**. The Ikus will carry out a start-test.

5. Wait for the start-test to finish (this takes a few minutes). Do not mute the acoustic signal. The messages in the message window inform the user of the current status of the test. If the system is operating correctly, the view *Select operating mode* will be displayed.
6. Select **Drive OFF**, then press **<Enter>** to confirm.
7. Respond to the prompt in the dialog window by pressing the **<X>** key or the **<1>** key. The system stops operation immediately and writes an operating log.
8. Wait until the log has completed (message: **Switch off drive with main switch!**). IMPORTANT: Do not turn the *Ikus* off yet.
9. Shut down the monitor program. Press **<F10>** and confirm by pressing the **<X>** key or the **<1>** key. The start menu is displayed on the laptop.
10. In the start menu, select **4. Save data** (**<4>**). The LOG files are copied onto the USB stick. After that the start menu appears again.
11. Turn off laptop. Take the USB stick out of the port (but never when the laptop is switched on).
12. Send the LOG files by e-mail to service@berlinheart.com.

16.4 Connecting the Patient to a Replacement Ikus

⚠ CAUTION

The Ikus must always be connected to the power supply when it is switched on. This is the only way to ensure that the start-up test is performed completely and possible malfunctions can be detected.

Ikus and all of its parts shall not be serviced or maintained while in use with a patient.

Turning on the replacement Ikus

INSTRUCTION

1. Prepare the replacement *Ikus* and connect it to the main power supply. Secure the mains cable with the plug clip. Ensure that the power switch (toggle switch) is set to *[I]* position.
2. Ensure both driving tube connectors are sealed.
3. Turn on the replacement *Ikus*. To do so, turn the key switch to the *[I]* position. The battery charge indicator will light up and the number of hours the Ikus has been used to date will be displayed. The main power indicator lights up.
4. Turn the laptop on. The menu *Select language* appears.
1. Select the desired language by pressing the corresponding number key. It is not necessary to press **<Enter>** to confirm this selection.
2. Select the **1. Start program** option (**<1>**). Enter user ID and password, confirming the password with **<Enter>**. The *Ikus* will carry out a start-test.
3. Wait for the start-test phase to finish (this takes a few minutes). Do not mute the acoustic signal. The messages in the message window inform the user of the current status of the test. When the test is complete, the view *Select operating mode* will be displayed.
4. Select **Univentricular (UVAD)** or **Biventricular (BVAD)**, then confirm the selected operating mode with **<Enter>**.

Setting the parameter values of the replacement Ikus

NOTICE

If no parameter values are entered into the replacement *Ikus*, the replacement *Ikus* will use the following default parameter values (standard parameters):

Systole [mmHg] left/ right	Diastole [mmHg] left/ right	Rate [bpm]	Rel. diast. duration [%] left/ right	Operation mode
210 / 130	-40 / -20	80	40 / 40	biventricular, synchronous and separate

Tab. 16-3 Default standard parameters

INSTRUCTION

5. In **biventricular** mode, the view *Pump size and single-step mode* is shown. In **univentricular** mode, a connector seal test is first performed (taking approx. 10 seconds). The *Ikus* will confirm that the driving tube connector with the blue marking has been sealed. Then the view *Pump size and single-step mode* is displayed.
6. Enter all operating parameters from the original *Ikus* to the replacement *Ikus*.
7. Move cursor to the field **Step left** and press **<Enter>** to confirm.
   Biventricular: move cursor to the field **Step right** and press **<Enter>** to confirm.
8. Move the cursor to the **OK** field. IMPORTANT: Do not confirm **OK** yet.

The default settings for systole, diastole and relative systole duration depend on whether the blood pump is registered as the left or right blood pump in the monitor program.

Univentricular: default setting as for left blood pump.

Connecting the blood pump(s) to the replacement Ikus

INSTRUCTION

1. For **univentricular operation**, unplug the connector marked in red. For **biventricular operation**, unplug both connectors by removing the seal plugs from their respective connector(s).
2. **If possible**, log into the monitor program of the original *Ikus*. Select **Drive OFF**, then press **<Enter>** to confirm. Respond to the prompt in the dialog window by pressing the **<X>** key or the **<1>** key. The system will stop. If it is not possible to select the **Drive OFF** option, proceed with triggering single steps (**Step left**/ **Step right**, see instructions in section 16.1: Replacing the Blood Pump(s), page 165) without stopping the *Ikus*.
3. As soon as the original *Ikus* has stopped, remove the driving tube(s) by taking hold of the release sleeve and pulling it out of the connector(s).
4. Connect the driving tube(s) to the replacement *Ikus*.
   IMPORTANT: Observe the colored markings. The sound of the plug snapping into place should be audible. Check to be sure the plug is securely connected by gripping the plug body above the release sleeve and pulling on it. Do not pull from the release sleeve or tube!

5. To confirm the **OK** selection, press **<Enter>**. The replacement *Ikus* will start up using the defined parameter settings.
6. Check to be sure the pump is filling correctly and, if necessary, adjust the parameters.
7. Turn off the original Ikus (see section 7.3.3: Drive OFF: Switching the Ikus off, page 56).

16.5 Driving Blood Pump(s) with the Manual Pump

Fig. 16-1 Patient on manual pump

This is necessary if …

- there is a problem with the power supply to which the Ikus is connected, or
- the Ikus has to be restarted (e.g. emergency operating mode) and there is no replacement Ikus available

⚠ WARNING

The manual pump should be used only by medical personnel specifically trained to use it.

To avoid risk of lung edema be sure the coloured markings on the driving tubes match the connectors of the manual pump (red to red and blue to blue).

Keep the manual pump attached to the Ikus in order to have it readily available in case of emergency.

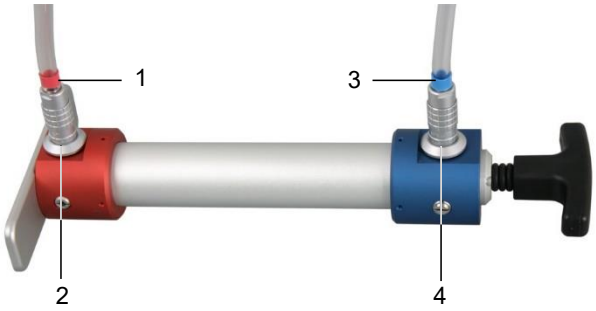
Ensure that the patient receives immediate support. Then call one or more persons to assist.

When operating the manual pump with one hand (using the base plate), do not block the valves with your feet (see valve "2" in Fig. 16-2, page 174).

IMPORTANT: In biventricular mode: the blood pumps are driven asynchronously by the manual pump.

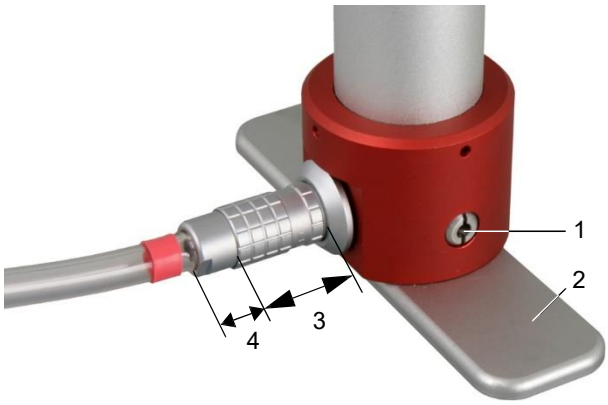
INSTRUCTION

1. Be sure the patient is lying down.
2. Disconnect the driving tube(s) from the Ikus by taking hold of the release sleeve and pulling it out of the connector.
3. Connect the driving tube(s) to the manual pump. IMPORTANT: Observe the colored markings to be sure they match.
4. Check to be sure that the plug is securely connected by gripping the plug body above the release sleeve and pulling on it. (see „4“ in Fig. 16-3, page 174) Do not pull from the release sleeve or tube!
5. Pump steadily and rhythmically at roughly 60 to 80 strokes per minute. Important: Move the piston so far that the membrane reaches its final position. The piston need not necessarily be moved to its end position.
6. Perform a visual check of the blood pump to verify that the membrane is moving and that blood is being pumped.



1 Driving tube with red marking
2 Connector for driving tube with red marking
3 Driving tube with blue marking
4 Connector for driving tube with blue marking

Fig. 16-2 Manual pump



1 Valve
2 Base plate
3 Release sleeve
4 Area above release sleeve

Fig. 16-3 Plug on the driving tube

Fig. 16-4 Examples to operate the manual pump

The manual pump can be operated with both hands or with one hand (placing the pump between the feet). Alternating between two-handed or one-handed pumping, as well as using the left or right hand, is allowed.

16.6 Main Power Supply Failure or Breakdown of Both Control Computers

INSTRUCTION

1. Assess the condition of the patient.
2. Check the filling and ejection behavior of the blood pump(s).
3. If possible: ensure support of patient with a replacement Ikus and turn off the original Ikus (see section 16.4: Connecting the Patient to a Replacement Ikus, page 171).

If both control computers fail at the same time or if there is a main power failure, the Ikus cannot generate any specific error messages in the message window. An acoustic alarm sounds and the indicator lamp on the handle lights up. Depending on the type of fault, the message **Error: no data from Master.** or **Error: no reaction from Master** appears in the message window.

Ikus is running in emergency pulse mode (see section 16.3: Emergency Pulse Mode, page 169).

HOTLINE

Call Service Hotline! 866.249.0128

16.7 Reading out the LOG Files

This is necessary if it is not possible to clearly identify function faults even after consultation with the service department.

WARNING

When reading out the log files: make sure the USB stick is inserted and that there is sufficient capacity on the stick.

To avoid losing any data, the Ikus laptop should be turned off before connecting and disconnecting the USB stick.

When the user exits the monitor program, incoming messages cannot be identified. Accordingly always restart the monitor program after saving data.it is not possible to identify any incoming messages. For this reason, always start the monitor program again immediately after saving the data.

INSTRUCTION

1. Press **<F10>** to exit the monitor program and confirm the intention in the dialog window by pressing the **<X>** key or the **<1>** key. The start menu is displayed. The Ikus will continue to operate using the current parameter settings.
2. Turn off the laptop. Insert the USB stick into the port (never do this while the laptop is switched on). Turn the laptop on again.
3. Select the **4. Save data** option in the start menu. The LOG files are saved onto the USB stick. After completion the start menu appears.
4. Turn off the laptop and remove the USB stick (never do this while the laptop is still switched on!)
5. Turn the laptop on again. To return to the monitor program select the **1. Start program** option in the start menu.
6. Enter user ID and password, confirming the password with **<Enter>**.
7. Send the LOG files by e-mail to service@berlinheart.com.

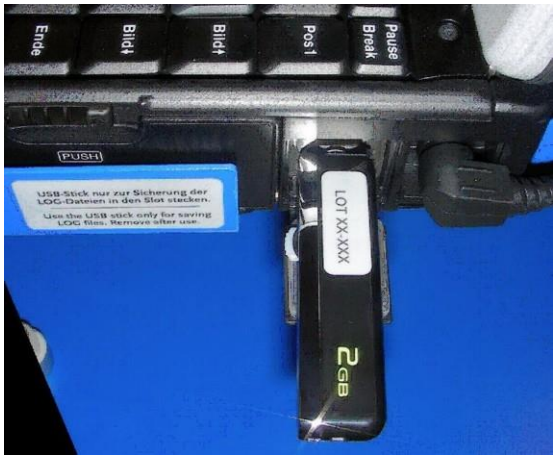


Fig. 16-5 Laptop CF30 with inserted USB stick

Fig. 16-6 Left: USB stick with extended plug (operating position); Right: USB- stick with retracted plug (position to transport and store the stick)

16.8 Circuit Breaker and Battery Fuse

The Ikus battery pack is protected against excessive current.

There is an internal battery fuse that protects against excessive load current.

A second fuse (the circuit breaker) protects against excessive charging current. The circuit breaker is located on the connection panel and it is resettable after one-time triggering (button circuit breaker flips out) by the operator.

Activated circuit breaker or internal battery fuse in mains operation

WARNING

Do not disconnect the Ikus from the main power supply if the circuit breaker or the internal battery fuse is activated. This will cause the Ikus to stop immediately.

INSTRUCTION

1. Ensure that the Ikus is connected to the mains.
2. Check if the circuit breaker was triggered. Push the button circuit breaker back in place to produce power supply again. Important: Only press the button briefly. Never keep the button pressed for a longer period, because otherwise the retriggering of the circuit breaker can not be noticed by the user.
3. If the circuit breaker is reactivated, do not press the button in again. Never keep the button pressed for a longer period of time. If possible, support the patient with a replacement Ikus (see section 16.4: Connecting the Patient to a Replacement Ikus, page 171).

HOTLINE

Call Service Hotline! 866.249.0128

Activated circuit breaker or internal battery fuse in battery operation mode

WARNING

The Ikus stops immediately. The blood pumps are no longer being driven.

NOTICE

If the circuit breaker or internal battery fuse is activated in battery operation, the Ikus generates an acoustic alarm.

INSTRUCTION

1. Check to see if the resettable circuit breaker was triggered.
   If yes: immediately push it back in place. Start the Ikus again if it does not happen automatically.
2. If the circuit breaker is triggered again, immediately support of the patient with the manual pump.

HOTLINE

Call Service Hotline! 866.249.0128

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17 Summary of Clinical Studies

17.1 Indications for Use

EXCOR® is intended to provide mechanical circulatory support as a bridge to cardiac transplantation for pediatric patients. Pediatric candidates with severe isolated left ventricular or biventricular dysfunction who are candidates for cardiac transplant and require circulatory support may be treated using EXCOR.

17.2 Contraindications

Patients unable to tolerate systemic anticoagulation therapy should not be implanted.

Magnetic Resonance Imaging (MRI) is contraindicated in patients after being implanted with EXCOR.

17.3 Alternative Practices or Procedures

FDA approved therapies include the Debakey Child device for left ventricular support for body surface area > 0.7 m^2 and < 1.5 m^2. EXCOR is the only Ventricular Assist Device approved for univentricular and biventricular support in children from 3-60 kg.

17.4 Marketing History

EXCOR was approved to apply the CE Mark in 1996. Since that authorization, EXCOR has been distributed to the following countries: Germany, Austria, Belgium, Bulgaria, Estonia, Switzerland, Denmark, Spain, Finland, France, Great Britain, Greece, Hungary, Italy, Lithuania, Netherlands, Poland, Portugal, Romania, Sweden, Slovakia, Turkey, Argentina, Australia, Azerbaijan, Brazil, Canada, Chile, Taiwan, China, Hong Kong, Israel, Iran, New Zealand, Serbia, Russia, Saudi Arabia, and South Africa.

17.5 Potential Adverse Effects

Serious adverse events (SAEs) for all primary cohort patients were reported in the primary study analysis for events per patient-day. The total time on device for Cohort 1 (BSA <0.7 m^2) subjects of 1411 days yielded a rate of 0.068 SAEs per patient-day. The total time on device for Cohort 2 (BSA >0.7 to < 1.5 m^2) subjects was 1376 days and yielded a rate of 0.079 SAEs per patient-day.

The following table details each SAE with the number of events experienced and the number and percent of subjects experiencing each SAE. Some of the SAEs have subcategories (see indented descriptions) which provide additional detail regarding the type of SAE.

Rates for subjects enrolled in the Cohorts 1 CAP (Continued Access Protocol which allowed continued access to the device following the conclusion of enrollment in the primary cohorts) and Compassionate/ Emergency Use Cohorts 3A and 3B are included to support the assessment of reasonable assurance of safety as specified in the IDE Investigational Plan.

Serious Adverse Event Summary per Cohort

EVENT	COHORT									
	1 Total	Per Subject (% of 24)	1 CAP Total	Per Subject (% of 20)	3A Total	Per Subject (% of 35)	2 Total	Per Subject (% of 24)	3B Total	Per Subject (% of 6)
Major Bleeding	**15**	**10 (41.7%)**	**12**	**7 (35.0%)**	**25**	**18 (51.4%)**	**22**	**12 (50.0%)**	**3**	**3 (50.0%)**
Cardiac Arrhythmia	**1**	**1 (4.2%)**	**2**	**2 (10.0%)**	**3**	**3 (8.6%)**	**6**	**4 (16.7%)**	**2**	**1 (16.7%)**
Sustained VT	1	1 (4.2%)	0	0 (0.0%)	2	2 (5.7%)	2	2 (8.3%)	2	1 (16.7%)
Sustained SVT	0	0 (0.0%)	2	2 (10.0%)	1	1 (2.9%)	4	3 (12.5%)	0	0 (0.0%)
Pericardial Fluid Collection	**3**	**3 (12.5%)**	**5**	**5 (25.0%)**	**4**	**4 (11.4%)**	**4**	**3 (12.5%)**	**1**	**1 (16.7%)**
With Tamponade	1	1 (4.2%)	3	3 (15.0%)	2	2 (5.7%)	2	2 (8.3%)	0	0 (0.0%)
Without Tamponade	2	2 (8.3%)	2	2 (10.0%)	2	2 (5.7%)	2	2 (8.3%)	1	1 (16.7%)
Hemolysis	**1**	**1 (4.2%)**	**1**	**1 (5.0%)**	**1**	**1 (2.9%)**	**1**	**1 (4.2%)**	**1**	**1 (16.7%)**
Hemolysis-Early	0	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	1	1 (16.7%)
Hemolysis-Late	1	1 (4.2%)	1	1 (5.0%)	1	1 (2.9%)	1	1 (4.2%)	0	0 (0.0%)
Hepatic Dysfunction	1	1 (4.2%)	0	0 (0.0%)	6	5 (14.3%)	1	1 (4.2%)	3	2 (33.3%)
Hypertension	12	12 (50.0%)	15	13 (65.0%)	9	9 (25.7%)	8	8 (33.3%)	1	1 (16.7%)
Major Infection	**35**	**15 (62.5%)**	**15**	**7 (35.0%)**	**39**	**16 (45.7%)**	**24**	**12 (50.0%)**	**8**	**4 (66.7%)**
Infection-Localized Non-Device	25	12 (50.0%)	10	6 (30.0%)	20	11 (31.4%)	18	10 (41.7%)	7	3 (50.0%)
Infection-Percutaneous Site or Pocket	4	4 (16.7%)	1	1 (5.0%)	0	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)
Infection-Sepsis	6	5 (20.8%)	4	2 (10.0%)	19	9 (25.7%)	6	6 (25.0%)	1	1 (16.7%)
Psychiatric Episode	**0**	**0 (0.0%)**	**0**	**0 (0.0%)**	**0**	**0 (0.0%)**	**1**	**1 (4.2%)**	**0**	**0 (0.0%)**

Tab. 17-1 Serious adverse event summary per cohort

Serious Adverse Event Summary per Cohort, *continued*

EVENT	COHORT											
	1 Total	Per Subject (% of 24)	1 CAP Total	Per Subject (% of 20)	3A Total	Per Subject (% of 35)	2 Total	Per Subject (% of 24)	3B Total	Per Subject (% of 6)
Neurological Dysfunction	8	7 (29.2%)	6	5 (25.0%)	6	6 (17.1%)	9	7 (29.2%)	4	3 (50.0%)
TIA	0	0 (0.0%)	1	1 (5.0%)	0	0 (0.0%)	0	0 (0.0%)	1	1 (16.7%)
Ischemic CVA	8	7 (29.2%)	5	5 (25.0%)	4	4 (11.4%)	7	7 (29.2%)	3	3 (50.0%)
Hemorrhagic CVA	0	0 (0.0%)	0	0 (0.0%)	2	2 (5.7%)	2	2 (8.3%)	0	0 (0.0%)
Renal Dysfunction	**3**	**2 (8.3%)**	**0**	**0 (0.0%)**	**7**	**7 (20.0%)**	**4**	**3 (12.5%)**	**2**	**1 (16.7%)**
Acute	3	2 (8.3%)	0	0 (0.0%)	7	7 (20.0%)	2	2 (8.3%)	2	1 (16.7%)
Chronic	0	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	2	2 (8.3%)	0	0 (0.0%)
Respiratory Failure	**3**	**3 (12.5%)**	**8**	**8 (40.0%)**	**6**	**5 (14.3%)**	**9**	**6 (25.0%)**	**6**	**5 (83.3%)**
Right Heart Failure	**2**	**2 (8.3%)**	**2**	**2 (10.0%)**	**8**	**7 (20.0%)**	**3**	**3 (12.5%)**	**1**	**1 (16.7%)**
Arterial Non-CNS Thromboembolism	**1**	**1 (4.2%)**	**1**	**1 (5.0%)**	**2**	**2 (5.7%)**	**0**	**0 (0.0%)**	**0**	**0 (0.0%)**
Venous Thromboembolism Event	**1**	**1 (4.2%)**	**1**	**1 (5.0%)**	**0**	**0 (0.0%)**	**0**	**0 (0.0%)**	**0**	**0 (0.0%)**
Wound Dehiscence	**0**	**0 (0.0%)**	**0**	**0 (0.0%)**	**1**	**1 (2.9%)**	**0**	**0 (0.0%)**	**0**	**0 (0.0%)**
Other	**10**	**6 (25.0%)**	**6**	**5 (25.0%)**	**17**	**12 (34.3%)**	**15**	**6 (25.0%)**	**7**	**4 (66.7%)**
Other Ischemic w/o symptoms	**0**	**0 (0.0%)**	**0**	**0 (0.0%)**	**1**	**1 (2.9%)**	**0**	**0 (0.0%)**	**0**	**0 (0.0%)**
Other Covert Stroke	**0**	**0 (0.0%)**	**0**	**0 (0.0%)**	**0**	**0 (0.0%)**	**0**	**0 (0.0%)**	**1**	**1 (16.7%)**

Tab. 17-2 Serious adverse event summary per cohort (table continued)

The rates of SAEs per patient-day were calculated and separated by whether the subjects were supported with ECMO pre-implant and are summarized in the following table.

