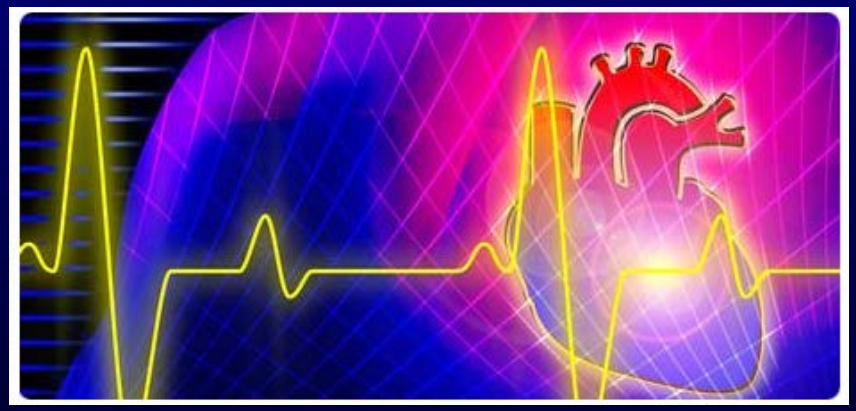
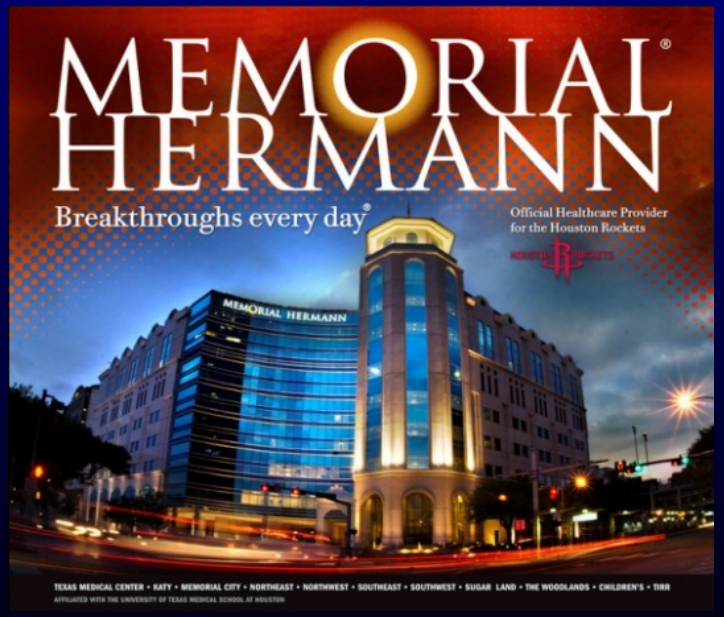
Heart Transplantation and MCS in Advanced Heart Failure

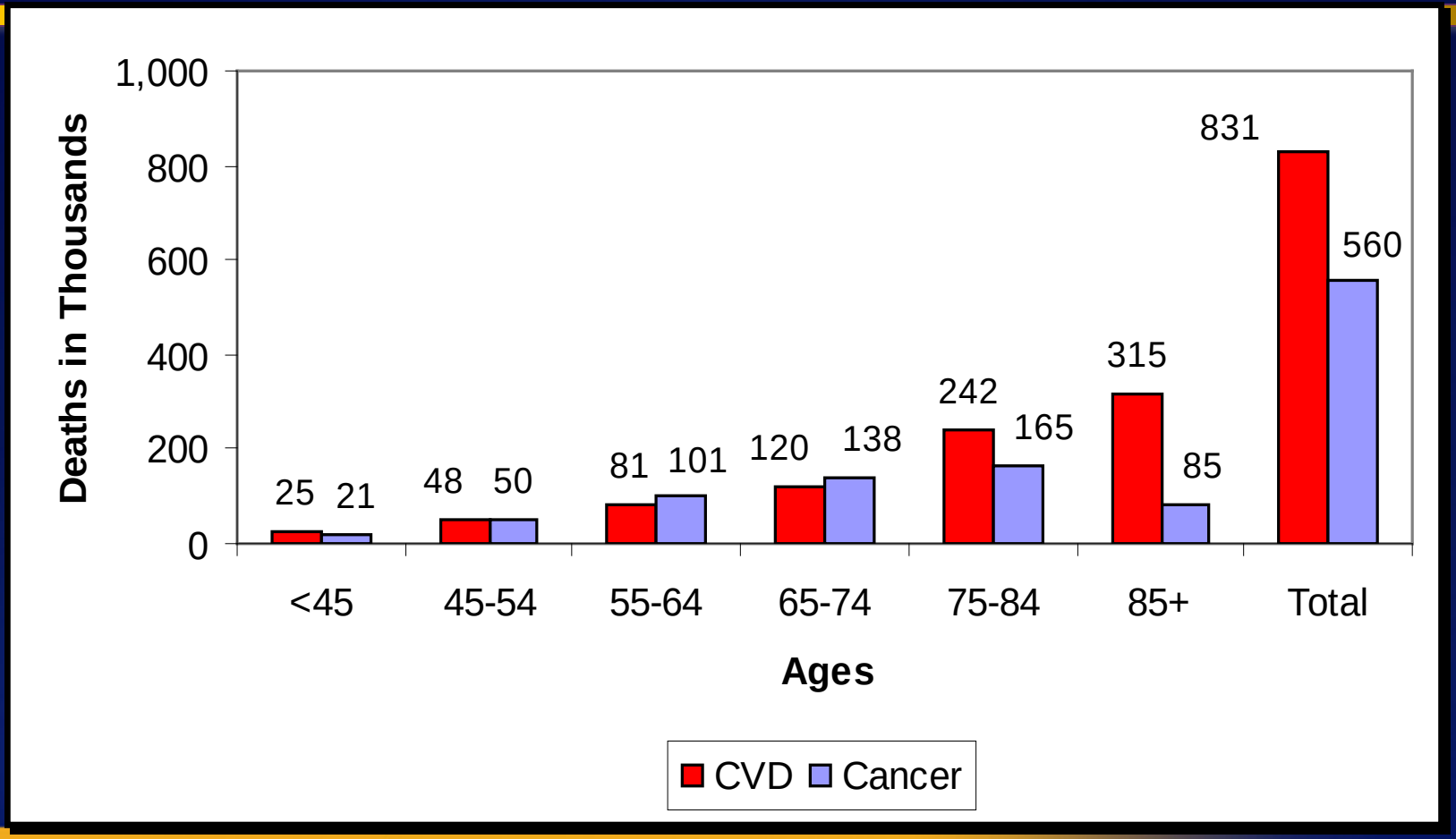
Igor D Gregoric, MD
Professor of surgery, Dept. of CV Surgery at UT, Houston TX
Chief and Program Director, Center for Advanced Heart Failure,
Memorial/Hermann Hospital, Houston, TX



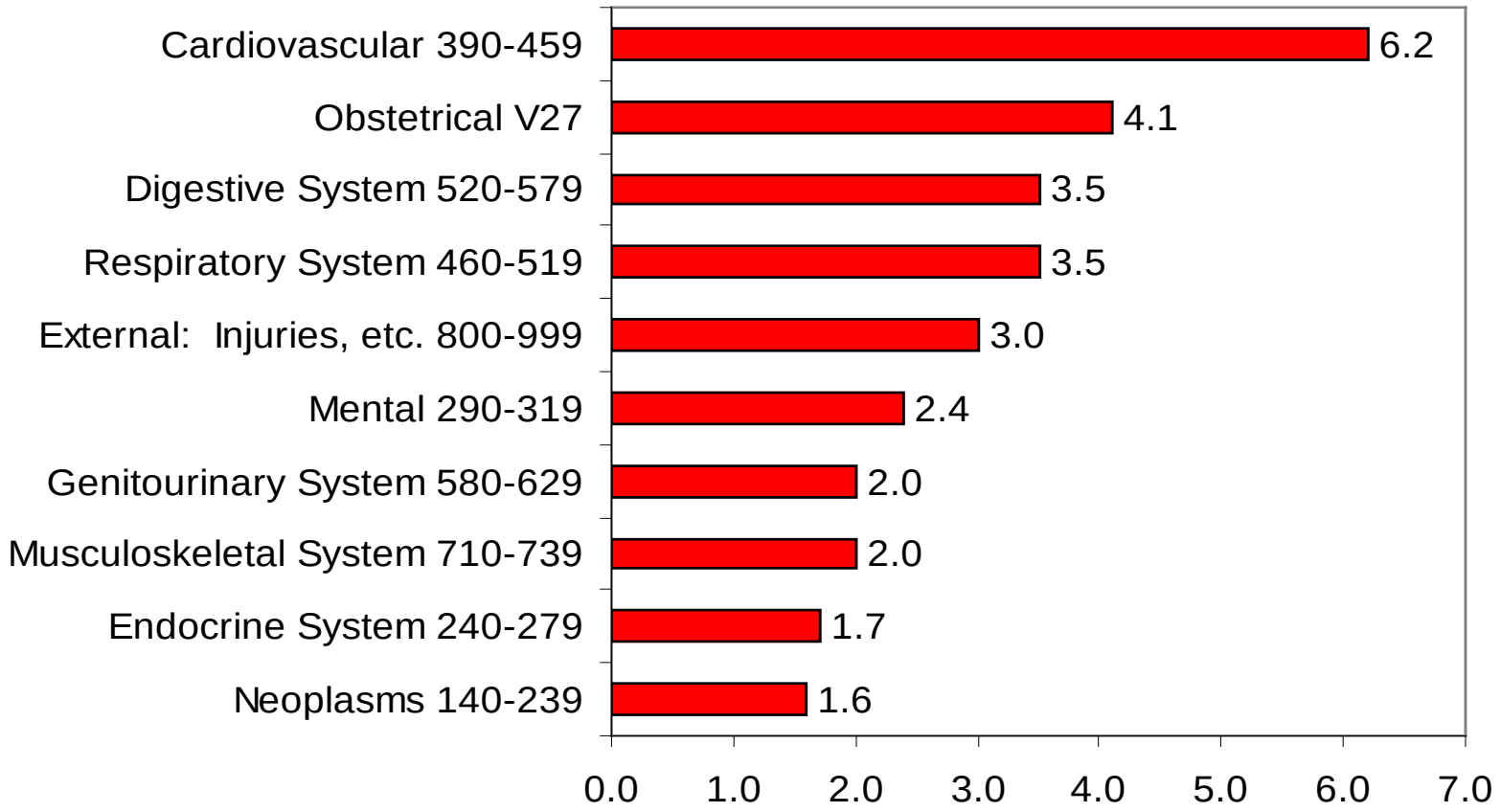


Univerza v Novi Gorici, October 11, 2017

CVD deaths vs. cancer deaths by age (US)



Hospital Discharges (in millions) for the 10 Leading diagnostic Groups



The University of Texas Medical School at Houston
UT★PHYSICIANS

CENTER FOR ADVANCED HEART FAILURE

MEMORIAL HERMANN
Heart & Vascular Institute
Texas Medical Center

NHDS/NCHS and NHLBI 2006

Heart Failure Facts

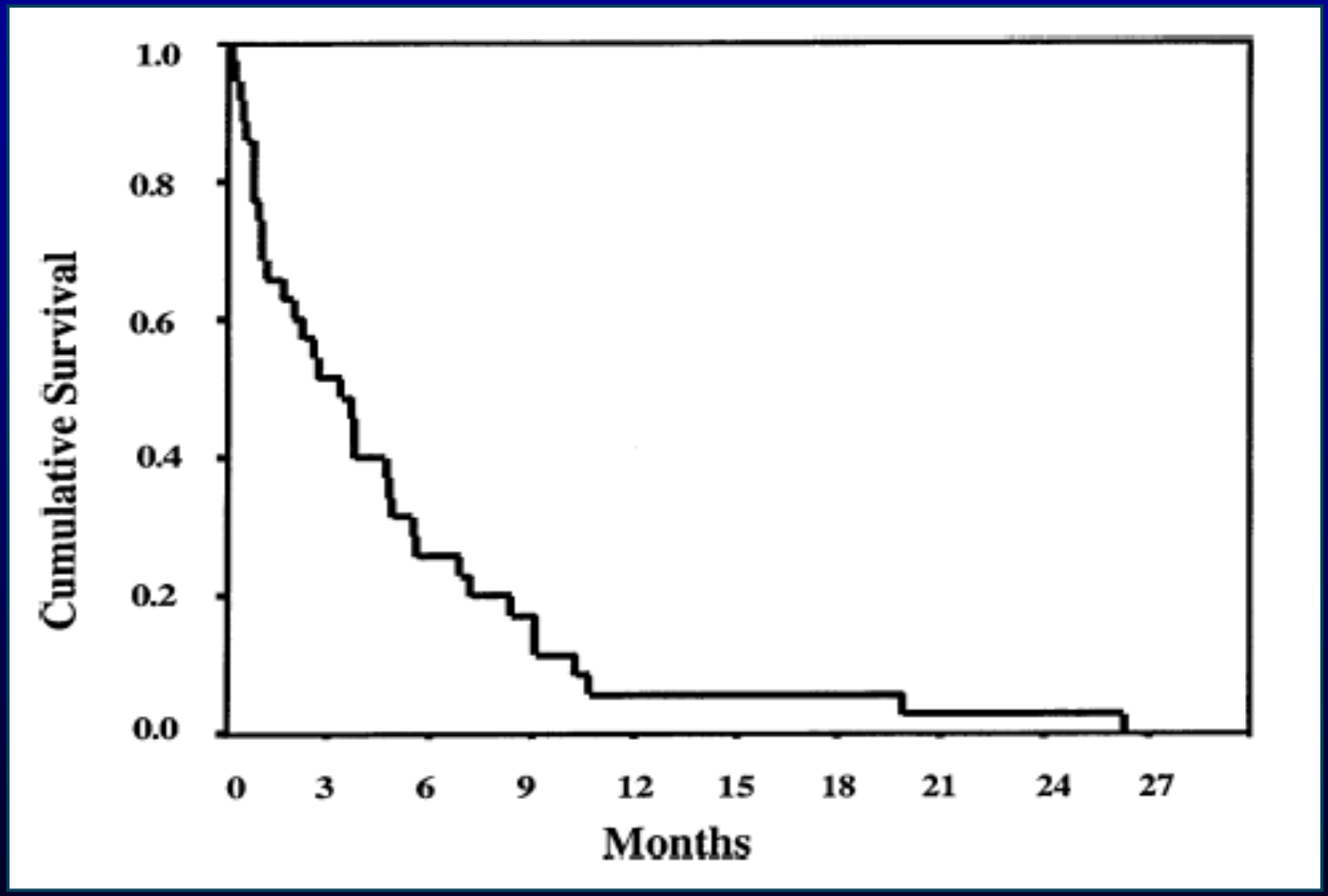
- U.S. prevalence 4.8 million
- 550,000 new cases CHF each year
- Survival outlook <5 years
- 287,000 deaths per year
- $45 billion spent on CHF

Source: American Heart Association

Etiologies of heart failure

- Coronary artery disease
- Idiopathic cardiomyopathy
- Peripartum cardiomyopathy
- Dilated cardiomyopathy
- Ischemic cardiomyopathy
- Acute valvular disease
- Arrhythmia (supraventricular or ventricular)
- Myocarditis
- Congenital heart disease
- Drug induced
- Diabetes mellitus
- Hypertension

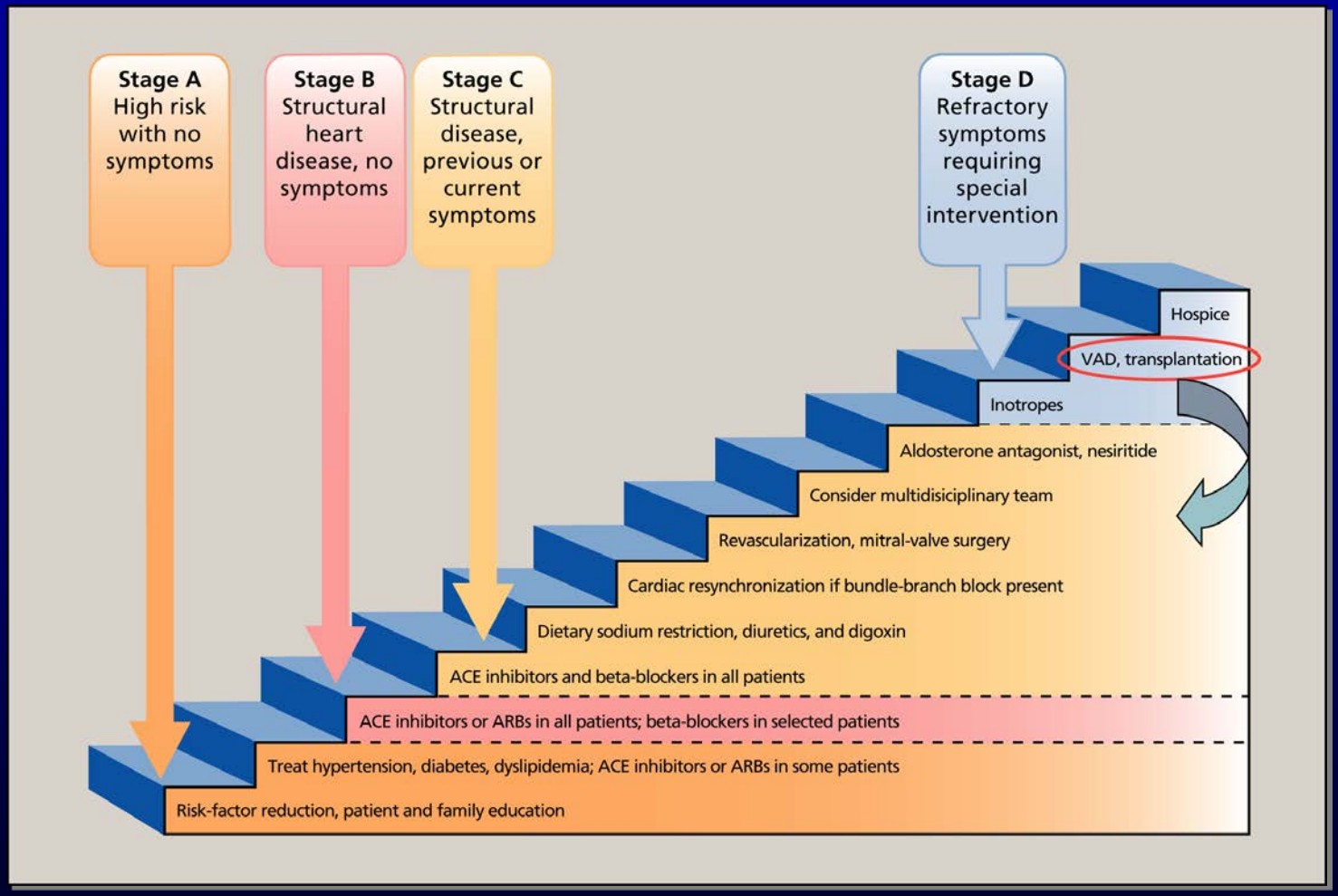
HF Mortality associated with Continuous Inotropic Infusions



Hershberger RE et al. *J Cardiac Failure* 2003;9:180.

End Stage Heart Failure

Heart failure



Jessup M, Brozena S. N Engl J Med 2003;348:2007-18.

Heart Transplantation

The University of Texas Medical School at Houston
UT★PHYSICIANS

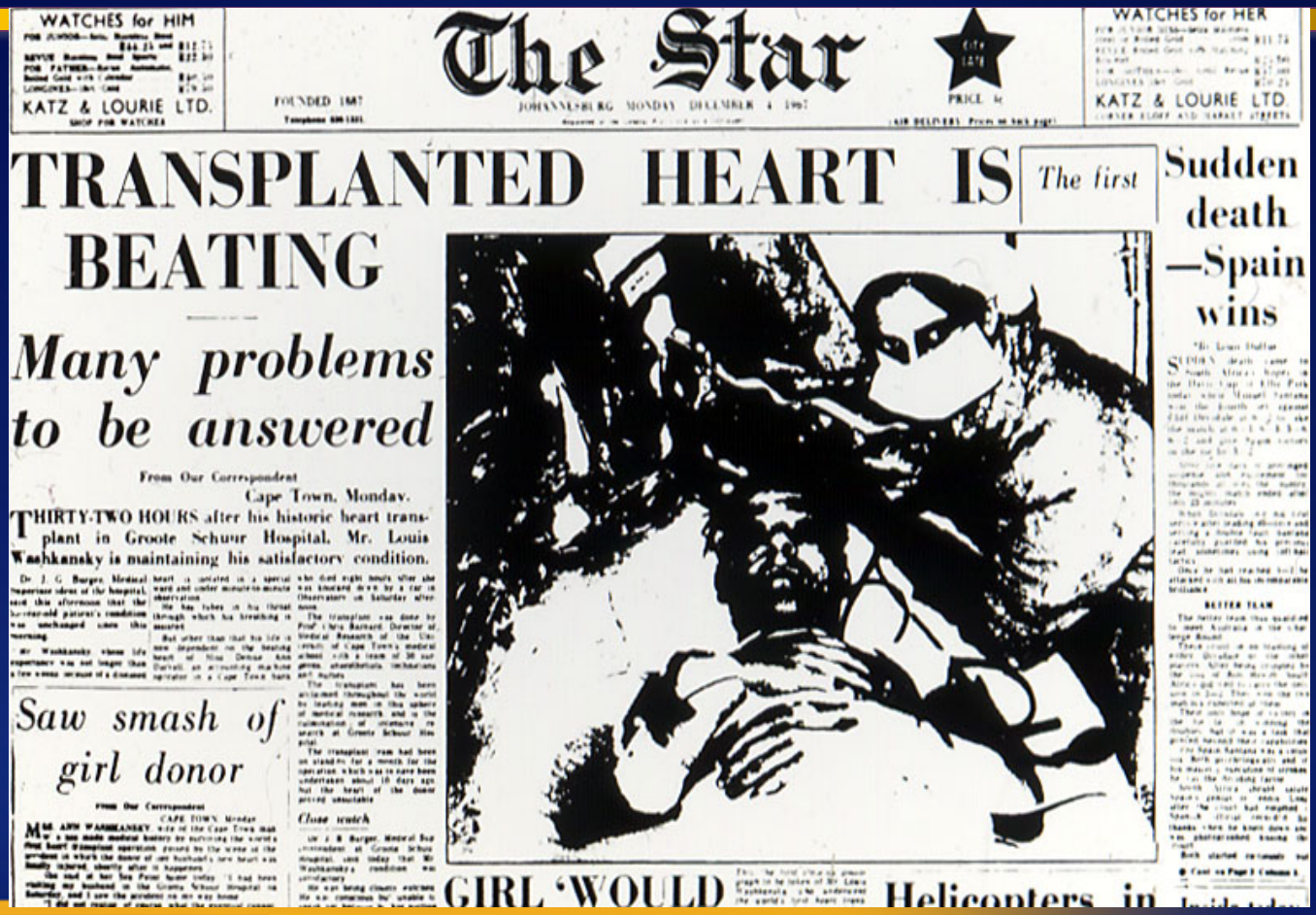
CENTER FOR ADVANCED HEART FAILURE

MEMORIAL HERMANN
Heart & Vascular Institute
Texas Medical Center

Christian Barnard

- Born in South Africa in 1922
- Studied heart surgery at the University of Minnesota then returned to set up a cardiac unit in Cape Town.
- December 1967: transplanted the heart of a road accident victim into a 59 year old patient
- Patient only survived 18 days due to infectious complications

Heart Transplantation Dec 3 1967



WATCHES for HIM

KATZ & LOURIE LTD.

The Star

JOHANNESBURG MONDAY DECEMBER 4 1967

PRICE 4c

WATCHES for HER

KATZ & LOURIE LTD.

TRANSPLANTED HEART IS BEATING

Many problems to be answered

From Our Correspondent

Cape Town, Monday.

THIRTY-TWO HOURS after his historic heart transplant in Groote Schuur Hospital, Mr. Louis Washkansky is maintaining his satisfactory condition.

Saw smash of girl donor

The first

Sudden death —Spain wins

GIRL 'WOULD

Helicopters in

The University of Texas Medical School at Houston

UT★PHYSICIANS

CENTER FOR ADVANCED HEART FAILURE

MEMORIAL HERMANN Heart & Vascular Institute Texas Medical Center

Summary of Heart Transplants

as of March 1, 1971

- Total No. of Transplants **170**
  - US 108
  - Foreign 62
- Total No. of Recpients **167**
  - Total No of Deaths 143
  - No of Survivors 24
    - US 18
    - Foreign 6
- Total No of Countries **20**

Richenbacher, MCS, 1999

The interest in cardiac transplantation waned during the 1970s as most recipients died within a few months of the transplant operation from infection or rejection.

1976– Discovery Cyclosporine A

- Severity and acuity of rejections decreased
- Lead to a renewed interest in cardiac transplantation in 1980s
- The need for bridge to transplant devices resurfaced
  - LVAD
  - TAH

Most Common Transplantation -Blood Transfusion-

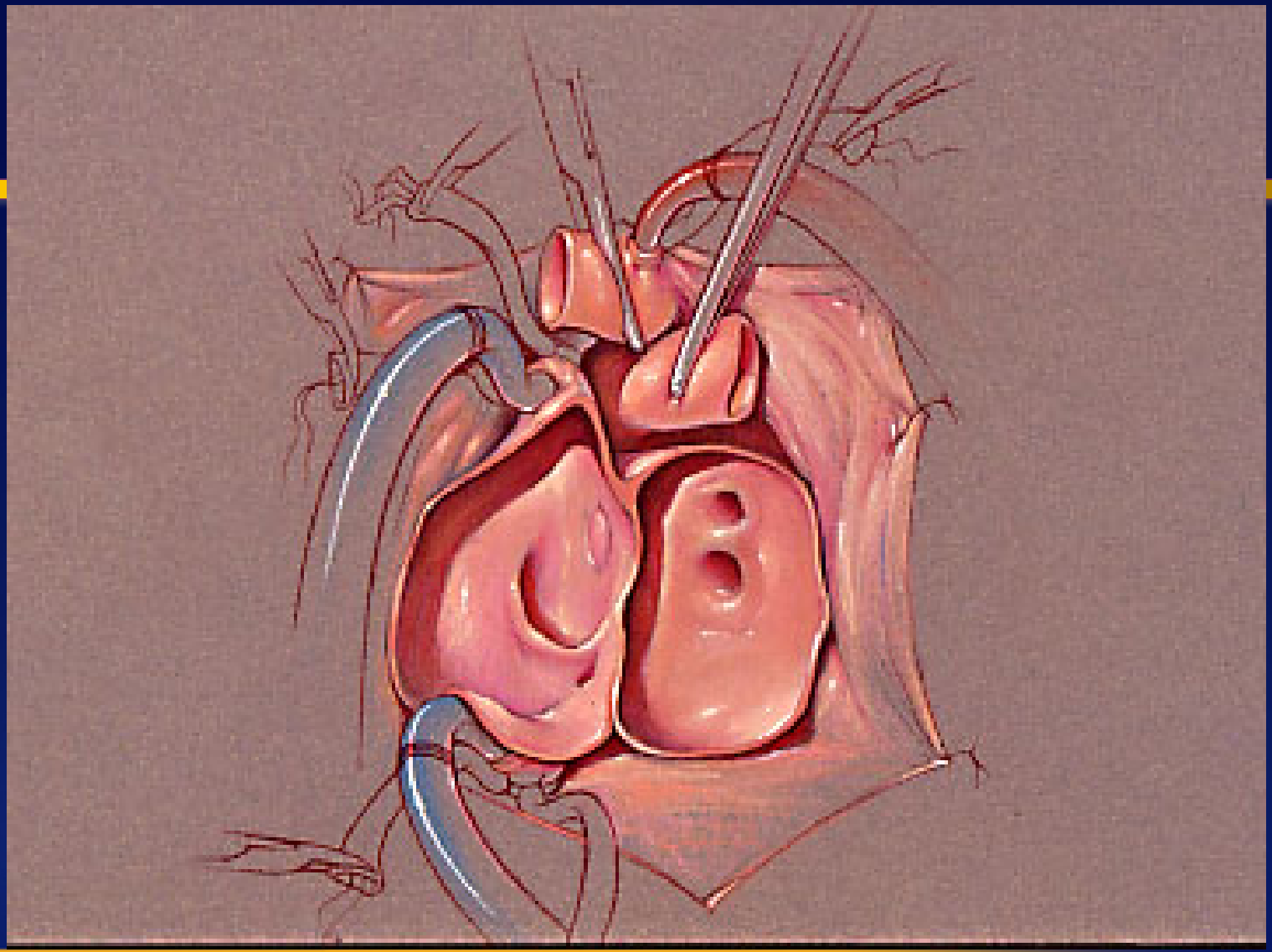
Recipient	Potential donor: O	Potential donor: A	Potential donor: B	Potential donor: AB
O Anti-A and anti-B antibodies				
A Anti-B antibodies				
B Anti-A antibodies				
AB No antibodies against A or B				

