Advances in Durable Mechanical Circulatory Support:

Current State and Future Directions

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Disclosures

Speaker – Abbott Laboratories, Inc.

Objectives

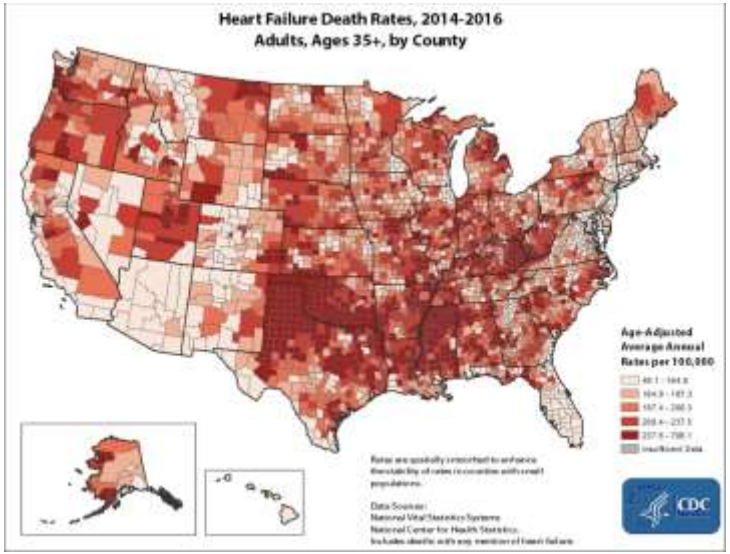
1. Understand current survival and longterm outcomes associated with contemporary, durable mechanical circulatory support
2. Review contra-indications to durable mechanical circulatory support
3. Discuss future devices and directions of durable mechanical circulatory support

Outline

1. History of durable MCS (dMCS)
2. Contemporary dMCS utilization and trends
   -outcomes in magnetically levitated dMCS
3. Future directions in dMCS

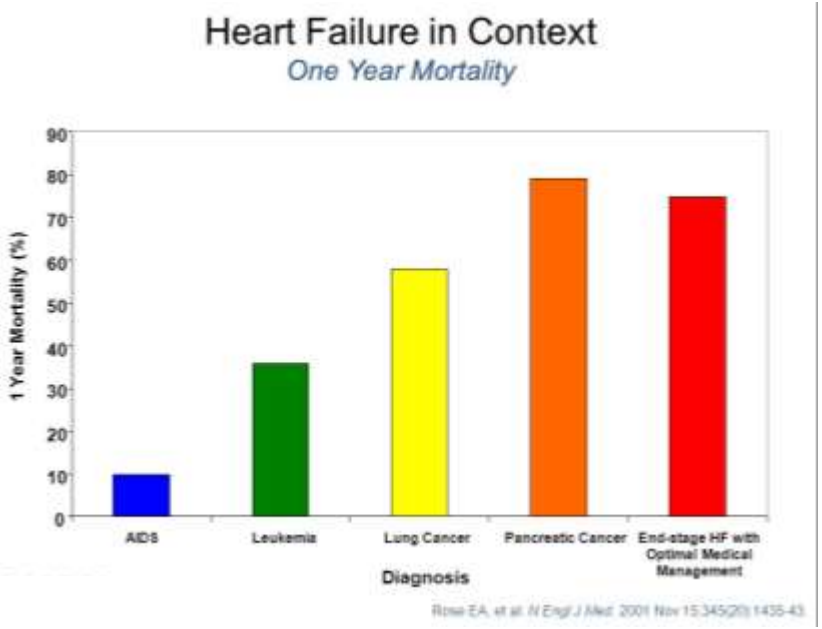
Epidemiology of Heart Failure

-There is an estimated 6.2[(2)] million Americans with heart failure and it is estimated that by 2030, there will be **>8 million**[(1)].
-Each year, **960,000** new cases of heart failure are diagnosed[(1)]
-In 2017, there were 1.2 million HF hospitalizations in the United States[(1)]
-By age **45 has a 1 in 5** lifetime risk of developing heart failure
-In 2018, heart failure was mentioned on 379,800 death certificates (13.4%) [(2)]
-Of incident hospitalized HF events, **53% had HF with reduced ejection fraction and 47% had preserved ejection fraction**

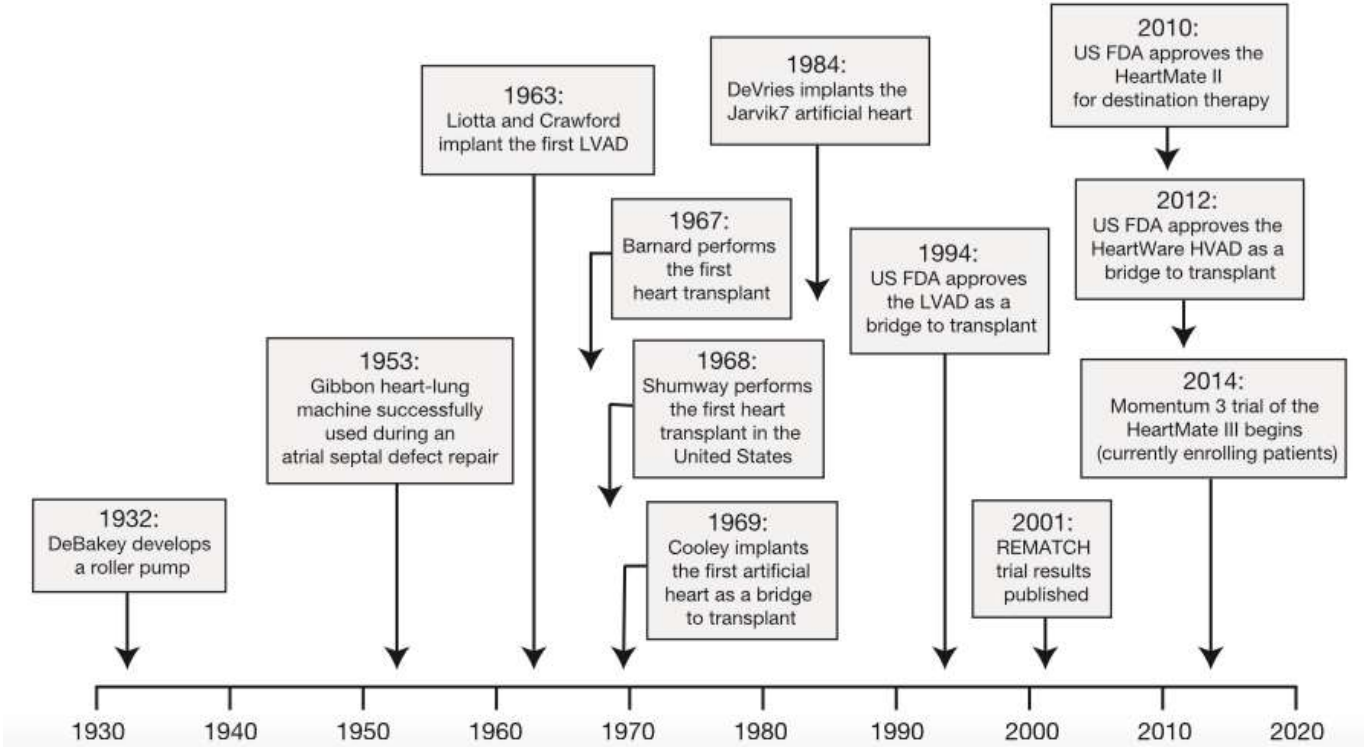


Epidemiology of Heart Failure

Despite advancement in cardiovascular disease management, the number of heart failure patients is increasing with **5% of heart failure patients progressing to Stage D heart failure and 5% dying annually.**



History of Left Ventricular Assist Devices



Initial success with heart-lung machines would spur the continued push to develop an artificial heart

History of Left Ventricular Assist Devices

-Atomic Energy Commission (AEC), NHI and private contractors developed proposals to utilize radioisotope powered engines

-"The ideal implantable device meant no external lines or connections from the patient to outside power sources and a ten-year reliability span."

-The **weight and safety** of a radio-isotopic powered engine for implantation in the human body were the perceived obstacles

-Based on favorable reports, the NHI and AEC described the prospect for developing a radioisotope engine for mechanical hearts as "good"

-The AEC subcontracted Westinghouse who in turn subcontract Philips of North America, who would utilize sixty grams of plutonium-238 to power their first engine for use in-vivo

-February 1972 John Norman of Harvard an NHLI-sponsored heart assist system powered by Pu-238 in a calf

-Successful for eight hours until a kinked inflow tube terminated the experiment

History of Left Ventricular Assist Devices

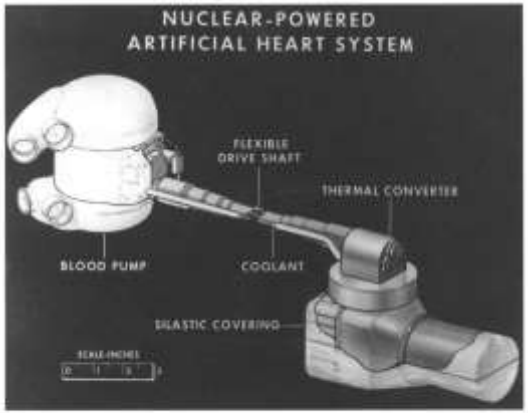


FIG. 1 AEC–Westinghouse atomic heart, developed by Westinghouse under contract from the AEC in the early 1970s. (Source: Willem J. Kolff Collection, box 5, book 5, folder 4, P0343, in Special Collections, Marriott Library, University of Utah, Salt Lake City. Reprinted with permission.)