In Cohort 1, those supported with ECMO pre-implant had twice as many events per patient-day of support. For Cohort 2, those supported with ECMO pre-implant had 1.5 times as many events per patient-day of support.

Serious Adverse Events per Patient-day by pre-implant ECMO

Group	ECMO Pre-Implant	# Events	Total Time on Support (Days)	Rates Success Criterion <0.25	
				Events per Patient-Day	Upper bound of CI
Cohort 1	Yes	38	345	0.110	0.151
	No	58	1066	0.054	0.070
Cohort 2	Yes	43	450	0.096	0.129
	No	64	926	0.069	0.088

Tab. 17-3 Serious adverse events per patient-day pre-implant ECMO

17.6 IDE Clinical Study

17.6.1 IDE Clinical Study Summary

Berlin Heart Inc. conducted a prospective, multi-center, single arm study to determine whether use of EXCOR for bridge-to-transplantation is associated with reasonable assurance of safety and probable benefit such that EXCOR merits approval by the Food and Drug Administration (FDA) under a Humanitarian Device Exemption (HDE).

17.6.2 Study Cohorts

The primary study population of 48 subjects aged 0-16 years consisted of 24 subjects with a body surface area (BSA) < 0.7 m^2 (Cohort 1) and 24 subjects with a body surface area (BSA) ³ 0.7 m^2 to < 1.5 m^2 (Cohort 2).

A third cohort of subjects was enrolled under Compassionate / Emergency Use regulations and is classified as Cohort 3. These subjects followed the study protocol unless otherwise noted within the approval documentation for the subject. This cohort is further divided into groups based on the subject's BSA similar to Cohorts 1 and 2 and is labeled Cohort 3A if the subject's BSA is < 0.7 m^2 and Cohort 3B if the BSA is ³ 0.7 m^2 and <1.5 m^2.

For the primary effectiveness endpoint, the protocol prescribed an ECMO historical control group. The historical ECMO control group was compiled from the Extracorporeal Life Support Organization (ELSO) registry, the most extensive registry of patients treated with ECMO in North America. The database was filtered to best match the EXCOR IDE study population. Patients included for comparison to the EXCOR cohorts included patients from both genders, age 0-16 years, with weight greater than 3 kg, cardiac only ECMO support, support initiation from 2000 onward who met critical eligibility criteria. The dataset for the ELSO registry included baseline and outcomes data comparable to the EXCOR dataset. The control group was then

created by matching the EXCOR subjects to the patients in the subset using a Propensity Score Analysis (PSA).

17.6.3 Inclusion / Exclusion Criteria

Subjects of both genders who satisfy all inclusion and exclusion criteria were eligible for entrance into the primary cohorts of the clinical study.

Inclusion Criteria

1. Severe New York Heart Association (NYHA) Functional Class IV (or Ross Functional Class IV for subjects ≤ 6 years) heart failure refractory to optimal medical therapy, and has met at least one of the following criteria:
   a. INTERMACS™ profile status 1 or 1A, i.e. critical cardiogenic shock (low BP unresponsive to support, compromised end organ perfusion, < 24 hour survival expected without mechanical support; may be due to VT/VF (1A)
   b. INTERMACS profile status 2 or 2A (i.e. progressive decline): not in imminent danger, but worsening despite optimal inotropic therapy; may be due to VT/VF (2A) AND at least one of the following criteria:
      a. Decline in renal function as defined by a 50 % reduction in estimated GFR despite optimization of subject volume status
      b. Decline in nutritional status as defined by a sustained (≥ 7 days) inability to tolerate an enteral nutritional intake sufficient to provide at least 75 % of the prescribed caloric needs for the subject, or signs of nutritional compromise (cachexia, nutritional weight loss) despite appropriate intervention
      c. Decline in mobility/ambulation as defined by sustained bed confinement (≥ 7 days without prospect for improvement) attributable to heart failure symptoms or its treatment (e.g. intubation for pulmonary edema)
   c. Support with extra-corporeal membrane oxygenation (ECMO) or other mechanical circulatory support device OR
   d. Unable to separate from cardiopulmonary bypass (must be listed for heart transplantation at time of transfer to the operating room)
2. Listed (UNOS status 1A or equivalent) for cardiac transplantation
3. Two-ventricle circulation, including cardiomyopathy, repaired structural heart disease (e.g. ALCAPA, aortic stenosis) or acquired heart disease (e.g. myocarditis, Kawasaki disease)
4. Age 0 to 16 years; corrected gestational (CGA) at least 37 weeks
5. Weight ≥ 3 kg and ≤ 60 kg
6. Legal guardian (and subject if age-appropriate) understands the nature of the procedure, are willing to comply with associated follow-up evaluations, and provide written informed consent and assent prior to the procedure

Exclusion Criteria

1. Support on ECMO for ≥ 10 days
2. Cardiopulmonary resuscitation (CPR) duration ≥ 30 minutes within 48 hours prior to device implantation
3. Body weight < 3.0 kg or BSA > 1.5 m^2
4. Presence of mechanical aortic valve
5. Unfavorable or technically-challenging cardiac anatomy including single ventricle lesions, complex heterotaxy, and restrictive cardiomyopathy
6. Evidence of intrinsic hepatic disease as defined by a total bilirubin level or AST/ ALT greater than five times the upper limit of normal for age, except in association with acute heart failure as determined by the principal investigator
7. Evidence of intrinsic renal disease as defined by a serum creatinine greater than 3 times the upper limit of normal for age, except in association with acute heart failure as determined by the principal investigator
8. Hemodialysis or peritoneal dialysis (not including dialysis or Continuous Veno-Venous Hemofiltration (CVVH) for volume removal
9. Evidence of intrinsic pulmonary disease (e.g. chronic lung disease, RDS) as defined by need for chronic mechanical ventilation, except in association with acute heart failure as determined by the principal investigator
10. Moderate or severe aortic and/or pulmonic valve insufficiency considered technically challenging to repair at the time of the device implantation as determined by the principal investigator
11. Apical VSD or other hemodynamically-significant lesion considered technically challenging to repair at the time of device implantation as determined by the principal investigator
12. Documented heparin induced thrombocytopenia (HIT) or idiopathic thrombocytopenia purpura (ITP) or other contraindication to anticoagulant/ antiplatelet therapy
13. Documented coagulopathy (e.g. Factor VIII deficiency, disseminated intravascular coagulation) or thrombophilic disorder (e.g. Factor V Leiden mutation)
14. Hematologic disorder causing fragility of blood cells or hemolysis (e.g. sickle cell disease)
15. Active infection within 48 hours of implant demonstrated by:
    a. Positive blood culture OR
    b. Temperature >38 degrees C and WBC >15, 000/ ml
16. Documented human immunodeficiency virus (HIV) infection or acquired immunodeficiency syndrome (AIDS)
17. Evidence of recent or life-limiting malignant disease
18. Stroke within past 30 days prior to enrollment, or congenital CNS malformation syndrome associated with increased risk of bleeding (e.g. arteriovenous malformation, moya moya)
19. Psychiatric or behavioral disease (e.g. antisocial disorder) with a high likelihood for non-compliance
20. Currently participating in another investigational device or drug trial and has not completed the required follow-up period for that study
21. Subject is pregnant or nursing

17.6.4 Study Enrollment

The following table summarizes the complete enrollment (including the subjects enrolled at non IDE sites) by subject's body size. As of the data cutoff for the final HDE report (February 2011 report with January 17, 2011 data cutoff), there were 151

smaller sized subjects (BSA < 0.7m^2) enrolled and 53 larger sized subjects (BSA ≥ 0.7 to <1.5 m^2) enrolled.

Subject Enrollment

Cohort	IDE Site Implants	Non-IDE Site Implants	Total
BSA < 0.7 m^2			
Cohort 1	24	*n/a*	24
Cohort 1 CAP	20	*n/a*	20
Cohort 3A	35	72	107
Subtotal	*79*	*72*	*151*
BSA ≥ 0.7 m^2 to < 1.5 m^2			
Cohort 2	24	*n/a*	24
Cohort 3B	6	23	29
Subtotal	*30*	*23*	*53*
TOTAL	**109**	**95**	**204**

Tab. 17-4 Subject enrollment

Note: Enrollment in Cohorts 1 CAP, 3A, 3B (IDE and non-IDE) are supportive data and are included only in the safety summary tables.

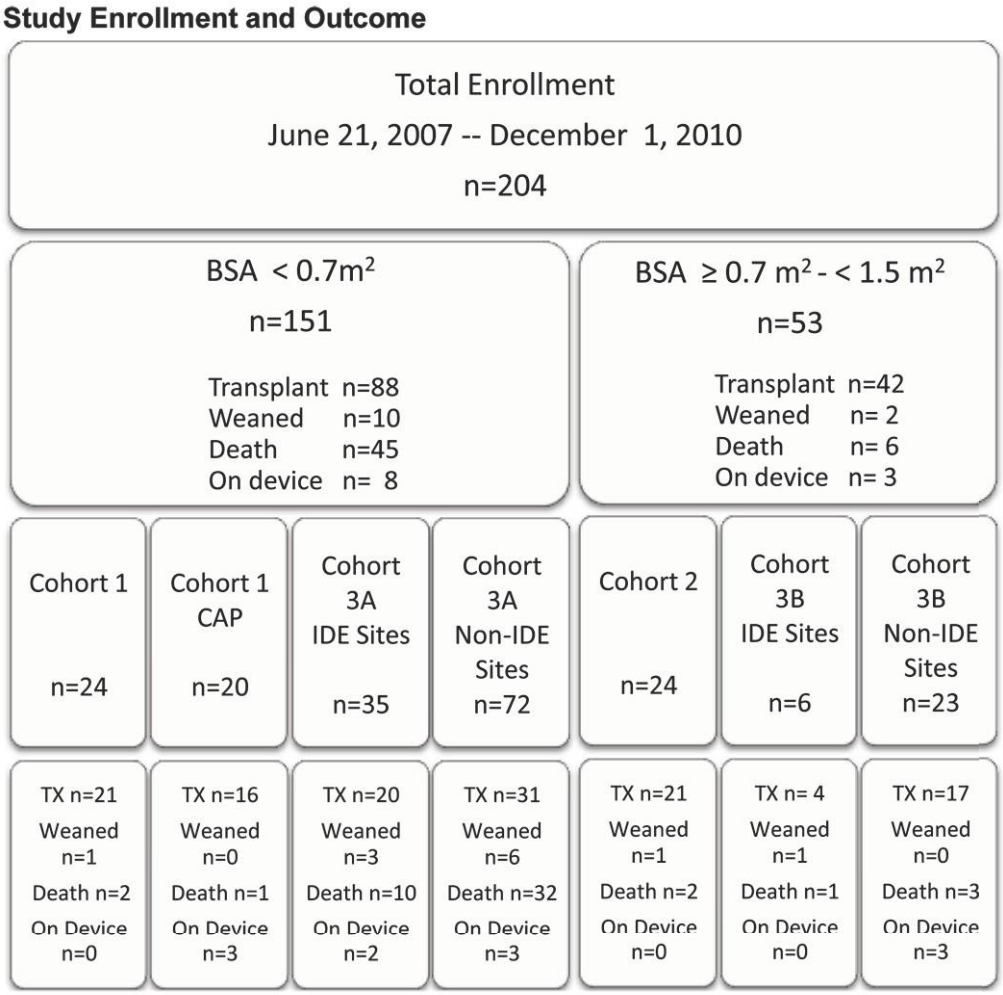


Fig. 17-1 Study enrollment and outcome

Enrollment in Cohorts 1 CAP, 3A, 3B (IDE and non-IDE) are supportive data and are only included in the safety summary tables.

17.6.5 Subject Demographics

The following table summarizes the demographic data for Cohorts 1 and 2. Males comprised the majority of the subjects in Cohort 2 (54 %) and half (50 %) of Cohort 1. The smaller group of subjects ranged in age from 2.6 to 45.6 months while the larger group ranged in age from 51 to 192 months (or 4.2 to 16 years). The weight range for Cohort 1 was 3.6 to 13.6 kilograms with a BSA range of 0.23 to 0.62 m^2 and the weight range for Cohort 2 was 16.0 to 58.1 kilograms with a BSA range of 0.71 to 1.66 m^2.

The most predominant cardiac diagnosis for Cohort 1 was dilated cardiomyopathy (79.2 %) and the majority of this group, 54.2 %, presented with progressive decline. The most predominant cardiac diagnosis for Cohort 2 was also dilated cardiomyopathy (70.8 %) and most (54.2 %) were listed as in critical cardiogenic shock.

Demographic Data Summary

Variable	Category	Cohort 1 n=24	Cohort 2 n=24
Gender	Female	12 (50.0%)	11 (45.8%)
	Male	12 (50.0%)	13 (54.2%)
Age (months)	Mean ± Std (N) Median Min – Max	15.4 ± 12.4 (24) 11.7 2.6 - 45.6	113.2 ± 37.6 (24) 111.2 50.8 - 191.8
BSA (m^2)	Mean ± Std (N) Median Min – Max	0.43 ± 0.10 (24) 0.44 0.23 - 0.62	1.09 ± 0.29 (24) 1.08 0.71 - 1.66
Weight (kg)	Mean ± Std (N) Median Min – Max	9.1 ± 2.7 (24) 9.2 3.6 - 13.6	32.2 ± 12.5 (24) 30.7 16.0 – 58.1
Race	African-American	7 (29.2%)	6 (25.0%)
	American Indian/Alaska Native	1 (4.2%)	0 (0.0%)
	Asian	0 (0.0%)	1 (4.2%)
	Hawaiian/other Pacific Islander	0 (0.0%)	1 (4.2%)
	White	13 (54.2%)	15 (62.5%)
	Other/none of the above	3 (12.5%)	1 (4.2%)
Ethnicity: Hispanic or Latino	Yes	7 (29.2%)	1 (4.2%)

Tab. 17-5 Demographic data summary (a)

Demographic Data Summary, *continued*

Variable	Category	Cohort 1 n=24	Cohort 2 n=24
Patient Profile/Status	1 Critical Cardiogenic Shock	11 (45.8%)	13 (54.2%)
	2 Progressive decline	13 (54.2%)	11 (45.8%)
	3 Stable but Inotrope dependent	0 (0.0%)	0 (0.0%)
Modifier A Arrhythmia (# Yes)		4 (16.7%)	4 (16.7%)
Primary Cardiac Diagnosis	Congenital Heart Disease	3 (12.5%)	6 (25.0%)
	Dilated Myopathy	19 (79.2%)	17 (70.8%)
	Hypertrophic cardiomyopathy	1 (4.2%)	0 (0.0%)
	Restrictive Myopathy	1 (4.2%)	1 (4.2%)
Secondary Cardiac Diagnosis (multiple Choices)	Congenital Heart Disease	2 (8.3%)	3 (12.5%)
	Coronary Artery Disease	0 (0.0%)	2 (8.3%)
	Dilated Myopathy: Familial	1 (4.2%)	0 (0.0%)
	Dilated Myopathy: Idiopathic	0 (0.0%)	2 (8.3%)
	Dilated Myopathy: Ischemic	0 (0.0%)	1 (4.2%)
	Dilated Myopathy: Myocarditis	0 (0.0%)	2 (8.3%)
	Dilated Myopathy: Viral	1 (4.2%)	0 (0.0%)
	Dilated Myopathy: Other	1 (4.2%)	2 (8.3%)
	Restrict Myopathy: Secondary to Radiation/Chemo	0 (0.0%)	1 (4.2%)
	Valvular Heart Disease	0 (0.0%)	1 (4.2%)
	CHD/Dilated Myopathy Familial	1 (4.2%)	0 (0.0%)
	None	18 (75.0%)	10 (41.7%)
Heart Rate	Mean ± Std (N) Min – Max	126.3 ± 25.5 (24) 91.0 - 175.0	117.9 ± 21.1 (24) 85.0 - 168.0
Systolic Blood Pressure	Mean ± Std (N) Min – Max	85.3 ± 16.0 (24) 45.0 - 110.0	95.2 ± 13.5 (24) 60.0 - 112.0
Diastolic Blood Pressure	Mean ± Std (N) Min – Max	56.0 ± 14.1 (24) 38.0 - 89.0	65.9 ± 14.8 (24) 46.0 - 100.0
Previous Cardiac operations (# Yes)		5 (20.8%)	8 (33.3%)

Tab. 17-6 Demographic data summary (b)

Pre-implant support for the subjects is detailed in the following table. ECMO support was used pre-implant for 25 % of Cohort 1 subjects and 33.3 % of Cohort 2 subjects.

Pre-Implant Support

Variable	Category	Cohort 1 n=24	Cohort 2 n=24
Prior support within 48 hours	No support	0 (0.0%)	0 (0.0%)
	Ventilator	20 (83.3%)	12 (50.0%)
	ECMO	6 (25.0%)	8 (33.3%)
	Ultrafiltration	3 (12.5%)	1 (4.2%)
	VAD	2 (8.3%)	0 (0.0%)
	Dialysis	0 (0.0%)	0 (0.0%)
	Feeding Tube	10 (41.7%)	7 (29.2%)
	IABP	0 (0.0%)	0 (0.0%)
	Inotropes	22 (91.7%)	21 (87.5%)

Tab. 17-7 Pre-implant support

17.6.6 Results

17.6.6.1 Probable Benefit

Efficacy for the IDE trial was assessed by comparing survival (defined by the interval of time from initiation of mechanical support as a bridge to transplant or recovery) to the historical ECMO control. Subjects who were transplanted were censored at the time of explant. Subjects who were explanted due to recovery of their ventricular function and survived to 30 days or discharged with acceptable neurologic status were censored at the time of explant. Subjects who were explanted due to recovery of their ventricular function and died within 30 days or discharge (whichever was longer) were counted as a failure with time to failure being the explant date.

For the 2 primary cohorts, the rate of successfully bridging the subjects to transplant was 87.5 % for Cohort 1 (21/24) and 91.7 % for Cohort 2 (22/24) or 89.6 % overall (43/48). The following table summarizes the survival to transplant/successful recovery for each primary Cohort ITT and PP as well as their matched ECMO control groups.

Three (3) of the Cohort 1 subjects (12.5 %) failed (2 deaths and 1 weaned subject with unacceptable neurological outcome at 30 days post-explantation) compared to 12 of the 48 (25 %) patients in the matched ECMO control group. The 3 subjects from Cohort 1 who died or were considered failures were all supported with ECMO at the time of implant. The failures occurred at day 0 (death), day 38 (death) and day 146 (weaned-failure).

The control group for Cohort 1 was on ECMO for a median of 4.9 days and a maximum of 20.5 days compared to the primary cohort subjects who were supported a median of 27.5 days and maximum of 174 days. Seventeen (17) of the 24 (71 %) Cohort 1 subjects were supported longer than the entire ECMO control group (i.e. longer than 20.5 days).

Two of the Cohort 2 subjects (8.3 %) failed compared to 16 of the 48 (33.3 %) patients in the matched ECMO control group. One of the subjects who died in Cohort 2 was supported with ECMO at the time of implant. The deaths occurred at day 19 and day 144.

