SynCardia Systems LLC
temporary Total Artificial Heart (TAH-t)
Instructions for Use with the
Companion 2 Driver System

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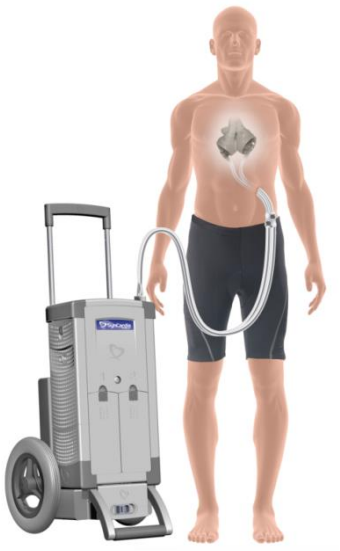

CAUTION: Federal (USA) law restricts this device to sale by or on order of a physician.

STERILE	EO

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Chapter 1. Device Description

The SynCardia temporary Total Artificial Heart (TAH-t) System is comprised of an implantable TAH-t (70cc or 50cc) and an external driver. The Companion 2 Driver System (**Figure 1-1**) includes a Hospital Cart and/or Caddy.

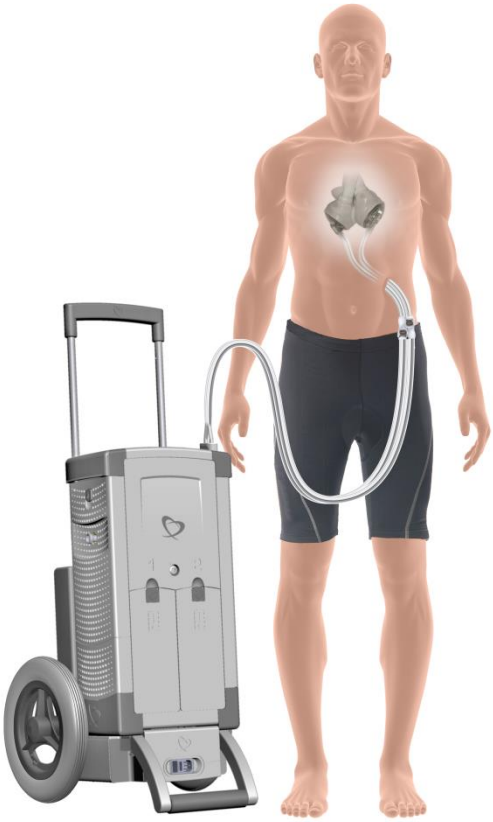

Figure 1-1 –TAH-t with Companion 2 Driver System

The SynCardia TAH-t is an implantable pulsatile biventricular device that replaces a patient's native ventricles and valves and pumps blood to both the pulmonary and systemic circulation systems. The TAH-t is available in two sizes: the 70cc TAH-t and a smaller version, the 50cc TAH-t.

The 70cc TAH-t left and right cannulae have one colored band at the end of each cannula: one red band for the left ventricle and one blue band for the right ventricle. These cannulae differ from the 50cc TAH-t which has two colored bands on each cannula, as shown in **Figure 1-2.**

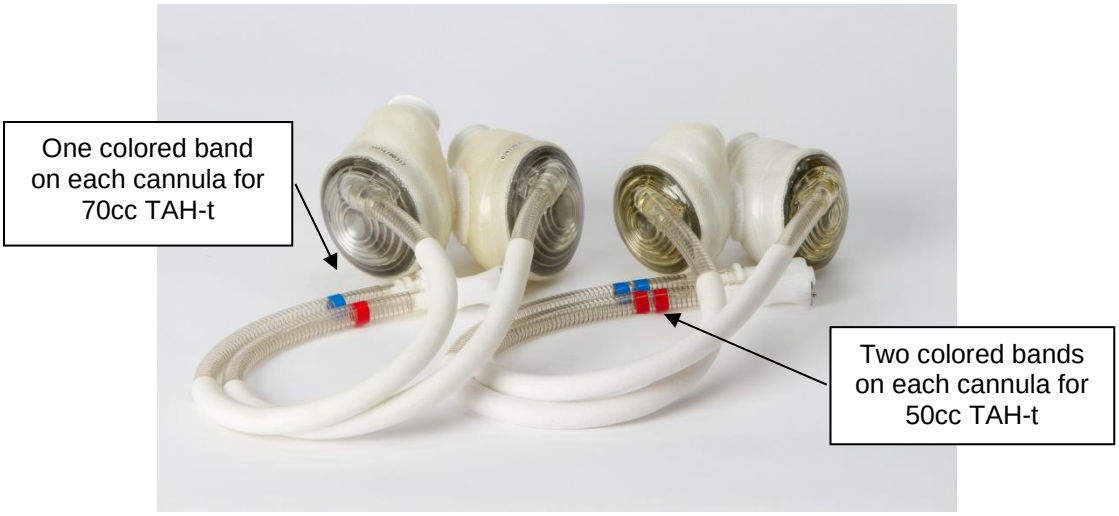

Figure 1-2 – 70cc TAH-t and 50cc TAH-t Ventricles and Cannulae

The Companion 2 Driver System (**Figure 1-3**) is a multi-component electro-mechanical unit designed to provide pneumatic power to the implanted TAH-t. The Companion 2 Driver System includes a Driver, a Hospital Cart, and a Caddy.

Figure 1-3 – Companion 2 Driver System Major Components

1.1 The Implantable TAH-t

The implantable TAH-t consists of two artificial ventricles, each made of a semi-rigid polyurethane housing with four flexible polyurethane diaphragms separating the blood chamber from the air chamber. The diaphragms allow the artificial ventricle to fill and then eject blood when compressed by air from the external driver. Valves, mounted in the inflow and outflow ports of each artificial ventricle, control the direction of blood flow. The maximum dynamic stroke volume of each ventricle allows for generating a flow rate up to 10.5 liters per minute (LPM) for the 70cc TAH-t and up to 7.5 LPM for the 50cc TAH-t.

The left artificial ventricle is connected via the left atrial inflow connector to the left atrium, and via the aortic outflow connector to the aorta. The right artificial ventricle is connected via the right atrial inflow connector to the right atrium and via the pulmonary artery outflow connector to the pulmonary artery. The cannula from each artificial ventricle is tunneled through the chest wall. The cannulae of the right and left artificial ventricles are attached to seven-foot pneumatic drivelines that connect to the driver.

1.2 Selection of TAH-t size: 50cc vs. 70cc

The SynCardia TAH-t is available in two sizes, 50cc and 70cc. The 50cc TAH-t is a smaller version of the 70cc TAH-t. When evaluating a patient, the following factors should be considered to determine which size device should be used:

- 50cc TAH-t
  - designed to typically provide a cardiac output of about 3.5 LPM to about 5.9 LPM
  - may provide a maximum cardiac output of 7.5 LPM (150 BPM @ 50cc)
  - can be used on patients with a body surface area (BSA) of ≤ 1.85m^2
- 70cc TAH-t
  - designed to typically provide a cardiac output of about 4.5 LPM to about 8.8 LPM
  - may provide a maximum cardiac output of 10.5 LPM (150 BPM @ 70cc)
  - can be used on patients with a body surface area (BSA) of ≥ 1.7m^2

1.3 TAH-t Theory of Operation

The theory of operation for the TAH-t is identical for both sizes of the device.

Blood enters the TAH-t through the patient's native atria, passing through an inflow cuff that has been anastomosed to the atrium at the level of the atrioventricular valve annulus. The cuff attaches to the rigid housing of the

TAH-t via an inflow valve that allows blood to enter the polyurethane ventricle.

Pulses of air generated by an external driver and delivered by a driveline distend the ventricle diaphragm and expel blood from the ventricle through an outflow valve into an outflow graft anastomosed to the aorta or pulmonary artery. The TAH-t will fully support the patient's circulation.

The basic concept for utilizing the TAH-t is "partial fill, full eject." A graphic representation of a typical pressure curve for the pulse of air delivered to the TAH-t ventricle is shown in **Figure 1-4** below. The pressure curves for the 50cc TAH-t and 70cc TAH-t have the same waveform.

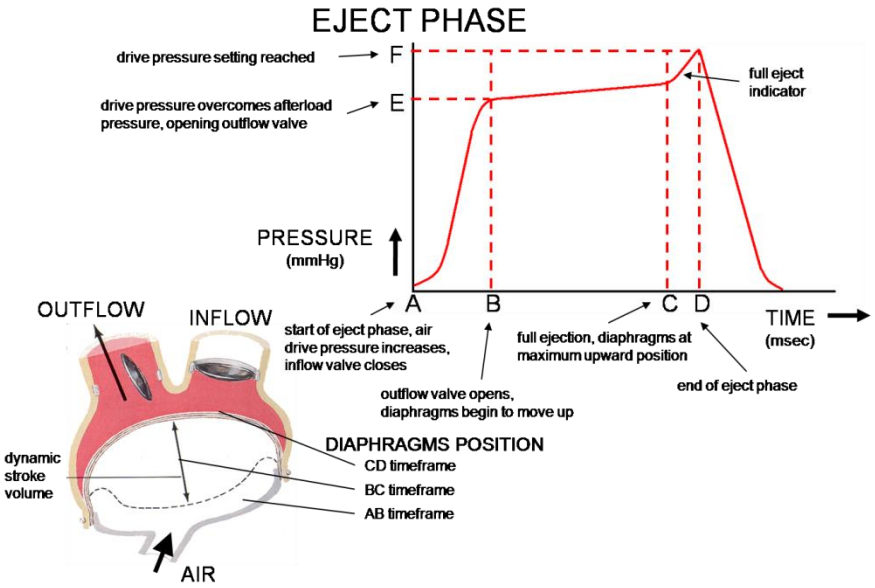

Figure 1-4 – Typical Pressure Waveform for the TAH-t

The pressure waveform contains features that are indicative of the implanted TAH-t performance during systole. The initial segment of the pressure waveform (A to B) communicates a quick rise in pressure as the air side of the ventricle is pressurized until the drive pressure overcomes the afterload pressure and the outflow valve is opened.

During the period between B and C, air continues to enter the air chamber of the ventricle as the diaphragm moves to eject blood, resulting in a sharply reduced rate of pressurization when compared to the front edge.

When the diaphragm is unable to move further, the pressure increases as air continues to enter the isovolumetric air chamber of the ventricle, resulting in a display of a "full eject" flag, indicated by the region from C to D. The Driver then begins diastole, pressure in the air chamber is vented, and the waveform moves towards the starting pressure line on the X-axis.

Reduction of the systolic drive pressure results in reduced cardiac output and increased venous pressures, as the pressure produced by the driver does not exceed the afterload pressure of the patient. Full ejection increases organ perfusion and diminishes blood stasis. Full ejection of the left ventricle is generally achieved by providing a drive pressure that is 30 – 40 mmHg higher than the aortic pressure.