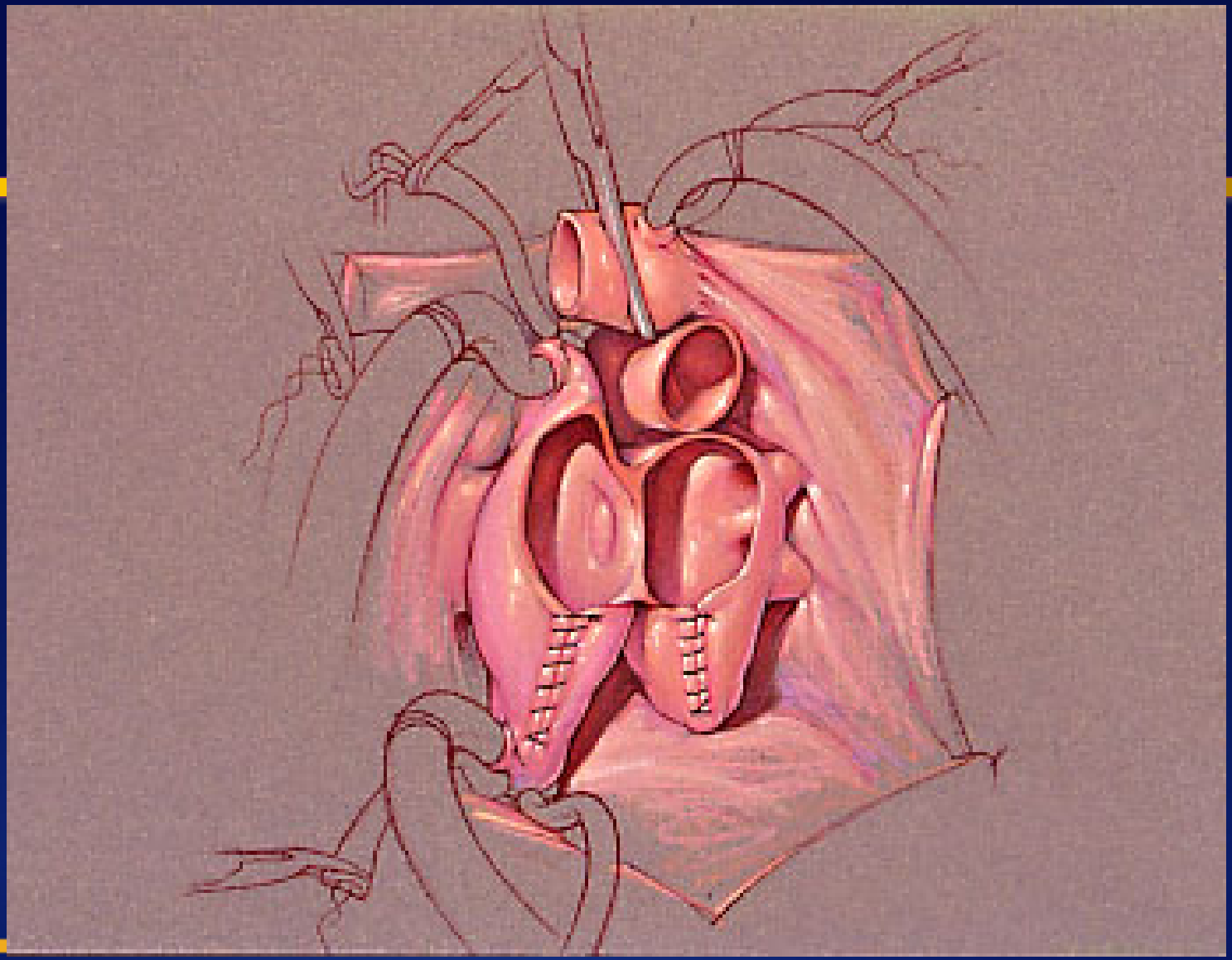
Transfuse Not transfused

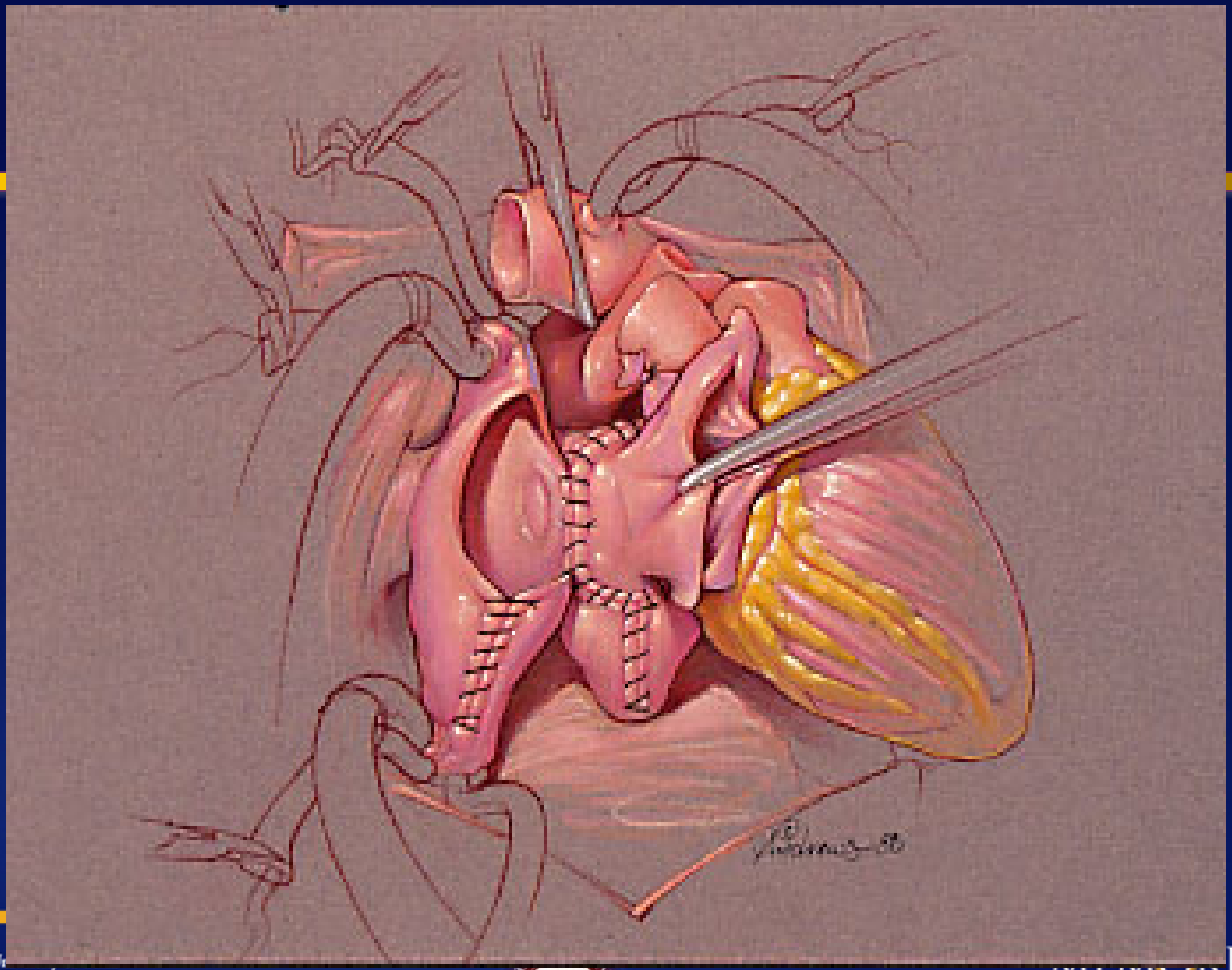
Immunologic Analysis

- HLA Tissue Typing
- Cytoscreen
- Cross Match

TECHNIQUE





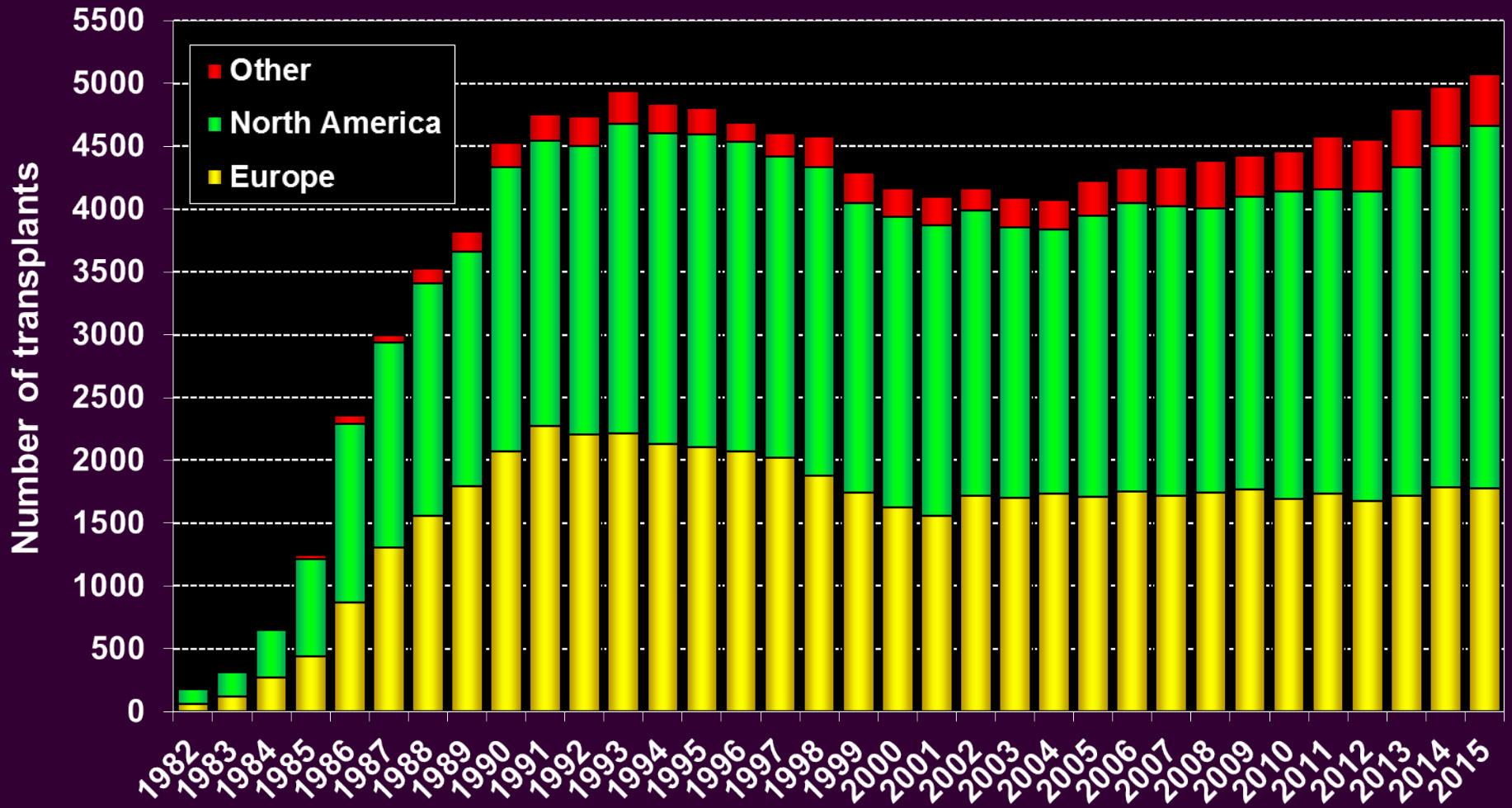


HEART TRANSPLANTATION

Overall

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2017
JHLT. 2017 Oct; 36(10): 1037-1079

Adult and Pediatric Heart Transplants
Number of Transplants by Year and Location



NOTE: This figure includes only the heart transplants that are reported to the ISHLT Transplant Registry. As such, the presented data may not mirror the changes in the number of heart transplants performed worldwide.

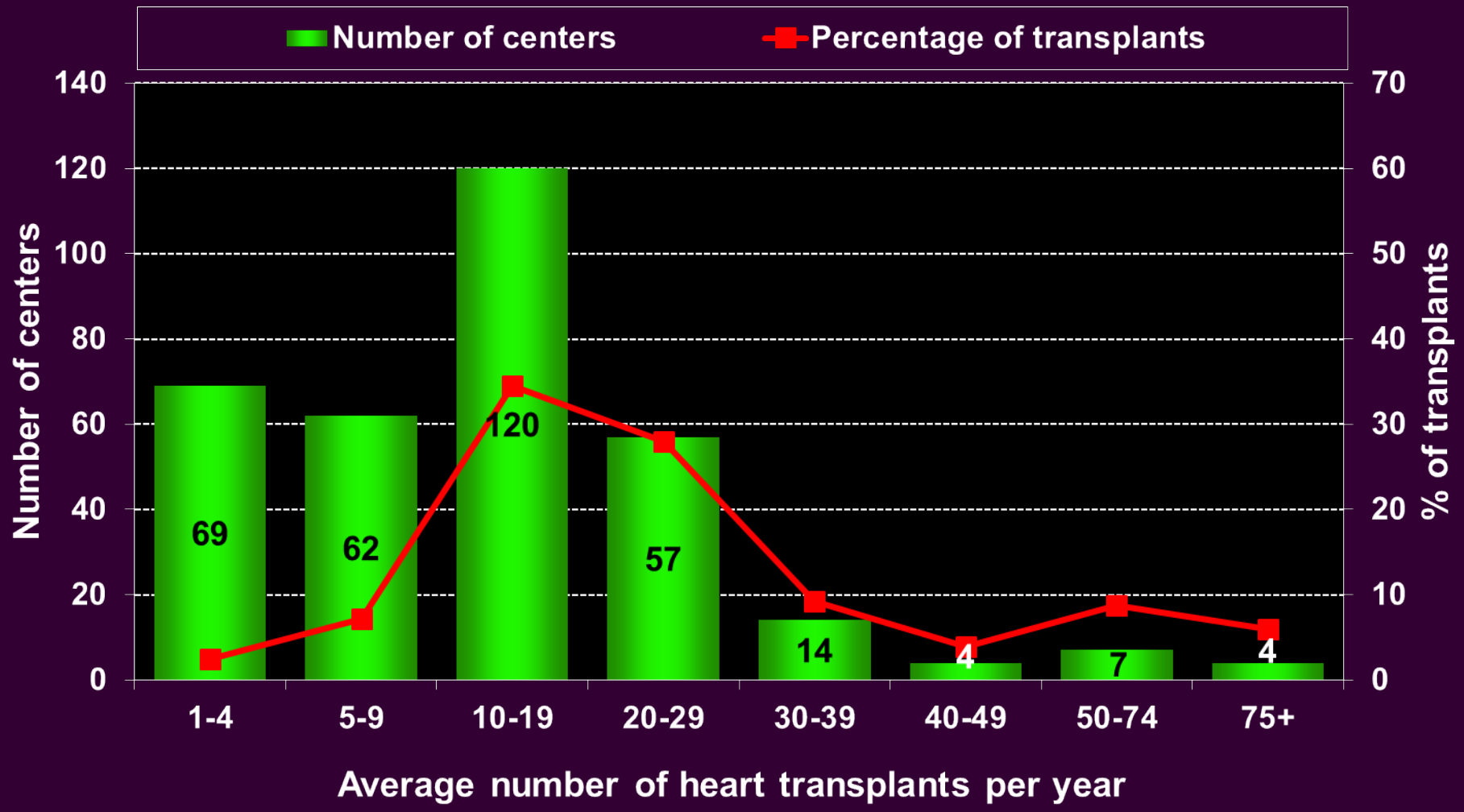
ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

2017

JHLT. 2017 Oct; 36(10): 1037-1079

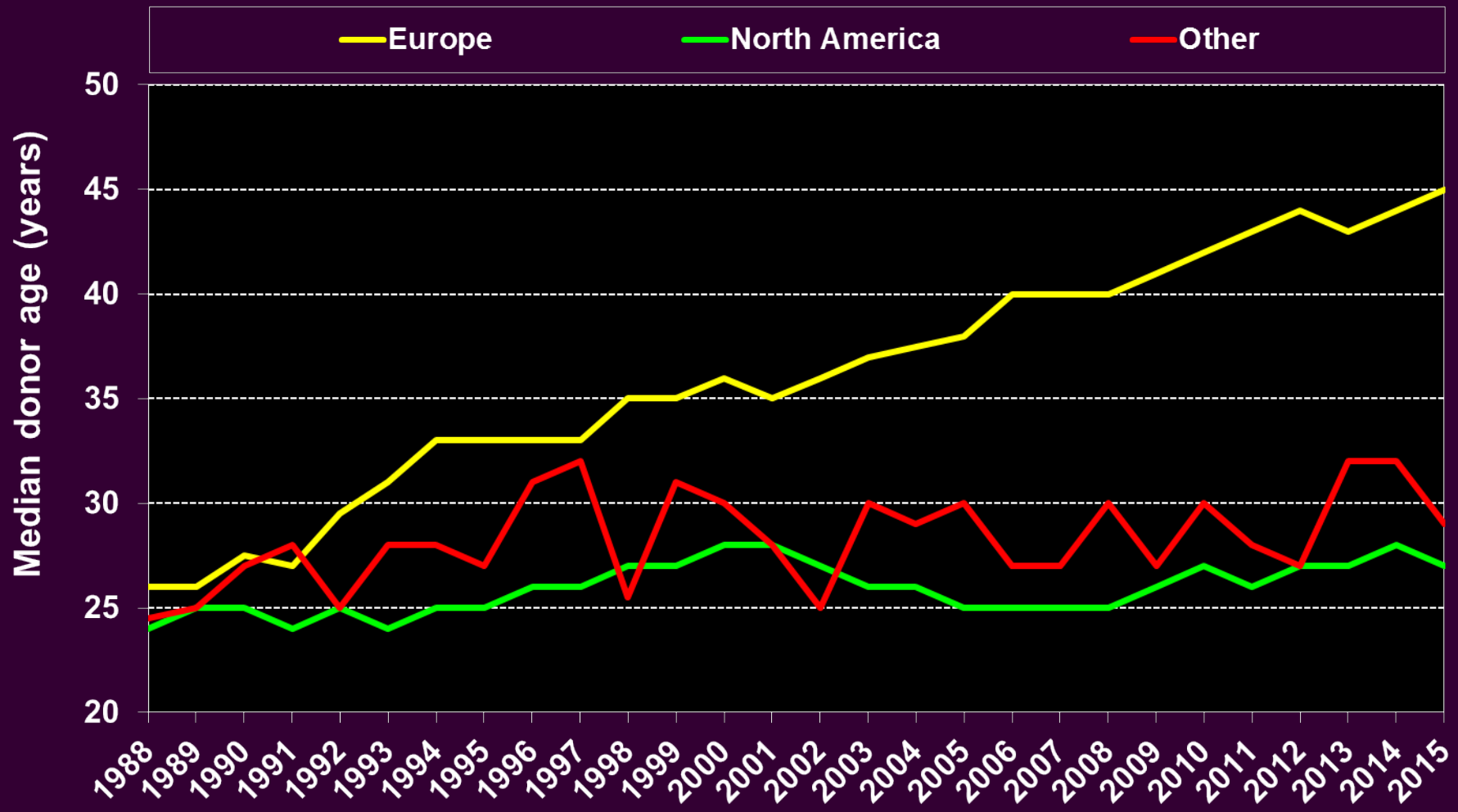
Adult and Pediatric Heart Transplants

Average Center Volume (Transplants: January 2009 – June 2016)



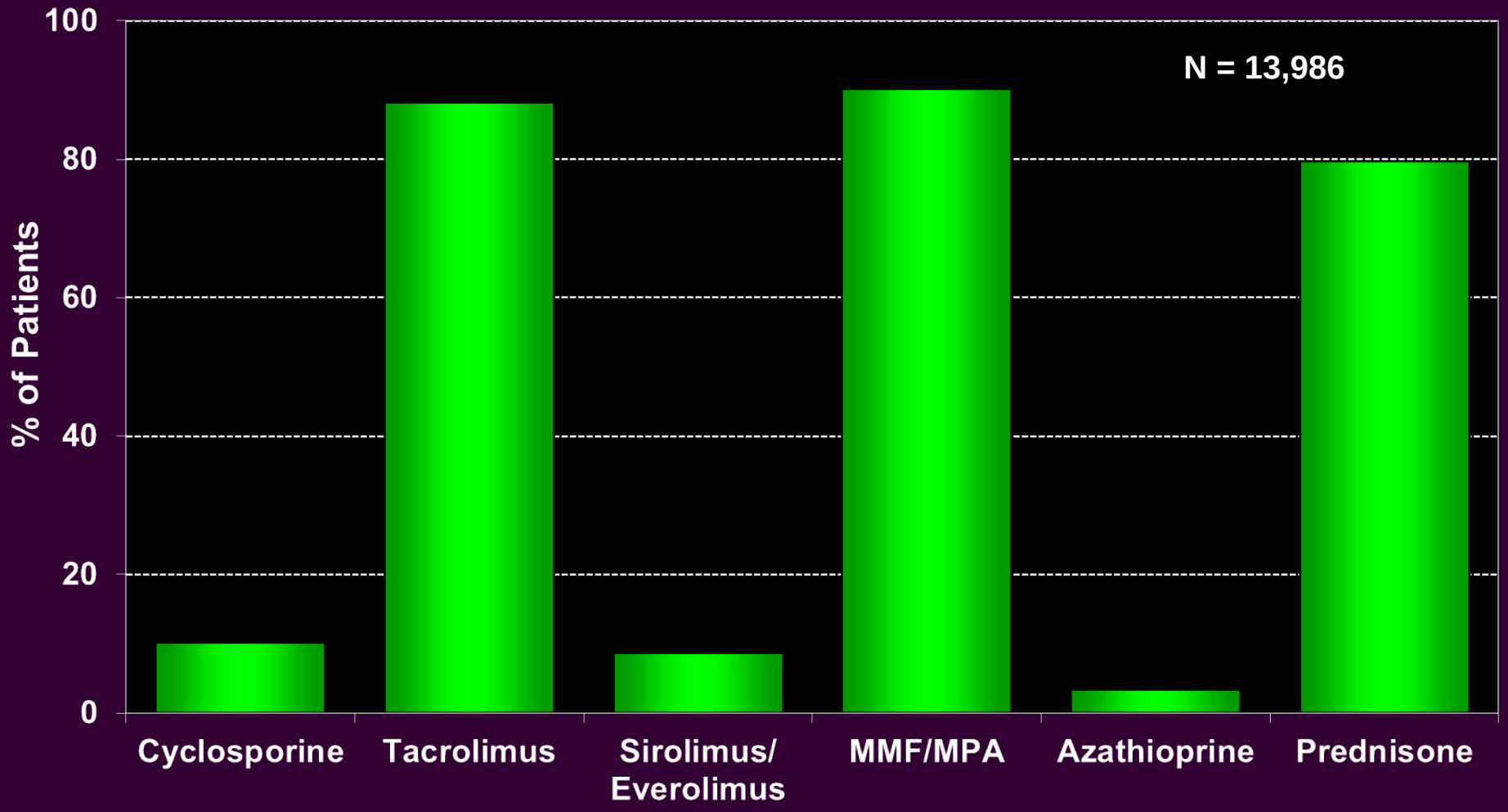
ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2017
JHLT. 2017 Oct; 36(10): 1037-1079

Adult and Pediatric Heart Transplants
Median Donor Age by Location



ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2017
JHLT. 2017 Oct; 36(10): 1037-1079

Adult Heart Transplants
Maintenance Immunosuppression at Time of 1 Year Follow-up (Follow-ups: January 2009 – June 2016)



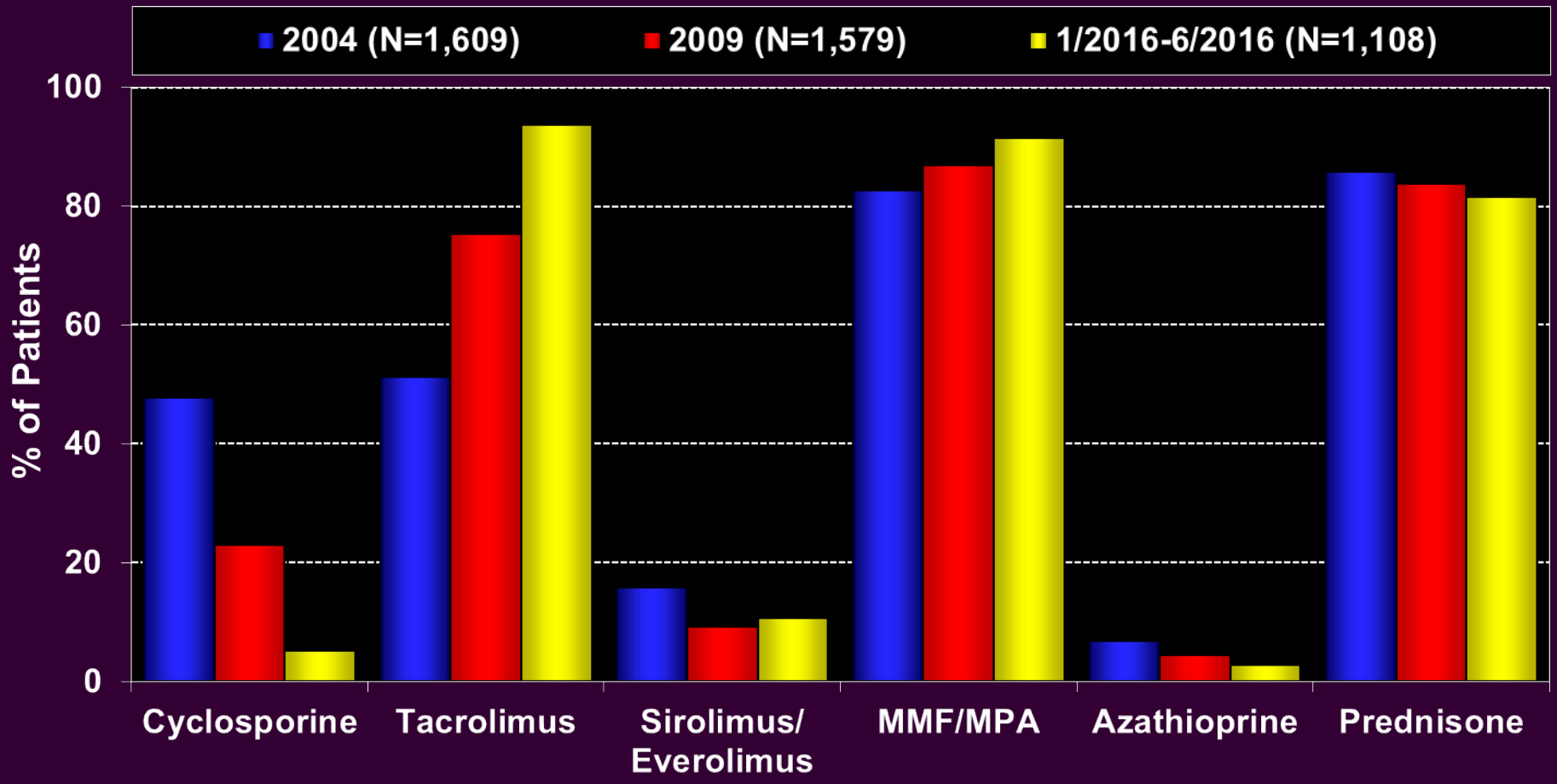
ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

2017

JHLT. 2017 Oct; 36(10): 1037-1079

Analysis is limited to patients who were alive at the time of the follow-up.

Adult Heart Transplants
Maintenance Immunosuppression at Time of 1 Year Follow-up by Year

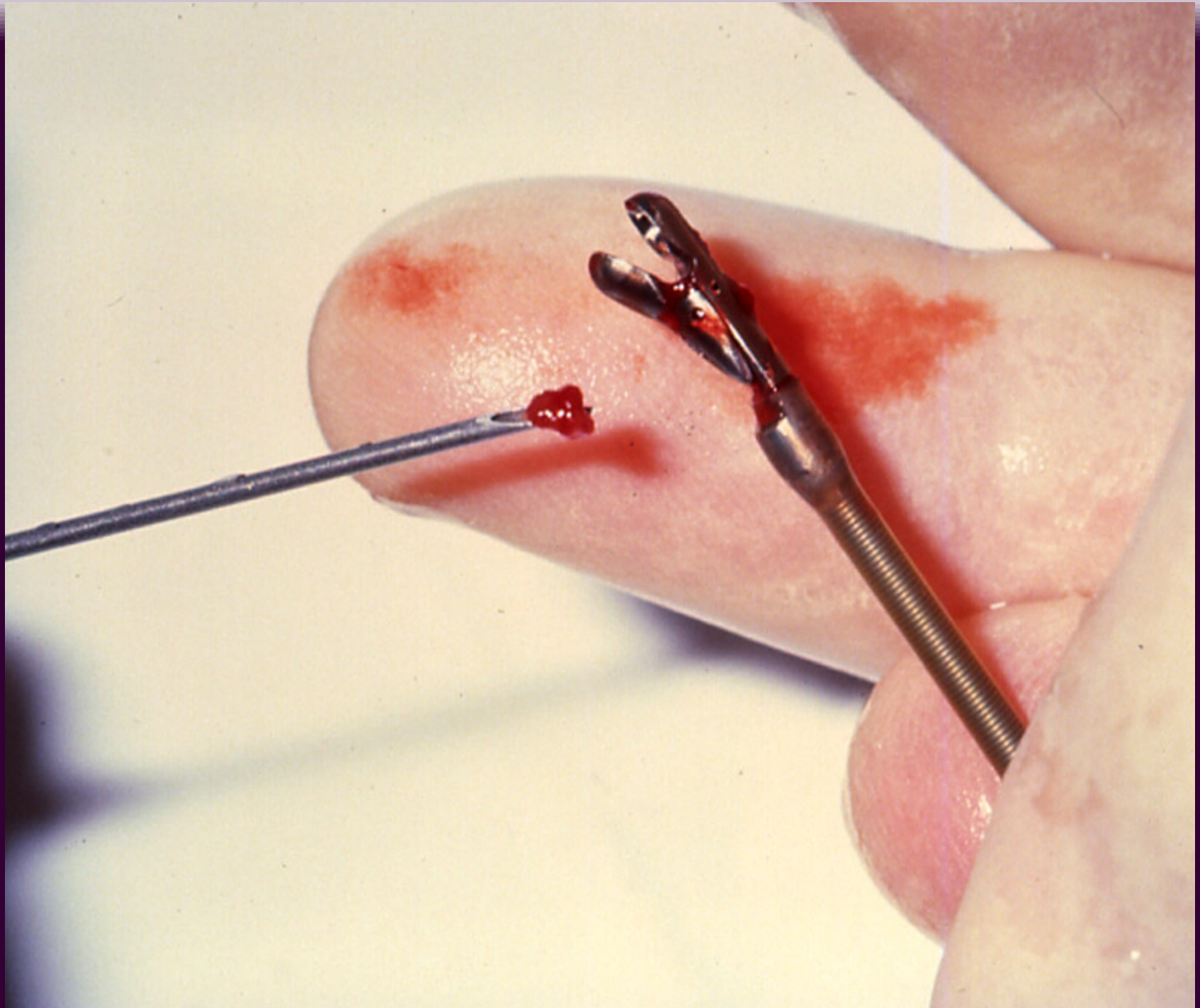


NOTE: Different patients are analyzed in each timeframe.

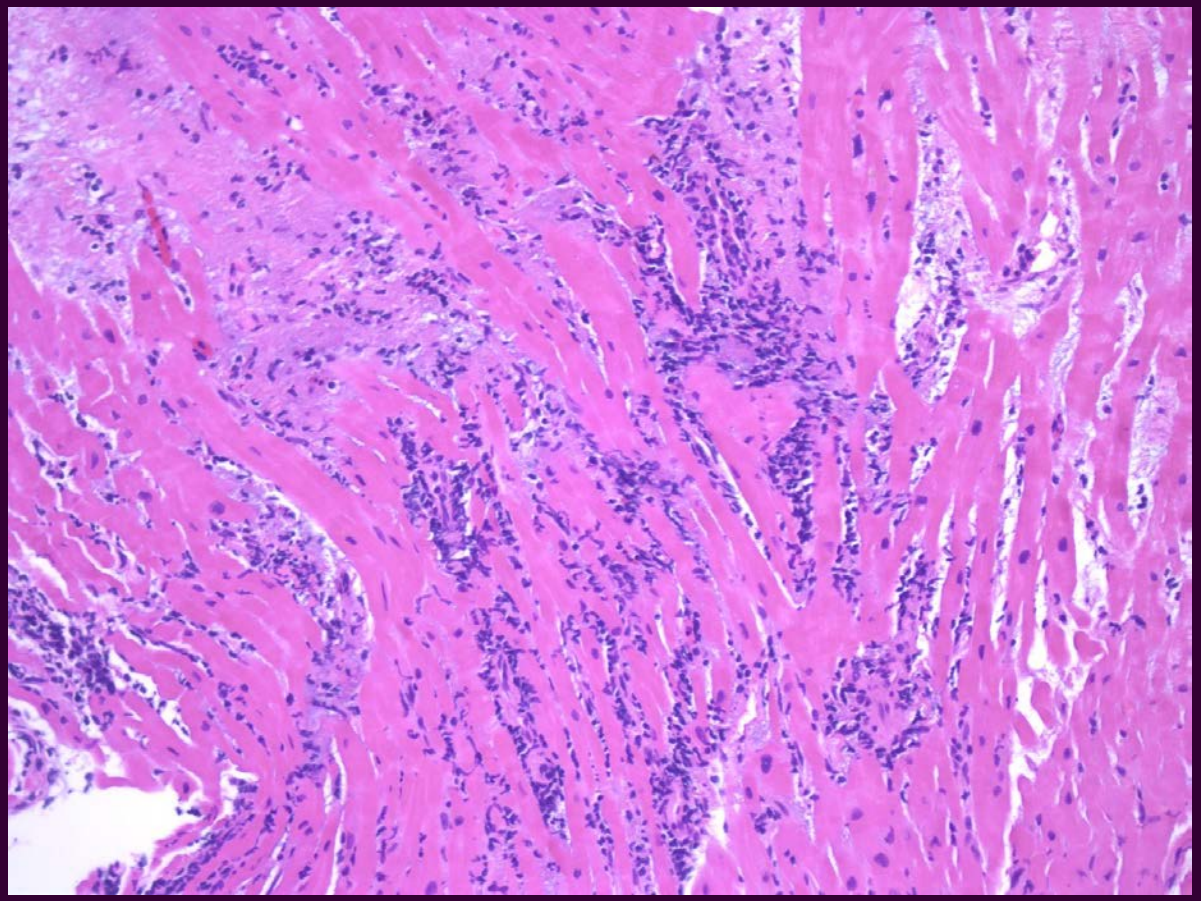
ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2017
JHLT. 2017 Oct; 36(10): 1037-1079

Analysis is limited to patients who were alive at the time of the follow-up.

