Surgical Heart Failure in 2023: Rise of the Machines

Carly Lodewyks MD MSc FRCSC
Cardiac Surgeon
Minneapolis Heart Institute

Allina Health
MINNEAPOLIS HEART INSTITUTE

Minneapolis Heart Institute Foundation

1

Objectives

- Review current indications for mechanical circulatory support
- Explore the latest devices available for support of patient with heart failure
- Discuss the use of organ preservation and perfusion systems in DCD and DBD heart procurement

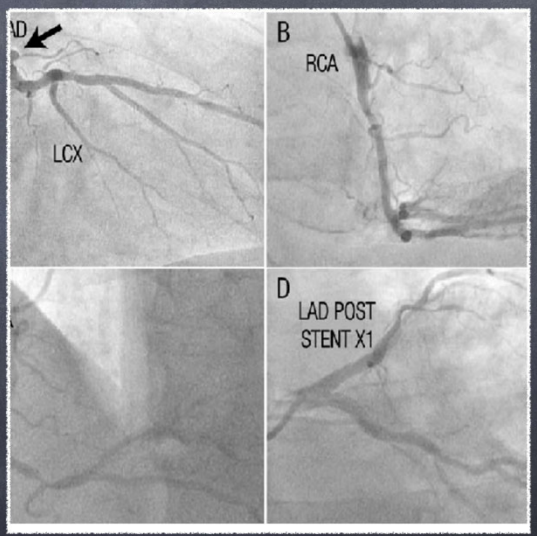
2

Disclosures…

3

A Case…. Of Course!

- 68 Year Old Male
  - PMHx: DM, smoker
  - Presented with late anterior STEMI:
    - 100% ostial LAD
    - Severe LCx, RCA disease
    - LAD and Cx stented
    - Left femoral IABP placed



4

Post Procedure

- Initial TTE: EF 20-25%, normal RV and valves
- In ICU:
  - DCCV for a fib
  - Initially some improvement in hemodynamics with IABP and inotropy but now…

5

Hemodynamics

- PA 30/15 (20)
- CVP 10
- PCWP 22
- O2M 47
- CO 3.57
- CI 1.77
- SVR 1142

Dobutamine 5
Milrinone 0.375
Amio 44/hr
IABP 1:1

6

"Hey Carly,
Can you see this guy in bed 38 for consideration of advanced therapies?"

7

The Heart Failure Decision Tree

- Type of shock
  - INTERMACS classification
- Which pump is the problem
- Oxygenation issues
- Clinical considerations

8

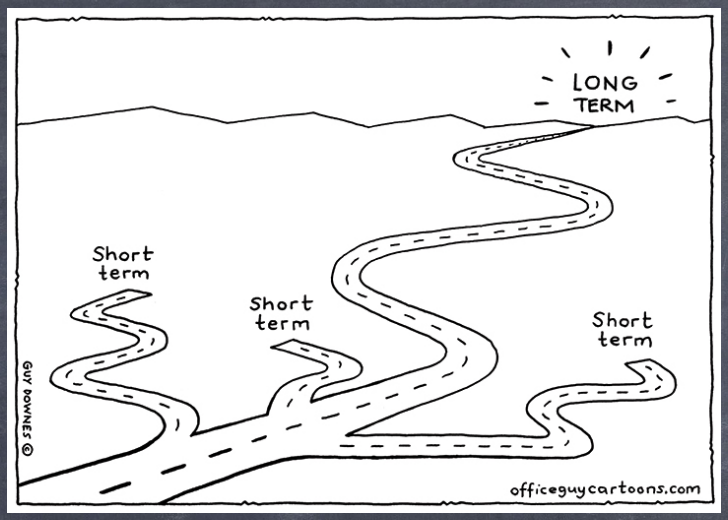
Short Term MCS Options

- ECMO
- Centrimags
- IABP
  - Femoral
  - Axillary
- Impella
  - CP
  - Axillary 5.5

9

DURABLE LVAD?
HEART TRANSPLANTATION?

10



Surgical Heart Failure Commandment:

You must always think about the long term goal!

11

Surgical Heart Failure Commandment:

Use "bridges" to your advantage

12

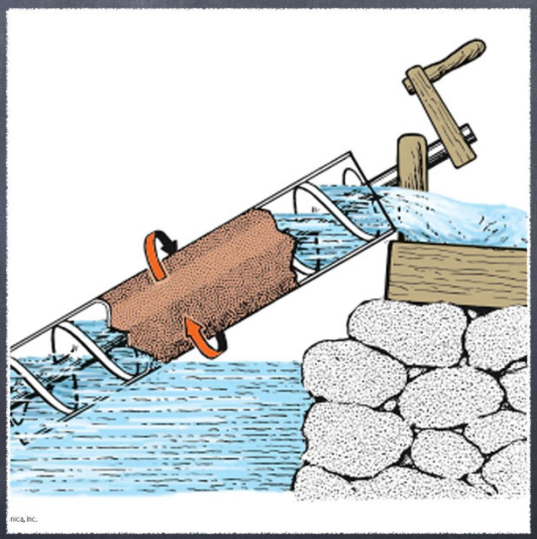
Impella

The little pump that could

13

Impella - A Brief History

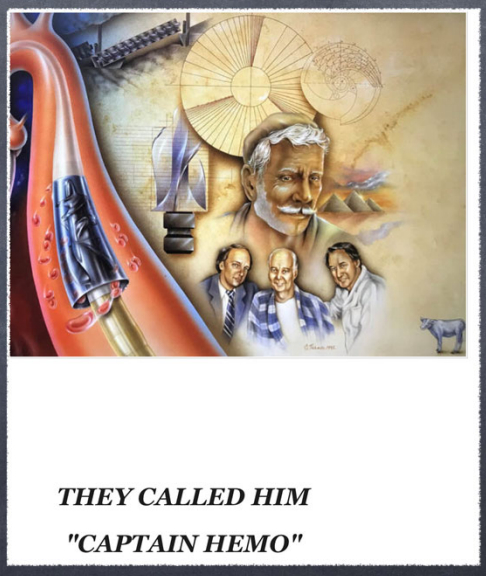
Archimedes Screw



14

Hemopump

Dr Richard Wampler
1985



15

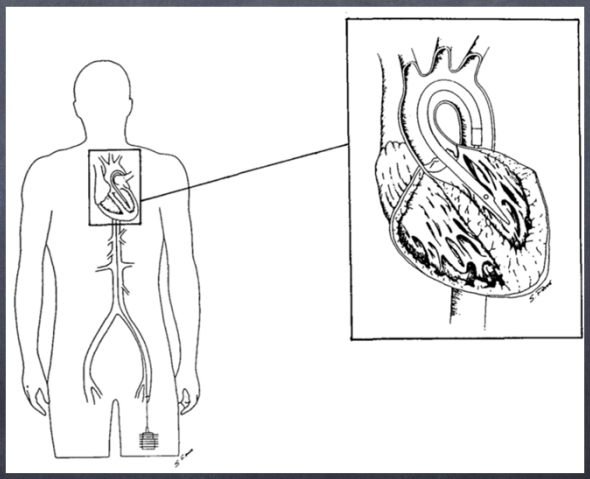
Nimbus Hemopump

- Continuous flow intra vascular pump
- Pumps from LV to aorta
- Purge assembly for blood seal integrity
- Hydrodynamic lubrication
- Console for power to pump and purge

16

Nimbus Hemopump

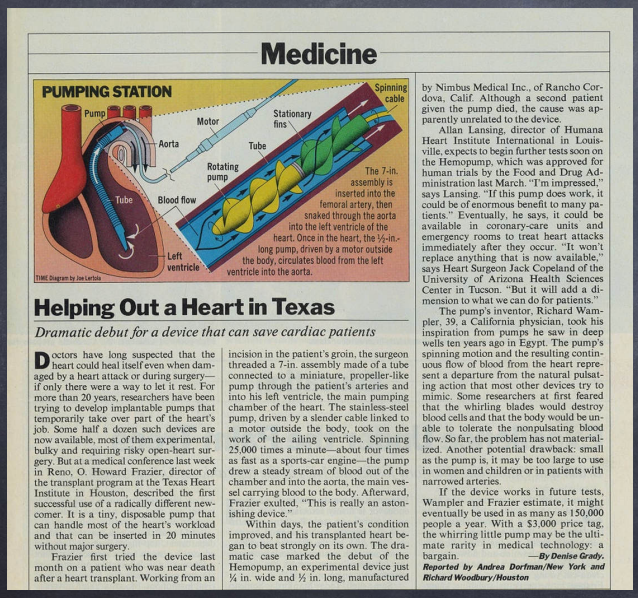
- Femoral, direct aortic access (? Abdominal aorta)
- Provided up to 3.5L/min of flow
- No need for LV contribution or synchronization
- Provides LV decompression



Wampler et al 1991

17

First In-Human Implant



Medicine

Helping Out a Heart in Texas

Dramatic debut for a device that can save cardiac patients

Doctors have long suspected that the heart could heal itself even when damaged by a heart attack or during surgery—if only there were a way to let it rest. For more than 20 years, researchers have been trying to develop implantable pumps that temporarily take over part of the heart's job. Some half a dozen such devices are now available, most of them experimental, bulky and requiring risky open-heart surgery. But at a medical conference last week in Reno, O. Howard Frazier, director of the transplant program at the Texas Heart Institute in Houston, described the first successful use of a radically different newcomer. It is a tiny, disposable pump that can handle most of the heart's workload and that can be inserted in 20 minutes without major surgery.

Frazier first tried the device last month on a patient who was near death after a heart transplant. Working from an incision in the patient's groin, the surgeon threaded a 7-in. assembly made of a tube connected to a miniature, propeller-like pump through the patient's arteries and into his left ventricle, the main pumping chamber of the heart. The stainless-steel pump, driven by a slender cable linked to a motor outside the body, took on the work of the ailing ventricle. Spinning 25,000 times a minute—about four times as fast as a sports-car engine—the pump drew a steady stream of blood out of the chamber and into the aorta, the main vessel carrying blood to the body. Afterward, Frazier exulted, "This is really an astonishing device."

Within days, the patient's condition improved, and his transplanted heart began to beat strongly on its own. The dramatic case marked the debut of the Hemopump, an experimental device just ¼ in. wide and ½ in. long, manufactured by Nimbus Medical Inc., of Rancho Cordova, Calif. Although a second patient given the pump died, the cause was apparently unrelated to the device.

Allan Lansing, director of Humana Heart Institute International in Louisville, expects to begin further tests soon on the Hemopump, which was approved for human trials by the Food and Drug Administration last March. "I'm impressed," says Lansing. "If this pump does work, it could be of enormous benefit to many patients." Eventually, he says, it could be available in coronary-care units and emergency rooms to treat heart attacks immediately after they occur. "It won't replace anything that is now available," says Heart Surgeon Jack Copeland of the University of Arizona Health Sciences Center in Tucson. "But it will add a dimension to what we can do for patients."

The pump's inventor, Richard Wampler, 39, a California physician, took his inspiration from pumps he saw in deep wells ten years ago in Egypt. The pump's spinning motion and the resulting continuous flow of blood from the heart represent a departure from the natural pulsating action that most other devices try to mimic. Some researchers at first feared that the whirling blades would destroy blood cells and that the body would be unable to tolerate the nonpulsating blood flow. So far, the problem has not materialized. Another potential drawback: small as the pump is, it may be too large to use in women and children or in patients with narrowed arteries.

If the device works in future tests, Wampler and Frazier estimate, it might eventually be used in as many as 150,000 people a year. With a $3,000 price tag, the whirring little pump may be the ultimate rarity in medical technology: a bargain.

—*By Denise Grady.*
Reported by Andrea Dorfman/New York and Richard Woodbury/Houston

18

Hemopump

- 53 patients with refractory cardiogenic shock
- Successful insertion in 41/53
- Significant hemodynamic improvement
- Minimal hemolysis
- No leg ischemia
- 30 day survival 31.7%

Treatment of Cardiogenic Shock With the Hemopump Left Ventricular Assist Device

Richard K. Wampler, MD, O. Howard Frazier, MD, Allan M. Lansing, MD, PhD, Richard W. Smalling, MD, PhD, John M. Nicklas, MD, Steven J. Phillips, MD, Robert A. Guyton, MD, and Leonard A. R. Golding, MD

Nimbus, Inc, Rancho Cordova, California; Texas Heart Institute and Hermann Hospital, Houston, Texas; Humana Hospital Audubon, Louisville, Kentucky; The University of Michigan Medical Center, Ann Arbor, Michigan; Mercy Hospital Medical Center, Des Moines, Iowa; Emory University and Crawford Long Hospitals, Atlanta, Georgia; and The Cleveland Clinic Foundation, Cleveland, Ohio

Annals of Thoracic Surgery

19

Comparative Study > J Invasive Cardiol. 1990 Jul-Aug;2(4):169-73.

The Nimbus Hemopump: a new left ventricular assist device that combines myocardial protection with circulatory support

M R Mooney [1], J F Mooney, R A Van Tassel, I F Goldenberg, J D Madison, K E Johnson, T Von Ruedon, L D Joyce, R W Emery, M R Pritzker

Affiliations – collapse

Affiliation

1 Divisions of Mechanical Support/Transplantation and Interventional Cardiology, Minneapolis Heart Institute, Abbott Northwestern Hospital, MN 55407.

A Minnesota Connection

20

Hemopump-> Impella

- Hemopump - no commercial success, discontinued
- Germany: early 1990s modified Hemopump design
  - Short rotating impeller rather than long screw
  - Mini motor on the catheter
- Experimental studies of impella in Belgium
- US- FDA approval of 2.5 2008, CP in 2012.

21

Impella- the next generation

22

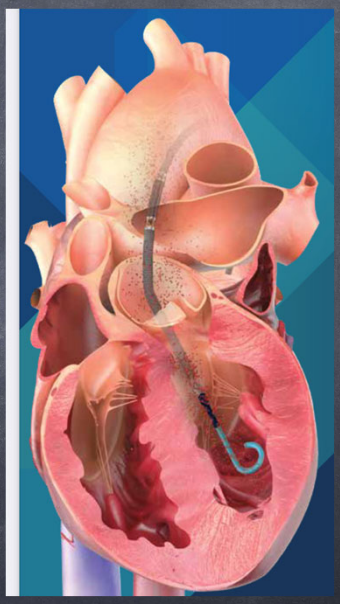
Impella 2.5 and CP

- Retrograde femoral approach
- 2.5 L/min, 4.0 L/min flow
- Approved for use:
  - 4 days (Cardiogenic shock)
- Primary Uses:
  - High risk PCI
  - Cardiogenic, Post cardiotomy shock
  - LV unloading - ECMO

23

Impella CP

- Issues
  - Limited flow capability
  - Small device
    - Hemolysis
      - CP= "Crushing Platelets"
    - Groin access- impaired mobility, vascular injury/bleeding
    - Limited duration of use
    - Upsizing to larger device often necessary for severe shock

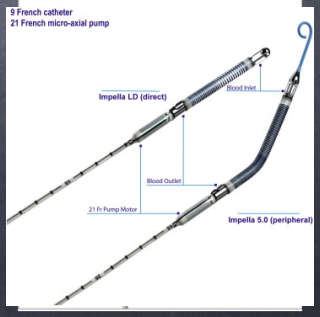


abiomed.com

24

Surgical Impellas

- Impella 5.0/LD
  - 4-5LPM
  - 7F pigtail at tip
  - 21F motor
  - 23F sheath
  - Femoral or axillary cut down
  - LD: direct aortic
  - Approval 14d
- Impella 5.5
  - 5.5 LPM
  - No pigtail, shorter motor
  - 19F motor
  - Smart Assist- positioning
  - Axillary cut down or direct aortic
  - Approval 14 d FDA, 30D CE



Ramzy et al, JHLT 2023

25

Improved clinical outcomes associated with the Impella 5.5 compared to the Impella 5.0 in contemporary cardiogenic shock and heart failure patients

Danny Ramzy, MD, PhD,[a] Edward G. Soltesz, MD, MPH,[b] Scott Silvestry, MD,[c] Mani Daneshmand, MD,[d] Manreet Kanwar, MD,[e] and David A. D'Alessandro, MD[f]

From the [a]Department of Cardiac Surgery, UTHealth McGovern School of Medicine Houston, Texas; [b]Department of Thoracic and Cardiovascular Surgery, Cleveland Clinic, Cleveland, Ohio; [c]Advent Health Transplant Institute, AdventHealth Orlando, Orlando, Florida; [d]Division of Cardiothoracic Surgery, Emory University School of Medicine, Atlanta, Georgia; [e]Cardiovascular Institute at Allegheny Health Network, Pittsburgh, Pennsylvania; and the [f]Division of Cardiac Surgery, Massachusetts General Hospital, Boston, Massachusetts.