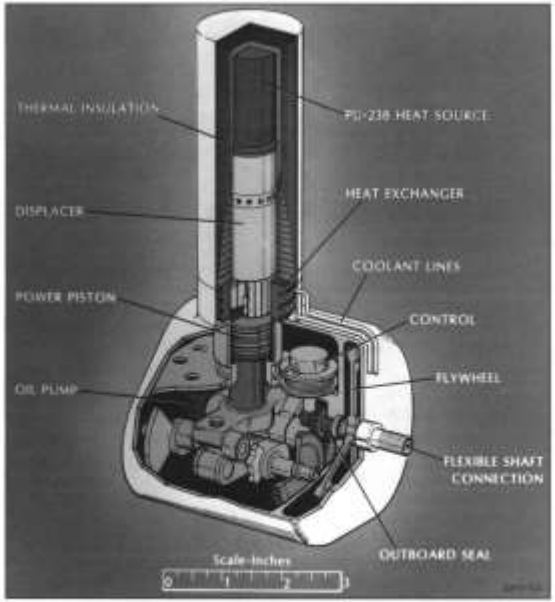


FIG. 2 Cutaway diagram of the AEC–Westinghouse atomic heart's thermal converter, fabricated by the engineering firm Philips of North America under subcontract to Westinghouse. (Source: Willem J. Kolff Collection, box 5, folder 21, P0343, in Special Collections, Marriott Library, University of Utah, Salt Lake City. Reprinted with permission.)

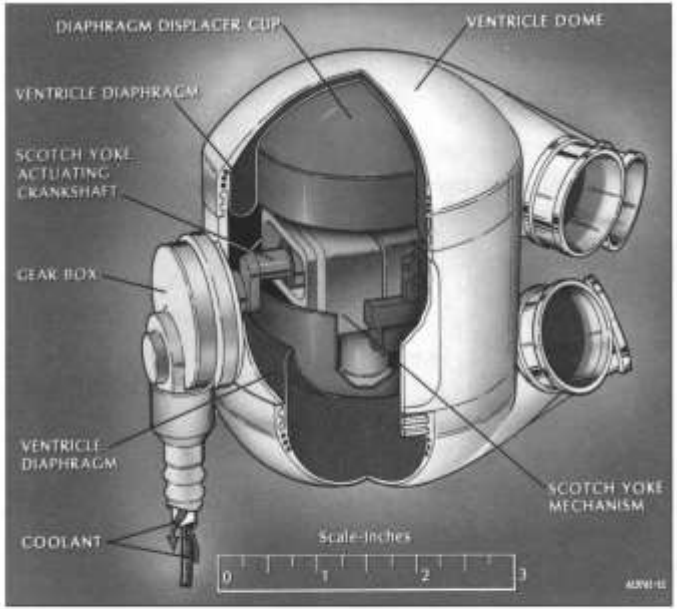


FIG. 3 Cutaway diagram of the AEC–Westinghouse atomic heart's blood pump, fabricated at Westinghouse's Astronuclear Laboratory in collaboration with Willem J. Kolff's artificial heart research team at the University of Utah. (Source: Willem J. Kolff Collection, box 5, folder 21, P0343, in Special Collections, Marriott Library, University of Utah, Salt Lake City. Reprinted with permission.)

History of Left Ventricular Assist Devices

FIG. 4 The NHLI atomic heart. This nuclear-powered heart assist system consisted of two main parts: (1) the blood pump or Model VIII assist pump (top), which is attached via hydraulic drive lines to (2) the thermal converter or nuclear engine (bottom). This photo shows the system being held in an assembly stand during the insertion of the plutonium-238 fuel capsule (center) into the engine prior to implantation. (Source: John C. Norman et al., "An Implantable Nuclear-Fueled Circulatory Support System," *Annals of Surgery* 176, no. 4 [October 1972]: 497. Reprinted with permission.)

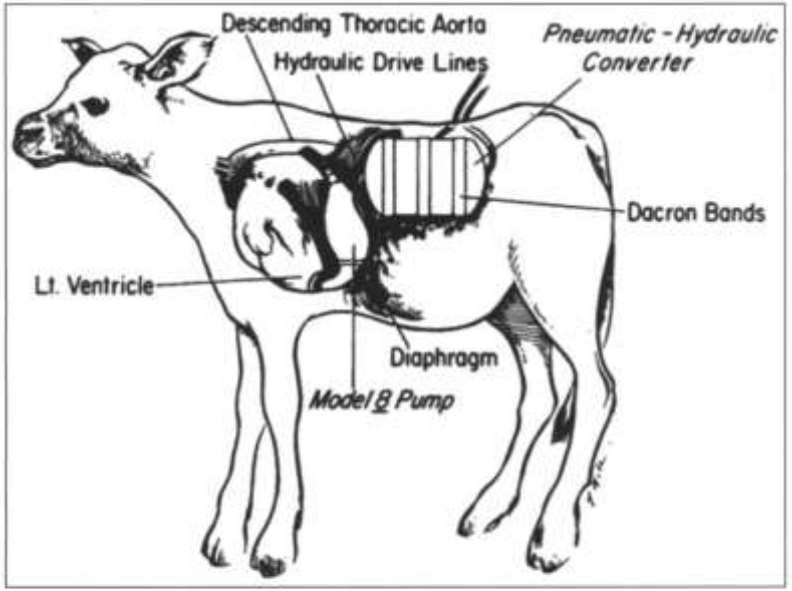


FIG. 5 The NHLI atomic heart functioning in a calf. The device consists of a converter (fueled by plutonium-238) attached via hydraulic drive lines to the Model VIII heart assist pump, which in turn connects to the natural heart. (Source: John C. Norman et al., "An Implantable Nuclear-Fueled Circulatory Support System," *Annals of Surgery* 176, no. 4 [October 1972]: 500. Reprinted with permission.)

History of Left Ventricular Assist Devices

Allocation of Resources: The Artificial Heart

An NIH Panel's Early Warnings

by HAROLD P. GREEN

In December 1682 Barney B. Clark, a retired Seattle dentist, entered the annals of medical history by becoming the first recipient of an artificial heart intended to be a permanent replacement for the diseased organ. (The few previous implants were intended as temporary substitutes until a heart for transplantation became available.) Dr. Clark lived for 112 days attached to the device, which had an external pump and power source. The debate that preceded the implantation went on for at least fifteen years and the one that followed it may last even longer.

The following articles illustrate how the assumptions underlying the debate have changed and how the moral dilemmas have become even more troubling. Harold P. Green, the chairman of the Artificial Heart Assessment Panel that examined the question in 1972 and 1973, describes the National Institutes of Health's cautiously optimistic assessment of the state of the technology on which the group based its deliberations. The panel concluded that a platinum-pyramid heart would not be in the public interest, because it posed a low risk of harm to many others every while offering the possibility of great benefit to a few recipients.

Samuel Gorovitz brings the debate up to date by addressing the tension between the autonomy of individual patients and physicians and the social costs of the artificial heart program. He finds we close out answer to the quandary; only some questions that ought to be asked and some that are irrelevant.

A new development may further alter the debate. In early August, Dr. William C. DeVries, the only surgeon authorized by the Food and Drug Administration to use the new artificial heart device, announced his move from the University of Utah to the Humana Heart Institute in Louisville, Kentucky, a private for-profit institution. This shift in emphasis for the artificial heart program from the academic nonprofit world to the private economic sector will alter not only the pace of the program but also its goals and the ability of the public to assess and control its implementation. The questions raised by both authors will become even more critical in the future.

A Plutonium-Powered Heart

On the other hand, one panel was asked to consider a device, including the energy source, that would be totally implanted within the recipient's body. The implanted energy source would be a capsule containing 55 grams of Plutonium 238. The entire device was designed by the pacemaker NIH-LI to provide the maximum benefits for its recipients. It would operate reliably and trouble-free, without any dependence on external machinery for a period of at least ten years. The recipient would be free to come and go, to work, to play, to travel to be or she pleased, and to lead an essentially normal and fully productive life.

We were told that clinical experimental implantations were likely within the next several years. We were also told to assume that all technical problems such as biocompatibility of materials had been overcome, that the device would in fact function as advertised, and that implantations would be made in patients whose cardiac conditions would otherwise lead to imminent death or severe cardiac conditions necessarily involved a very low quality of existence (life).