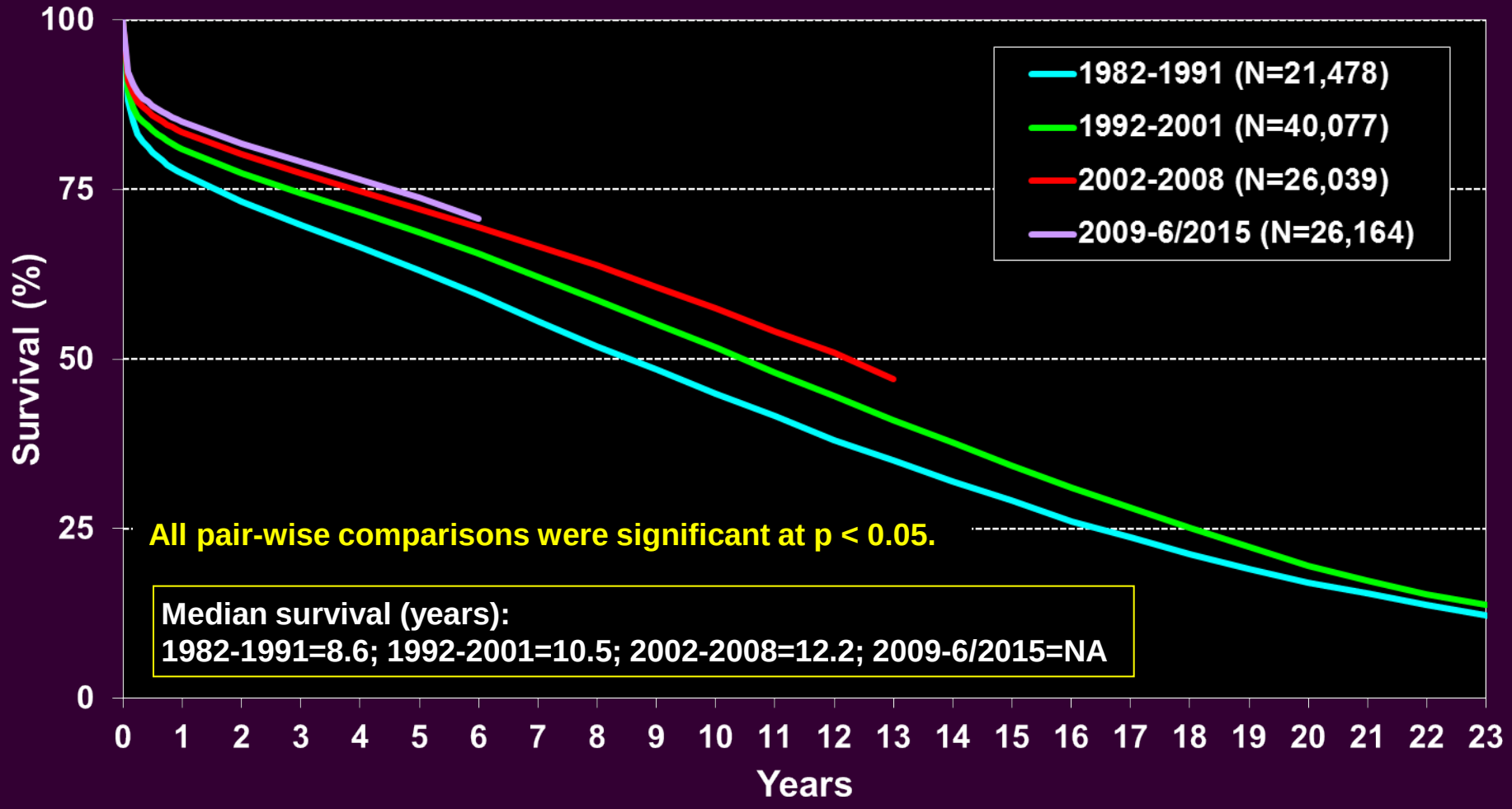
Rejection



Grade 3R, Severe (3B)

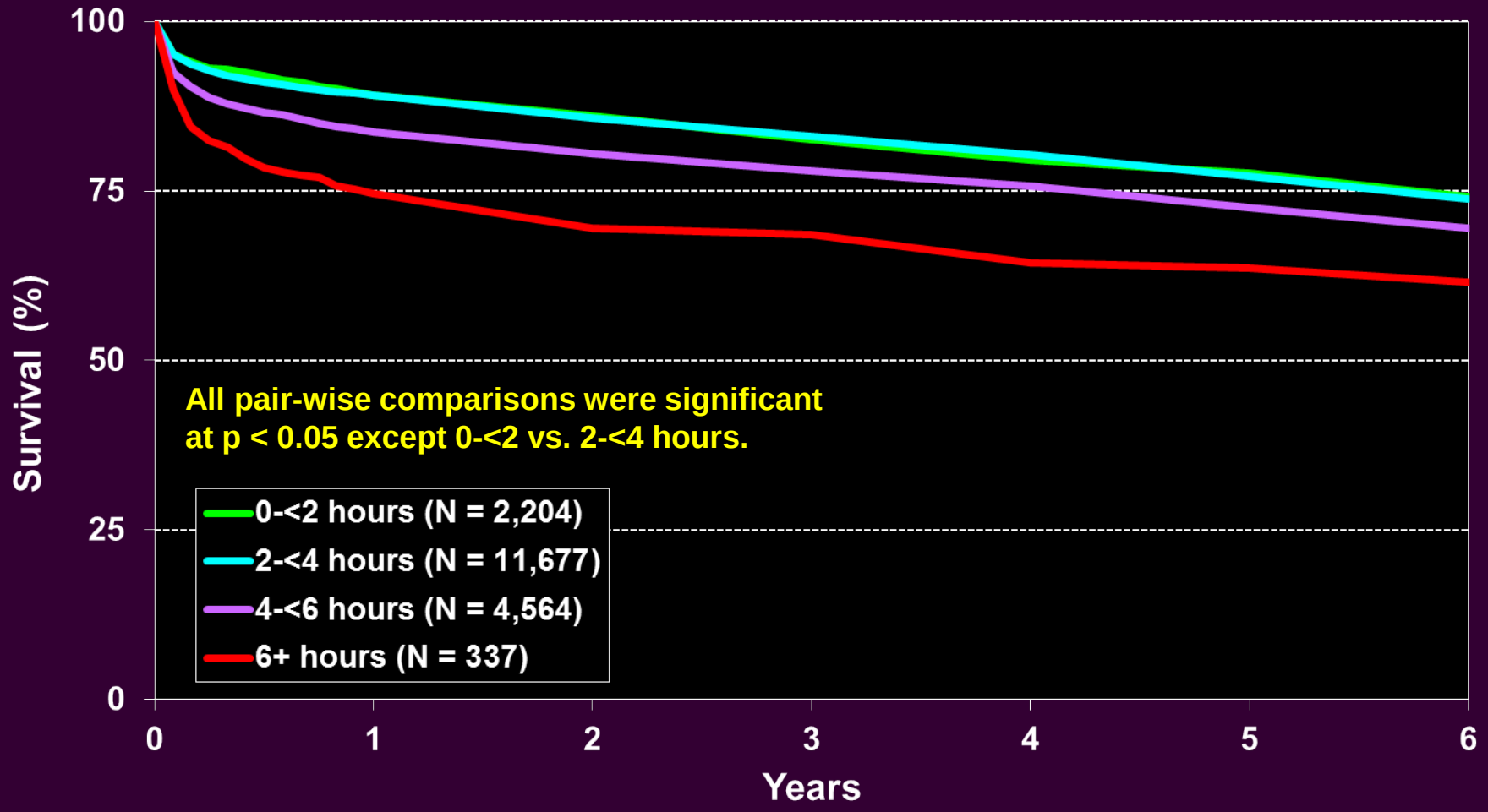


Adult Heart Transplants
Kaplan-Meier Survival by Era
(Transplants: January 1982 – June 2015)



ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2017
JHLT. 2017 Oct; 36(10): 1037-1079

Adult Heart Transplants
Kaplan-Meier Survival by Ischemic Time
(Transplants: January 2009 – June 2015)

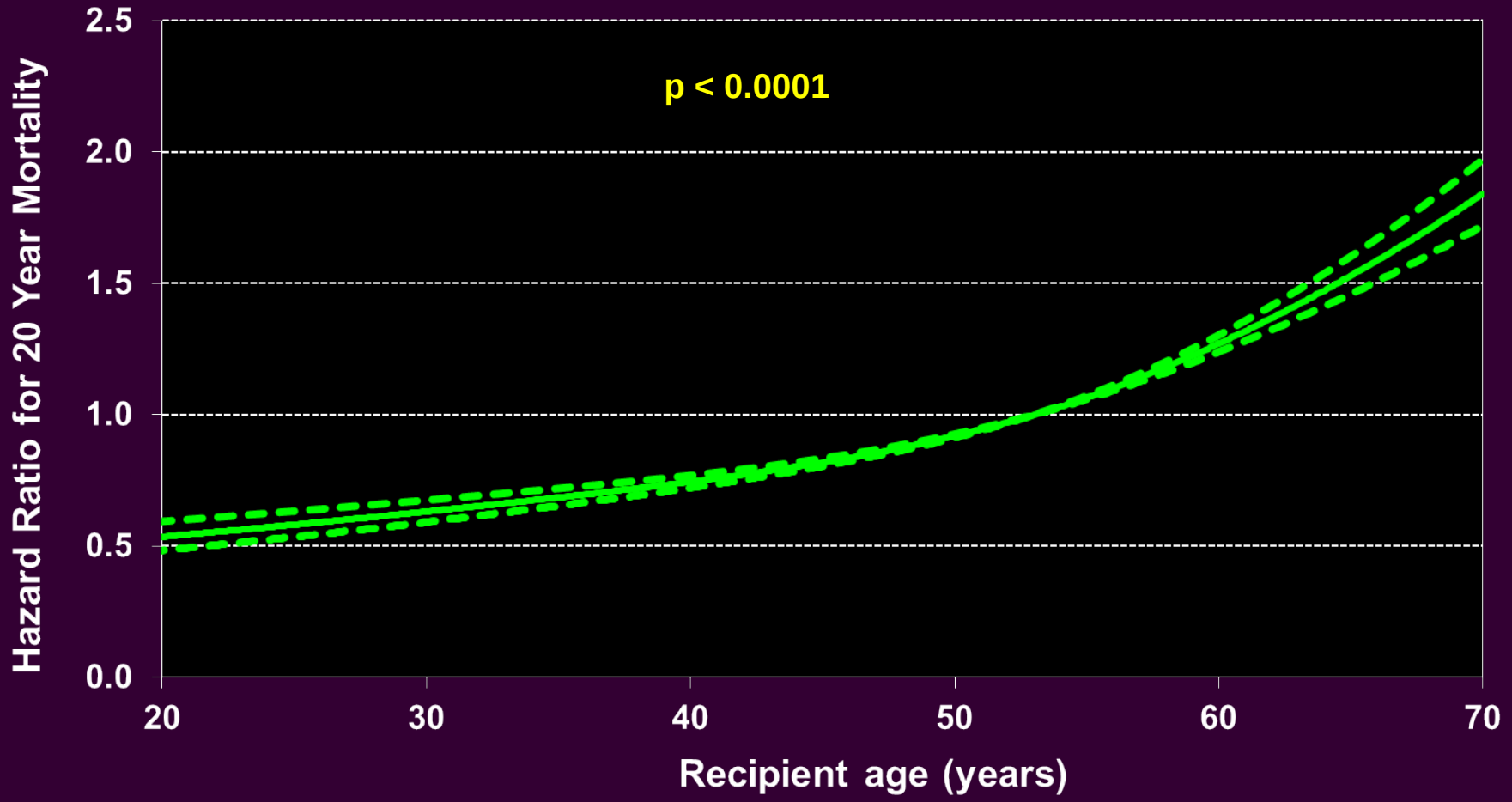


ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2017
JHLT. 2017 Oct; 36(10): 1037-1079

Adult Heart Transplants (1991-6/1996)

Risk Factors For 20 Year Mortality with 95% Confidence Limits

Recipient age



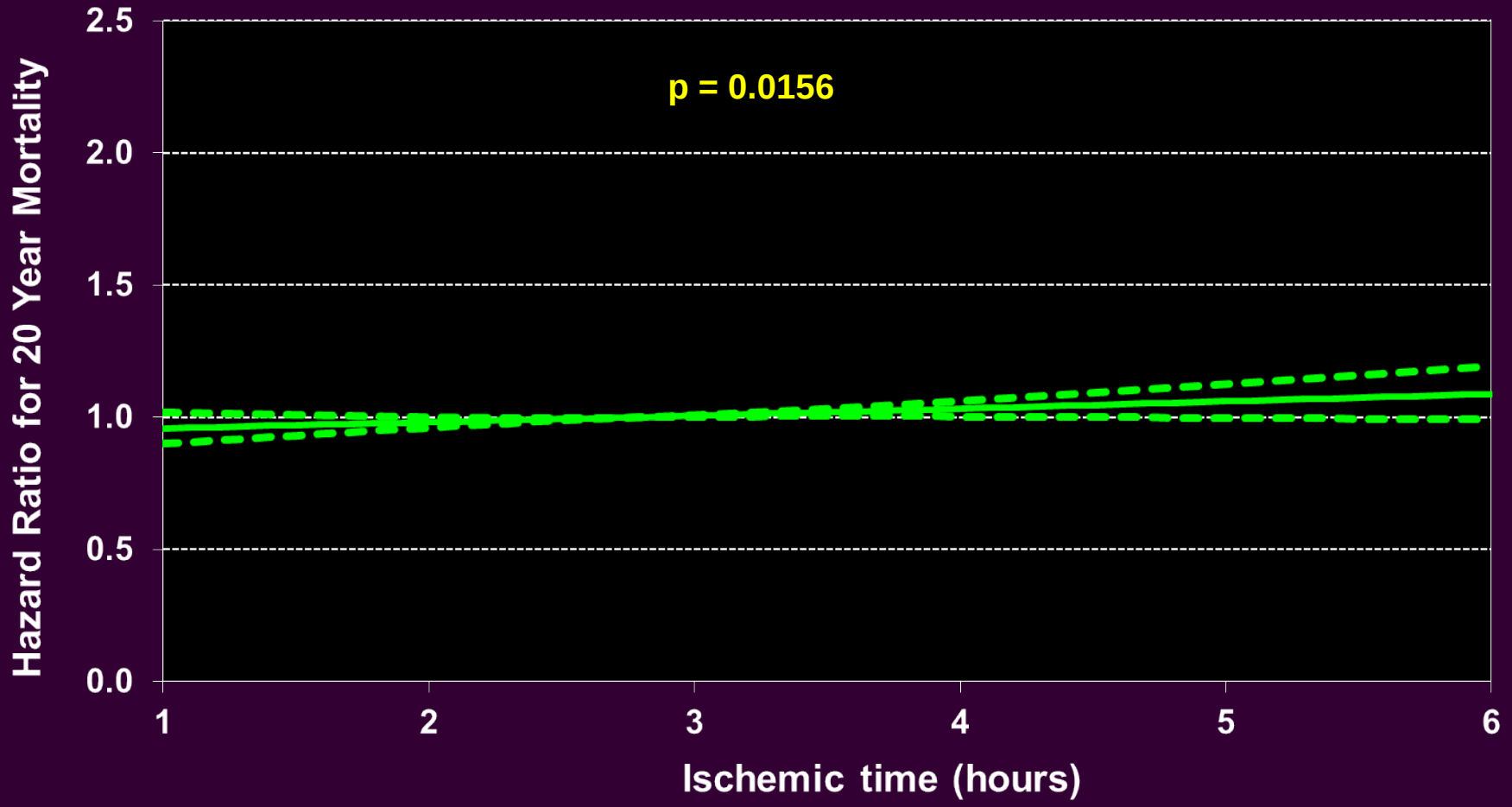
(N = 22,629)

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2017
JHLT. 2017 Oct; 36(10): 1037-1079

Adult Heart Transplants (1991-6/1996)

Risk Factors For 20 Year Mortality with 95% Confidence Limits

Ischemic time



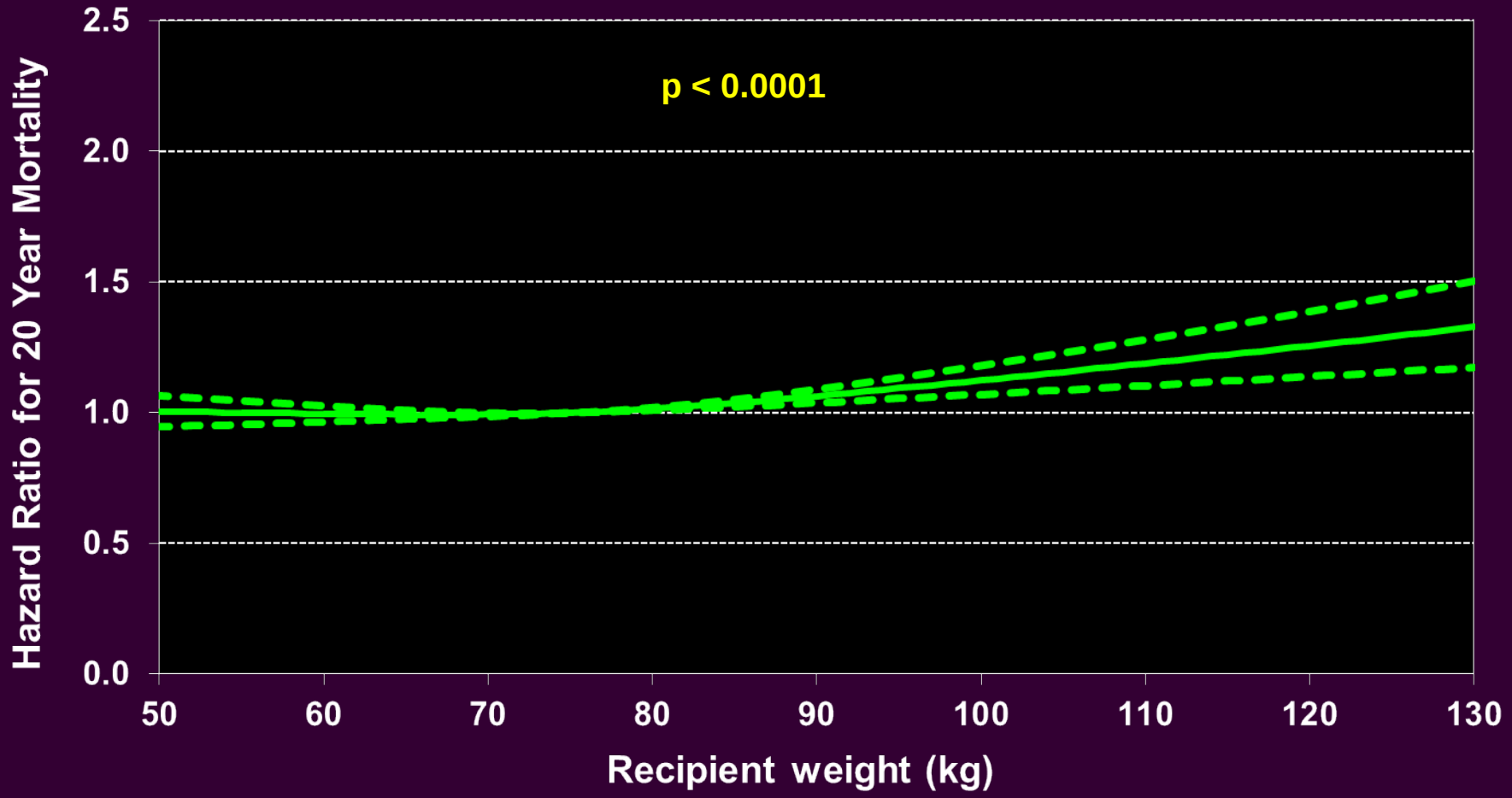
(N = 22,629)

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2017
JHLT. 2017 Oct; 36(10): 1037-1079

Adult Heart Transplants (1991-6/1996)

Risk Factors For 20 Year Mortality with 95% Confidence Limits

Recipient weight (kg)



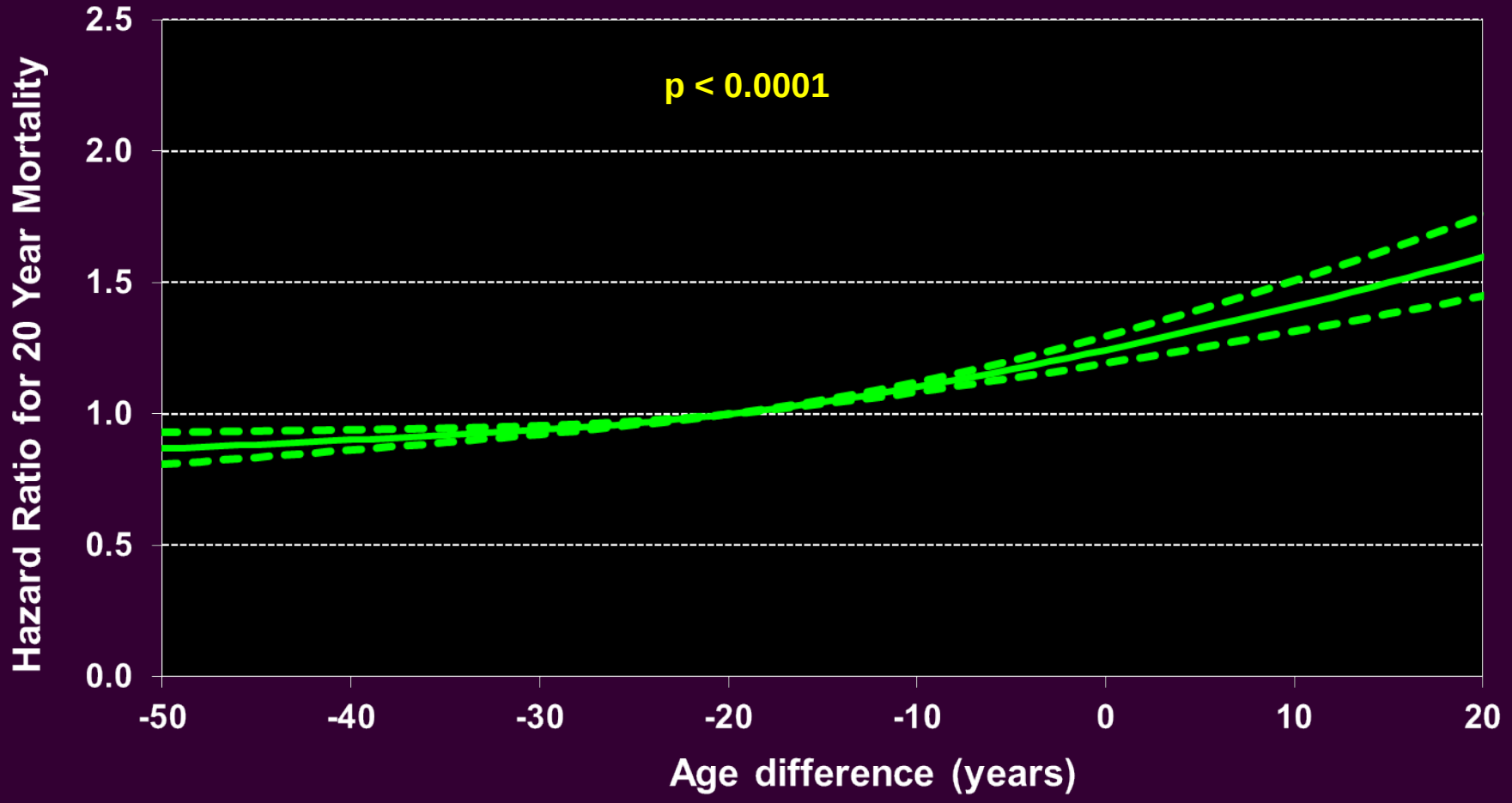
(N = 22,629)

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2017
JHLT. 2017 Oct; 36(10): 1037-1079

Adult Heart Transplants (1991-6/1996)

Risk Factors For 20 Year Mortality with 95% Confidence Limits

Age difference



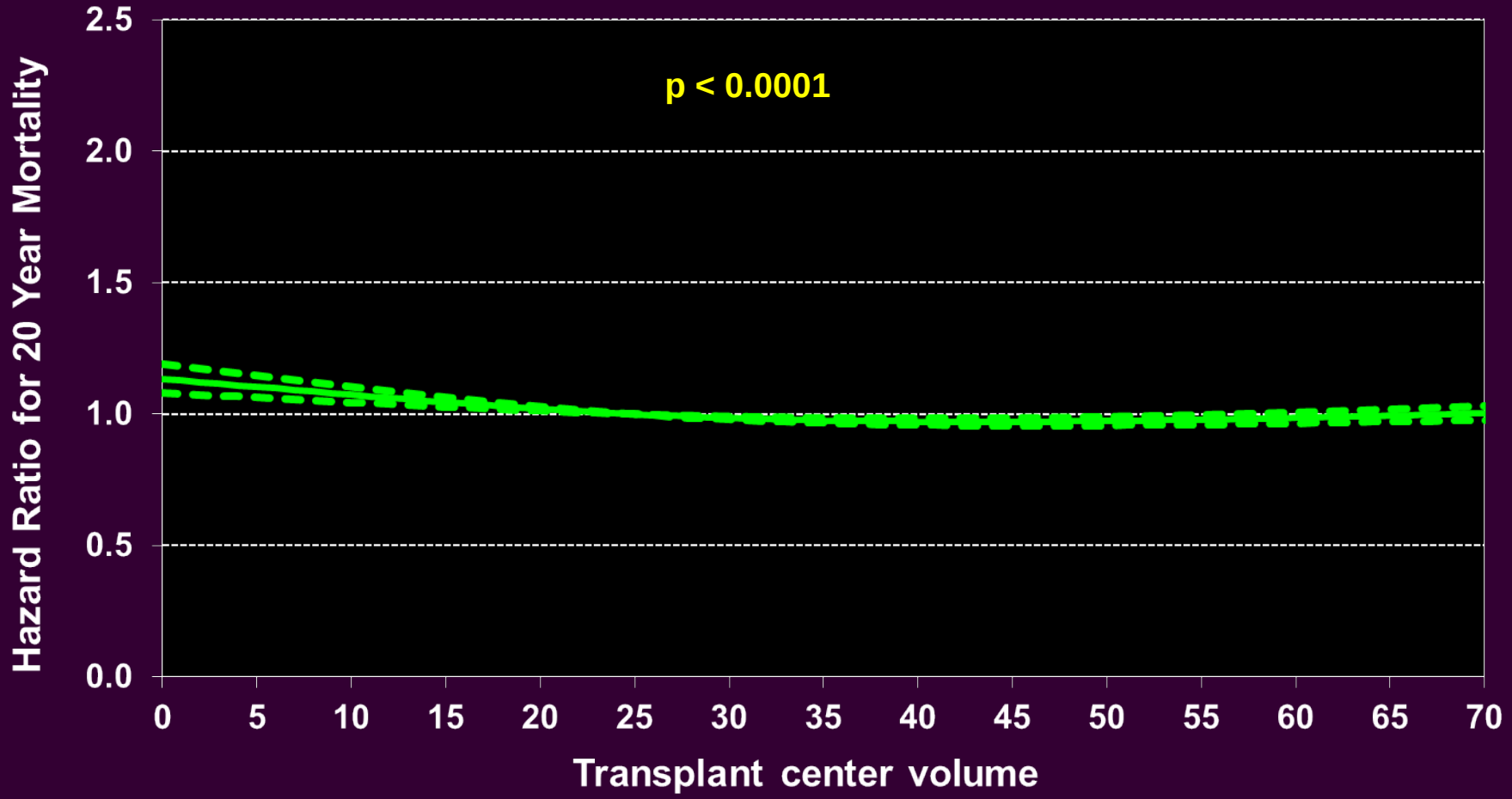
(N = 22,629)

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2017
JHLT. 2017 Oct; 36(10): 1037-1079

Adult Heart Transplants (1991-6/1996)

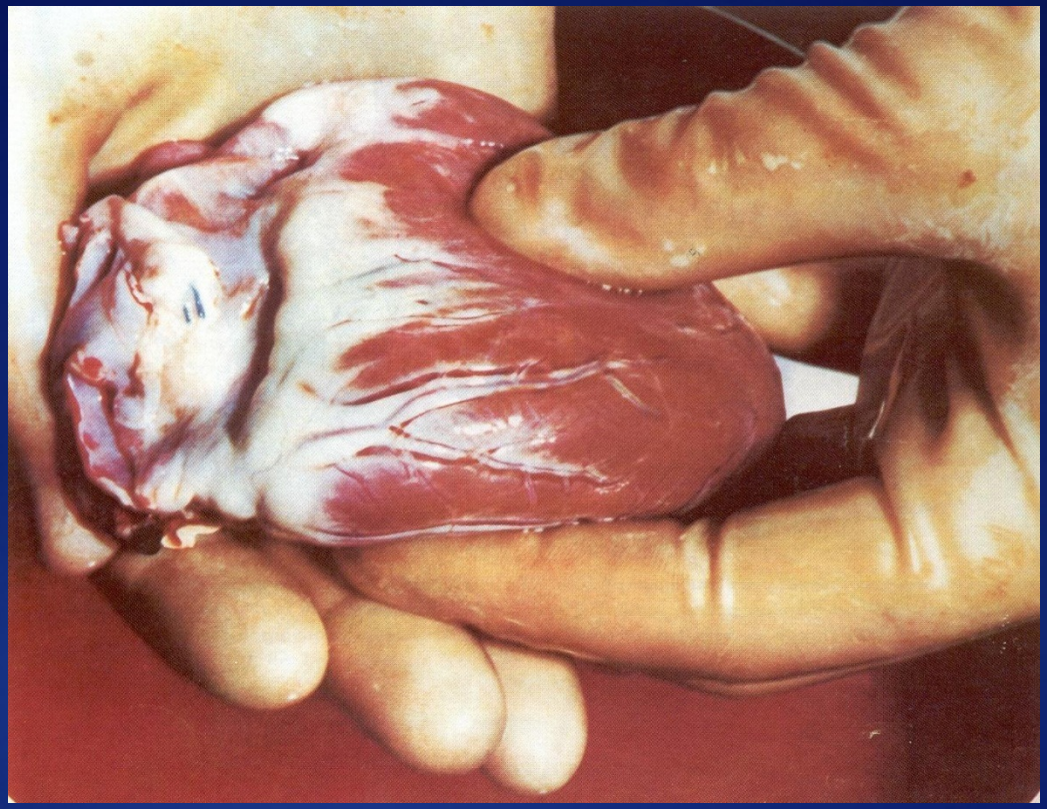
Risk Factors For 20 Year Mortality with 95% Confidence Limits

Transplant center volume



(N = 22,629)

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2017
JHLT. 2017 Oct; 36(10): 1037-1079

