Is an Artificial Heart a Realistic Solution for Younger Patients with Circulatory Failure?

A UK Perspective...

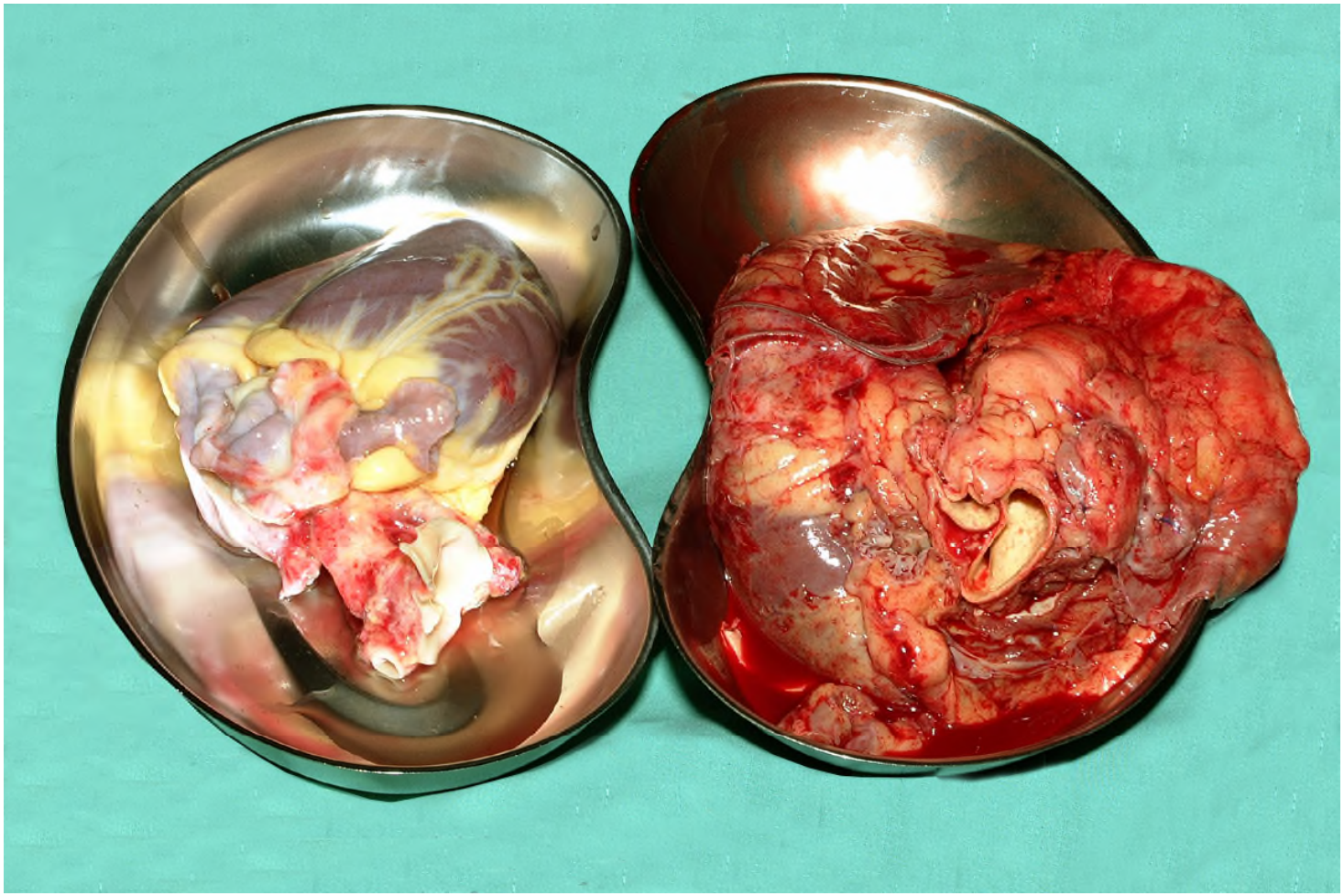
Disclosures

- Consultant:
  - Transmedics
  - ReliantHeart
  - Heartware/Medtronic

Questions:

- **Younger**: Under 60, under 50 or under 40?
- **Artificial Heart**: LVAD, RVAD, BiVAD, TAH?
- **Realistic Solution**: What is the reality out there, what are the results etc….
- **Developments**: What can we expect?

Heart Transplant



Therapeutical Concepts

HTx	
Destination Therapy	

A Brief History of Heart Transplantation

A short story…

The first Heart Transplantation

3rd centrury BC

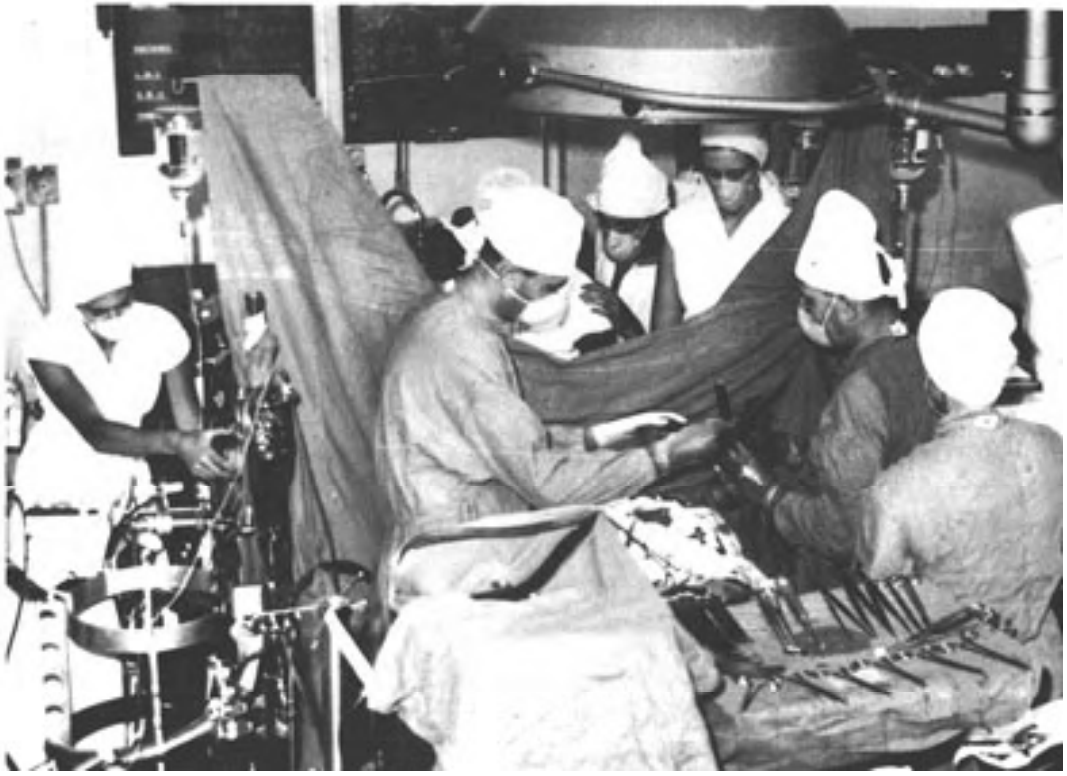
A report from 3rd centrury BC China states how the phsician and surgeon Pien Ch'iao exchanged the hearts between two soldiers (Kung He und Ch'I Ying), who suffered from "dysbalance".

He administered sedative medication, opened their chests and continued to exchange their hearts.

The patients awoke three days after surgery. They had to take strong medication, derived from mountain herbs and were discharged home healthy.

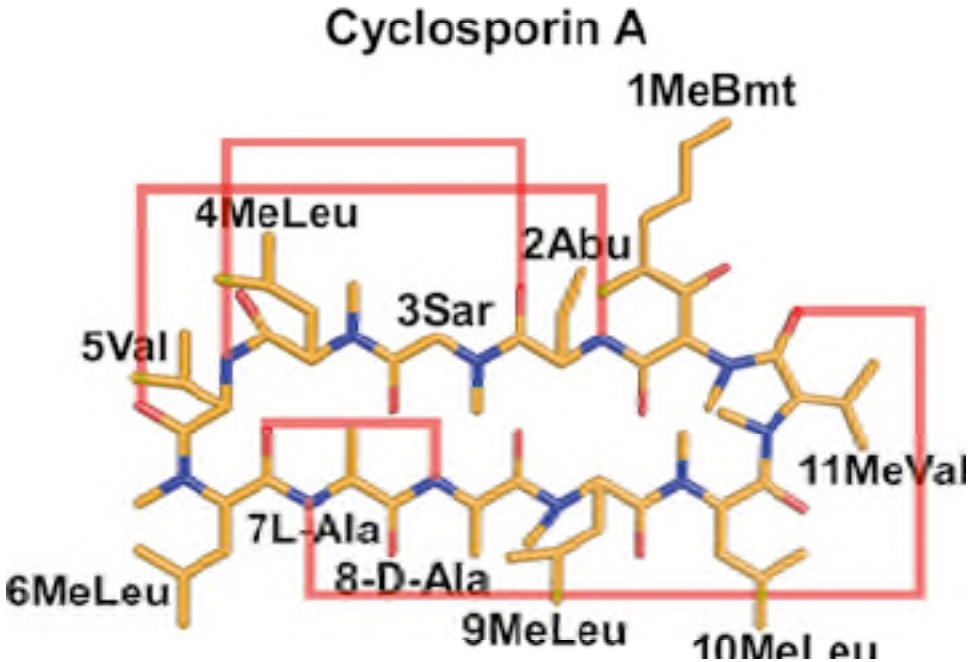
The second Heart Transplantation

1967 AD



The Discovery of Cyclosporine A

1972 AD



The End

ENGINE
TRANSPLANT
Guaranteed new sub assemblies
and cylinder heads

Results….

Heart Transplantation (US)

- Number of Patients on WL HTx: 4022
- Transplants 2016: 3191
- Increase in HTx (US) 2010-15: 37%

- % transplants of WL HTx: 79%

- Median survival: 10.7 yrs.

- Deaths on HTx WL (2016, active Pts.): 128
- % of deaths of Pts. On HTx WL (active): 3%

The Relevance….

The Impact of Heart Failure

- One in 9 deaths has HF mentioned on the death certificate (NCHS, NHLBI).[21]
- In 2013, HF any-mention mortality was 300,122 (140 126 males and 159 996 females). HF was the underlying cause in 65 120 of those deaths in 2013.[21] Table 20-1 shows the numbers of these deaths that were coded for HF as the underlying cause.
- The number of any-mention deaths attributable to HF was approximately as high in 1995 (287 000) as it was in 2013 (300 000; NCHS, NHLBI).[21]
- Survival after HF diagnosis has improved between 1979 and 2000, as shown by data from the Olmsted County Study.[22] However, the death rate remains high: ≈50% of people diagnosed with HF will die within 5 years.[22,23]

Dariush Mozaffarian et al. Circulation. 2016;133:e38-e360

The Impact of Heart Transplantation (US)

- 2013 : 300,122 deaths
- Survival rate: 50% at 5 years

- HTx: n=2614
- Survival rate 50% at 11 years

- Impact 1%

Dariush Mozaffarian et al. Circulation. 2016;133:e38-e360

The Impact of Heart Transplantation (UK)

- US population (2013): ca. 318,000,000
- UK pupuation (2013): ca. 64,000,000

- HTx (US): n=2614
- HTx (UK): n=164

- Ratio population US/UK: ca. 5/1
- Ratio HTx US/UK: ca. 16/1

- Impact: NONE

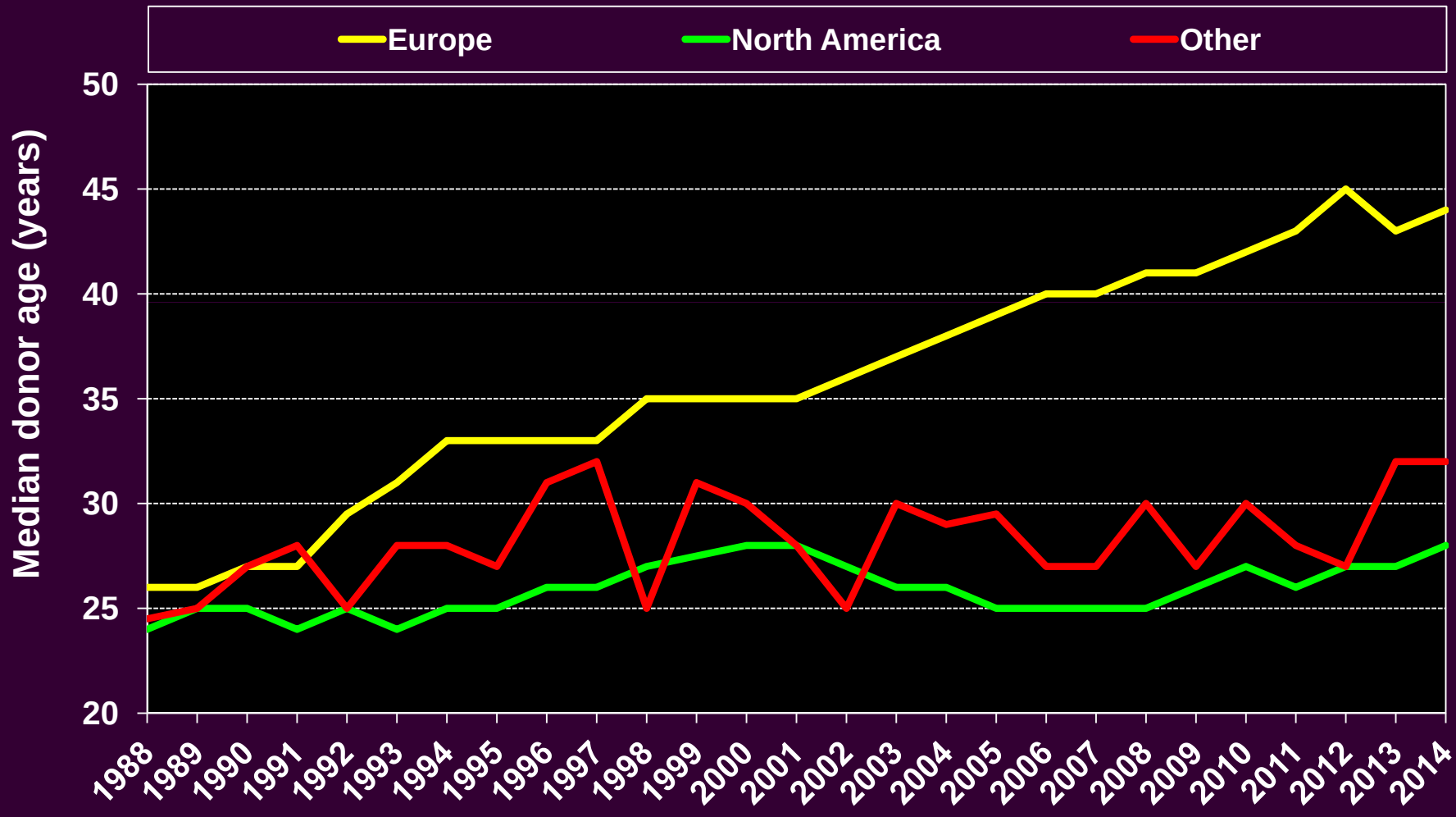
Dariush Mozaffarian et al. Circulation. 2016;133:e38-e360

Is HTx a Realistic Solution for Younger Patients with Circulatory Failure?