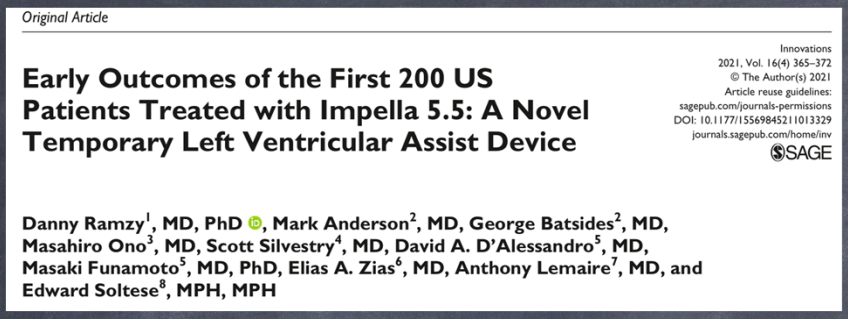
JHLT 2023

- Impella 5.0 vs 5.5 for acute MI shock, cardiomyopathy, post cardiotomy shock
- 1238 patients in Impella Quality (IQ) registry
- 290 US centers, Oct 2019- Dec 2020

26

- Impella 5.5- higher survival for all indications **WAHOO IMPELLA 5.5!**
- Higher percentage 5.5 CM patients bridged to transplant
- Impella 5.5 patients had higher rate of successful weaning in PCCS
- Duration of support longer with 5.5 in AMICS (9.2 d vs 6.1d) and CM (10.7d vs 8.1d)
- Lower hemolysis with 5.5 CM patients (?no more pigtail, easier repositioning)

27



Original Article

Early Outcomes of the First 200 US Patients Treated with Impella 5.5: A Novel Temporary Left Ventricular Assist Device

Innovations
2021, Vol. 16(4) 365–372
© The Author(s) 2021
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/15569845211013329
journals.sagepub.com/home/inv
SAGE

Danny Ramzy[1], MD, PhD, Mark Anderson[2], MD, George Batsides[2], MD, Masahiro Ono[3], MD, Scott Silvestry[4], MD, David A. D'Alessandro[5], MD, Masaki Funamoto[5], MD, PhD, Elias A. Zias[6], MD, Anthony Lemaire[7], MD, and Edward Soltese[8], MPH, MPH

- IQ registry retrospective analysis, October 2019 to MArch 2020
- 200 patients at 42 centers
- CM, AMICS, PCCS
- 88% via right axillary artery, 6% left ax, 6% aorta
- Median duration support 10 d (0.001 to 64.4 d)
- 35 patients (17%)- ECPELLA

28

- 5 patients (2.5%) adverse event
  - Bleeding - 4 (hematoma 2, anastomosis 1, GI 1)
  - CVA - 1 (LV thrombus, VT, shocks)
- 74% weaned or bridged (ie. survived)
- 19% died/withdrawal of care (almost half of these-ECPELLA)

- GOOD OUTCOMES, LOW COMPLICATION RATES

29

Impella 5.5 - Bridge to Transplantation

OPTIMIZE!!!

- End organ dysfunction
- Pulmonary hypertension
- Reduction in vasoactives
- Mobilization potential
  - NO GROIN
- Prolonged use/support
  - Facilitate workup/buys time
- Status 2….

30

UNOS Listing Criteria Change

1999-2018

Status 1A
- Admitted with TAH/ IABP/ ECMO
- LVAD with complications
- Continuous ventilation
- Continuous single or multiple inotropes requiring hemodynamic monitoring
- Dischargeable LVADs for 30 days

October 2018

Status 1
- ECMO (up to 7 days)*
- Non-dischargeable surgically implanted VAD
- MCSD with life threatening ventricular arrhythmia

Status 2
- Intra-aortic balloon pump (up to 14 days)*
- Sustained Ventricular tachycardia/ventricular fibrillation
- Non-dischargeable, surgically implanted, non-endovascular LVAD (up to 14 days)*
- MCSD with device malfunction/ mechanical failure
- Total artificial heart
- Dischargeable BiVAD or RVAD
- Acute endovascular percutaneous circulatory support (up to 14 days)*

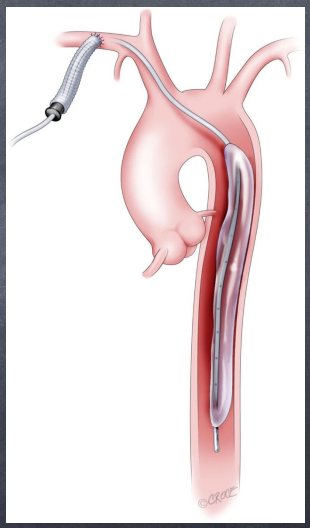
Status 3
- Dischargeable LVAD for up to 30 days
- Multiple inotropes or single high dose inotropes with continuous hemodynamic monitoring
- MCSD with device infection, hemolysis, pump thrombosis, right heart failure, mucosal bleeding, and aortic insufficiency
- ECMO after 7 days or any other temporary MCSD after 14 days

Nallamothu et al, Circ outcomes 2020

31

[Sidebar- Axillary IABP]

- Alternative bridging strategy
  - Status 2
- Less hemodynamic support than impella 5.5
- Allows mobilization
- Positioning issues…
- Specific populations
  - NB mechanical aortic valve, LV thrombus, severe AS etc.



32

Clin Transplant. 2023 Jul 1;e15066. doi: 10.1111/ctr.15066. Online ahead of print.

Impella 5.5 as a bridge to heart transplantation: Waitlist outcomes in the United States

Marisa Cevasco [1], Max Shin [2], William Cohen [2], Mark R Helmers [1], Noah Weingarten [1], David Rekhtman [2], Joyce W Wald [3], Amit Iyengar [1]

- UNOS Database
- Sept 2019 (FDA Approval)-Dec 31, 2021
- 464 patients
- Impella 5.5 at any time while on wait list
- 54% DCM, 23% ICM

75% Status 2
13% status 1

33

- Median time on wait list: 19 days
  - 10 d if listed with impella
  - 37 days if added later
- Median duration of support 16 days

- 86.8% transplanted
  - 96% BTT directly
  - 3.8% device removed prior to txp
    - 11 patients - device failure, 4 patients- LVAD

34

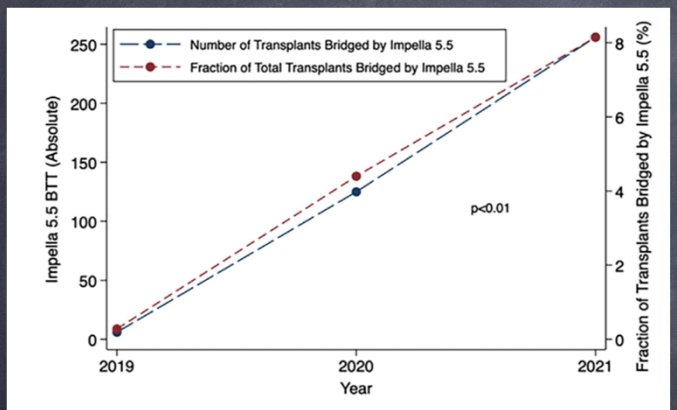


FIGURE 1 Trends in use of Impella 5.5 as a bridge to transplant.

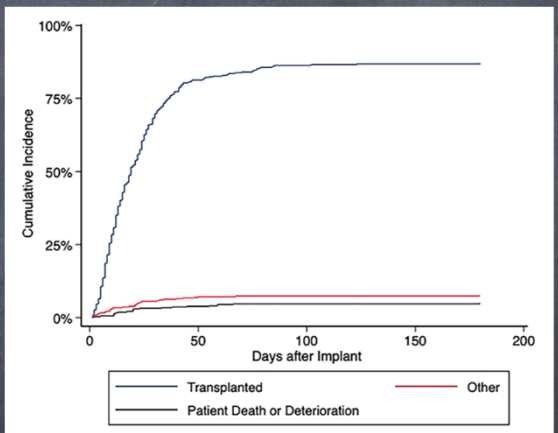


FIGURE 2 Composite waitlist outcomes in patients supported by Impella 5.5.

35

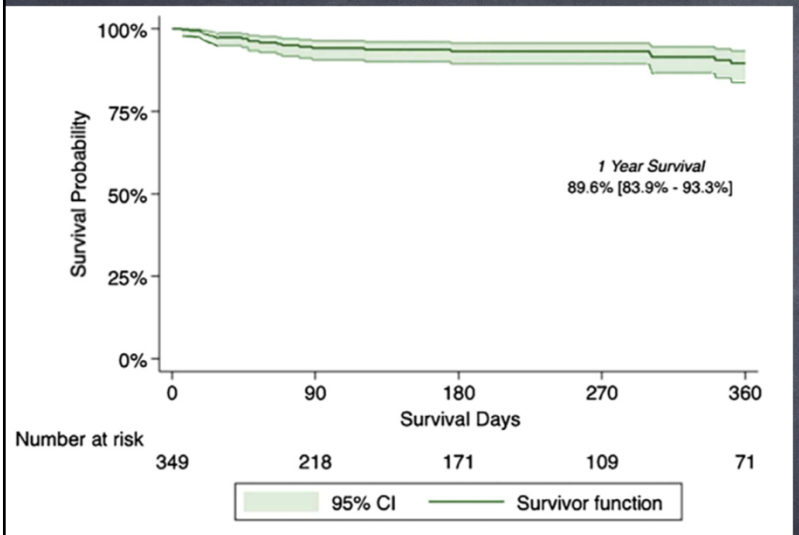


FIGURE 4 Post-transplant survival of patients bridged by Impella 5.5.

Excellent 1 year survival
Low rates of complications

TABLE 4 Post-transplant complications among patients bridged with Impella 5.5.

Complication	Total (%)
Acute Kidney Injury requiring Dialysis	55 (15.7)
Stroke	14 (4.0)
Pacemaker	3 (.9)
Acute rejection episode	21 (4.5)

36

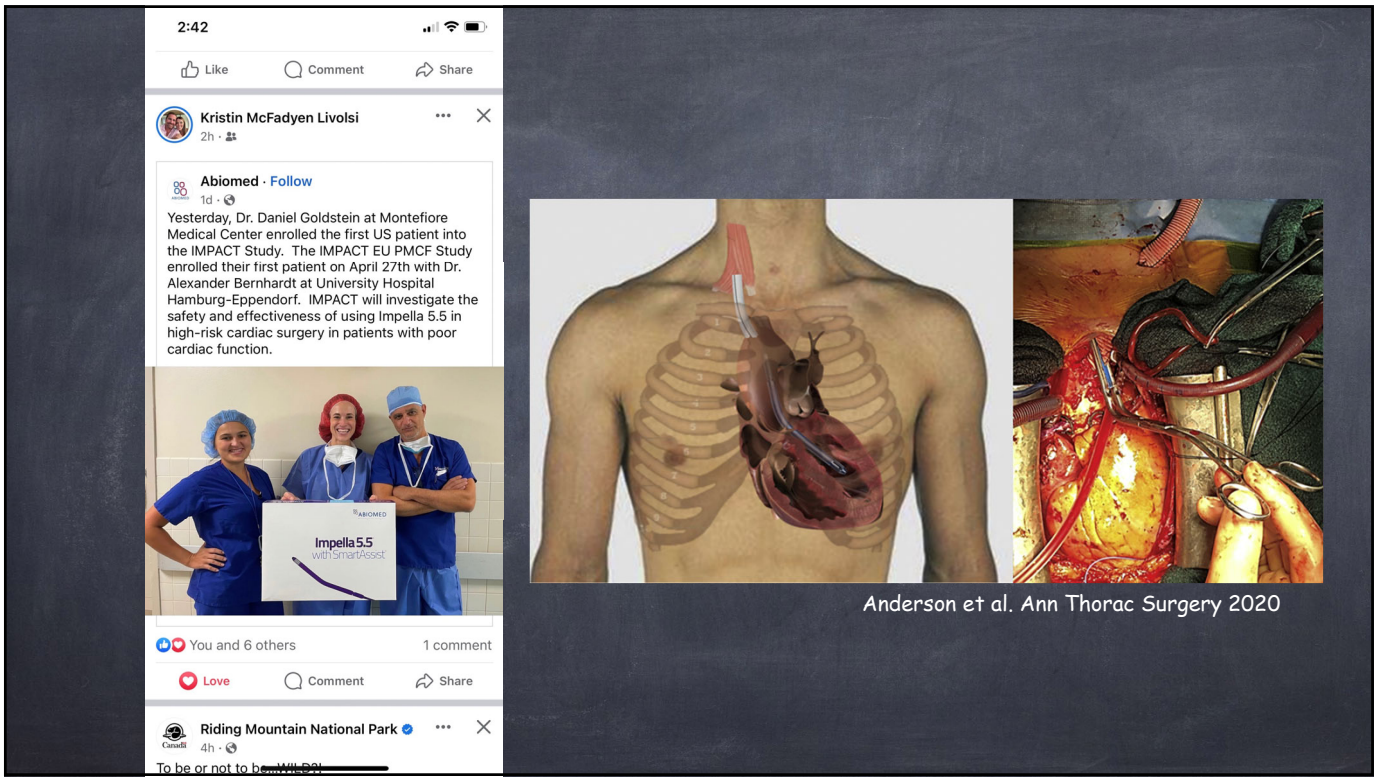
WORLD RECORD IMPELLA 5.5 RUN:
269 DAYS (SINGLE DEVICE) BTT IN FLORIDA!