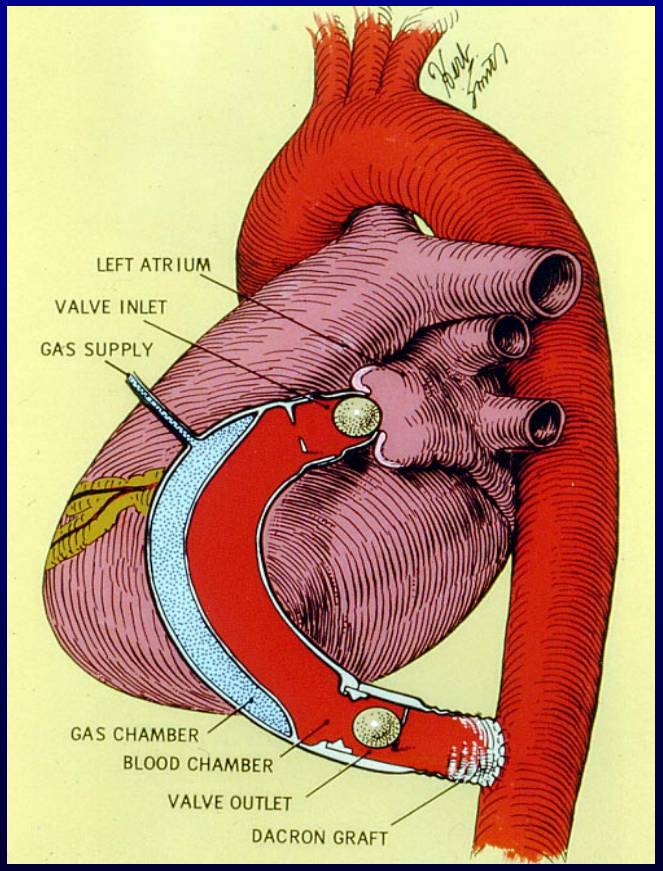


SLEH 1987

MCS in Chronic Heart Failure

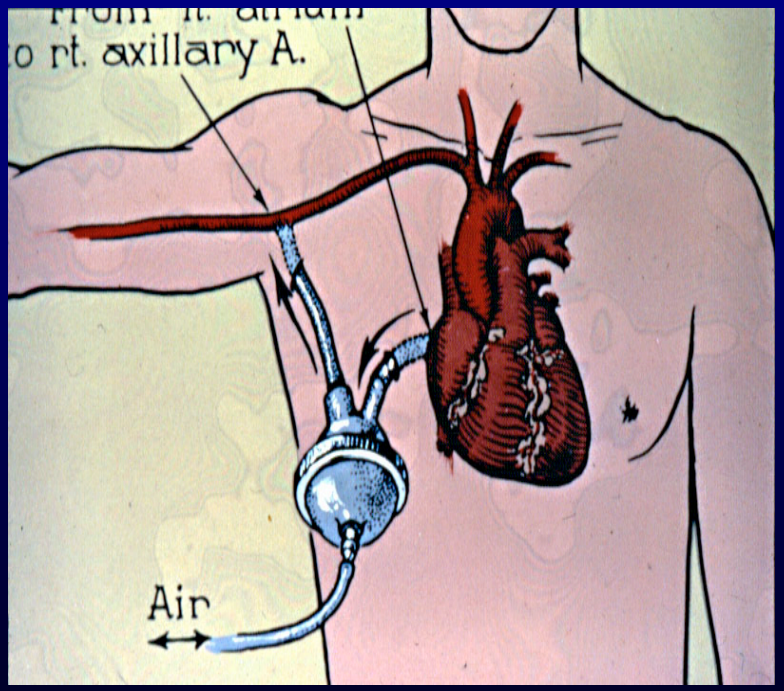
First Clinical LVAD

- 1963, Michael E. DeBakey
- 42-year-old patient
- Supported for 4 days
- Pump functioned well
- Pt. died of lung complications



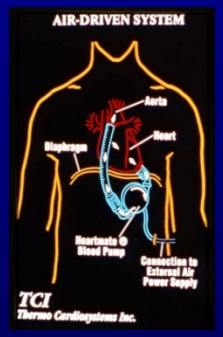
First Clinical LVAD Success

- 1966, Michael E. DeBakey
- 37-year old patient
- Postcardiotomy
- Supported for 10 days
- Long-term survivor



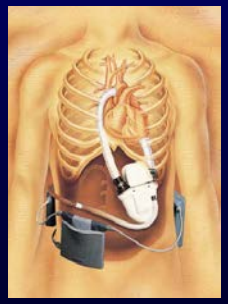
Mid 80’s

- Clinical trials with

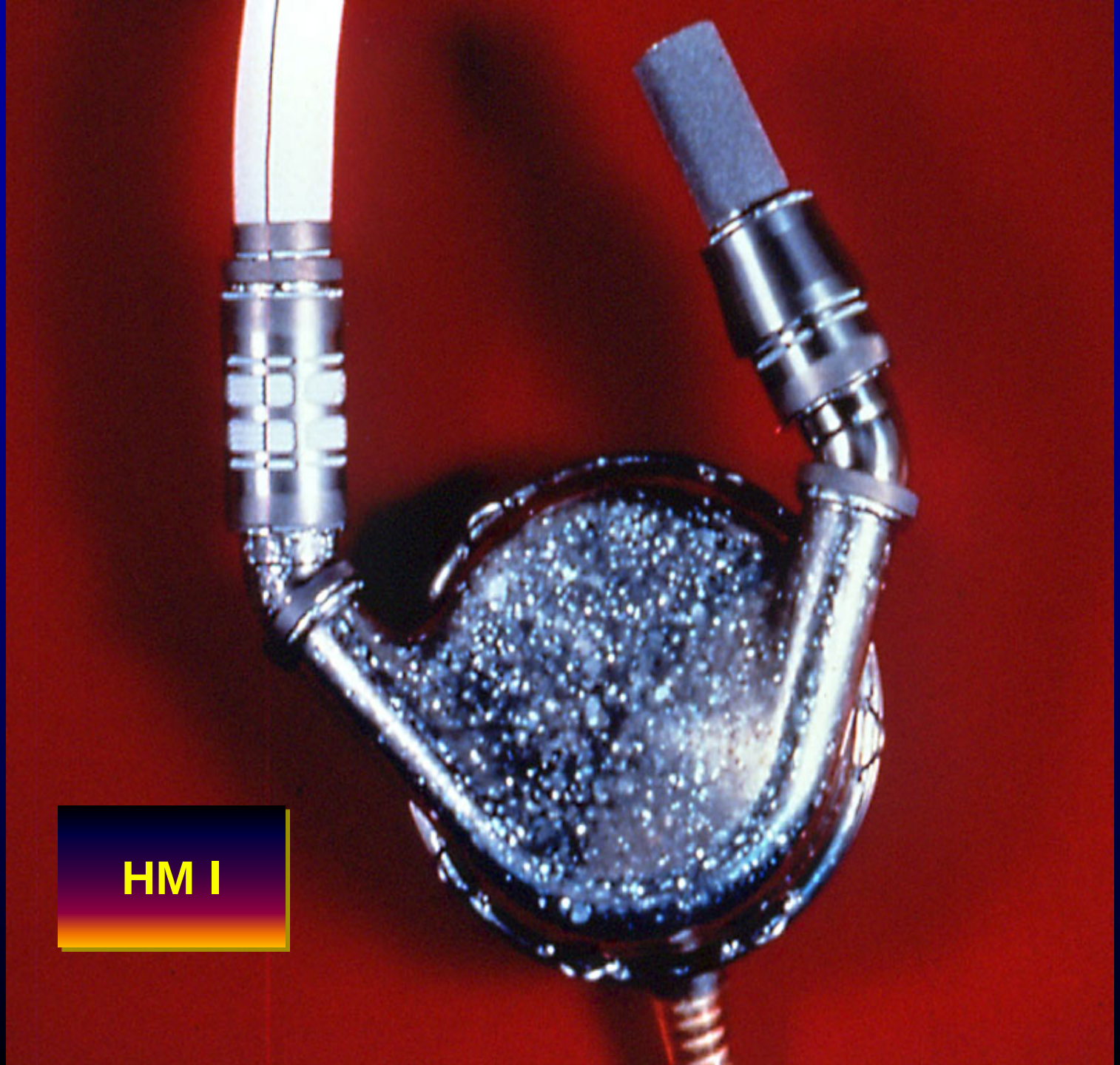


  - Pneumatic HM I

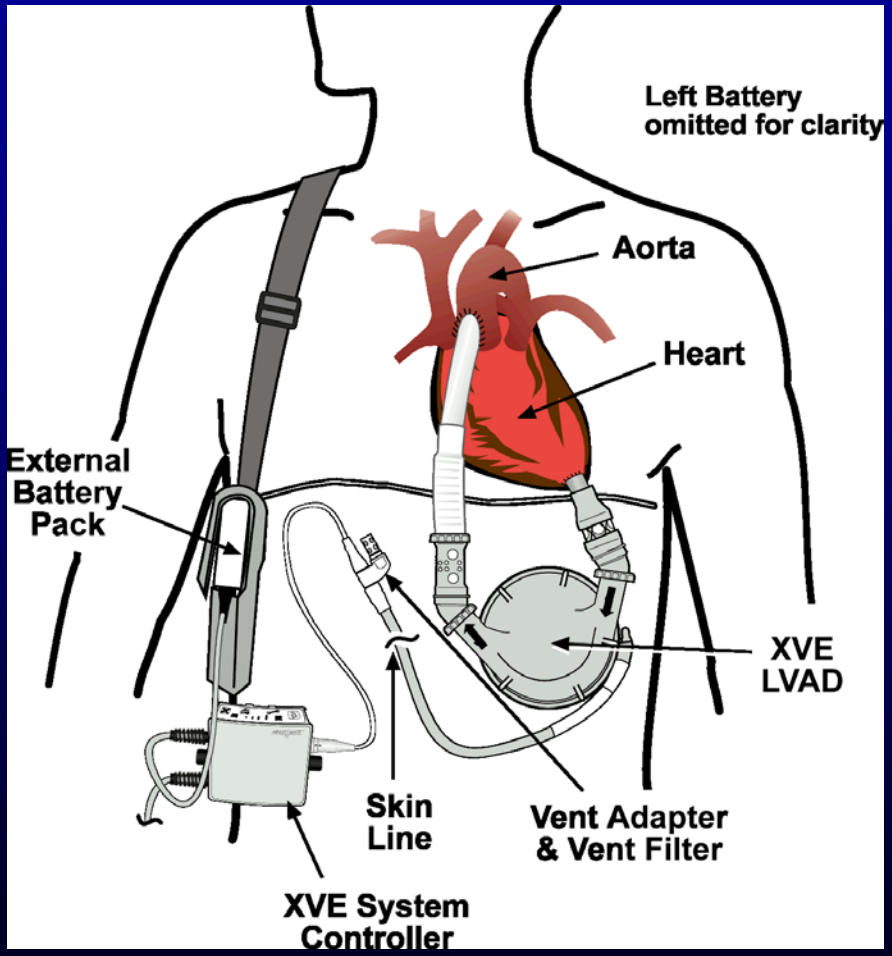
  - Novacor



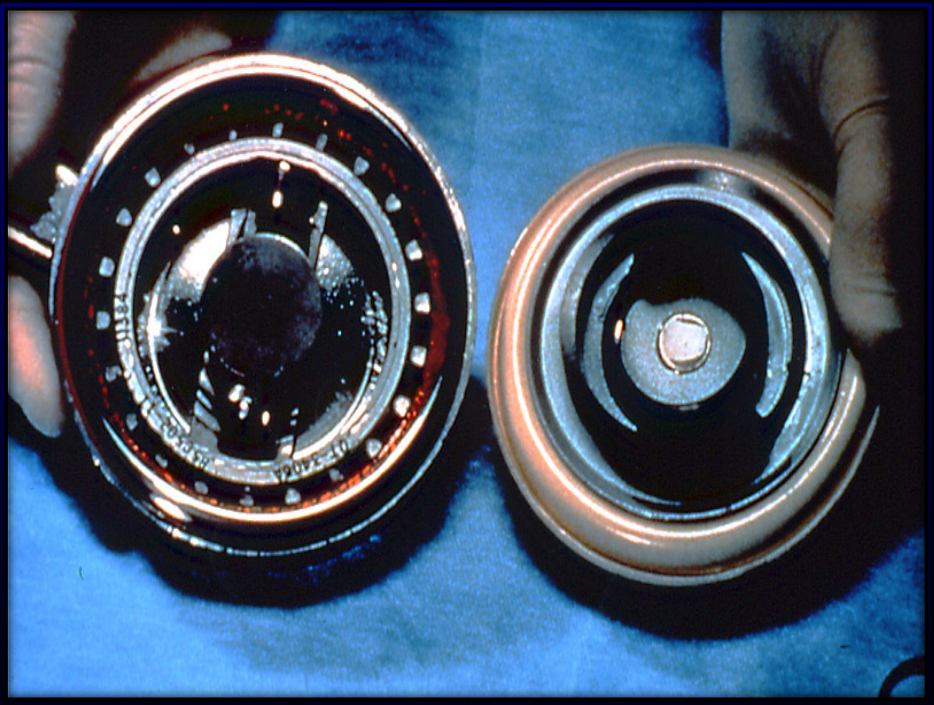
First generation Pulsatile Devices for Long Term Use


HM I

HeartMate XVE

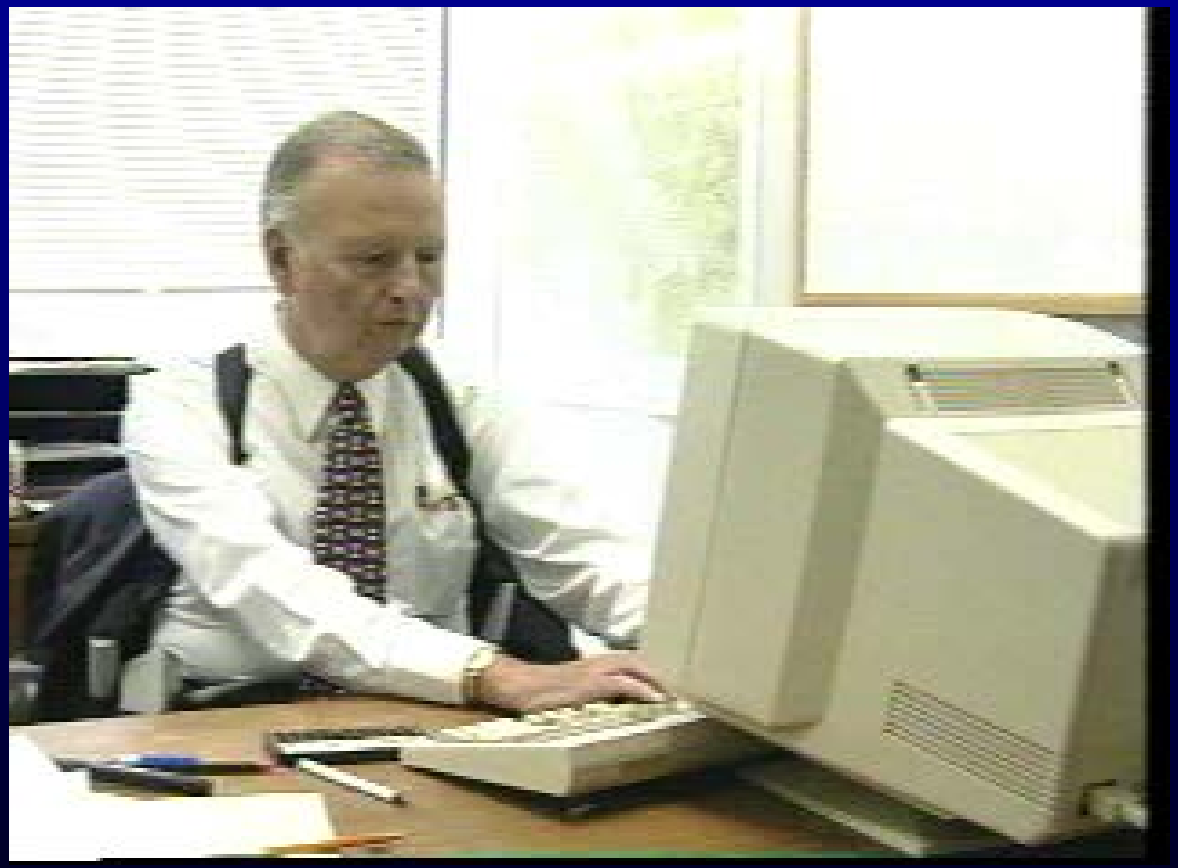


HM IP



HM XVE

Working With HM I



HeartMate XVE® - First FDA Approved Device for Destination Therapy

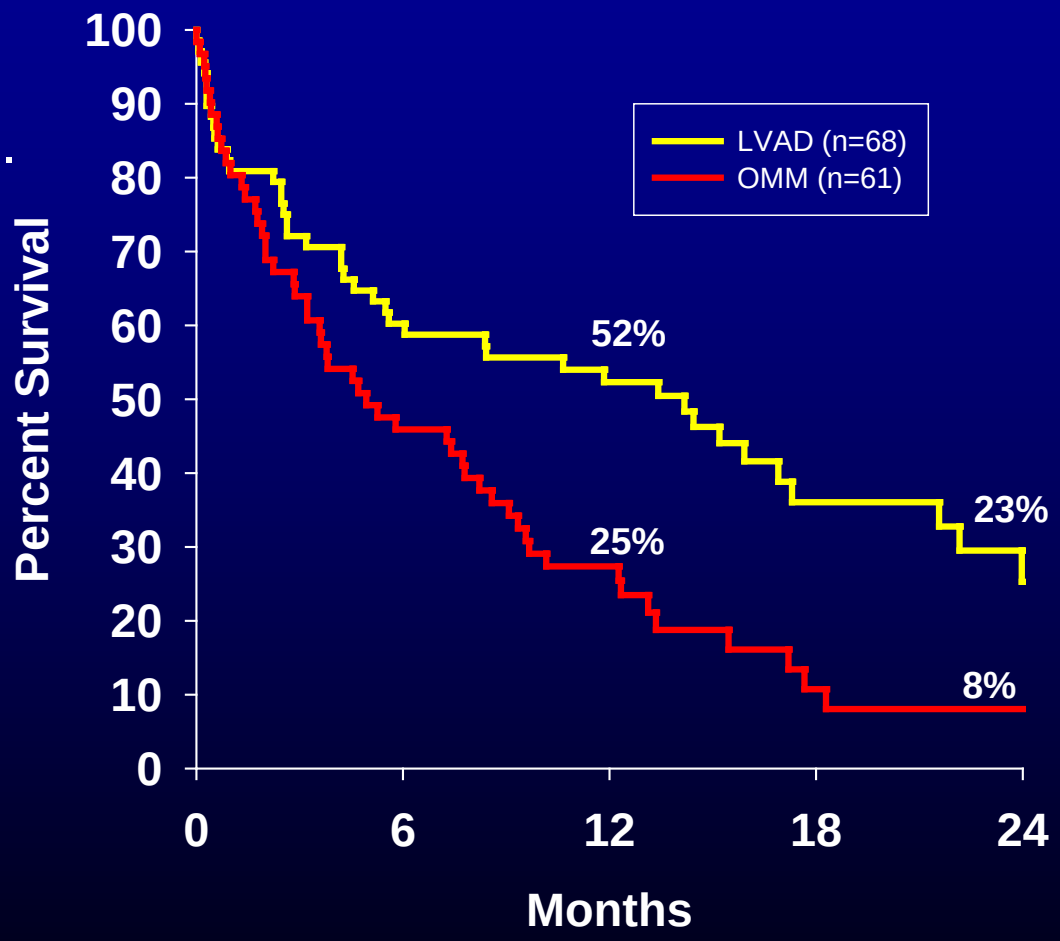
- NYHA class IV end-stage LV failure
- Received optimal medical therapy for at least 60 of the last 90 days
- Life expectancy of < 2 years
- Not a candidate for cardiac transplantation
- LVEF < 25%
- MVO_2 < 12 ml/kg/min or on inotropes
- BSA ≥ 1.5 m^2

Data from HeartMate XVE Left Ventricular Assist System Instructions for Use

REMATCH

Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure

- Randomized clinical trial
  - optimal medical therapy vs. pulsatile flow LVAD
- Non-transplant candidates (n=129)
  - EF ≤ 25%,
  - peak VO2 < 12 ml/kg/min,
  - or continuous infusion inotropes
- FDA approval for XVE as destination therapy



N Engl J Med 2001; 345:1435-43

Evolution of LVAD Technology

1st Generation *Pulsatile Pump* → **2nd Generation** *Axial Flow Pump* → **3rd Generation** *Rotary Pump*

DuraHeart
3rd Generation

Ventrassist
3rd Generation

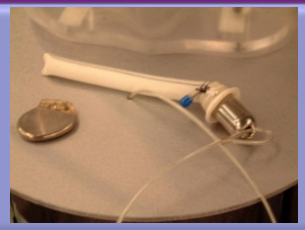
HeartWare
3rd Generation

Levacor
3rd Generation

Heartmate III
3rd Generation

Heartmate II
2nd Generation

DeBakey VAD
2nd Generation



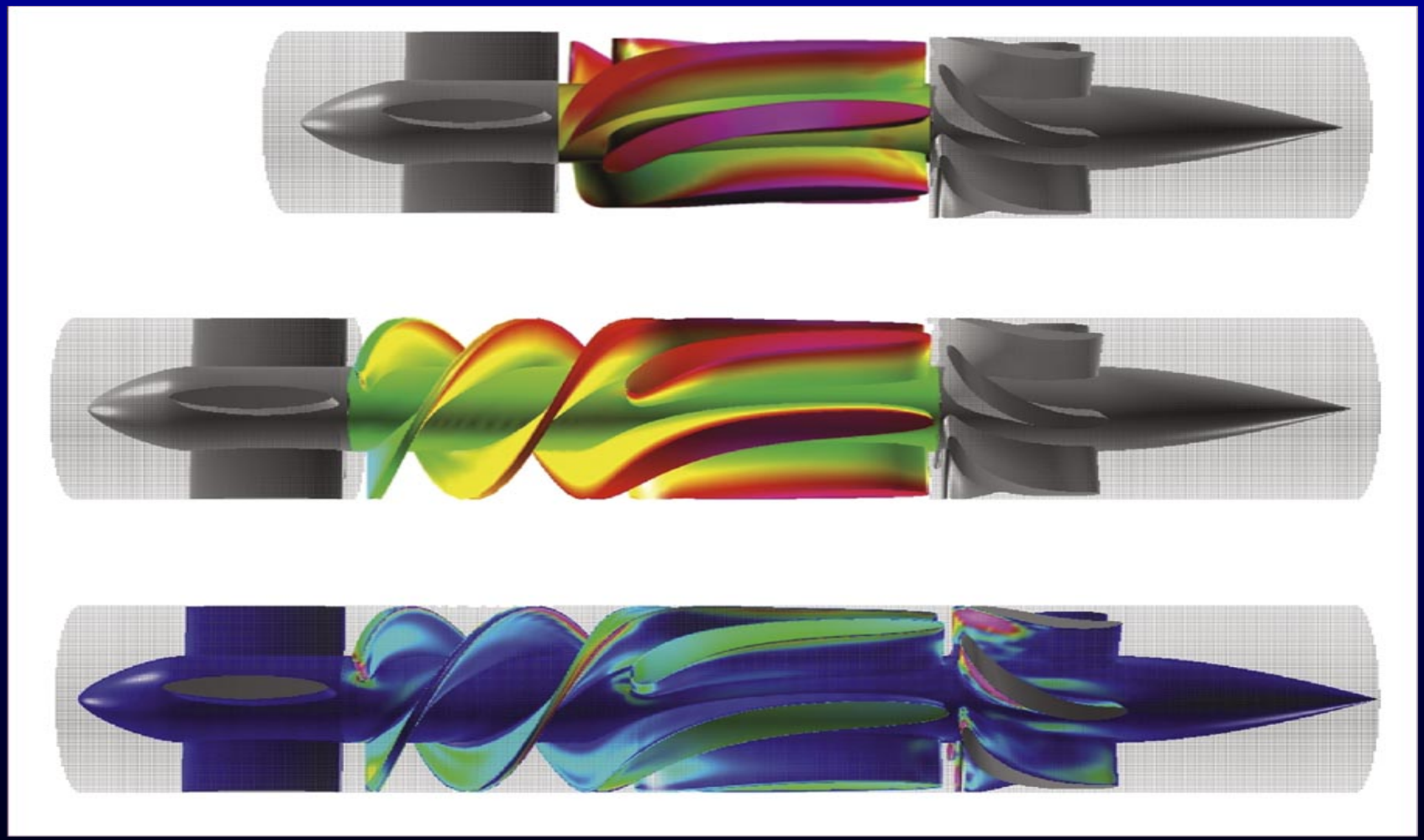
Jarvik 2000
2nd Generation

Heartmate I
1st Generation

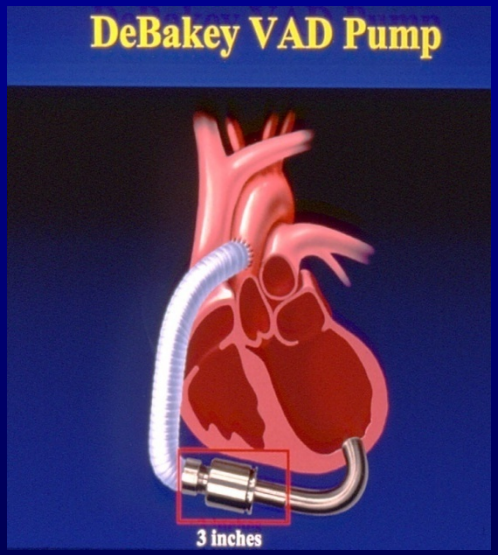
Novacor
1st Genertion

Axial flow second generation LVAD's

New Technology



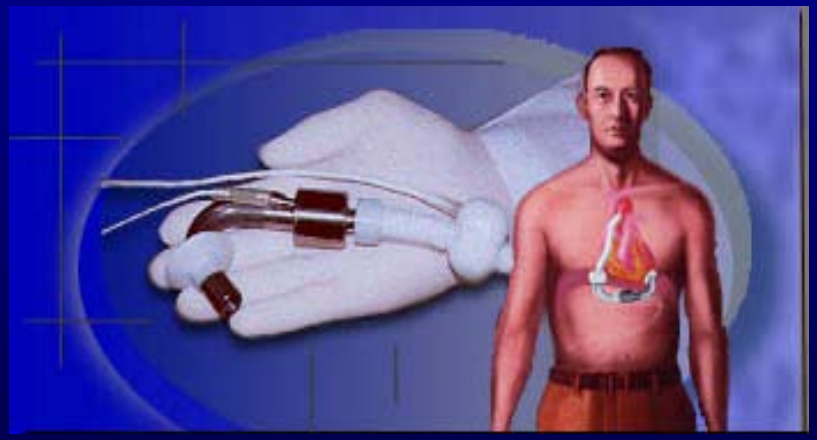
Axial Flow Pumps



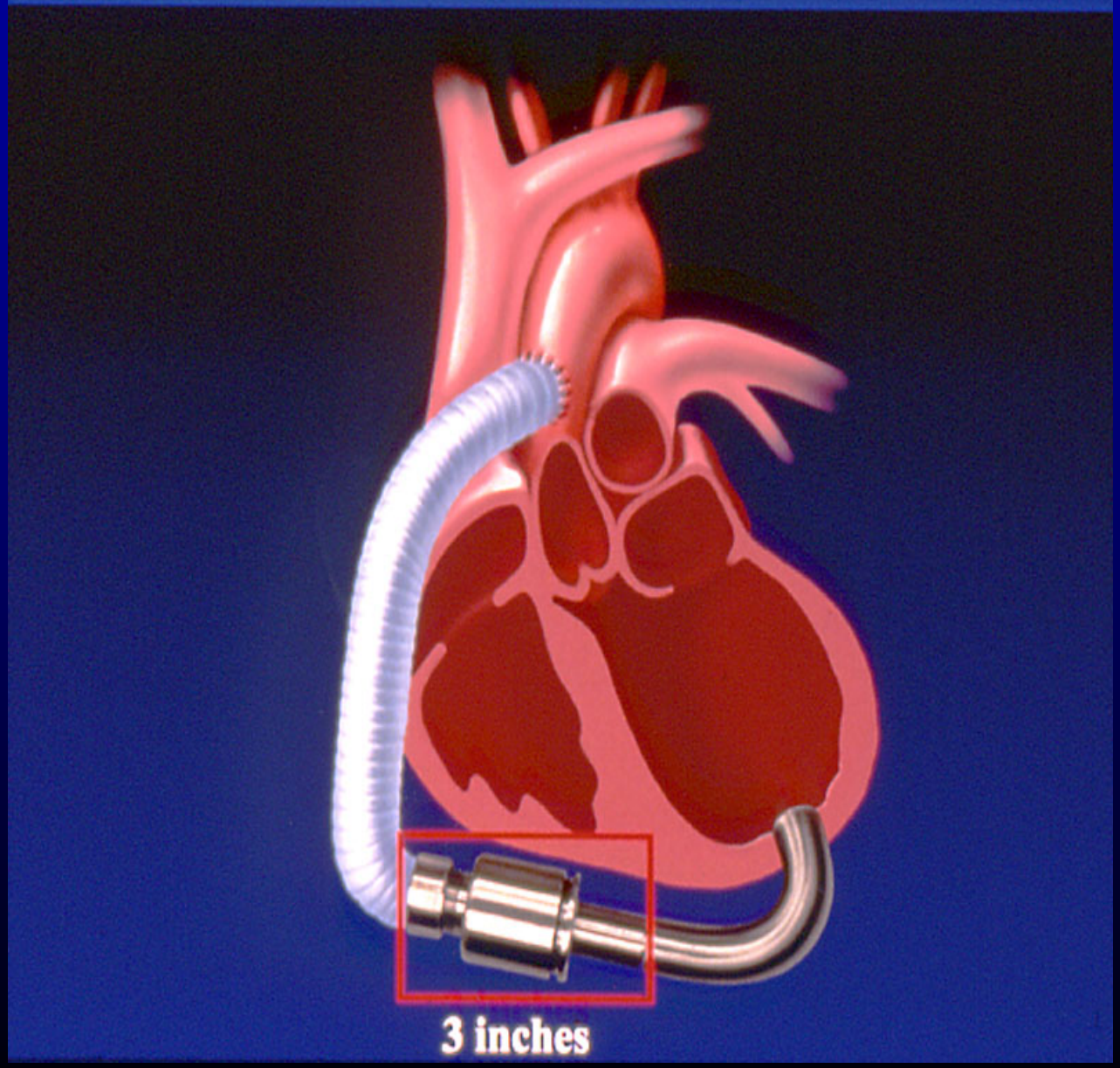
Jarvik 2000 HeartMate II DeBakey

DeBakey/NASA

- Axial flow
- Inflow cannula
- Fixed speed
- Integrated flow probe
- Subdiaphramatic