The control group for Cohort 2 was on ECMO for a median of 4.7 days and a maximum of 27.5 days compared to the primary cohort subjects who were supported a median of 42.5 days and a maximum of 192 days. Seventeen(17) of the 24 (71 %) subjects in Cohort 2 were supported longer than the entire ECMO control group (i.e. longer than 27.5 days).

Primary Efficacy Study and Control Groups

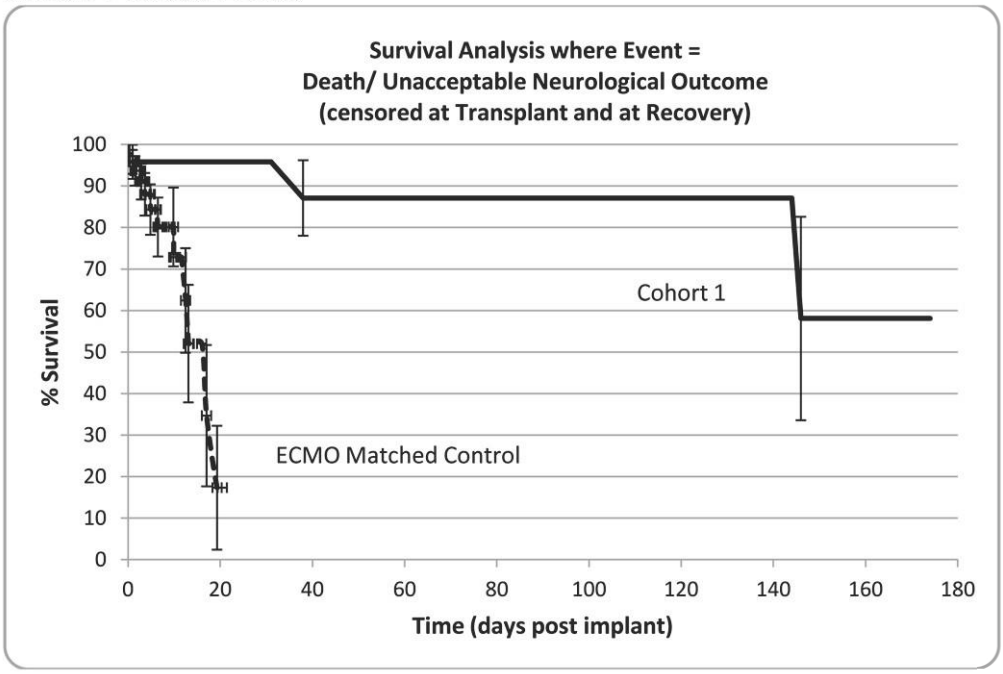
Group	Total	Max Time on Device (days)	# Successes	# Failures	Survival Time		
					30 days	60 days	90 days
Cohort 1 ITT	24	174	21 (87.5%)	3 (12.5%)	95.8%	87.1%	87.1%
Cohort 1 Per-Protocol	22	174	19 (86.4%)	3 (13.6%)	95.5%	86.8%	86.8%
ECMO Control Group	48	20.5	36 (75.0%)	12 (25.0%)	NA	NA	NA
Cohort 2 ITT	24	192	22 (91.7%)	2 (8.3%)	94.7%	94.7%	94.7%
Cohort 2 Per-Protocol	22	144	20 (90.9%)	2 (9.1%)	94.1%	94.1%	94.1%
ECMO Control Group	48	27.5	32 (66.7%)	16 (33.3%)	NA	NA	NA

Tab. 17-8 Primary Efficacy Study and Control Groups

Comparison of the ITT groups to their respective matched ECMO control group survival rates were both statistically significant (log-rank p value <0.0001). Therefore, there is a significantly higher survival rate of Cohort 1 and 2 subjects as compared to their respective ECMO control group.

The following figures display the Kaplan-Meier curves for the endpoint of death/ weaned with unacceptable outcome for both Cohort 1 ITT and Cohort 2 ITT and their respective ECMO control groups.

Survival to Death/Weaned with Unacceptable Neurological Outcome: Cohort 1 versus ECMO

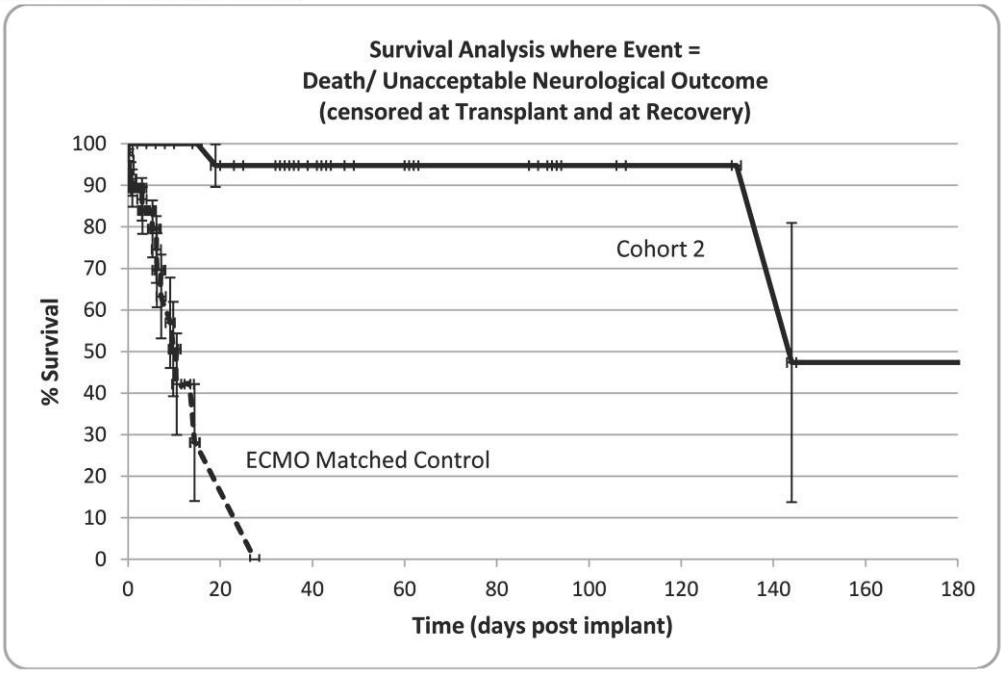


	Interval Ending (Days Post Implant)									
COHORT 1	**0**	**1**	**7**	**14**	**30**	**45**	**60**	**90**	**120**	**150**
# Left	24	21	21	20	12	10	9	6	5	1
Total # Failed	0	1	1	1	1	2	2	2	2	3
Survival	100%	95.8%	95.8%	95.8%	95.8%	87.1%	87.1%	87.1%	87.1%	58.1%
Std Error	0%	4.1%	4.1%	4.1%	4.1%	9.1%	9.1%	9.1%	9.1%	24.5%

	Interval Ending (Days Post Implant)					
ECMO CONTROL	**0**	**1**	**7**	**14**	**30**	
# Left	48	46	16	4	0	
Total # Failed	0	2	7	10	12	
Survival	100%	95.8%	80.1%	52.0%	17.3%	
Std Error	0%	2.9%	7.1%	14.2%	14.9%	

Fig. 17-2 Cohort 1 Survival

Survival to Death/Weaned with Unacceptable Neurological Outcome: Cohort 2 versus ECMO



	Interval Ending (Days Post Implant)									
COHORT 2	**0**	**1**	**7**	**14**	**30**	**45**	**60**	**90**	**120**	**150**
# Left	24	23	21	20	17	11	9	6	3	1
Total # Failed	0	0	0	0	1	1	1	1	1	2
Survival	100%	100%	100%	100%	94.7%	94.7%	94.7%	94.7%	94.7%	47.4%
Std Error	0%	0%	0%	0%	5.1%	5.1%	5.1%	5.1%	5.1%	33.6%

	Interval Ending (Days Post Implant)					
ECMO CONTROL	**0**	**1**	**7**	**14**	**30**	
# Left	48	41	12	3	0	
Total # Failed	0	5	10	15	16	
Survival	100%	89.4%	69.6%	42.2%	0%	
Std Error	0%	4.5%	8.9%	12.2%	.	

Fig. 17-3 Cohort 2 Survival

Because the Kaplan-Meier analysis censors subjects at time of transplant, “Competing Outcomes” curves were constructed to show a more complete picture of the endpoints.

The following figure shows the “Competing Outcomes” for Cohort 1. The curves represent each of the outcomes and at any time point the sum of the proportions of outcomes equals 100 %.

Of the 24 Cohort 1 subjects, 21 were transplanted between 1 to 174 days of support. The 2 deaths in this Cohort occurred at 0 and 38 days post implant. One subject was weaned after 146 days due to poor prognosis.

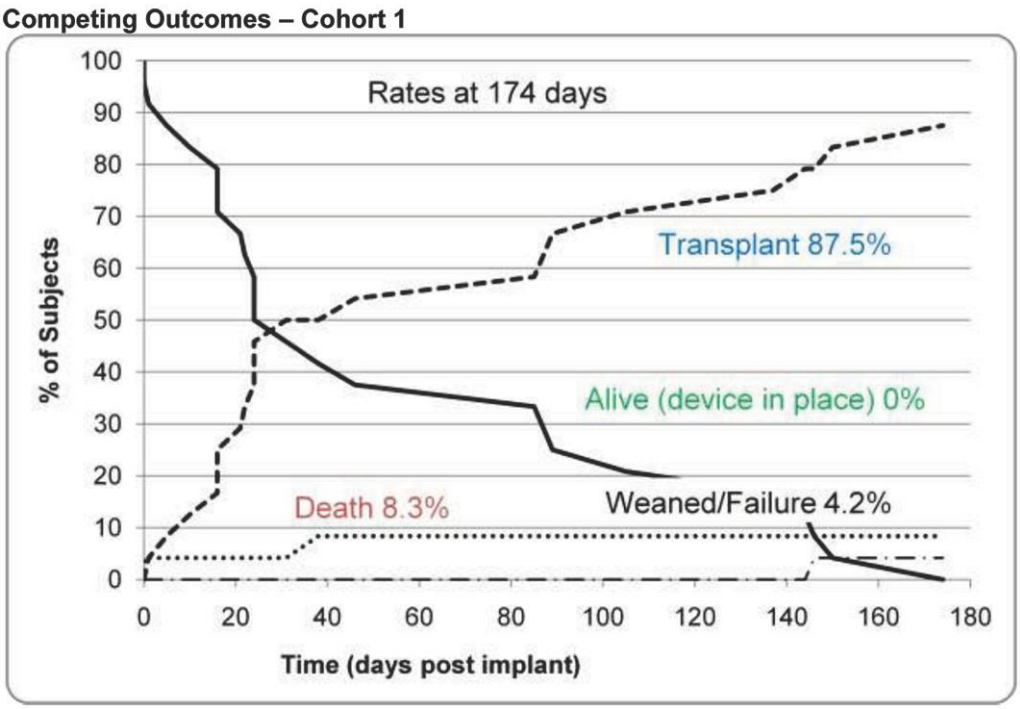


Fig. 17-4 Cohort 1 Competing outcomes

The next figure shows the “Competing Outcomes” for the ECMO control group for Cohort 1. The longest support time was 20.5 days at which time 75 % were weaned from ECMO for recovery or transplant.

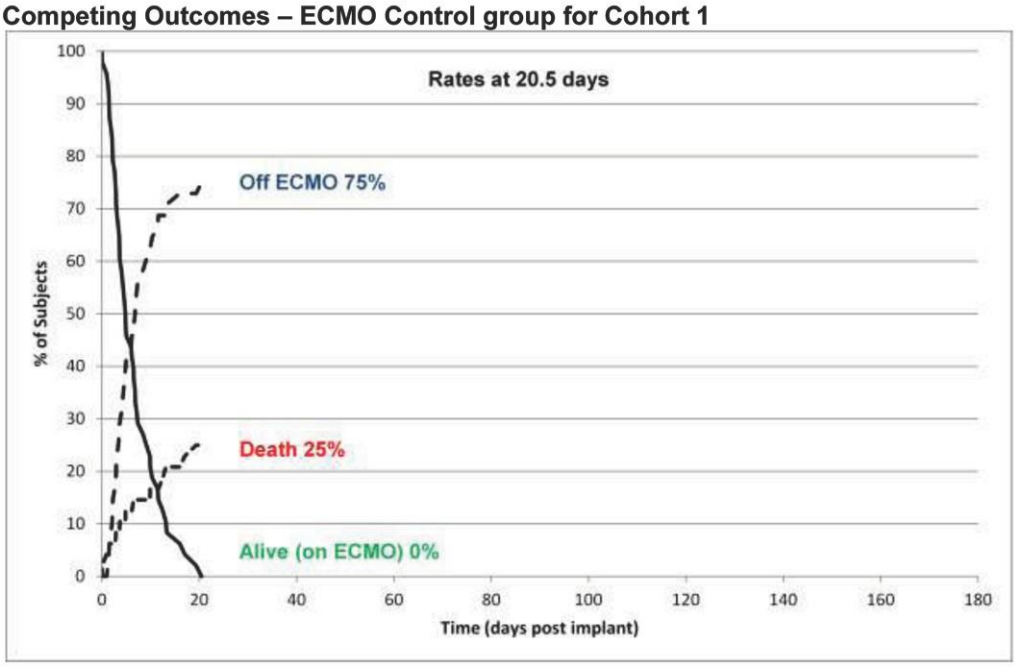


Fig. 17-5 Cohort 1 control group competing outcomes

The following figure shows the “Competing Outcomes” for Cohort 2. Of the 24 Cohort 2 subjects, 21 were transplanted between 3 to 192 days of support. The 2 deaths in this Cohort occurred at 19 and 144 days post implant. One subject was successfully weaned to recovery after 9 days.

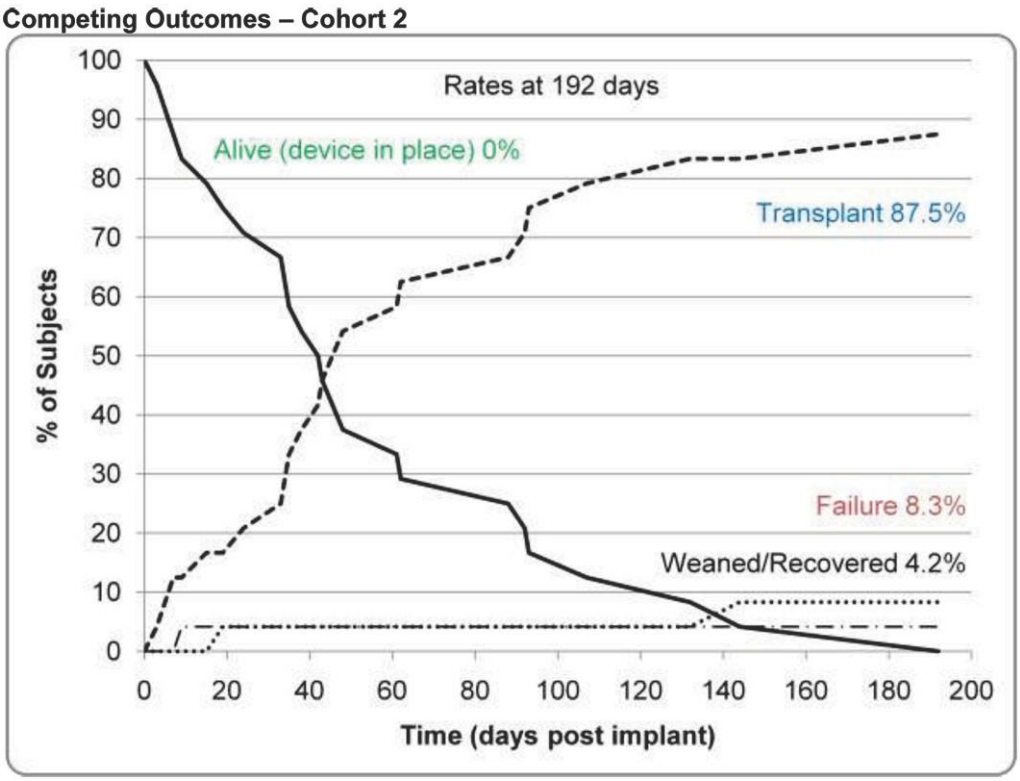


Fig. 17-6 Cohort 2 competing outcomes

The next figure shows the “Competing Outcomes” for the ECMO control group for Cohort 2. The longest support time was 27.5 days at which time 67 % were weaned from ECMO for recovery or transplant.

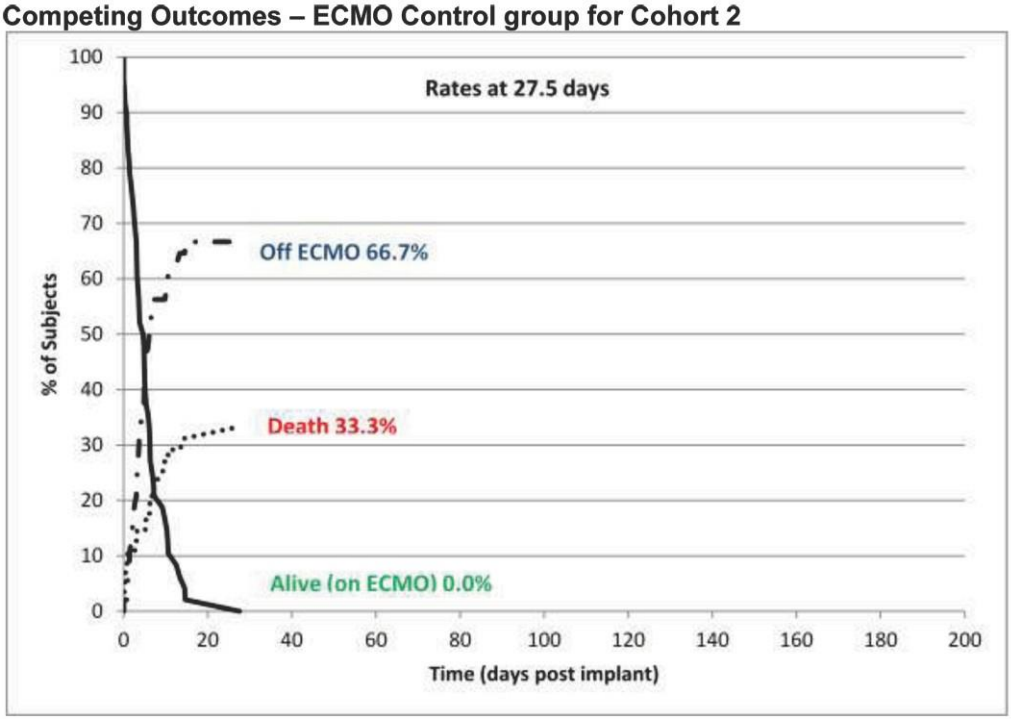


Fig. 17-7 Cohort 2 Control Group Competing Outcomes

a) Secondary Efficacy Results

There were two secondary efficacy objectives of the study. The first was to summarize the days of transplant eligible support.

Only one subject was removed from the transplantation listing at any point during their support. The subject (in Cohort 2) was first listed on day 3 of support (10/03/09) and then was delisted from 01/15/10 to 02/22/10 due to a neurological event. The subject was successfully transplanted on 04/10/10. The summary statistics of time of eligible support are detailed in the following table.

Days of Transplant Eligible Support

Cohort	N	Median	Mean ± Std	Range
Cohort 1	24	27.5	58.8 ± 56.1	0 – 174
Cohort 2	24	42.5	55.6 ± 44.3	3 – 151

Tab. 17-9 Days of transplant eligible support

The second objective was to show the ability to de-intensify concomitant hemodynamic support. At each visit, the subject's status was recorded with the following choices: sedated, intubated, on ECMO, awake, ambulating or eating. The following table summarizes those choices pre-implant, and at 2 weeks and 1 month post-implant. A subject could have more than one status subcategory checked.

Prior to implant, 22 of the 24 Cohort 1 subjects (92 %) and 16 of 24 Cohort 2 subjects (67 %) were sedated and/or intubated and over 30 % were supported by ECMO immediately prior to device implant.

In Cohort 1 there were 7 subjects (7/20=35 %) who were sedated and intubated at 2 weeks with 1 sedated and awake (1/20=5 %). The other 12 (12/20=60 %) were awake with some of those also ambulating and eating.

In Cohort 2, 6 subjects (6/20=30 %) were still sedated and intubated at 2 weeks with 1 awake and intubated (1/20=5 %) and the remaining 13 awake (13/20=65 %). At 1 month post, those numbers drop to only 3 of the Cohort 1 and 4 of the Cohort 2 subjects remaining sedated and intubated.