37

Direct Aortic Impella

- Post cardiotomy cardiogenic shock
- Low EF cardiac surgery - planned implantation
- FDA approved implant technique and use.
- Provides significant hemodynamic support in periop period
- Avoid open chest, return to OR for removal (bedside ICU)

38



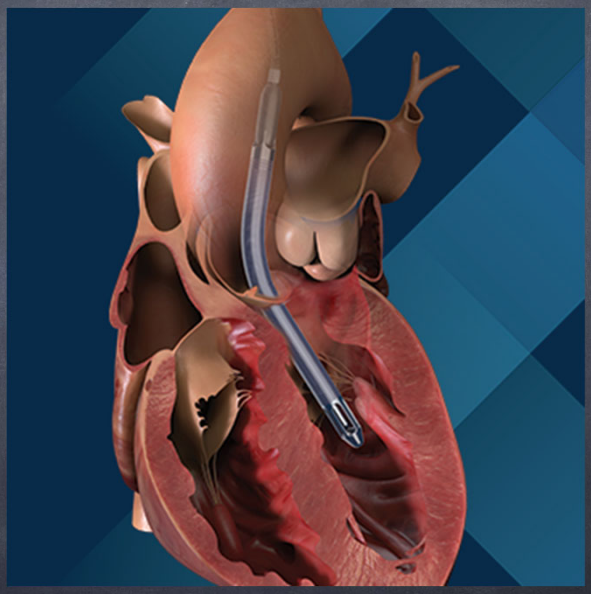
39

Contraindications to Impella

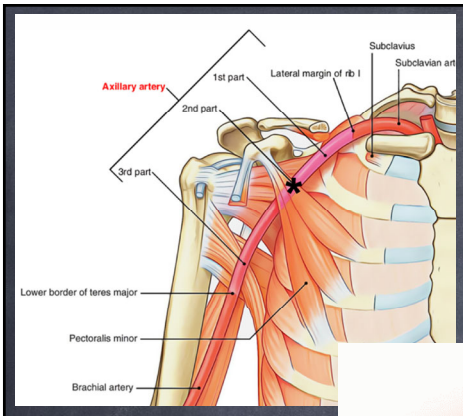
- Mural thrombus in LV
- Mechanical AV or heart constrictive device
- Aortic stenosis/calcification (EOA < 0.6cm2)
- Mod-severe AI
- Severe arterial disease precluding placement
- Significant RHF
- LV rupture
- Tamponade
- Combined cardio respiratory failure
- ASD [or VSD (including PIVSD)]