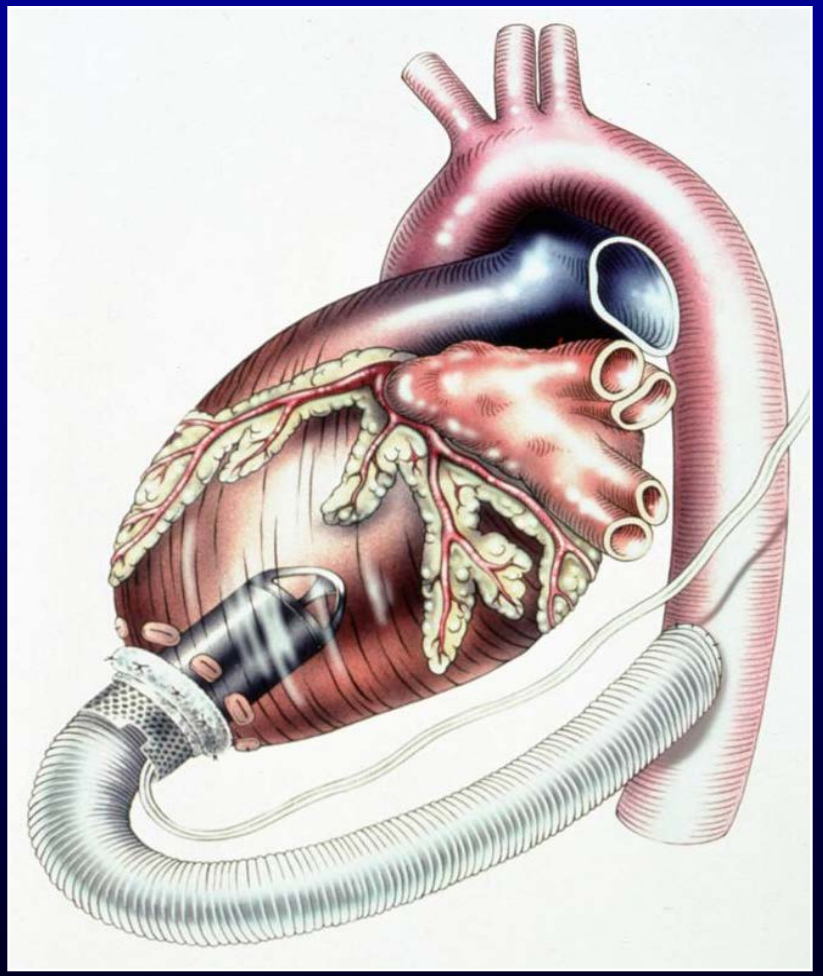


DeBakey VAD Pump

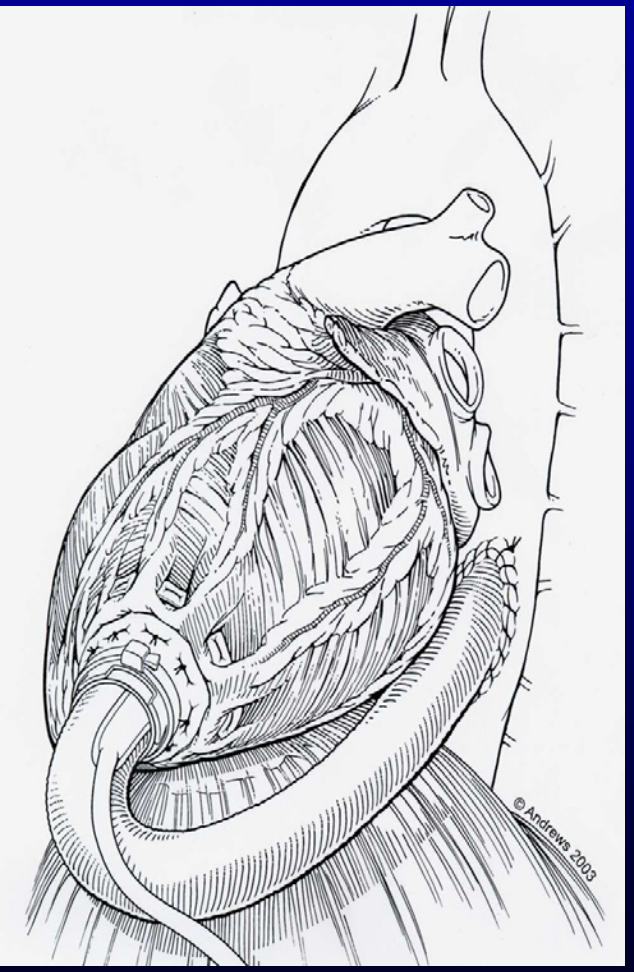


Implantation of the Jarvik 2000

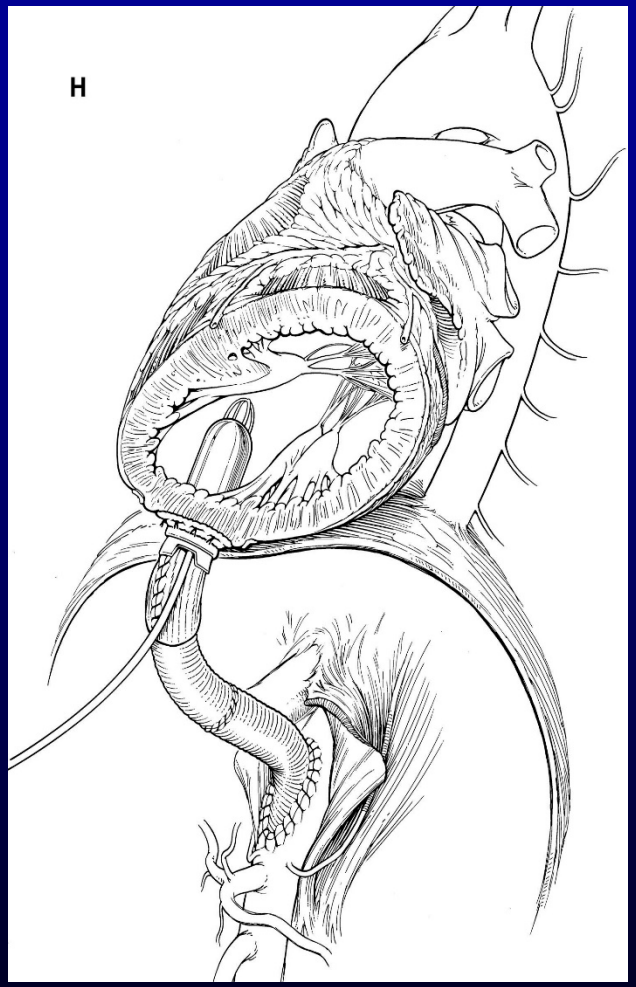
- Left Thoracotomy or Sternotomy
- Non Thoracic
- Partial Cardiopulmonary Bypass or No CPB
- Silastic Cuff on Apex
- Pump Placed in LV
- Outflow Graft Anastamosed to Aorta



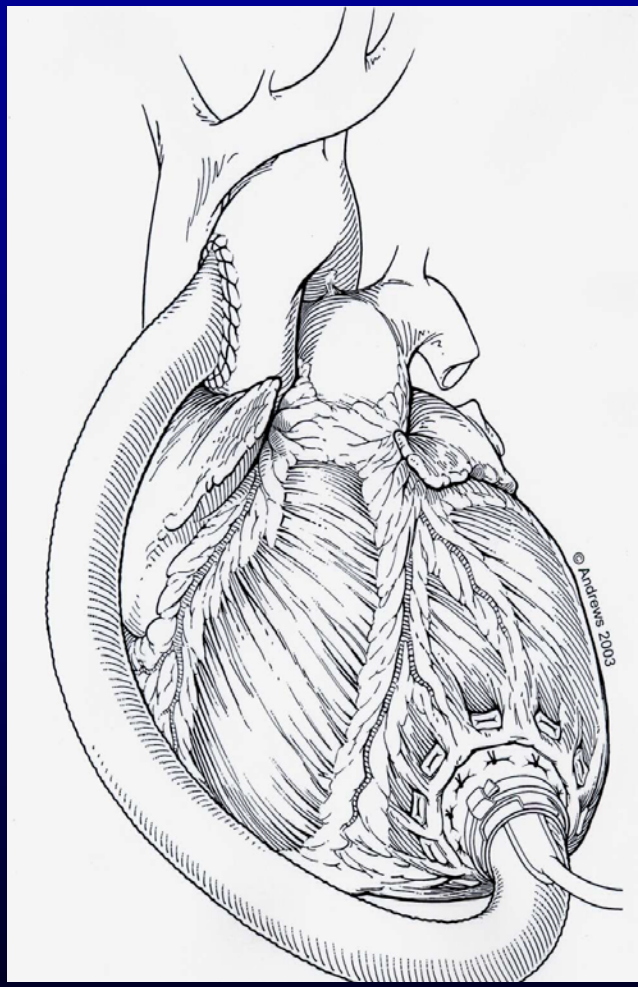
Different Surgical Approaches



Left Thoracotomy
Descending Ao

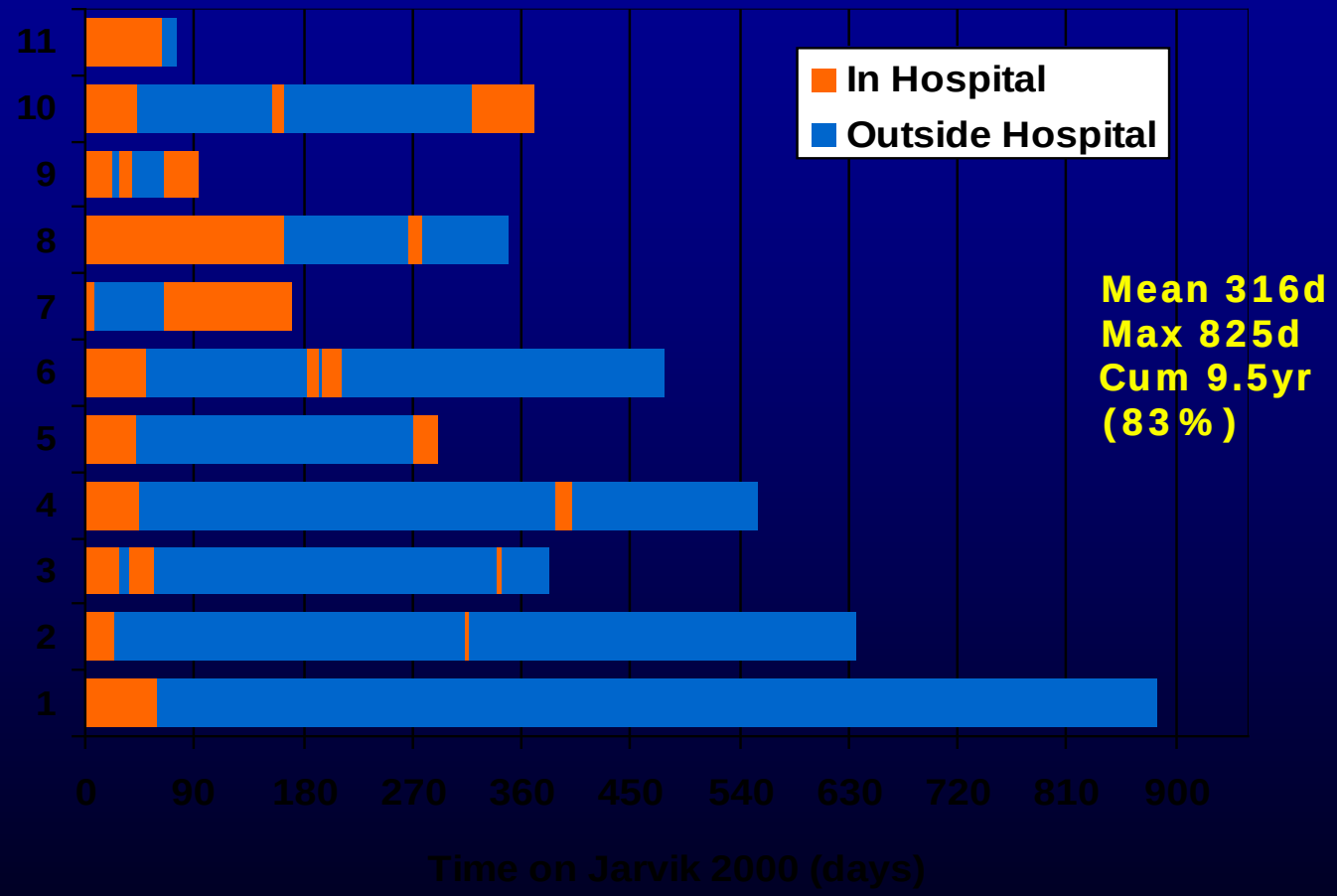


Subcostal
Supraceliac Ao



Median Sternotomy
Ascending Ao

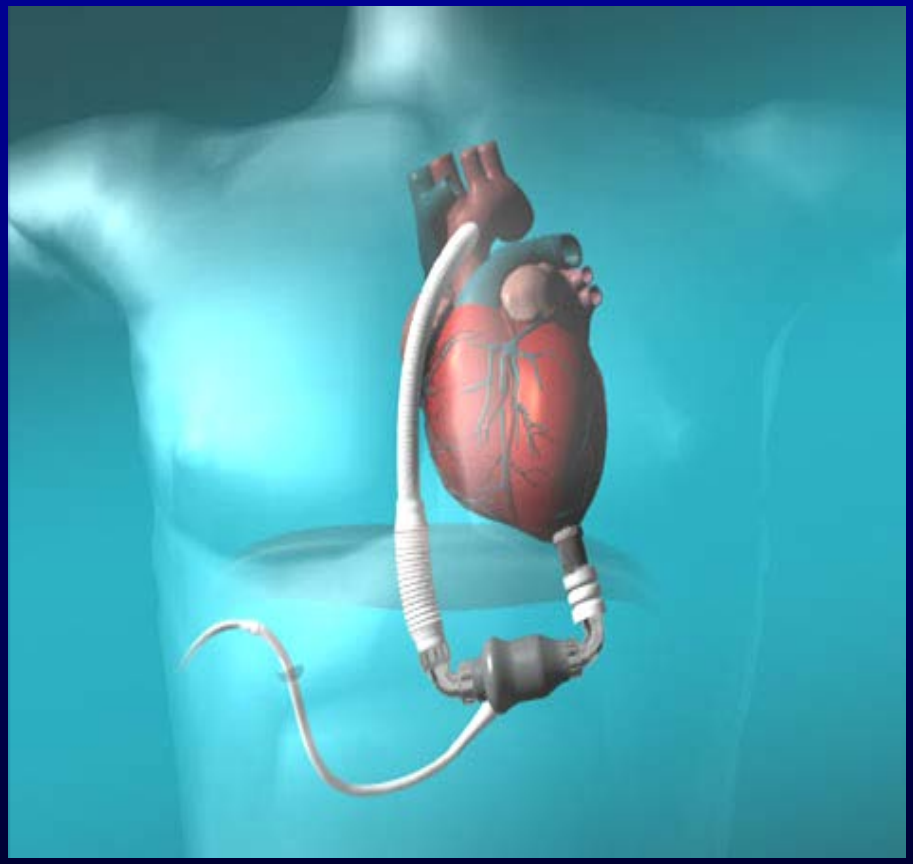
Home Discharge Experience

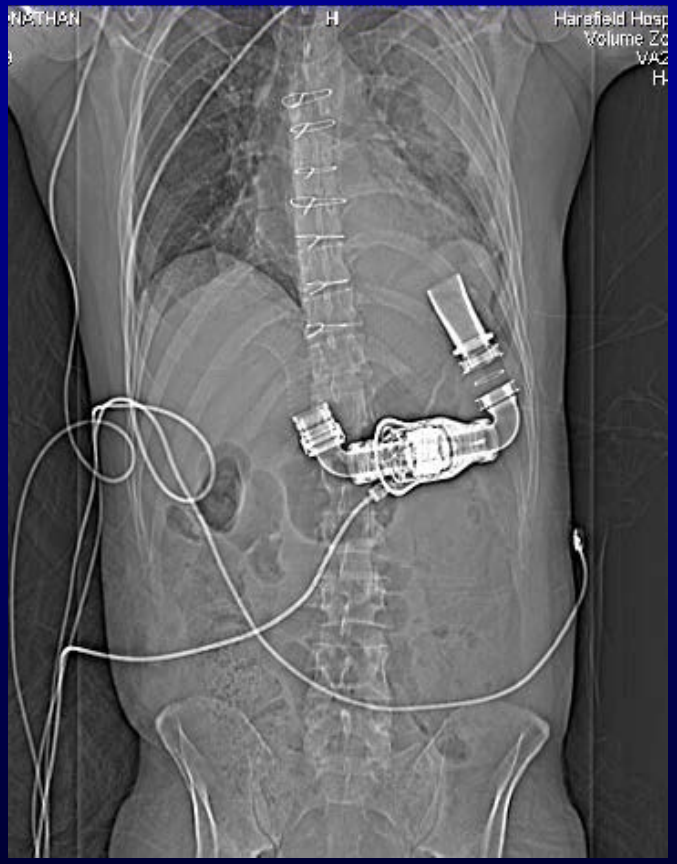


HeartMate II™

- Axial flow
- Brushless DC motor
- Inflow cannula
- Textured surfaces
  - excluding impeller
- Small (65cc 260g)
- Power requirements
  - (>14 watts)

HMII Anatomical Placement





The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

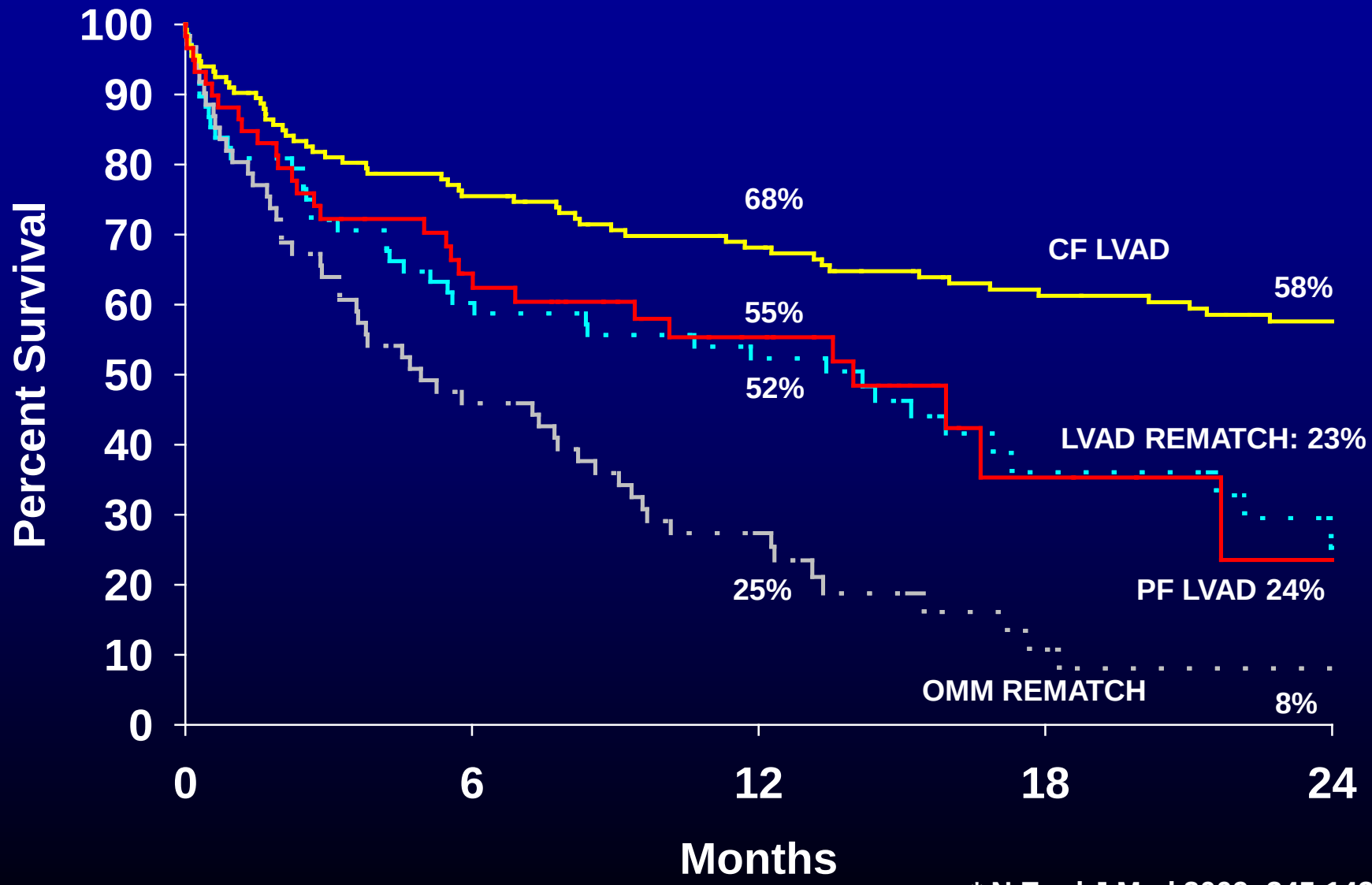
Advanced Heart Failure Treated with Continuous-Flow Left Ventricular Assist Device

Mark S. Slaughter, M.D., Joseph G. Rogers, M.D., Carmelo A. Milano, M.D., Stuart D. Russell, M.D., John V. Conte, M.D., David Feldman, M.D., Ph.D., Benjamin Sun, M.D., Antone J. Tatooles, M.D., Reynolds M. Delgado, III, M.D., James W. Long, M.D., Ph.D., Thomas C. Wozniak, M.D., Waqas Ghumman, M.D., David J. Farrar, Ph.D., and O. Howard Frazier, M.D., for the HeartMate II Investigators*

N Engl J Med 2009;361:2241-51.

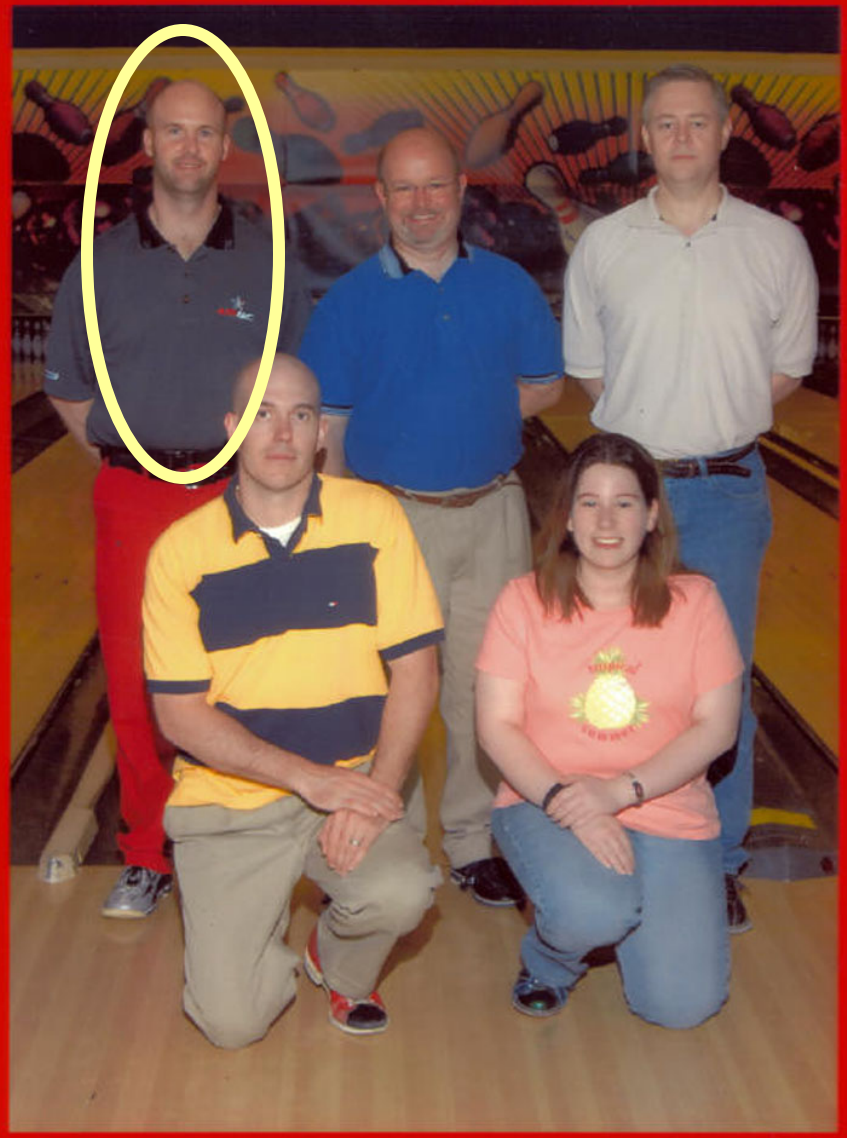
Actuarial Survival vs REMATCH*

HeartMate II Destination Therapy Trial



* N Engl J Med 2009; 345:1435-43

Patient Quality of Life



HeartMate II

Patient DXP

- 14 y/o Caucasian male BSA=1.87
- Dilated viral cardiomyopathy
- Pre Implant:
  - PCWP=22 CO=2.68
  - EF<10%
- Implanted on 9-24-04
- Pump speed maintained at 8600 rpm for 2 months
- Pump speed currently maintained at 10000 rpm since Nov ‘04
- On 03-08-05 patient fell (skateboarding) damaged device and had pump exchanged
- Device was explanted on 10-25-06

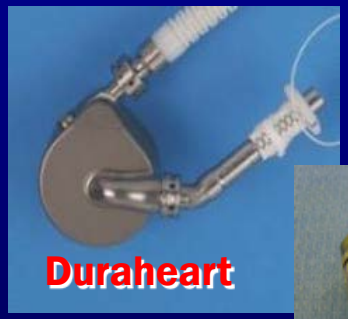
Third Generation Blood Pumps

No Valves or Mechanical Bearings

Magnetically-Suspended Impeller

Hydrodynamically Suspended Impeller

Centrifugal-Flow

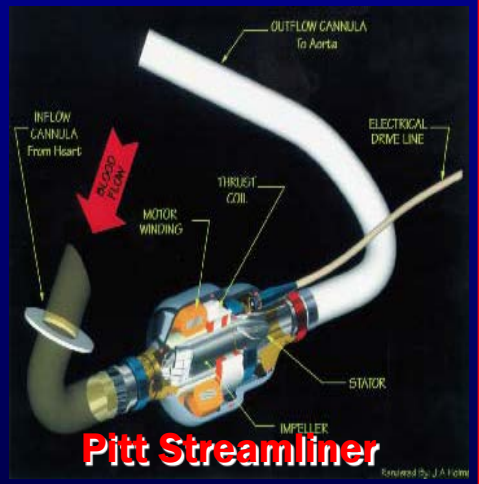

Duraheart


HeartQuest

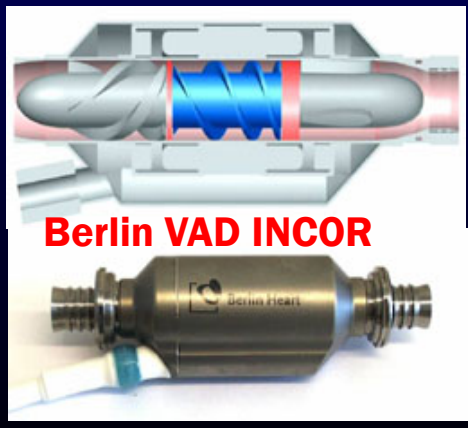

HeartMate III


CentriMag

Axial-Flow



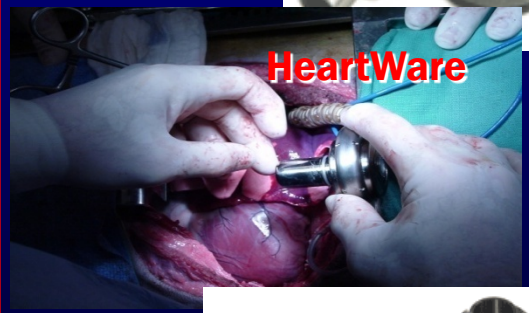
Pitt Streamliner



Berlin VAD INCOR

Hydrodynamically Suspended Impeller


CorAid


HeartWare


VentrAssist

DuraHeart LVAD

- Protocol #08-02-251-181

  "Evaluation of the Safety and Effectiveness of the DuraHeart Left Ventricular Assist System in Patients Awaiting Transplant"

The world's first commercially available Mag-Lev 3rd Generation implantable LVAS

DuraHeart External Components

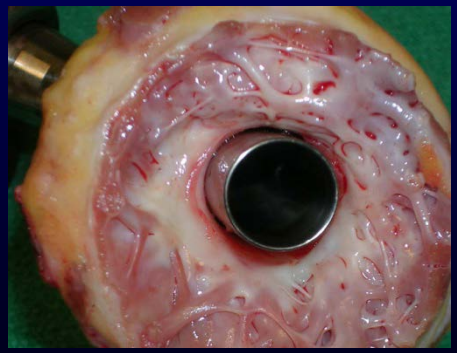
DuraHeart™ Long Term Biocompatibility

The pump after more than 16 months implantation

(Clear indication of enhanced wash-out and reduced shear)