Support Status at each Follow-up Visit

Time Point	Status (more than 1 could be checked)	Cohort 1 n=24	Cohort 2 n=24
Pre-implant N=24 In each cohort	Sedated	21 (87.5%)	16 (66.7%)
	Intubated	21 (87.5%)	14 (58.3%)
	On ECMO/other	8 (33.3%)	9 (37.5%)
	Awake	3 (12.5%)	12 (50.0%)
	Ambulating	0 (0.0%)	5 (20.8%)
	Eating	0 (0.0%)	8 (33.3%)
2 Weeks N=20 In each cohort	Sedated	8 (40.0%)	6 (30.0%)
	Intubated	7 (35.0%)	6 (30.0%)
	Awake	13 (65.0%)	14 (70.0%)
	Ambulating	3 (15.0%)	4 (20.0%)
	Eating	6 (30.0%)	12 (60.0%)
1 Month N=12 Cohort 1 N=17 Cohort 2	Sedated	4 (33.3%)	5 (29.4%)
	Intubated	3 (25.0%)	5 (29.4%)
	Awake	9 (75.0%)	13 (76.5%)
	Ambulating	3 (25.0%)	8 (47.1%)
	Eating	4 (33.3%)	9 (52.9%)

Tab. 17-10 Support status at each follow-up visit

17.6.6.2 Primary Safety

The total time on device of the Cohort 1 subjects was 1411 days. There were 96 serious adverse events (SAEs) for this cohort yielding a rate of **0.068 events per patient-day**. The 95 % Poisson confidence interval was calculated as: [0.055, 0.083]. The total time on device for Cohort 2 was 1376 days. There were 109 SAEs for this cohort yielding a rate of **0.079 events per patient-day** with the confidence interval as [0.065, 0.096]. A summary of SAEs rates for each cohort is included in the first table of this clinical study section.

a) Infection Serious Adverse Events

Major Infection events were reported according to the Investigational Plan definition (which is the same as the INTERMACS definition). Any time an additional medication was added for treating a different organism a new SAE was reported (or adjudicated as an event). The study design was intentionally broad with regard to setting a low threshold for calling an event an infection. Fever was defined at 38 degrees, WBC > 15,000, positive cultures from any source, or decision to start antibiotics with or without positive cultures were listed as an SAE and subsequently adjudicated. Each infection was counted as a separate event even when occurring concurrently in one patient, ensuring that the infection rate would not be under-reported.

In Cohort 1, 15 subjects had 35 total infectious events reported. In Cohort 1, a majority of subjects had pre-existing risks for infection including ventilation (83 %), pre-implant ECMO support (33 %), and previous cardiac surgery (21 %).

In the larger subjects (Cohorts 2) there were fewer events (12 subjects with 24 events) which is as expected based on age and body size.

Outcomes of any of the subjects did not appear to be affected by infections as the deaths that occurred were not solely related to infection, even when one was present. These cases tended to have multi-factorial contributors such as stroke, end-organ failure, arrhythmias, or thromboembolism. All other subjects with a noted infectious SAE were transplanted or weaned. Infection had little impact on the transplant wait time since 99.3 % of the total time the subjects were on support was considered transplant eligible time.

b) Major Bleeding Serious Adverse Events

Major Bleeding was the third most frequently reported SAE in Cohort 1 (10 subjects with at least one event). All bleeding events for Cohort 1 occurred in subjects less than 2 years old. Five of the 10 subjects in Cohort 1 with bleeding events were younger than 9 months old. Young infants have some degree of ineffective erythropoiesis. Hemoglobin subsequently falls to a nadir at around 2–3 months of age due to decreased RBC production. Anemia in acute or critical illness may be exacerbated by numerous factors including blood loss (due to hemorrhage or sampling), reduced RBC production (due to nutritional deficits, inflammatory processes or low erythropoietin levels) and increased RBC turnover due to hemolysis.

Cohort 1 subjects had a pre-implant history of transfusion in 92 % (22/24), history of ECMO or previous VAD in 33 % (8/24), and 21 % (5/24) of subjects had previous cardiac surgeries. These factors along with the strict Major Bleeding definition could have contributed to the percentage of events reported.

Major Bleeding was one of most prevalent events in Cohort 2 with 12 of 24 (50 %) subjects experiencing a bleeding event.

c) Hypertension Serious Adverse Events

Hypertension was reported per the protocol definition (consistent with the INTERMACS definition). An event was logged each time a subject's blood pressure reached the 95th percentile for age and was treated with an IV agent. Several hypertension events were reported in the early post-op periods. However, 75 % (15/20) of the hypertension events were in Cohort 1 and 2 subjects who only received LVAD support. This is not surprising as it is common for patients supported only with left sided devices to require pharmacological support in order to optimize right ventricular function with agents that can cause hypertension, resulting in the concomitant need for agents to lower the blood pressure in the early post-operative period. Additionally, hypertension is one of the leading post operative cardiac surgical events for children, especially younger children, possibly due to their reactive vasculature. In order to follow the event definition, hypertension events were reported when the values met the definition even if the subject was also on a pressor or in a period where the site was trying to optimize the overall hemodynamic status of the subject in the early post-op period. There did not appear to be a correlation between Hypertension and Major Bleeding.

d) Neurological Dysfunction Serious Adverse Events

Four of the 48 (8.3 %) Cohort 1 and 2 subjects experienced a neurological dysfunction with long term severe results (PSOM scores ≥2) and another 2 (4.2 %) were withdrawn from support due to the neurological injury.

In Cohort 1, 7 of the 24 subjects experienced a neurological event. One subject experienced 2 ischemic events. Of the 7 subjects, 1 was withdrawn from support as a

result of the neurological injury. Of the remaining 6 subjects, PSOM exams were performed post explant and 1 had no deficit (assessed 17 days post explant); 2 had mild deficits (23 and 221 days post explant), 1 had moderate deficit (82 days post) and 2 had severe deficits (PSOM score of 3 at 34 days post and score 4 at 54 days post).

In Cohort 2, 7 of the 24 subjects experienced a neurological event. Two of those subjects experienced both an ischemic and hemorrhagic event. Of the 7 subjects, 1 was withdrawn from support as a result of the neurological injury. Of the remaining 6 subjects, PSOM exams were performed post explant and 1 had no deficit (50 days post explant); 2 had mild deficits (27 and 49 days post explant), 1 had moderate deficit (357 days post) and 2 had severe deficits (PSOM scores of 10 at 29 and 38 days post).

The following table summarizes the status information.

Summary of Neurological Event Status

Long term Result	Cohort 1 N=24	Cohort 2 N=24	Total N=48
No Deficit (PSOM 0.0)	1 (4.2%)	1 (4.2%)	2 (4.2%)
Mild (PSOM 0.5-1.0)	2 (8.3%)	2 (8.3%)	4 (8.3%)
Moderate (PSOM 1.5-2.0)	1 (4.2%)	1 (4.2%)	2 (4.2%)
Severe (PSOM ≥ 2.5)	2 (8.3%)	2 (8.3%)	4 (8.3%)
Support withdrawn	1 (4.2%)	1 (4.2%)	2 (4.2%)
TOTAL	**7 (29.2%)**	**7 (29.2%)**	**14 (29.2%)**

Tab. 17-11 Summary of neurological event status

Pump Replacement Due to Thrombus

During the course of the support, a clinician may have identified that a pump required replacement due to visualized thrombus within the blood pump. These replacements were not considered adverse events. However, these were nonetheless regarded as sentinel events due to their frequency and association with thromboemboli.

In the primary cohorts, 24 (50 %) of the subjects had at least one pump replacement due to suspected thrombus (11 Cohort 1, 13 Cohort 2). The number of pump replacements ranged from 0 to 4 per subject. The average number of replacements per subject was 0.9 ± 1.2. However, subjects were supported on the device for varying lengths of time therefore it may be more informative to consider the replacements per length of time on device. The average replacements-per-day on device was 0.02 ± 0.03 per day.

At the IDE sites, 57 (52.3 %) of the 109 subjects had at least one pump replacement due to thrombus (11 Cohort 1, 14 Cohort 1 CAP, 13 Cohort 2, and 19 Cohort 3). The number of pump replacements ranged from 0 to 6 per subject. The average number of replacements per subject was 1.1 ± 1.4 and the average replacements-per-day on device was 0.02 ± 0.03 per day.

Additionally, 95 subjects were enrolled at non-IDE sites. Of the 204 subjects, 93 (45.6 %) subjects had at least one pump replacement due to thrombus (11 Cohort 1, 14 Cohort 1 CAP, 13 Cohort 2, and 19 Cohort 3, 36 Cohort 3 Non-IDE). The number of pump replacements ranged from 0 to 6 per subject. The average number of replacements per subject was 1.1 ± 1.4 and the average replacements-per-day on device was 0.02 ± 0.03 per day.

Cohort	N	# Subjects with at least 1 replacement	Total number of replacement	Replacements per Subject	Total Days on Device	Replacements per Days on Support	Time to first replacement (days)
primary Cohorts*	48	25 (50.0 %)	43	0.9 ± 1.2 0 - 4	2787	0.02 ± 0.03 0.00 - 0.13	24.1 ± 19.7 4 - 105
IDE Cohorts	109	57 (52.3 %)	114	1.1 ± 1.4 0 - 6	6350	0.02 ± 0.03 0.00 - 0.18	19.1 ± 16.9 2 - 105
Non-IDE Cohorts	95	36 (37.9 %)	58	0.6 ± 1.0 0 - 4	7240	0.01 ± 0.03 0.00 - 0.27	41.9 ± 44.6 2 - 198
Total	204	93 (45.6 %)	172	0.8 ± 1.2 0 - 6	13590	0.02 ± 0.03 0.00 - 0.27	27.8 ± 32.3 2 - 198

Tab. 17-12 Pump replacement

* Note: the 48 subjects in the “Primary Cohorts” group are a subset of the “IDE Cohorts” group (n=109)

17.6.6.3 Death Information

Two subjects in each of the primary cohorts died after support was withdrawn. The 4 subjects were supported a median time of 28.5 days ranging from 0 to 144 days (mean ± std: 50.3 ± 64.4 days). Of the 4 subjects who died, 75 % (3/4) were supported with ECMO at the time of EXCOR implant.

The CEC reviewed all deaths at the IDE sites and assigned primary and secondary causes of death. These causes are summarized by subject in the following table.

Patient	Days on Device	Primary Cause	Secondary Cause(s)
COHORT 1 (2 deaths/ 24 subjects)			
#1	0	Pulmonary Respiratory Failure	Cardiovascular: Left A-V valve regurgitation
#2	38	CNS: Multiple ischemic strokes	None
COHORT 2 (2 deaths/ 24 subjects)			

Tab. 17-13 Primary and secondary cause of death

Patient	Days on Device	Primary Cause	Secondary Cause(s)
#3	144	Other: Arterial CNS and non-CNS Thromboembolism	Infection
#4	19	CNS: Large ischemic strokes with hemorrhagic conversion	Other: Tonsillar herniation

Tab. 17-13 Primary and secondary cause of death

17.6.7 Conclusion

Despite the reported SAEs, 42 of the 48 subjects supported by EXCOR were adequately supported to transplant and 1 subject was able to be weaned successfully from the device after 9 days of support yielding an 89.6 % success rate (43/48). The device supported children safely to cardiac transplantation for a median transplant eligible time of 27.5 and 42.5 days for cohort 1 and 2 respectively. Only one subject was temporarily removed from transplant eligibility during their support and was eventually relisted and transplanted.

Data that strongly supports the consideration for probable benefit is summarized for both Cohort 1 and 2 subjects as shown in the following tables.

Probable Benefit

Cohort	N	Outcome				Success (Transplant or Weaned-Recovered)
		Transplant	Weaned-Recovered	Weaned-Failure	Died	
Cohort 1	24	21	0	1	2	21/24 (87.5%)
Cohort 2	24	21	1	0	2	22/24 (91.7%)
Total	**48**	**42**	**1**	**1**	**4**	**43/48 (89.6%)**

Tab. 17-14 Probable Benefit

Post-Explant/Transplant Follow-up

Cohort		Outcome	30 days post-explant		1 year post-explant	
	N	# Explanted	# (%) alive 30 days	Lost to Follow-up	# (%) alive 1 Year	Lost to Follow-up
Cohort 1	24	22	22/22 (100%)	n/a	17/22 (77%)	0
Cohort 2	24	22	21/22 (95%)	1*	16/17 (94%)**	1
Total	**48**	**44**	**43/44 (97.7%)**	**1**	**33/39 (85%)**	**1**

* 1 subject was weaned and returned to home

** 5 subjects have regular contact with the site for post transplant care but are not 1 year post-explant as of this report: 3 subjects are due in June (last report alive at 313, 257 and 250 days), 1 subject is due in July (last report alive at 170 days) – verbal report; denominator includes 1 LTF

Tab. 17-15 Post-explant/transplant status follow up

Beyond the primary endpoint of survival to transplant, the majority of subjects remain alive at 1 year post-explant/transplant as noted in the previous table.

HDE regulations require the device under study to show **reasonable safety and probable benefit**. In the EXCOR® Pediatric IDE trial the device demonstrated probable benefit as a bridge to transplantation in patients who are transplant eligible with severe left ventricular or biventricular dysfunction. The majority of patients implanted with EXCOR were transplant eligible during device support with adequate end organ function and decreasing need for hemodynamic support such as intubation, sedation or ECMO support. While the concomitant support decreased, the subjects were able to spend more time awake, eating and ambulating.

The benefits offered to subjects implanted with the EXCOR® Pediatric include additional time to await transplant and improved hemodynamics allowing removal of pre-implant hemodynamic support allowing for increase time awake, ambulating and eating contributing to post implant transplant eligible wait times. These far-reaching benefits outweigh the risks associated with the adverse events that occurred.

17.7 Post Approval Study Summary

17.7.1 Study Objective

The purpose of the Post Approval Study (PAS) of the EXCOR® Pediatric VAD was to evaluate whether safety and outcomes of the device use in the commercial setting were comparable to the safety and outcomes of the device use in the IDE study.

17.7.2 Study Design

The study was an “all-comers” prospective study maintained by Berlin Heart consisting of pediatric patients aged 0-21 years implanted according to the IFU with the EXCOR® Pediatric who were transplant eligible children in need of mechanical circulatory support and who consented to be enrolled into the study.

17.7.3 Study Population

The study included subjects who met the Inclusion and Exclusion Criteria included below and for whom the EXCOR® Pediatric was indicated and not contraindicated per the product labeling.

Inclusion Criteria

- Patient requires mechanical circulatory support and is eligible for cardiac transplantation; and
- Legal guardian and patient (if age appropriate) understands the nature of the implant procedure and are willing to comply with associated follow-up evaluations, and provide written informed consent and assent prior to the procedure

Exclusion Criteria

- Patient is currently enrolled in EXCOR® Pediatric pre market study; and/or
- Patient is currently participating in another investigational device or drug trial which would confound the results of the study

17.7.4 Data Source

Berlin Heart sponsored web-based Registry.

17.7.5 Key Study Endpoints

Primary Safety Objective / Endpoint

The primary safety objective of the study was to demonstrate that the Serious Adverse Event (SAE) rate in subjects implanted with the EXCOR® Pediatric in this study was not greater than the rate experienced in the IDE study.

The primary endpoint was the SAE rate which was calculated as the total number of SAEs divided by the sum of days all subjects were supported on the EXCOR® Pediatric device.

A Clinical Events Committee (CEC) met regularly during the course of the study to adjudicate the protocol-specified SAEs: major bleeding, major infection and neurological dysfunction events, and device malfunctions. The CEC also reviewed and assigned cause of death to any subject who died as a result of withdrawal of device support.

Primary Efficacy Objective / Endpoint

The primary effectiveness objective for the study was to assess the outcome following implantation of the EXCOR® Pediatric for transplant eligible children in need of mechanical circulatory support. The endpoint was defined as transplant, recovery of left ventricular function or death.

17.7.6 Total Number of Enrolled Study Sites and Subjects, Follow-up Rate

A total of 39 subjects were enrolled at 19 investigational sites. All subjects were followed for the duration of device support. Subjects explanted from the device will continue to be followed for 24 months post explant.

17.7.7 Study Visits and Length of Follow-up

Clinical data recorded in hospital records was collected at the time of pre-implant, implant, planned follow-ups (3 weeks, 6 weeks, 3 months, 6 months and every 3 months thereafter while on device support and up to transplant/recovery). Following explant of the device, follow-up visits were scheduled at hospital discharge, 12 months post explant and 24 months post explant.

17.7.8 Results

17.7.8.1 Primary Safety

The total time on device support for the study subjects was 4216 days. There were 102 SAEs reported for the 39 subjects yielding a rate of 0.024 events per patient-day (95 % Poisson confidence interval: 0.020 – 0.029). The difference between the event rate in the PAS study and the IDE rate 0.071 was statistically significantly lower (p-value <0.0001).

SAEs have been reported in 32 of the 39 subjects (82 %).The following table summarizes the reported SAEs with their adjudicated results.

Event Category	# event	# subjects with event n (% of 39)	Events / Subject # /39
Adjudicated SAEs			
Major Bleeding	23	16 (41.0 %)	0.59
Major Infection:	20	15 (38.5 %)	0.51
Localized non-device	3	3 (7.7 %)	0.08
Percutaneous Site and/or Pocket Infection	8	6 (15.4 %)	0.21
Internal Pump Component, Inflow or Outflow Tract Infection	2	2 (5.1 %)	0.05
Sepsis	7	7 (17.9 %)	0.18
Neurological dysfunction:	17	13 (33.3 %)	0.44
TIA	0	0 (0.0 %)	0.00
Ischemic CVA	8	6 (15.4 %)	0.21
Hemorrhagic CVA	5	5 (12.8 %)	0.13
Ischemic/Hemorrhagic CVA	4	3 (7.7 %)	0.10
New abnormality of head ultrasound	0	0 (0.0 %)	0.00
EEG positive for seizure activity with or without clinical seizure	0	0 (0.0 %)	0.00
Other • Covert stroke • Seizure • Encephalopathy	 3 2 1	 3 (7.7 %) 2 (5.1 %) 1 (2.6 %)	 0.08 0.05 0.03
Other SAEs			
Hepatic Dysfunction	2	2 (5.1 %)	0.05
Hypertension	4	4 (10.3 %)	0.10
Pericardial effusion with tamponade	1	1 (2.6 %)	0.03
Pericardial effusion without tamponade	3	3 (7.7 %)	0.08
Psychiatric episode	1	1 (2.6 %)	0.03
Renal Dysfunction-Chronic	1	1 (2.6 %)	0.03
Respiratory failure	9	7 (17.9 %)	0.23
Right heart failure	3	3 (7.7 %)	0.08

Tab. 17-16 EXCOR® Pediatric Post Approval Study Serious Adverse Events

Event Category	# event	# subjects with event n (% of 39)	Events / Subject # /39
Venous Thromboembolism	3	2 (5.1 %)	0.08
Other	9	8 (20.5 %)	0.23
TOTAL	102	32 (82.0 %)	2.36

Tab. 17-16 EXCOR® Pediatric Post Approval Study Serious Adverse Events

17.7.8.2 PAS Neurological Summary

Of the 39 PAS subjects, 13 subjects had 17 neurological dysfunction events; 8 of the events were ischemic, 5 were hemorrhagic and 4 were ischemic/hemorrhagic. Of the 13 subjects who had a neurological event, 5 were successfully transplanted (n=4) or weaned (n=1). The other 8 subjects had support withdrawn (n=7) or died less than 30 days following explant (n=1). Of those 8 subjects, 3 were on ECMO prior to the EXCOR Pediatric implant.

Of the 5 subjects who had a neurological event that were successfully transplanted/ weaned, all are alive 24 months post explant and 3 have had long term (24 month post explant) PSOMs performed. The 3 subjects had PSOM scores one each of mild (score 1), moderate (score 2) and severe (score 4).

17.7.8.3 Primary Efficacy Endpoints

Twenty-seven (27) of the 39 (69.2%) subjects were successfully transplanted or weaned from the device. Total support time ranged from 0 to 457 days with an average time of 108.1 days (standard deviation=118.9) and median of 63 days (IQR=20, 160).

The following table details the outcomes for the study subjects.