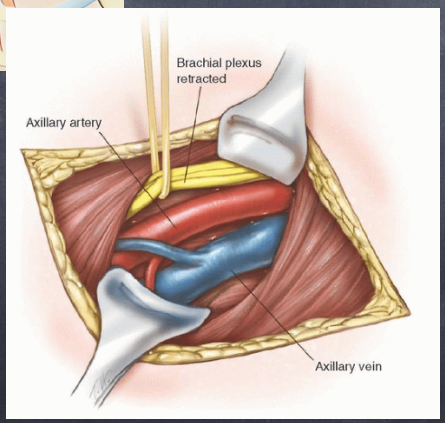
40

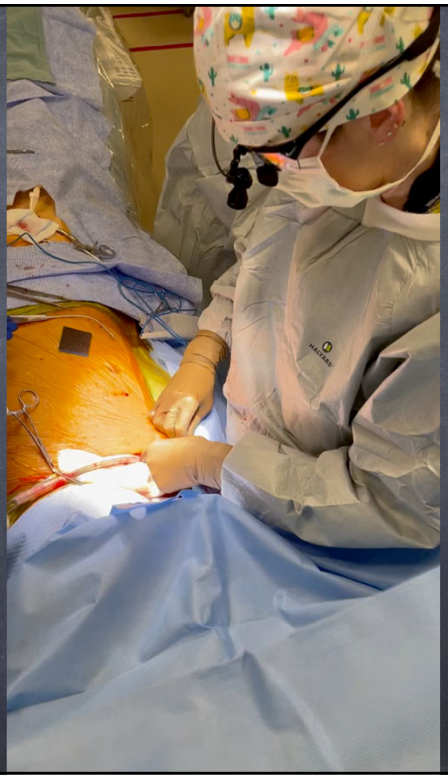
Our case - Impella 5.5 Insertion



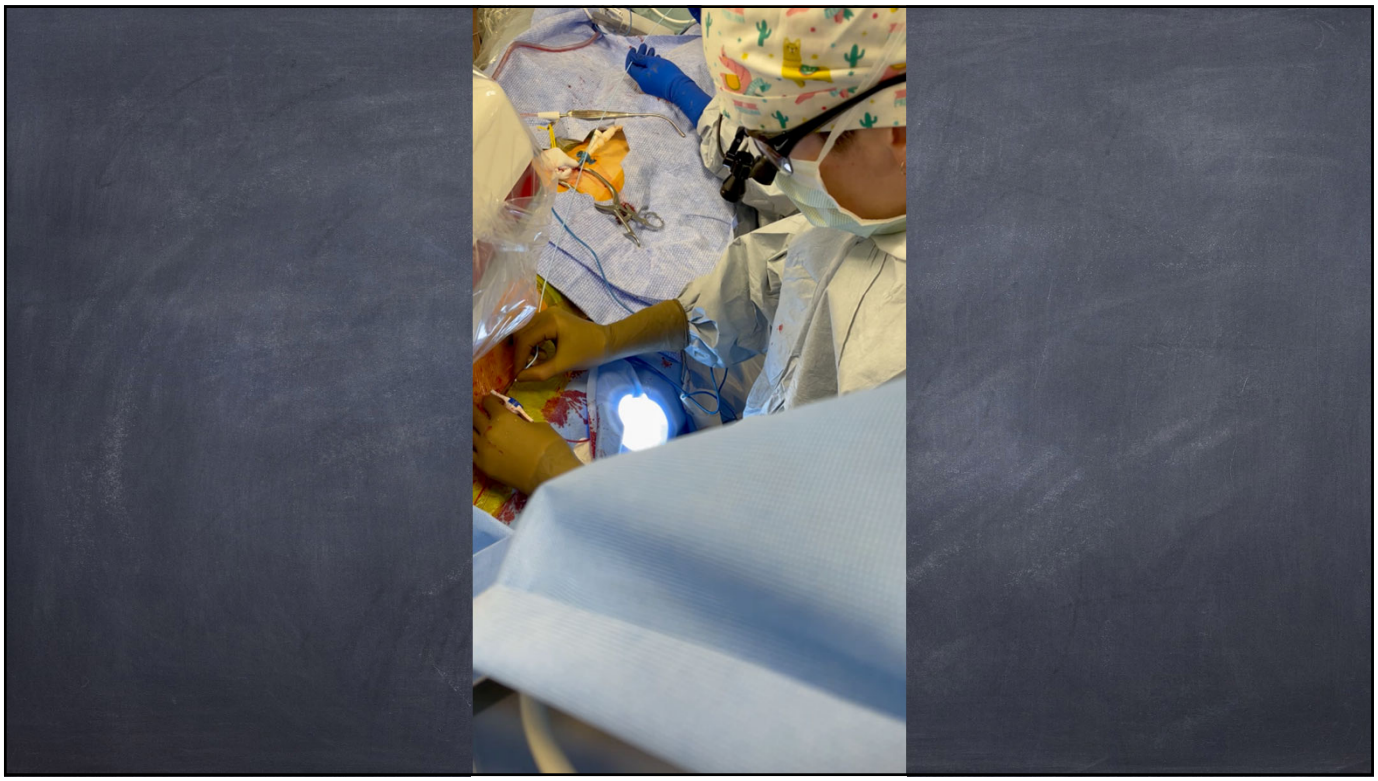
41



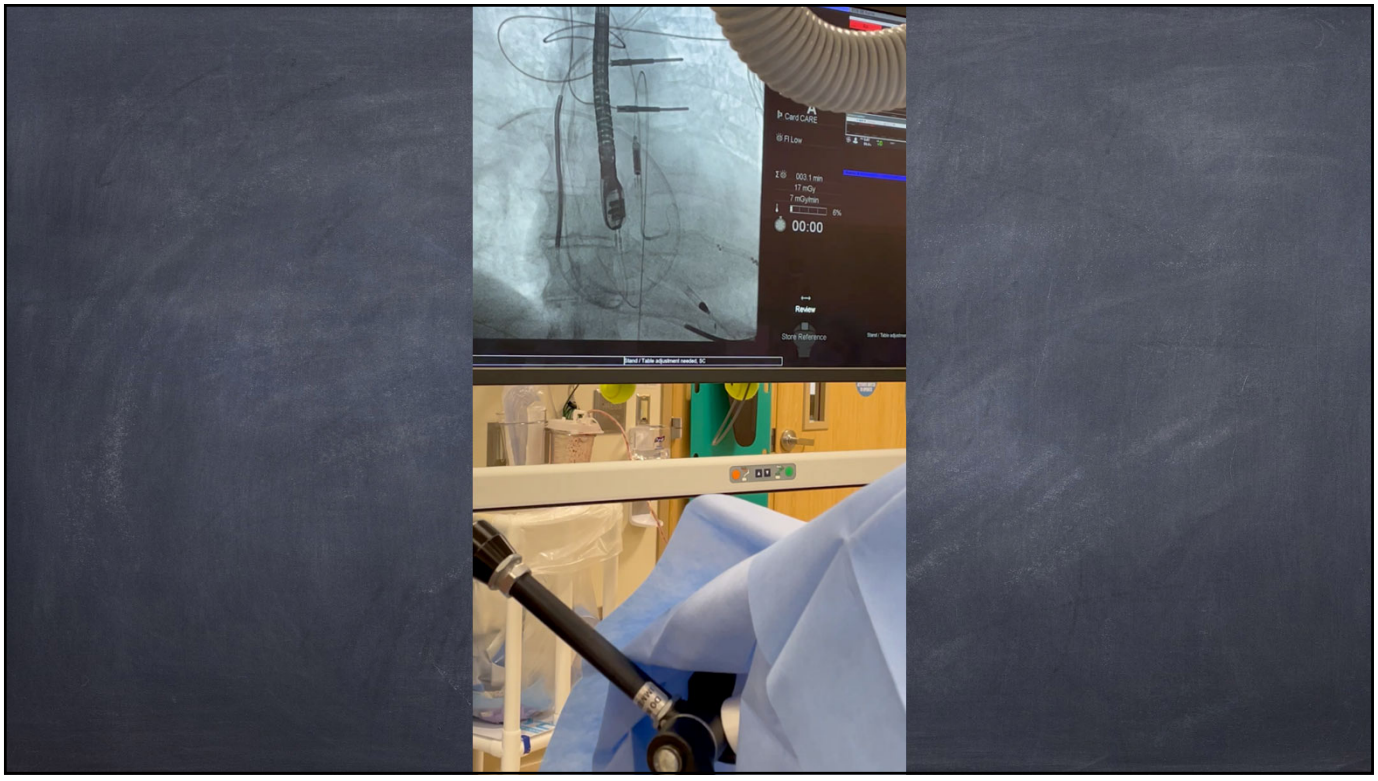




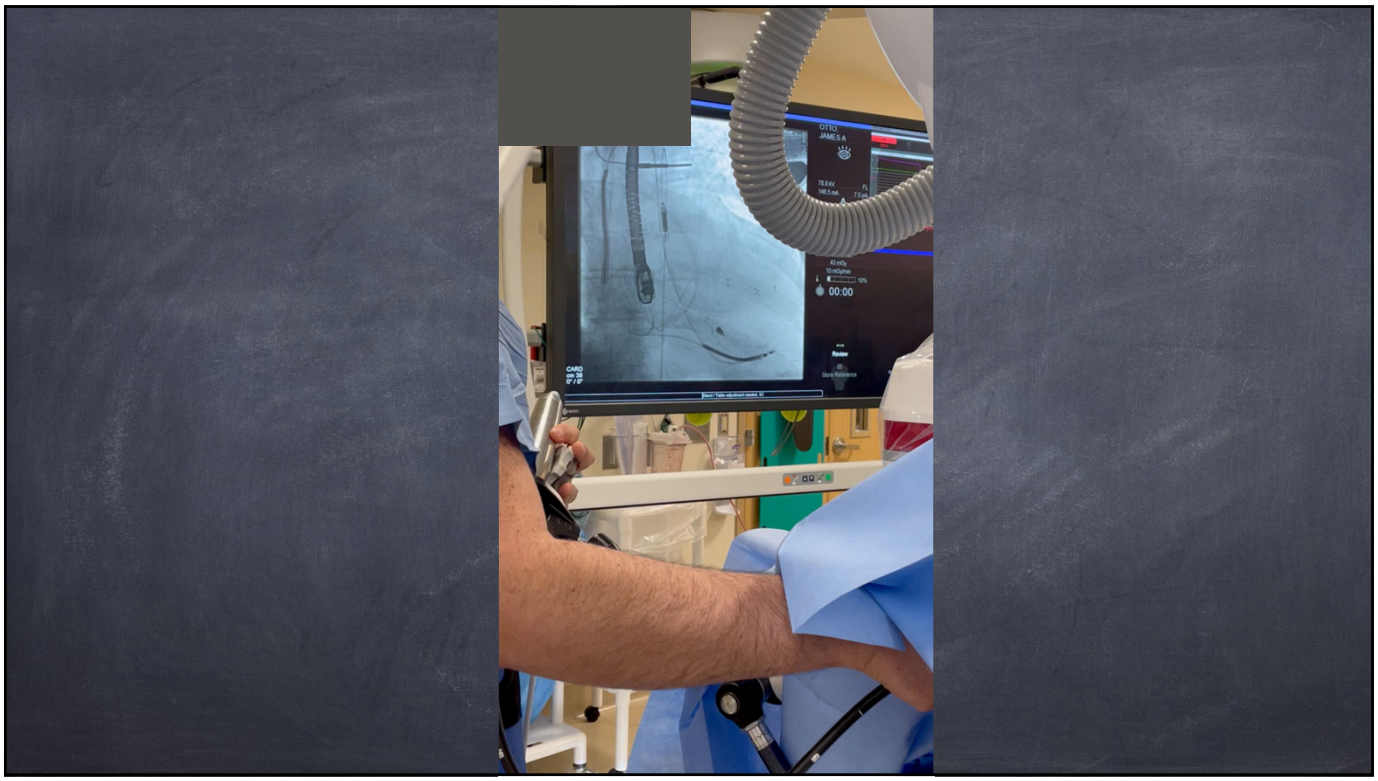
42



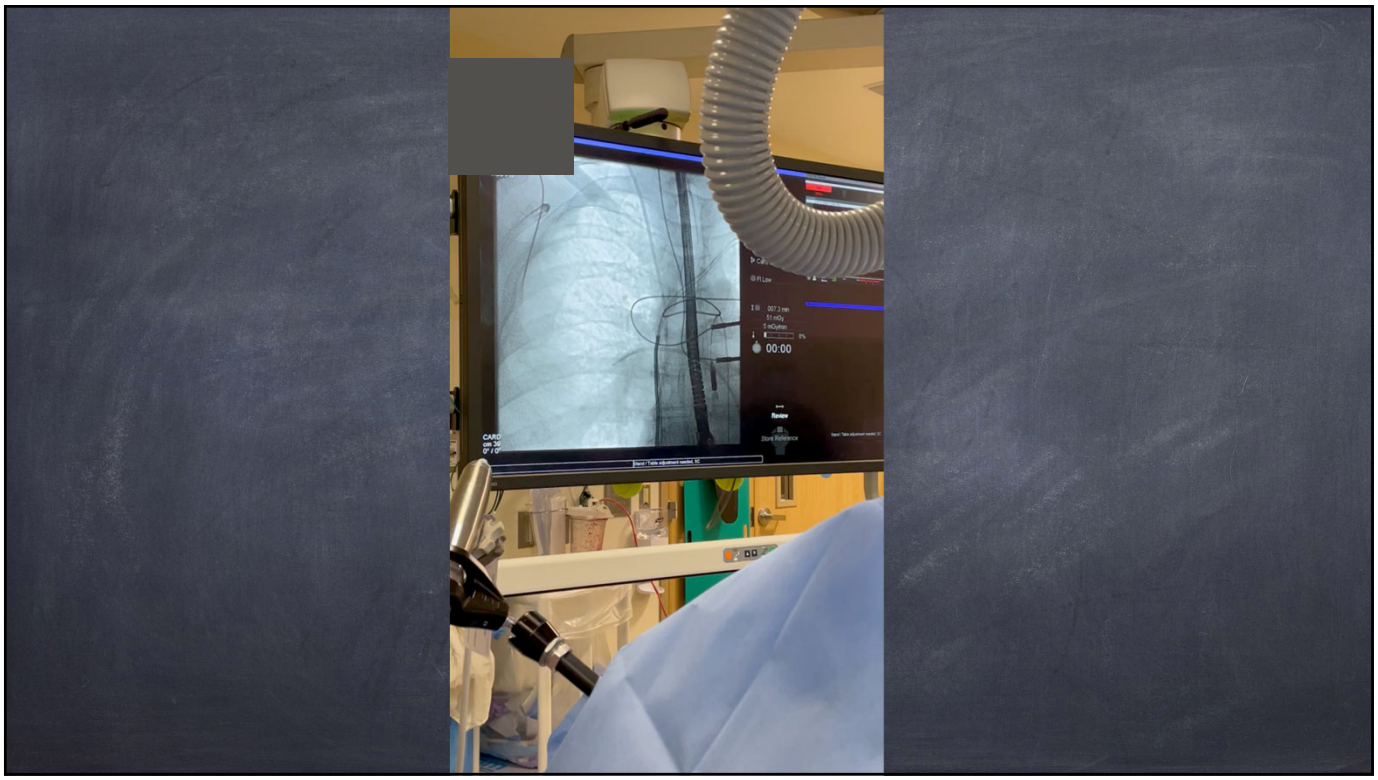
43



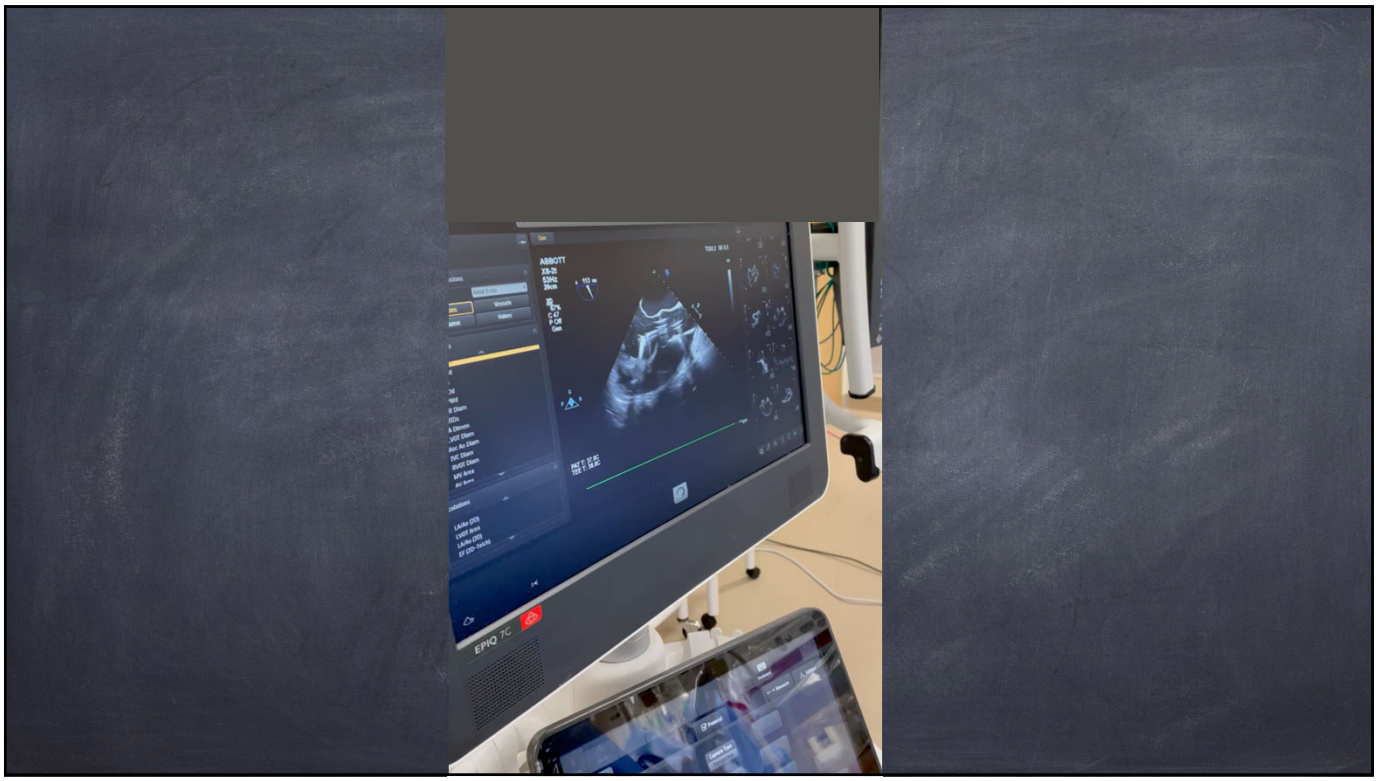
44



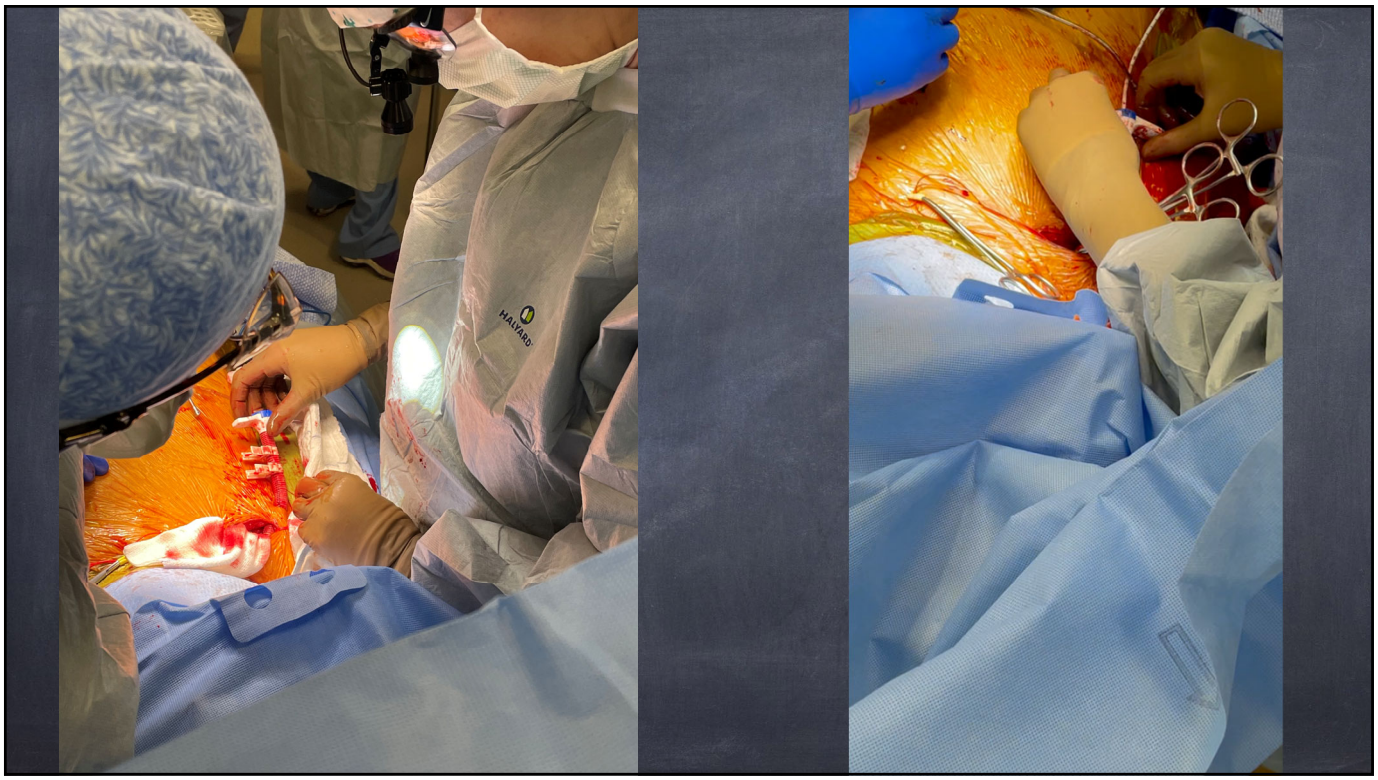
45



46



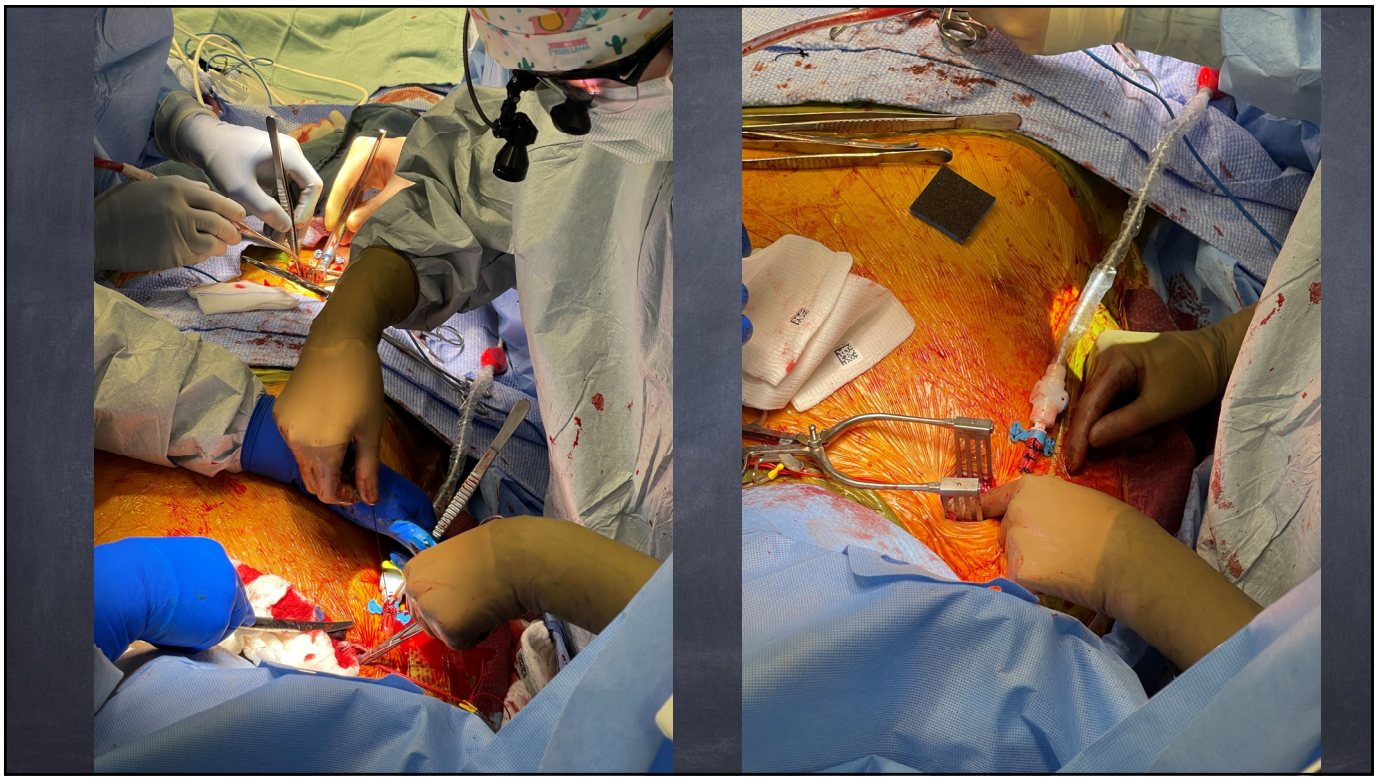
47



48

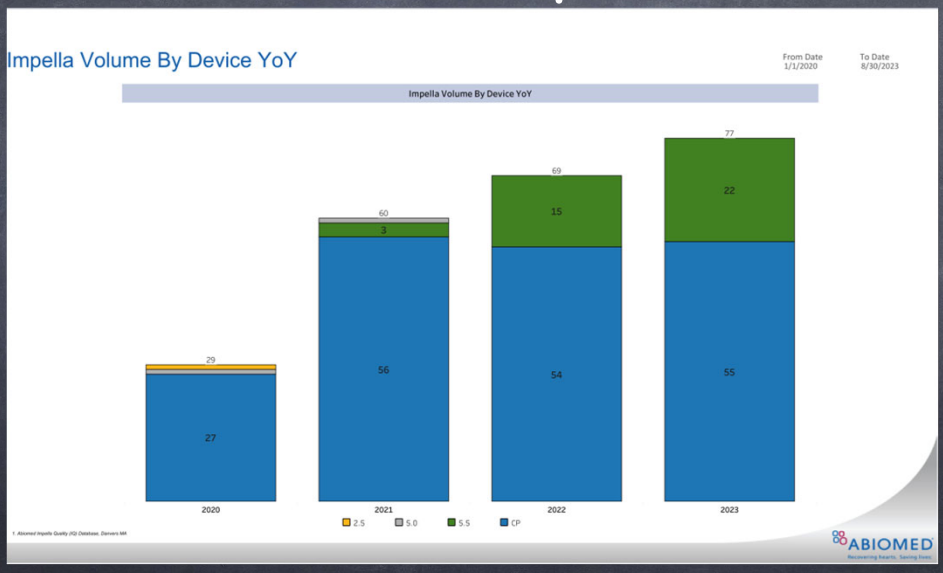

Frozen
ABBOTT
X8-2t
53Hz
20cm
Vessels
Valves
PAT T: 37.0C
TEE T: 39.0C
Dist 4.66 cm

49



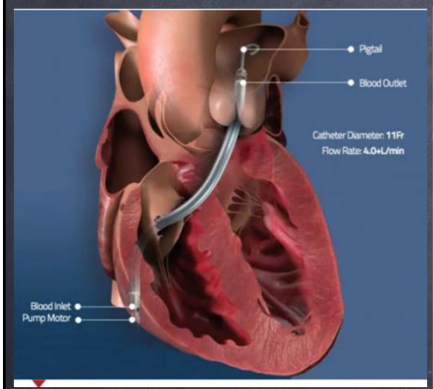
50

ANW and Impella 5.5

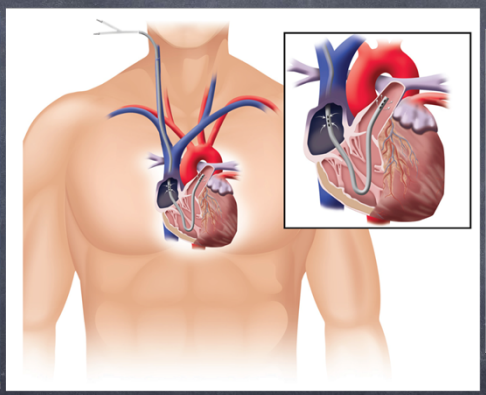


51

What about the right side?