A closer look…

US vs. UK

Adult and Pediatric Heart Transplants
Median Donor Age by Location

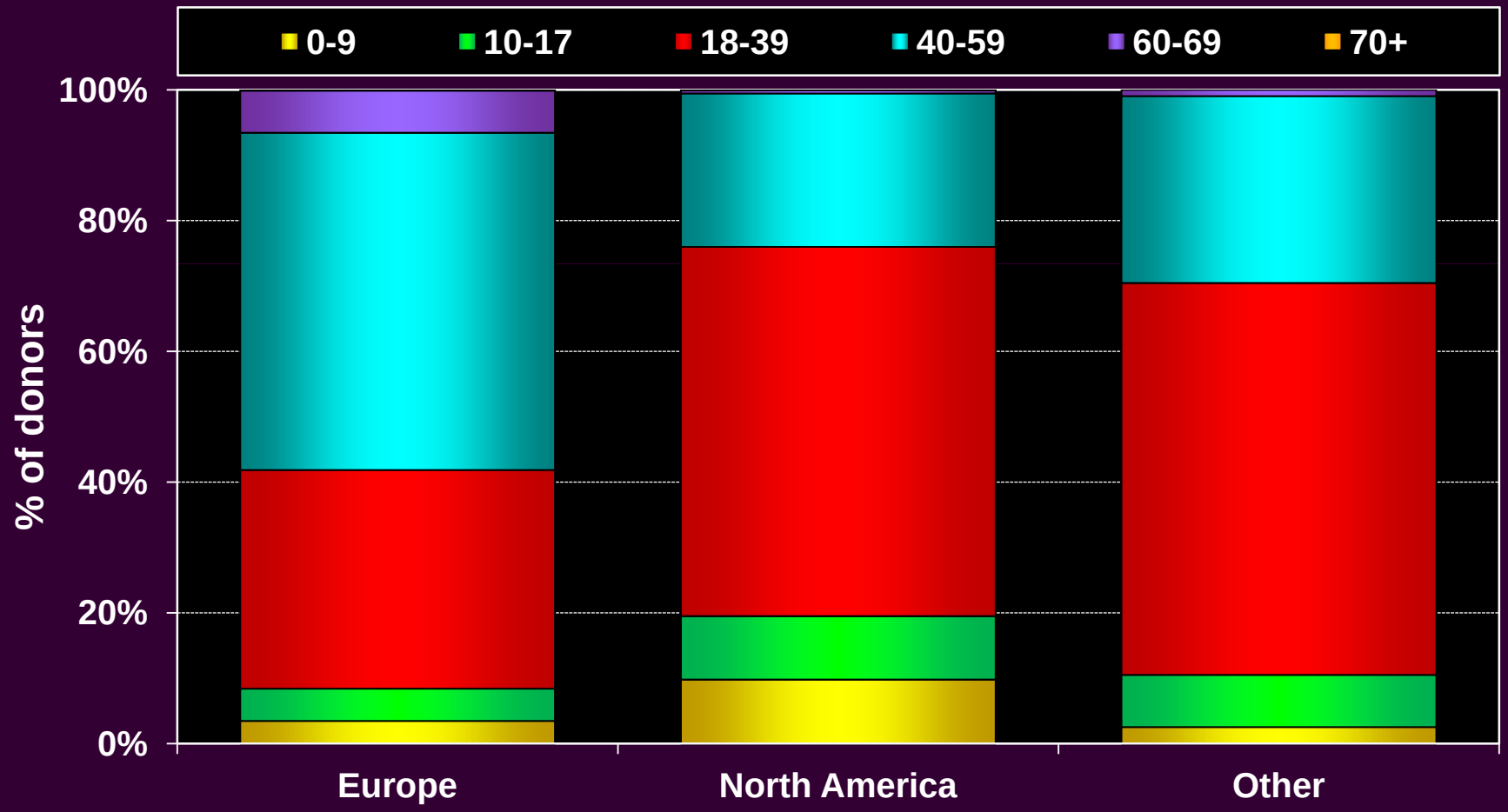


ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

2016

JHLT. 2016 Oct; 35(10): 1149-1205

Adult and Pediatric Heart Transplants
Donor Age Distribution by Location
(Transplants: January 2009 – June 2015)



ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

2016

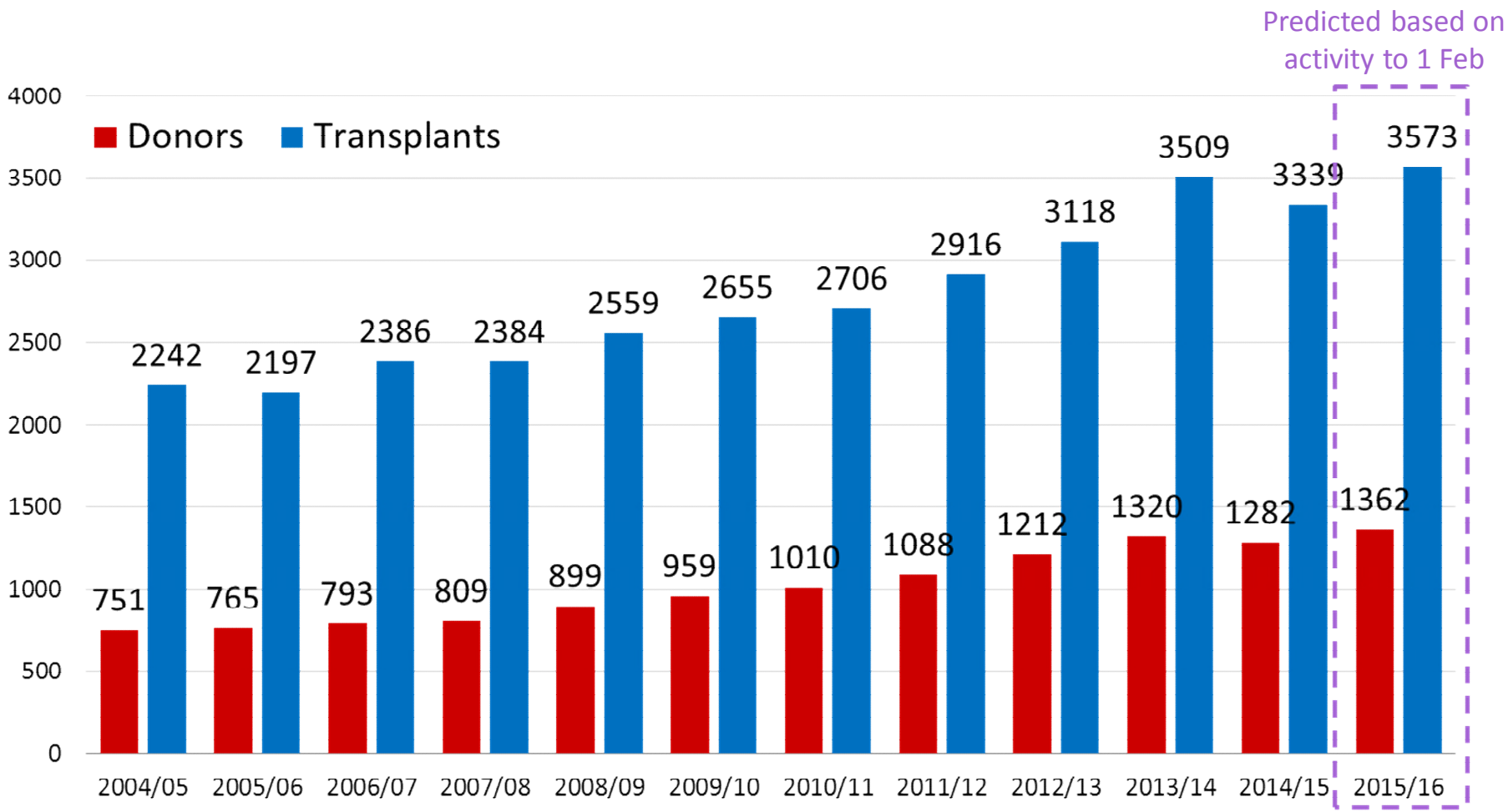
JHLT. 2016 Oct; 35(10): 1149-1205

Donor age (years): mean/median

Europe = 40/43; North America = 28/27; Other = 32/29

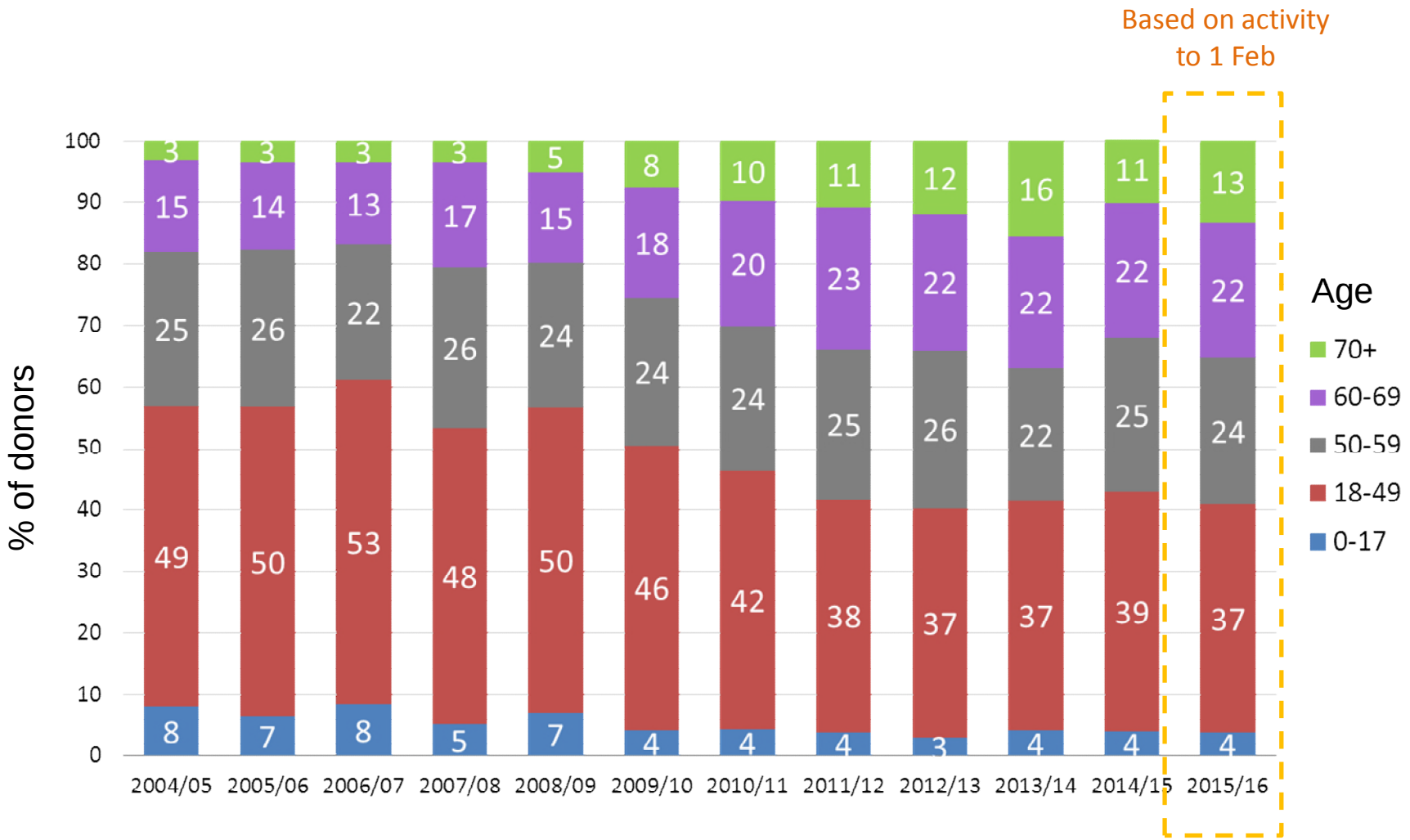
Deceased donors & transplants

NHS
Blood and Transplant



NHS
Blood and Transplant

Age of deceased donors



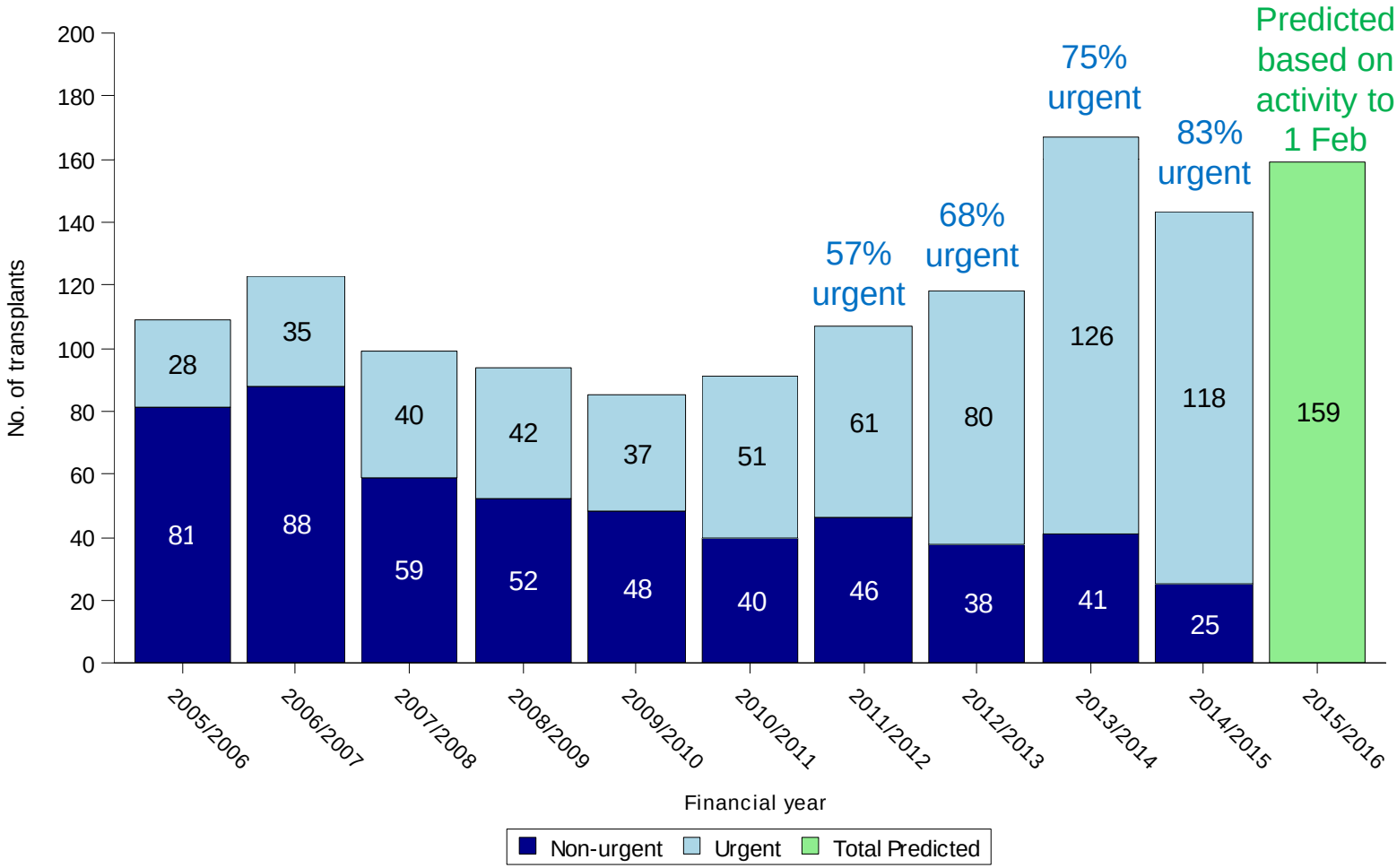
Differences in Allocation

Patient Status	Status US	Status UK
TAH	1a	Normal (=2)
ECMO/IABP	1a	Super Urgent (1a)
High dose inotrope dependent	1a (revalidation 7d)	Urgent (1b)
Mechanical Ventilation	1a (revalidation 14d)	Unlikely to be listed for long
VAD (not in hospital)	1a (30 days)	Normal (2)
Mechanical Ventilation MCS c. significant complication	1a (revalidation 14d)	Urgent (1b)
VAD	1b	Normal (2)
Inotrope infusion	1b	Normal (2) (level dependent)

NHS
Blood and Transplant

Heart Transplants

Number of adult heart transplants in the UK, 1 April 2005 to 31 March 2015, by financial year and urgency status



Heart Transplantation Developments

- Increase in HTx EU/rest 2010-15: 0%

- Increase in HTx (US) 2010-15: 37%

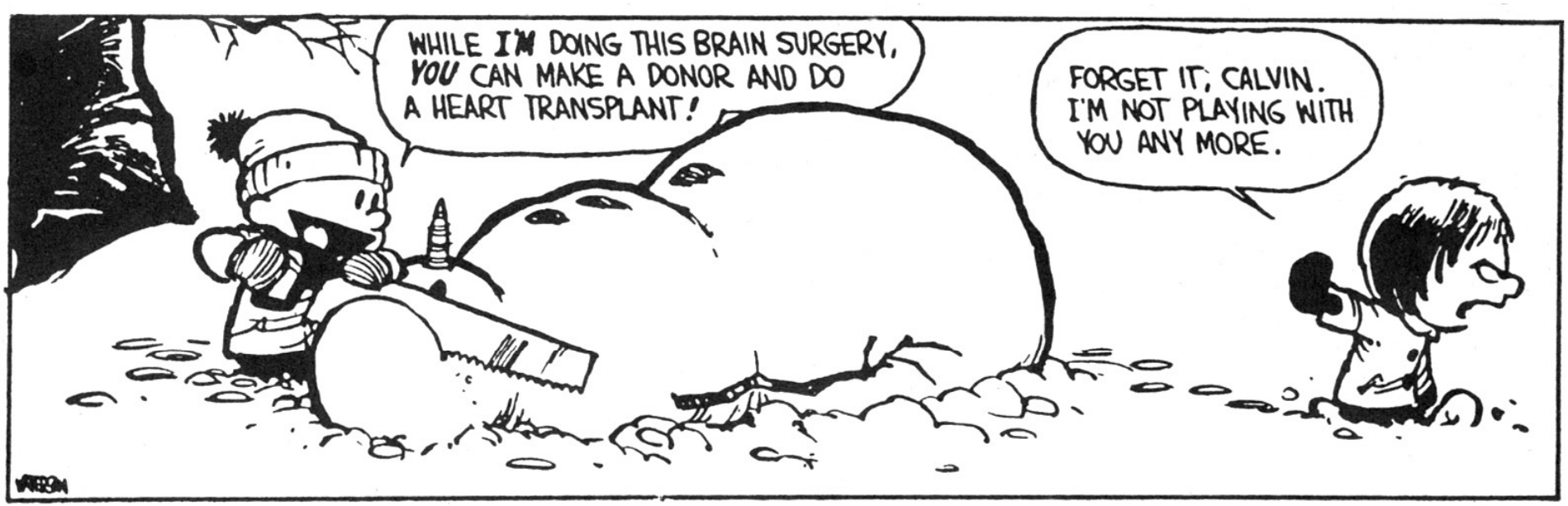
Conclusion HTx:

- On an individual level, HTx is highly successful
- On epidemiological level, HTx is irrelevant
- HTx is a very expensive orphan therapy
- In the UK, it is almost completely irrelevant

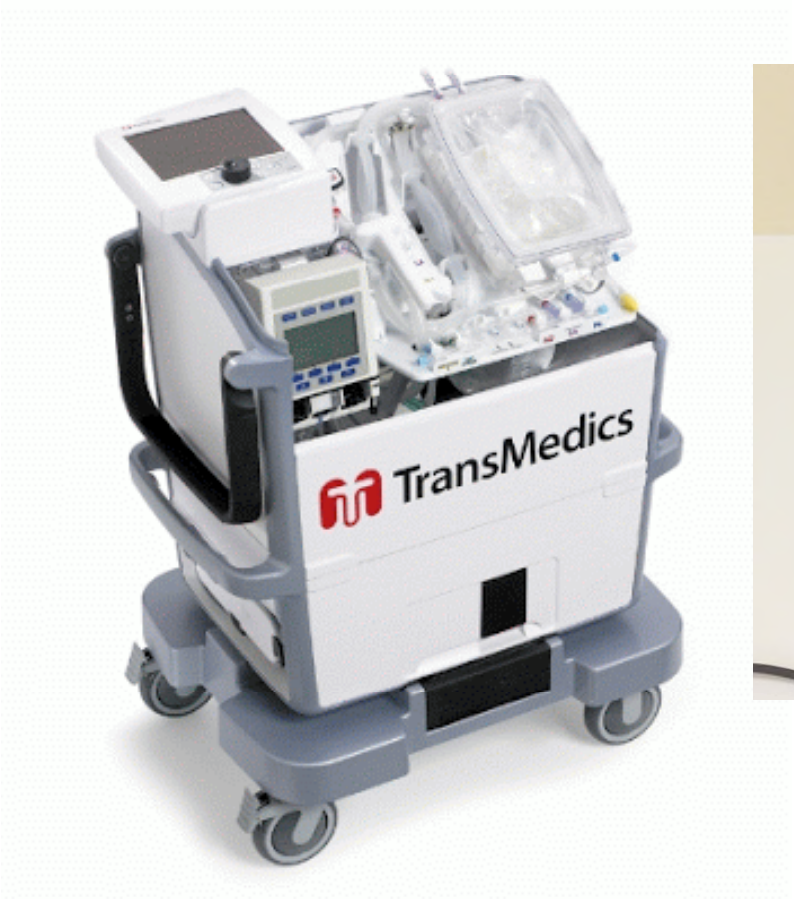
What is a Realistic Solution for Younger Patients with Circulatory Failure?

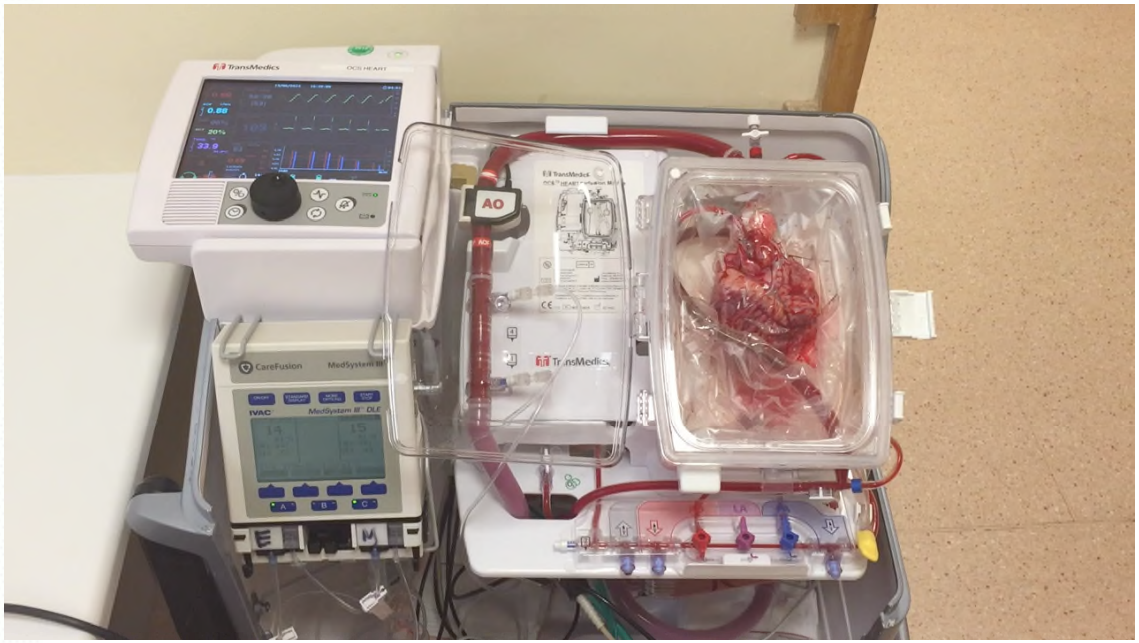
Potential Solutions

- Maximize Organ Utilization



Ex Situ Perfusion





DCD Heart Transplantation

Electrician undergoes pioneering heart transplant using an organ that had STOPPED beating and was revived before being implanted

Potential Solutions

- Maximize Organ Utilization
- Explore alternatives

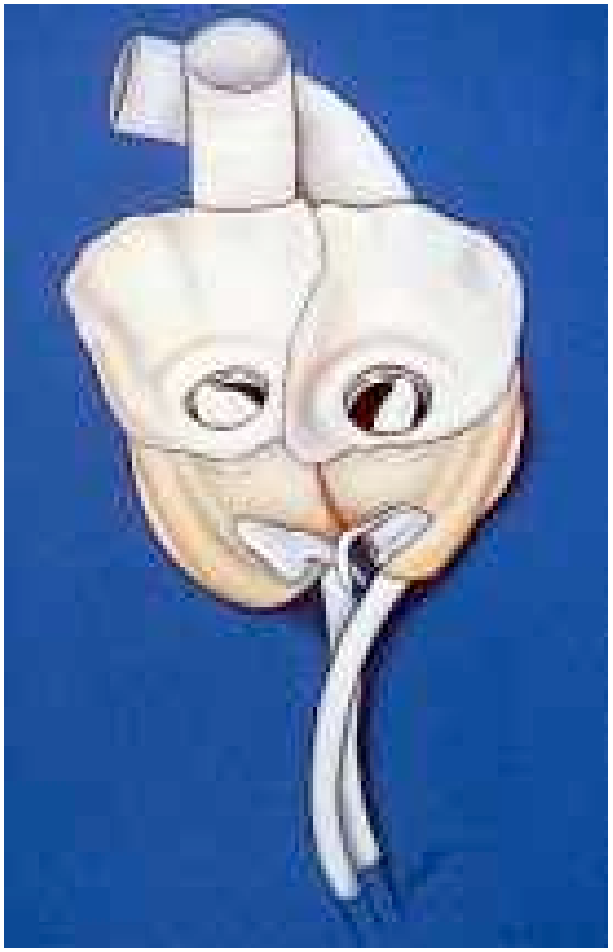
Assist Devices

A Brief History of Ventricular Assist Devices

Moore's law applied?

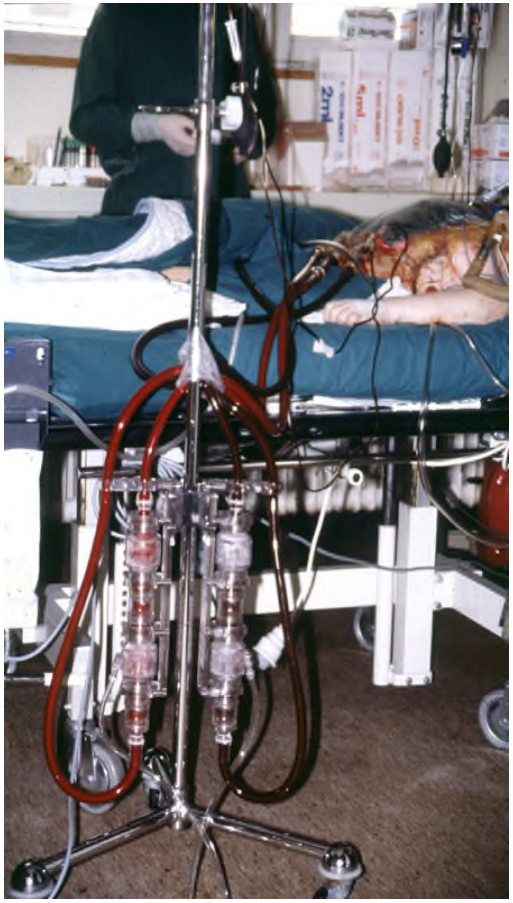
Orthotopic Cardiac Prosthesis for Two-Staged Cardiac Replacement (1969)

V24 (1969), *American Journal of Cardiology* (pp. 723-730).