We estimated that when the totally implantable artificial heart was fully available about 50,000 candidates would be eligible for implantation each year, and that, accordingly, these 50,000 individuals could then look forward to an active and productive life for an additional ten-year period (unless, of course, they died sooner because of some noncardiac condition or event).

The totally implantable artificial heart had been under development with NIH

The Hastings Center

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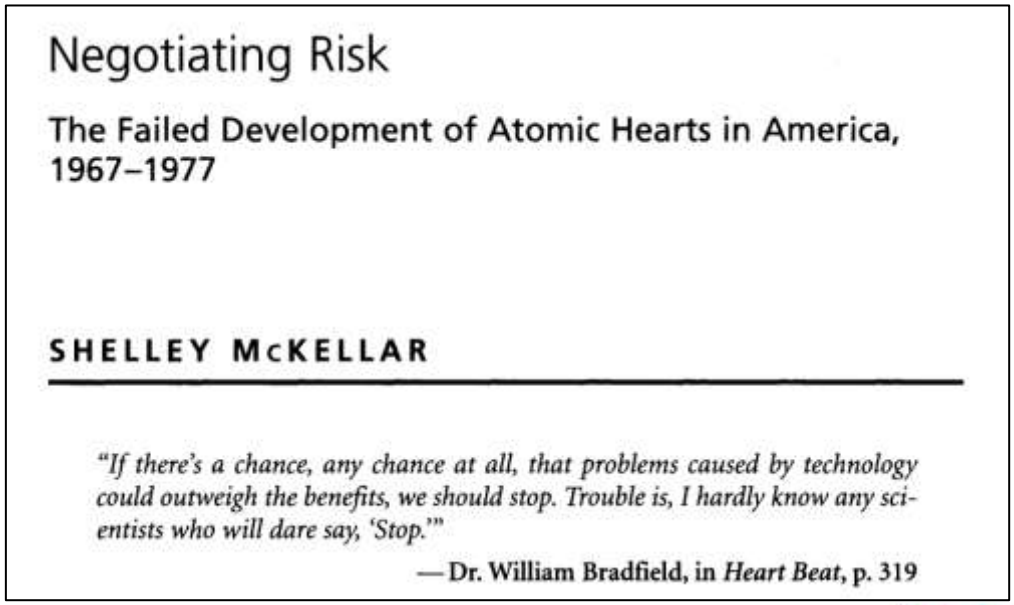


Negotiating Risk

The Failed Development of Atomic Hearts in America, 1967–1977

SHELLEY McKELLAR

"If there's a chance, any chance at all, that problems caused by technology could outweigh the benefits, we should stop. Trouble is, I hardly know any scientists who will dare say, 'Stop.'"

— Dr. William Bradfield, in *Heart Beat*, p. 319

History of Left Ventricular Assist Devices

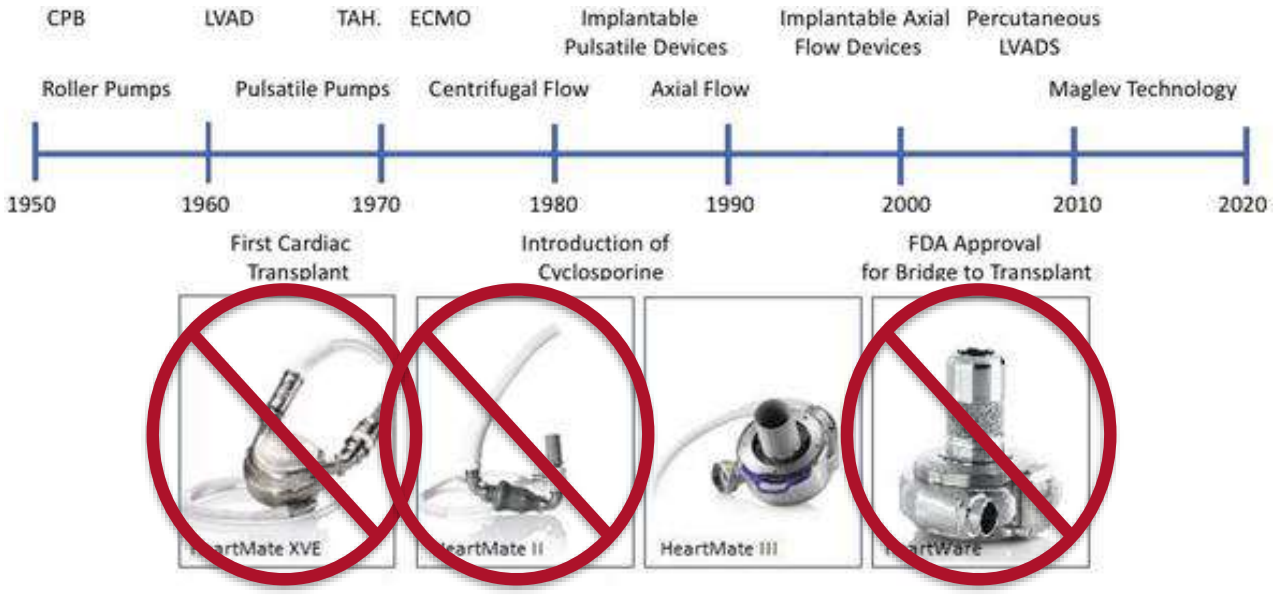
DeBakey Ventricular Assist Device-1966

The Liotta-DeBakey LVAD on display at the Smithsonian Institute

History of Left Ventricular Assist Devices

-Progressive changes to the dMCS landscape have essentially decreased the number of commercially available LVADs

-Currently, only one CF-LVAD is used



Durable MCS Today:

Pump Design and Modifications

External Components

-Inflow Cannula

-Pump Chamber/Motor

-Outflow Graft

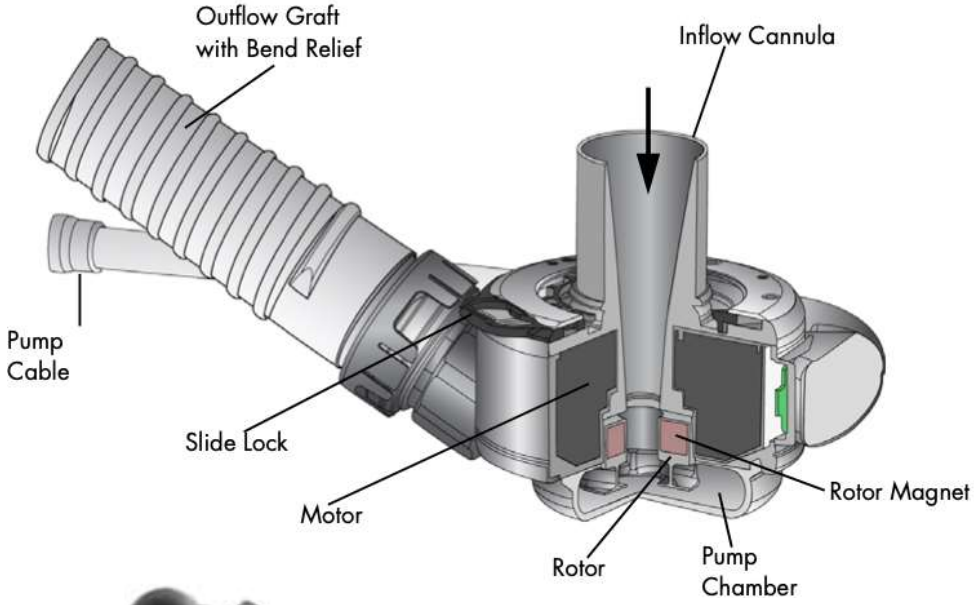
-Pump Cable

Unique Features

Full Magnetic Levitation or “MagLev”

Widened ”Gaps” for less RBC shear stress

Pulsitility of 30 bpm



Durable MCS Today:

Pump Design and Modifications

-200 grams (7 oz) composed of titanium

-Priming volume of 21 cc

-Gelatin-impregnated 14 mm woven polyester

-Driveline of silicone and velour

-Pump Speed Range:

3-9000 rpm

-Minimum Speed:

3000 rpm

Durable MCS Today:

Pump Design and Modifications

-200 grams (7 oz) composed of titanium

-Priming volume of 21 cc

-Gelatin-impregnated 14 mm woven polyester

-Driveline of silicone and velour

-Pump Speed Range:

3-9000 rpm

-Minimum Speed:

3000 rpm

1. Pump

2. Pocket Controller

4. Mobile Power Unit (MPU)

3. Modular Driveline

5. Batteries (17hr)

6. Battery Charger

Durable MCS Today:

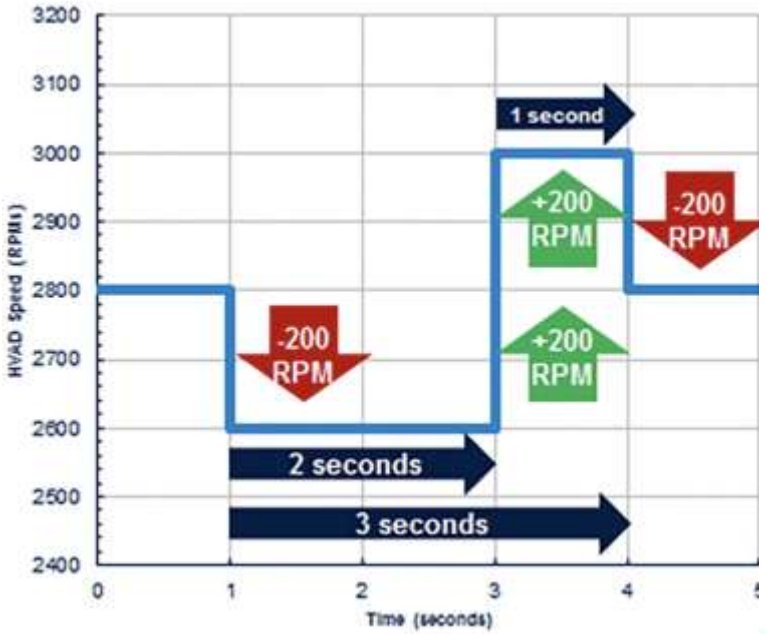
Pump Design and Modifications

-Average speed is approx. 5300 rpm

-Afterload and preload sensitive

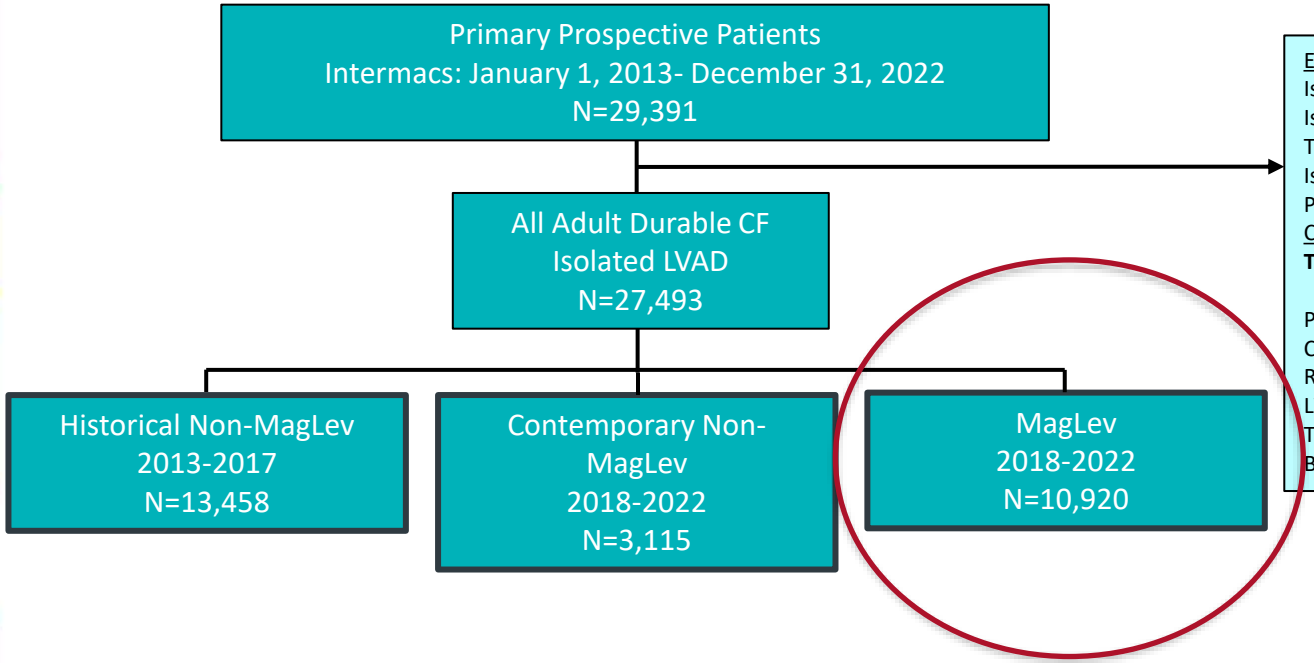
-”Pulsitility” with speed change every

-Every 2 seconds, the rotor will decrease by 2000 RPM, from the set speed, for 0.15 seconds, then increase by 4000 RPMs for 0.20 seconds, and finally return to the set speed.



Durable MCS Today:

STS (INTERMACS) Registry Data



Exclude:	n
Isolated PF RVAD	2
Isolated CF RVAD	19
TAH	379
Isolated PF LVAD	15
PF BiVAD	57
CF BiVAD	1426
Total	**1898**

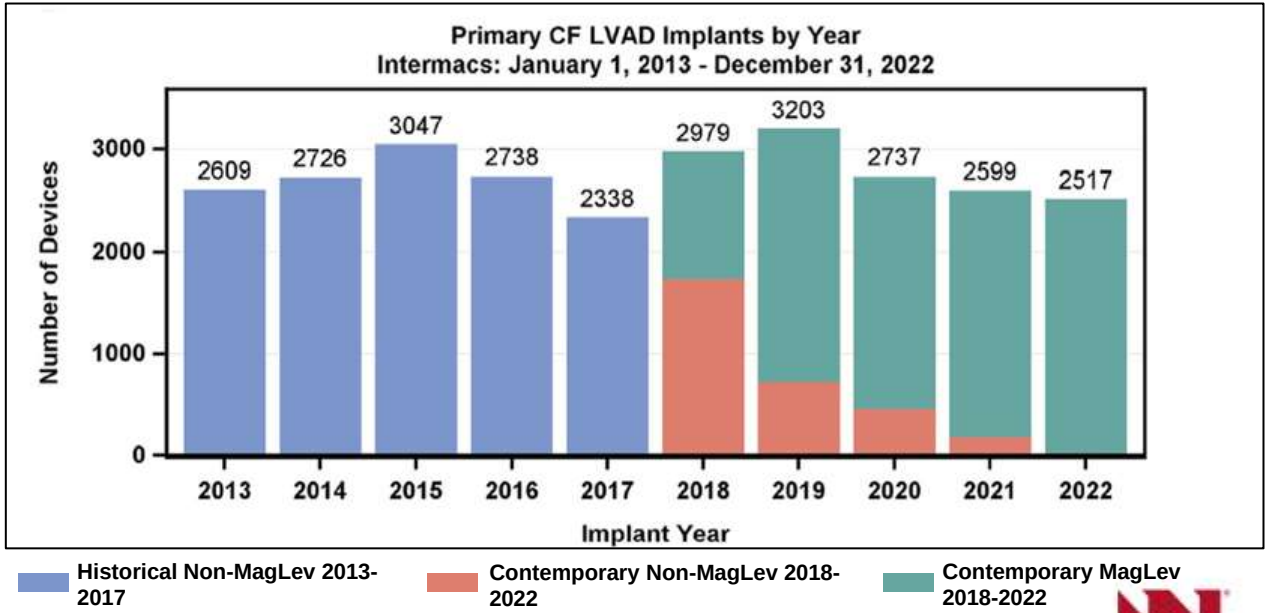
PF= pulsatile flow pump
CF= continuous flow pump
RVAD= right ventricular assist device
LVAD= left ventricular assist device
TAH= total artificial heart
BiVAD= biventricular assist device

Durable MCS Today:

STS (INTERMACS) Registry Data

LVAD Implants by Year grouped by Non-MagLev and MagLev in its historical and contemporary form