Pump chamber

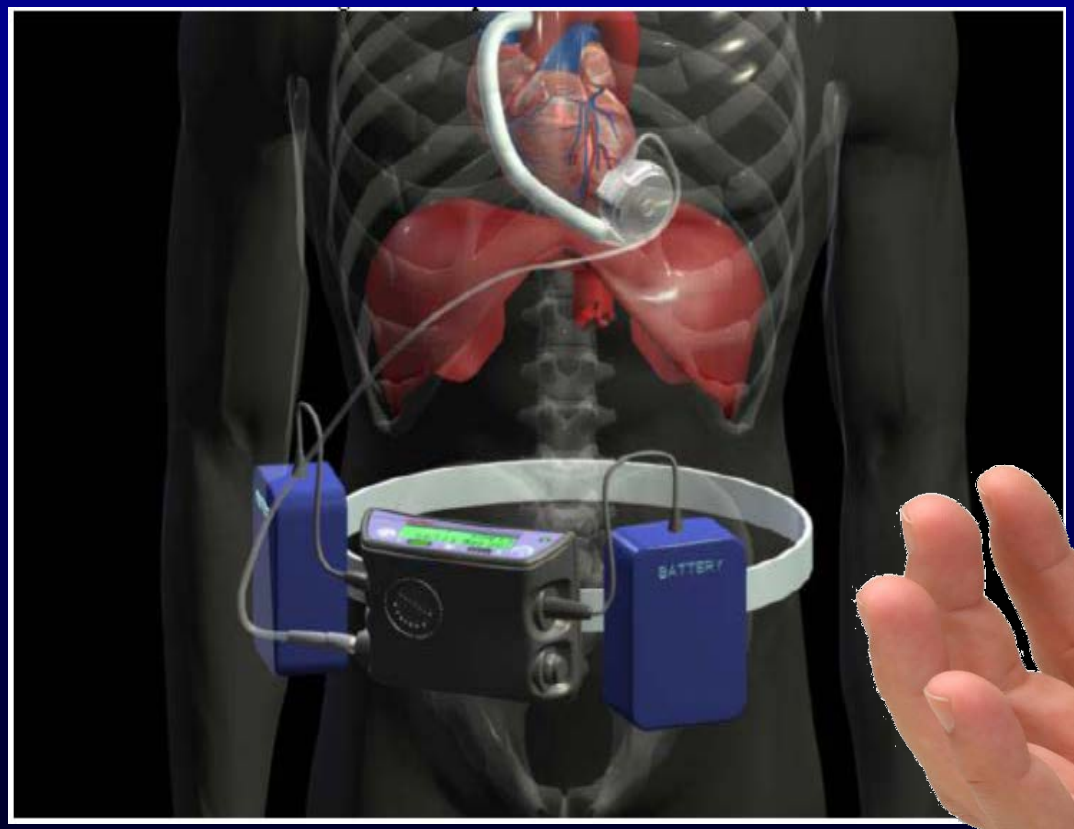
Impeller

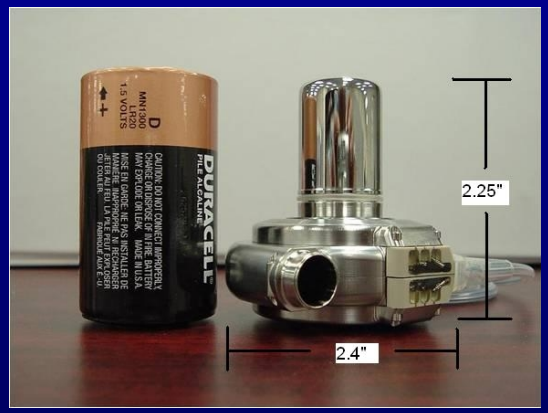


LV apex and inflow tip

Inflow conduit

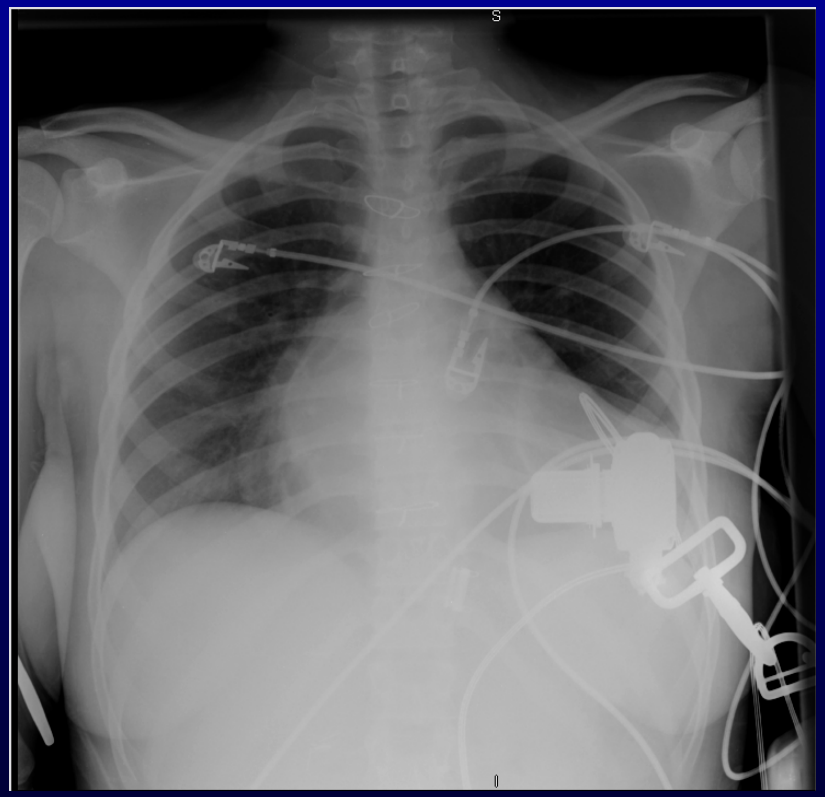
HeartWare LVAD



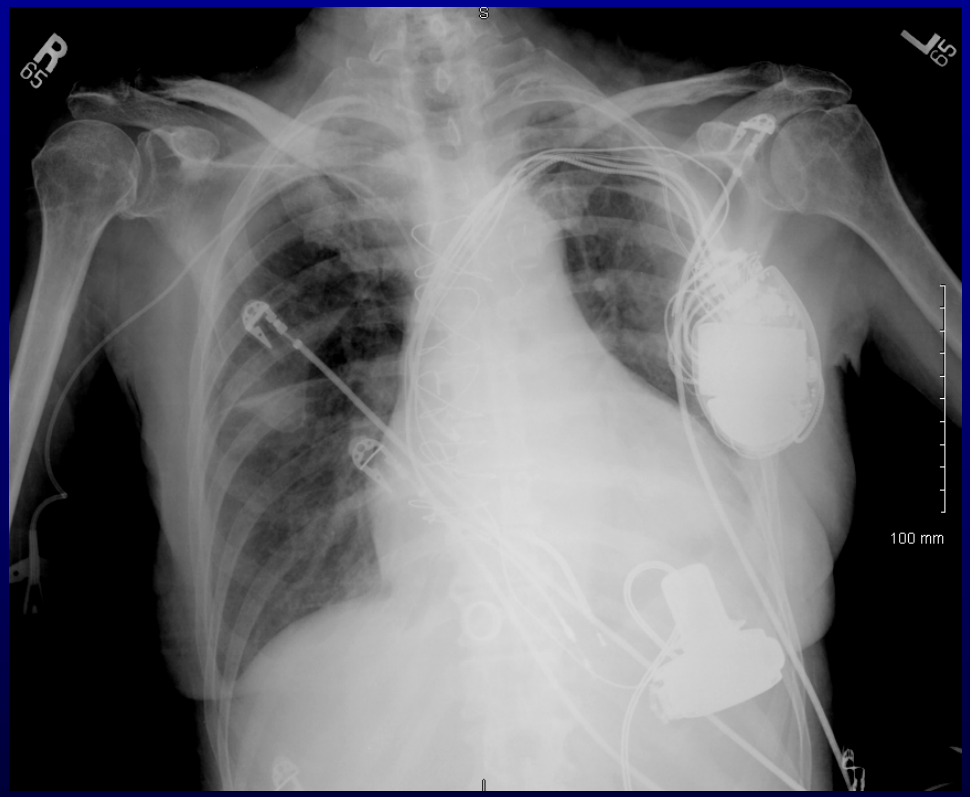


HeartWare LVAS

Surgical Implant and Inlet Position



Apical



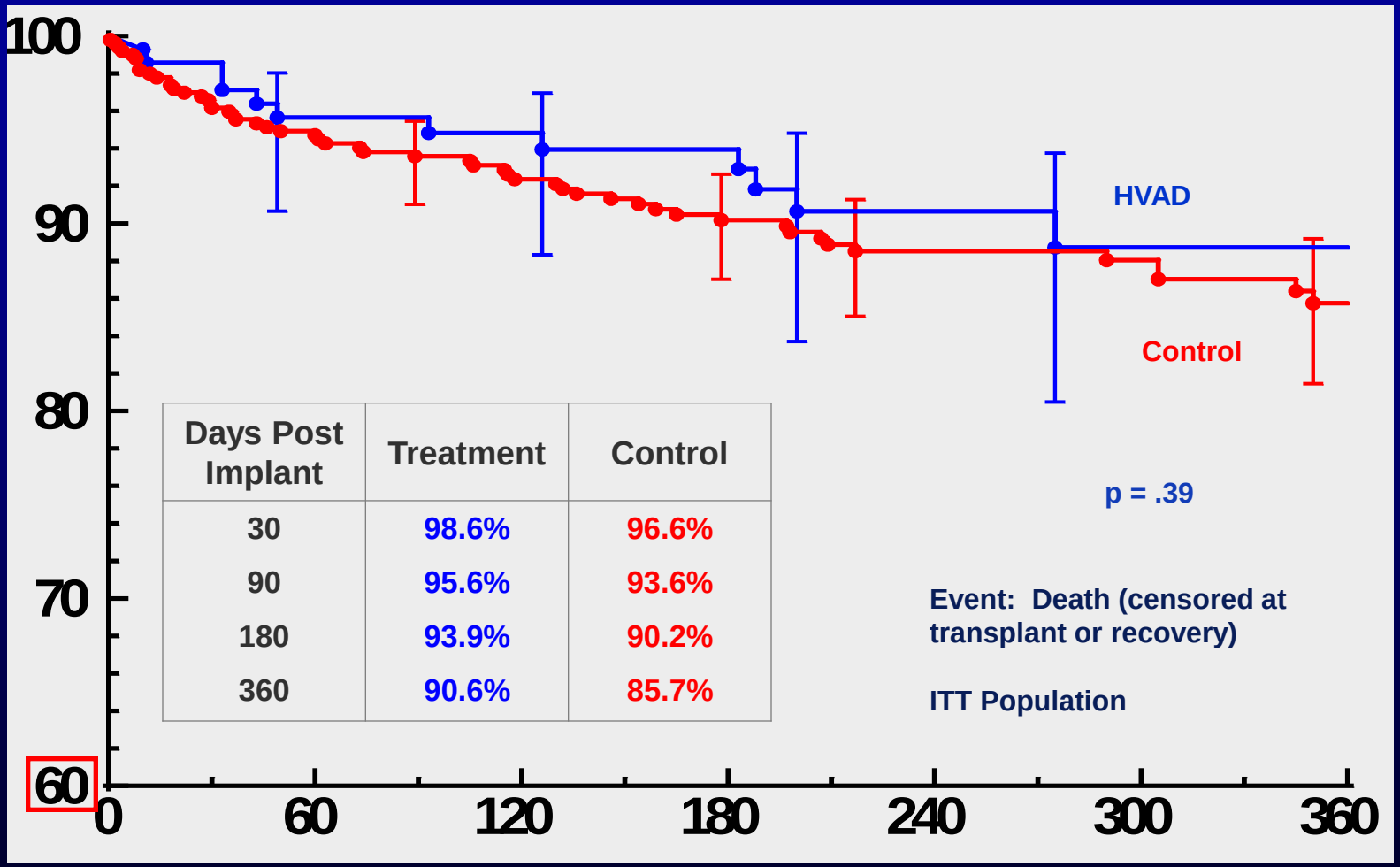
Diaphragmatic

Evaluation of the HeartWare HVAD Left Ventricular Assist System for the Treatment of Advanced Heart Failure: Results of the ADVANCE Bridge to Transplant Trial

Keith Aaronson, Mark Slaughter, Edwin McGee, William Cotts, Michael Acker, Mariell Jessup, Igor Gregoric, Pranav Loyalka, Valluvan Jeevanandam, Allen Anderson, Robert Kormos, Jeffrey Teuteberg, Francis Pagani, Steven Boyce, David Hathaway, Leslie Miller for the HeartWare ADVANCE Investigators

February 2011

ADVANCE Trial Secondary Outcome: Survival



Days Post Implant	Treatment	Control
30	98.6%	96.6%
90	95.6%	93.6%
180	93.9%	90.2%
360	90.6%	85.7%

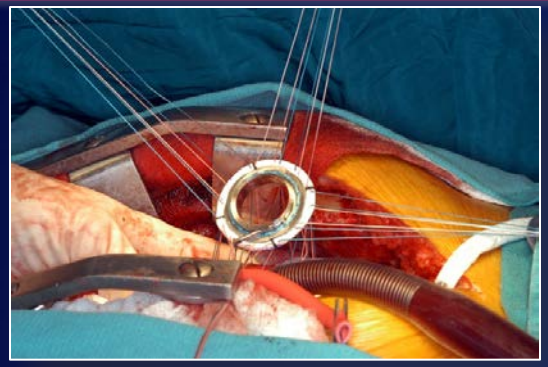
Patients at Risk							
Treatment	140	128	108	92	63	36	26
Control	499	440	370	305	228	176	127

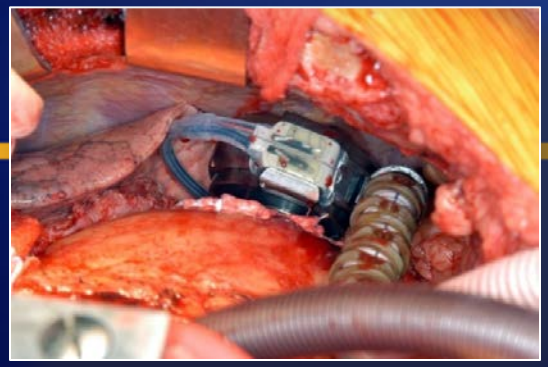
MCS Complications

LVAD Complications

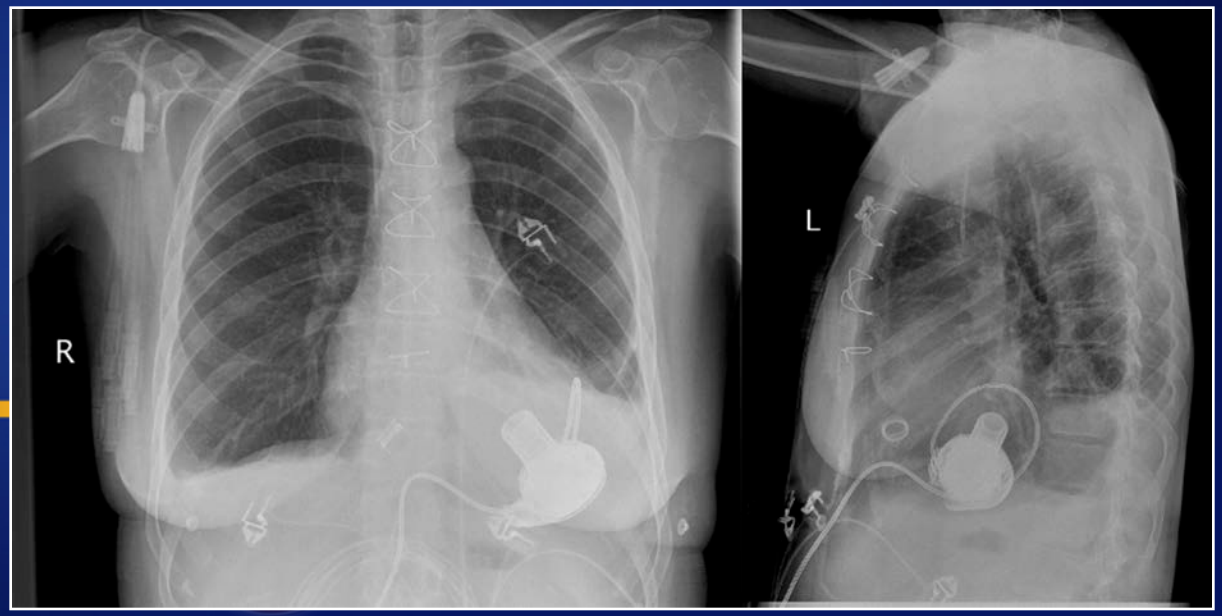
Perioperative Bleeding

Pericardial Placement with no pocket – a Key Advantage





- No abdominal surgery
- No pump pocket
- Low blood loss
- Potential for shorter implant time



Blood transfusion

Table 3. Comparison of blood product transfusion between the off-CPB group and CPB groups.

Blood product	Off-CPB	CPB	P value
Red blood cells (units)	1.4 ± 1.8	8.1 ± 8.2	0.007
Fresh frozen plasma (units)	1.3 ± 2.0	6.0 ± 5.6	0.007
Platelets (units)	0.4 ± 0.9	2.7 ± 1.9	<0.0001
Cryoprecipitate (units)	0.0 ± 0.0	0.3 ± 0.6	0.073

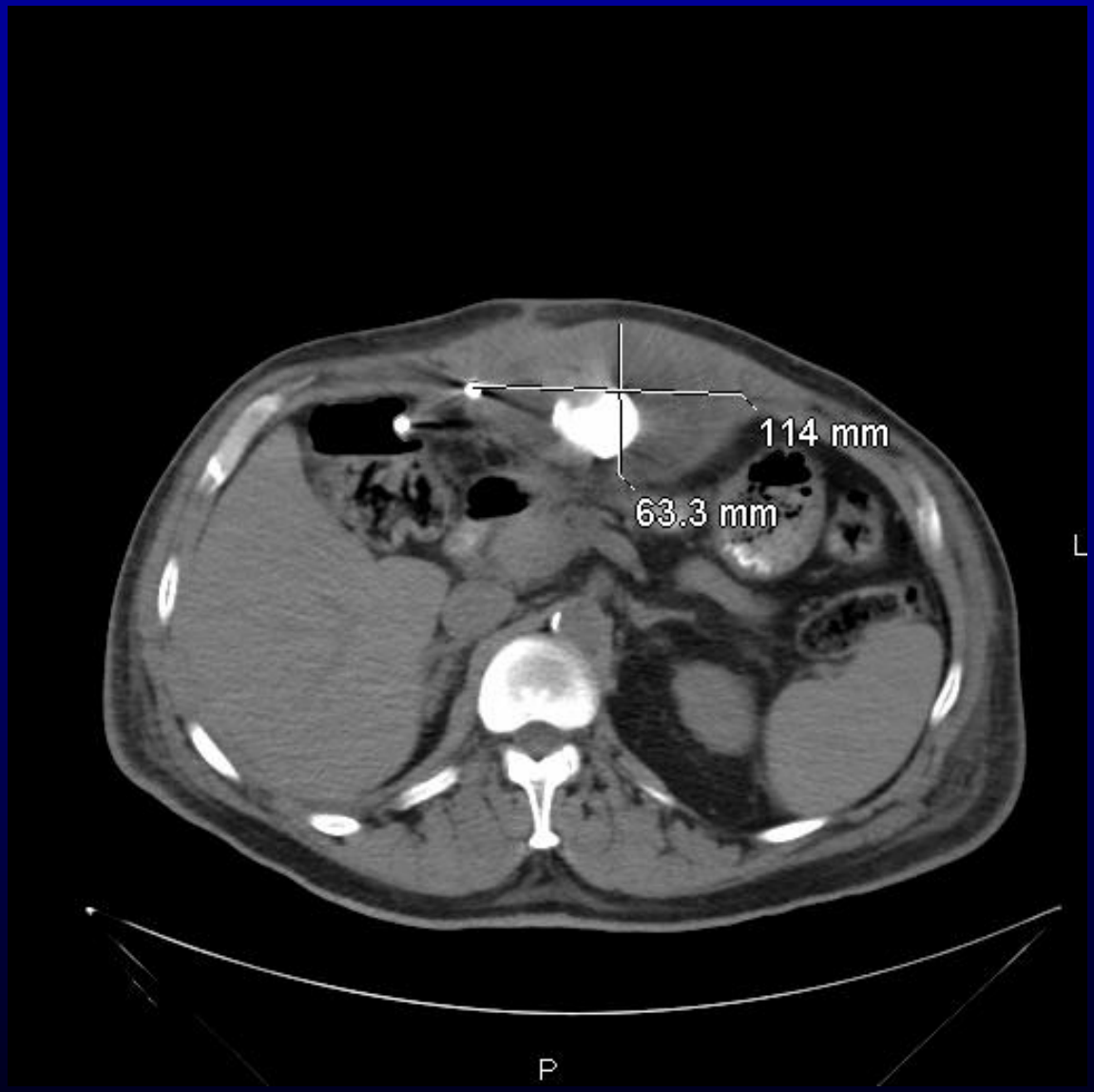
Abbreviations: CPB = cardiopulmonary bypass

LVAD Complications

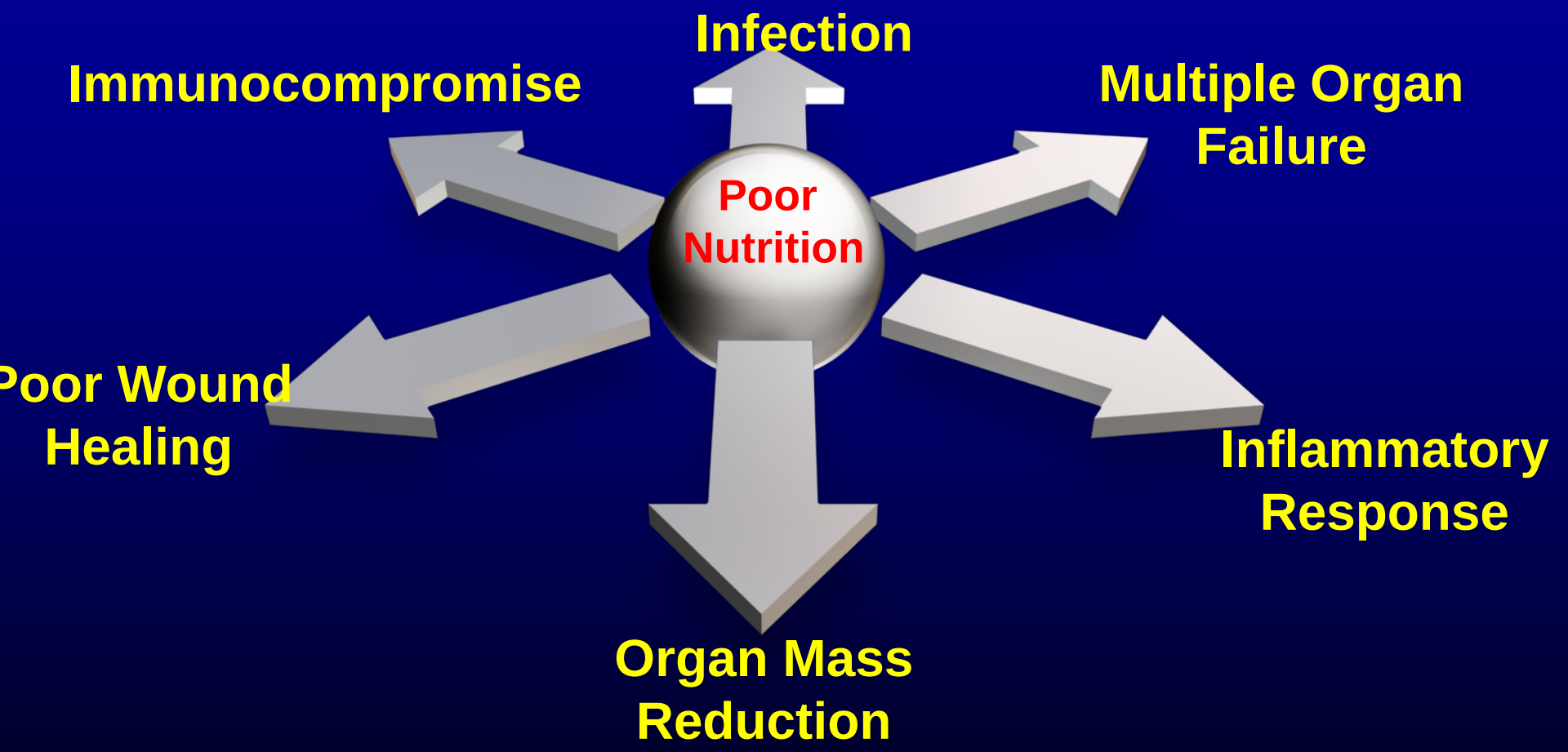
Driveline infection

Infection

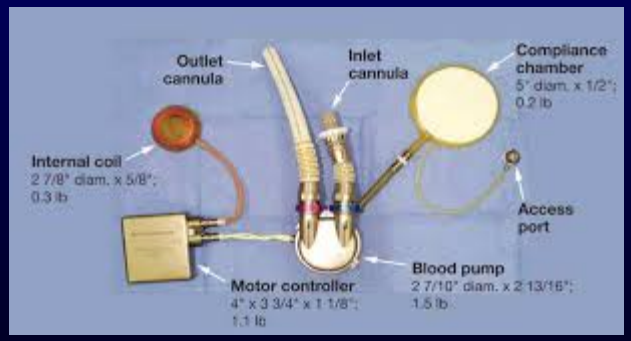
- S/S and exam:
  - Leukocytosis, fever, erythema, drainage, tenderness around driveline site, positve cultures, hyperdynamic flows, hypotension
- Etiology: (multifactorial)
  - Poor dressing technique, improper immobilization of driveline, immunosuppression (ANC < 1000), diabetes, low albumin/poor nutritional status
- Tx:
  - Antibiotics (po/IV depending on severity), Possible OR for exploration, fluid resuscitation, dressing changes/Vacs etc.

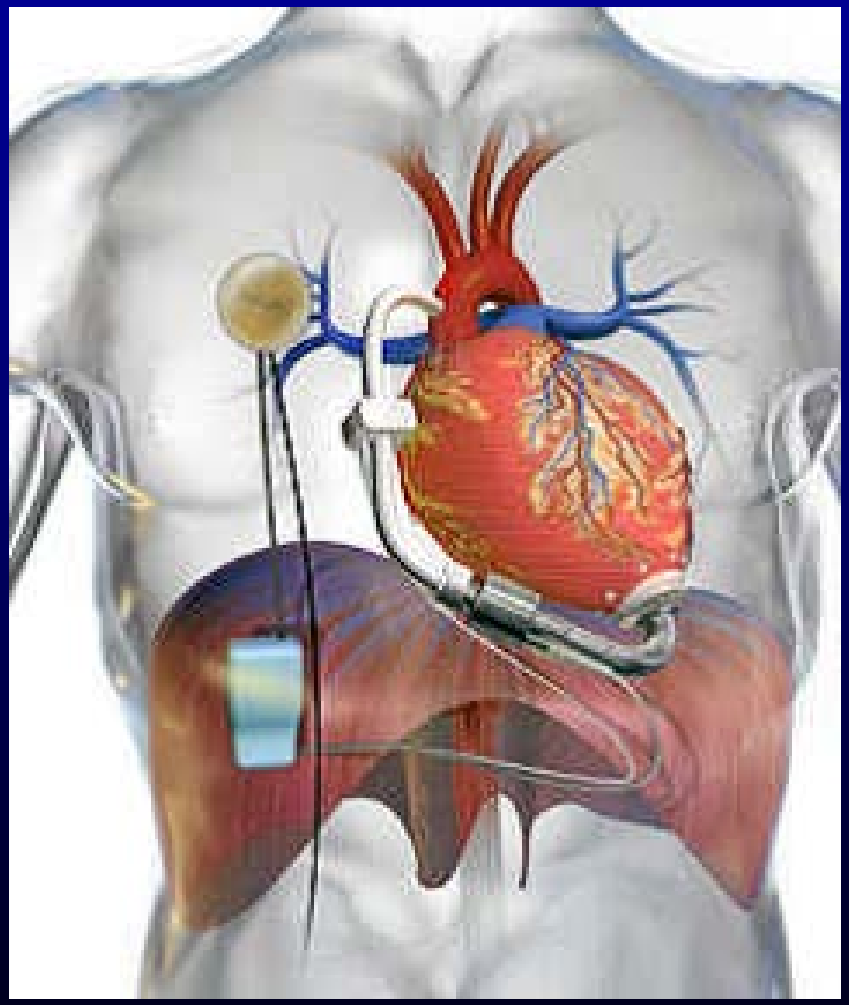

114 mm
63.3 mm
L
P

Importance of Nutrition



TET systems


Outlet cannula
Inlet cannula
Compliance chamber
5" diam. x 1/2";
0.2 lb
Internal coil
2 7/8" diam. x 5/8";
0.3 lb
Access port
Blood pump
2 7/10" diam. x 2 13/16";
1.5 lb
Motor controller
4" x 3 3/4" x 1 1/8";
1.1 lb



LVAD Complications

GI Bleeding

GI bleeding/AVMs

- S/S:
  - Abdominal pain, low H/H, blood in stool or emesis
- Dx:
  - Colonoscopy, IR, guiac stool
- Etiology:
  - Continuous flow/high pump speed?, supratherapeutic INR, antiplatelet, HIT pts
- Tx:
  - Decrease coumadin dosing, antiplatelet agents, transfuse if indicated,

Tx

Arteriovenous Malformation and Gastrointestinal Bleeding in Patients with the HeartMate II Left Ventricular Assist Device

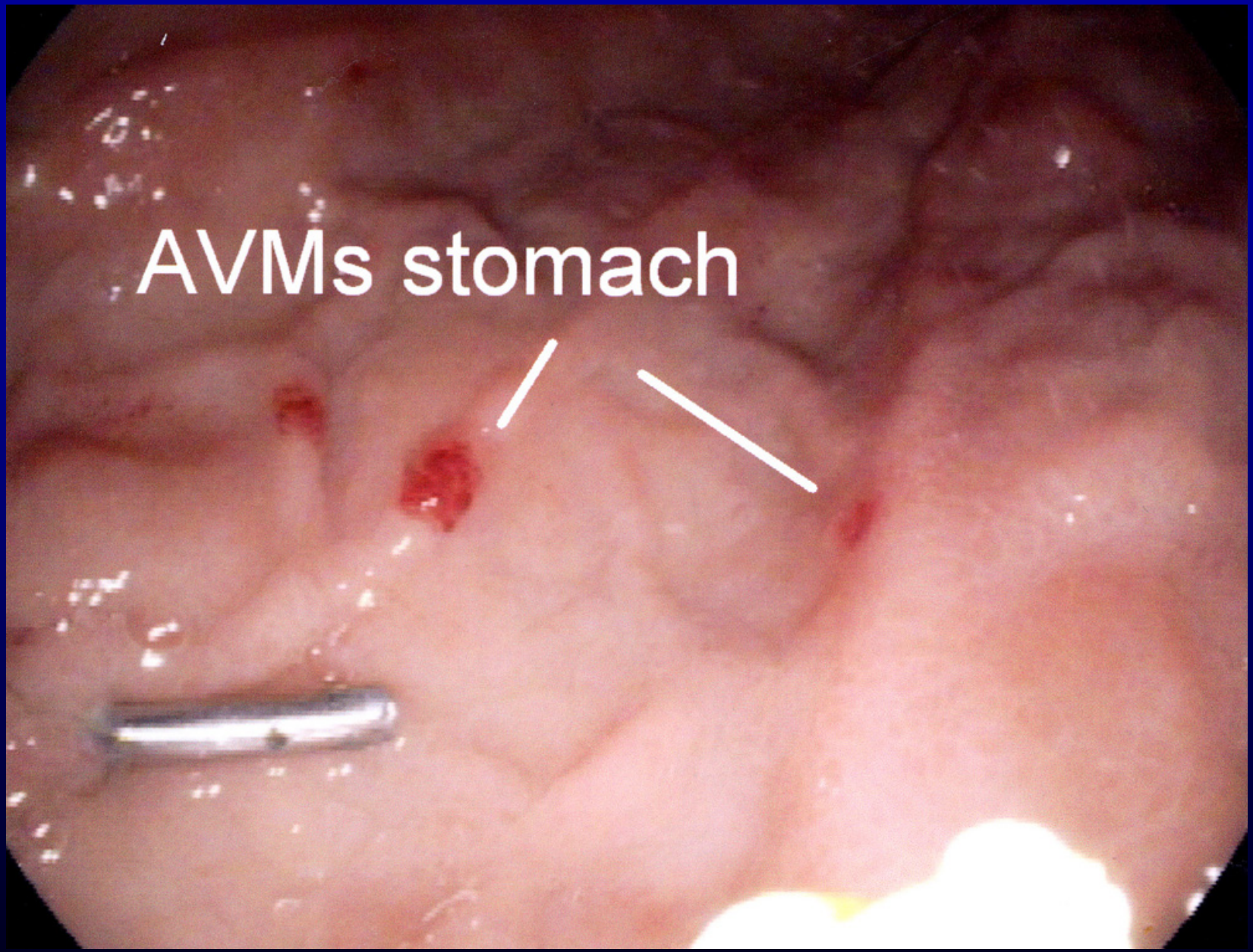
Zumrut T. Demirozu,
Rajko Radovancevic, Lyone Hochman,
Igor D. Gregoric, George V. Letsou, Biswajit Kar,
Roberta C. Bogaev, O. H. Frazier

Cardiopulmonary Transplantation and Center for Circulatory Support

Texas Heart Institute at St. Luke's Episcopal Hospital, Houston, Texas

Patients and Methods

- Of 184 patients, 31 patients (17%) met the criteria for GI bleeding.
- Duration of LVAD support in the study group: 351 ± 272 days
- Average time from LVAD implantation to 1st bleeding episode: 84 ± 132 days (8-707 days)