The “partial fill” portion of the operating concept is derived from the Frank-Starling mechanism, which states that the heart has the intrinsic capability of increasing its force of contraction, and therefore its stroke volume, in response to an increase in venous return. The Frank-Starling principle is based on the length-tension relationship within the ventricle. If ventricular end diastolic volume (preload) is increased, it follows that ventricular fiber length is also increased, resulting in an increased ‘tension’ of the muscle. In this way, cardiac output is directly related to venous return, the most important determining factor of preload.

When the heart rate is constant, cardiac output is directly related to preload, up to a certain point. An increase in preload will increase the cardiac output until very high end diastolic volumes are reached. At this point cardiac output will not increase with any further increase in preload, and may even decrease after a certain preload is reached.

In the TAH-t, the Frank-Starling mechanism is implemented by balancing three other parameters: heart rate, percent systole, and vacuum. By reserving a space within the ventricle that is not used when the patient is at rest, the venous return may increase, which results in a higher stroke volume. As long as volume overload is avoided, the TAH-t can behave along a Frank-Starling curve with venous return translated into increased cardiac output.

The fill volumes are established using the flow waveform generated during diastole, as depicted in **Figure 1-5**. The flow curves for the 50cc TAH-t and 70cc TAH-t have the same waveform. The initial part of the curve, (A to B) is characterized by a rapid movement of air as the pressure in the air chamber of the TAH-t is relieved and the outflow valve closes. The inflow valve of the ventricle opens at point B and blood enters the blood chamber of the ventricle, while air is exhausted from the ventricle through the driveline.

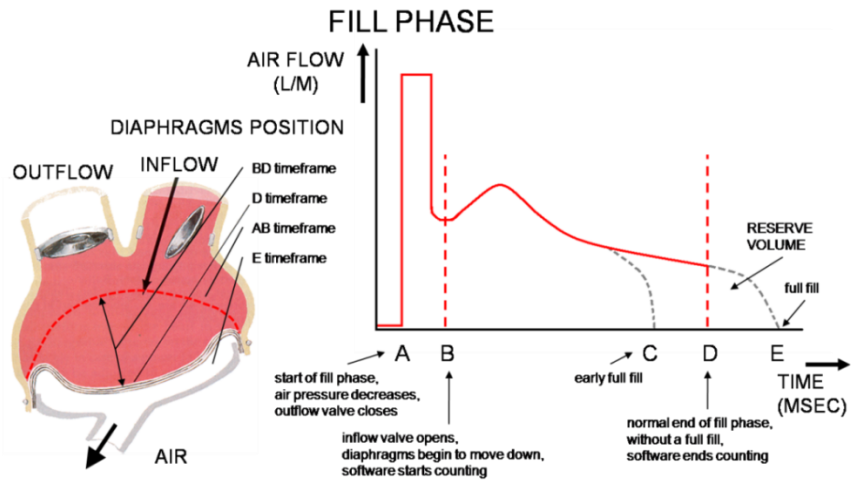

Figure 1-5 – Typical Flow Waveform for the TAH-t

The duration of the period indicated from B to C, D or E, prior to initiation of systole, is indicative of whether the device is partial or full filling the ventricle. It is this region that is measured to determine the fill volume of the ventricle. Integrating the area under the flow curve once the inflow valve has opened provides the stroke volume of the ventricle, provided that full ejection has occurred. The fill volume multiplied by the heart rate provides the device cardiac output.

Full filling of the ventricle is represented by an abrupt mid-diastolic drop of flow rate to zero, as indicated by point C. Increasing the heart rate will increase the cardiac output, but will also decrease the blood fill volume by decreasing the amount of time allowed for filling the ventricle. Adjustment of the percent systole control will vary the time of the cardiac cycle that the device remains in systole. Modification of the percent systole can be used to optimize the filling time of the ventricle. The vacuum control provides another means to control ventricular filling such that increasing the negative diastolic pressure will result in increased ventricular filling.

1.4 The Companion 2 Driver System

The Companion 2 Driver System operates and monitors the TAH-t throughout the implantation, surgical recovery phase in the ICU and step-down units and also the ambulatory phases of patient support. The Companion 2 Driver System includes a Driver, a Hospital Cart, a Caddy and an optional Hand Pump.

- The Companion 2 Driver powers the TAH-t pneumatically and docks into the Hospital Cart or Caddy. The TAH-t is monitored non-invasively by the Driver so there are no electrical connections to the patient.

- The Hospital Cart is a large cart with wheels, into which the Companion 2 Driver docks. It is intended for use in the hospital during the TAH-t implant procedure and subsequent surgical recovery phase.
- The Driver Caddy is a small cart with wheels, into which the Companion 2 Driver docks. It is designed to facilitate mobility of ambulatory patients within the hospital.
- The optional Hand Pump is a manually-operated driver that is intended to provide pulses of pneumatic pressure through the right and left Drivelines. The Hand Pump is designed for emergency use when a backup Driver is not immediately available. See the SynCardia Hand Pump Operator Manual for additional details.

See the *SynCardia Companion 2 Driver System Operator Manual* for detailed information on the Companion 2 Driver System.

1.5 The Freedom Driver System

The Freedom® Driver System is a portable multi-component electro-mechanical unit designed to provide pneumatic power to the implanted SynCardia TAH-t to support clinically stable TAH-t patients in and out of the hospital. Clinically stable patients implanted with the TAH-t can be transferred from the Companion 2 Driver to the Freedom Driver.

See the *SynCardia Freedom Driver System Operator Manual* for detailed information on the Freedom Driver System.

Chapter 2. Indications for Use

2.1 The SynCardia temporary Total Artificial Heart (TAH-t) is indicated for use as a bridge to transplantation in cardiac transplant-eligible candidates at risk of imminent death from biventricular failure.

2.2 Companion 2 Driver System Intended Use

The Companion 2 Driver System, used with the TAH-t, is intended for use inside the hospital and on the hospital grounds.

Chapter 3. Contraindications

3.1. The TAH-t System is contraindicated for use in:

- Patients who are not transplant-eligible and for whom clinical indices indicate a remote likelihood of becoming eligible for a transplant.
- Patients who cannot be adequately anticoagulated on the TAH-t.

3.2. The 70cc TAH-t System is contraindicated for use in:

- Patients who do not have sufficient space in the chest area vacated by the natural ventricles [generally, patients who have a distance between the sternum and the 10th anterior vertebral body measured by computed tomography imaging (CT scan) < 10 cm may not be able to accommodate the device].

3.3. The 50cc TAH-t is contraindicated for use in:

- Patients who do not have sufficient space in the chest area vacated by the natural ventricles.
- Patients who have a body surface area (BSA) of > 1.85 m^2.
- Patients who cannot be adequately anticoagulated on the 50cc TAH-t.

Chapter 4. Warnings

4.1 Setup and operation of the TAH-t System should only be performed by personnel trained and certified in accordance with the SynCardia training program. A thorough understanding of the technical principles, clinical applications, and risks associated with the device is necessary. Prior to use, refer to the *SynCardia Companion 2 Driver System Operator Manual*.

4.2 Sterile components of the TAH-t are intended for single use only. Do not use if the package is opened or damaged. Do not re-sterilize or reuse.

4.3 Safe use of the TAH-t System has not been established in pregnant patients.

4.4 Do not subject patients implanted with the TAH-t to magnetic resonance imaging (MRI) scans.

4.5 Do not use the TAH-t System if the implantable artificial ventricles cannot fit in the chest area vacated by the natural ventricles. Compression of the inferior vena cava and left pulmonary vein are possible consequences.

4.6 Do not allow any catheter to get near the inflow valves of the TAH-t. If a catheter migrates into an inflow valve, the valve could become stuck, limiting flow. Confirm the position of the catheter by x-ray after catheter insertion and repeat an x-ray immediately if any unexplained sudden drop in cardiac output occurs. A percutaneously inserted central catheter may migrate into the inflow valve when the patient raises his or her arm.

4.7 There is a potential for air embolism. De-air the artificial ventricles to minimize the possibility of air inadvertently entering the device.

4.8 Do not allow the external drivelines to become kinked. If there is any low cardiac output alarm, inspect the external drivelines for kinking.

4.9 A reduction in the maximum stroke volume with full eject on the external driver monitoring computer to below 50 milliliters for the 70cc TAH-t and 30 milliliters for the 50cc TAH-t may indicate a failure of one of the diaphragms in a ventricle.

4.10 Do not administer CPR to TAH-t patients. Defibrillation, cardioversion, and CPR are ineffective on patients implanted with the TAH-t.

Chapter 5. Precautions

5.1 Surgical, nursing, and perfusion staff responsible for the SynCardia TAH-t program at each hospital must complete the SynCardia TAH-t Training program.

5.2 The SynCardia TAH-t and Drivelines are provided sterile; caution must be taken in opening the package. Do NOT resterilize. Do NOT use if package is damaged. Storage temperature for the drivelines is 10 - 50°C.

5.3 Measures should be taken to prevent infection or sepsis. Use strict aseptic techniques during implantation.

5.4 The outflow grafts must be pre-clotted before use.

5.5 Do not use an antifibrinolitic agent like Amicar with an active clotting agent like FEIBA.

5.6 Each Companion 2 Driver contains two independent compressor subassemblies, each capable of providing independent support for operation of the TAH-t. Hospitals and patients supported with the Companion 2 Driver must have an additional Companion 2 Driver available as a backup to be used in the event of a failure of the primary Companion 2 Driver.

Personnel should be trained how to exchange the primary Companion 2 Driver with a backup Companion 2 Driver in the event of system failure. The backup Companion 2 Driver should be connected as quickly as possible. See the *SynCardia Companion 2 Driver System Operator Manual*, *Switching from Primary Companion 2 Driver to Backup Companion 2 Driver*.

5.7 The TAH-t System contains ferro-magnetic metal components. Do NOT perform MRI imaging procedures on patients implanted with the TAH-t.

5.8 Manage the exit site in accordance with hospital procedures.

5.9 Use only water-soluble antiseptic cleaners around the exit site. Ointments may delay tissue in-growth around the cannulae.

5.10 The Cannulae and Drivelines must be inspected daily to make sure they are intact and have no holes. If a hole is detected in the Cannulae or Driveline the hospital should apply a self-fusing silicone tape to seal the hole. The hospital must contact SynCardia for possible further instructions.

5.11 Monitor cardiac output when closing the chest. A reduction in TAH-t output while closing the chest may indicate inflow obstruction. Reposition the TAH-t ventricles by anchoring to a rib or moving it into the left pleural space.

5.12 A sudden reduction in TAH-t flow may be caused by a kink in the pneumatic drivelines (check for and correct), or some inflow obstruction to the TAH-t, such as tamponade (surgical intervention may be required).

5.13 Maintain proper washing of the blood contacting surfaces of the ventricles. This is typically achieved by keeping Fill Volume between 30ml to 40ml for the 50cc TAH-t and between 50ml to 60ml for the 70cc TAH-t.