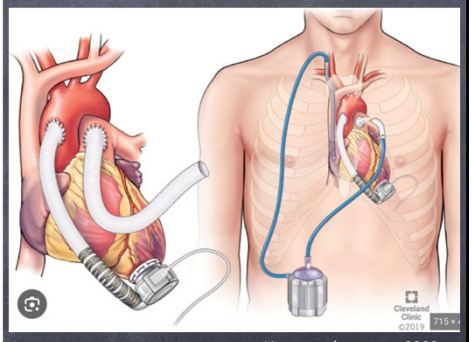


Impella RP



Kazui et al. J Cardiothorac Surg 2016

Protek Duo



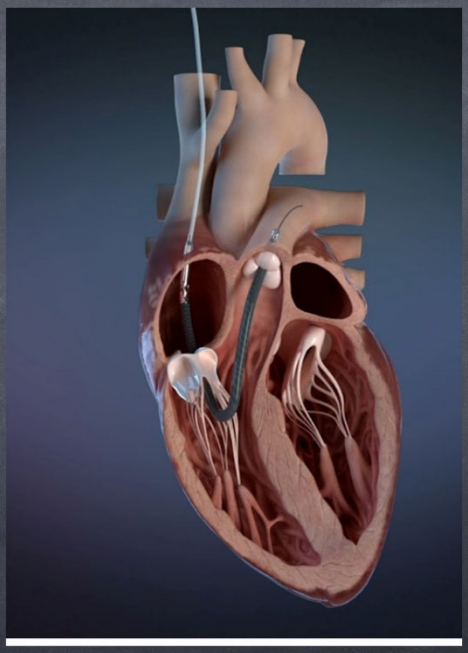
Vargo et al sem ctvs 2020

Centrimag

52

Impella RP FLEX

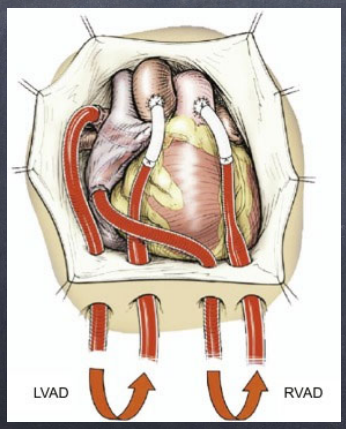
Coming soon…

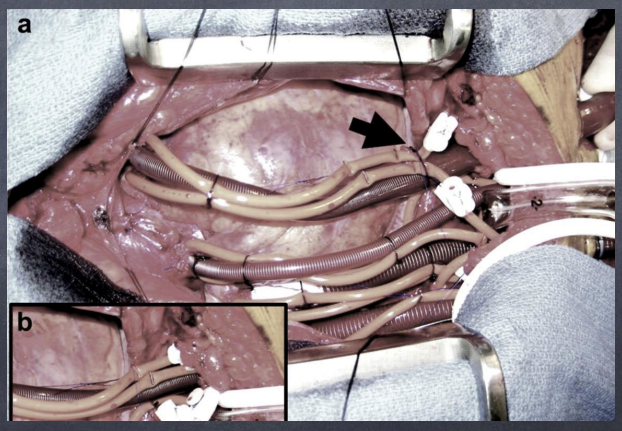


53

BIVADS

- Centrimag- historically





Perfusion.com

54

A new era of BIVADS

- BIPELLA
  - Impella CP/5.5 + Impella RP
- Impella 5.5/Protek

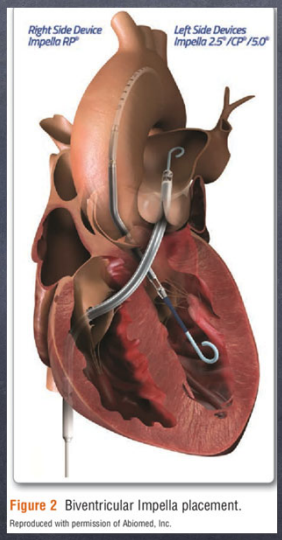
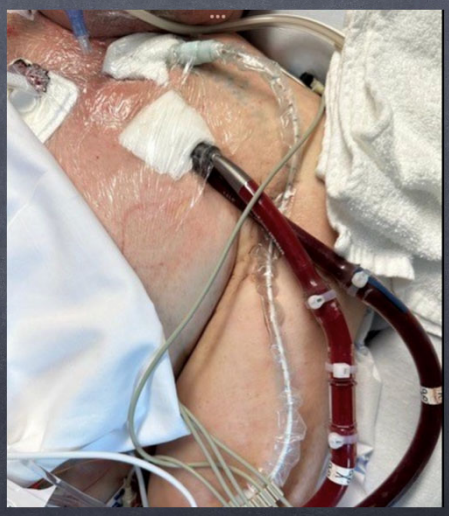


Figure 2 Biventricular Impella placement.
Reproduced with permission of Abiomed, Inc.



55

Advanced Heart Failure Therapies:

Durable Options

56

Advanced Heart Failure Therapies: A Bridge to…Durable LVADs

ABBOTT HEARTMATE 3

57

Medtronic Heartware HVAD

- Biggest competition for Heartmate 3 until….

Medtronic HVAD™ System

Medtronic has stopped the distribution and sale of the HVAD™ system as of June 3, 2021, and has notified physicians to cease new implants of the Medtronic HVAD™ system and transition to an alternative commercial LVAD for all future implants.

Indications, Safety, and Warnings

ProductDetails

58

FDA Activities Related to the HVAD System

Date	Event
August 25, 2022	The FDA issued a recall notice indicating the FDA classified the June 2022 recall related to the increase in battery electrical faults due to an interaction between the battery software and an internal component as Class 1.
June 23, 2022	The FDA issued a recall notice indicating the FDA classified the May 2022 recall related to a welding defect affecting internal HVAD Battery components from a single lot as Class 1.
June 10, 2022	The FDA issued a recall notice indicating the FDA classified the April 2022 recall related to actions to alert healthcare providers to a possibility of a weld defect in the internal pump as Class 1.
April 28, 2022	The FDA issued a letter to health care providers to alert health care providers to the possibility that patients who have the Medtronic HVAD System and appear to present with pump thrombosis may have a weld defect in the internal pump causing the pump to malfunction.
August 12, 2021	The FDA issued a recall notice indicating the FDA classified the June 3, 2021 actions to stop the sale and distribution of the HVAD System as Class 1.
June 3, 2021	The FDA issued a letter to health care providers stating that Medtronic has stopped the sale and distribution of the Heartware Ventricular Assist Device (HVAD) System because: • There is an increased risk of neurological adverse events and mortality associated with the internal pump. • There is a potential for the internal pump to stop. If the internal pump stops, it may delay restarting or fail to restart.

Multiple Recalls:
- Batteries
- Failure to restart
- Auto log issues

59

So now what?

- How to improve upon HM3?
  - Driveline infection
  - External power source

<u>FILVAS??</u>

60

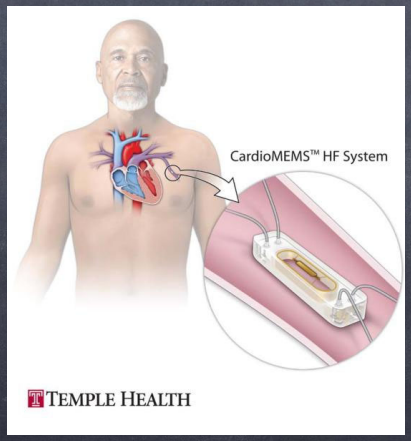
The Road to FILVAS

- Engineering hurdles
  - How to make efficient?
  - Temperature issues
- Multiple acquisitions
- How do we get there?

61

Cardiomems + HM3

- Use of cardiomems for hemodynamic monitoring and optimization of the LVAD pre and post op



62

Check for updates

Circulation: Heart Failure

ORIGINAL ARTICLE

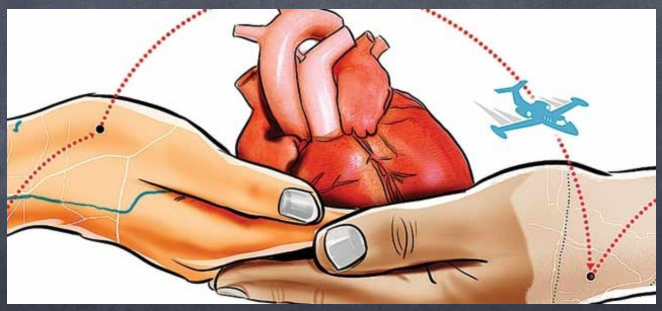
Use of a Pulmonary Artery Pressure Sensor to Manage Patients With Left Ventricular Assist Devices

Vinay Thohan, MD; Jacob Abraham, MD; Adam Burdorf, DO, MS; Nasir Sulemanjee, MD; Brian Jaski, MD; Maya Guglin, MD, PhD; Francis D. Pagani, MD, PhD; Himabindu Vidula, MD, MS; David T. Majure, MD, MPH; Rebecca Napier, MD; Thomas J. Heywood, MD; Rebecca Cogswell, MD; Nicholas Dirckx, MPH; David J. Farrar, PhD; Stavros G. Drakos, MD, PhD; on behalf of the INTELLECT 2-HF Investigators*

- HM2/HM3 + Cardiomems
- Reduction in PAD at 6 mo, improved 6mwt, if PAD < 20mm = less heart failure hospitalizations
- Feasible, functional and clinical benefits.

63

Advanced Heart Failure Therapies: A Bridge to… Heart Transplantation



Kauveryhospital.com

64

Donor Heart Management: Machine Perfusion

- Revolutionizing donor heart management
- Expanding the donor pool
- Improving transport over longer distances

65

Remember - Two Types of Donors!

DBD- Donation after Brain Death

DCD- Donation after Circulatory Death

66

Donor Type - DBD vs DCD

DBD- They must be confirmed brain dead!!

ADULT BRAIN DEATH DETERMINATION

BRAIN DEATH CRITERIA

- **Definition: "Irreversible cessation of all brain function, including the brain stem"**
- Evaluate and correct potentially reversible causes of abnormal neurological evaluation:
  - Absence of hypotension/shock, hypothermia, metabolic disturbances, significant drugs or medications known to cause CNS unresponsiveness
- Determination is to be made by a physician specialist during a recommended observation period of at least 6 hours
- Confirmatory studies and apnea test must be performed by a specialist
- Injuries or injuries that may result in non-survivable neurological injuries:
  - Head Trauma
  - Cerebrovascular accident (embolic or hemorrhagic)
  - Localized brain tumor
  - Cerebral anoxia 2° drowning, smoke inhalation, or prolonged cardiac arrest

St Luke's

BRAIN STEM REFLEX TESTING

- **No Pupillary** reflex
- **No Corneal** reflex
- **No Oculocephalic** (doll's eyes) reflex
- **No Oculovestibular** (cold or iced calorics) reflex
- **No Pharyngeal** and **laryngeal** reflexes (cough and gag)
- No Response to **painful stimuli** *(excluding spinal cord reflexes)*

APNEA TESTING

- Pre-oxygenate with 100% FIO_2 for 20 minutes
- Normalize $PaCO_2$, draw baseline ABG
- Disconnect ventilator and provide passive O_2 via cannula @ 8-12 L/min-Observe for spontaneous breathing
- Draw ABG at 5 and 10 minute intervals; conclude test when a $PaCO_2 \geq 60$ mmHg is obtained or if patient becomes hemodynamically unstable*
- Reconnect the ventilator. Test is consistent with brain death if $PaCO_2 \geq 60$ mmHg (or 20 mmHg greater than baseline), and there is no breathing.

***If patient becomes hemodynamically unstable, immediately draw ABG and reconnect the ventilator. Consider other confirmatory tests.**

67

Donor Type - DCD

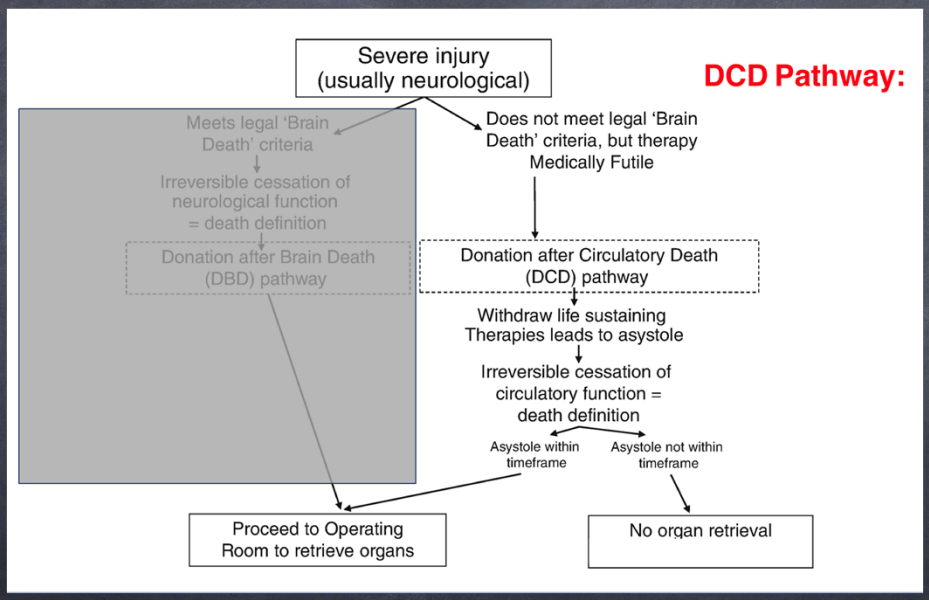
- Modified Maastricht criteria for donation after cardiac death

	Sub-category	Description
Category I—Found dead (Uncontrolled)	IA	Unexpected cardiac arrest out of hospital without attempted resuscitation
	IB	Unexpected cardiac arrest in hospital without attempted resuscitation
Category II—Witnessed cardiac arrest (Uncontrolled)	IIA	Unexpected cardiac arrest out of hospital with unsuccessful resuscitation
	IIB	Unexpected cardiac arrest in hospital with unsuccessful resuscitation
Category III—Withdrawal of life support (Controlled)		Expected, planned cardiac arrest after withdrawal of care
Category IV—Cardiac arrest whilst brain dead (Uncontrolled, controlled)		Sudden cardiac arrest following brain death but prior to planned organ recovery

Categories used to classify donation following cardiac death (22).