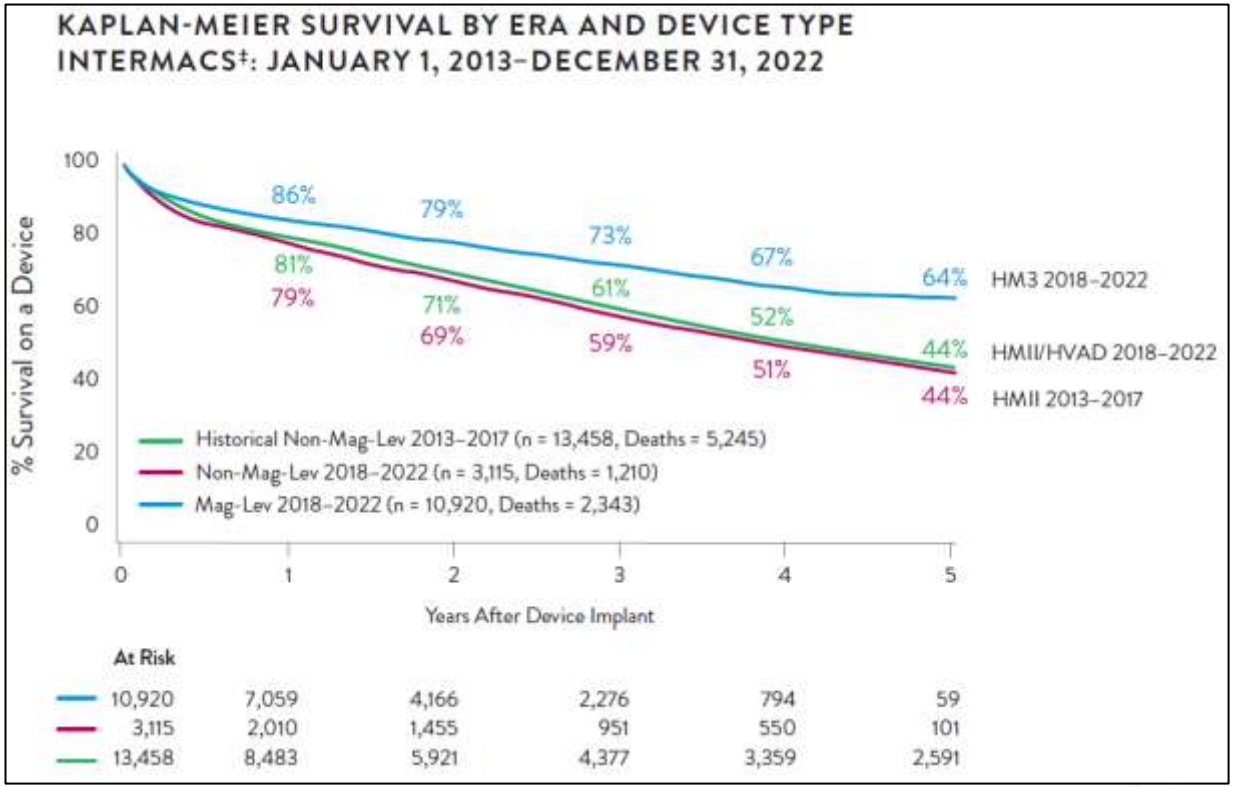
-In 2022, 99.8% of LVADs were HM3



Durable MCS Today:

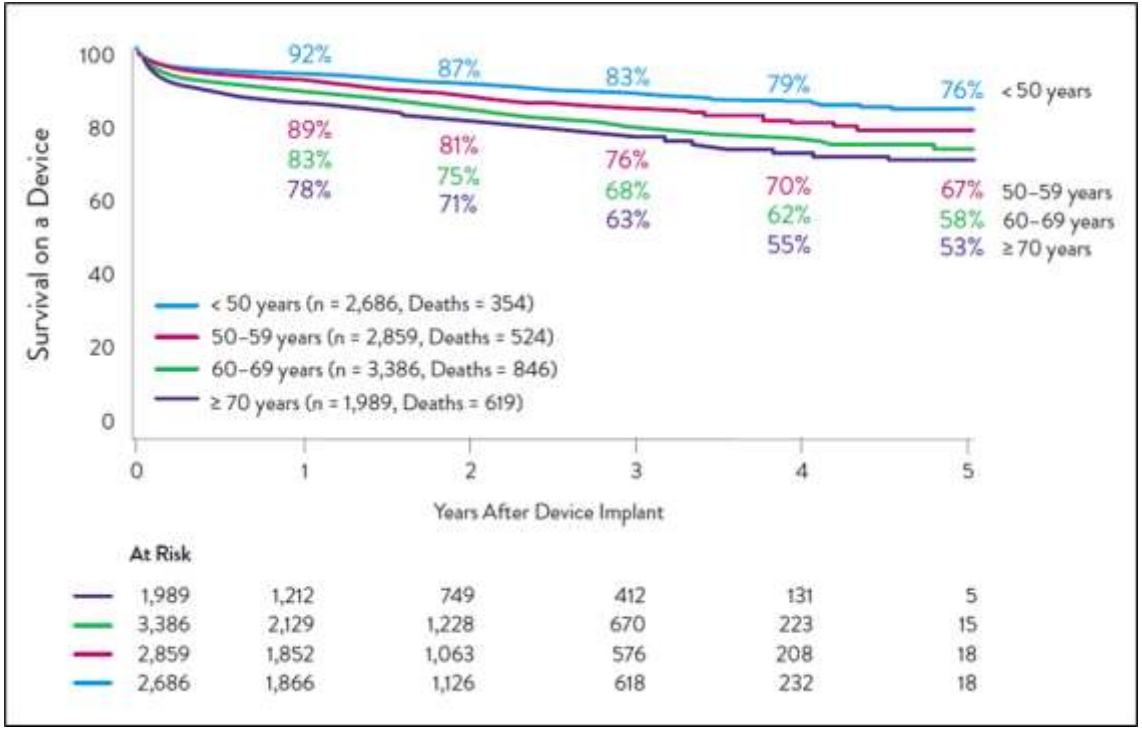
STS (INTERMACS) Registry Data

At 5-years, **64%** of people who have undergone implant of contemporary, MagLev LVAD were alive



Durable MCS Today:

STS (INTERMACS) Registry Data



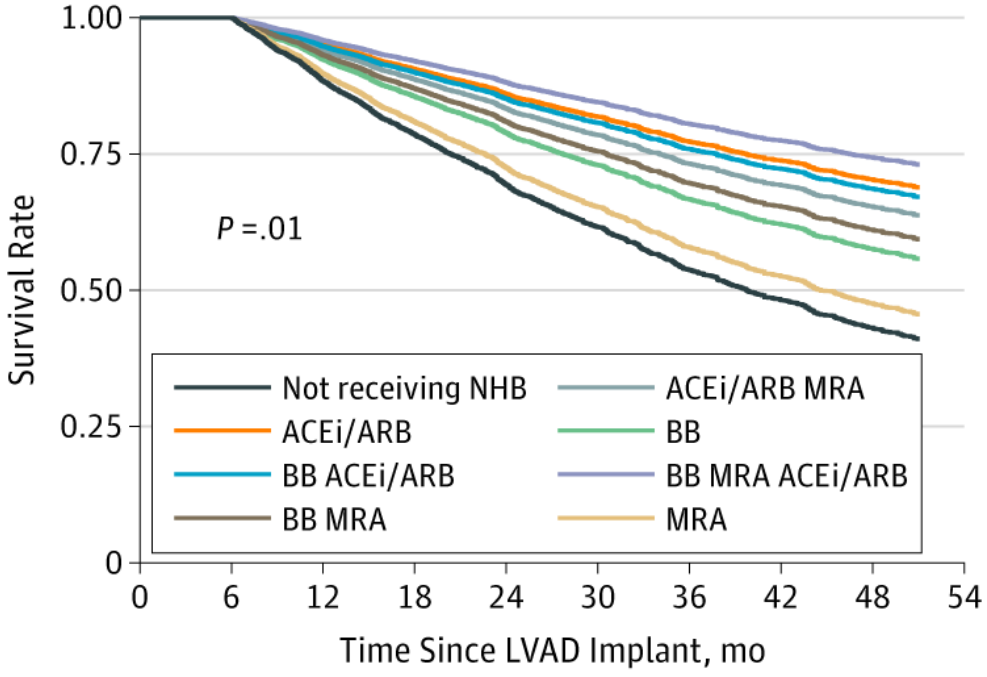
76% of patients under 50 years of age were alive at 5 years

-Decrease in survival with subsequent decades but even those >70 years of age had a 53% survival

Durable MCS Today:

Clinical Management

Improved survival rate with utilization of GDMT in LVAD patients yet limited guidance on medical management of LVAD patients.



McCullough M, Caraballo C, Ravindra NG, Miller PE, Mezzacappa C, Levin A, Gruen J, Rodwin B, Reinhardt S, van Dijk D, Ali A, Ahmad T, Desai NR. Neurohormonal Blockade and Clinical Outcomes in Patients With Heart Failure Supported by Left Ventricular Assist Devices. JAMA Cardiol. 2020 Feb 1;5(2):175-182. doi: 10.1001/jamacardio.2019.4965. PMID: 31738366; PMCID: PMC6865330.

Durable MCS Today:

Clinical Management

-Titrate GDMT and educate patients on their disease, living with an LVAD and medication education

-January 2019- March 2021

-150% increase in beta blocker

-140% increase in ARNi

-17% increase in aldosterone antagonist -41% reduction in loop diuretic

-7 patients were started on SGLT2i

The Journal of
Heart and Lung Transplantation
The Official Publication of the International Society for Heart and Lung Transplantation

LVAD OPTIMIZE Clinic Improves Medication Use and Reduces Hospitalizations Post-Implant

S. Lundgren, T. Diederich, B. Pozehl, T. Ryan and A. Burdorf. University of Nebraska Medical Center, Omaha, NE.

Variable	LVAD OPTIMIZE (N=26)	Control Group (N=43)	p-value
Patients on beta blocker, N (%)	20 (76.9)	23 (53.4)	0.05
Patients on ACEi/ARB/ARNi, N (%)	21 (80.8)	19 (44.2)	0.003
Patients on ARNi, N (%)	12 (46.2)	6 (14)	0.003
Patient on aldosterone antagonist, N (%)	21 (80.8)	24 (55.8)	0.03
Patients on SGLT2i, N (%)	7 (26.9)	3 (7)	0.02
Patients on loop diuretic, N (%)	10 (38.5)	23 (53.4)	0.23
Brain Natriuretic Peptide, pg/mL (SD)	305.1 (±265.2)	208.6 (±150.6)	0.12
Creatinine, mg/dL (SD)	1.1 (±0.3)	1.3 (±0.4)	0.08
Glomerular Filtration Rate, mL/min/1.73m2 (SD)	71.2 (±27)	62.6 (±27.6)	0.2
Sodium, mmol/L (SD)	138.1 (±2)	137.6 (±3.2)	0.5
LVIDD, cm (SD)	4.9 (±0.9)	5.4 (±1.1)	0.05
Total hospitalizations per year, N (SD)	2 (±0.4)	3 (±0.5)	0.11
# of patients with HF hospitalization post-implant, N (%)	2 (8.7%)	11 (25.6%)	0.11
HF hospitalizations per year	0.08	0.53	0.03

Table 1. Comparison of medication utilization, lab values, LVIDD, and hospitalizations at the end of LVAD OPTIMIZE clinic between groups.