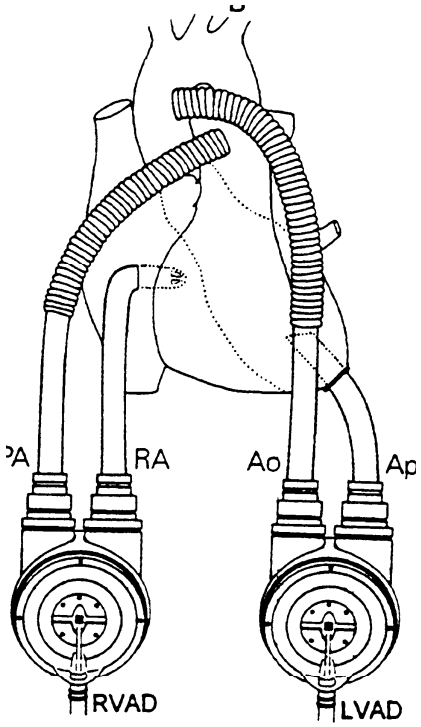
- On April 4, 1969, Dr. Denton A. Cooley performed the first total artificial heart implant in the world. The device, developed by Dr. Domingo Liotta, was implanted in a 47-year-old patient with severe heart failure. The Liotta heart supported the patient for nearly three days, at which time a donor heart was found for transplantation. This experience showed doctors that patients could be "bridged" to transplantation, meaning that mechanical circulatory support systems could be used to keep a patient alive until a donor heart is found.

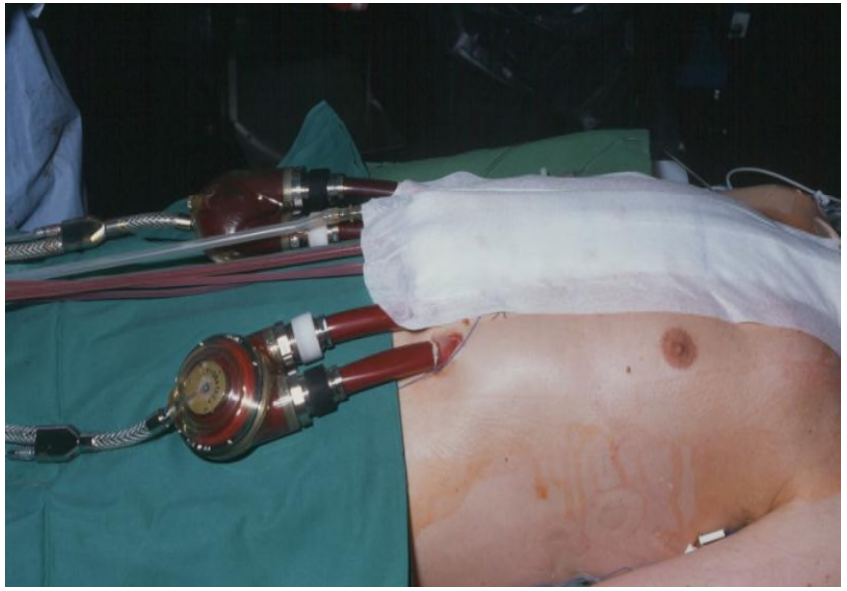
ABIOMED BVS 5000 (1988)



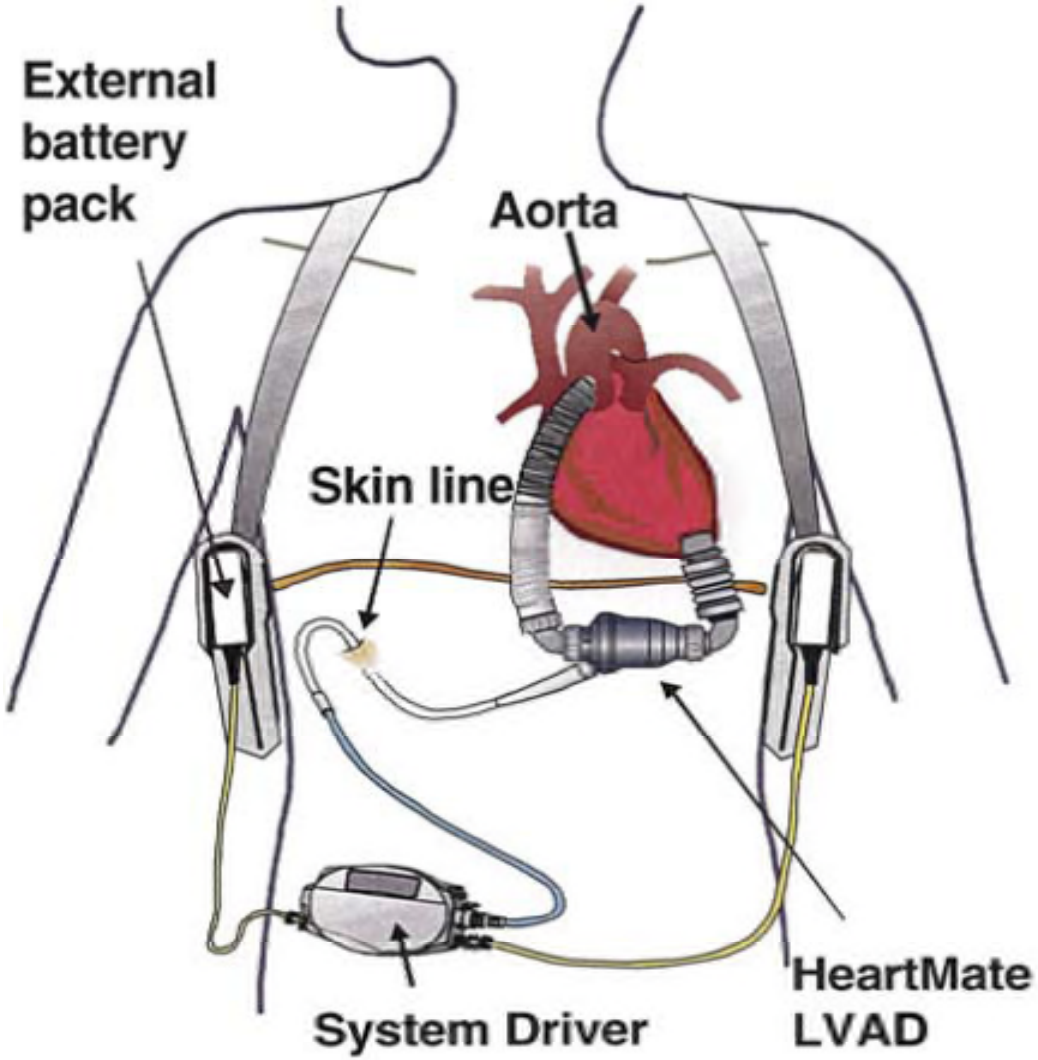
An air-driven extracorporeal pump. The design provides support for either the left or right ventricle, or both.
The pump consistts of two polyurethane chambers: an atrial chamber that fills with blood through gravitational force and a ventricular chamber that pumps blood by air-driven power. The atrial chamber is vented outside the patient. The ventricular chamber is connected to the power console by pneumatic air line. Two trileaflet valves separate the atrial and ventricular chambers. The pump can produce blood flow of up to 5 liters per minute.

Thoratec PVAD

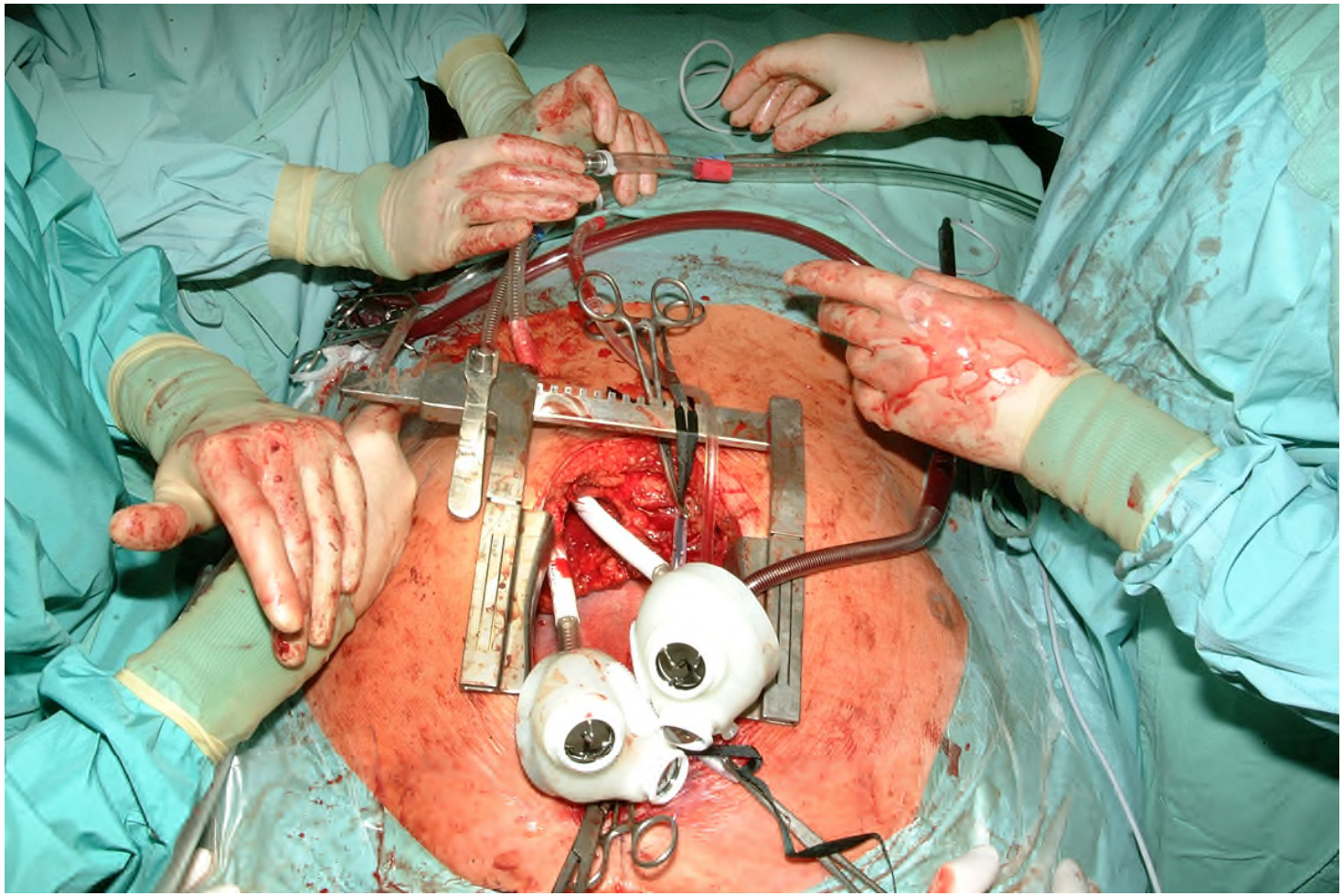




HeartMate I (1991)



Total Artificial Heart (1982)

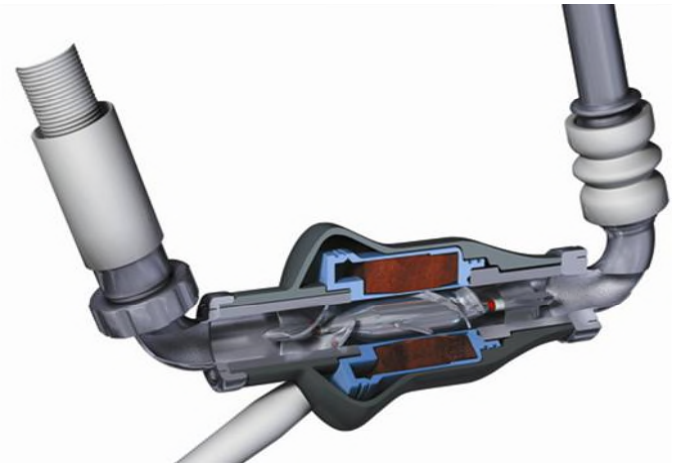


HeartMate II

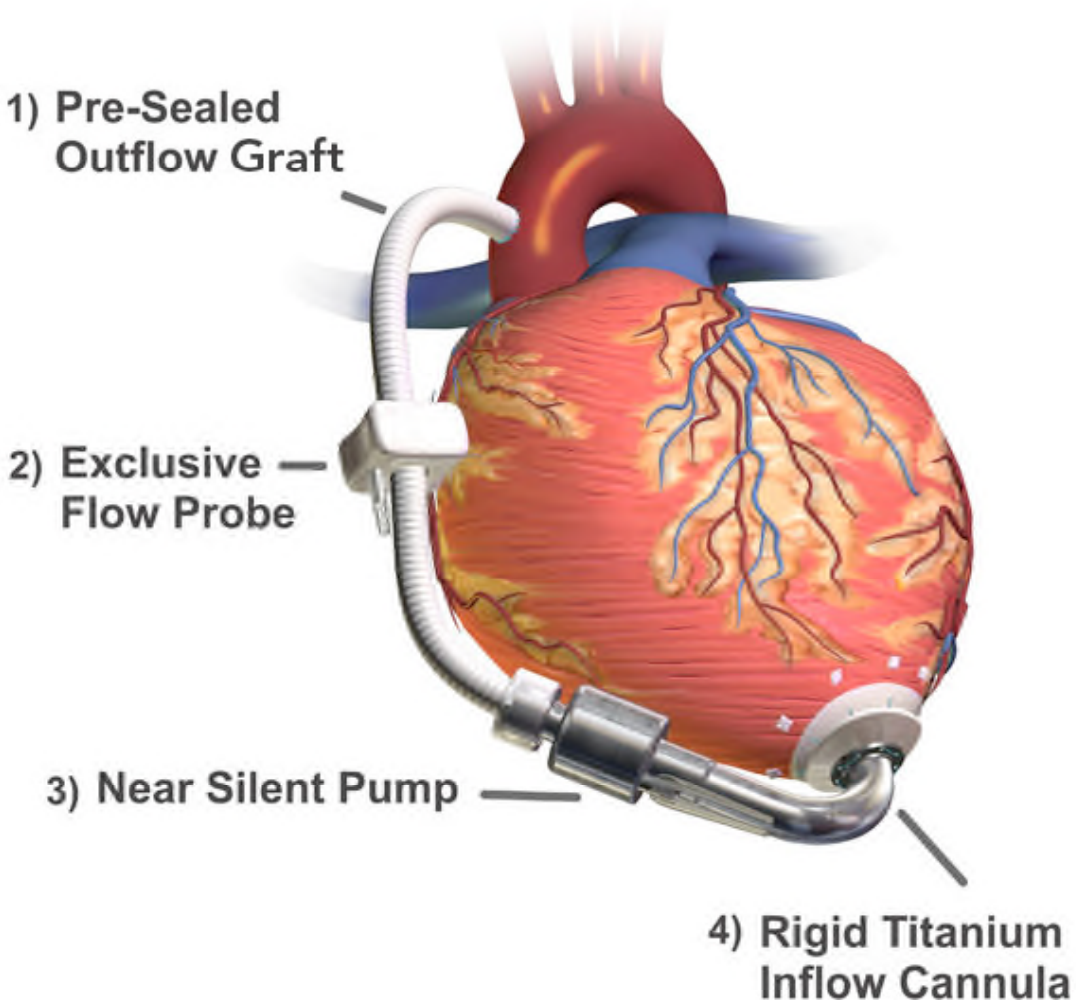
Technical details:

- Axial flow pump
- Non-pulsatile
- Speed: 9,000-13,000 rpm
- Flow: 3 - 10 l/min
- BSA: >1.2m²

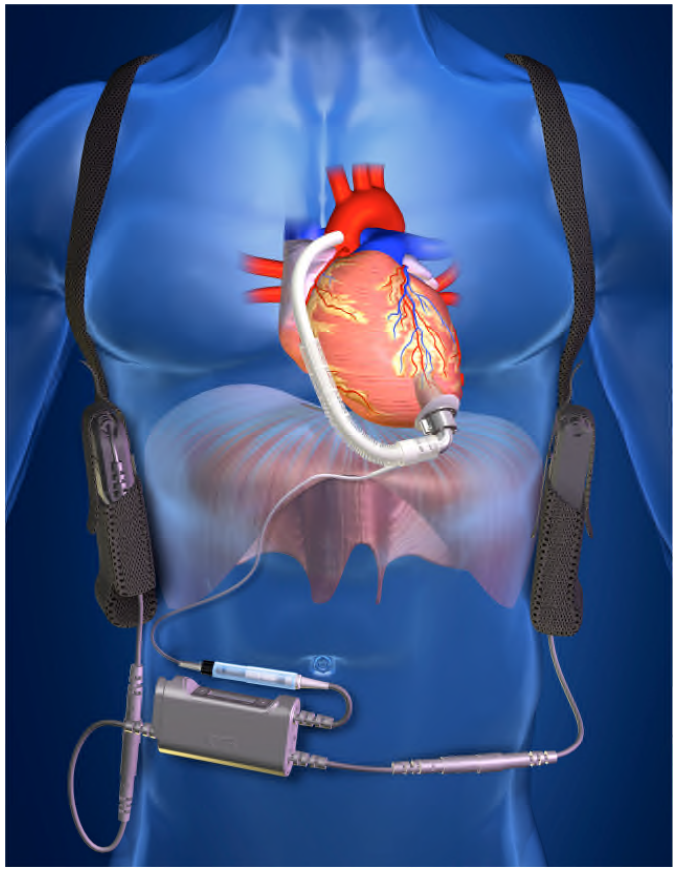
- Since 2004



Heart Assist5



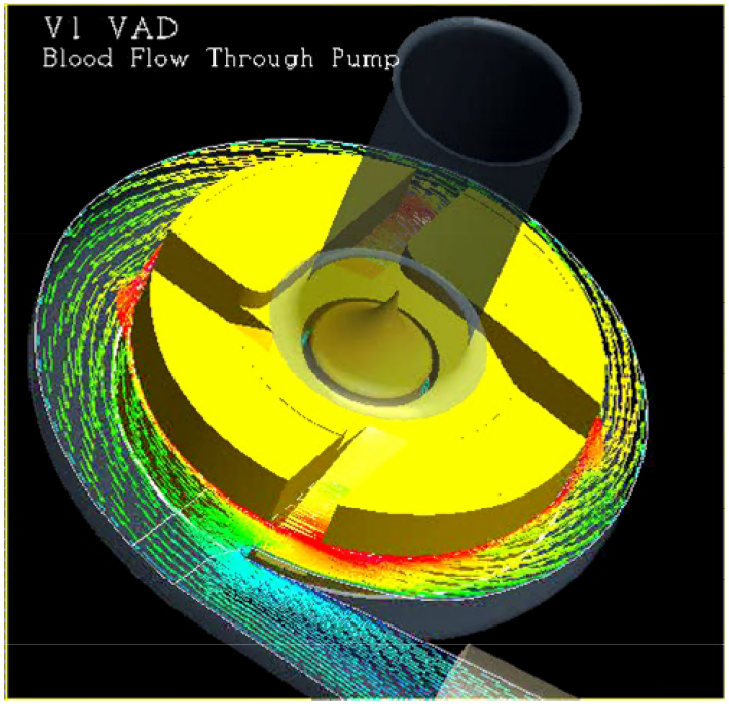
AVAD

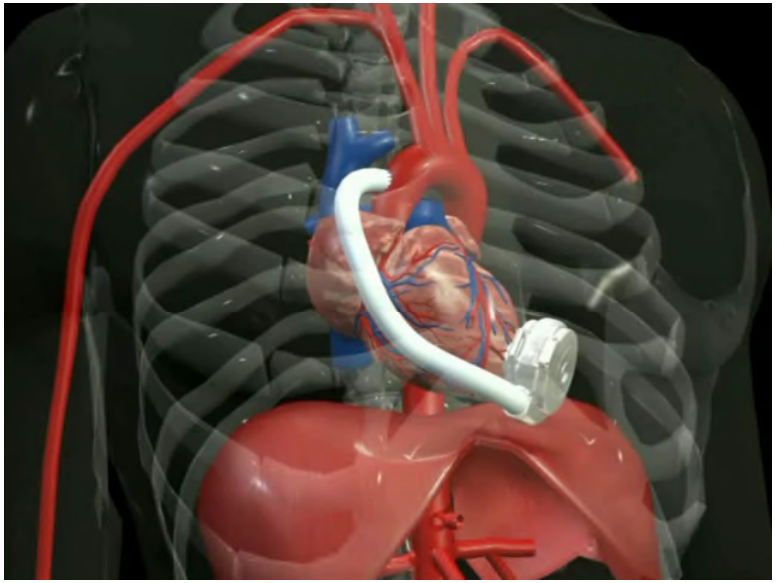


HVAD

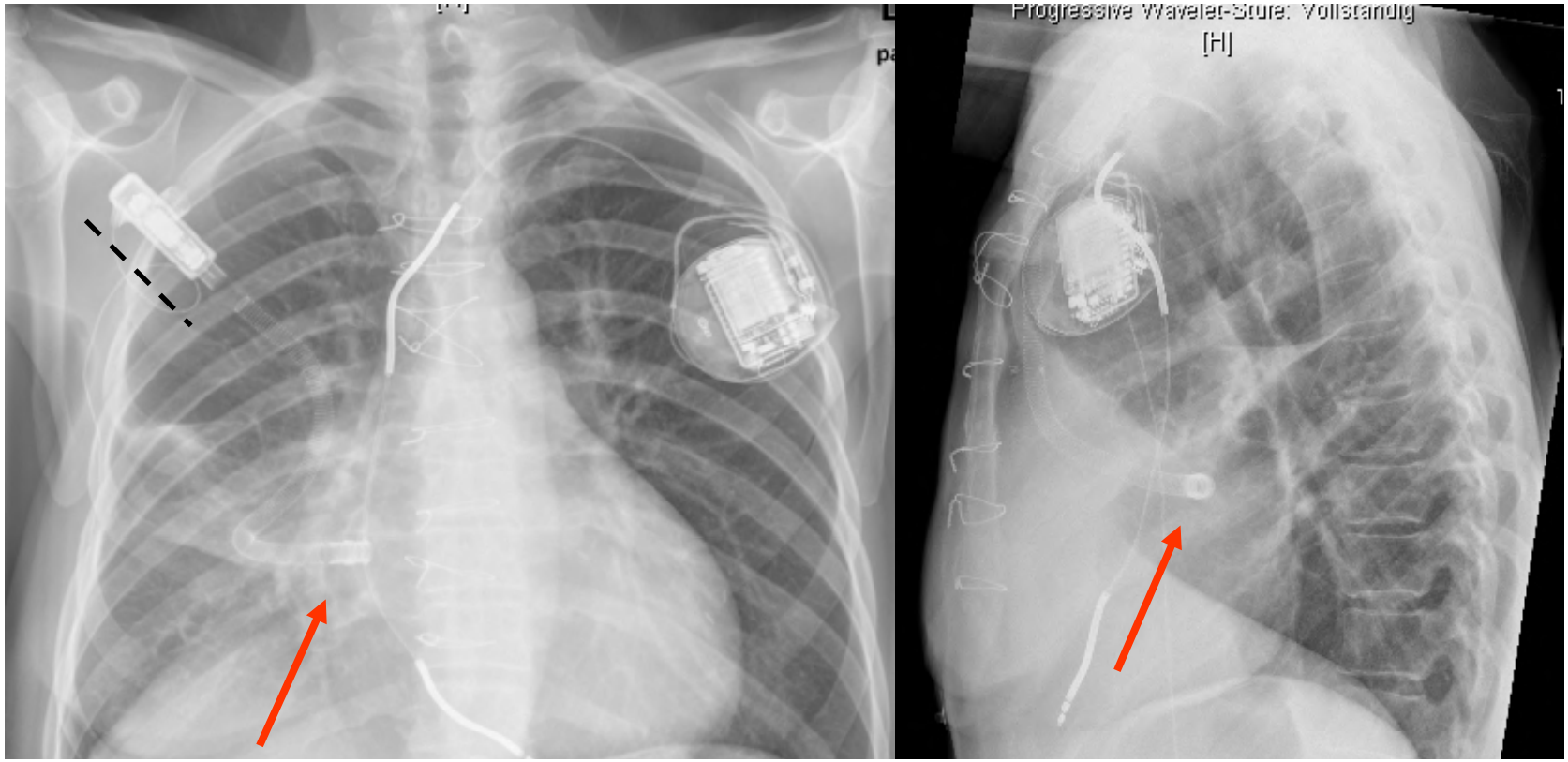
Technical details:

- Centrifugal pump
- Speed: 2,000-3,000rpm
- Flow: 3-10l/min





Synergy (Partial Support)

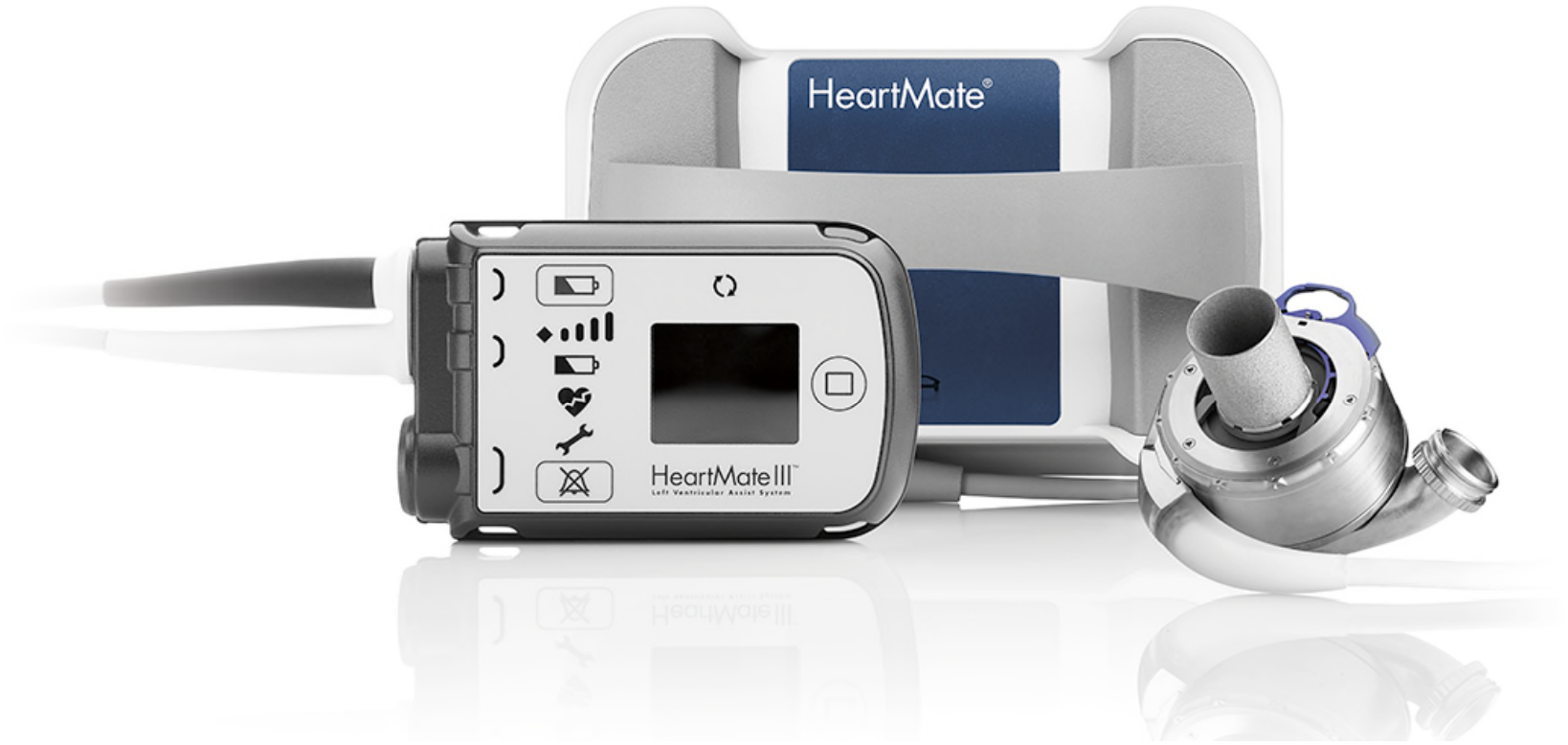


Inflow Cannula: Tip visible on PA (profile) and lateral (head on) views and Cannula exits thorax at 2nd intercostal space

Micro-pump : Position over 2nd intercostal space and parallels clavicle

HeartMate III

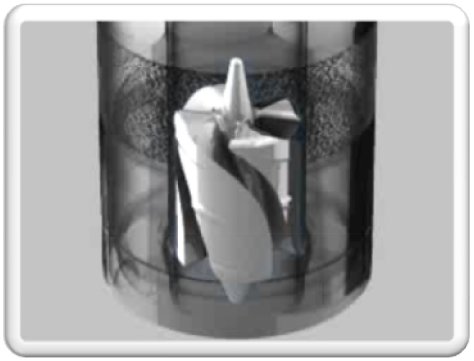
Thoratec



Future Developments….