5.14 The level of anticoagulation will vary depending on the patient's coagulation status. Clinical experience has shown that, typically, patients supported with the TAH-t require systemic antithrombotics similar to those used for patients with mechanical valves.

Chapter 6. Summary of Studies

6.1 70cc TAH-t with CSS Console

A multi-center (5) clinical study was conducted of the 70cc TAH-t with a large external driver, the Circulatory Support System (CSS) Console. The purpose of the study was to evaluate the device system configuration as a bridge to cardiac transplantation in transplant-eligible patients at risk of imminent death from biventricular failure.

Ninety-five patients (ages 16-67 years) were implanted with the 70cc TAH-t; 81 (70 males, 11 females) met all inclusion/exclusion criteria and were designated the core implant group. All patients were in NYHA Class IV at time of enrollment. Additional characteristics of the core implant group at the time of entry into the study are:

- 15 patients were on heart-lung machine/ECMO support,
- 51 patients had central venous pressure > 18 mmHg,
- 11 patients had right ventricular ejection fraction < 20%, and
- all patients had relative or absolute contraindications to VAD support, as evidenced by refractory arrhythmias or unresuscitatable cardiac arrest (25), hypokinetic right/left/global ventricles (23), aortic regurgitation, stenosis or prosthesis (13), massive myocardial infarction or direct myocardial injury that affects technical insertion of a VAD through the left ventricle (10), failure to wean from cardiopulmonary bypass with biventricular injury (4), left, right ventricular or mural thrombus (3) or septal defect (3).

All patients were on maximal medical therapy and at imminent risk of death before a donor heart could be obtained.

6.1.1 Trial Success

Treatment success was defined as patients who, at 30 days post-transplant, were: 1) alive; 2) NYHA Class I or II, 3) ambulatory; 4) not ventilator dependent; and 5) not on dialysis.

Trial success was achieved in 56 (69%) of the 81 core patients. Sixty-four of the 81 core patients (79%) reached transplant after a mean time of 79 days (range 1-414). Fifty-eight (72%) survived to 30 days post-transplant.

6.1.2 Hemodynamics

The hemodynamic performance of the 70cc TAH-t was assessed through a comparison of pre- and post-implant values of cardiac index, systolic arterial blood pressure, and central venous pressure. Hemodynamic indices were effectively restored to near normal values. Average cardiac index increased from 1.9 to 3.0 L/min/m^2, average systolic blood pressure increased from 93mmHg to

120mmHg, and average Central Venous Pressure (CVP) decreased from 20mmHg to 14mmHg.

The average perfusion pressure (mean aortic pressure minus CVP) increased from 49mmHg to 63mmHg, which was associated with recovery of renal and hepatic function.

6.1.3 Adverse Events

Adverse events collected for all 81 core patients while on the 70cc TAH-t System are presented in descending order in **Table 6-1**. The adverse events represent 17.6 device years of experience for an overall event rate of 1.9 events per month while on the device awaiting transplant.

Table 6-1
Incidence of Adverse Events in Core Patients
During 70cc TAH-t Device Implantation
in Decreasing Order of Frequency
(Represents 17.6 years or 6411 days on the device)

Adverse Event	Number of Events	Number (%) of Patients n=81
Any Adverse Event	400	76 (93.8%)
Infection	125	58 (71.6%)
Bleeding	55	34 (42.0%)
Respiratory Dysfunction	44	24 (29.6%)
Hepatic Dysfunction	30	29 (35.8%)
Neurological Event	26	20 (24.7%)
Renal Dysfunction	23	21 (25.9%)
Reoperation	18	17 (21.0%)
Device Malfunction	18	15 (18.5%)
Peripheral Thromboembolism	14	9 (11.1%)
Reduced Blood Pressure	13	12 (14.8%)
Reduced Cardiac Index	11	7 (8.6%)
Technical/Procedural	11	3 (3.7%)
Fit Complication	5	5 (6.2%)
Hemolysis	3	3 (3.7%)
Miscellaneous	3	3 (3.7%)

6.2 50cc TAH-t as a Bridge to Transplant (BTT) IDE Study

A multi-center (30) clinical study was conducted of the 50cc TAH-t as a BTT. The primary objective of the study was to evaluate whether the 50cc TAH-t could safely support transplant-eligible pediatric patients (aged 10 - 18 years) and transplant-eligible adult patients (aged 19 - 75 years) at imminent risk of death from biventricular failure without experiencing permanent disabling, stroke-related deficits.

The study was conducted as a three-arm trial of the 50cc temporary Total Artificial Heart (TAH-t) as a bridge to transplant:

- The Primary Adult Arm of the trial evaluated the safety and efficacy of the 50cc TAH-t for transplant-eligible patients 19 through 75 years of age.
- The Primary Pediatric Arm of the trial evaluated the safety and probable benefit of the 50cc TAH-t for transplant-eligible patients 10 through 18 years of age.
- The Secondary Arm captured pediatric and adult patients who did not meet enrollment criteria for a Primary Arm, but met the less restrictive Secondary Arm enrollment criteria, in order to further characterize the use of the device.

Thirty-one (31) patients were supported by the 50cc TAH-t in the United States during the study period. Thirteen (13) adults and two (2) pediatric patients met all inclusion/exclusion criteria and were enrolled in the study. The remaining 16 patients were supported by the 50cc TAH-t under compassionate or emergency use requests.

6.2.1 Trial Success

Treatment success in the primary study arms was measured at six months post-implant as either transplanted during the first six months, or continuing on support at six months on the same 50cc TAH-t, without experiencing permanent disabling stroke-related deficits.

Of the 15 enrolled patients, 10 were successfully bridged to transplant and five (5) died on device within the first 91 days on support. Of the 10 patients bridged to transplant, none had permanent disabling stroke-related deficits when measured at six months on support.

6.2.2 Hemodynamics

The hemodynamic performance of the 50cc TAH-t was assessed by calculating the mean cardiac index achieved between each study visit through the first six months of support.

The 50cc BTT enrolled patients revealed a baseline mean cardiac index of 2.2 liters per minute per meter squared ($L/min/m^2$) compared to a post-50cc TAH-t implant mean cardiac index

ranging from 3.3 to 4.0 L/min/m^2. The cardiac index on 50cc TAH-t support demonstrated an upward trend over time with the maximum mean cardiac output occurring at six months post-implant.

6.2.3 Adverse Events

Adverse events collected for the 15 enrolled patients while on the 50cc TAH-t system represent 5.8 years of experience. **Table 6–2** provides the number of events, the number of patients experiencing each event and the percentage of patients who experienced each event.

Table 6-2
Incidence of Adverse Events in Patients
During 50cc TAH-t Device Implantation
(Represents 5.8 years or 2,102 days on the device)

STS Intermacs AE Definitions	Number of Events	Number and Percentage of Subjects N=15 (%)
Arterial Non-CNS Thromboembolism	**5**	**5 (33.3%)**
Device Malfunction	**36**	**8 (53.3%)**
Major	0	0 (0.0%)
Minor	36	8 (53.3%)
Hemolysis*	**35**	**14 (93.3%)**
Major	13	9 (60.0%)
Minor	22	10 (66.7%)
Hepatic Dysfunction	**3**	**3 (20.0%)**
Hypertension	**3**	**3 (20.0%)**
Major Bleeding	**13**	**8 (53.3%)**
During the First Seven Days	1	1 (6.7%)
After First Seven Days	12	8 (53.3%)
Major Infection	**14**	**10 (66.7%)**
Localized Non-Device Infection	11	9 (60.0%)
Percutaneous Site and/or Pocket Infection	2	2 (13.3%)
Internal Pump Component, Inflow, or Outflow Tract Infection	0	0 (0.0%)
Sepsis	1	1 (6.7%)

STS Intermacs AE Definitions	Number of Events	Number and Percentage of Subjects N=15 (%)
Neurological Dysfunction	**5**	**5 (33.3%)**
TIA	1	1 (6.7%)
Ischemic Stroke	3	3 (20.0%)
Acute Symptomatic ICH	1	1 (6.7%)
Clinically Covert Ischemic Stroke or ICH	0	0 (0.0%)
Hypoxic-Ischemic Encephalopathy	0	0 (0.0%)
Acute New Encephalopathy	0	0 (0.0%)
Pericardial Fluid Collection	**4**	**4 (26.7%)**
Psychiatric Episode	**8**	**7 (46.7%)**
Renal Dysfunction	**6**	**6 (40.0%)**
Acute	6	6 (40.0%)
Chronic	0	0 (0.0%)
Respiratory Failure	**11**	**6 (40.0%)**
Venous Thromboembolism	**2**	**2 (13.3%)**
Wound Dehiscence	**0**	**0 (0.0%)**
Other	**6**	**4 (26.7%)**
Any Adverse Event	**152**	**15 (100.0%)**

*Captured as a triggered event per Rev 004 of the STS Intermacs A/E definition.

All adverse events reported through 12/20/2019.

6.3 SynCardia 50cc TAH-t Global Experience

A total of 89 implants of the 50cc temporary Total Artificial Heart (TAH-t) have occurred world-wide as of September 17, 2019. Of those 89 implants, 57 (64.0%) occurred outside the United States (US) and 32 (36.0%) occurred inside the US. Of the 32 implants that occurred in the US, 14 (43.8%) were enrolled in the 50cc TAH-t as a Bridge to Transplant (BTT) Investigational Device Exemption (IDE) Study, 14 (43.8%) were implanted under Emergency Use and four (12.5%) were implanted under Compassionate Use. The average world-wide duration of 50cc TAH-t support was 166 days with a range of 0 to 999 days.

6.3.1 Outcomes

As of September 17, 2019, thirty-seven (37) patients (41.6%) were successfully bridged to transplant. The average duration of support of the transplanted patients was 197 days and ranged from 11 to 909 days. Six of the 89 (6.7%) patients were continuing on 50cc TAH-t support with an average duration of support of 345 days and range of 77-812 days. The remaining 46 (55.4%) patients died on 50cc TAH-t support with an average duration of support of 118 days and a range of support of 0-999 days.

The two most prevalent causes of death in the 46 patients who died on 50cc TAH-t support was multiple organ system failure and sepsis, which accounted for 30 (65.2%) of the 46 deaths. Cerebrovascular accident (CVA) was reported as the cause of death in only one (2.2%) of the 46 patients.

Table 6-3 summarizes the implant outcomes and status of disabling stroke-related deficits in patients who experienced strokes, for all subjects implanted with the 50cc TAH-t world-wide as of September 17, 2019. The summary includes subjects enrolled in the SynCardia 50cc TAH-t as a BTT IDE Study, the Compassionate Use and Emergency Use patients implanted in the US and the real word experience of patients implanted outside the US. The information provided includes the region of the implant, the age at the time of implant, the gender, the implant date, the outcome date, duration of support, stroke occurrence and impact (including post-operative day of occurrence), the outcome status (alive on device, transplanted, deceased) and the primary cause of death in patients who died on 50cc TAH-t support.