UNMC LVAD OPTIMIZE Clinic

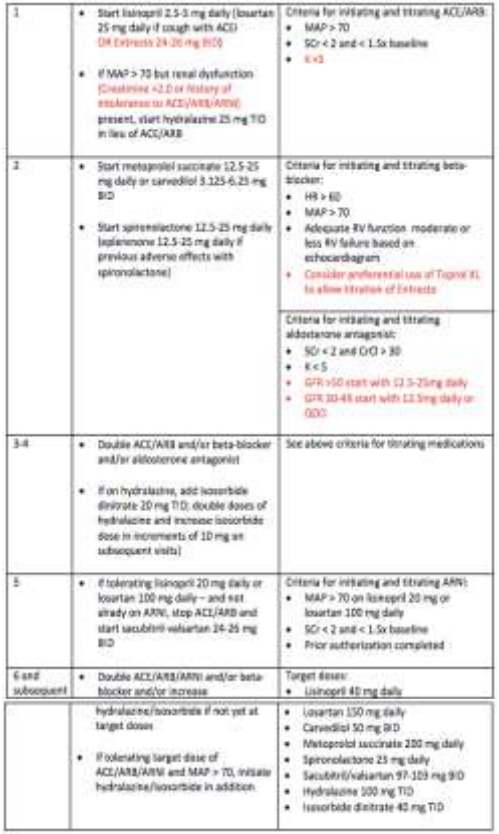
-Similar concept to our HF-OPTIMIZE Clinic already in existance

-Multidisciplinary

- -APP → **medication titration**
- -Nutrition
- -Dietary

-Promote education of the disease process and lifestyle modifications as well as education about the management of VADs

-**Evaluation for CardioMEMs** as well as clinic research studies, etc



1	• Start lisinopril 2.5-5 mg daily (losartan 25 mg daily if cough with ACEI OR Entresto 24-26 mg BID) • If MAP > 70 but renal dysfunction (Creatinine >2.0 or history of intolerance to ACEI/ARB/ARNI) present, start hydralazine 25 mg TID in lieu of ACEI/ARB	Criteria for initiating and titrating ACEI/ARB: • MAP > 70 • SCr < 2 and < 1.5x baseline • K <5
2	• Start metoprolol succinate 12.5-25 mg daily or carvedilol 3.125-6.25 mg BID • Start spironolactone 12.5-25 mg daily (eplerenone 12.5-25 mg daily if previous adverse effects with spironolactone)	Criteria for initiating and titrating beta-blocker: • HR > 60 • MAP > 70 • Adequate RV function moderate or less RV failure based on echocardiogram • Consider preferential use of Toprol XL to allow titration of Entresto Criteria for initiating and titrating aldosterone antagonist: • SCr < 2 and CrCl > 30 • K < 5 • GFR >50 start with 12.5-25mg daily • GFR 30-49 start with 12.5mg daily or QOD
3-4	• Double ACEI/ARB and/or beta-blocker and/or aldosterone antagonist • If on hydralazine, add isosorbide dinitrate 20 mg TID; double doses of hydralazine and increase isosorbide dose in increments of 10 mg on subsequent visits)	See above criteria for titrating medications
5	• If tolerating lisinopril 20 mg daily or losartan 100 mg daily – and not already on ARNI, stop ACEI/ARB and start sacubitril-valsartan 24-26 mg BID	Criteria for initiating and titrating ARNI: • MAP > 70 on lisinopril 20 mg or losartan 100 mg daily • SCr < 2 and < 1.5x baseline • Prior authorization completed
6 and subsequent	• Double ACEI/ARB/ARNI and/or beta-blocker and/or increase	Target doses: • Lisinopril 40 mg daily
	hydralazine/isosorbide if not yet at target doses • If tolerating target dose of ACEI/ARB/ARNI and MAP > 70, initiate hydralazine/isosorbide in addition	• Losartan 150 mg daily • Carvedilol 50 mg BID • Metoprolol succinate 200 mg daily • Spironolactone 25 mg daily • Sacubitril/valsartan 97-103 mg BID • Hydralazine 100 mg TID • Isosorbide dinitrate 40 mg TID

UNMC LVAD OPTIMIZE Clinic

Improvement Projects in Progress	Barriers of Threats to Program	What are we excited to share?
• Reducing rehospitalizations -HF (VAD Optimize) -Anticoagulation (Adjustments to anticoagulation protocol) • Reducing infections -Driveline dressing kits	• LVAD implants decreasing	• Joint Commission Recertification August 2023 • Intracycle Call Recertification August 2024

UNMC LVAD OPTIMIZE Clinic

Heart failure hospitalizations were a significant source of rehospitalization

->35% for 3 years between 2017-2020

Year	Nebraska Medicine	INTERMACS
2009	18.8%	22.8%
2010	33.3%	25.4%
2011	15%	28.7%
2012	18.5%	28.4%
2013	25%	32.2%
2014	29.1%	29.3%
2015	28.2%	30.4%
2016	26.4%	29.6%
2017	38.2%	30%
2018	39.5%	28.3%
2019	35.5%	25.8%
2020	19%	48.9%

INTELLECT-2 HF:

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

Multicenter prospective study in patients with HeartMate II (n=52) or HeartMate 3 (n=49) LVADs and CardioMEMS PA Sensors over 6-month period:

-Pulmonary artery pressure

-6-minute walk distance

-Quality of life (EQ-5D-5 L scores)

-Heart failure hospitalization rates (HFH)

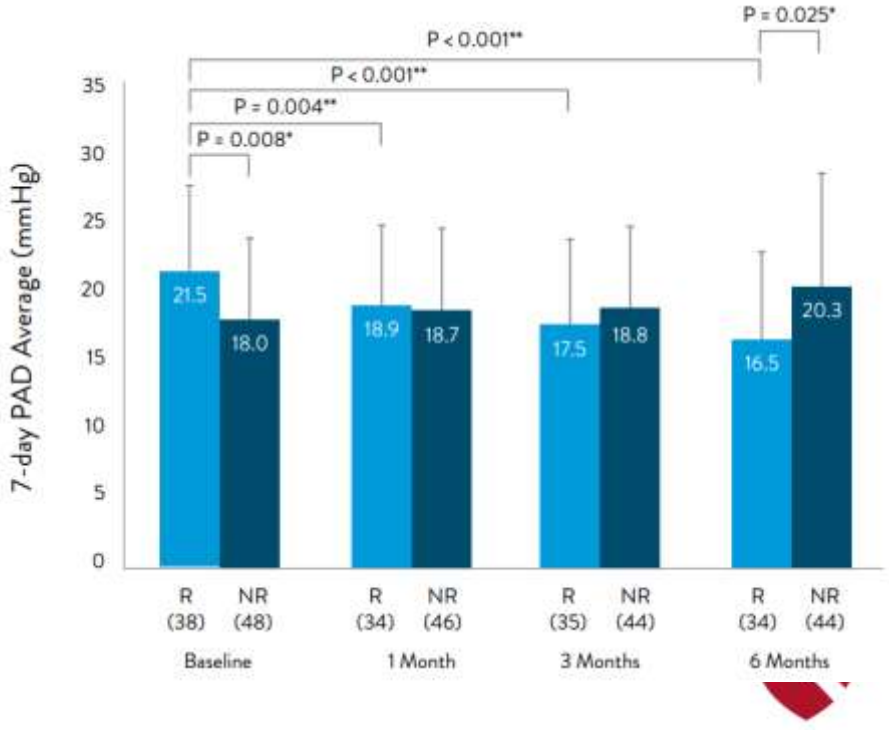
Post-hoc stratified as clinical responders (cR) and non-responders(cNR)