AVMs stomach

LVAD Complications

Pump Thrombosis

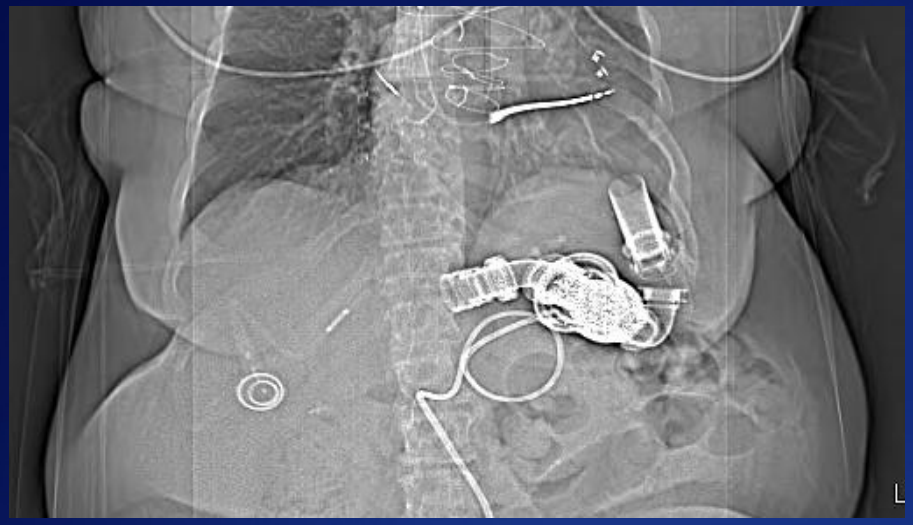
LVAD Thrombosis

- Pump Related
- Not Pump related

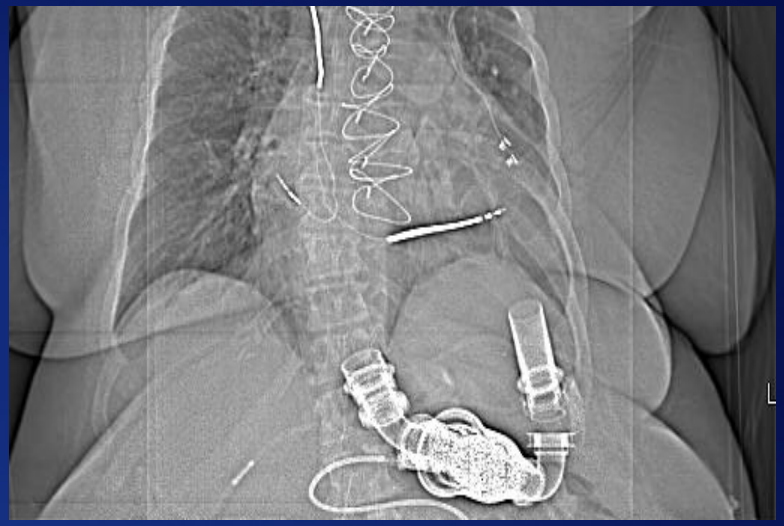
Non Pump related Thrombosis of LVAD

Dislodgement of outflow cannula

Pump replacement

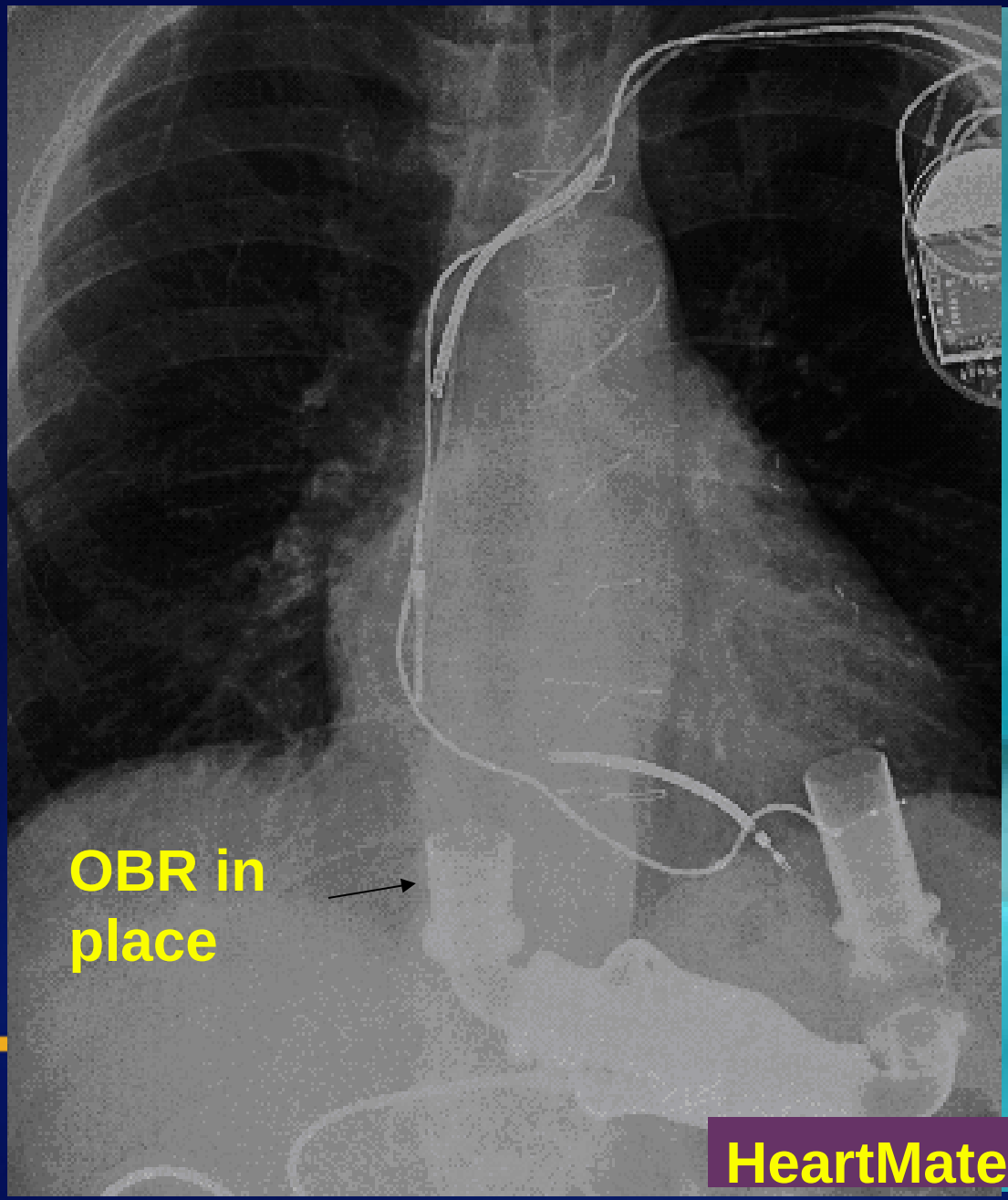


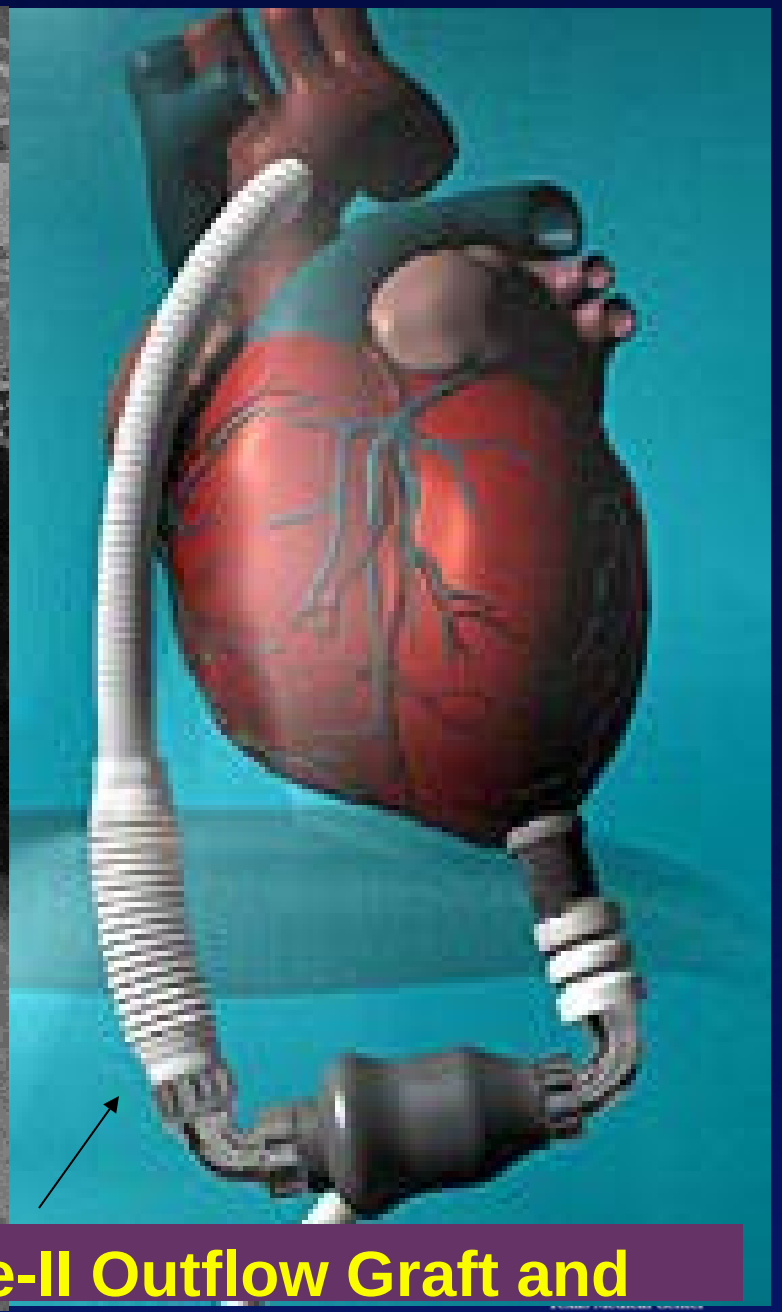
Before



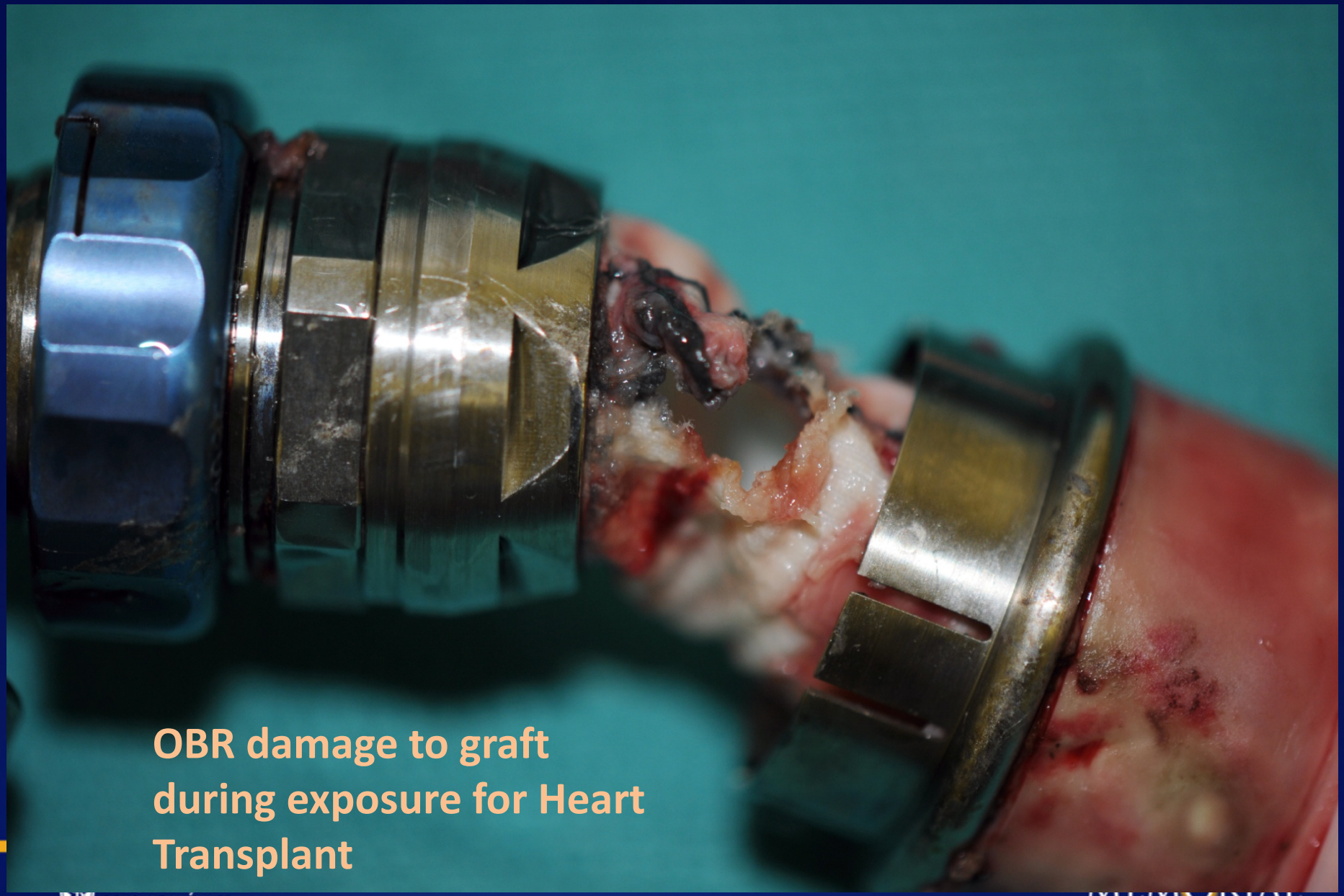
After

Disconnected
Bend relief graft



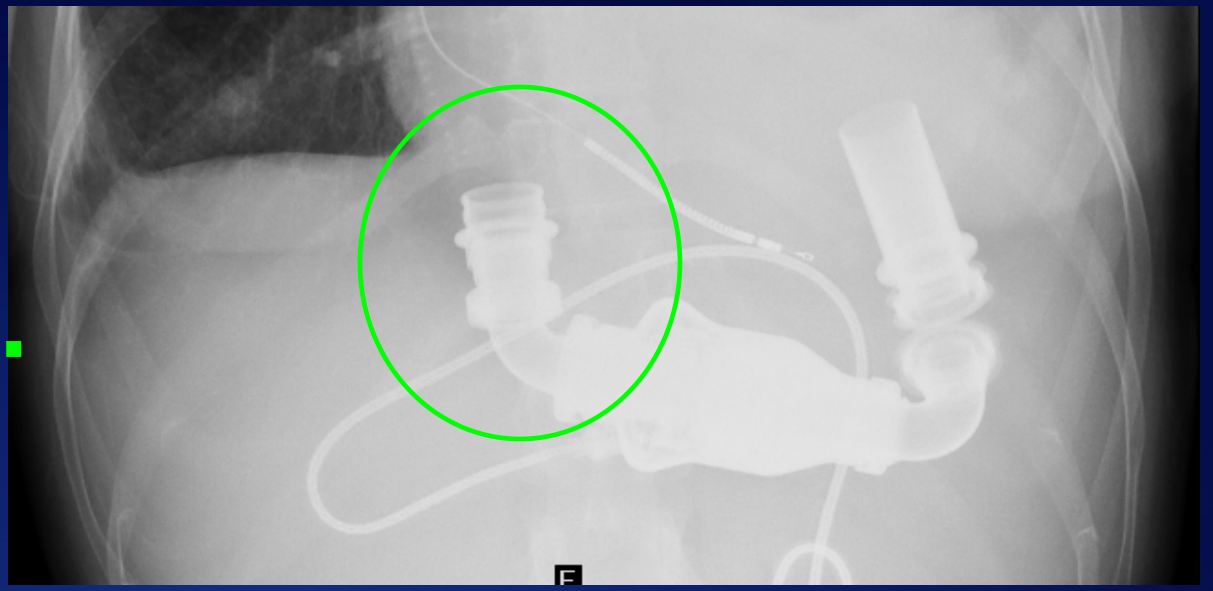


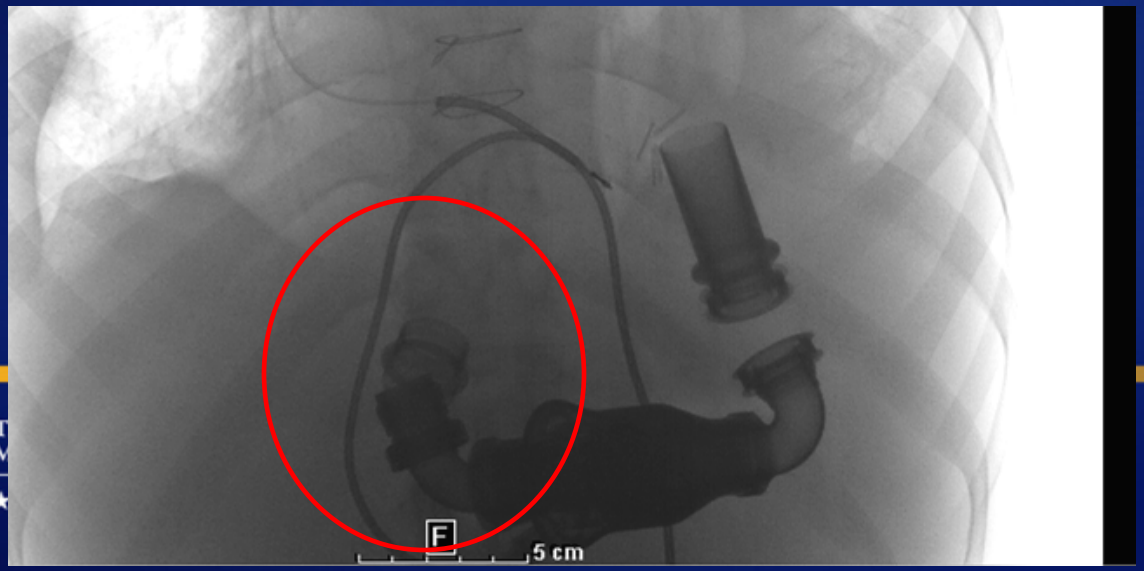
HeartMate-II Outflow Graft and Bend Relief



OBR damage to graft during exposure for Heart Transplant

Normal connection…





…Slipped Bend Relief !

Evolution of LVAD Technology

1st Generation *Pulsatile Pump* → **2nd Generation** *Axial Flow Pump* → **3rd Generation** *Rotary Pump*

DuraHeart
3rd Generation

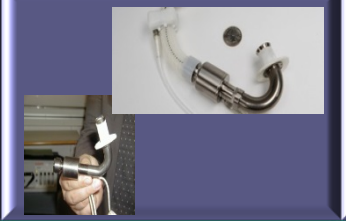
Ventrassist
3rd Generation

HeartWare
3rd Generation

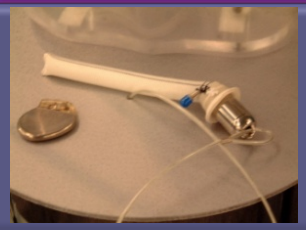
Levacor
3rd Generation

Heartmate III
3rd Generation

Heartmate II
2nd Generation



DeBakey – Reliant VAD
2nd Generation



Jarvik 2000
2nd Generation

Heartmate I
1st Generation

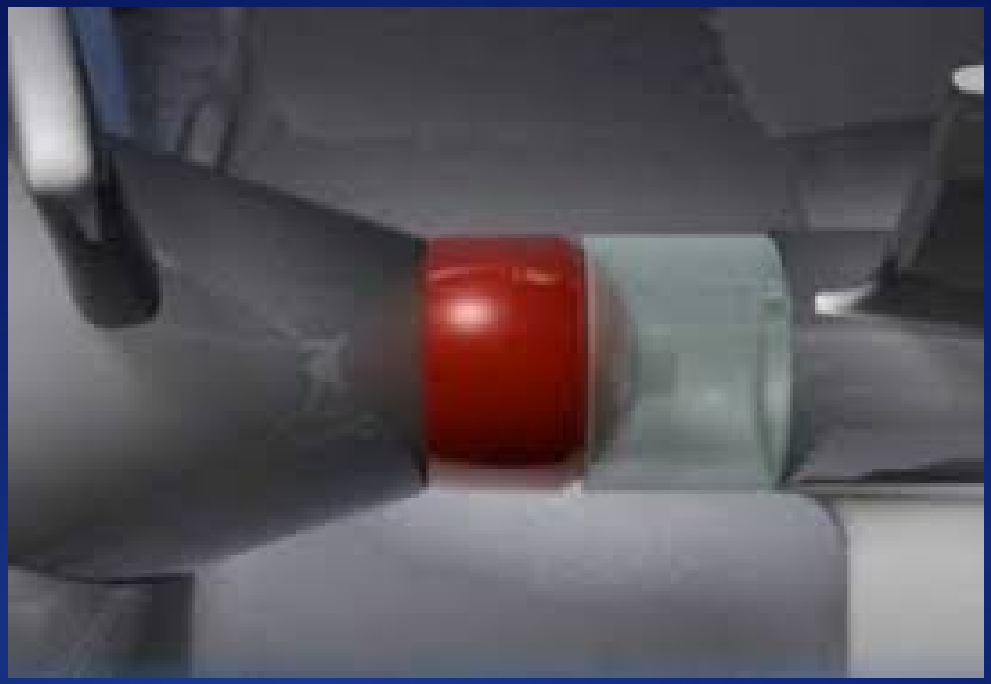
Novacor
1st Generation

The University of Texas Medical School at Houston
UT★PHYSICIANS

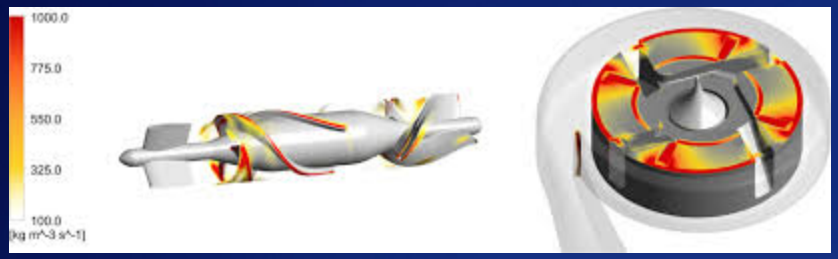
MEMORIAL HERMANN
Heart & Vascular Institute
Texas Medical Center

Pump related Thrombosis of LVAD

Bearings – Potentially heat generated in this area



Blood Damage



Numerical Analysis of Blood Damage Potential of the HeartMate II and HeartWare HVAD Rotary Blood Pumps

1.Bente Thamsen[1,*],
2.Bastian Blümel[2],
3.Jens Schaller[1],
4.Christian O. Paschereit[2],
5.Klaus Affeld[1],
6.Leonid Goubergrits[1] and
7.Ulrich Kertzscher[1]

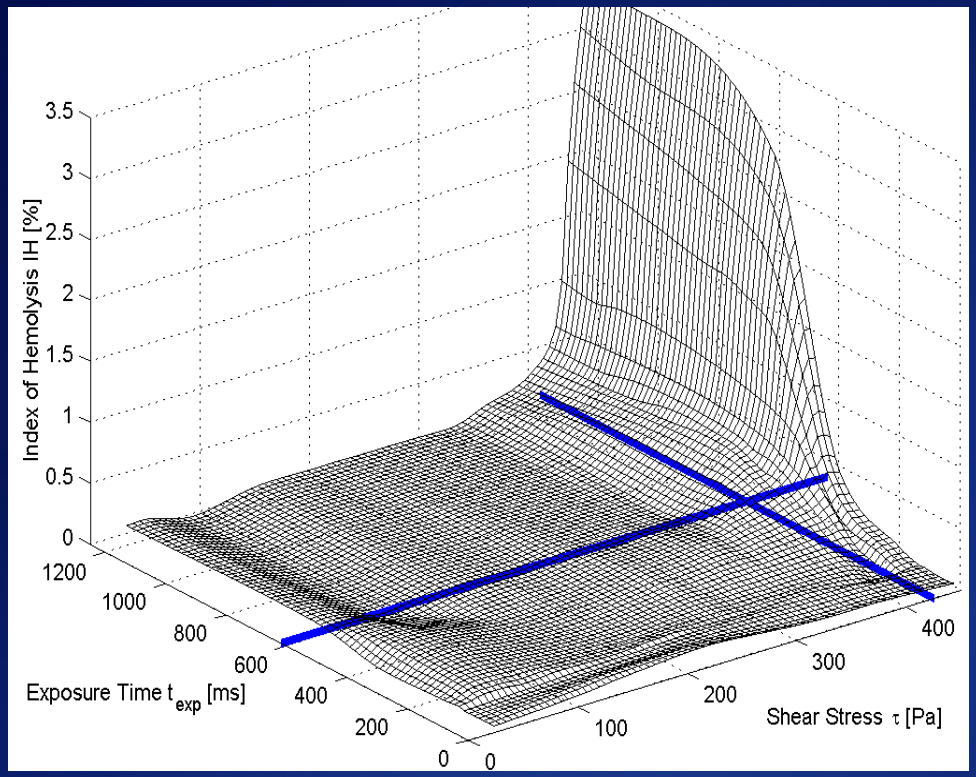
Artificial Organs
Volume 39, Issue 8, pages 651–659, August 2015

The University of Texas Medical School at Houston
UT★PHYSICIANS

MEMORIAL HERMANN
Heart & Vascular Institute
Texas Medical Center

Hemolysis

Hemolysis is a function of shear stress level and exposure time
For most rotary pumps the exposure times are very short (ms), thats the secret for low hemolysis!



Shear stress induced blood damage:

Below exposure times of 620 ms and/or shear stresses of 425 Pa, the index of hemolysis is negligible

Paul et al, Artif Organs 2003, 27(6)

Platelet Trajectories

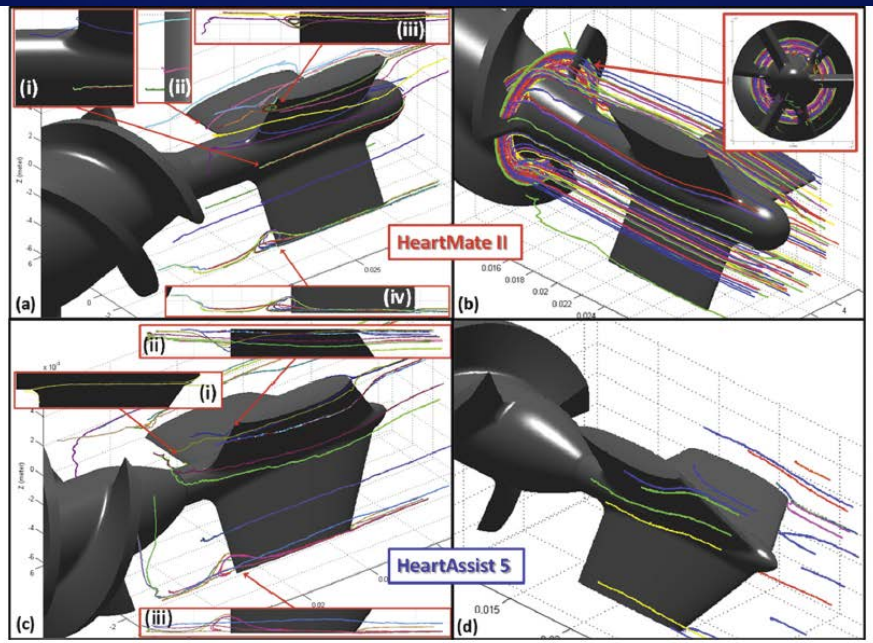


Fig. 5 Stagnant platelet trajectories and recirculation zones in HMII and HA5- (*a*) The recirculation zones and stagnant platelet trajectories were observed at the downstream of the flow straightener blades of HMII, with approximately 2 mm of the average eddy diameter. (*b*) Several entrapped platelet trajectories were observed at the entry of the impeller blades of the HMII, and closely following the rotational motion of impeller. (*c*) Fewer stagnant trajectories were observed at the rear hub region of the HA5 comparing to the HMII, and no recirculation zone was found. (*d*) No entrapped platelet trajectory was observed at the entry of the HA5 impeller. These platelet trajectories were represented as a time average of their residence time (184 ms).

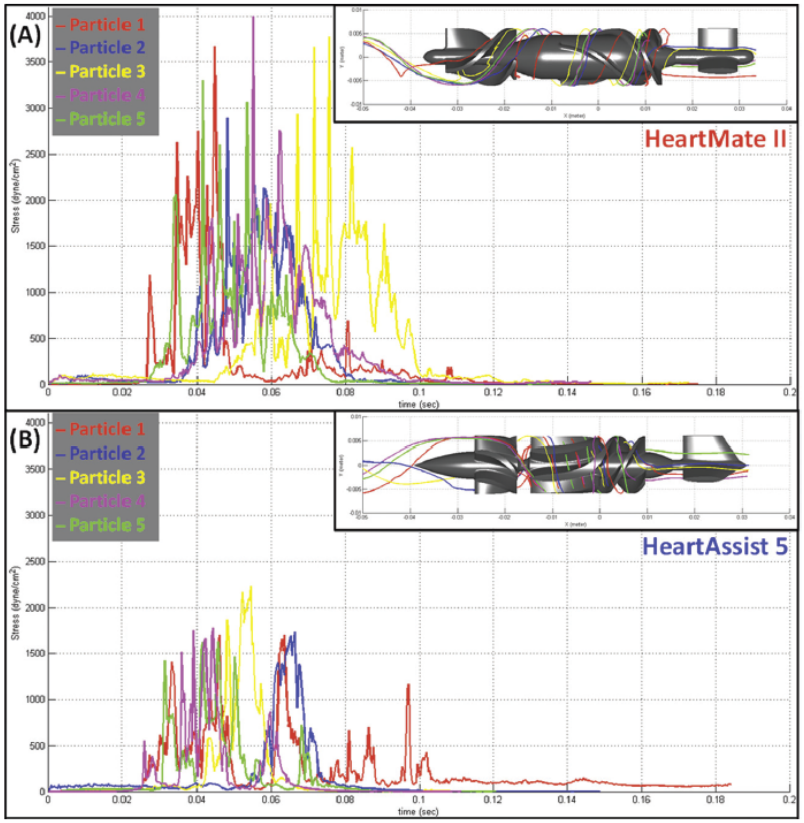


Fig. 7 Markedly lower stress accumulation of platelet trajectories flow through impeller-shroud gap of HA5 representative shear stress and exposure time of five platelet trajectories flow through the impeller-shroud gap of (*a*) HMII and (*b*) HA5 VADs are shown. The platelet trajectories flowing through the HA5 has lower shear stress magnitude and shorter exposure time comparing to the trajectories flowing through the HMII.

Simulation of centrifugal blood pump

Computational fluid dynamics

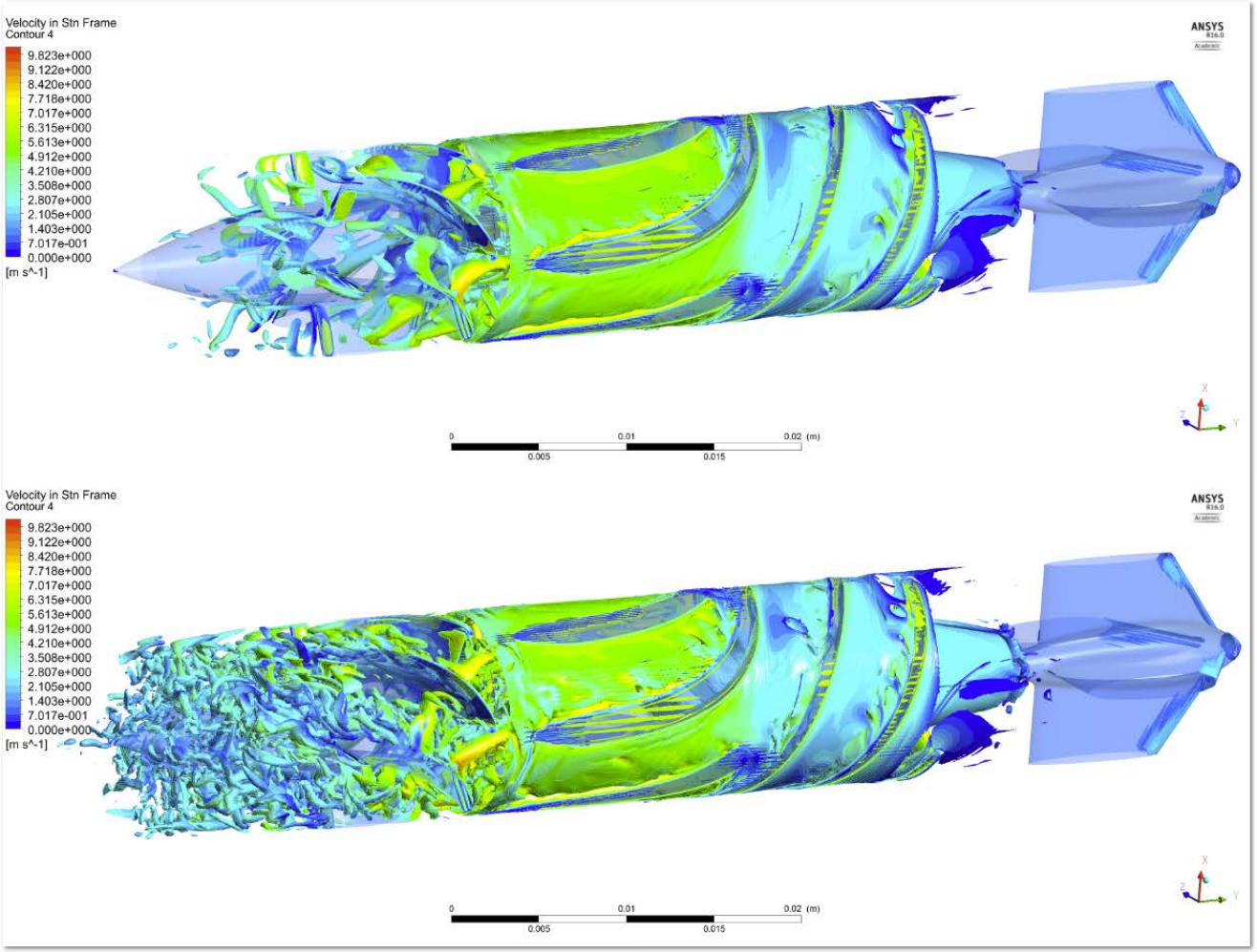
University of Ljubljana
Faculty of Mechanical Engineering

Preliminary report R02

Preliminary report R02

Primož Drešar

Mentor: Dr. Jože Duhovnik
Co-Metnor: Dr. Igor Gregorič


Velocity in Stn Frame
Contour 4
9.823e+000
9.122e+000
8.420e+000
7.718e+000
7.017e+000
6.315e+000
5.613e+000
4.912e+000
4.210e+000
3.508e+000
2.807e+000
2.105e+000
1.403e+000
7.017e-001
0.000e+000
[m s^-1]
ANSYS
R16.0
0
0.01
0.02 (m)
0.005
0.015
Velocity in Stn Frame
Contour 4
9.823e+000
9.122e+000
8.420e+000
7.718e+000
7.017e+000
6.315e+000
5.613e+000
4.912e+000
4.210e+000
3.508e+000
2.807e+000
2.105e+000
1.403e+000
7.017e-001
0.000e+000
[m s^-1]
ANSYS
R16.0
0
0.01
0.02 (m)
0.005
0.015