6.3.2 Adverse Events

For patients supported by the 50cc TAH-t who were not enrolled under the IDE Study or supported under a Compassionate Use provision, complete adverse event data is not available. However, device malfunctions are typically captured in customer experience reports and investigated, when possible. Cerebrovascular accidents (CVAs) are known only if reported by the hospital to SynCardia.

6.3.2.1 Device Malfunction Adverse Events

A review of customer experience reports of the 89 patients revealed 84 confirmed device malfunctions which were reported in relation to patients supported by the 50cc TAH-t world-wide through September 17, 2019. Of those confirmed device malfunctions, two (2) cannulae tears were classified as major device malfunction adverse events which resulted in no reported adverse patient impact. The remaining 82

device malfunctions were classified as minor device malfunction adverse events as per STS Intermacs Registry AE Definition (Rev 004).

6.3.2.2 Cerebrovascular Accidents (CVAs)

CVAs were reported in five (5.6%) of the 89 patients who were implanted with the 50cc TAH-t world-wide. Three of the five CVAs occurred in subjects enrolled in the IDE Study, one of the five CVAs occurred in a Compassionate Use patient and one of the five CVAs occurred in a patient who was implanted outside of the US.

All three subjects enrolled in the IDE Study who experienced CVAs were successfully bridged to transplant. The mRS Stroke-Related Score in two of those three subjects showed complete resolution of the stroke-related deficits prior to transplantation. The remaining subject had an mRS Stroke-Related Score of 1 at the time of the event which was indicative of no significant disability despite symptoms and the subject was able to carry out all usual duties and activities. This subject was subsequently transplanted on post-operative day 42 and no additional mRS assessments were completed prior to transplant for comparison.

A neurology consult performed on the Compassionate Use patient who experienced a CVA on 50cc TAH-t support concluded that the patient had pre-implant thromboembolic disease based on the intracardiac thrombus and wedge-shaped encephalomalacia on a previous CT, which were suggestive of prior embolic infarct in the left parietal lobe. A repeat CT scan of the head at the time of the event identified white matter and cortical hypodensity involving the lateral occipital lobes, right side greater than left side, with focus of acute hemorrhage seen in the right occipital lobe. The extent of the stroke-related deficits was not defined because the mRS assessment was not completed. The patient subsequently had 50cc TAH-t support withdrawn on Post-Operative Day (POD) 110 because of acute respiratory failure and chronic protein-losing enteropathy. The CVA was not reported as a contributing cause of death.

The patient who was implanted outside the US who suffered a CVA died on TAH-t support on POD 122. CVA was the reported cause of death in this patient.

Table 6-3
Summary of 50cc TAH-t Patients Worldwide
as of September 17, 2019
(Represents 40.5 years or 14,793 days on the device)

Number	Region	Age	Gender	Duration of Support	Stroke Occurrence and Impact	Outcome Status	Cause of Death
1	OUS	48	M	45	None Reported	Deceased	Sepsis
2	OUS	63	M	152	None Reported	Deceased	Multi-organ failure
3	OUS	57	M	21	None Reported	Deceased	Sepsis
4	OUS	45	M	433	None Reported	Alive on Device	N/A
5	OUS	15	M	604	None Reported	Transplant	N/A
6	OUS	27	M	999	None Reported	Deceased	Multi-organ failure, Sepsis
7	OUS	46	F	8	None Reported	Deceased	Sepsis
8	OUS	22	M	135	None Reported	Transplant	N/A
9	OUS	51	F	849	None Reported	Deceased	Metastases
10	OUS	43	F	812	None Reported	Alive on Device	N/A
11	OUS	39	F	122	Disabling Stroke (POD not reported)	Deceased	CVA
12	OUS	39	M	120	None Reported	Transplant	N/A
13	OUS	57	M	56	None Reported	Deceased	Multi-organ failure
14	OUS	23	M	10	None Reported	Deceased	Unknown

Number	Region	Age	Gender	Duration of Support	Stroke Occurrence and Impact	Outcome Status	Cause of Death
15	OUS	14	M	59	None Reported	Transplant	N/A
16	OUS	72	F	56	None Reported	Deceased	Unknown
17	OUS	59	F	27	None Reported	Deceased	Multi-organ failure
18	OUS	60	M	12	None Reported	Deceased	Multi-organ failure
19	OUS	64	F	31	None Reported	Deceased	Multi-organ failure, Sepsis
20	OUS	48	F	189	None Reported	Deceased	Multi-organ failure, Sepsis
21	OUS	60	F	74	None Reported	Deceased	Septic pulmonary embolism
22	OUS	60	F	133	None Reported	Deceased	Multi-organ failure
23	OUS	62	M	388	None Reported	Deceased	Multi-organ failure, Sepsis
24	OUS	55	M	401	None Reported	Deceased	Unknown
25	OUS	56	F	13	None Reported	Deceased	Multi-organ failure
26	OUS	45	F	73	None Reported	Deceased	Sepsis
27	OUS	67	F	55	None Reported	Deceased	Multi-organ failure, Sepsis
28	OUS	63	F	375	None Reported	Transplant	N/A
29	OUS	30	F	378	None Reported	Transplant	N/A

Number	Region	Age	Gender	Duration of Support	Stroke Occurrence and Impact	Outcome Status	Cause of Death
30	OUS	51	F	8	None Reported	Deceased	Respiratory Failure (Failure to wean from VV ECMO)
31	OUS	53	M	68	None Reported	Deceased	Multi-organ failure, Sepsis
32	OUS	39	F	159	None Reported	Transplant	N/A
33	OUS	26	M	135	None Reported	Deceased	Sepsis from mediastinitis
34	OUS	58	M	14	None Reported	Deceased	Unknown
35	OUS	39	F	476	None Reported	Transplant	N/A
36	OUS	16	M	72	None Reported	Transplant	N/A
37	OUS	15	M	36	None Reported	Transplant	N/A
38	OUS	23	F	382	None Reported	Transplant	N/A
39	OUS	48	M	43	None Reported	Deceased	Unknown
40	OUS	16	F	348	None Reported	Alive on Device	N/A
41	OUS	39	M	179	None Reported	Alive on Device	N/A
42	OUS	20	F	0	None Reported	Deceased	Unknown
43	OUS	33	M	59	None Reported	Transplant	N/A
44	OUS	64	M	58	None Reported	Deceased	Multi-organ failure, Sepsis

Number	Region	Age	Gender	Duration of Support	Stroke Occurrence and Impact	Outcome Status	Cause of Death
45	OUS	26	F	88	None Reported	Transplant	N/A
46	OUS	60	M	99	None Reported	Transplant	N/A
47	OUS	48	F	15	None Reported	Deceased	Unknown
48	OUS	62	M	4	None Reported	Deceased	Mesenteric infarction
49	OUS	47	M	195	None Reported	Transplant	N/A
50	OUS	15	F	99	None Reported	Transplant	N/A
51	OUS	12	M	13	None Reported	Transplant	N/A
52	OUS	18	M	103	None Reported	Deceased	Multi-organ failure following cardiogenic shock
53	OUS	12	F	11	None Reported	Transplant	N/A
54	OUS	NR	F	14	None Reported	Deceased	Multi-organ failure
55	OUS	53	M	81	None Reported	Deceased	Sepsis
56	OUS	46	F	104	None Reported	Deceased	Unknown
57	OUS	40	M	218	None Reported	Alive on Device	N/A
58	US - IDE	45	F	38	None Reported	Deceased	Metabolic Acidosis
59	US - IDE	66	F	91	None Reported	Deceased	Support withdrawn per subject's request

Number	Region	Age	Gender	Duration of Support	Stroke Occurrence and Impact	Outcome Status	Cause of Death
60	US - IDE	65	F	21	None Reported	Transplant	N/A
61	US - IDE	23	M	68	None Reported	Transplant	N/A
62	US - IDE	26	M	3	None Reported	Deceased	Multi-organ failure
63	US - IDE	22	F	38	None Reported	Transplant	N/A
64	US - IDE	15	M	37	None Reported	Transplant	N/A
65	US - IDE	17	M	62	None Reported	Deceased	Multi-organ failure associated with extensive bleeding complications involving retroperitoneal soft tissues and GI tract
66	US - IDE	22	F	11	None Reported	Transplant	N/A
67	US - IDE	38	F	205	None Reported	Transplant	N/A
68	US - IDE	26	F	798	CVA POD 42; Resolved	Transplant	N/A
69	US - IDE	38	F	668	None Reported	Transplant	N/A
70	US - IDE	19	M	33	CVA POD 3; Resolved	Transplant	N/A
71	US - IDE	30	F	42	CVA POD 30; No significant disability	Transplant	N/A
72	US - Compassionate Use	44	F	37	None Reported	Deceased	Multi-organ failure

Number	Region	Age	Gender	Duration of Support	Stroke Occurrence and Impact	Outcome Status	Cause of Death
73	US - Compassionate Use	18	M	110	CVA POD 20*	Deceased	Acute respiratory failure and chronic protein-losing enteropathy
74	US - Compassionate Use	55	F	909	None Reported	Transplant	N/A
75	US - Compassionate Use	22	M	581	None Reported	Deceased	Multi-organ failure
76	US - Emergency Use	43	F	92	None Reported	Transplant	N/A
77	US - Emergency Use	54	F	103	None Reported	Transplant	N/A
78	US - Emergency Use	40	F	104	None Reported	Transplant	N/A
79	US - Emergency Use	35	F	77	None Reported	Alive on Device	N/A
80	US - Emergency Use	11	M	280	None Reported	Transplant	N/A
81	US - Emergency Use	41	M	206	None Reported	Transplant	N/A
82	US - Emergency Use	39	F	65	None Reported	Deceased	Sepsis preceded by bowel infarction
83	US - Emergency Use	10	M	69	None Reported	Transplant	N/A
84	US - Emergency Use	44	F	22	None Reported	Transplant	N/A
85	US - Emergency Use	53	F	42	None Reported	Deceased	N/A
86	US - Emergency Use	17	F	238	None Reported	Transplant	N/A

Number	Region	Age	Gender	Duration of Support	Stroke Occurrence and Impact	Outcome Status	Cause of Death
87	US - Emergency Use	NR	M	4	None Reported	Deceased	Multi-organ failure; Support withdrawn
88	US - Emergency Use	20	M	10	None Reported	Deceased	Multi-organ failure, Sepsis
89	US - Emergency Use	53	M	18	None Reported	Deceased	Multi-organ failure, Family withdrew care

Chapter 7. Implant Procedures

Patients are prepared for the implant pursuant to standard hospital procedures for any cardiac surgery. An arterial line, a central line, and standard artificial ventilation are required prior to the start of surgery. Transesophageal echocardiography is recommended.

The implantation of the 50cc TAH-t is the same as the 70cc TAH-t. The TAH-t is de-aired using an aortic sump.

Prepare the Companion 2 Driver prior to surgery as described in **Section 8.2, *Readying the Companion 2 Driver for Clinical Use***.