Leveraging Core Impeller Design

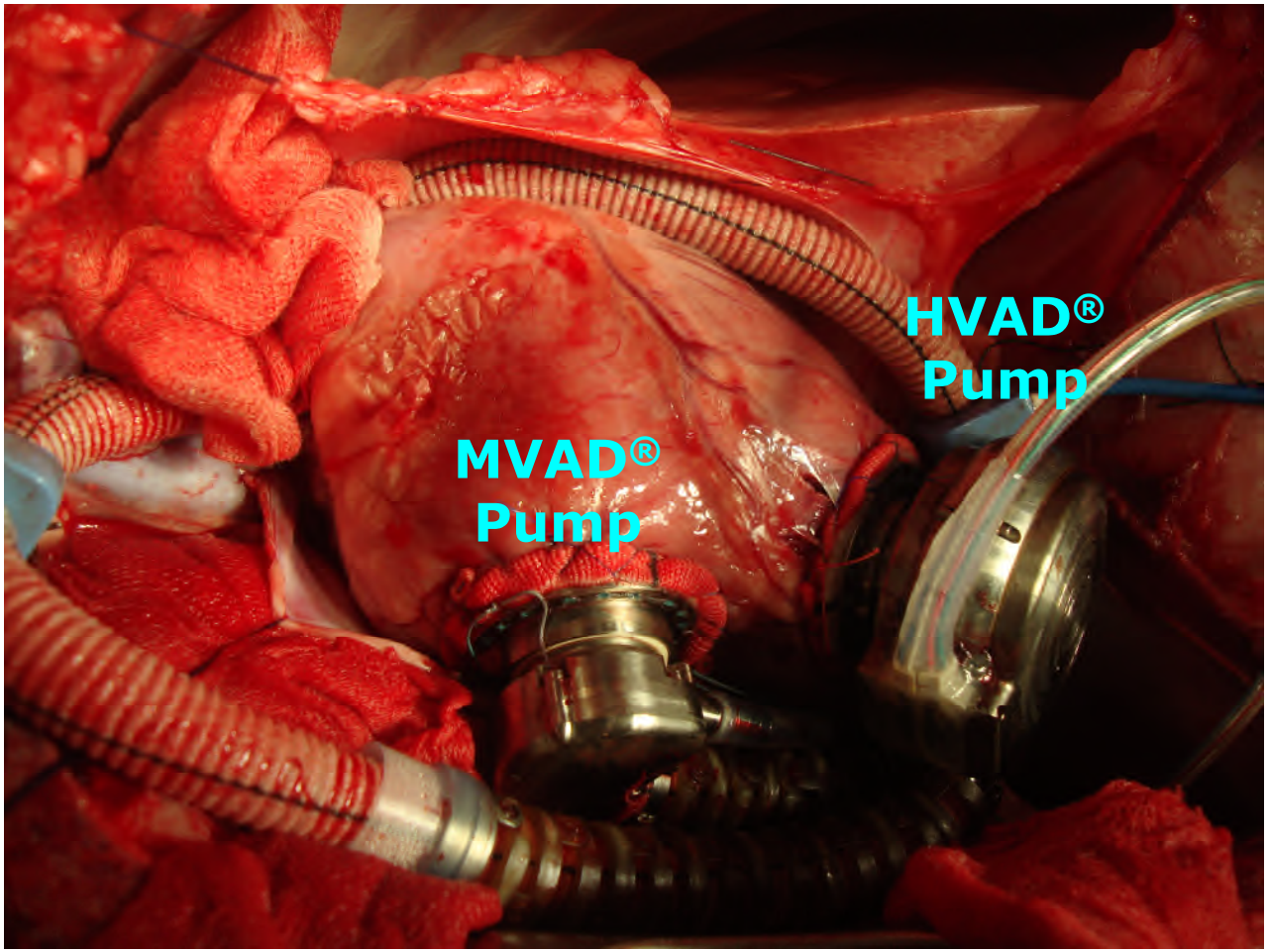
MVAD® Pump
Full-support device;
BTT/DT patient



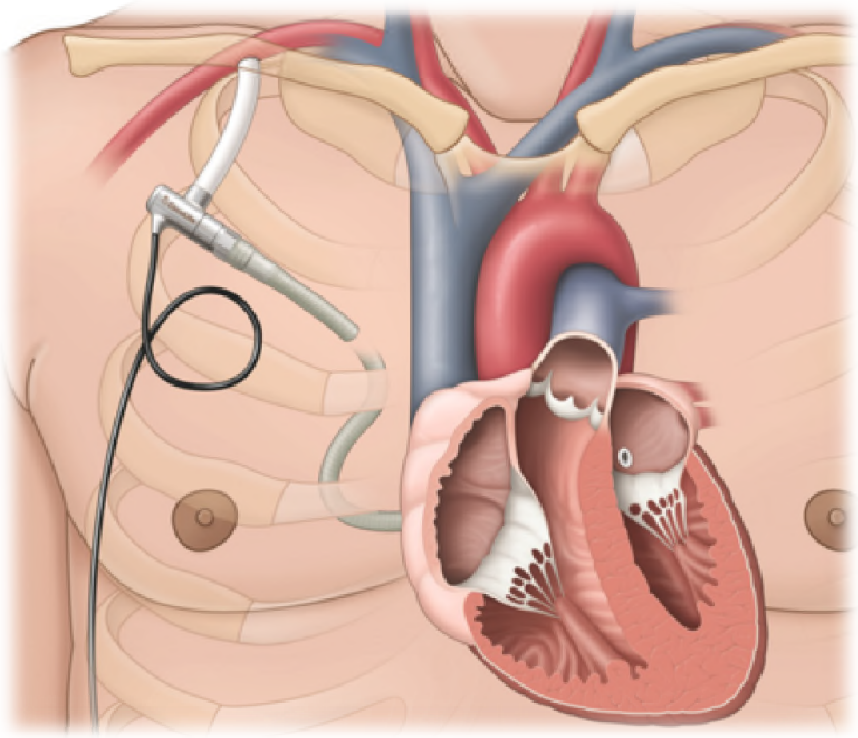
Longhorn
Full-support; elderly and high-risk patients

CircuLite
Partial-assist device;
Class III patients, HFpEF patients

Bi-Ventricular Support



CircuLite C-Pump Surgical System



Advances HTWR into Class III patient population

- Targeting patients who fail CRT therapy
- Large unmet need

Pump in subcutaneous pacemaker pocket

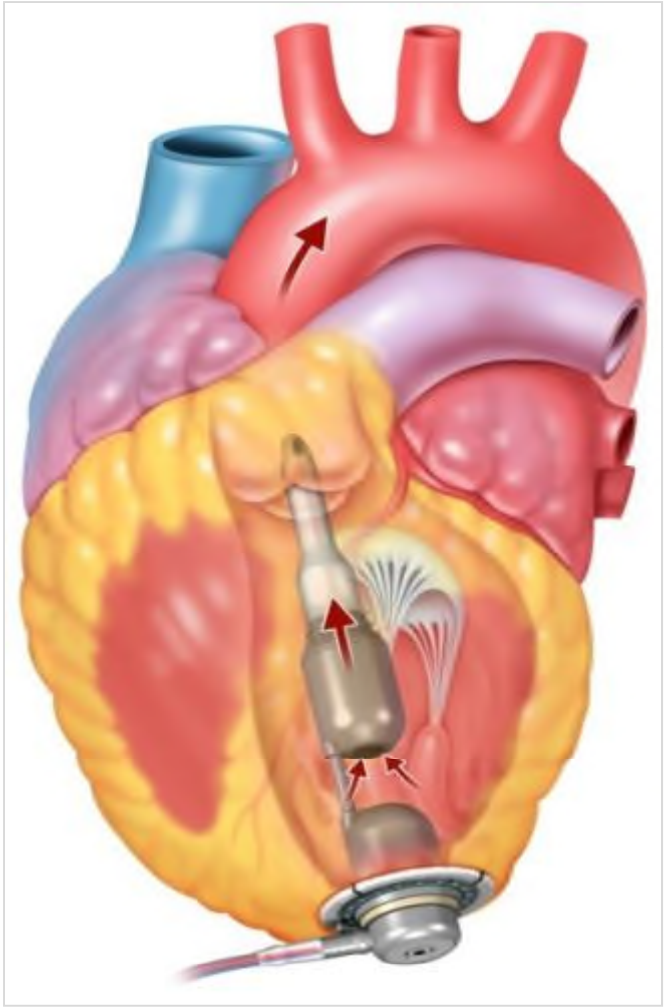
Right sided mini-thoracotomy

Off-pump procedure

Extubation in OR possible

Longhorn Transapical Pump

- **Intracardiac device with no arterial anastomosis required**
  - Outflow cannula across aortic valve
- **Designed for:**
  - Small, single incision, minimally invasive implant (similar to Transapical TAVR)
  - ‘Off pump’ implant procedure
- **Potential benefits:**
  - Eliminate CPB
  - Reduce LOS
  - Reduce blood utilization
  - Expand treatment population
    - Elderly/High Risk

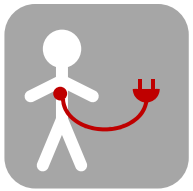


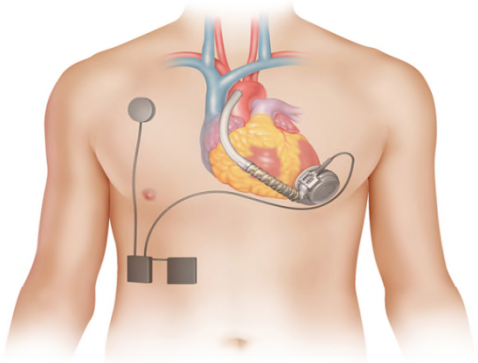
Fully-Implantable System

Free

Mobile

Tethered





Advanced Technology

- Based on Transcutaneous Energy Transfer (**"TET"**) technology
- Periodically recharged using inductive coupling across the skin
- Fully-implantable controller & battery optimized for long-term support and patient mobility
- Wireless monitoring and management of VAD parameters

Patient Benefits

- Designed for both HVAD® Pump and MVAD® Pump
- No exit site care or risk of trauma to exit site
- Patient physical freedom from external components
- Discreet physical appearance

CAUTION: In development and not available for clinical use.

Ongoing…

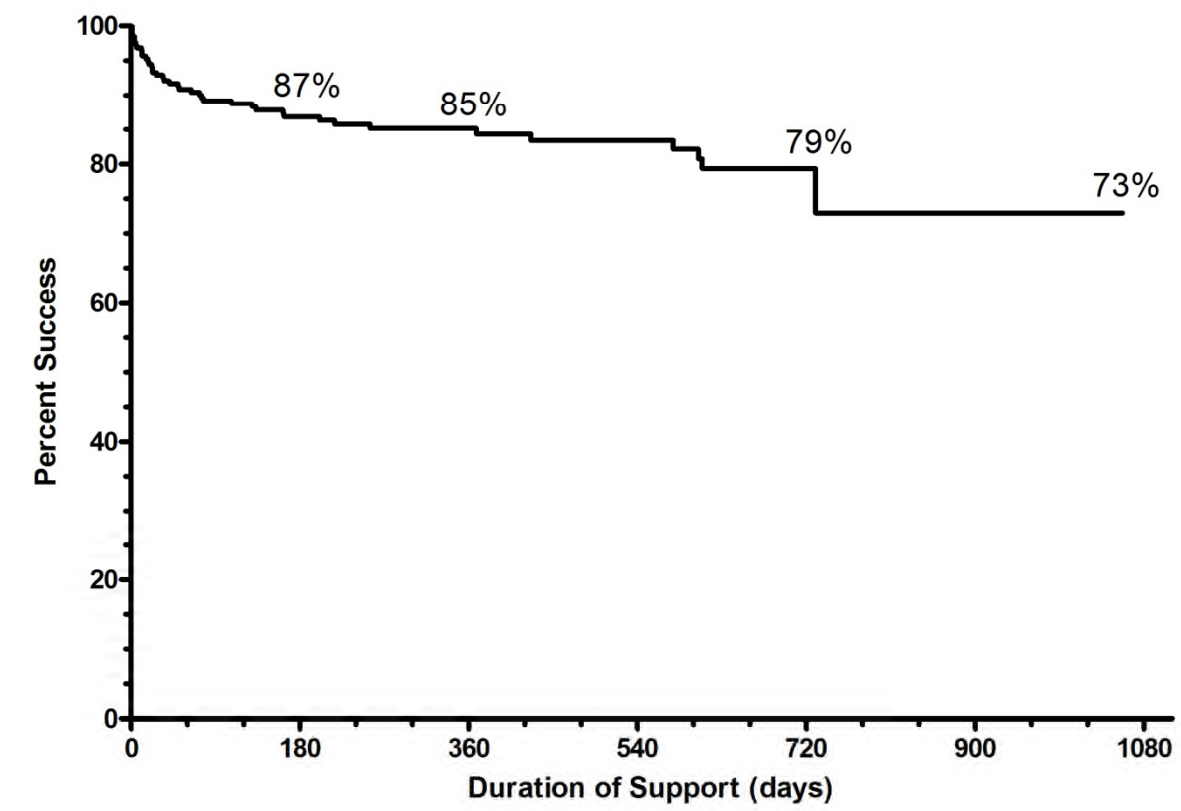
Therapeutical Concepts

HTx	VAD
	Bridge to Recovery
Destination Therapy	Destination Therapy Bridge to Decision Bridge to Transplantation

The Harefield Experience

- Largest transplant/ MCS program in the UK
- Currently, 75 long-term MCS patients
- 2014/15 we implanted 48 long term devices
- Longest on-going VAD patient 10 years on support
- In 2016, > 100 pts. on ECLS
- 2014/15, 25 heart transplants
- 17 of these transplants were on patients supported by MCS

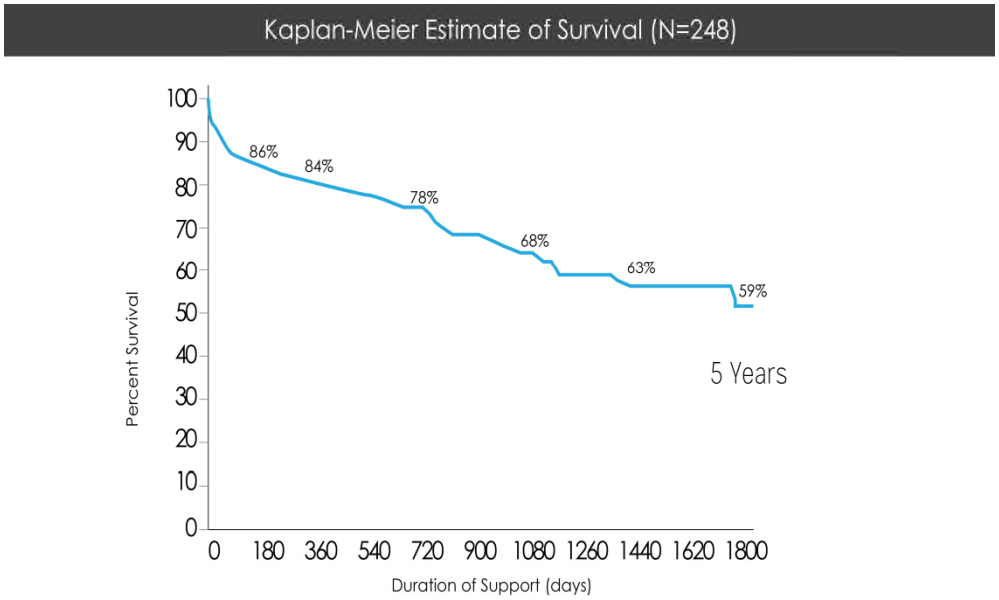
Success rate after HVAD Implantation



Success was defined as survival to transplant, successful recovery with device explant, or on continued HeartWare System support.