68

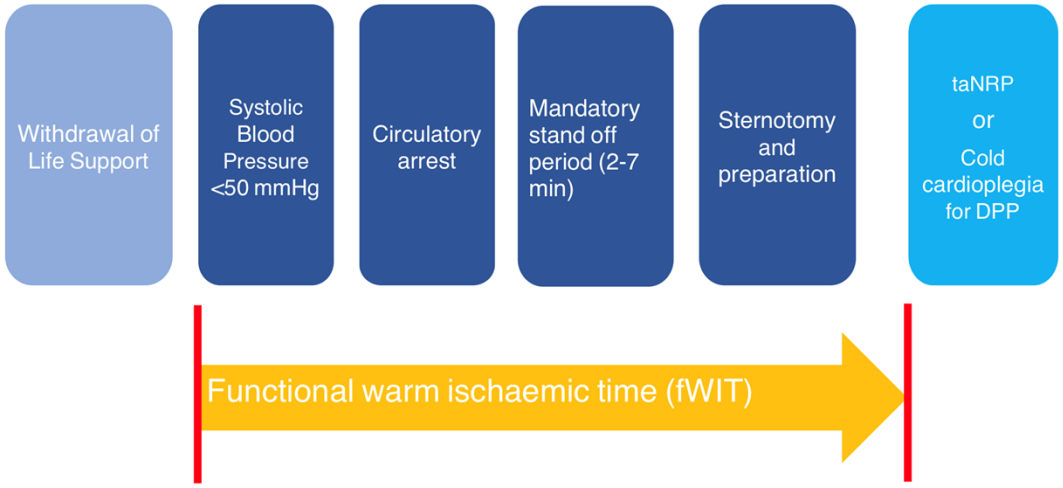
DCD Organ Donation



Courtesy of Jacob N. Schroder

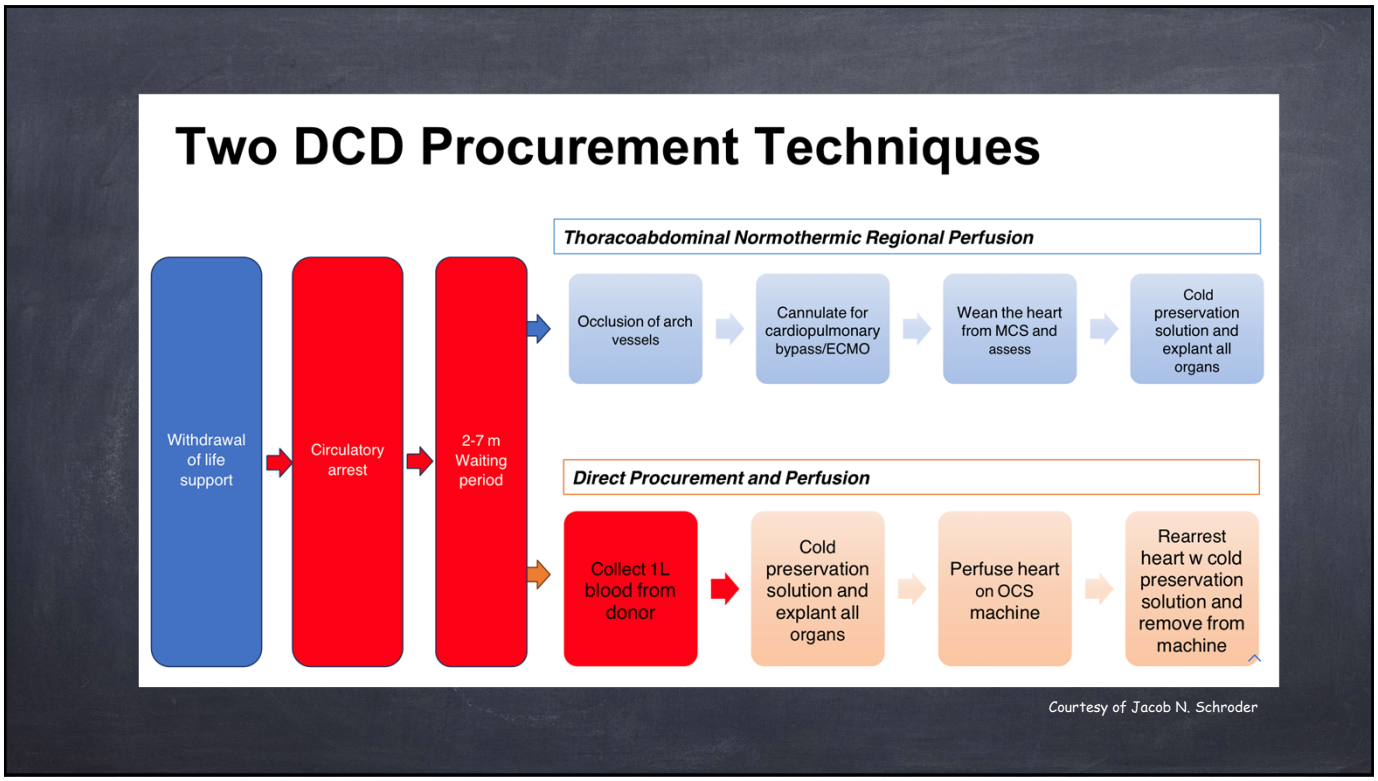
69

Functional Warm Ischemic Time (FWIT)

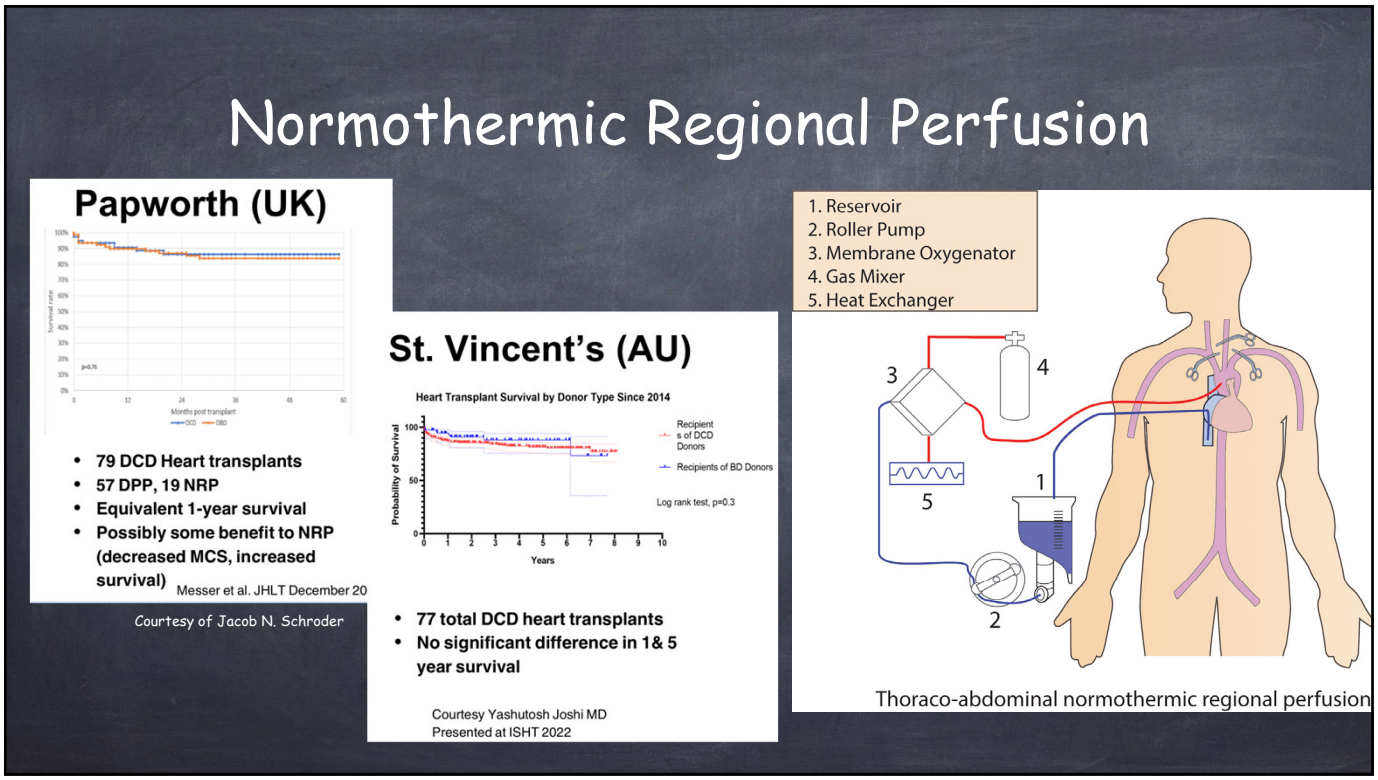


Courtesy of Jacob N. Schroder

70


Two DCD Procurement Techniques
Thoracoabdominal Normothermic Regional Perfusion
Withdrawal of life support
Circulatory arrest
2-7 m Waiting period
Occlusion of arch vessels
Cannulate for cardiopulmonary bypass/ECMO
Wean the heart from MCS and assess
Cold preservation solution and explant all organs
Direct Procurement and Perfusion
Collect 1L blood from donor
Cold preservation solution and explant all organs
Perfuse heart on OCS machine
Rearrest heart w cold preservation solution and remove from machine
Courtesy of Jacob N. Schroder

71


Normothermic Regional Perfusion
Papworth (UK)
79 DCD Heart transplants
57 DPP, 19 NRP
Equivalent 1-year survival
Possibly some benefit to NRP (decreased MCS, increased survival)
Messer et al. JHLT December 20
Courtesy of Jacob N. Schroder
St. Vincent's (AU)
Heart Transplant Survival by Donor Type Since 2014
Probability of Survival
Years
Recipients of DCD Donors
Recipients of BD Donors
Log rank test, p=0.3
77 total DCD heart transplants
No significant difference in 1& 5 year survival
Courtesy Yashutosh Joshi MD
Presented at ISHT 2022
1. Reservoir
2. Roller Pump
3. Membrane Oxygenator
4. Gas Mixer
5. Heat Exchanger
Thoraco-abdominal normothermic regional perfusion

72

The international experience of in-situ recovery of the DCD heart: a multicentre retrospective observational study

John Louca,[a,*] Marco Öchsner,[a] Ashish Shah,[b] Jordan Hoffman,[b] Alexandra Debose-Scarlett,[b] Francisco González Vilchez,[c] Iris Garrido,[d] Mario Royo-Villanova,[d] Beatriz Domínguez-Gil,[e] Deane Smith,[f] Leslie James,[f] Nader Moazami,[f] Filip Rega,[g] Janne Brouckaert,[g] Johan Van Cleemput,[g] Katrien Vandendriessche,[g] Vincent Tchana-Sato,[h] Diawara Bandiougou,[h] Marian Urban,[i] Alex Manara,[j] Marius Berman,[k] Simon Messer,[l] and Stephen Large,[k] on behalf of WISPG[m,n]

Journal of eClinical Medicine / the Lancet - April 2023

- 157 taNRP DCD vs 673 DBD
- 15 centers
- TaNRP- 23% increase in transplant activity
- Similar 30d, 1 year and 5 year survival
- TaNRP= effective organ preservation and procurement

73

Normothermic Regional Perfusion

- Advantages:
  - Continuous warm blood perfusion- restores heart function, reduces myocardial injury, promotes energy storage and maintains homeostasis
  - Visual assessment of heart for viability
  - Reduces warm ischemia
  - Equipment less cumbersome than OCS
  - ? Cheaper

74

Normothermic Regional Perfusion

- Disadvantages
  - Ethical debate- concern for 'reanimation'
    - ? Donors 'alive' at time of organ recovery since circulation re-established
  - Logistics can still be challenging, need perfusionists as well

75

Direct Procurement and Perfusion (DPP)

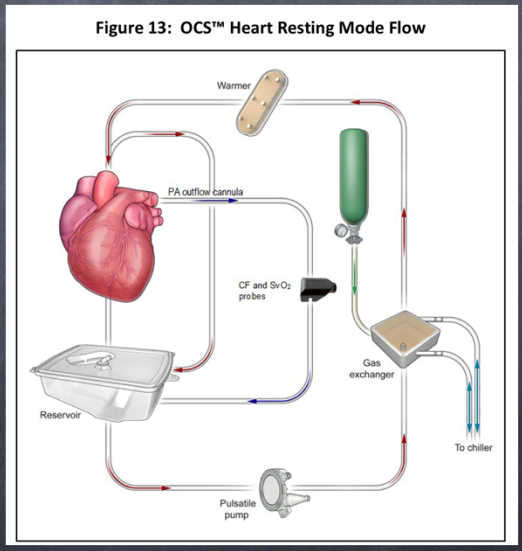
- Most commonly used device - Transmedics Organ Care System (OCS)
  - Cold preservation
  - Procurement (DCD OR DBD)
  - Preparation and placement on rig
  - Warm perfusion

76

Transmedics OCS

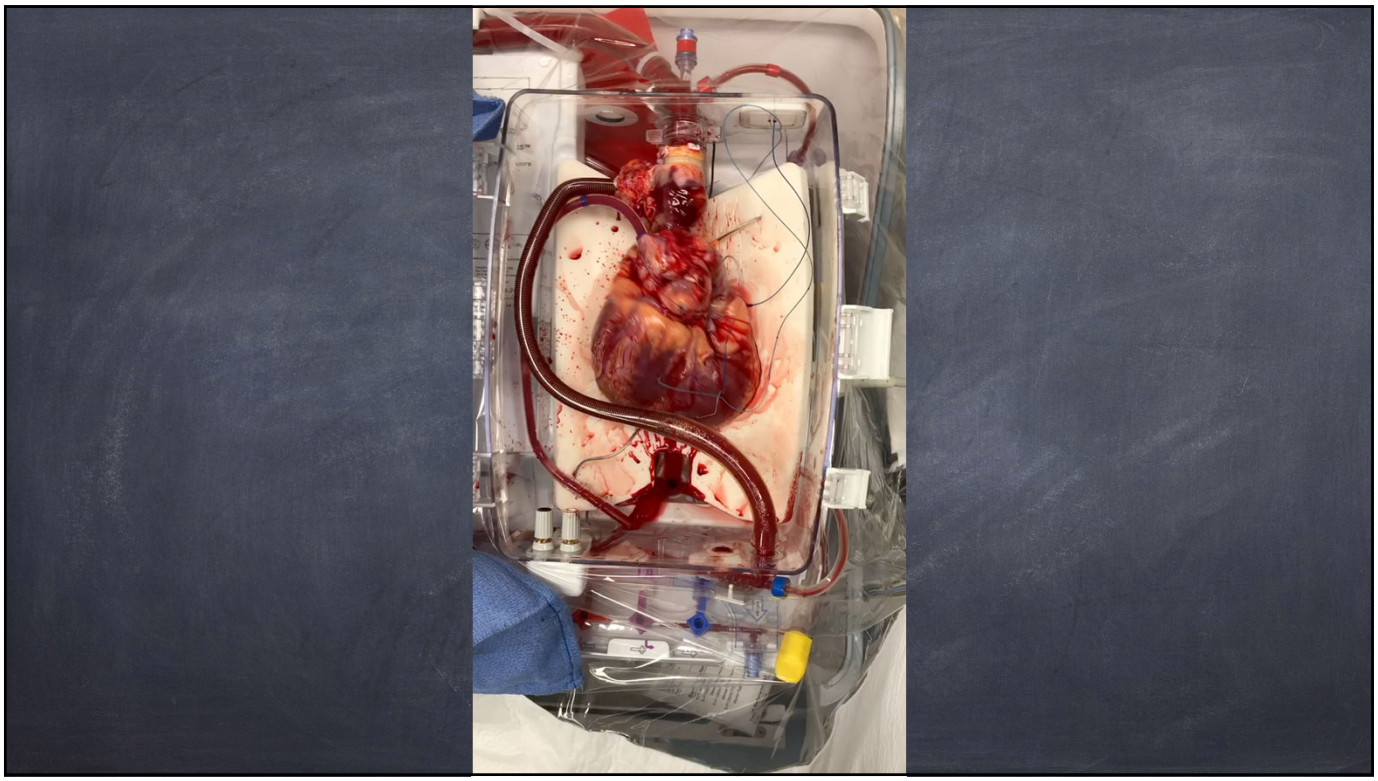
- Parameters
  - Aortic pressure
  - Flow
  - Coronary flow
  - Heart rate
- Metabolics - blood gas analysis, electrolytes

- Monitoring of cardiac function via arterial and venous lactates
  - Venous lactate higher = heart is secreting lactate