7.1 Materials Needed but not Provided

The following materials are needed for the surgery but are not provided by SynCardia. They are typically ordered and maintained by the implanting hospital.

- *Three 15 cm by 20 cm sheets of PTFE pericardial membrane material (e.g., GORE® PRECLUDE® Pericardial Membrane)* are used to create a neo-pericardium to prevent adhesions.
- *Surgical sealant* is used to coat the outflow grafts.
- Aortic sump for de-airing the ventricles.
- *Optional: Teflon felt buttress strips* are cut to approximately 10-12 mm in width and are generally 10 cm in length. It usually takes at least two of these to extend around the entire atrial cuff. (See **Section 7.3**, ***Removal of Native Ventricles***)

7.2 Preparation

7.2.1 Pass each sterile TAH-t component onto the sterile field by opening the non-sterile outer bag and dropping or passing the sterile inner bag using sterile technique.

7.2.2 Perform a standard median sternotomy.

7.2.3 Apply surgical sealant to the two arterial outflow connectors. This is done before cannulation so that there is plenty of time for the outflow connectors to dry before use.

7.2.4 Prepare the two inflow connectors for atrial anastomoses by trimming them to appropriate size for the patient's anatomy (typically a radius extending out from the connector of 5-7 mm). The surgeon may elect to invert the inflow connector prior to suturing to the native anatomy.

7.2.5 Tunnel the cannulae of the artificial ventricle through their subcutaneous pathways before heparinization of the patient.

7.2.5.1 Position the left ventricle cannula in the epigastrium at the level of the midclavicular line and approximately 2 inches below the costal margin. Make a semicircular skin flap incision on the left midclavicular line approximately 5 to 10 cm below the costal margin.

7.2.5.2 Place a long clamp through the subcutaneous tissue, rectus fascia, rectus muscle, and into the chest as a chest tube would be placed. Use a similar approach to place the cannula for the prosthetic right ventricle, approximately 4 to 5 cm medial to the left ventricle cannula so that no necrosis between the two exit sites will result.

7.2.5.3 Enlarge the pathway by opening the clamp and inserting a one-inch Penrose drain through the pathway. Place the end of the cannula in the Penrose drain and advance approximately 8-10 cm. Pull the Penrose drain through the pathway that delivers the cannula. Position the artificial ventricles laterally to the wound and cover with a towel while the rest of the procedure takes place. This provides ample opportunity for small bleeders in the cannula pathway to clot.

7.3 Removal of the Native Ventricles

7.3.1 Cannulation of the aorta and both superior and inferior vena cavae is done in a standard fashion. Umbilical tape chokers are used on the cavae. Dissection around the aorta and pulmonary artery is limited to the proximal portion of the aorta in anticipation of transplantation, thus leaving some untouched areas that will not be very fibrotic. Cardiopulmonary bypass is instituted and the heart is fibrillated. Total bypass is instituted by pulling on the choker tapes.

7.3.2 The heart is fibrillated and excision of the ventricles is begun. The excision is different from that used for transplantation. It seeks to preserve the annulus of both the tricuspid and mitral valves. Thus, an incision is made on the ventricular side of the AV groove of the right ventricle (**Figure 7-1**).

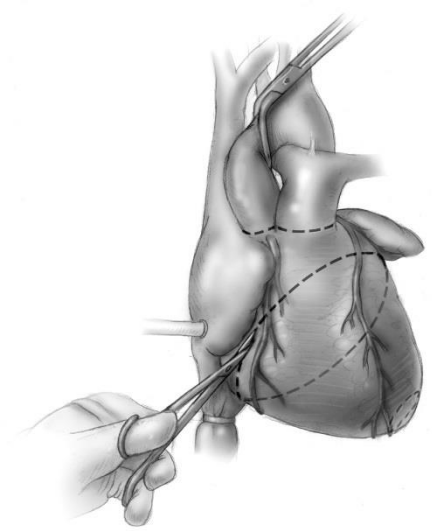

Figure 7-1 – First Incision of Ventricle Excision

7.3.3 Incision can be done with a knife and extended with a knife or scissors. It is extended anteriorly across the right ventricular outflow tract and just proximally to the pulmonary valve. Posteriorly, it is extended to the interventricular septum and across the septum, staying on the left side of the atrioventricular (AV) groove and preserving the entirety of the mitral annulus. The anterior and posterior lines of incision are dissected apart from each other out to the level of the pulmonary bifurcation.

7.3.4 Trim the excess muscle on the right and left sides down to near the AV valves. All chordae are trimmed away, and a 2 mm edge of valve tissue along with the annulus is left intact. The atrial cuff generally extends 1 cm beyond the AV valves and consists of residual ventricular muscle and fat in the AV groove. The portion of the cuff in the left ventricular outflow tract consists of the residual anterior leaflet of the mitral valve and some aortic tissue. Most of the aortic tissue is trimmed away; however, some is left intact because it may present strong tissue for the sewing of the inflow connector. The great vessels are then separated from the remaining ventricular myocardium above the valvular level. The great vessels are separated from each other (**Figure 7-2**).

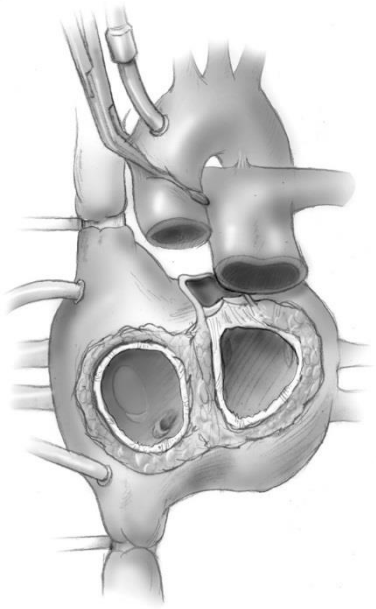

Figure 7-2 – Ventricles Removed

7.3.5 Over-sew the coronary sinus entrance into the right atrium (**Figure 7-3**). This prevents backflow of blood through the coronary sinus and out to the cut vessels on the AV groove.

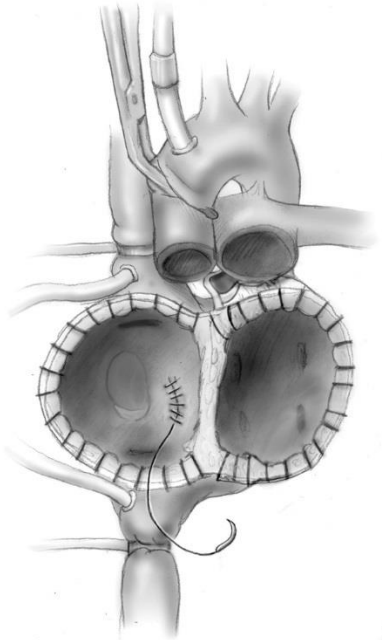

Figure 7-3 – Ligate Coronary Sinus

7.3.6 Three 15 cm by 20 cm sheets of PTFE pericardial membrane are used to create a neo-pericardium to prevent adhesions. On the right side, a sheet is anchored with non-absorbable suture to the pericardial reflection at the level of the superior vena cava, pulmonary veins and inferior vena cava. On the left side, a second sheet is sutured to the pericardial reflection just anterior to the left pulmonary veins. On the diaphragmatic side, a third sheet is sutured so as to cover the entire diaphragmatic pericardial surface. The three sheets are then folded upon themselves to keep them out of the operative field while the TAH-t is implanted.

7.4 Preparing the Atria

7.4.1 The surgeon may elect to encircle the outer walls of the atrial cuff complex with Teflon felt buttresses to strengthen the anastomosis to the inflow connector and also to tamponade and control all possible bleeding from the AV groove portion of the connectors. The felt is cut to approximately 10-12 mm wide by 10 cm long and can be sewn in place with a running 3-0 polypropylene with an MH needle.

7.4.2 The atrial inflow connector is sewn first. It may be inverted if desired and is placed inside the left atrial cuff on the lateral wall. 3-0 polypropylene is used with an MH needle with a running stitch, taking care to tailor the atrial cuff and the inflow connector into a single hemostatic suture line, including both free walls of the atrium. A similar procedure is done with the right inflow connector. After completing both suture lines, return inverted inflow connectors to their normal positions (**Figure 7-4**).

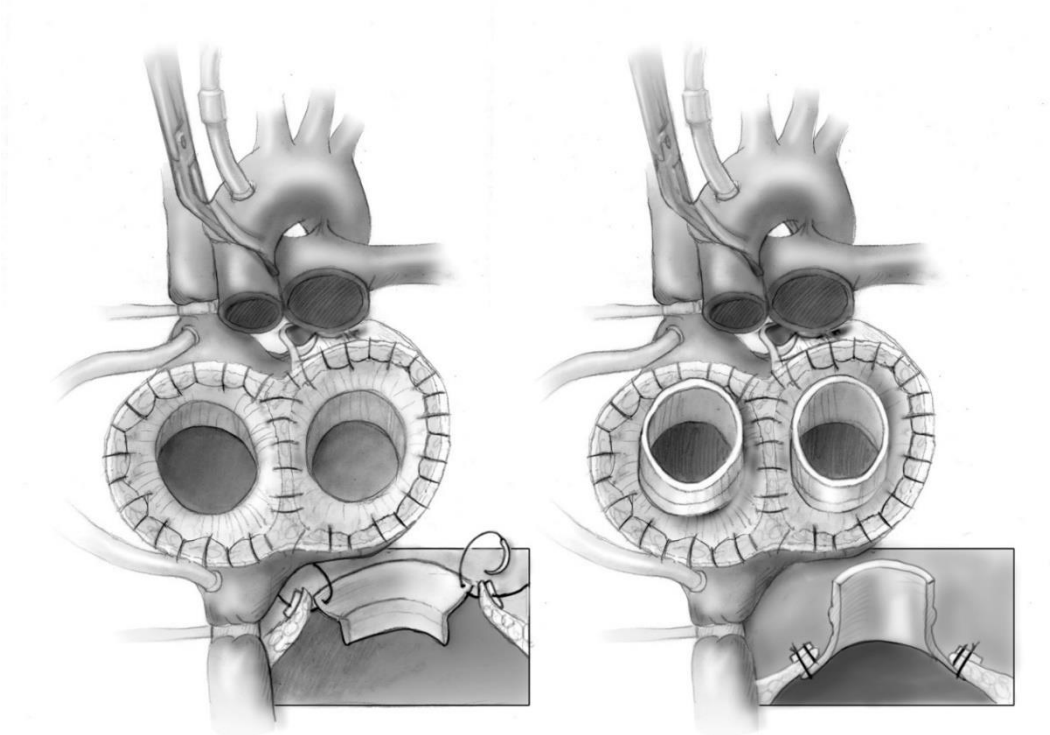

Figure 7-4 – Inflow Connector Inverted for Suturing (left), and Finished Normal Position (right)

7.4.3 Check for hemostasis with the plastic leak tester made to fit within the inflow connector (**Figure 7-5**). A syringe (60-100 cc) is used to inject saline into a three-way stopcock connected with the tester to test the left atrial suture line. The surgeon places his hand posterior to the left atrium and compresses the right and left pulmonary veins, while the assistant injects saline mixed with a small amount of blood into the left atrium. An alternative test medium is methylene blue. Observe for leaks. A dental tool (freer elevator or tonsil elevator) is used to break the seal between the tester and connector. If there are any leaks, sutures are placed at this time. On the right side, fluid is simply injected into the right atrium under pressure, since the inferior and superior venae cavae are already obstructed by the caval tapes. Again, closure of leaks with a 3-0 MH polypropylene suture is done at this time.