HVAD® Long-Term Survival

Long-term follow-up in a post-CE mark Commercial Registry (ReVOLVE) demonstrated improvedt long-term survival; with low adverse event rates (59% at 5 years).



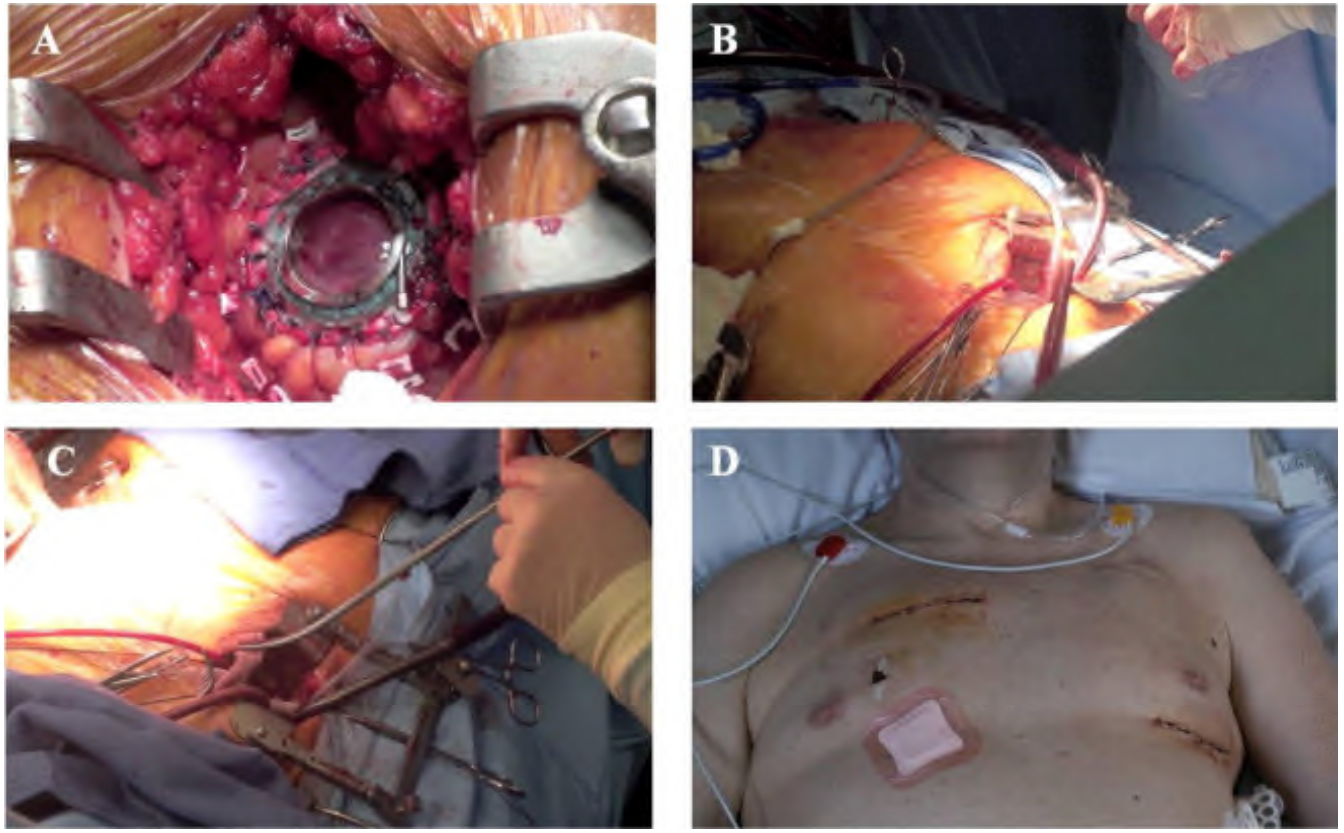
* Schmitto, J. Long Term Support of Patients Receiving an LVAD for Advanced Heart Failure: A Follow-up Analysis of the Registry to Evaluate the HeartWare Left Ventricular Assist System (The ReVOLVE Registry), Presentation at ISHLT, April 16, 2015, Nice France

Surgical Technique

HeartWare Left Ventricular Assist Device Implantation Through Bilateral Anterior Thoracotomy

Aron Frederik Popov, MD, Morteza Tavakkoli Hosseini, MD, Bartlomiej Zych, MD, Andre Ruediger Simon, MD, PhD, Toufan Bahrami, MD,

The Annals of Thoracic Surgery Volume 93, Issue 2, Pages 674-676 (February 2012



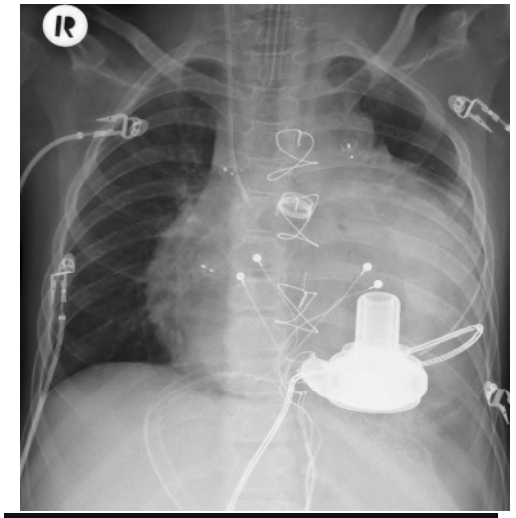
(A) Implantation of the sewing ring. (B) Establishment of cardiopulmonary bypass. (C) Tunneling of the outflow graft toward the right thoracotomy incision. (D) Postoperative result.

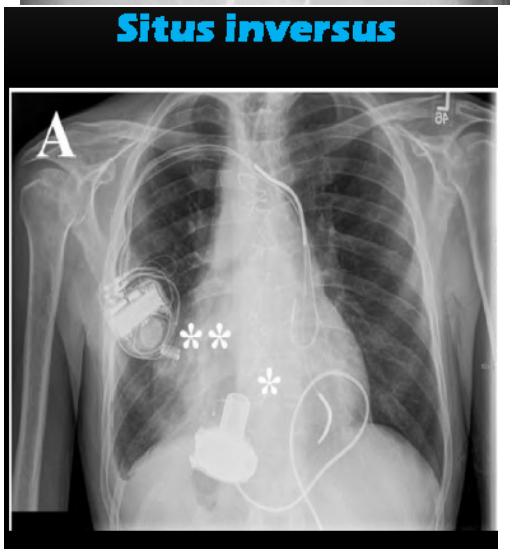
The Annals of Thoracic Surgery 2012 93, 674-676DOI: (10.1016/j.athoracsur.2011.09.055)
Copyright © 2012 The Society of Thoracic Surgeons

Congenital

- **Primary Anatomy[1]**
  - Failed Fontan's
  - Systemic RV/transposition of great vessels

- **CMO associated with Muscular Dystrophy:**
  - Duchenne MD
    - It's the most common lethal genetic disease in children worldwide
    - 80% die from advanced heart failure





The first female with Duchenne Muscular Dystrophy is implanted with an LVAD at Cincinnati Children's Hospital

[1]Shah et al, 2013, JHLT

Left Ventricular Assist Device Implantation With Dor Procedure via Bilateral Limited Thoracotomy.

Artif Organs. 2015 Jul;39(7):641-2.

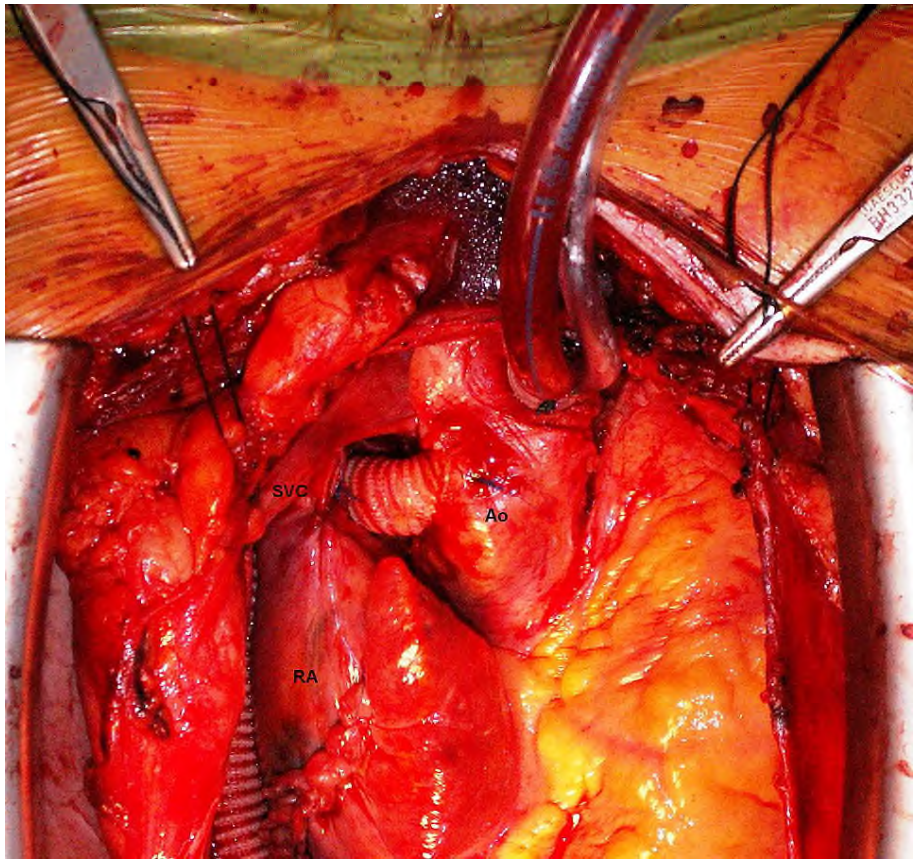
Patil NP, Popov AF, Simon AR.

Left ventricular assist device implantation with concomitant left ventricular reconstruction without patchplasty

J Artif Organs. 2014 Dec;17(4):370-2.

Fatullayev J1, Butters T, Sabashnikov A, Garcia Saez D, Mohite PN, Edwards G, Hoegerle B, Wahlers T, Popov AF, Simon AR.

Anticipation of Future Operation



Tunneling of ventricular assist device outflow graft rostral to superior vena cava

Prashant N. Mohite, MCh, Aron F. Popov, MD, Tarun K. Mittal, MD, Andre R. Simon, MD

The Journal of Thoracic and Cardiovascular Surgery, Volume 144, Issue 6, Pages 1519-1520 (December 2012)

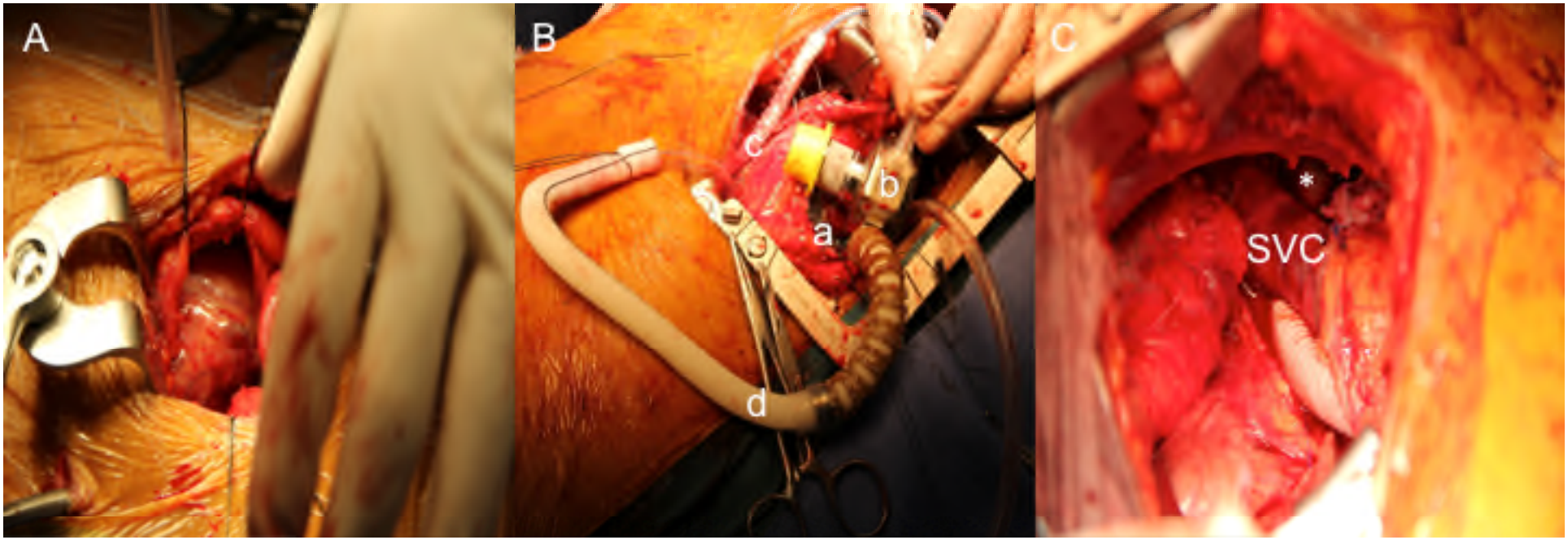
The Journal of Thoracic and Cardiovascular Surgery 2012 144, 1519-1520DOI: (10.1016/j.jtcvs.2012.07.027)