Outcome	n (% of 39)
Transplant	25 (64.1 %)
Weaned; alive > 30 days	2 (5.1 %)
Escalated to ECMO [1]	2 (5.1 %)
Death	10 (25.6 %)

[1] subjects died after transition

Tab. 17-17 EXCOR® Pediatric Post Approval Study Outcomes

17.7.8.4 Study Strength and Weaknesses

Strengths:

The study was a prospective study with pre-defined hypotheses and statistically calculated sample size. A central committee adjudicated the major serious adverse events (major bleeding, major infection, neurological dysfunction) as well as device malfunctions and deaths. Follow-up rate was 100 % as all subjects remained in the hospital while on device support and, therefore, all follow-up visits were conducted.

Weaknesses:

The enrolled subjects showed a higher risk profile when compared to the IDE cohort and were smaller, younger, spent longer time on support, and more patients presented with CHD, especially single ventricle physiology.

17.8 FDA Study Progress and Commercial Use

Pre-IDE / Retrospective Experience

Prior to IDE study approval, from 2000 to 2007, Berlin Heart provided access to the EXCOR Pediatric device under Emergency Use regulations. A total of 97 patients were implanted with the device in that time period.

Pre-Market IDE Study

Approval for the IDE study was granted in 2007. The IDE primary study population of 48 subjects included in the primary Cohorts 1 and 2 completed enrollment in August 2010 with the final subject outcome being met in October 2010. Berlin Heart submitted an HDE application in February 2011 containing analyses of the study endpoints for both primary cohorts. An additional 46 subjects were enrolled in a Continued Access Protocol which allowed continued access to the device following the conclusion of enrollment in the primary cohorts, Cohort 1 and Cohort 2. Implants that were performed under Compassionate/Emergency Use Regulations, 54 at IDE sites and 133 at non-IDE sites (labeled as Cohorts 3A and 3B) were included in the HDE application to support the assessment of reasonable assurance of safety as specified in the IDE Investigational Plan.

FDA granted HDE approval on December 16, 2011 at which time the IDE study was closed to further enrollment. A total of 281 subjects received EXCOR Pediatric implants during the study time period.

Post Approval Study

A condition of the 2011 HDE approval was a post approval study. Following the approval of the Post Approval Study (PAS) protocol, Berlin Heart contacted sites that were involved in the IDE study as well as all other active pediatric transplant centers in the United States to invite them to participate in the post approval study. IRB approval was obtained at 26 sites who agreed to participate.

The last implanted patient was enrolled into the PAS on March 10, 2014. The final subject reached an outcome February 20, 2015. The final study report was submitted to FDA February 8, 2017 after completion of long term follow-up requirements.

Post Approval Commercial Use

In March 2012, FDA requested that Berlin Heart gather information for patients implanted with the EXCOR Pediatric in the United States following HDE approval (December 16, 2011) who were not enrolled in the post approval study. Berlin Heart receives basic patient, device and mechanism of implantation information through the device ordering and return processes. Additionally Berlin Heart receives verbally-reported information regarding patient status and outcome through routine site communication.

A total of 245 patients have been implanted with the EXCOR Pediatric at 45 hospitals following approval but outside the post approval study through December 31, 2015.

This yields a total of 565 implants from June 21, 2007 to December 31, 2015; 187 implants under a study protocol, 133 implants at sites following the IDE protocol but

not participating in the IDE study and 245 implants occurring post approval outside a study.

17.8.1 Disposition of Subjects

Tab. 17-18 summarizes the implants for each time period.

Study Group	Implant Period	N
IDE study Primary Cohorts	2007-2011	94
IDE study Compassionate Use	2007-2011	54
Non-IDE site Compassionate Use	2007-2011	133
Post Approval Study	2013-2015	39
Post approval non study	2011-2015	245
Total	**2007-2015**	**565**

Tab. 17-18 Implants per time period

Fig. 17-8 details the complete implantation of EXCOR Pediatric since the initiation of the IDE.

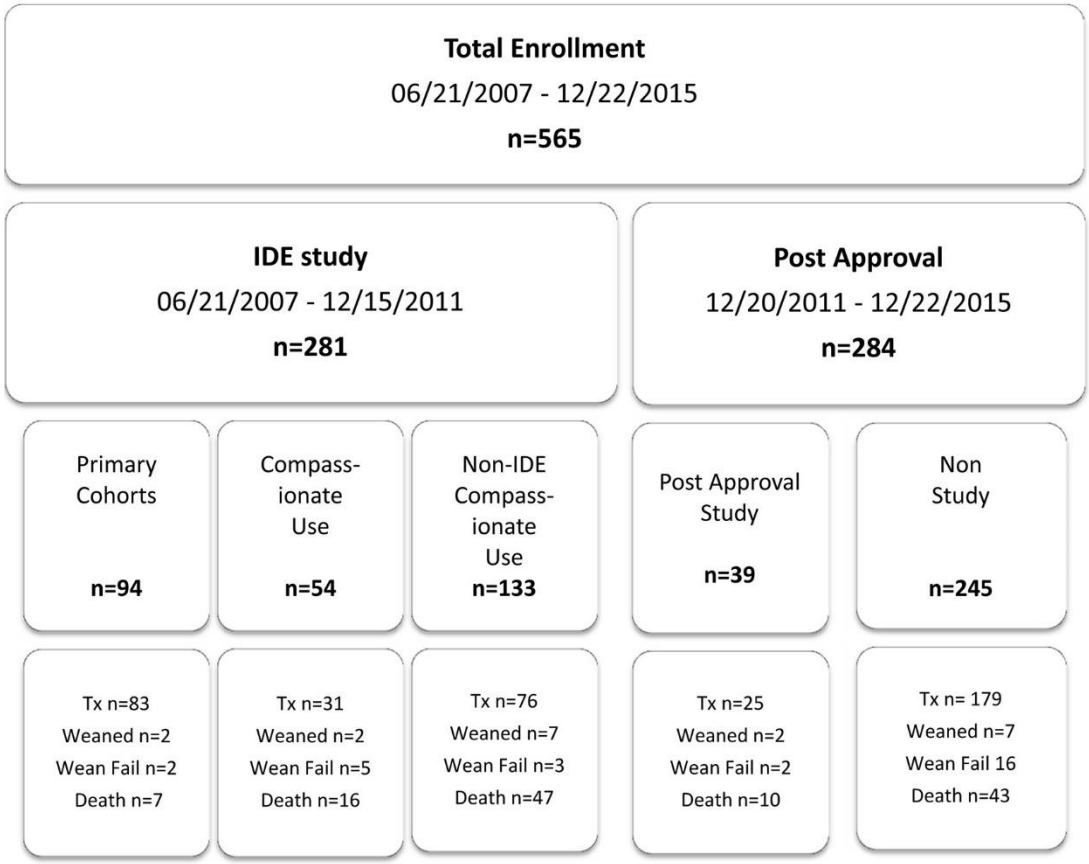


Fig. 17-8 Study Enrollment and Outcome

17.8.2 Brief Summary of Results

Summary data is presented in three groups. The first group (Study Group) contains the IDE study data that was monitored and adjudicated combined with the PAS data. The second group (Database Group) contains the IDE study and PAS data along with the Compassionate Use data from sites that agreed to enter data into the study database. The third group (All Implant Group) is a comprehensive group containing all pre and post approval patients from the time of IDE approval in 2007 through 2015.

Tab. 17-19 summarizes the basic demographic and pre-implant data that is available for all implants. Tab. 17-20 and Tab. 17-21 summarize the demographic and pre-implant data that is available for the study and database groups. Overall, the patients ranged in age from 0 days to 389.3 months, the weight ranged from 2.8 to 112 kilograms and the BSA ranged from 0.13 to 2.3 m^2.

Variable	**Category**	**Study Group (IDE + PAS) n=187**	**Database Group (IDE + Comp Use + PAS) n=320**	**All Implant Group n=565**
Age (mo)	Median [Range]	19.8 [0 – 194.7]	20.5 [0 – 239.3]	19.8 [0.0 – 389.3]
Weight (kg)	Median [Range]	10.6 [3.0 – 70.0]	10.7 [2.8 – 71.0]	10.7 [2.8 – 112.0]
Height (cm)	Median [Range]	82.0 [45.0 – 171.0]	82.0 [44.0 – 171.0]	81.0 [44.0 – 181.0]
BSA (m^2)	Median [Range]	0.50 [0.20 – 1.76]	0.50 [0.19 – 1.76]	0.49 [0.19 – 2.30]
Device Type	LVAD BVAD	118 (63.1%) 69 (36.9%)	201 (62.8%) 119 (37.2%)	382 (67.6%) 183 (32.4%)

Tab. 17-19 Basic demographic data

The majority of study subjects were female (51%) who presented with cardiomyopathy (53%). Other prevalent diagnoses were congenital heart disease (28%), and myocarditis (12%). Most of the subjects presented with either progressve decline (48%) or critical cardiogenic shock (48%) with the remaining presenting as stable but inotrope dependent (3%) or other (1%).

Prior to implantation, 90% of the subjects in the database groups were receiving inotrope therapy, 74% ventilatory support and over 41.8% ECMO or temporary VAD support. Additionally, 80% of subjects had a history of transfusion.

Variable	**Category**	**Study Group** (IDE + PAS) **n=187**	**Database Group** (IDE + Comp Use + PAS) **n=320**
Gender	Male Female	90 (48.1%) 97 (51.9%)	158 (49.4%) 162 (50.6%)

Tab. 17-20 Demographic data for study and database groups

Variable	Category	Study Group (IDE + PAS) n=187	Database Group (IDE + Comp Use + PAS) n=320
Device strategy	Bridge to Transplant (BTT)	176 (94.1%)	298 (93.1%)
	Possible BTT-Likely to be eligible	6 (3.2%)	13 (4.1%)
	Possible BTT-Mod Likelihood	3 (1.6%)	3 (0.9%)
	Possible BTT-Unlikely to be eligible	0 (0.0%)	1 (0.3%)
	Bridge to Recovery	1 (0.5%)	3 (0.9%)
	Other	1 (0.5%)	2 (0.6%)
Patient Profile/Status	1 Critical Cardiogenic Shock	81 (43.3%)	154 (48.1%)
	2 Progressive decline	100 (53.5%)	152 (47.5%)
	3 Stable but Inotrope dependent	5 (2.7%)	11 (3.4%)
	4 Recurrent advanced heart failure	0 (0.0%)	1 (0.3%)
	7 Advanced NYHA Class 3	1 (0.5%)	1 (0.3%)
	Not reported	0 (0.0%)	1 (0.3%)
Pre-implant support: ECMO		66 (35.3%)	123 (38.4%)
Pre-implant support: Ventilator		134 (71.7%)	237 (74.1%)
Pre-implant support: Inotropes		169 (90.4%)	288 (90.0%)
Pre-implant support: VAD		7 (3.7%)	11 (3.4%)
History of transfusions		147 (78.6%)	256 (80.0%)
Heart Failure Classification Pre-implant	NYHA I	1 (0.5%)	1 (0.3%)
	NYHA II	1 (0.5%)	5 (1.6%)
	NYHA III	2 (1.1%)	3 (0.9%)
	NYHA IV	42 (22.5%)	70 (21.9%)
	Ross Class II	3 (1.6%)	5 (1.6%)
	Ross Class III	5 (2.7%)	9 (2.8%)
	Ross Class IV	122 (65.2%)	210 (65.6%)
	Not reported	11 (5.9%)	17 (5.3%)

Tab. 17-20 Demographic data for study and database groups

Variable	Category	Study Group (IDE + PAS) n=187	Database Group (IDE + Comp Use+ PAS) n=320
Primary Cardiac Diagnosis	CHD	49 (25.2%)	91 (28.4%)
	DCMP	99 (52.9%)	169 (52.8%)
	Myocarditis	23 (12.3%)	39 (12.2%)
	RCMP/HCMP	9 (4.8%)	13 (4.1%)
	Other	7 (3.7%)	8 (2.5%)

Tab. 17-21 Primary and secondary diagnoses for study and database groups

Variable	Category	Study Group (IDE + PAS) n=187	Database Group (IDE + Comp Use+ PAS) n=320
Secondary	None	115 (61.5%)	197 (61.6%)
Cardiac	DCMP	30 (16.0%)	56 (17.5%)
Diagnosis	Congenital Heart Disease	15 (8.0%)	21 (6.6%)
	Coronary Artery Disease	4 (2.1%)	4 (1.3%)
	RCMP	3 (1.6%)	5 (1.6%)
	Heart Disease	3 (1.6%)	10 (3.1%)
	Myocarditis	3 (1.6%)	3 (0.9%)
	CHD/Heart disease	3 (1.6%)	4 (1.3%)
	CHD/DCMP	1 (0.5%)	1 (0.3%)
	CHD/CAD	1 (0.5%)	1 (0.3%)
	DCMP/Heart disease	0 (0.0%)	2 (0.6%)
	RCMP/Heart disease	0 (0.0%)	1 (0.3%)
	Other	5 (2.7%)	6 (1.9%)
	Unknown	4 (2.1%)	9 (2.8%)

Tab. 17-21 Primary and secondary diagnoses for study and database groups

17.8.3 Efficacy Evaluation

Efficacy Results

Efficacy was assessed by measuring survival (defined by the interval of time from initiation of mechanical support as a bridge to transplant or recovery). Subjects were censored at time of explant. Subjects who were explanted due to recovery of their ventricular function and died within 30 days were counted as a failure with time to failure being the explant date. Subjects who were explanted due to escalation to ECMO or alternative device of support were counted as a failure with time to failure being the explant date.

A total of 73.3% (414 of 565) were successfully transplanted (n=394) or weaned due to recovery of their ventricular function (n=20). Twenty-eight (28) patients required escalation of support to ECMO or another supportive device or were weaned due to poor prognosis and died within 30 days of being weaned. A total of 123 patients (21.8%) died as a result of withdrawal of support.

Subjects participating in a study (Study Group) were successfully weaned or transplanted in 78% of the cases.

The subjects participating in a study (Study Group) were supported on the device for a median time of 42 days but overall, the median time was 47 days.

Tab. 17-22 details the outcomes and support time for each group.

Outcome	**Study Group** (IDE + PAS) **n=187**	**Database Group** (IDE + Comp Use + PAS) **n=320**	**All Implant Group** **n=565**
Transplant	139 (74.3%)	215 (67.2%)	394 (69.7%)
Weaned	6 (3.2%)	13 (4.1%)	20 (3.5%)
Wean-Failure*	9 (4.8%)	12 (3.8%)	28 (5.0%)
Death	33 (17.7%)	80 (25.0%)	123 (21.8%)
Success**	145 (77.5%)	228 (71.3%)	414 (73.3%)
Support Time, Median [Range]	42.0 [0 – 457]	40.5 [0 – 457]	47.0 [0 – 504]

* Failure if escalated to other support or weaned from support and died within 30 days

** Successful transplant or wean of those who met an endpoint

Tab. 17-22 Outcomes and support time

Fig. 17-9 details the Kaplan-Meier survival curve for the endpoint of death for the All Implant group. Fig. 17-10 shows the “Competing Outcomes” for the All Implant group. The lines represent each of the outcomes and at any time point the sum of the proportions of outcomes equals 100%.

It has been documented that patients who were on ECMO prior to implant[1] and those with congenital heart disease[2] are less successful, therefore the outcomes have been summarized for those groups in Tab. 17-23. The data for these variables are available for 320 subjects participating in the IDE or PAS studies (Database Group).

Fig. 17-11 and Fig. 17-12 show the “Competing Outcomes” by pre-implant ECMO and Figures Fig. 17-13 and Fig. 17-14 show the plots stratified by primary diagnosis of CHD or non-CHD.

Of the 320 subjects in the database group, 123 were on ECMO prior to the EXCOR Pediatric implant. Only 61% of the subjects who were on ECMO prior to implant were successfully transplanted/weaned compared to 78% of the subjects not on ECMO prior to EXCOR Pediatric. Of the 320 subjects in the database group, 91 were diagnosed with congenital heart disease. Only 52% of the subjects with congenital heart disease were successfully transplanted/weaned compared to 79% of the subjects which did not have a congenital heart disease diagnosis.

	ECMO prior to Implant		**Primary Diagnosis Group**	
Outcome	**Not on ECMO n=197**	**On ECMO n=123**	**Non-CHD n=229**	**CHD n=91**
Transplant	147 (74.6%)	68 (55.3%)	169 (73.8%)	46 (50.6%)
Weaned	6 (3.1%)	7 (5.7%)	12 (5.2%)	1 (1.1%)
Wean-Failure*	5 (2.5%)	7 (5.7%)	7 (3.1%)	5 (5.4%)
Death	39 (19.8%)	41 (33.3%)	41 (17.9%)	39 (42.9%)

Tab. 17-23 Outcomes and support time by pre-implant ECMO and CHD diagnosis

1. FDA Summary of Safety and Probably Benefit – H100004; EXCOR
2. Submitted Manuscript July 2016: Berlin Heart EXCOR use in Patients with Congenital Heart Disease; Morales, Zafar, Almond et al.

	ECMO prior to Implant		Primary Diagnosis Group	
Outcome	**Not on ECMO n=197**	**On ECMO n=123**	**Non-CHD n=229**	**CHD n=91**
Success**	153 (77.7%)	75 (61.0%)	181 (79.0%)	47 (51.7%)
Support Time, Median [Range]	45.0 [0 – 457]	35.0 [0 – 424]	42.0 [0 – 457]	39.0 [0 – 435]

* Failure if escalated to other support or weaned from support and died within 30 days

** Successful transplant or wean of those who met an endpoint

Tab. 17-23 Outcomes and support time by pre-implant ECMO and CHD diagnosis

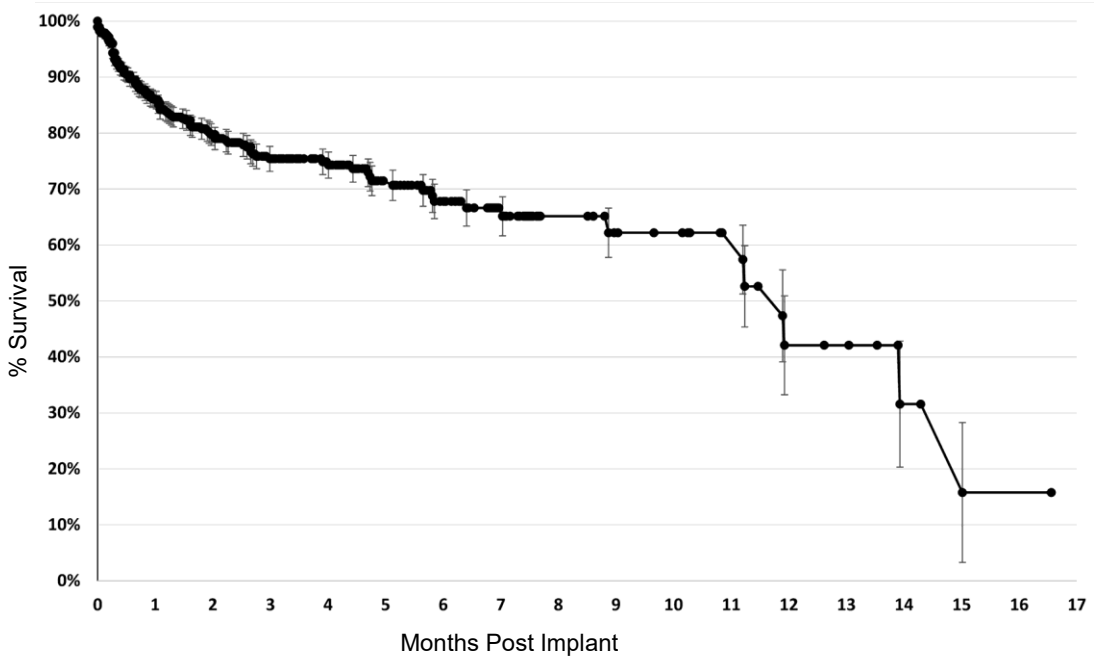


Fig. 17-9 Kaplan-Meier freedom from death for all implant group (n=565)

Interval Beginning (Months Post Implant)

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
# At Risk	565	356	227	175	130	90	68	45	25	20	18	13	8	7	3	2	1
Total # Die	0	70	93	104	105	110	114	115	116	117	117	117	121	121	122	122	123
Survival %	100	86.1	79.7	75.4	74.9	71.4	67.7	66.6	65.1	62.2	62.2	62.2	42.1	42.1	31.6	31.6	15.8
Std Error %	0	1.6	1.9	2.2	2.3	2.6	3.1	3.2	3.5	4.4	4.4	4.4	8.8	8.8	11.3	11.3	12.5