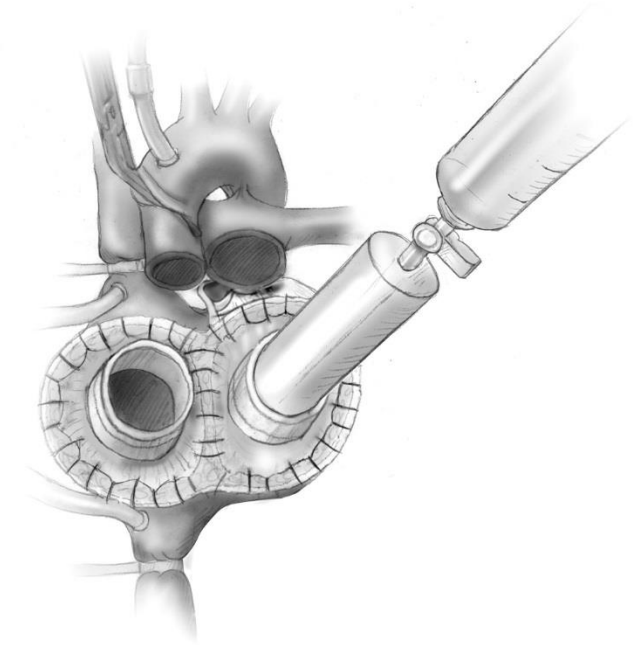

Figure 7-5 – Checking Inflow Connector for Hemostasis

7.5 Outflow Connectors

7.5.1 Great vessel connections are made. The pulmonary artery anastomosis is made first. The lengths of the outflow connectors are determined by placing the artificial ventricles in position within the pericardial cavity. Place the outflow connector between the aortic or pulmonic valve and its respective great vessel and measure the distance. Cut outflow connectors to the appropriate lengths, usually 3 to 5 cm.

7.5.2 The pulmonary artery anastomosis is made in an end-to-end fashion, beginning with the lateral wall and running the back wall of the anastomosis from the inside (**Figure 7-6**).

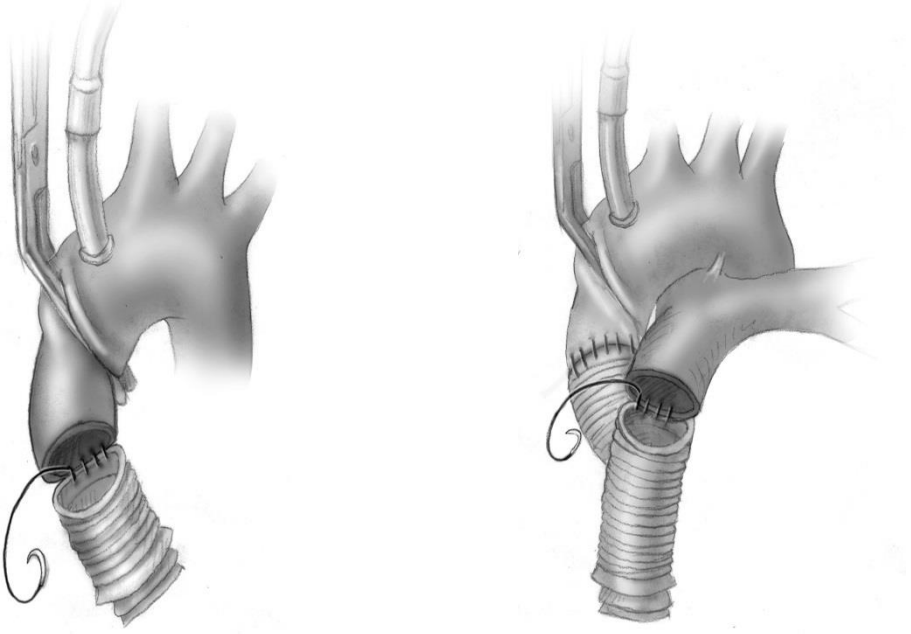

Figure 7-6 – Aorta (left) and Pulmonary Artery (right) Outflow Connector Suturing

7.5.3 A similar anastomosis is made with the aortic suture line (**Figure 7-7**). Then, the outflow connector leak tester is inserted into the aortic outflow connector. Saline is injected under pressure, observed for leaks, and then any leaks are closed. The pulmonary artery needs to be cross-clamped in order to test the integrity of the pulmonary artery-to-connector anastomosis. The pulmonary artery/aortic tester is the same, but smaller, than the one utilized for the atrial inflow connector (**Figure 7-7**).

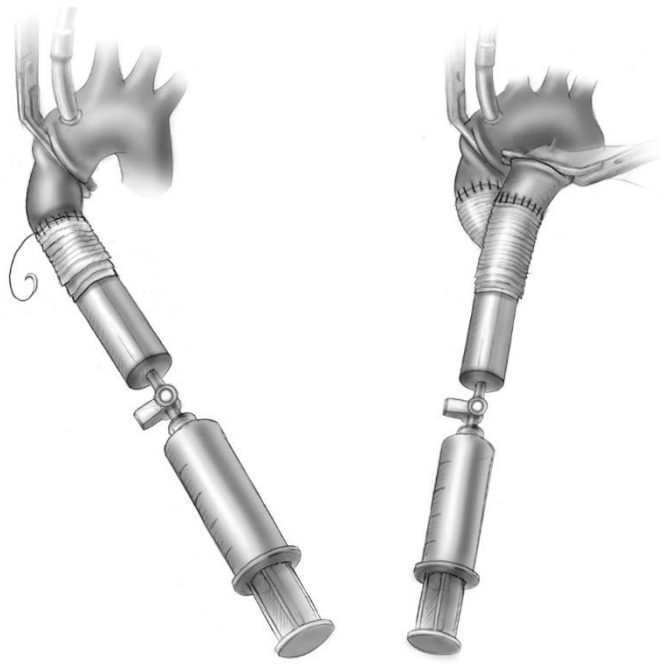

Figure 7-7 – Aorta (left) and Pulmonary Artery (right) Leak Testers

7.6 Connect Ventricles

7.6.1 Once adequate hemostasis of all suture lines is established, placement of the ventricles begins. First, the left ventricle is connected (**Figure 7-8**).

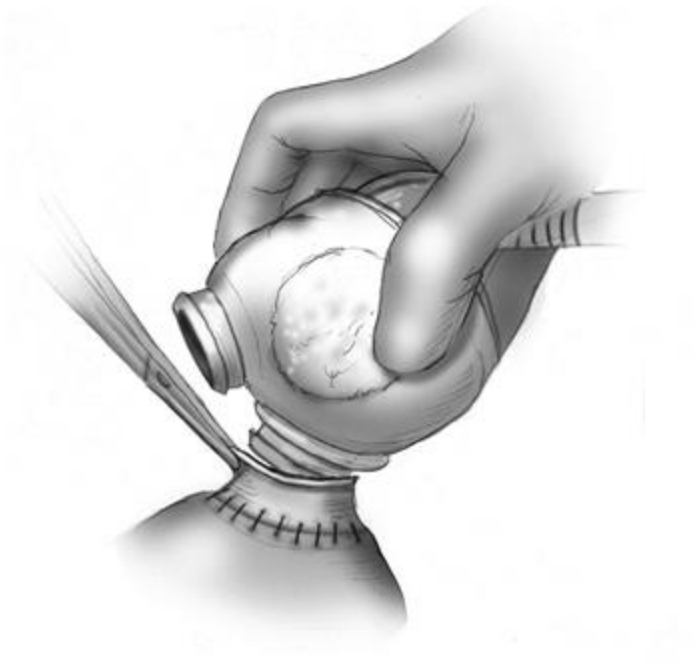

Figure 7-8 – Connect Ventricles

7.6.2 Grasp the left inflow connector with two large Mayo needle holders placed side by side, with a good hold of the connector. The opposite side of the plastic fitting for the connector of the left ventricle is placed within the connector, and the operator pulls with the Mayo clamps and pushes the left ventricle into the inflow connector. The position in which the heart sits for the duration of the support of the patient is determined by the orientation of the left ventricle as it is placed into the left atrial inflow connector. Therefore, a careful assessment of exactly where the aortic outflow connector will connect to the left ventricle and the anticipated position of the left ventricle should be made before the connection of the atrial inflow connector is completed. Snap on the aortic outflow connector, taking care not to twist the connector or aorta. While this is being done, fill the left ventricle with saline through the aortic valve as well as the outflow connector. Once the connection is made, place the patient in a steep Trendelenburg position, and place large vent sites in the highest point of the aortic outflow connector and the aorta for removal of air.

7.6.3 Connect the right ventricle. Make the atrial connection first, again taking care with the orientation of the right ventricle, so that the

direction of flow from the outlet valve is appropriate for the anatomy of the patient. After the atrial connection is made, make the pulmonary outflow connection, again, taking care not to twist. Before connecting the pulmonary outflow connector graft, remove the chokers on the superior and inferior vena cavae. This allows a flow of blood into the right atrium and the right ventricle, and flushes air out as the connection to the pulmonary artery is made (**Figure 7-9**).