Copyright © 2012 The American Association for Thoracic Surgery

Tunneling of ventricular assist device outflow graft rostral to superior vena cava

Prashant N. Mohite, MCh, Aron F. Popov, MD, Tarun K. Mittal, MD, Andre R. Simon, MD

The Journal of Thoracic and Cardiovascular Surgery
Volume 144, Issue 6, Pages 1519-1520 (December 2012)

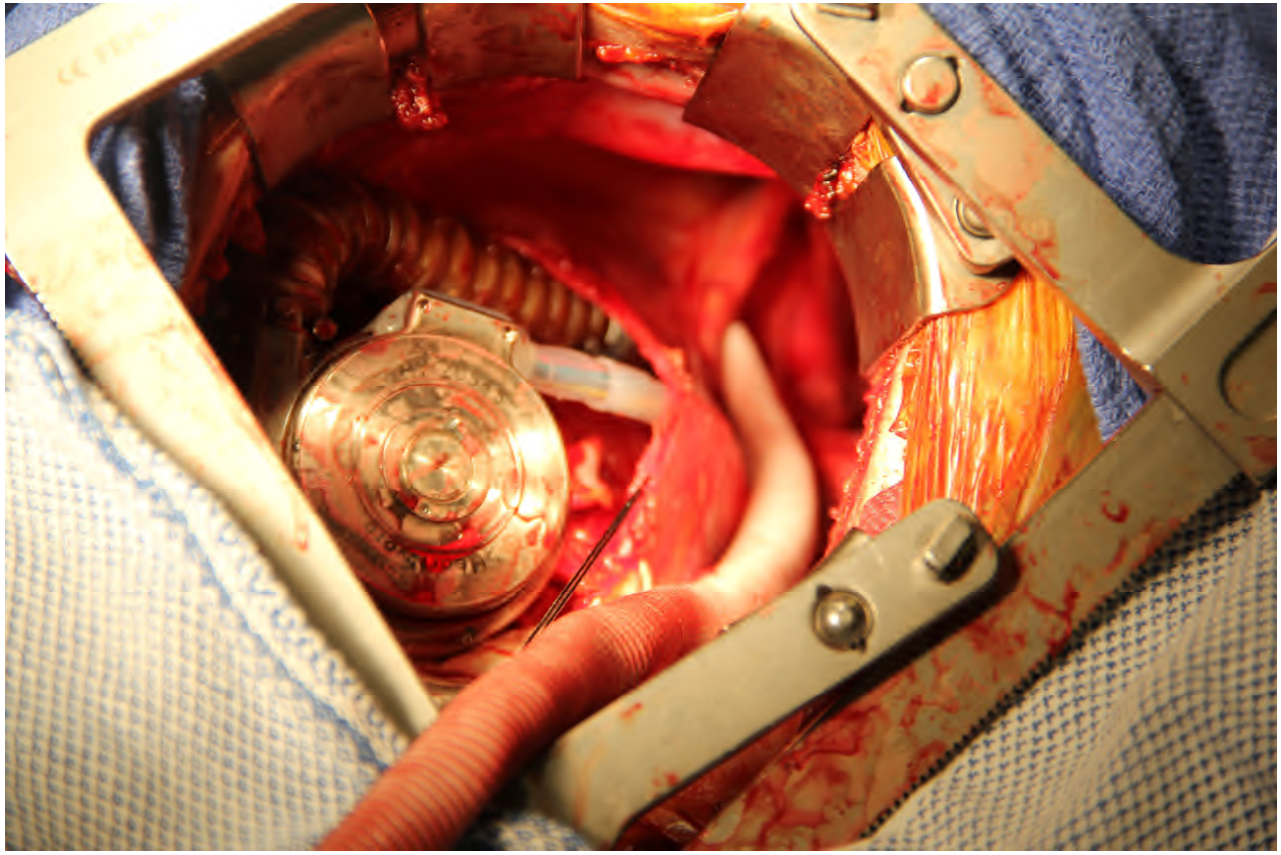


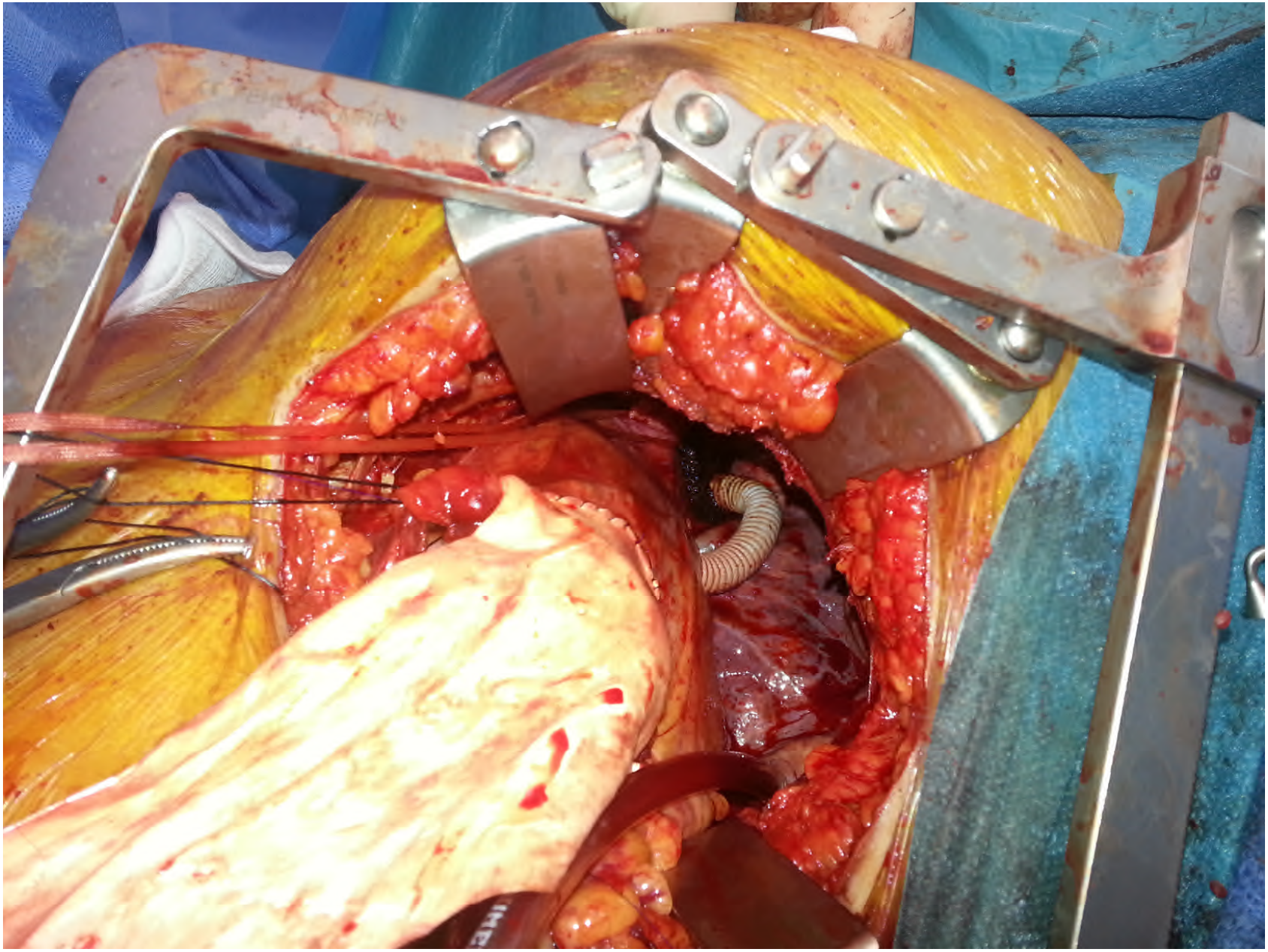
Copyright © 2012 The American Association for Thoracic Surgery

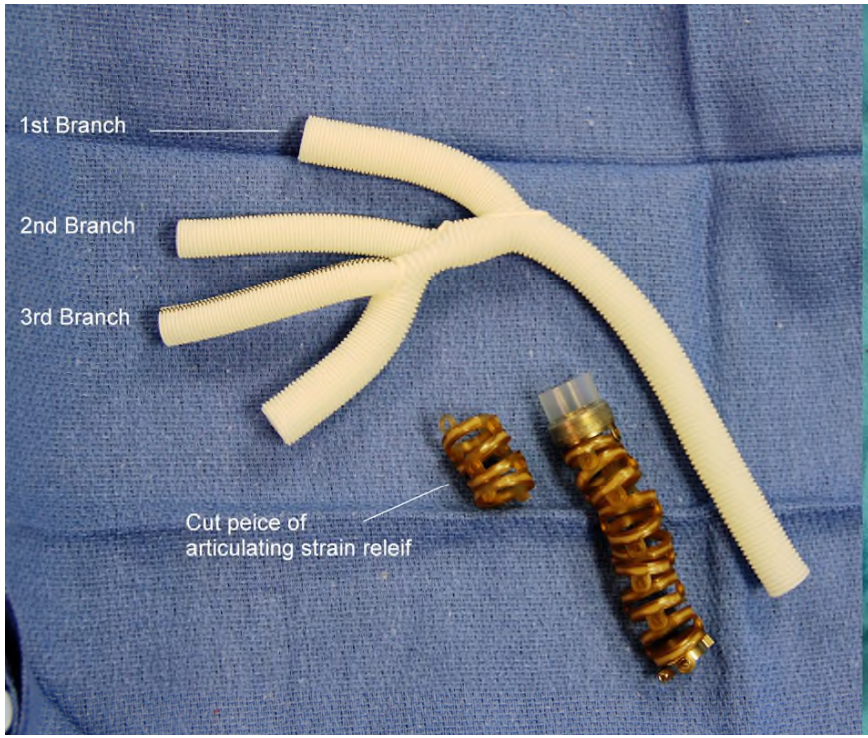
Minimally invasive HeartWare LVAD implantation through single left thoracotomy

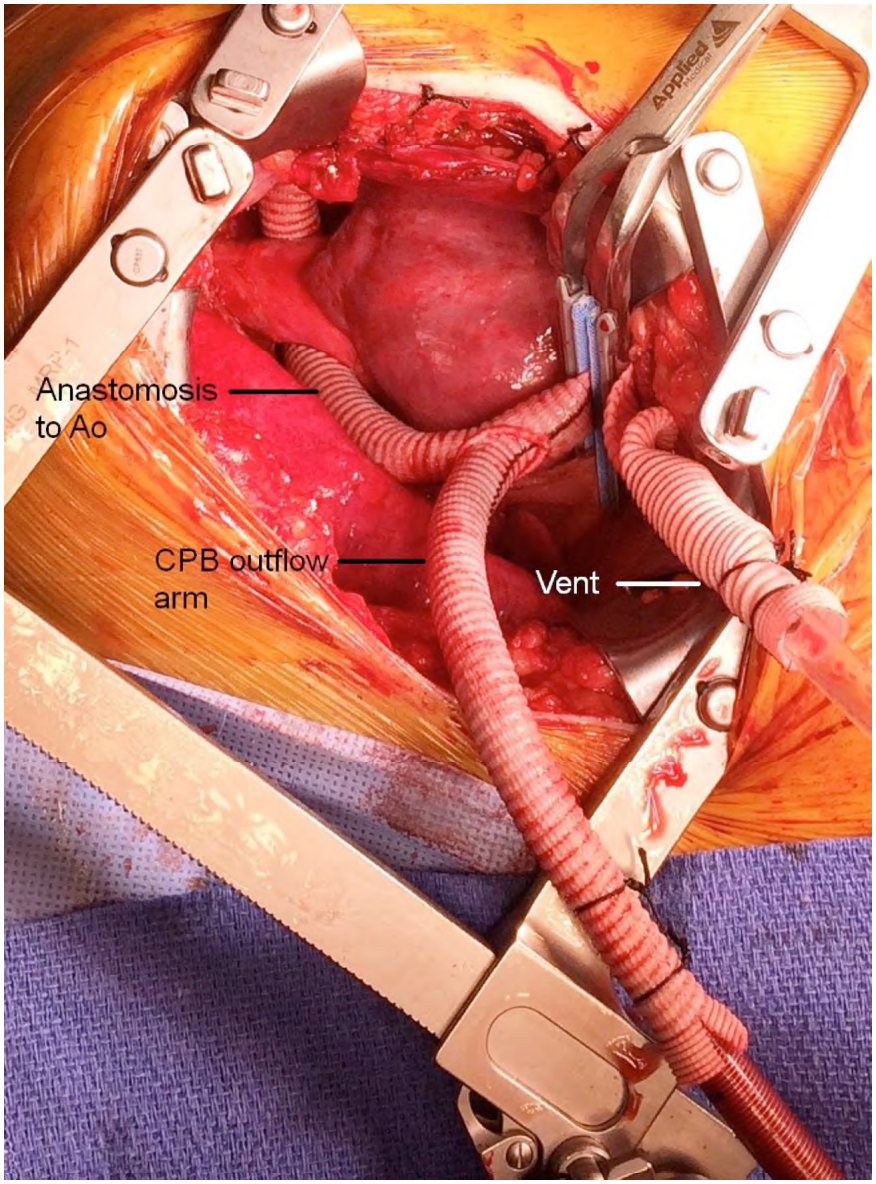
J Artif Organs. 2015 Jun;18(2):170-2..

Popov AF1, Mohite PN, Sabashnikov A, Weymann A, Patil NP, Sáez DG, Simon AR.






1st Branch
2nd Branch
3rd Branch
Cut peice of
articulating strain releif


Anastomosis
to Ao
CPB outflow
arm
Vent

Current Results

- 3 year survival comparable or better when compared to HTx in select groups (75% HH ongoing)
- 5 year survival 59% in non selected patients (HTx: 69%)
- Excellent QoL
- Used as destination or chronic support (outside UK) therapy routinely

Conclusion (UK)

- Heart transplantation does not present a feasible therapeutical concept in real life.
- Medium term VAD results are VAD results are acceptable, long term results acceptable in selected groups and results continue to improve rapidly.
- As suggested by NICE, destination/chronic support should be funded.
- VAD therapy should become the standard long term therapy for patients with end stage heart failure
- HTx should be restricted to a highly selected patient population

Conclusion (UK)

Artificial Hearts have become a Realistic Solution for Younger Patients with Circulatory Failure

Real Life…