-R → PAD ≥ 1mmHg @

-PAD lower in cR @ 6 months

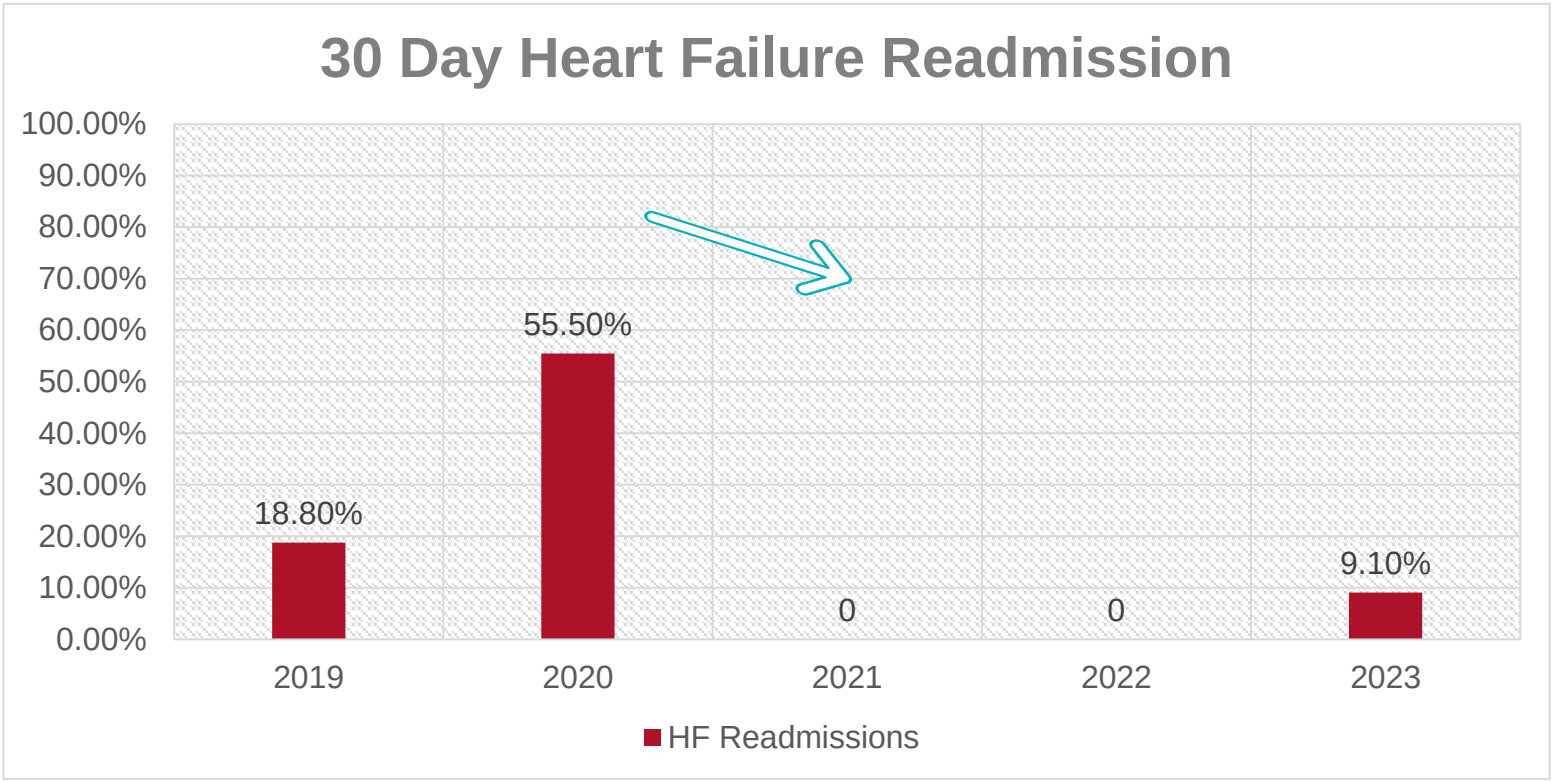
-No change in QoL or HFH cR vs cNR

-Pts w/ PAD < 20mmHg with DECREASED HFH



Thohan V, Abraham J, Burdorf A, et al. Use of a pulmonary artery pressure sensor to manage patients with left ventricular assist devices. *Circulation: Heart Failure*. 2023. doi:10.1161/CIRCHEARTFAILURE.122.009960

UNMC LVAD OPTIMIZE Clinic



Medical Therapy with Durable MCS

A large portion of the success of our VAD Optimize Clinic has been utilizing CardioMEMs to monitor LVAD patients.

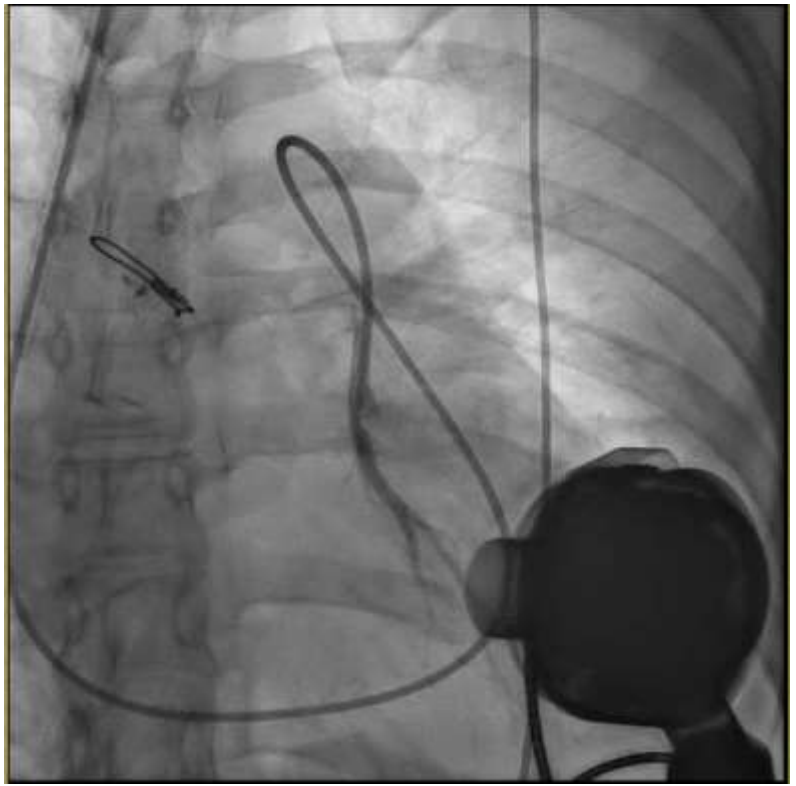
-Right Heart Failure

-Distance from UNMC

-Those with Elevated Pulmonary Pressures

-Patients with a history of heart failure hospitalizations

To date, we have implanted **47 LVAD** patients with the CardioMEMs system.

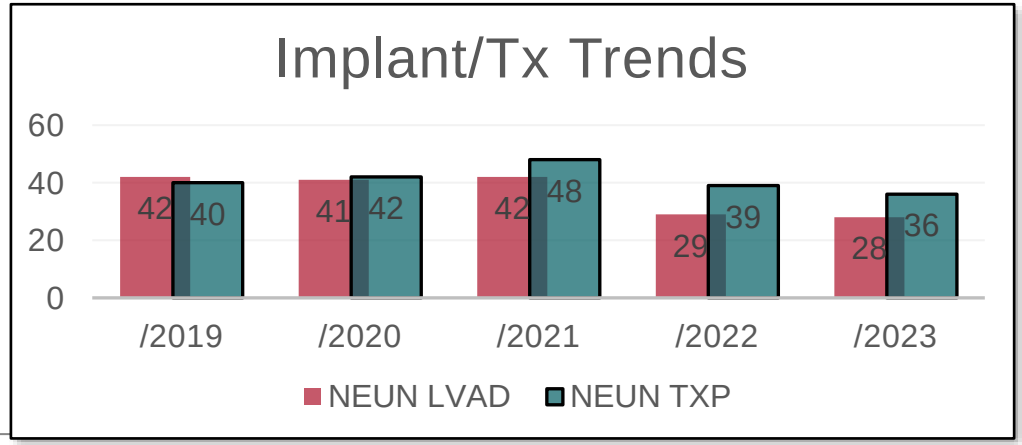


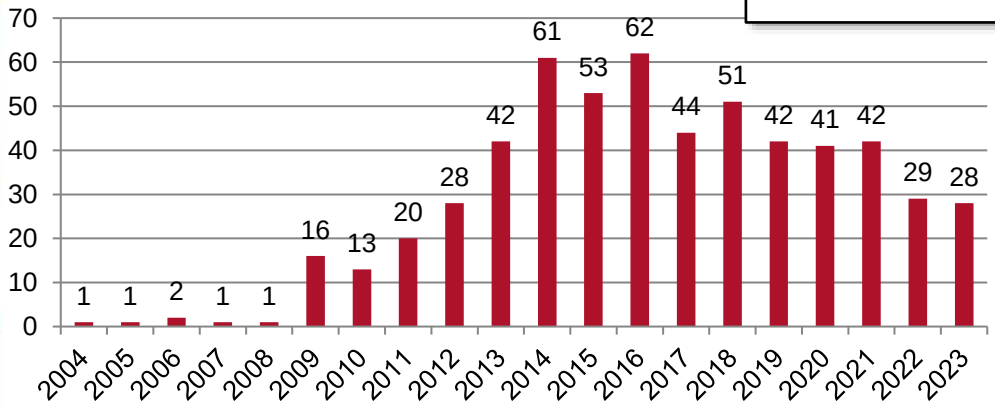
Heart Replacement by the Numbers

Our contemporary durable Left Ventricular Assist Device (LVAD) and Transplant program started in 2009