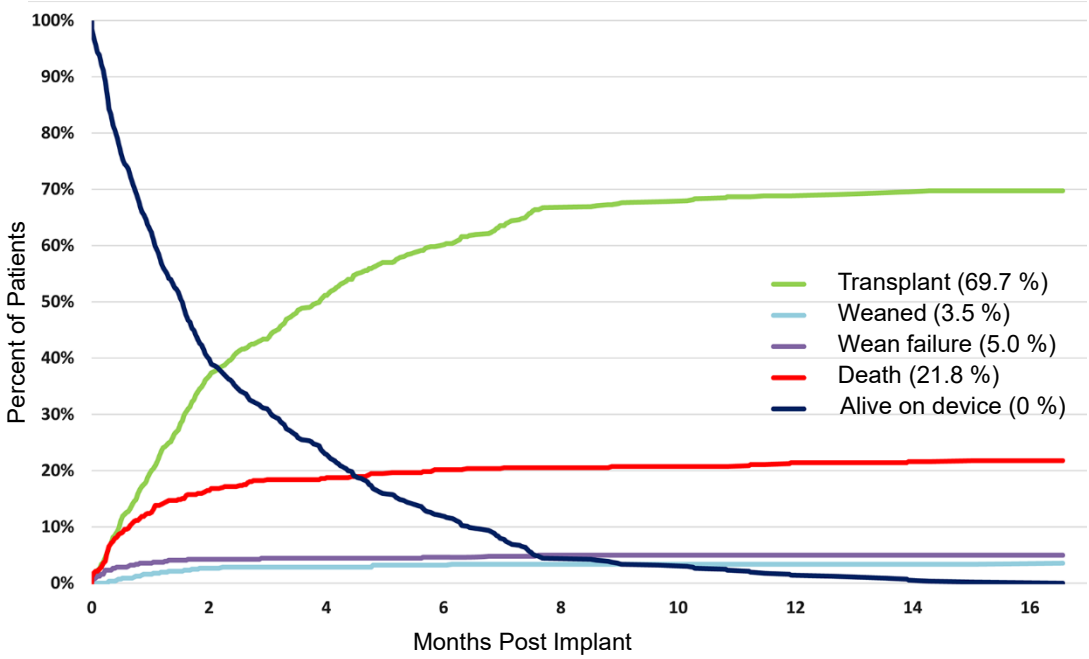


Fig. 17-10 Competing outcome plot for all implant group (n=565)

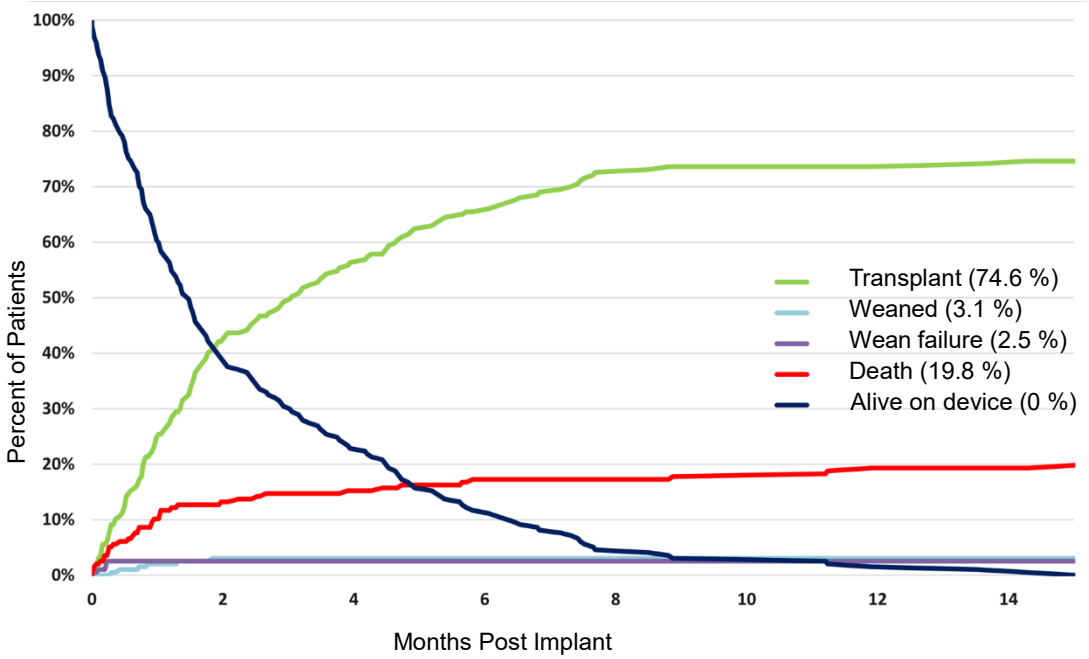


Fig. 17-11 Competing outcome plot for database group: no ECMO prior to implant (n=197)

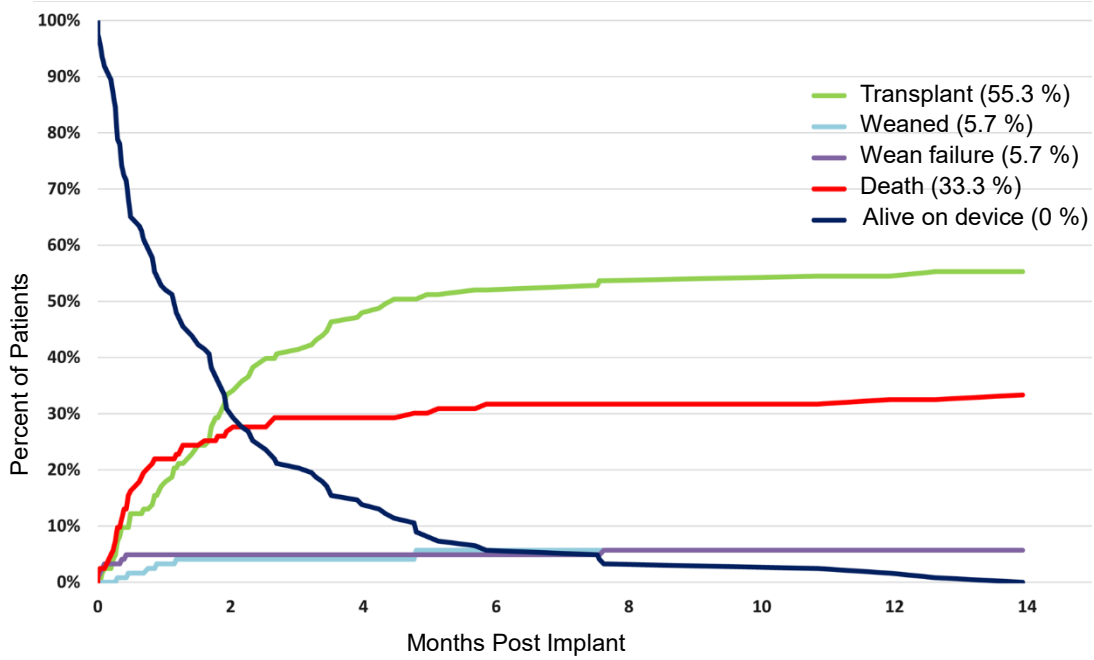


Fig. 17-12 Competing outcome plot for database group: ECMO prior to implant (n=123)

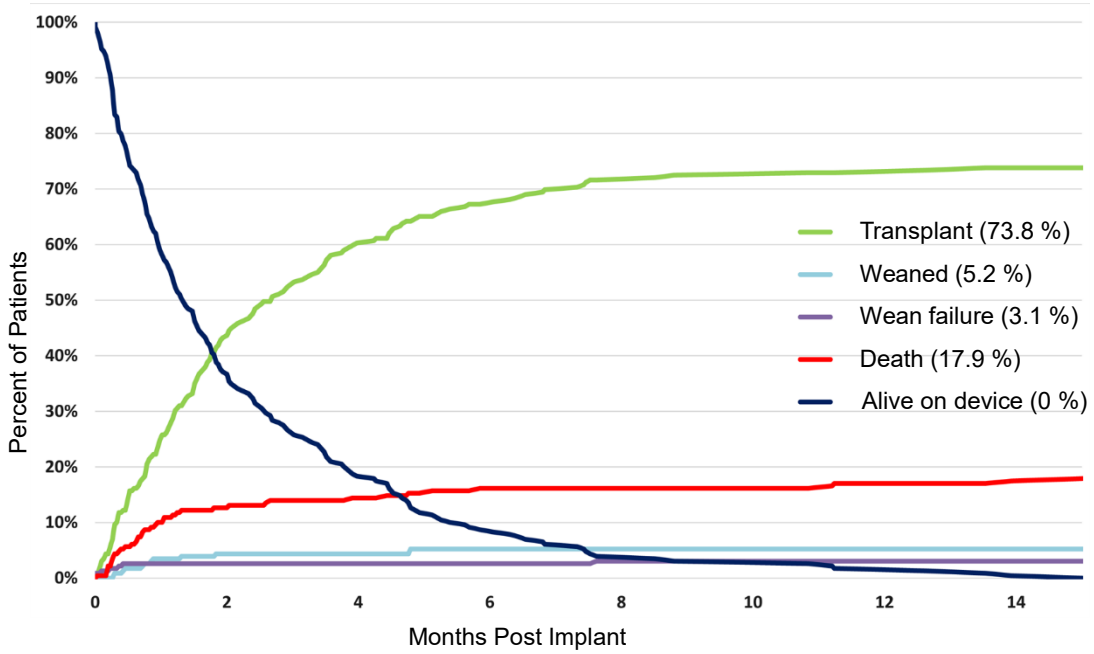


Fig. 17-13 Competing outcome plot for database group: non-CHD (n=229)

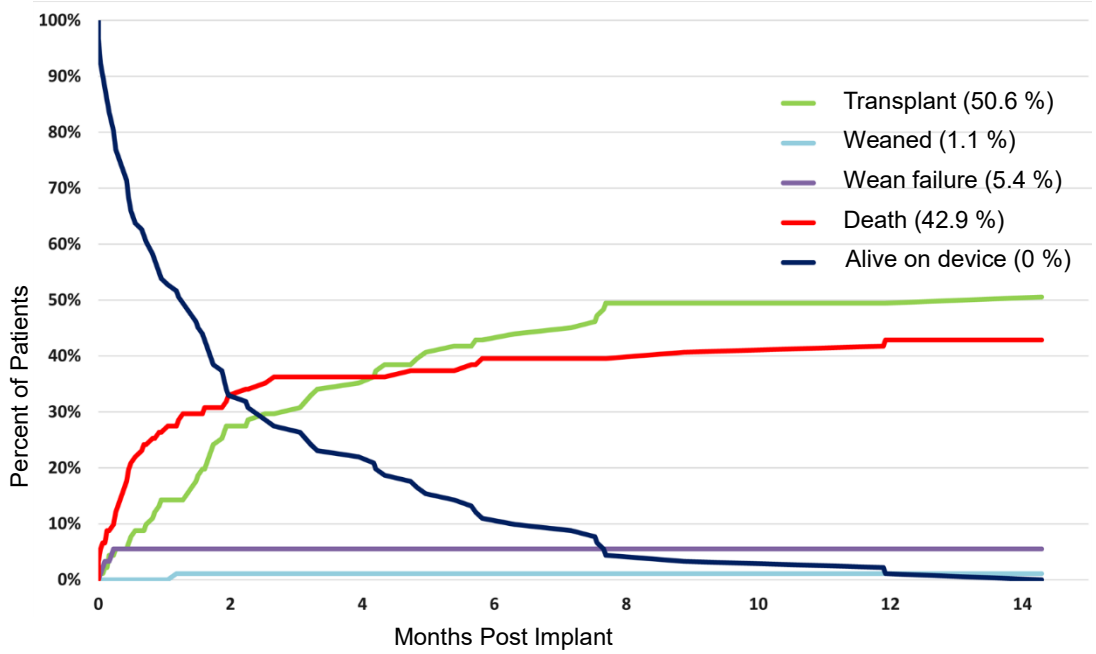


Fig. 17-14 Competing outcome plot for database group: CHD (n=91)

17.8.4 Safety Evaluation

Serious Adverse Events

Serious Adverse Events (SAEs) were collected on study subjects per the study protocol. The IDE data submitted to FDA in the February 2011 HDE application along with the Compassionate use data at the IDE sites (109 subjects total) were centrally adjudicated by a clinical events committee (CEC). A subset of the events (major bleeding, major infection, neurological dysfunction) were adjudicated per protocol in the post approval study (39 subjects). SAEs for the non-study data were gathered through Berlin Heart's complaint system per MDR guidelines. Tab. 17-24 summarizes the SAEs and rates per patient days.

No unanticipated adverse events have been reported to date.

Serious Adverse Event	**Study Group** (IDE + PAS) **n=187**		**Database Group** (IDE+Comp Use+PAS) **n=320**		**All Implant Group** **n=565**	
Total Days of support	**13137 days**		**22,742 days**		**43551 days**	
	# events	**Event Per Patient Day**	**# events**	**Event Per Patient Day**	**# events**	**Event Per Patient Day**
Major Bleeding	120	0.0091	231	0.0102	247	0.0057
Major Infection	181	0.0138	280	0.0123	294	0.0068
Neurological Dysfunction	57	0.0043	101	0.0044	134	0.0031

Tab. 17-24 Serious Adverse Event summary

Serious Adverse Event Total Days of support	**Study Group** (IDE + PAS) **n=187**		**Database Group** (IDE+Comp Use+PAS) **n=320**		**All Implant Group** **n=565**	
	13137 days		**22,742 days**		**43551 days**	
	# events	**Event Per Patient Day**	**# events**	**Event Per Patient Day**	**# events**	**Event Per Patient Day**
Cardiac Arrhythmia	19	0.0014	32	0.0014	32	0.0007
Hemolysis	7	0.0005	11	0.0005	11	0.0003
Hepatic Dysfunction	17	0.0013	35	0.0015	35	0.0008
Hypertension	59	0.0045	81	0.0036	81	0.0019
Myocardial Infarction	1	0.0001	1	0.0000	1	0.0000
Pericardial Fluid Collection	22	0.0017	37	0.0016	37	0.0008
Pericardial Effusion	4	0.003	4	0.0002	4	0.0001
Psychiatric Episode	3	0.0002	5	0.0002	5	0.0001
Renal Dysfunction	19	0.0014	34	0.0015	34	0.0008
Respiratory Failure	55	0.0042	114	0.0050	114	0.0026
Right Heart Failure	25	0.0019	39	0.0017	39	0.0009
Thromboembolism-Arterial Non CNS	4	0.0003	7	0.0003	8	0.0002
Thromboembolism-Venous	5	0.0004	8	0.0004	8	0.0002
Wound Dehiscence	1	0.0001	2	0.0001	2	0.0000
Other: Seizure	5	0.0004	15	0.0007	17	0.0004
Other: Silent Stroke	5	0.0004	5	0.0002	5	0.0001
Other	66	0.0050	94	0.0041	101	0.0023

Tab. 17-24 Serious Adverse Event summary

17.8.4.1 Summary of Neurological Dysfunction Events and Outcomes

The results of the Berlin Heart EXCOR Pediatric studies demonstrate that 73.2% of patients survived to successful weaning or cardiac transplantation. The majority of patients (64%) survived to successful weaning or cardiac transplantation with no neurologic adverse events. Study results demonstrated that patients on the device who did not meet the strict entrance criteria of the IDE study and those who were not implanted at experienced centers experienced a higher rate of mortality.

Outcome	**Study Group** (IDE + PAS) **n=187**	**Database Group** (IDE + Comp Use + PAS) **n=320**	**All Implant Group n=565**
Successful transplant or wean*	145 (77.5%)	228 (71.3%)	414 (73.3%)
No Ischemic/hemorrhagic Neurological events	143 (76.5%)	257 (80.3%)	477 (84.4%)
Successful transplant or wean with no neurological events	116 (62.0%)	189 (59.1%)	359 (63.5%)

* Successful transplant or wean of those who met an endpoint

Tab. 17-25 Outcomes and neurological events

Stroke Category	**Study Group (IDE + PAS) N=187**		**Database Group (IDE+ Comp Use + PAS) N=320**		**All Implant Group N=565**	
	Total Events	**# (%) with Event**	**Total Events**	**# (%) with Event**	**Total Events**	**# (%) with Event**
Ischemic	42	37 (19.8%)	63	55 (17.2%)	85	76 (13.5%)
Hemorrhagic	14	13 (7.0%)	16	15 (4.7%)	26	23 (4.1%)
Ischemic or Hemorrhagic	56	44 (23.5%)	79	63 (19.7%)	111	88 (15.6%)

Tab. 17-26 Incidence of each category of stroke for each group

Stroke Category		**N**	**Treatment Failure n=151**	**Treatment Success n=414**
Ischemic	No events	489	121 (24.7%)	368 (75.3%)
	At least one event	76	30 (39.5%)	46 (60.5%)
Hemorrhagic	No events	542	144 (26.6%)	398 (73.4%)
	At least one event	23	7 (30.4%)	16 (69.6%)
Ischemic or Hemorrhagic	No events	477	118 (24.7%)	359 (75.3%)
	At least one event	88	33 (37.5%)	55 (62.5%)

Tab. 17-27 Incidence of treatment failure/success for each category of stroke

17.8.4.2 Summary of Death/Withdrawal of Support

A total of 123 of 565 subjects (21.8%) died as a result of withdrawal of support. The 123 subjects were supported a median time of 22 days ranging from 0 to 457 days.

Of the 320 subjects in the database group, 80 subjects died (25%). Of the 80 subjects who died, 41 (51%) were on ECMO prior to the EXCOR Pediatric implant. The use of ECMO prior to EXCOR Pediatric implant is identified with increased mortality and increased occurrence of adverse events.

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18 Appendix

18.1 Overview: Product Range and Possible Combinations

18.1.1 Blood Pumps

Article number	Volume [ml]	∅ Inflow / outflow [mm]
P10P-001	10	6
P15P-001	15	9
P25P-001x01	25	9
P30P-001x01	30	9
P50P-001	50	12
P60P-001	60	12

Tab. 18-1 Blood pumps PU valves

18.1.2 Overview: Relationship: Body Weight – Pump Size

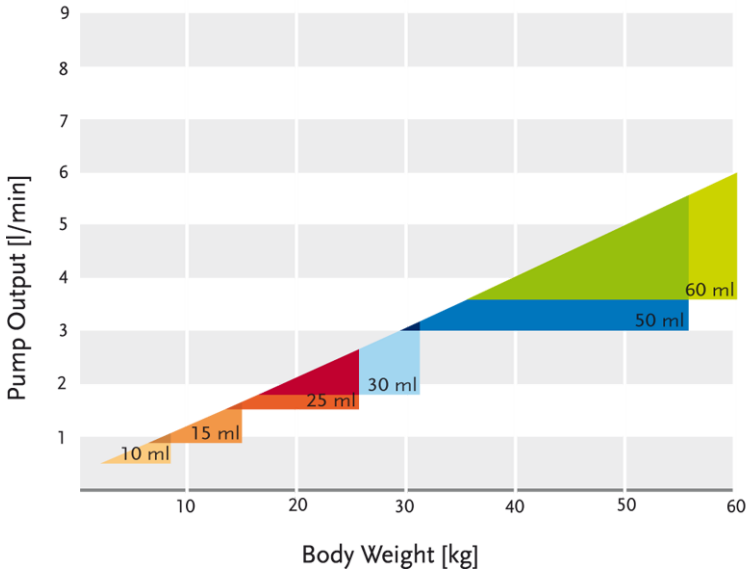

Fig. 18-1 Relationship: body weight - pump size

The final decision of pump selection should be made by the implanting physician based on the individual patients needs and the weight/pump output guidance represented in this graph. Note that the graph represents common clinical use and not the maximum technical performance of the blood pumps.