77

78



79

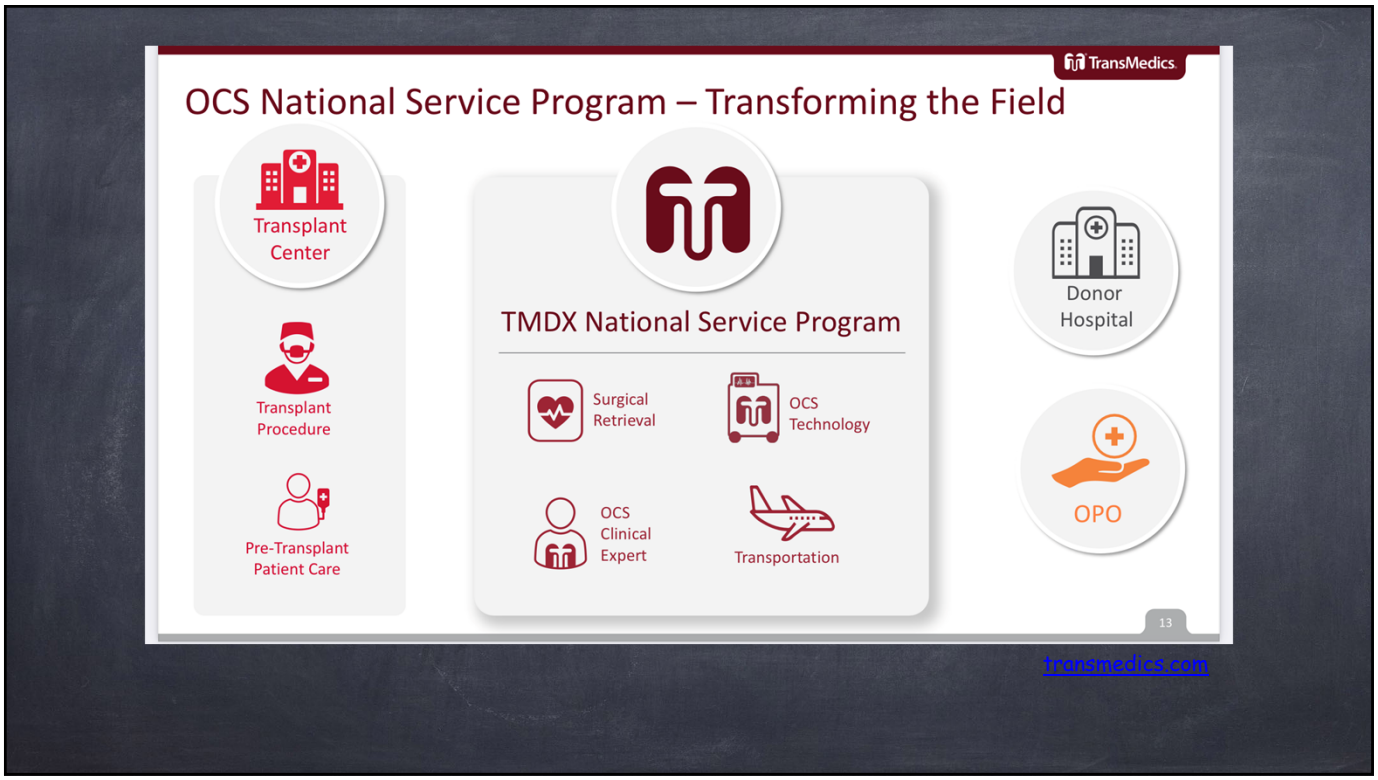
Transmedics OCS

- Advantages
  - Decreases ischemic time
  - Warm organ perfusion
  - Assessment of organ function
  - Expand organ utilization
  - Support for extended criteria donors
    - NB: Long ischemic times (9hours!)
- Disadvantages
  - COST - module + disposables
  - Equipment cumbersome- transport logistics
  - Need perfusionist/preservationist
  - Boggy hearts/RV dysfunction…

80


TransMedics
7 TM OCS Items:
- Rig
- Base
- Huge box
- Run bag
- Dolly
- Drug bag
- Cooler

81


TransMedics
OCS National Service Program – Transforming the Field
Transplant Center
Transplant Procedure
Pre-Transplant Patient Care
TMDX National Service Program
Surgical Retrieval
OCS Technology
OCS Clinical Expert
Transportation
Donor Hospital
OPO
13
transmedics.com

82

TransMedics
Bringing new life to organ transplant

TransMedics Signs Definitive Agreement to Acquire Summit Aviation to Expand TransMedics Aviation Capabilities for Organ Transplantation

Aug 1, 2023 at 11:00 AM EDT

Establishes the first national provider of air logistics dedicated to organ transplantation in the U.S.

ANDOVER, Mass., Aug. 1, 2023 /PRNewswire/ -- TransMedics Group, Inc. ("TransMedics") (Nasdaq: TMDX), a medical technology company that is transforming organ transplant therapy for patients with end-stage lung, heart, and liver failure, announced today that it has signed a definitive agreement to acquire Summit Aviation, a premier U.S. charter flight operator. The deal is expected to close in the third quarter of 2023, subject to the satisfaction of closing conditions. Upon closing, Ben Walton, Founder of Summit, will join TransMedics as VP of Aviation Services.

83

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 8, 2023 VOL. 388 NO. 23

Transplantation Outcomes with Donor Hearts after Circulatory Death

J.N. Schroder, C.B. Patel, A.D. DeVore, B.S. Bryner, S. Casalinova, A. Shah, J.W. Smith, A.G. Fiedler, M. Daneshmand, S. Silvestry, A. Geirsson, V. Pretorius, D.L. Joyce, J.Y. Um, F. Esmailian, K. Takeda, K. Mudy, Y. Shudo, C.T. Salerno, S.M. Pham, D.J. Goldstein, J. Philpott, J. Dunning, L. Lozonschi, G.S. Couper, H.R. Mallidi, M.M. Givertz, D.T. Pham, A.W. Shaffer, M. Kai, M.A. Quader, T. Absi, T.S. Attia, B. Shukrallah, B.C. Sun, M. Farr, M.R. Mehra, J.C. Madsen, C.A. Milano, and D.A. D'Alessandro

RCT: DCD (OCS) vs DBD (cold storage)

180 patients (90 / 90)
13 centres

84

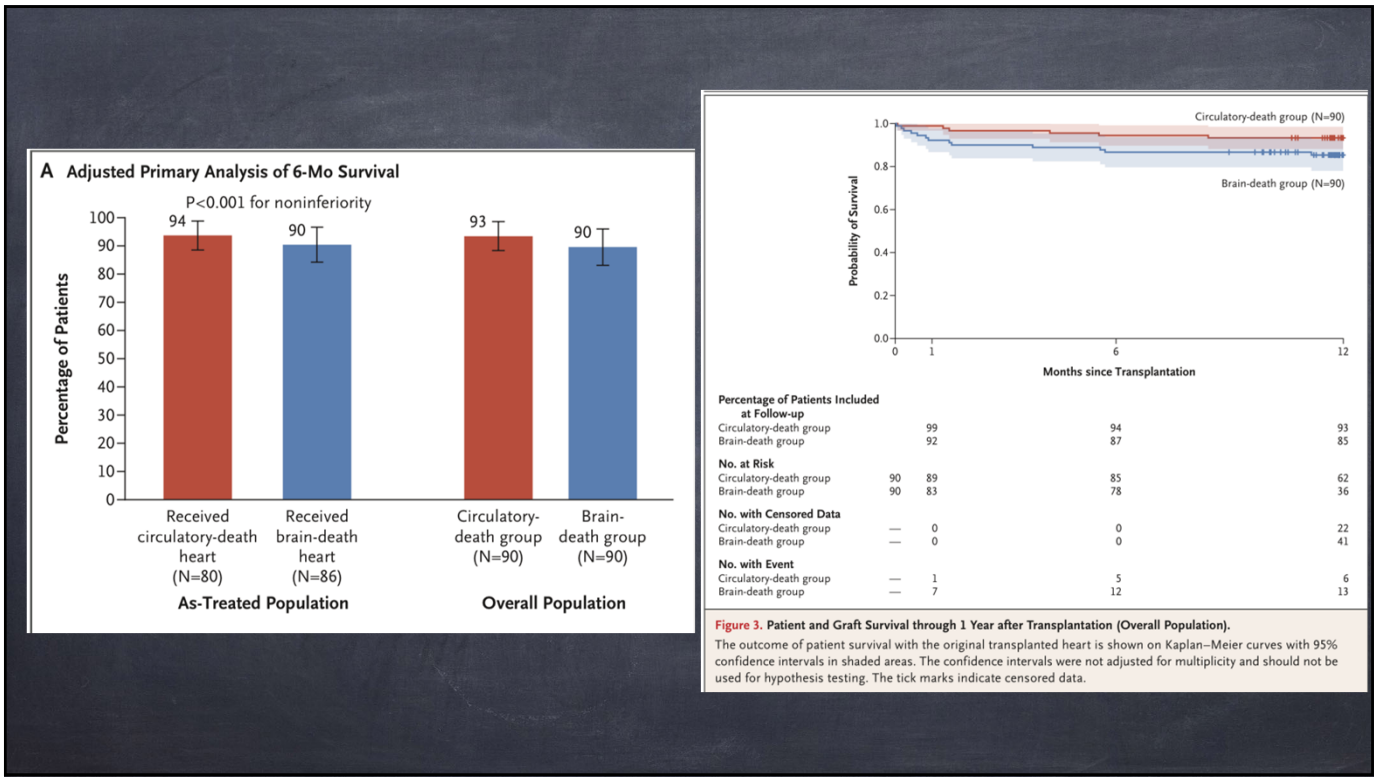


Figure 3. Patient and Graft Survival through 1 Year after Transplantation (Overall Population).
The outcome of patient survival with the original transplanted heart is shown on Kaplan–Meier curves with 95% confidence intervals in shaded areas. The confidence intervals were not adjusted for multiplicity and should not be used for hypothesis testing. The tick marks indicate censored data.

85

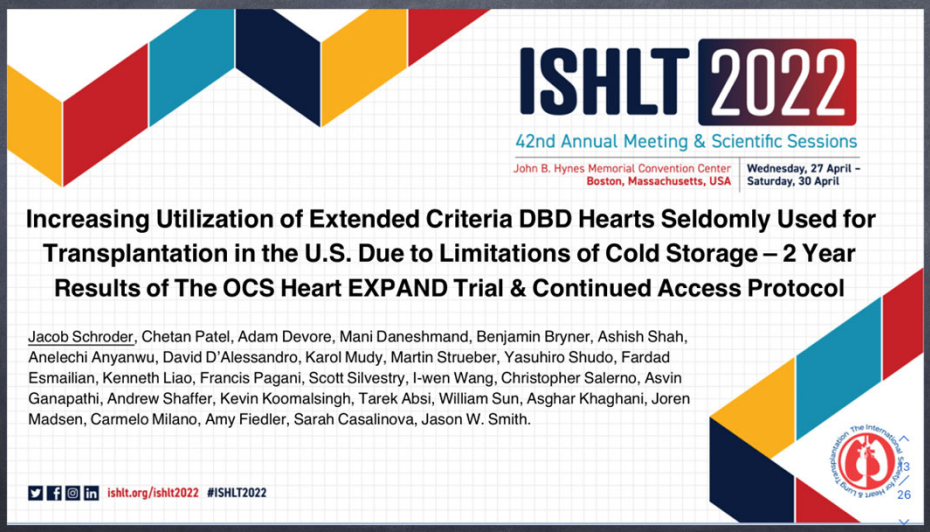
Table 2. Serious Adverse Events Associated with the Heart Graft in the 30 Days after Transplantation (As-Treated Population).*

Variable	Recipients of Heart from Circulatory-Death Donor (N=80)	Recipients of Heart from Brain-Death Donor (N=86)†
Occurrence per patient‡		
Mean (95% CI)	0.2±0.42 (0.1–0.3)	0.1±0.39 (0.0–0.2)
Median (range)	0 (0–1)	0 (0–2)
Primary graft dysfunction — no./total no. (%)		
Left or right ventricle, moderate or severe	18/80 (22)	8/84 (10)
Left ventricle, moderate	5/80 (6)	4/84 (5)
Left ventricle, severe	12/80 (15)	4/84 (5)
Right ventricle	1/80 (1)	0/84
Primary graft failure and retransplantation — no./total no. (%)	0/80	2/86 (2)

- Higher incidence of moderate or severe PGD in DCD
- PGD did not affect patient or graft survival at 30d or 1 year
- Overall patient survival with original transplanted heart in DCD was higher than DBD at 1 year

86

OCS for DBD Hearts- The EXPAND Trial



87

Extended Criteria Donors

- Expected total cross clamp time of >/= 4 hours OR
- Expected total XC time of >/= 2 hours PLUS >/= 1 additional risk factor:
  - Age >/= 55y
  - Age 45-55 with no cath data
  - Reported down time >/= 20min with stable hemostat at final assessment
  - LVH 13-16mm
  - LVEF 40-50%
  - Angiogram with luminal irregularities with no significant CAD
  - CO poisoning with good cardiac function
  - Hx DM or alcoholism with good cardiac function

88

- Single arm trial, benchmarked long term results with standard criteria HTx outcomes in US (SRTR)
- 138 extended criteria DBD donors, 1813 std criteria DBD donors
  - EC DBD - 88% freedom from severe PGD
  - Long term survival to 2 years- not significantly different from concurrent controls
    - 92% at 6mo, 89% 1y, 85% 2y

89

TransMedics

TransMedics, Inc Press Release | Sept 7, 2021

TransMedics Receives FDA Approval for its OCS™ Heart System Enabling Broader Utilization of Donor Hearts for Transplantation in the U.S

Andover, Mass. – September 7, 2021 – TransMedics Group, Inc. ("TransMedics") (Nasdaq: TMDX), a medical technology company that is transforming organ transplant therapy for patients with end-stage lung, heart, and liver failure, today announced that the U.S. Food and Drug Administration (FDA) has granted premarket approval (PMA) of its OCS Heart System for use with organs from donors after brain death (DBD).

TransMedics

Bringing new life to organ transplant

TransMedics Receives FDA PMA Approval of OCS™ DCD Heart Indication

April 28, 2022

ANDOVER, Mass., April 28, 2022 /PRNewswire/ -- TransMedics Group, Inc. ("TransMedics") (Nasdaq: TMDX), a medical technology company that is transforming organ transplant therapy for patients with end-stage lung, heart, and liver failure, today announced that the U.S. Food and Drug Administration (FDA) has granted premarket approval (PMA) of its OCS™ Heart System for use with organs from donors after circulatory death (DCD). The landmark approval stands to significantly expand the pool of eligible donor hearts in the United States and follows FDA PMA approval of the OCS™ Heart System for use with organs from donors after brain death (DBD) received in September 2021.

90

91

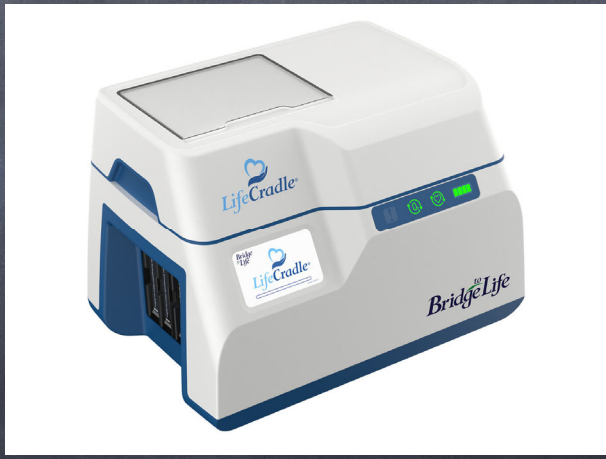
Hypothermic Machine Perfusion

- Not currently available in US
- Continuous perfusion with cold oxygenated cardioplegia nutrient rich solution
- Potentially extend ischemic time for cold storage
- ? Better event free survival, decreased PGD compared to SCS
- ?safer and simpler than NMP

92

Bridge to Life: Lifecradle…

- Hypothermic oxygenated nutrient rich perfusion
- No blood required
- "Plug and play"
- "Streamlined workflow"



93

CISION
PR Newswire

Send a Release

TransMedics Acquires Warm Perfusion EVOSS™ and Cold Perfusion LifeCradle® Technologies from Bridge to Life

TransMedics

NEWS PROVIDED BY
TransMedics Group, Inc. →
02 Aug, 2023, 17:00 ET

SHARE THIS ARTICLE

94

PARAGONIX SHERPAPAK®
CARDIAC TRANSPORT SYSTEM

TEMPERATURE PROBE	Continuous monitoring of temperature
PURGE MECHANISM	Enables flushing system to remove trapped air pockets for even cooling
HEART CONNECTOR	Four sizes of heart connector to fully suspend heart immersed in preservation solution
NESTED CANISTER SYSTEM	Pressure controlled and leak-proof rigid canister to safeguard heart
PARAGONIX SHERPACOOL® RIBBONS AND POUCH	Consistent storage environment validated to maintain temperature over 40 hours
SHIPPER WITH TELESCOPING HANDLE AND WHEELS	Light-weight, easy to handle system designed to fit in standard aircraft and ground vehicles
DISPLAY AND BLUETOOTH® DATA TRANSMISSION	Real-time monitoring and data reporting via Bluetooth® connected devices