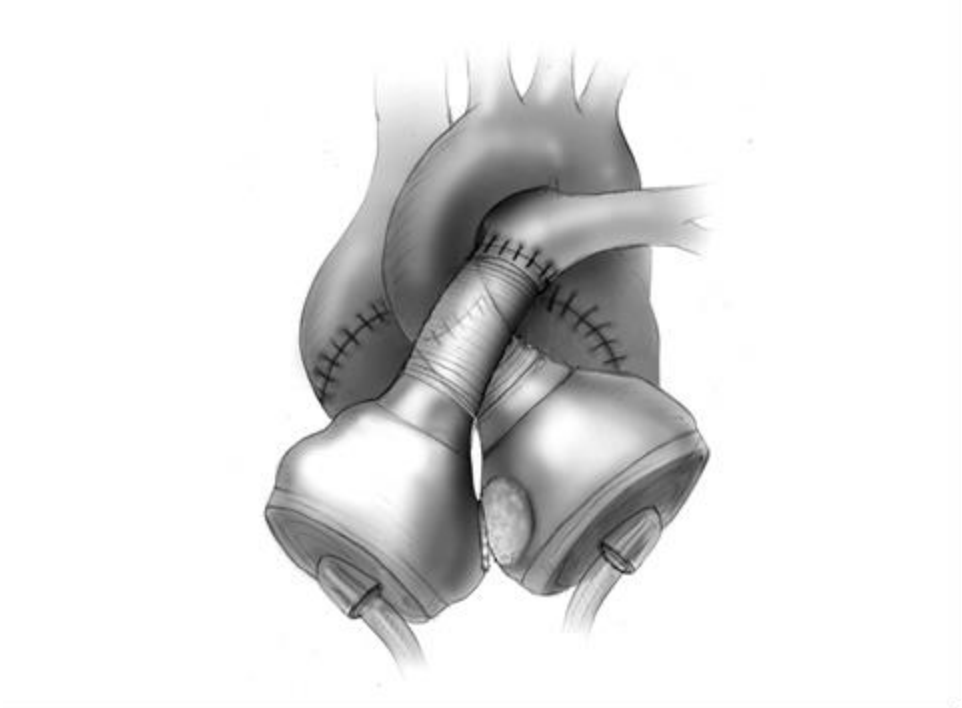

Figure 7-9 – TAH-t Final Position

7.6.4 Perform Start Up of the Companion 2 Driver System as described in **Section 8.3*, TAH-t Startup Procedure***.

7.6.5 Verify that the following parameters are programmed into the Driver:

- Rate: : "--" indicates single pulse mode
- % Systole: 50
- LDP: 180 mmHg
- RDP: 80 mmHg
- Right/Left Vacuum: 0 mmHg

7.6.6 Attach the drivelines to the Companion 2 Driver

7.6.7 Place the patient in a steep Trendelenburg position and slowly ventilate the lungs.

7.6.8 De-air the ventricles using an aortic sump.

Deliver a single pulse from the Driver at the set pressure and vacuum. (Companion 2 operator presses the “1x” button on the Driver for each pulse). Alternatively, the rate can be set to a value desired by the surgeon for the de-airing process.

Agitate the ventricles, as well as the atria, to facilitate removal of air from the system.

Complete the de-airing process by beginning to pump at a low rate. (Companion 2 operator presses the rate “+” button to go from single pulse mode to 40 bpm.) Decrease flow on the heart-lung machine temporarily to help move air through the lungs and into the TAH-t.

Use transesophageal echocardiography to help determine when the device has been completely de-aired.

7.6.9 Once satisfied that all the air is out of the TAH-t, remove the aortic cross clamp, close the vent sites and continue to increase rate as the patient is weaned off the heart-lung machine.

7.6.10 The patient should be kept in steep Trendelenburg for an additional 15-20 minutes to ensure that any remaining air in the system does not cause neurologic complications. The stroke volumes will be low until the patient is completely weaned off cardiopulmonary bypass. As the perfusionist begins to slow venous return, TAH-t filling should increase.

7.6.11 A small amount of vacuum may be applied while the chest is open. If vacuum is desired, apply up to -10mmHg vacuum on the left and then on the right. After the chest is closed vacuum may be further adjusted as needed.

7.6.12 As the table is flattened out, try to position the ventricles within the mediastinum. The pleura on both sides should not be opened and the pericardium should be left intact for closure.

7.6.13 In smaller patients, there may be a need to force the right ventricle under the left edge of the sternum. Care should be taken to examine the left pulmonary veins and the inferior vena cava for evidence of compression. This is facilitated with transesophageal echo.

7.6.14 Pass rectangular strips of PTFE pericardial membrane material (e.g., GORE® PRECLUDE® Pericardial Membrane) or sterilized polyisoprene blue band strips around the SVC, IVC, and aorta and secure loosely with non-absorbable suture or surgiclips. This provides access to surgical planes at explant.

7.6.15 Check for hemostasis. After protamine has been administered and hemostasis obtained, use towel clips to perform a trial closure of the sternum. If the fit of the device is judged to be adequate by

hemodynamic stability and by transesophageal echo examination of the caval and pulmonary venous flows, reopen the chest and bring together the edges of the PTFE pericardial membrane material (e.g., GORE® PRECLUDE® Pericardial Membrane) to form a tent or neo-pericardium. Take care to make a loose fit, without impinging upon the cavae and placing tension on the device.

7.6.16 Place one chest tube in the neo-pericardium and a second in the native pericardial space. Irrigate with antibiotic solution before closure. Close the sternum and remaining incision in a routine fashion. Check device output, central venous pressure, and device filling when the chest is closed, because chest closure may alter the anatomy, causing pressure on the left pulmonary veins, inferior vena cava, and occasionally the right pulmonary veins. If decreased flow is noted, reopen the chest and make changes in the position of the device. One possible change is to mobilize the diaphragmatic attachment of the pericardium, allowing the device to sit more leftward in the chest. This requires opening the left pleura, allowing the TAH-t to slightly migrate into the left pleural space. If decreased flow is still observed, the right ventricle may need to be anchored to a rib, using umbilical tape (**Figure 7-10**).

7.6.17 A SynCardia Heart Tracking Implant Form is included with each TAH-t Implant Kit. Complete the information on all pages of the form for each patient and return to SynCardia as instructed on the form.

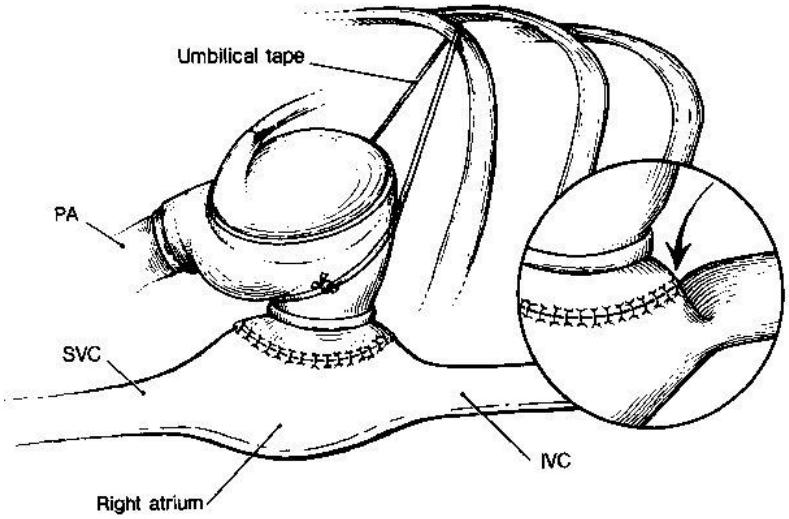

Figure 7-10 – Solution to a Fit Problem

Chapter 8. Companion 2 Driver System

The *SynCardia Companion 2 Driver System Operator Manual* contains detailed information on the setup and operation of the Companion 2 Driver System. It contains the following sections:

- Device Description
- Indications for Use
- Contraindications
- Warnings
- Precautions
- Companion 2 Driver
- Hospital Cart
- Driver Caddy
- Operating Modes – Surgical (O.R.) Environment
- Operating Modes – I.C.U. Environment
- Operating Modes – Ambulatory Mode
- List of Symbols
- Companion 2 Driver Operating Cautions
- Power Management
- Alarms and Notification
- Switching to Backup Companion 2 Driver
- Switching from Companion 2 Driver System to the Freedom Driver System
- Equipment Maintenance and Care
- Unpacking and System Setup
- Companion 2 Driver System Specifications

8.1 Companion 2 Driver Operation Dos and Don'ts

- **Do** set backup Driver parameters to the same values as the primary Driver.
- **Do** keep wheel casters locked except for transport.
- **Do** connect the A/C power cord only to grounded mains outlets with ratings that match those given on the device identification label. Only connect the mains input of these components to suitable mains outlets complying with the electrical safety regulations of the respective country of use.
- **Do** protect all components from exposure to dampness and moisture. Do not store the Companion 2 Driver System in damp rooms.
- **Do** protect all components against temperatures lower than 10°C (50°F) and above 30°C (95°F), as well as against sudden temperature changes and overheating. Avoid exposing the components to direct heat radiation.
- **Do** protect all Companion 2 Driver System components against interference from strong electromagnetic fields (as generated by mobile/cell phones, magnetic resonance tomography equipment, etc.). This also applies to the Batteries not currently connected.
- **Do** ensure that the Companion 2 Driver System always receives an adequate amount of power. **Never disconnect both Batteries from the Driver at the same time.** Recharge depleted Batteries immediately.
- **Do** use only the power cords and Batteries supplied with the Companion 2 Driver System. Do not connect the Companion 2 Driver System to multiple-outlet adapters or mains extension cables.
- **Do** make sure that the Driver is not covered by textiles, clothing or similar items.
- **Do** protect all components against dirt and contamination (IP30 rating). Prevent foreign objects from falling or working their way into the connectors and ventilation slits.
- **Do** use only Batteries that you know are in full working order. Immediately replace Batteries that are not working correctly.
- **Do** protect the components against mechanical shocks, and ensure that they are not dropped.
- **Do** keep a backup Companion 2 Driver System ready for use and near the patient at all times.

- **Do not** operate or adjust the Companion 2 Driver System without proper training.
- **Do not** use a Driver outside of its planned maintenance cycle.
- **Do not** operate a Driver having only one functional compressor for any longer than is necessary to switch to a backup Driver.
- **Do not** leave the OR with the Driver set to O.R. Mode, because audible alarms are muted, and the system may be stopped by setting the rate to zero.
- **Do not** leave the key in the key switch while the Driver is operating. Remove the key once the Driver is turned on. Store in a location determined by the clinical staff.
- **Do not** use the Driver System in areas with explosive atmospheric conditions.
- **Do not** touch or manipulate the components with pointed or sharp-edged objects (surgical instruments, wire brushes etc.). Also be careful with clothing items, such as sharp-edged belt buckles.
- **Do not** let the Driver come into contact with any chemicals other than those permitted for disinfection.
- **Do not** place other objects on the Driver.

8.2 Readying the Companion 2 Driver for Clinical Use

8.2.1 Dock the Driver without External Batteries into the Hospital Cart. If necessary, this may be done with the help of another trained user.

8.2.2 Connect the Hospital Cart to a wall AC power source.

8.2.3 Insert two External Batteries into the Driver.

8.2.4 Connect the Driver to external air. If external air is not available, the Driver will operate with its internal compressors

8.2.5 Turn the Driver to the ON position using the key, and then remove the key and store in a location determined by the clinical staff.

8.2.6 Immediately upon start-up, the Driver will perform several self-checks to verify that all the internal electronics are functioning properly. The Driver will operate at the default parameters until the software is fully loaded. It will then operate at the previously chosen settings in Ambulatory Mode.

8.2.7 Change from Ambulatory Mode to O.R. Mode using the password.

8.2.8 Perform System Check – Select MENU, SYSTEM, and SYSTEM CHECK, then follow the onscreen prompts.

8.2.9 Enter data for the new patient's profile.

8.2.10 Set the startup parameters in O.R. Mode to the following values:

- Rate: "--" indicates single pulse mode
- % Systole: 50
- LDP: 180 mmHg
- RDP: 80 mmHg
- Right/Left Vacuum: 0 mmHg
- **NOTE**: When in O.R. Mode, audible alarms are always muted.