18.1.3 LV Apex Cannulae

Article number	∅ Lumen [mm]	Overall length [mm]	Length of head [mm]	Angle of head [°]
C14A-040	5	220	14	0
C18A-020	6	250	18	0
C22A-004	12/9[1]	270/220[1]	28	0
C27A-001	12	265	38	0
[1] with stage/with stage cut off				

Tab. 18-2 LV apex cannulae

18.1.4 Atrial Cannulae

Article number	∅ Lumen [mm]	Length of corpus [mm]	Length of head [mm]	Angle of head [°]
C15V-040	5	200	15	80
C19V-020	6	250	19	80
C22V-004	12/9[1]	280/240[1]	22	45
C25V-004	12/9[1]	280/240[1]	25	45
C22V-002	12	330	22	45
C26V-002	12	330	26	45
[1] with stage/with stage cut off				

Tab. 18-3 Atrial cannulae

18.1.5 Arterial Cannulae

Article number	∅ [mm]	Overall length [mm]	Length of head [mm]	Angle of head [°]	Remarks
C80G-040	5	200	4,5	80	
C80G-021	6	250	5	80	
C60G-004	12/9[1]	280/240[1]	0	60	with flexible reinforcement
C85G-004	12/9[1]	280/240[1]	0	85	with flexible reinforcement

Tab. 18-4 Arterial cannulae

Article number	∅ [mm]	Overall length [mm]	Length of head [mm]	Angle of head [°]	Remarks
C60G-002	12	330	0	60	with flexible reinforcement
C85G-002	12	330	0	85	with flexible reinforcement
[1] with stage/with stage cut off					

Tab. 18-4 Arterial cannulae

18.1.6 Overview: Which Cannulae Should be Used for Which Blood Pump?

Which pump?	Pump connector Ø [mm]	Cannula lumen Ø [mm] where cannula joins pump	Which inflow cannula?	Which outflow cannula?
P10-001	6	5 5 6 6	C15V-040 (AT) C14A-040 (AP) C19V-020 (AT) C18A-020 (AP)	C80G-040 C80G-021
P15P-001	9	6 6 9 9 9	C19V-020 (AT;CS) C18A-020 (AP;CS) C22V-004 (AT;SC) C25V-004 (AT;SC) C22A-004 (AP;SC)	C80G-021 (CS) C60G-004 C85G-004
P25P-001x01 P30P-001x01	9	6 6 9 9 9	C19V-020 (AT;CS) C18A-020 (AP;CS) C22V-004 (AT;SC) C25V-004 (AT;SC) C22A-004 (AP;SC)	C80G-021 (CS) C60G-004 (SC) C85G-004 (SC)
P50P-001 P60P-001	12	12 12 12 12 12 12	C22V-004 (AT;SO) C25V-004 (AT;SO) C22V-002 (AT) C26V-002 (AT) C22A-004 (AP; SO) C27A-001 (AP)	C60G-004 (SO) C85G-004 (SO) C60G-002 C85G-002
Explanation:	AT: atrial cannula AP: apex cannula SO: staged (stepped diameter) cannula, original diameter SC: staged (stepped diameter) cannula, diameter after cutting to size CS: connecting set required (A06-009 or A09-012 accordingly)			

Tab. 18-5 Which cannula for which pump?

18.1.7 System Accessories

Article number	Designation
T00L-002	Accessory set for blood pumps with PU valves (membrane set, de-airing set and tube connecting set) accessory set for blood pumps with PU valves
L20H-002x01	Driving tube, red; length: 200 cm
L20H-003x01	Driving tube, blue; length: 200 cm

Tab. 18-6 System Accessories

18.1.8 Driving Unit

Article number	Designation
D03I-111	EXCOR® Stationary Driving Unit Ikus (115V/ 60Hz)

Tab. 18-7 Driving unit

18.1.9 Special Components

Article number	Designation
A06-006	Cannula extension set, ∅ 6/6 mm
A09-009	Cannula extension set, ∅ 9/9 mm
A12-012	Cannula extension set, ∅ 12/12 mm
A06-009	Connecting set for cannulae, ∅ 6/9 mm
A09-012	Connecting set for cannulae, ∅ 9/12 mm

Tab. 18-8 Connecting set and cannula extension set

18.1.10 Maximum Rates for the Blood Pump - Cannula Combinations

WARNING

Pump-cannula combinations which are not recommended are leading to an increased risk of blood clots and hemolysis.

The pumping rate should not be greater than the respective value found in the table below. The blood pump will not eject its full volume at higher rates.

Cannulation[1]		**Blood pumps**					
Ø inflow cannula	**Ø outflow cannula**	**10 ml**	**15 ml**	**25 ml**	**30 ml**	**50 ml**	**60 ml**
5 mm	**5 mm**	130 bpm					
6 mm	**5 mm**	130 bpm	130 bpm				
6 mm	**6 mm**	130 bpm	130 bpm	80 bpm	65 bpm		
9 mm	**6 mm**		130 bpm	100 bpm	90 bpm		
9 mm	**9 mm**		130 bpm	130 bpm	130 bpm	130 bpm	105 bpm
12 mm	**9 mm**					130 bpm	105 bpm
12 mm	**12 mm**					130 bpm	125 bpm

Tab. 18-9 Maximum rates for the pump-cannula combinations

[1] For components with multiple lumen: the smaller lumen determines the classification of the cannulae. This also applies to the use of the connection set.

	Recommended pump-cannulae combination
	Pump-cannula combinations in which not every parameter combination is recommended (pump rate, % systole, systolic and diastolic pressure) can lead to incomplete filling and emptying of the blood pump.
rate value (bpm)	The value indicated is the upper threshold for pump rates. Values that are below the upper threshold are within the acceptable range. Values that are higher than the upper threshold are not recommended.

The threshold values have been determinated (in vitro) taking a mean arterial blood pressure of 120 mmHg as a basis.

rate value (bpm)	Red marked values displayed on the laptop: these parameter combination (pump rate, % systole, systolic and diastolic pressure) for these pump-cannula combination can lead to incomplete filling and emptying of the blood pump(s). Be sure to observe the filling behavior of the blood pump(s)!
in biventricular mode	The lower value of both pump rates (corresponding to the pump sizes used) is the relevant parameter.

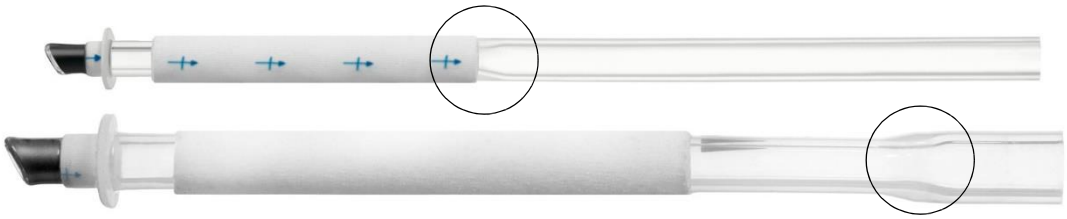

Fig. 18-2 Multiple lumen e.g. C14A-040m and C22A-004

18.1.11 Blood Pump Combinations in Biventricular Mode

Left blood pump	Right blood pump
10 ml	10 ml
15 ml	15 ml
30 ml	25 ml
60 ml	50 ml

Tab. 18-10 Recommended combinations

Check to be sure the blood pump combination selected for the patient is recommended, as indicated above.

18.1.12 Relative Systolic Duration

The relative systolic duration can be adjusted between a range of 20 % to 70 %. The upper and lower threshold (20-30 % and 60-70 %) are marked in red on the laptop. When using these upper or lower threshold the blood pump may not filling and ejecting completely. Visually check the filling and ejecting.

18.2 Technical Specifications

Electro pneumatic extracorporeal Ventricular Assist Device **EXCOR® Pediatric VAD with Stationary Driving Unit Ikus**	
Manufactured by:	Berlin Heart GmbH Wiesenweg 10 12247 Berlin Germany
Classification	Class 3
Overall system (except sterile products)	
Recommended ambient temperature in operation	+10 °C to +30 °C; with restrictions of the battery performance up to +35°C
Recommended ambient temperature, transportation and storage	-10 °C to +50 °C ; 6 h warming-up period before commissioning after transportation
Max. permitted ambient magnetic field strength	10 A/m
Relative humidity of environment	45 to 75 %
Ambient atmospheric pressure	Max. 2000 m (6562 ft) above MSL (mean sea level)
Pump	
Dimensions	Refer to product data sheets
Material	Casing and membranes: polyurethane Driving tube adapter: polyoxymethylene Connectors: titanium
Coating of blood contact surfaces	Carmeda® BioActive Surface (CBAS®)
Max. period of use	Max. 1 year
Cannulae	
Dimensions	Refer to product data sheets

Tab. 18-11 Technical specifications

Electro pneumatic extracorporeal Ventricular Assist Device **EXCOR® Pediatric VAD with Stationary Driving Unit Ikus**	
Material	Silicone, partially reinforced with plastic webbing, partially encased with suture-suitable polyester velour; some equipped with flexible metal reinforcement: wire 2 mm, circular steel Rd 1.4301; apex cannula with a titanium alloy shell
For all sterile products	
Long-term storage conditions	Temperature: +15°C to 25°C Relative humidity: 35 % to 50 % Store in a dry place!
Ikus	
Dimensions (W x H x D)	46 x 95 x 73 cm with laptop cover down (approx. 18.5 x 37.5 x 29 in) 46 x 120 x 73 cm with laptop cover open (approx. 18.5 x 47.5 x 29 in)
Weight	100.6 kg (approx. 219 lb)
Input voltage	AC 115 V
Frequency	60 Hz
Power drawn	575 VA
Main fuse	5 A
Main cable	10 A, hospital grade
Connector External alarm	Electrical data: max 1 A, 24 V insulation specifications: 2.5 mm/ 4 mm clearance and creepage distance between alarm contact and 24 V extra low voltage inside the device (coil-sided) insulation test voltage: 500 V
Protection class	IPX1 (protection against touching live parts not tested, tested safety from vertically dripping water)
Pump rate	30 to 150 bpm
Sound level of acoustic alarm	71 dB (A)

Tab. 18-11 Technical specifications

Electro pneumatic extracorporeal Ventricular Assist Device EXCOR® Pediatric VAD with Stationary Driving Unit Ikus	
Systolic pressure:	60 to 350 mmHg
Diastolic pressure	-100 to 0 mmHg
Pressure display accuracy	±10 %
Relative systolic duration	20 % to 70 %
Off-mains operating time	Max. 30 minutes
Battery charging time	6 h
Maintenance interval	2000 operating hours (at the latest after 6 months). In the event of permanently higher ambient temperatures than recommended, the maintenance intervals can shorten drastically.
Product life Ikus	Max. 8 years

Tab. 18-11 Technical specifications

18.3 Symbols and Tags

 Refer to instruction booklet / manual	 Example of symbol for NumLk and Caps Lock status LED on laptop
 Caution	 Type B applied part
 General warning sign	 Type CF applied part
 Catalogue number	 MR unsafe (Magnetic Resonance Imaging unsafe)
 Batch code	 Keep dry
 Serial number	 WEEE symbol: not to be disposed of with consumer waste
 Manufacturer	 Can be disposed of with consumer waste
 Date of manufacture	 Use-by date
 Sterilized using ethylene oxide	 Do not use if package is damaged
 Do not re-use	 Do not resterilize
 Humidity limitation	 Temperature limit

Fig. 18-3 Symbols used on labeling

For symbols on the connection panel: See section 5.2.1: Connection Panel, page 26.

18.4 Sample Copy: Ikus Incoming Checklist

IKUS INCOMING CHECKLIST

Berlin Heart®

Always refer to the Instructions for Use of EXCOR Pediatric VAD!

Ikus LOT#: (located under red drive tube connection port) ..... – ..... Name of clinical site: .....

Please ensure that the checklist below has been satisfactorily completed:

	checked
Ikus driver and replacement driver are available	☐
Remove Ikus drivers from crates and inspect for damage and/or broken parts	☐
Manual pump included (located and secured under laptop)	☐
Locate and inspect for the following accessories (either loose or in white box):	
⇨ Mains power supply cable ☐	⇨ Keys ☐
⇨ Envelope with default password ☐	⇨ Connector Plug for External Alarm ☐

⚠ If the driver is damaged or there are missing parts:
Do not use the driver. Notify Berlin Heart Clinical Affairs (866) 249 - 0128

Ikus driver initial start-up:

Caution! - Keep the driving tube connectors covered at all times when not in use.
- The Ikus mains power switch (rocker switch) should always be in the ON/ EIN position – even when Ikus is in battery mode or is switched off (i.e. not in operation).

	checked
Connect the Ikus to the mains power (emergency outlet). Secure the mains cable with the plug clip on the Ikus driver. Ensure that the mains power switch (rocker switch) is set to ON/ EIN.	☐
Turn the key switch to the ON [I] position. The battery charge indicator (LED lights) will light up and the number of hours the driving unit has been operated to date will be displayed. The mains power indicator lights up.	☐
Switch on the laptop. The language selection menu appears. Select the desired language by pressing the corresponding number key. You do not have to press <Enter> to confirm this selection.	☐
The start menu is displayed on the laptop. Select the "Start program" option (<1>). Enter your user number and password. Confirm the password with <Enter>. Ikus will carry out a self-test. Wait for the test phase to be concluded (this takes several minutes). Do not acknowledge the acoustic signal. The messages in the message window will inform you of the status of the test. If Ikus is found to be operating correctly, the "Operating mode" view will be displayed next.	☐
Check that the batteries are adequately charged (full bar of LED lights).	☐
Shut down the monitoring program as instructed in the dialog window.	☐
When instructed in the message window, use the key switch to switch off Ikus. Important: The mains power switch (rocker switch) remains set to ON/ EIN.	☐

⚠ If the Ikus has detected a fault during start-up or the self test:

An error message will appear in the message window. Switch the Ikus off, wait for at least 10 minutes, and begin the start procedure again as described above. If the error message persists, notify Berlin Heart Clinical Affairs: (866) 249 - 0128

Remarks:

..... Name ..... Signature ..... Date

Please complete and fax this form back to Berlin Heart, Inc. Fax No: (877) 237 - 5464

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18.5 Implantation Record Form

Berlin Heart®

IMPLANTATION RECORD FORM

EXCOR® VAD Ped

This form applies **only** to USA and Canada

Please fill out the form (5 pages), and fax it to Berlin Heart, Inc. *immediately* after implantation (fax: 866.540.5026)
After replacing a blood pump, please fill out the "Pump Replacement" section (page 2), list the supplies used on page 3-5, and fax (5 pages) to Berlin Heart Inc. (fax: 866.540.5026)

PATIENT INFORMATION

Hospital			City/Country	
Patient's initials:	**Sex** m ☐ f ☐	**Age:**	**Height** [cm]	**Weight** [kg]
Patient-No.: (BH Site No. followed by the patient No. ie: 004-103)	**Indication** Ischemic CMP ☐	Idiopathic CMP ☐	Acute Myocarditis ☐	
	Postcardiotomy ☐	Acute Myocardial Infarction ☐		
	Congenital ☐	.....	Other ☐	

PRE- IMPLANTATION CONDITION

Urgency of implantation elective ☐ urgent ☐ emergency ☐

INTERMACS level

1 ☐ Critical cardiogenic shock despite escalating support
2 ☐ Progressive decline with inotropic dependence
3 ☐ Clinically stable with mild to moderate inotropic dependence
4 ☐ Recurrent, no refractory, advanced heart failure that can be stabilized with intervention
5 ☐ Exertion intolerant but is comfortable at rest and able to perform activities of daily living with slight difficulty
6 ☐ Exertion limited; is able to perform mild activity, but fatigue results within a few minutes of any meaningful physical exertion
7 ☐ Advanced NYHA functional class III

On ventilator	no ☐	yes ☐	since ..... (days)	
Other MCS	no ☐	yes ☐		
		IABP ☐	since ..... (date)	
		ECMO ☐	since ..... (date)	
Another VAD support	no ☐	yes ☐	since ..... (date)	
On transplantation list	no ☐	yes ☐	since ..... (date)	
CPR within 24h	no ☐	yes ☐	unknown ☐	
Dialysis/Hemofiltration within 72h	no ☐	yes ☐	unknown ☐	
History of stroke	no ☐	yes ☐	unknown ☐	
History of prev. thor. surg.	no ☐	yes ☐	unknown ☐	

PRE- IMPLANTATION HEMODYNAMICS (most recent – if any parameter is not available please mark: n.a.)

MAP [mmHg]	**CVP** [mmHg]	**PAP mean** [mmHg]	**LVEDP** [mmHg]	**LVEF %** **FS %**
Cardiac output [l/min]	**Cardiac Index** [l/min/sqm]	**LVEDD** [mm]		

IMPLANTATION DETAILS

Implantation date [mm/dd/yy]	**Surgeon** [name]	**Type** BVAD ☐ LVAD ☐ RVAD ☐	**Left-sided cannulation** apical ☐ atrial ☐	**Pump type** Tilting-disk valve ☐ PU valve ☐

LVAD pump size:	10 ml ☐	15 ml ☐	25 ml ☐	30 ml ☐	50 ml ☐	60 ml ☐	80 ml ☐
RVAD pump size:	10 ml ☐	15 ml ☐	25 ml ☐	30 ml ☐	50 ml ☐	60 ml ☐	80 ml ☐

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The Woodlands, TX 77380
www.berlinheart.com

1000068x08

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☐ **Pump replacement**

Left pump ☐	Reason for replacement .....
Date:	Location of deposit inflow valve ☐ outflow valve ☐ pump chamber ☐
Right pump ☐	Reason for replacement .....
Date:	Location of deposit inflow valve ☐ outflow valve ☐ pump chamber ☐

☐ **Device Explant**

Date:	HTx ☐ weaned ☐ died ☐ primary cause: ..... Remarks: ....

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Please record the lot numbers of the used EXCOR® components and indicate the availability of replacement components and fax all to Berlin Heart, Inc. *immediately* after implantation (fax: 866.540.5026).

Hospital/City ..... **Date of Implantation** .....

Patient ID (BH Site No. followed by the patient No. ie: 004-103) .....

Ikus-No. ..... **Ikus hours of operation** .....

Replacement Ikus available ? yes ☐ no ☐ **Replacement Ikus hours of operation**

Replacement Ikus-No. ....

Item	Article No.	Lot-No. LVAD used	RVAD used	Replacement available ? yes	no
EXCOR Blood Pumps with PU valves					
10 ml in/out Ø 6 mm	P10P-001			☐	☐
15 ml in/out Ø 9 mm	P15P-001			☐	☐
25 ml in/out Ø 9 mm	P25P-001x01			☐	☐
30 ml in/out Ø 9 mm	P30P-001x01			☐	☐
50 ml in/out Ø 12 mm	P50P-001			☐	☐
60 ml in/out Ø 12 mm	P60P-001			☐	☐
80 ml in/out Ø 12 mm	P80P-001***			☐	☐
EXCOR Blood Pumps with Tilting-disk valves					
50 ml in/out Ø 12 mm	P50M-001***			☐	☐
60 ml in/out Ø 12 mm	P60M-001***			☐	☐
80 ml in/out Ø 12 mm	P80M-001***			☐	☐
80 ml **out/in** Ø 12 mm (in/out exchanged)	P80M-005***			☐	☐
80 ml in/out Ø 16 mm	P80M-003***			☐	☐
80 ml **out/in** Ø 16 mm (in/out exchanged)	P80M-004***			☐	☐

*** Not available for general use in the US or Canada
+++ Not available for general use in the US

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Item	Article No.	Lot-No. LVAD used	RVAD used	Replacement available ? yes	no
EXCOR Apex Cannulae					
Ø 5 mm, L 22 cm (Apex cannula for infants)	C14A-040			☐	☐
Ø 6 mm, L 25 cm (Apex cannula for small children)	C18A-020			☐	☐
Ø 12/9 mm, L 27 cm (Apex pediatric cannula, staged)	C22A-004			☐	☐
Ø 12 mm, L 26,5 cm (Apex cannula, one-piece)	C27A-001			☐	☐
Ø 16 mm, L 33 cm (Apex cannula)	C41A-050***			☐	☐
EXCOR Atrial Cannulae					
Ø 5 mm, L 20 cm, head 15 mm (Atrial cannula for infants)	C15V-040			☐	☐
Ø 6 mm, L 25 cm, head 19 mm (Atrial cannula, small children)	C19V-020			☐	☐
Ø 12/9 mm, L 28 cm, head 22 mm (Atrial ped. cannula, stag.)	C22V-004			☐	☐
Ø 12/9 mm, L 28 cm, head 25 mm (Atrial ped. cannula, stag.)	C25V-004			☐	☐
Ø 12 mm, L 33 cm, head 22 mm (Atrial cannula)	C22V-002			☐	☐
Ø 12 mm, L 33 cm, head 26 mm (Atrial cannula)	C26V-002			☐	☐
EXCOR Arterial Cannulae					
Ø 5 mm, L 20 cm (Arterial cannula for infants)	C80G-040			☐	☐
Ø 6 mm, L 25 cm (Arterial cannula for small children)	C80G-021			☐	☐
Ø 12/9 mm, L 26 cm (Graft-adapter ped. cannula, staged)	C00P-004+++			☐	☐
Ø 12/9 mm, L 28 cm, 85° (Arterial ped. cannula, staged)	C85G-004			☐	☐
Ø 12/9 mm, L 28 cm, 60° (Arterial ped. cannula, staged)	C60G-004			☐	☐
Ø 12 mm, L 33 cm, 60° (Arterial cannula)	C60G-002			☐	☐
Ø 12 mm, L 33 cm, 85° (Arterial cannula)	C85G-002			☐	☐
Ø 12 mm, L 26 cm (Graft-adapter cannula)	C00P-001+++			☐	☐
Ø 16/12 mm, L 36 cm, 85° (Arterial cannula, staged)	C85G-050+++			☐	☐
Ø 16 mm, L 26 cm (Graft-adapter cannula)	C00P-050+++			☐	☐

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Item	Article No.	Lot-No. LVAD used	RVAD used	Replacement available ? yes	no
Connecting Set for Cannulae					
Ø 6/9 mm	A06-009			☐	☐
Ø 9/12 mm	A09-012			☐	☐
Ø 12/16 mm	A12-016***			☐	☐
Cannula Extension Set					
Ø 6/6 mm	A06-006			☐	☐
Ø 9/9 mm	A09-009			☐	☐
Ø 12/12 mm	A12-012			☐	☐
Accessories					
Accessory set Tilting-disk valves	T00L-001***			☐	☐
Accessory set PU-valves	T00L-002			☐	☐
Driving tube, red Ø 6/8 mm, L 2 m	L20H-002			☐	☐
Driving tube, blue Ø 6/8 mm, L 2 m	L20H-003			☐	☐
Tank unit	1600422			☐	☐

*** Not available for general use in the US or Canada
+++ Not available for general use in the US

Date	Signature
Name	Contact Phone No.