95

OPEN

ASAIO Journal 2023 Clinical Cardiovascular

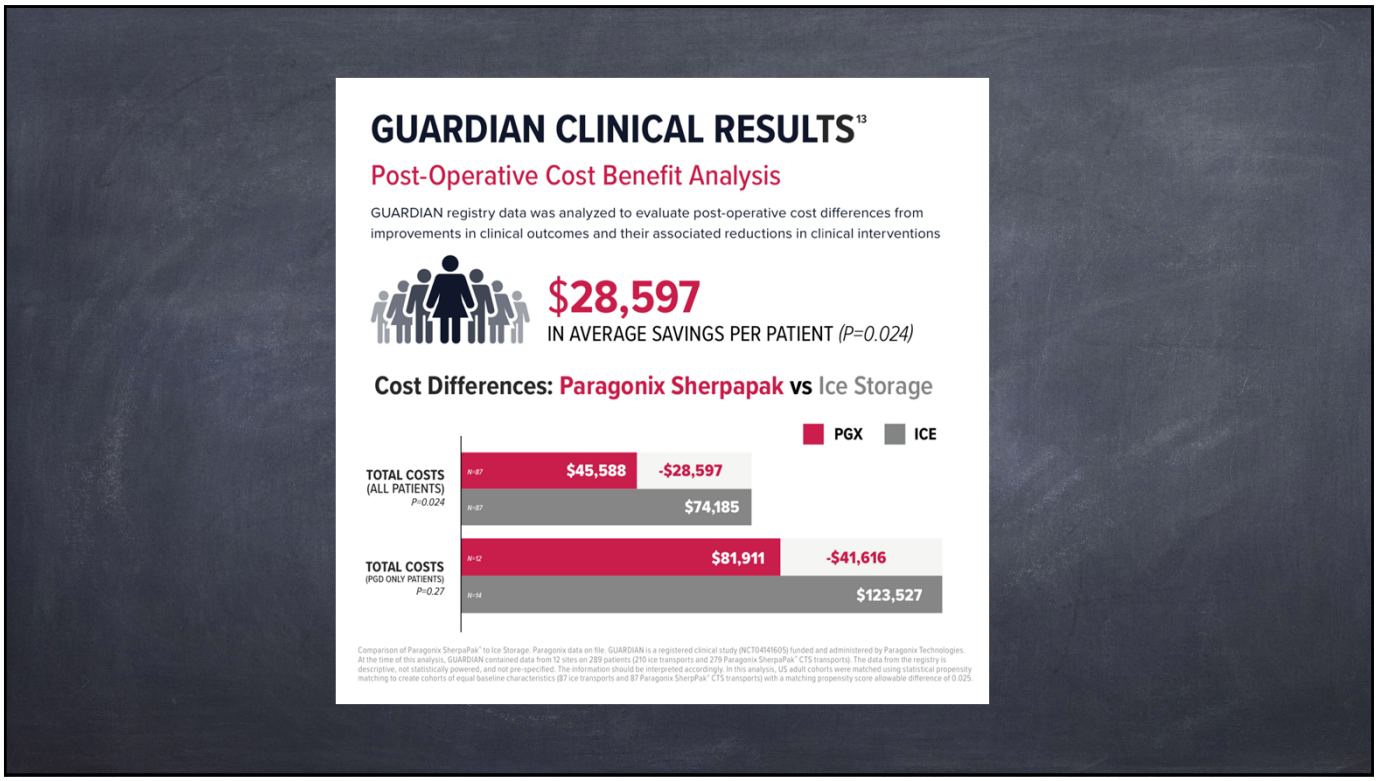
A Paradigm Shift in Heart Preservation: Improved Post-transplant Outcomes in Recipients of Donor Hearts Preserved with the SherpaPak System

Yasuhiro Shudo,* Marzia Leacche,† Hannah Copeland,‡ Scott Silvestry,§ Si M. Pham,¶ Ezequiel Molina,|| Jacob N. Schroder,# Christopher M. Sciortino,** Jeffrey P. Jacobs,†† Masashi Kawabori,‡‡ Dan M. Meyer,§§ Andreas Zuckermann,¶¶ and David A. D'Alessandro,||||

- Retrospective
- 1 year outcomes
- Oct 2015-Jan 2022
- 569 US adults
  - Sherpapak - 255
  - Ice- 314

- Sherpapak:
  - 67% reduction severe PGD
  - PM: reduced severe PGD
    - Trend: improved 1 y survival, reduced MCS
  - Ischemic time > 4 h- reduced MCS, severe PGD, better 30d survival
  - ICE- 3.4x increased chance of severe PGD

96


GUARDIAN CLINICAL RESULTS[13]
Post-Operative Cost Benefit Analysis
GUARDIAN registry data was analyzed to evaluate post-operative cost differences from improvements in clinical outcomes and their associated reductions in clinical interventions
$28,597
IN AVERAGE SAVINGS PER PATIENT (P=0.024)
Cost Differences: Paragonix Sherpapak vs Ice Storage
PGX
ICE
TOTAL COSTS (ALL PATIENTS) P=0.024
N=87
$45,588
-$28,597
N=87
$74,185
TOTAL COSTS (PGD ONLY PATIENTS) P=0.27
N=12
$81,911
-$41,616
N=14
$123,527
Comparison of Paragonix SherpaPak™ to Ice Storage. Paragonix data on file. GUARDIAN is a registered clinical study (NCT04141605) funded and administered by Paragonix Technologies. At the time of this analysis, GUARDIAN contained data from 12 sites on 289 patients (210 ice transports and 279 Paragonix SherpaPak™ CTS transports). The data from the registry is descriptive, not statistically powered, and not pre-specified. The information should be interpreted accordingly. In this analysis, US adult cohorts were matched using statistical propensity matching to create cohorts of equal baseline characteristics (87 ice transports and 87 Paragonix SherpPak™ CTS transports) with a matching propensity score allowable difference of 0.025.

97

98

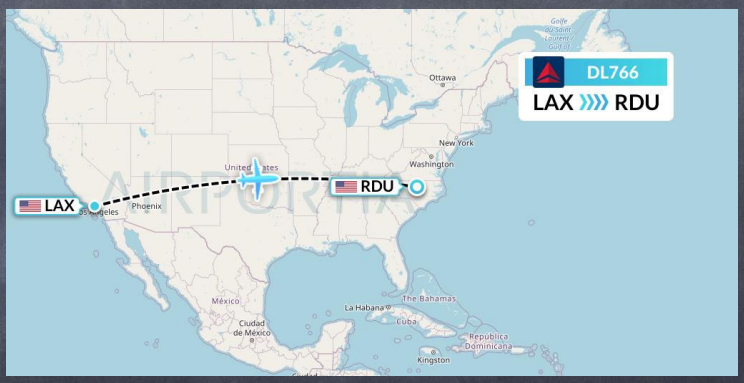
Pushing the Boundaries of Cold Storage

A heart was flown from Alaska to Boston, breaking a transplant record. Here's how it was done.

Adrianna Rodriguez
USA TODAY

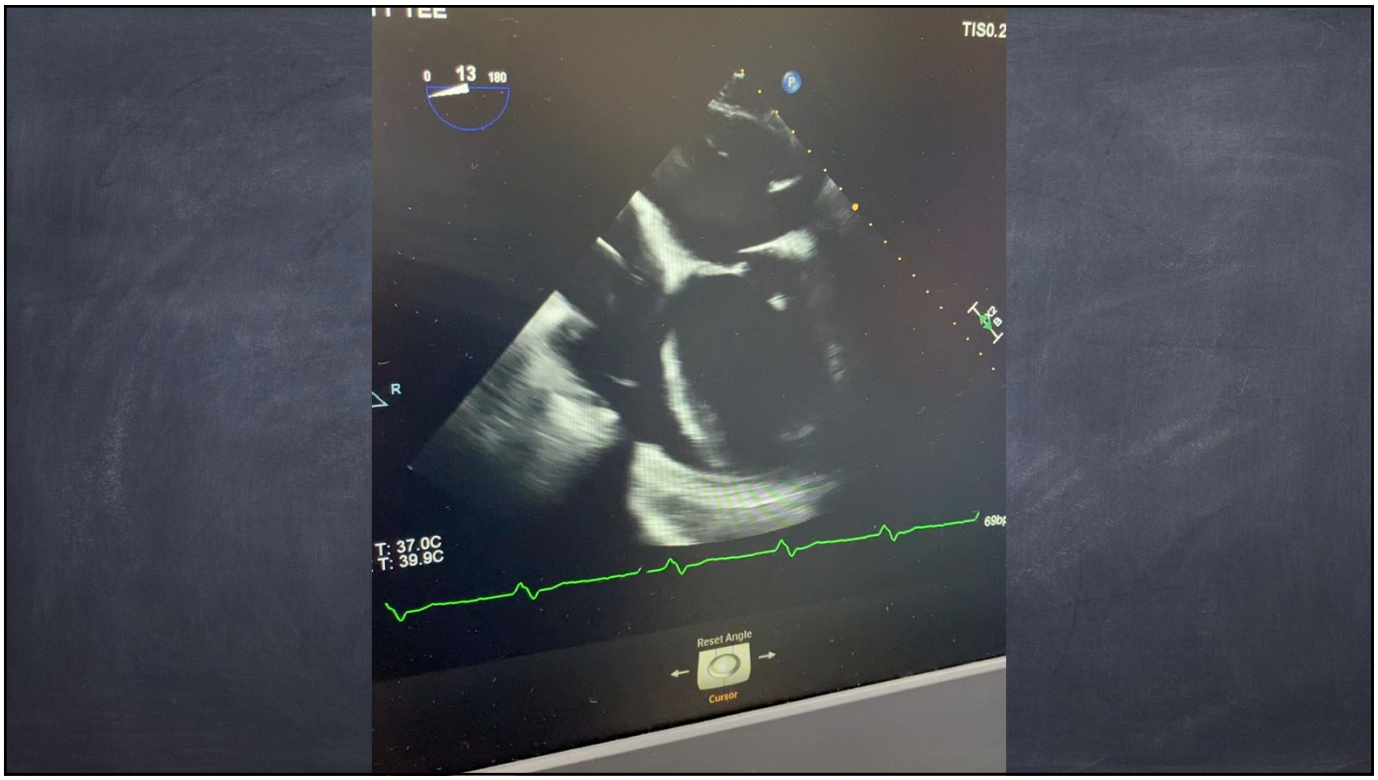
Published 10:35 a.m. ET May 23, 2023 | Updated 1:51 p.m. ET May 23, 2023

2506 miles
7.5 hr travel time



2238 miles
? 6 hr travel time

99



100

AESON CARMAT TAH

Biventricular, hemocompatible, autoregulated support

101

https://www.carmat-phrt.com

102

Transplant & Mechanical Support: Case Repo

The First Autoregulated Total Artificial Heart Implant in the United States

Jacob N. Schroder, MD,[1]
Sharon L. McCartney, MD,[2]
Piet Jansen, MD, PhD,[3] Ryan Plichta, MD,[1]
Jason N. Katz, MD, MHS,[4]
David M. Smadja, PhD,[5]
Krish C. Dewan, MD,[1] and
Carmelo A. Milano, MD[1]

The Aeson total artificial heart provides right- and left-sided heart replacement for biventricular failure with notable improvements from prior generations. These include enhanced hemocompatibility and autoregulation enabling increased output in response to higher filling pressures. We report the first clinical implantation in the United States as part of an early feasibility study. The patient was successfully bridged to transplant after 5 months of support on the device and has made a full recovery.

(Ann Thorac Surg Short Reports 2023;1:185-187)

Duke Surgeons First in U.S. to Place New-Generation Artificial Heart

The Procedure, Followed by Heart Transplant, Saves Man's Life

December 06, 2021

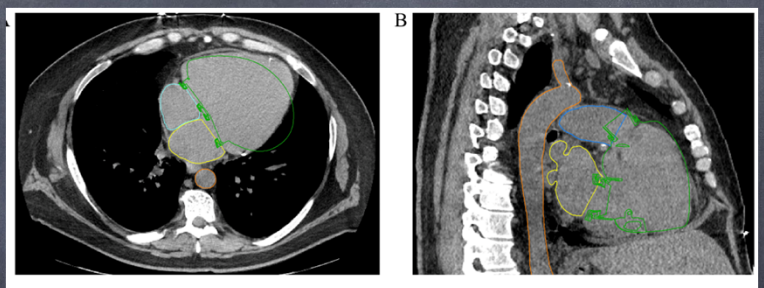
Share:

Duke University Hospital

103

Case Report

- 39yo M ICM - admitted with CHF
- V fib - central VA ECMO
- Impella 5.5
- VT/RHF, end organ dysfunction
- Too sick to transplant



Supplemental Figure 1. Adequate antero-posterior dimension and adequate pulmonary artery to diaphragm dimension on axial (A) and sagittal (B) computed tomography imaging of patient chest; Pump outline overlayed in green.

Minimum Sternal to vertebral body distance 12.6cm
Patient Diaphragm to mPA distance 10.8cm

104

- Implanted per protocol
- Put in 'Autoregulatory mode'- beat rate changes with change in filling pressure
  - Maintained in this mode
  - First 30 d- only one alarm, when patient bared down. Spontaneously resolved
- Anticoagulation: heparin -> daily enoxaparin + ASA
- Normalized platelets and VWF
- Correction of EOD
- No major complications

105

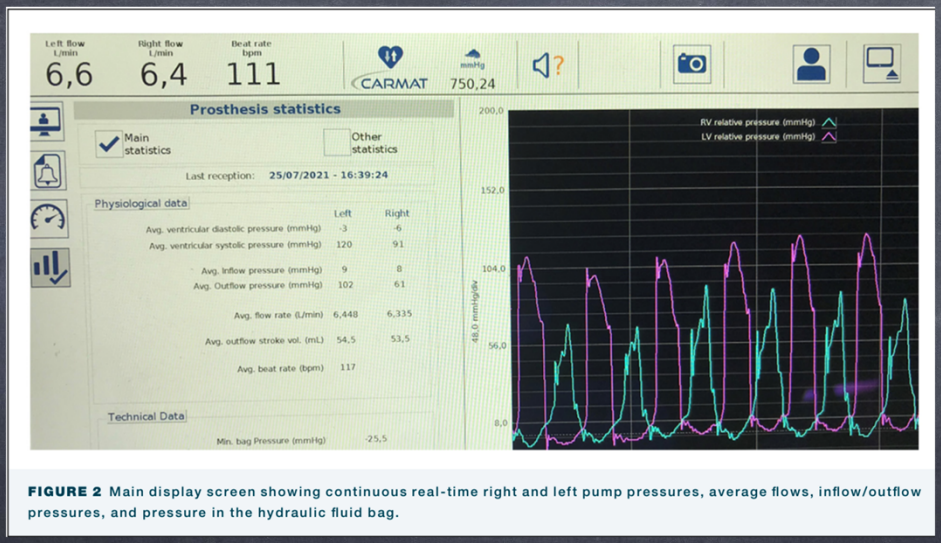


FIGURE 2 Main display screen showing continuous real-time right and left pump pressures, average flows, inflow/outflow pressures, and pressure in the hydraulic fluid bag.

106

Happy Ending!

- Transplanted 4 months later
- 8 month post transplant follow up- good graft function

107

- Potential for fewer CVA/bleeding events with newer generation TAH
- Improved patient quality of life with autoregulation
- CARMAT clinical trial now ongoing again…
  - Primarily in Europe - France

108

Summary

- The world of surgical heart failure is rapidly changing!
- So many new tools in the toolkit!
- Art of medicine
  - When do we use what, and in whom…

109

Questions?

110