8.2.11 Before moving the Driver (and Hospital Cart) to the Operating Room, moisten a clean cloth with an antibacterial agent and wipe down all exterior surfaces of the Hospital Cart.

8.2.12 Do not spray any cleaning agent directly on the Driver or Hospital Cart.

8.1.13 Move the Driver (and Hospital Cart) into the O.R. and plug the Hospital Cart into a wall outlet.

8.3 TAH-t Startup Procedures

8.3.1 Position the rear side of the Hospital Cart within driveline length of the patient's chest and lock the casters (wheels).

8.3.2 Verify that the Driver is in O.R. mode with the following values:

- Rate: "--" indicates single pulse mode
- % Systole: 50
- LDP: 180 mmHg
- RDP: 80 mmHg
- Right/Left Vacuum: 0 mmHg
- **NOTE**: When in O.R. Mode, audible alarms are always muted.

8.3.3 Attach drivelines to Driver.

8.3.4 When instructed by the surgeon, deliver a single pulse at the set pressure and vacuum by pressing the "1x" button to de-air the

ventricles. Continue to deliver single pulses by pressing the “1x” button as directed by the surgeon. Alternatively, the rate can be set to a value desired by the surgeon to complete the de-airing process.

8.3.5 When directed by the surgeon, press the rate “+” button to begin pumping at 40 bpm.

8.3.6 If the surgeon requests that the TAH-t be turned off, the drivelines can be disconnected from the Driver using the single connector to immediately cease TAH-t pneumatic support, or the rate “-” button can be held down to decrease the rate until single pulse mode is enabled and the TAH-t rate is zero.

8.3.7 When the surgeon is ready to wean the patient from cardiopulmonary bypass, continue to increase the rate as requested. Pressing the “+” button will increase rate by 1 BPM. Press and hold the “+” button to increase rate in 10 BPM increments.

8.3.8 Stroke volumes will be low until the patient is completely weaned from cardiopulmonary bypass. As the perfusionist begins to slow venous return, TAH-t filling should increase.

8.3.9 Pneumatic drive ejection pressures should be set to achieve full ejection. Monitor the pressure tracings to assure the right drive pressure is set to overcome the pulmonary systolic pressure, and the left drive pressure is set to overcome the aortic systolic pressure.

8.3.10 The fill volumes will be approximately 45 $\pm$ 5 milliliters for the 70cc TAH-t and 30 $\pm$ 5 milliliters for the 50cc TAH-t until volume is added and vacuum is applied.

8.3.11 A small amount of vacuum may be applied while the chest is open. If vacuum is desired, apply up to -10mmHg vacuum on the left and then on the right. After the chest is closed vacuum may be further adjusted as needed.

8.3.12 The 70cc TAH-t Rate should be set on the Hospital Cart Display to achieve a stroke volume between 50 and 60 milliliters. The 50cc TAH-t Rate should be set on the Hospital Cart Display to achieve a stroke volume between 30 and 40 milliliters. The TAH-t Rate for either size device is typically between 110 - 130 BPM.

8.3.13 Prior to moving to ICU, press MENU on the Driver, then MODE and enter ICU Mode to enable audible alarm functions of the Driver, to add additional security for changing operating parameters, and to prevent changes of rate to a single pulse mode or other non-therapeutic settings (e.g., 40 BPM).

8.3.14 When moving the patient to ICU from the OR, the Driver should be wheeled in proximity to the patient's bed while docked in the Hospital Cart or Caddy.

8.3.15 In ICU, continue to monitor Driver settings to ensure partial fill volumes and full eject and adjust as necessary.

8.3.16 When the patient is ready to be moved from ICU to the Step Down Unit, change user mode to Ambulatory Mode to prevent unauthorized changes to device settings.

Chapter 9. Explantation Procedures

9.1 Explantation of the TAH-t should be handled like any other redo cardiac procedure. Great care should be taken in the separation of the sternum from the TAH-t, the great vessel connector, and the cannulae. Explantation may be easier if the TAH-t is covered with PTFE pericardial membrane material *(e.g., GORE® PRECLUDE® Pericardial Membrane)*.

9.1.1 Initiate cardiopulmonary bypass with dual caval cannulation with tourniquets. Cross-clamp the aorta, and turn off the TAH-t System.

9.1.2 Separate the artificial ventricles from the atrial inflow cannula. Amputate the great vessels outflow connectors at the level of the connector/great vessel anastomosis. Transect the artificial ventricles at the base to the cannula connection, and remove the TAH-t from the operating field.

9.1.3 Pull the cannulae through the skin. The remaining atria inflow connectors are still in the remaining portion of ventricular muscle where they were initially sutured. Remove them by transecting the AV groove throughout.

9.1.4 Trim the remaining atria and great vessels to accept the donor heart.

9.2 All explanted TAH-t devices should be returned to SynCardia whenever possible. A Device Retrieval Kit is provided by SynCardia for this purpose.

9.2.1 Immediately upon explant, rinse both TAH-t ventricles (inside and out) gently, yet thoroughly, with physiological saline.

9.2.2 Prepare the ventricles, connectors and cannulae for shipment according to the directions accompanying the Device Retrieval Kit.

9.2.3 Contact SynCardia to obtain a return authorization and shipping label.

9.3 A SynCardia Heart Tracking Patient/Device Outcome Form is included with each TAH-t Implant Kit. Fill out all information on all pages of this form for each patient and return to SynCardia as instructed on the form.

Chapter 10. System Components

10.1 SynCardia TAH-t System with the TAH-t

The TAH-t System is comprised of the following:

- 50cc Implant Kit - Part # 570500 (Sterile) or 70cc Implant Kit - Part # 500101 (Sterile)

  Contains left artificial ventricle, right artificial ventricle, two inflow connectors, two outflow connectors, and an ancillary pack with inflow pressure test plug, outflow pressure test plug and locking ties (all sterile). Companion 2 Drivelines are not included in the Implant Kit. All sterile components are packaged in double aseptic transfer packages.

  The components in the 50cc Implant Kit are specific to the 50cc TAH-t and cannot be mixed with components from the 70cc Implant Kit.

- 50cc Surgical Spares Kit - Part # 550177 (Sterile) or 70cc Surgical Spares Kit - Part # 500177 (Sterile)

  Contains two inflow connectors, two outflow connectors, inflow pressure test plug, outflow pressure test plug, and locking ties.

  The components in the 50cc Surgical Spares Kit are specific to the 50cc TAH-t and cannot be mixed with components from the 70cc Surgical Spares Kit

- External Pneumatic Driver:

  Companion 2 Driver System – Part # 397002-001 (non-sterile).

- Device Retrieval Kit

  All explanted TAH-t devices should be returned to SynCardia whenever possible. A Device Retrieval Kit is provided by SynCardia for this purpose.

- SynCardia Heart Tracking Patient/Device Outcome Form

  The Heart Tracking Patient/Device Outcome Form is included with each TAH-t Implant Kit. Complete the information on all pages of this form for each patient and return to SynCardia as instructed on the form.

10.2 Companion 2 Driver System

The Companion 2 Driver System is comprised of the following components:

- Driver (plus one additional backup Driver) – Part # 397002-001
- 2 Batteries (plus two additional Batteries for backup Driver) - Part # 293001-001

- Hospital Cart - Part # C-400002 / Part # 397003-001
- Caddy - Part # C-400003 / Part # 397001-001
- AC Power Cord - Part # 197053-001 for US
  Part # 197053-002 for EU
  Part # 197053-003 for AUS
  Part # 197053-004 for UK
- Drivelines - Part # C-400008 / Part # 193002-001
- Optional Hand Pump – Part # 397004-001

Chapter 11. List of Symbols

Table 11-1 – Symbols Used in TAH-t Labeling

Symbol	Description
	Do not use if package is damaged
	Consult instructions for use
	Keep Dry
	Catalog Number
	Batch Code
	Use By Date
	Date of Manufacture
	Manufacturer
	Temperature Limitation
	Sterilized using ethylene oxide
	Do not resterilize

Appendix A – Patient Selection and Management

Management and coordination of successful TAH-t support requires a multidisciplinary team that has experience with circulatory support systems. Teams can include surgeons, cardiologists, heart transplant coordinators, perfusionists, engineers, nurses, cardiac rehabilitation therapists and coagulation specialists.

The following is a report of the experience of one of the clinical site users, Banner University (formally University of Arizona) Medical Center, Tucson, Arizona with the 70cc TAH-t.

Patient Selection

Based on previous experience with the 70cc TAH-t, successful bridge to transplant with the TAH-t involves selecting patients who are transplant eligible and who additionally are assessed in two main areas: 1) evaluation of fit of the TAH-t in the patient's chest, and 2) evaluation of the potential for reversal of any end organ dysfunction.

Once the TAH-t is implanted, and there are no fit issues, flow is maximized through the TAH-t.

With normalized hemodynamics, device outputs remain relatively constant, changing as the CVP fluctuates. This "Frank-Starling-like response" (where an increase in CVP fills the TAH-t with more volume, which is ejected on the next beat, increasing device output), requires no controller adjustments. Constant device output and high flow under normal CVP provides washing of the blood contacting surfaces of the artificial ventricles.

Antithrombotic Therapy

Based on previous experience with the 70cc TAH-t, the level of anticoagulation will vary depending on the patient's coagulation status. Typically, patients supported with the TAH-t require systemic antithrombotics similar to that used for patients with mechanical valves.

Driveline Exit Site Management

Take care to keep driveline exit sites clean and dry. Infections should be treated according to hospital protocol.

Appendix B – Outline of Training Program

Operation of the TAH-t System with the TAH-t should only be undertaken by personnel trained in accordance with the SynCardia Certification Program. The program will include the following topics:

(1) Indications and Contraindications

(2) System Overview

(3) Implant Procedures

(4) Operation of the Drive Systems

(5) Explant Procedures

(6) Patient Management

(7) Summary of Clinical Studies

(8) Animal Procedure – a minimum of one implant needs to be performed.

(9) Practical Experience - Physicians will be required to minimally view one live implant procedure or have their first procedure proctored. SynCardia will maintain centers of excellence where surgeons may view implantations. Proctors will be made available by SynCardia for surgical teams during their first case.

(10) Patient Management for Discharge

Appendix C – Materials Matrix

The TAH-t components are manufactured from the raw materials as defined in **Table C-1**. The artificial ventricles and cannulae have met the test requirements of ISO 10993, *Biological Evaluation of Medical Devices.*

Table C-1 - TAH-t Patient Contacting Materials Matrix

Component	***Material***
Ventricle and diaphragm	Segmented polyurethane
	Nylon
Inflow connector	Segmented polyurethane
	Polyester fabric
Outflow connector	Segmented polyurethane
	Polyester material
Valves	Titanium and pyrolytic carbon
Cannulae	Polyvinyl chloride tubing