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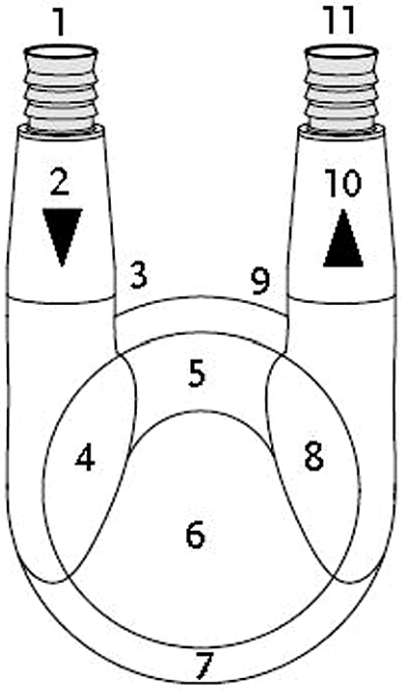
18.6 Sample Copy: EXCOR Pump Log



1 transition inflow cannula – inflow connector
2 inflow stub in front of inflow valve
3 inflow valve
4 inflow stub behind inflow valve
5 area between inflow and outflow stubs
6 remaining area of blood chamber
7 transition blood chamber - membrane (directly above the reinforcement ring)
8 outflow stub in front of outflow valve
9 outflow valve
10 outflow stub behind outflow valve
11 transition outflow connector – outflow cannula

Fig. 18-4 EXCOR blood pump with checkpoint numbers

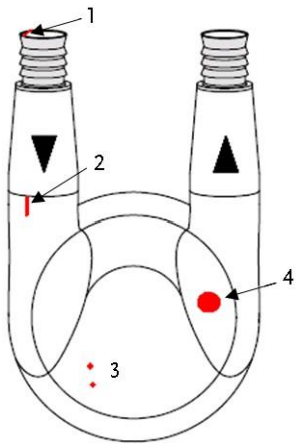
ADVICE

To briefly describe the findings, use the following letter codes:

p	Small punctual deposit	f	Small strand
P	Large punctual deposit	F	Large strand
a	Small area of deposit	t	Small thrombus
A	Large area of deposit	T	Large thrombus
~ above the respective letter indicates floating deposits			

Tab. 18-12 Notation for letter code

Example: Plotting of the deposits



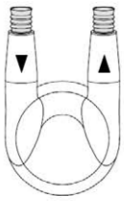
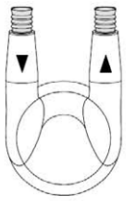
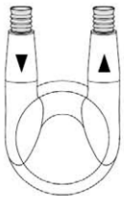
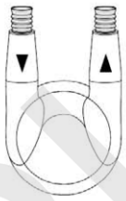
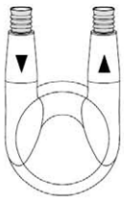
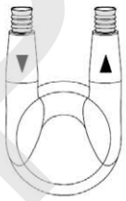
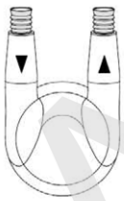
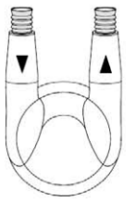
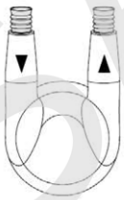
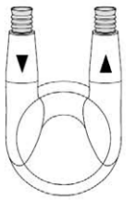
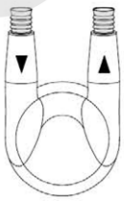
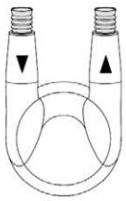
1 small laminar deposit
2 small suture on the inflow valve
3 small specks
4 larger laminar deposit

Fig. 18-5 Plotting of the deposits

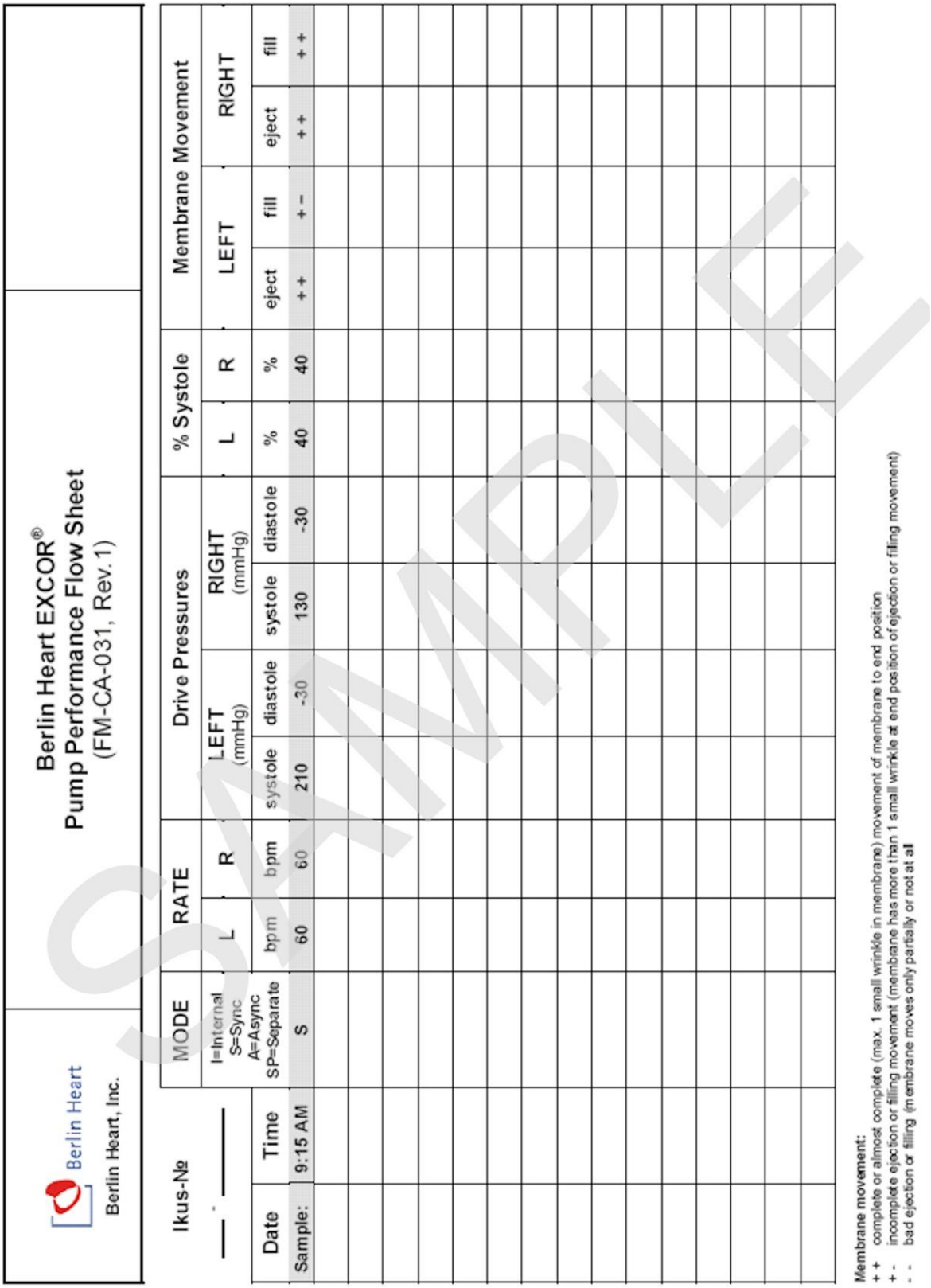
Example: Notation with letter code

			Linke Pumpe/ Left pump	ml: 50ml				No.: 0815						
Datum date	Zeit time	Name Sign.		1	2	3	4	5	6	7	8	9	10	11
01.01.	8:00	z.B.		a		F			p		A			

Fig. 18-6 Example: Notation with letter code

			Linke Pumpe/ Left pump	ml:				No.:							Rechte Pumpe/ Right pump	ml:				No.:						
Datum date	Zeit time	Name Sign.		1	2	3	4	5	6	7	8	9	10	11		1	2	3	4	5	6	8	7	9	10	11
																										
																										
Datum date	Zeit time	Name Sign.		1	2	3	4	5	6	7	8	9	10	11		1	2	3	4	5	6	8	7	9	10	11
																										
Datum date	Zeit time	Name Sign.		1	2	3	4	5	6	7	8	9	10	11		1	2	3	4	5	6	8	7	9	10	11
																										

18.7 Pump Performance Flow Sheet



Berlin Heart
Berlin Heart, Inc.

Berlin Heart EXCOR®
Pump Performance Flow Sheet
(FM-CA-031, Rev. 1)

Ikus-№ ___ - ___

Date	Time	MODE	RATE		Drive Pressures				% Systole		Membrane Movement			
		I=Internal S=Sync A=Async SP=Separate	L	R	LEFT (mmHg)		RIGHT (mmHg)		L	R	LEFT		RIGHT	
			bpm	bpm	systole	diastole	systole	diastole	%	%	eject	fill	eject	fill
Sample:	9:15 AM	S	60	60	210	-30	130	-30	40	40	+ +	+ –	+ +	+ +

Membrane movement:
+ + complete or almost complete (max. 1 small wrinkle in membrane) movement of membrane to end position
+ - incomplete ejection or filling movement (membrane has more than 1 small wrinkle at end position of ejection or filing movement)
- - bad ejection or filling (membrane moves only partially or not at all

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19 EMC Tables

19.1 Essential Performance

The following essential performance was verified in the electromagnetic immunity tests: the Ikus must drive the EXCOR blood pumps with the set parameters, by monitoring the following acceptance criteria:

- The pump rate may not deviate by more than 10 % or 50 ms (the higher value is valid).
- The relative systolic duration may not deviate by more than 10 % or 50 ms (the higher value is valid).
- The driving pressure in engaged condition at the end of the systole or diastole may not deviate by more than 10 % or 20 mmHg (the higher value is valid).
- No failure alarms may occur.
- No undesired change may occur between mains and battery operation.
- In battery operation the battery alarms must occur correctly.
- No switch to emergency pulse mode may occur.

19.2 Electromagnetic Emissions

The Ikus is intended for use in the electromagnetic environment specified below. The customer or the user of the Ikus should ensure that Ikus is used in such an environment

Emissions test	**Compliance**	**Electromagnetic environment - guidance**
RF emissions CISPR 11	Group 1	The Ikus uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
RF emissions CISPR 11	Class B	The Ikus is suitable for use in all establishments, including domestic establishments and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
Harmonic emissions IEC 61000-3-2	Class A	
Voltage fluctuations/ flicker emissions IEC 61000-3-3	Complies	

Tab. 19-1 Emissions characteristics

19.3 Electromagnetic Immunity - Part 1

The Ikus is intended for use in the electromagnetic environment specified below. The customer or the user of the Ikus should ensure that it is used in such an environment.

Immunity test	**IEC 60601 test level**	**Compliance level**	**Electromagnetic environment -guidance**
Electrostatic discharge (ESD) IEC 61000-4-2	± 6 kV contact ± 8 kV air	± 6 kV contact ± 8 kV air	Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30 %.
Electrical fast transient / burst IEC 61000-4-4	± 2 kV for power supply lines ± 1 kV for input/ output lines	± 2 kV for power supply lines ± 1 kV for input/ output lines	Mains power quality should be that of a typical commercial or hospital environment.
Surge IEC 61000-4-5	± 1 kV line(s) to line(s) ± 2 kV line(s) to earth	± 1 kV line(s) to line(s) ± 2 kV line(s) to earth	Mains power quality should be that of a typical commercial or hospital environment.
Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11	< 5 % U_T (>95 % dip in U_T) for 0.5 cycle 40 % U_T (60 % dip in U_T) for 5 cycles 70 % U_T (30 % dip in U_T) for 25 cycles < 5 % U_T (>95 % dip in U_T) for 5 sec	< 5 % U_T (>95 % dip in U_T) for 0.5 cycle 40 % U_T (60 % dip in U_T) for 5 cycles 70 % U_T (30 % dip in U_T) for 25 cycles < 5 % U_T (>95 % dip in U_T) for 5 sec	Mains power quality should be that of a typical commercial or hospital environment. If the user of the Ikus requires continued operation during power mains interruptions, it is recommended that the Ikus be powered from an uninterruptible power supply or a battery.
Power frequency (50/ 60 Hz) magnetic field IEC 61000-4-8	3 A/m	100 A/m	The Ikus can be used up to 1 m from power cables carrying up to 100 A.
NOTE U_T is the a.c. mains voltage prior to application of the test level.			

Tab. 19-2 Electromagnetic immunity - part 1

19.4 Electromagnetic Immunity - Part 2

The Ikus is intended for use in the electromagnetic environment specified below. The customer or the user of the Ikus should ensure that it is used in such an environment

Immunity test	IEC 60601 test level	Compliance level	Electromagnetic environment - guidance
			Portable and mobile RF communications equipment should be used no closer to any part of the Ikus, including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter. Recommended separation distance
Conducted RF IEC 61000-4-6	3 V [e)] 150 kHz to 80 MHz outside ISM bands[a] 10 V [e)] 150 kHz to 80 MHz in ISM bands [a)]	10 V 10 V	d=0.35√P d=1.2√P
Radiated RF IEC 61000-4-3	10 V/ m 80 MHz to 2,5 GHz	30 V/m 80 MHz to 6 GHz	d=0.4 √P 80 MHz to 800 MHz d=0.77√P 800 MHz to 2,5 GHz
			Where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and d is the recommended separation distance in metres (m).[b] Field strengths from fixed RF transmitters, as determined by an electromagnetic site surv ey,[c] should be less than the compliance level in each frequency range.[d] nterference may occur in the vicinity of equipment marked with the following symbol: 

Tab. 19-3 Electromagnetic immunity - part 2

Immunity test	IEC 60601 test level	Compliance level	Electromagnetic environment - guidance
NOTE 1: At 80 MHz and 800 MHz, the higher frequency range applies.			
NOTE 2: These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.			

Tab. 19-3 Electromagnetic immunity - part 2

a) The ISM (industrial, scientific and medical) bands between 150 kHz and 80 MHz are 6.765 MHz to 6.795 MHz; 13.553 MHz to 13.567 MHz; 26.957 MHz to 27.283 MHz; and 40.66 MHz to 40.70 MHz.

b) The compliance levels in the ISM frequency bands between 150 kHz and 80 MHz and in the frequency range 80 MHz to 2.5 GHz are intended to decrease the likelihood that mobile/portable communications equipment could cause interference if it is inadvertently brought into patient areas. For this reason, an additional factor of 10/ 3has been incorporated into the formulae used in calculating the recommended separation distance for transmitters in these frequency ranges.

c) Field strengths from fixed transmitters, such as base stations for radio (cellular/ cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the Ikus is used exceeds the applicable RF compliance level above, the Ikus should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as re-orienting or relocating the Ikus.

d) Over the frequency range 150 kHz to 80 MHz, field strengths should be less than 10V/m.

e) r.m.s., before modulation is applied.

19.5 Recommended Separation Distances Between Portable and Mobile RF Communications Equipment and the Ikus

The Ikus is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The customer or the user of the Ikus can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and the Ikus as recommended below, according to the output power of the communications equipment.

Rated maximum output power of transmitter [W]	Separation distance according to frequency of transmitter [m]			
	150 kHz to 80 MHz outside ISM bands **$d=0,35\sqrt{P}$**	**150 kHz to 80 MHz in ISM bands** **$d=1,2\sqrt{P}$**	**80 MHz to 800 MHz** **$d = 0.4\sqrt{P}$**	**800 MHz to 6 GHz** **$d = 0.77\sqrt{P}$**
0.01	0.04	0.12	0.04	0.08
0.1	0.11	0.38	0.13	0.24
1	0.4	1.2	0.4	0.8
10	1.11	3.8	1.3	2.4
100	3.5	12	4	7.7
For transmitters rated at a maximum output power not listed above, the recommended separation distance *d* in metres [m] can be determined using the equation applicable to the frequency of the transmitter, where *P* is the maximum output power rating of the transmitter in watts [W] according to the transmitter manufacturer.				

Tab. 19-4 Separation distance depending on frequency of transmitter

NOTE 1 At 80 MHz and 800 MHz, the separation distance for the higher frequency range applies.

NOTE 2 The ISM (industrial, scientific and medical) bands between 150 kHz and 80 MHz are 6.765 MHz to 6.795 MHz; 13.553 MHz to 13.567 MHz; 26.957 MHz to 27.283 MHz; and 40.66 MHz to 40.70 MHz.

NOTE 3 An additional factor of 10/3 has been incorporated into the formulae used in calculating the recommended separation distance for transmitters in the ISM frequency bands between 150 kHz and 80 MHz and in the frequency range 80 MHz to 2.5 GHz to decrease the likelihood that mobile/portable communications equipment could cause interference if it is inadvertently brought into patient areas.

NOTE 4 These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.

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Abbreviations

A

ALA: Alpha-linolenic acid
aPTT: Activated partial prothrombin time
ASA: Acetylsalicylic acid
AST: Aspartate aminotransferase

B

BSA: Body surface area
BTR: Bridge to recovery
BTT: Bridge to transplant
BUN: Blood urea nitrogen
BVAD: Biventricular assist device

C

CBAS: Carmeda® BioActive Surface
CEC: Clinical Events Committee
CPB: Cardiopulmonary Bypass
CRP: C-reactive protein
CVP: Central venous pressure , ,

E

ECG: Electrocardiogram
ECMO: Extracorporeal membrane oxygenation
ELSO: Extracorporeal Life Support Organization
EMC: Electromagnetic Compatibility
ETO: Ethylene oxide

F

FDA: Food and Drug Administration

H

HCT: Hematocrit
HDE: Humanitarian Device Exemption
HIT: Heparin-induced thrombocytopenia

I

i.v.: Intravenous
ICU: Intensive care unit
IFU: Instructions for Use
INR: International normalized ratio
IR: Initial rate
IU: International unit

L

LAD: Left anterior descending artery
LMWH: Low molecular weight heparin
LV: Left ventricular
LVAD: Left ventricular assist device
LVEDD: Left ventricular end-diastolic diameter

M

MAP: Mean arterial pressure
MRI: Magnetic Resonance Imaging

N

NO: Nitric oxide
NYHA: New York Heart Association

O

OR: Operating room

P

PAP: Pulmonary artery pressure ,
PCWP: Pulmonary capillary wedge pressure
POD: Postoperative day
PSA: Propensity Score Analysis

Q

q12h: quaque 12 h, every 12 hours

R

RFID: Radio frequency identification
RR: Reduced rate

S

SAE: Serious adverse event

T

TEG: Thrombelastography
TIA: Transient ischemic attack
TWI: Total weaning interval

U

UFH: Unfractionated heparin

V

VAD: Ventricular Assist Device

W

WR: Weaning rate

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