-Year to date we have implanted 578 LVAD

-583 Transplants

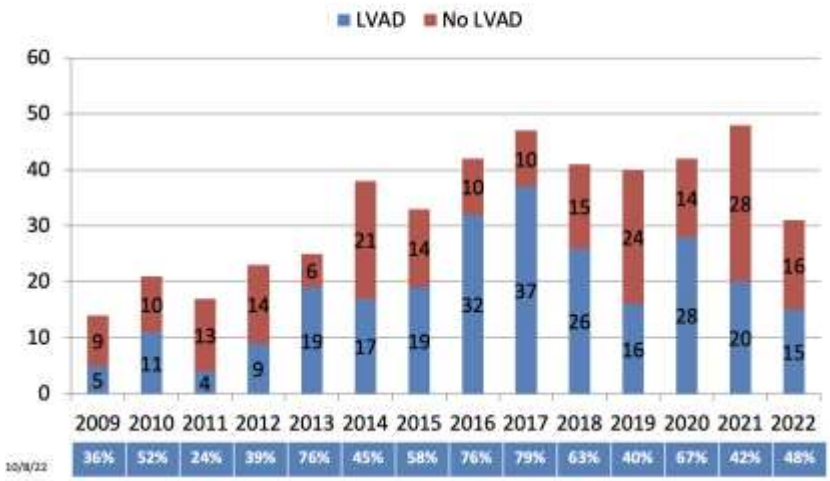




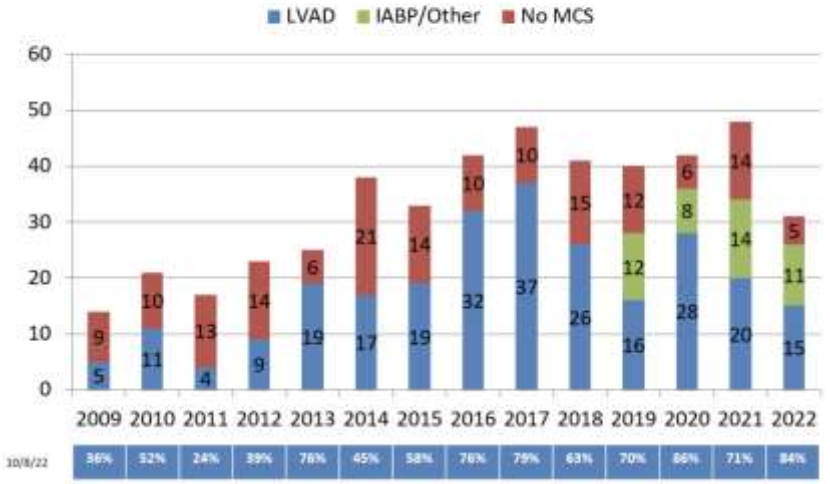
Durable MCS Today:

STS (INTERMACS) Registry Data

Transplants from Durable LVAD by Year



Transplants from MCS by Year



INTO TO THE FUTURE...

Durable MCS:

The TORVAD

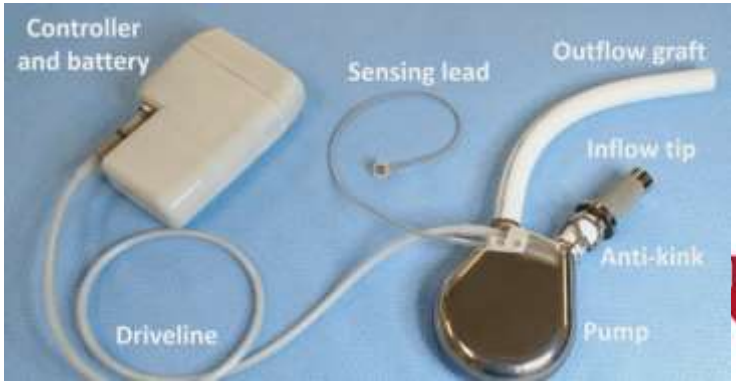
-is a positive displacement pump with rotary flow design which contains a ring-shaped pumping chamber which moves in a “toroidal fashion” at very low rotational speeds (60-150 rpm) with blood ejection accomplished by means of two pistons that “skate” around a rale.

-The pistons are magnetically coupled to motors and an epicardial sensing lead synchronizes to the heartbeat, and rhythm data is used to automatically adjust pump flow according to physiologic needs.

-Counterpulsation device

-Ex-vivo and large animal studies with preserved von Willebrand Factor (vWF) and low levels of hemolysis even without anticoagulation.

-The device remains in the pre-clinical phase



Durable MCS:

The Corwave

-Unique in that it does not rely on a turbine or spinning impeller to provide blood flow rather, a pulsating disc.

-Aims to improved hemocompatibility and hemodynamics through use of said disc wave membrane that creates what is termed a “high fidelity” pulse aiming to mimic systole and diastole

-Electromagnetic actuator, to generate magnetic fields within the pump in order to create oscillations, propagated along the membrane with an algorithm that synchronizes to native left ventricular contraction.

-3 modes: continuous (similar to rotary pump fixed RPM), synchronous co-pulsation providing full LV support and up to 30 mmHg aortic pulse pressure, and synchronous counter-pulsation providing partial LV support

-Clinical study in the near future but currently only investigational

Durable MCS:

The BrioVAD

-Centrifugal magnetically levitated rotor similar to the HM3

-Differences between the HM3 and BrioVAD-

- -narrow (3.5 mm outer diameter) and flexible driveline that **MAY** improve patient comfort and potentially reduce risk of infection;
- -a smaller outflow cannula (driveline durability
- -2 peripherals (a controller with integrated battery, and 1 system battery) made with lighter materials (1 kg weight)
- -patient is only required to carry two peripherals (a controller with integrated battery, and 1 system battery) manufactured from lighter materials (1 kg weight)

-First implant performed in 2017, with >3 years of survival on pump support reported

-25 patient single arm clinical study, with data contributing to device approval in China. Overall, more than 150 patients have been implanted with the technology in China

-INNOVATE study to begin enrolling in 2024

Durable MCS:

Total Artificial Hearts- BiVACOR TAH

-Continuous flow TAH with two centrifugal impellers affixed to a single rotor activated through magnetic levitation

-Hemocompatible due to large gaps through which blood flow through and has a left-right flow balancing system for dynamic adaptation to changes in physiologic demand.

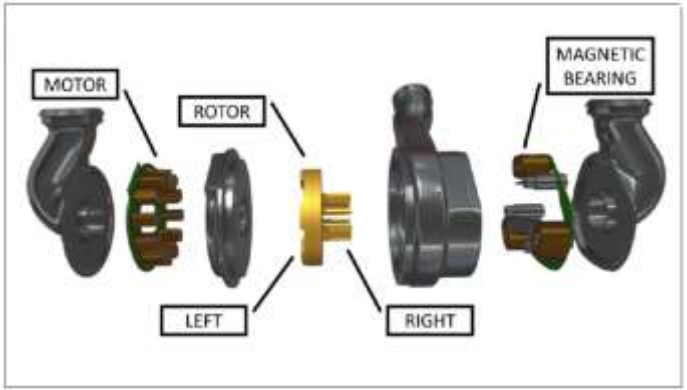
-Cyclic changes in pump speed allow pulsatile flow

-Theoretically can fit in adults and children

-Early Feasibility Study (EFS) approval from the FDA in December 2023. The first implant is anticipated at one of nine U.S. centers in 2024 as part of a bridge to transplant study

-July 9th at Texas Heart Institute

-Plan for TET



Durable MCS:

Total Artificial Hearts- BiVACOR TAH

-Plan for long-term use of up to 10 years

-Single moving part to reduce the risk of failure with redundant electromagnetic motor and driveline components

Durable MCS:

Total Artificial Hearts- Carmat SA- AESON TAH

-Electro-hydraulic device with a shape meant to mimic the human heart

-Composed of two ventricular chambers with bioprosthetic valves, each of which is separated by a membrane into a blood component and a driving fluid component

-The driving fluid generates pulsatile flow according to patient physiologic demands

-Study of 10 patients on support for a cumulative total of 2087 days, the device showed minimal hemolysis and preservation of vWF.

-Device is large needing standard chest CTs for measurement of thoracic dimensions prior to implant.

-Commercially available in Europe and is presently under EFS trial (n=10 patients) in the U.S. for a bridge to transplant intent with the first cohort of 3 patients enrolled. Initiation of enrollment of the second cohort of 7 patients is currently pending FDA approval.

Summary

Despite a decrease in the number of LVAD implants, current use of contemporary MagLev systems are safe and improve QoL and reduce mortality in end-stage heart disease

More devises on the market will likely drive future innovations:

-TCT of energy

-Smaller/lighter devices

-Less invasive surgery

University of Nebraska Medical Center℠

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