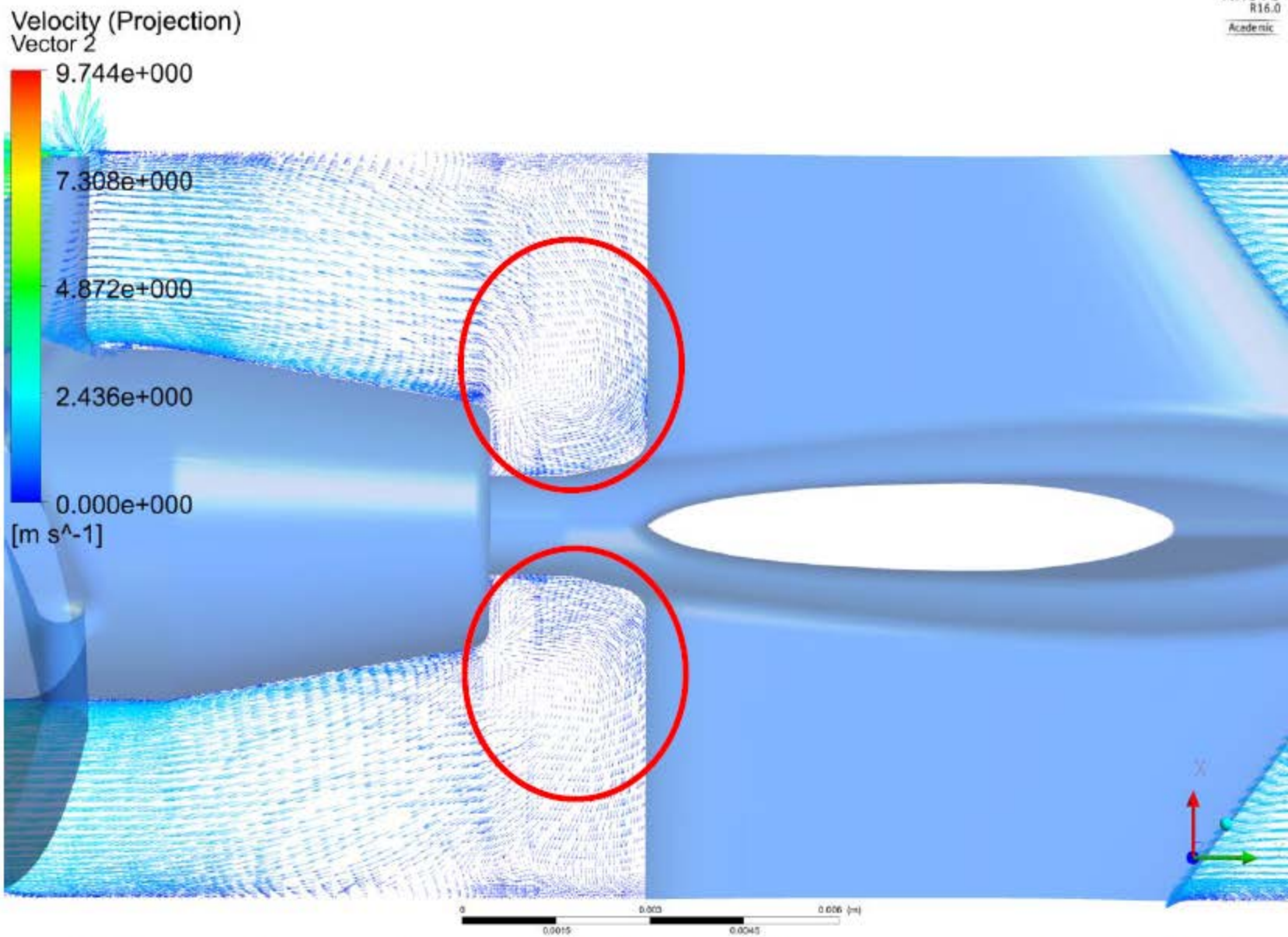


Figure 13: Rotational flow encircled in red behind driving blades (vector representation of velocity [m on XY plane)

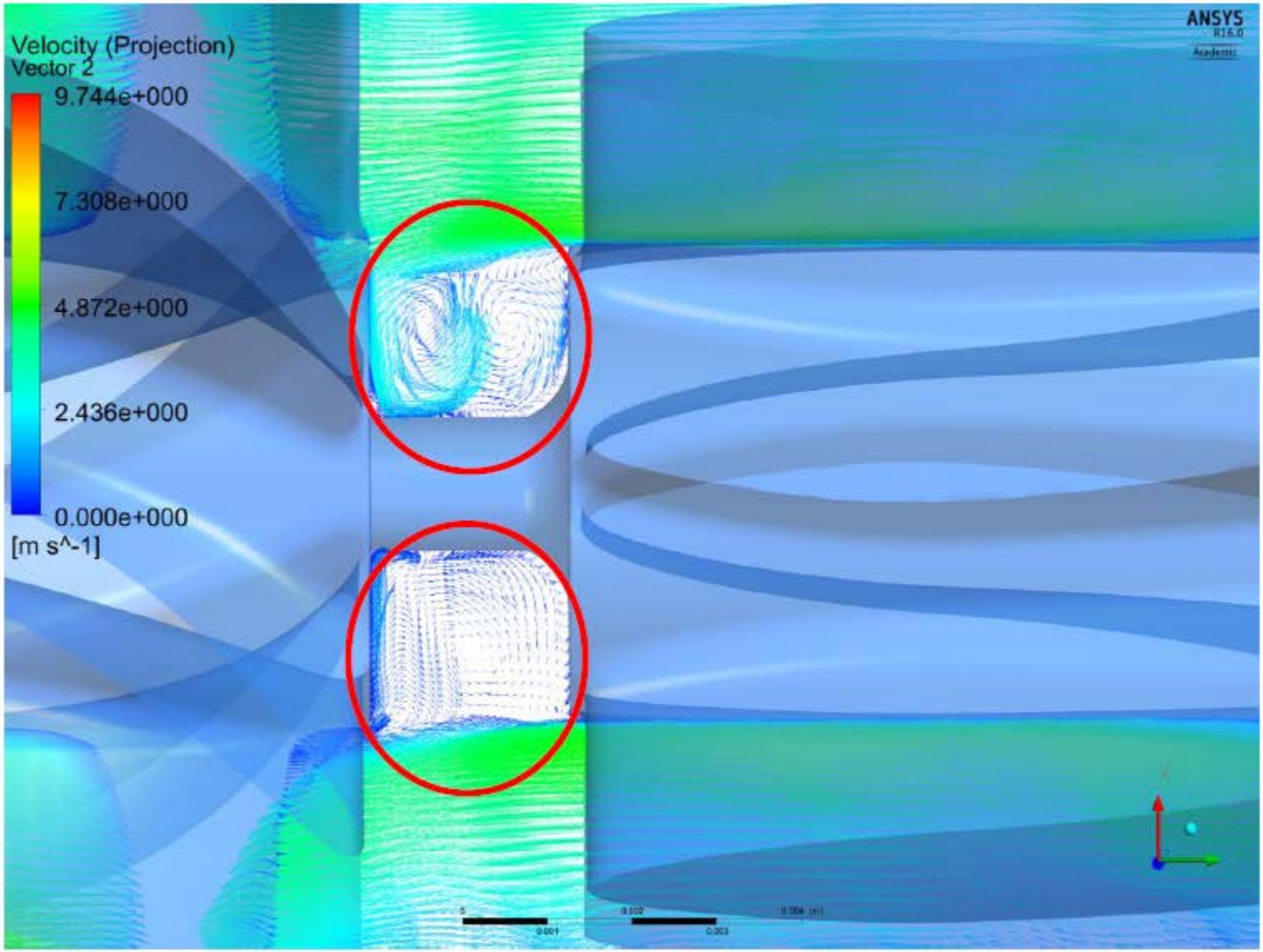


Figure 14: Rotational flow encircled in red behind rotor blades and before diffuser (velocity vec representation on XY plane)

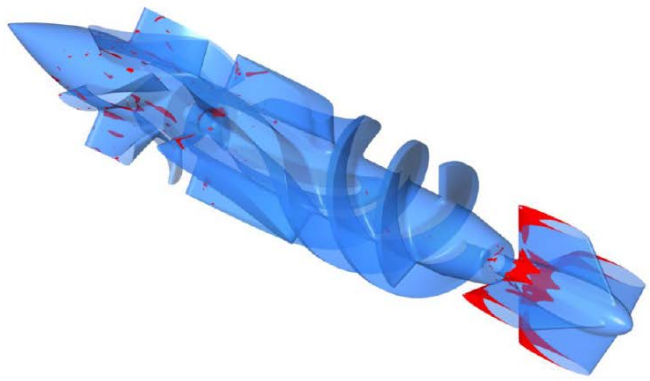


Figure 20: Wall Shear Stress of 0.8 Pa [Pa] projected on boundary surfaces

Wall Shear Stress

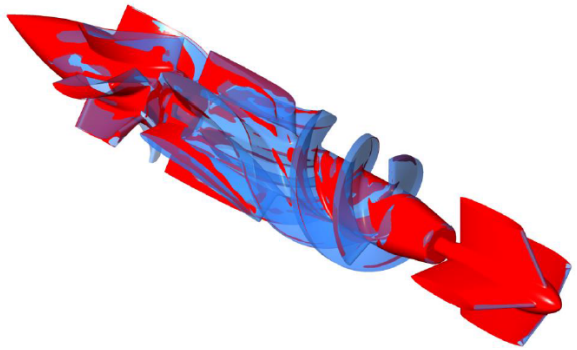


Figure 21: Wall Shear Stress of 150 Pa [Pa] projected on boundary surfaces

The representation of WSS is limited to surface projection. For improved shear stress evaluation some other methods were developed.

According to authors [4] shear stress of τ >150 Pa is correlated to hemolysis. Volume with τ >9 Pa which may contribute to platelet activation (Figure 20) and finally locations with τ <0,8 Pa may correlate with thrombosis.

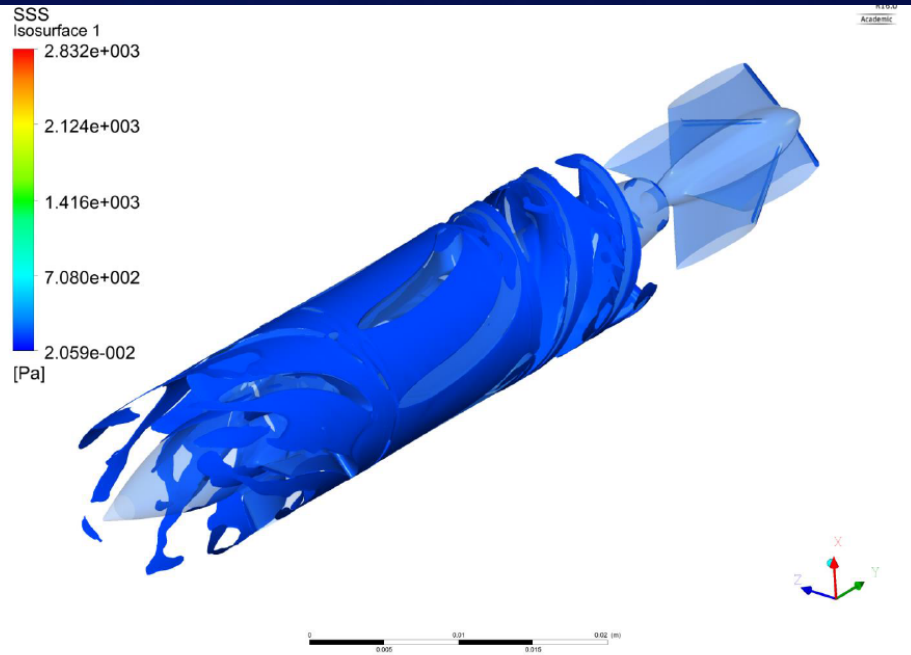


Figure 24: Scalar Shear Stress of 150 Pa applied to iso-surfaces closing a volume

Table 4: Volumes for critical Shear Stress Scalar (SSS) magnitudes

0.8 Pa volume	1.657E-6 m^3
9 Pa volume	2.26117E-6 m^3
150 Pa volume	5.03871E-8 m^3

Table 4 show calculated volumes of fluid with critical SSS values (K.H.Fraser et. ali, 2012).

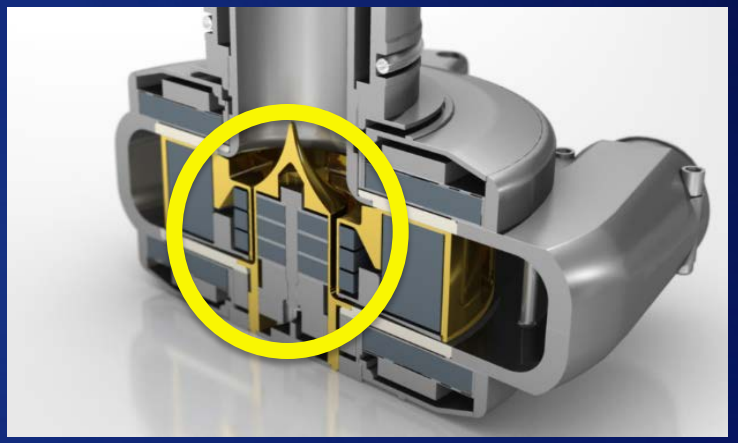
Findings

- Distinguished flow is showing detachment behind diffuser blades. In this case improvement in diffuser blade geometry would be suggested.

- Taking into account that the bearing is also located behind guiding blades, it might suggest the reason for thrombosis appearance in the same location

Clinical studies

H-Vad



Endurance trial

(for NEJM publ. / Presented by F. Pagani last year)

Treatment of Patients with Advanced Heart Failure Ineligible for Cardiac Transplantation with an Intra-pericardial Left Ventricular Assist Device

*Joseph G. Rogers[1], *Francis D.Pagani[2], Antone J. Tatooles[3], Geetha Bhat[3], Mark S. Slaughter[4], Emma J Birks[4], Steven W. Boyce[5], Samer S. Najjar[5], Valluvan Jeevanandam[6], Allen S Anderson[7], Igor D. Gregoric[8], Hari Mallidi[9], Katrin Leadley[10], Keith D. Aaronson[2], O.H Frazier[9], Carmelo A. Milano[1]

Table 3: Summary of Adverse Events Occurring Through 2 Years for Subjects Receiving Study or Control Device

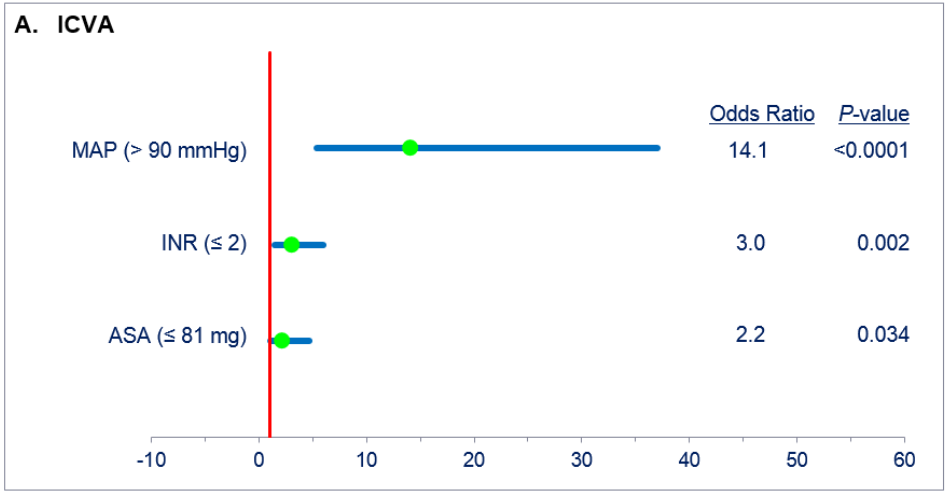
As treated population	Study Device N=296			Control Device N=149			*P* value
	Patients with event	No. of events	EPPY (410.0 PY)	Patients with event	No. of events	EPPY (203.9 PY)	
Overall Bleeding events	96 (60.8%)	426	0.83	93 (62.4%)	219	0.84	0.76
Requiring Reoperation*	45 (15.2%)	52	0.13	27 (18.1%)	28	0.14	0.50
Requiring Transfusion >4 U within 7 days*	45 (15.2%)	47	0.11	33 (22.1%)	36	0.18	0.09
GI Bleed	103 (34.8%)	225	0.55	51 (34.2%)	90	0.44	0.92
Cardiac Arrhythmia	111 (37.5%)	175	0.43	61 (40.9%)	82	0.40	0.54
Hepatic Dysfunction	13 (4.4%)	13	0.03	12 (8.1%)	12	0.06	0.13
Hypertension	47 (15.9%)	62	0.15	24 (16.1%)	28	0.14	>0.99
Sepsis	69 (23.3%)	83	0.20	23 (15.4%)	28	0.14	0.06
Driveline Exit Site Infection	56 (18.9%)	72	0.18	21 (14.1%)	25	0.12	0.23
Stroke	85 (28.7%)	110	0.27	18 (12.1%)	19	0.09	<0.001
Ischemic Cerebrovascular Event	50 (16.9%)	65	0.16	13 (8.7%)	13	0.06	0.021
Hemorrhagic Cerebrovascular Event	42 (14.2%)	45	0.11	6 (4.0%)	6	0.03	0.001
TIA	24 (8.1%)	27	0.07	7 (4.7%)	7	0.03	0.24
Renal Dysfunction	43 (14.5%)	54	0.13	19 (12.8%)	22	0.11	0.67
Respiratory Dysfunction	84 (28.4%)	114	0.28	38 (25.5%)	48	0.24	0.57
Right Heart Failure	110 (37.2%)	129	0.31	39 (26.2%)	45	0.22	0.025
RVAD*	8 (2.7%)	8	0.02	5 (3.4%)	6	0.03	0.77
Pump replacement#	23 (7.8%)	NA	NA	20 (13.4%)	NA	NA	0.06

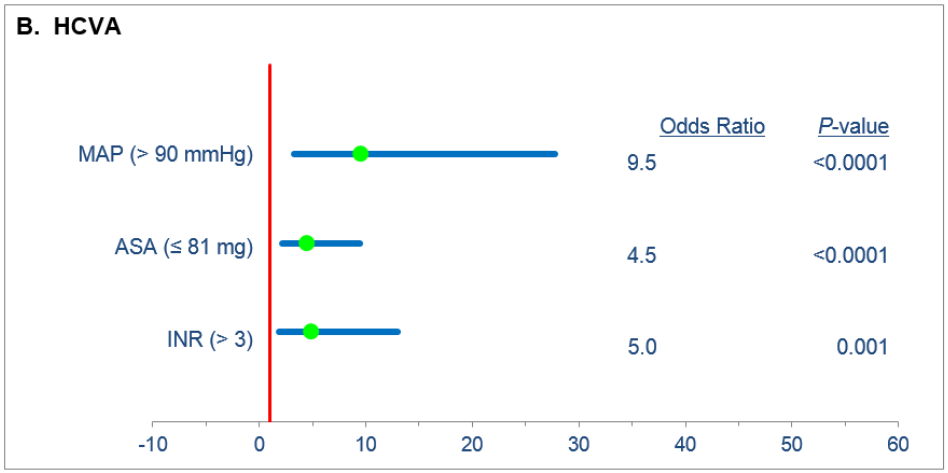
*Site-reported event. #Events and EPPY are not applicable for pump replacement since only the first event is counted.

Abbreviations: EPPY – events per patient year; PY – patient years; GI - gastrointestinal; RVAD - right ventricular assist device; TIA – transient ischemic attack (<24 hours).

Note: *P*-values for the comparisons between percent of patients with events determined by the Proportion Method.

Figure 5: Forrest Plot of Risk Factors for: (A) Ischemic Cerebrovascular Accident (ICVA) and (B) Hemorrhagic Cerebrovascular Accident (HCVA) in the As-Treated Population for Subjects Receiving the Study Device.





PREVENTion of HeartMate II Pump Thrombosis Through Clinical ManagemenT (PREVENT)

PREVENT Clinical Study

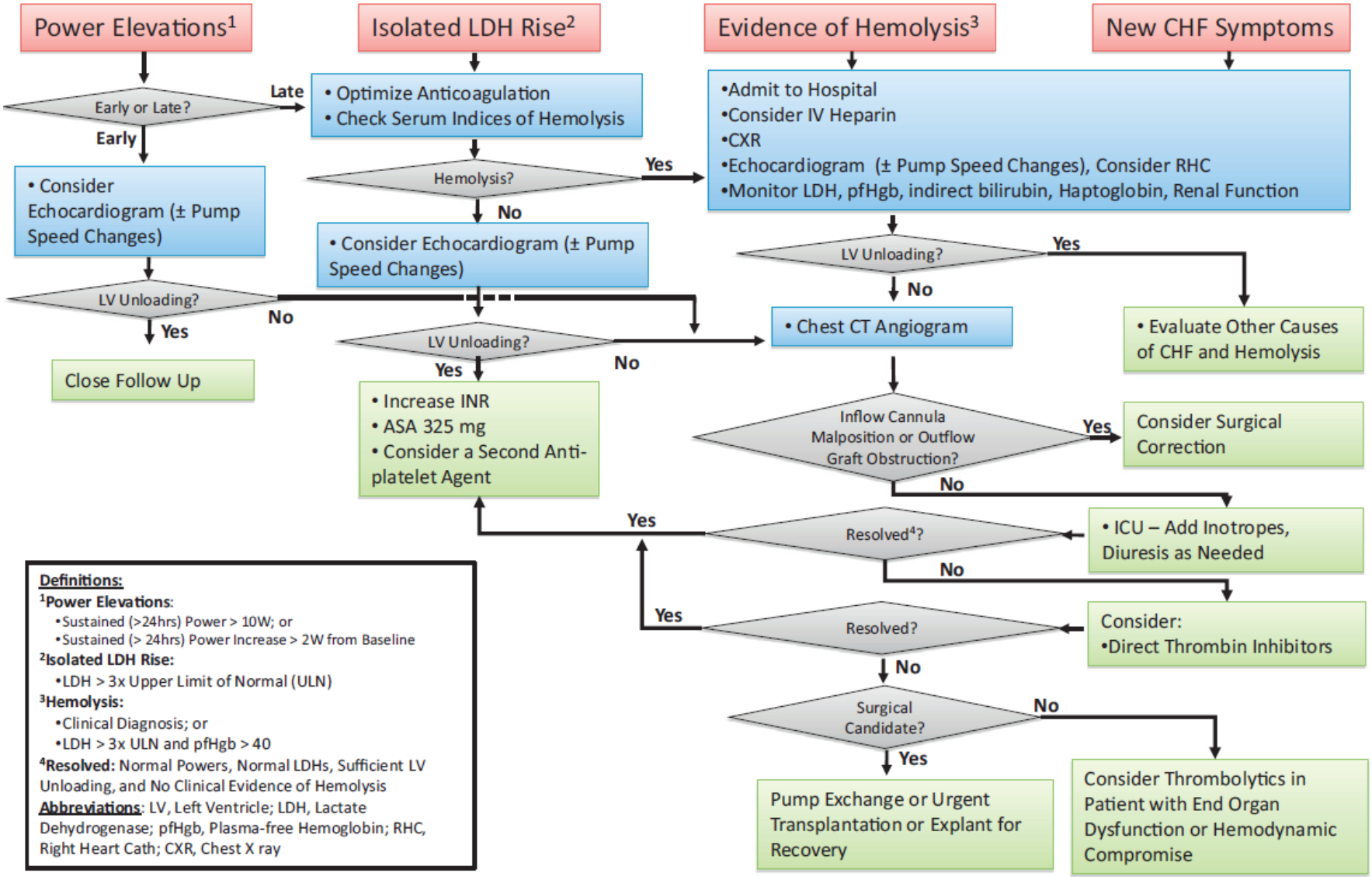
THORATEC CORPORATION

PREVENT

- **PREVEN**tion of HeartMate II Pump Thrombosis Through Clinical Managemen**T**
- Prospective Multi-Center Study (US)
  - Up to 20 sites
  - Up to 300 patients
- Objectives:
  - Assess the incidence of HMII pump thrombosis in the current era when recommended clinical practices are adopted
  - Identify risk factors associated with pump thrombosis events

PREVENT Clinical Study

Algorithm for the Diagnosis and Management of Pump Thrombosis[1]



Definitions:

[1]Power Elevations:
- Sustained (>24hrs) Power > 10W; or
- Sustained (> 24hrs) Power Increase > 2W from Baseline

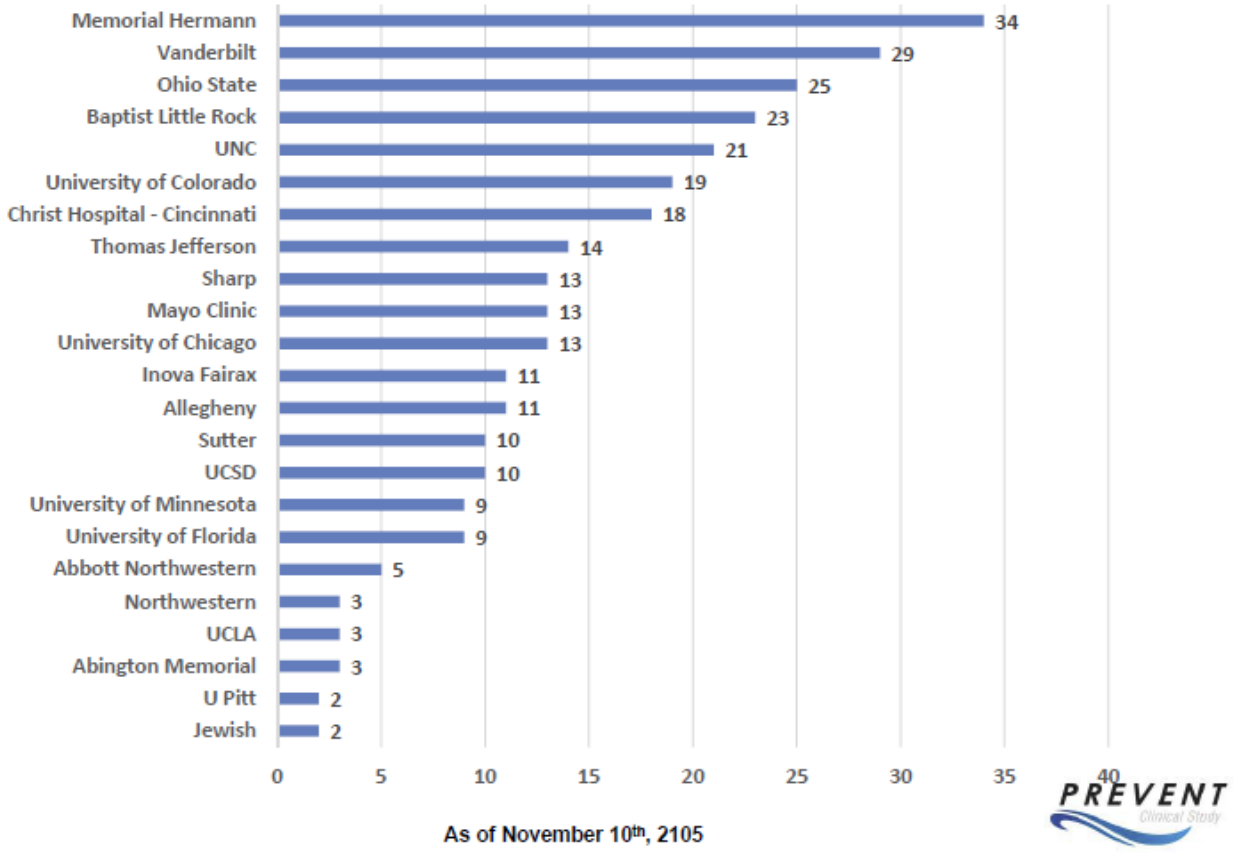
[2]Isolated LDH Rise:
- LDH > 3x Upper Limit of Normal (ULN)

[3]Hemolysis:
- Clinical Diagnosis; or
- LDH > 3x ULN and pfHgb > 40

[4]Resolved: Normal Powers, Normal LDHs, Sufficient LV Unloading, and No Clinical Evidence of Hemolysis

Abbreviations: LV, Left Ventricle; LDH, Lactate Dehydrogenase; pfHgb, Plasma-free Hemoglobin; RHC, Right Heart Cath; CXR, Chest X ray

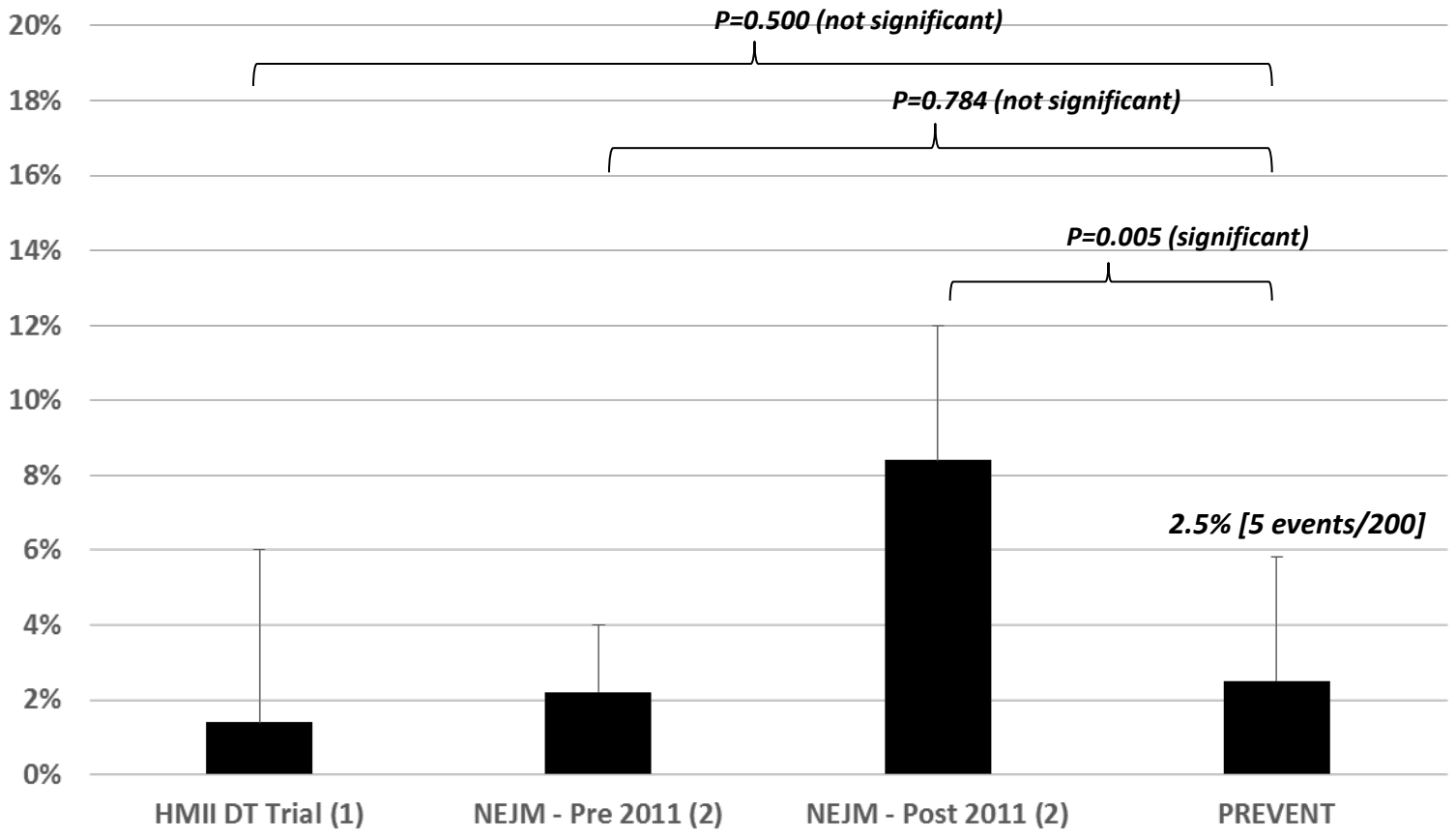
PREVENT Enrollment by Site



As of November 10th, 2105

Results - Primary Endpoint

Confirmed Pump Thrombosis at 90 Days 200 pts



1: Evaluated from the dataset published in: Park SJ, Milano CA, Tatooles AJ et al. Outcomes in advanced heart failure patients with left ventricular assist devices for destination therapy. Circ Heart Fail. 2012 Mar 1;5(2):241-8.

2: Starling RC, Moazami N, Silvestry SC et al. Unexpected abrupt increase in left ventricular assist device thrombosis. N Engl J Med. 2014 Jan 2;370(1):33-40

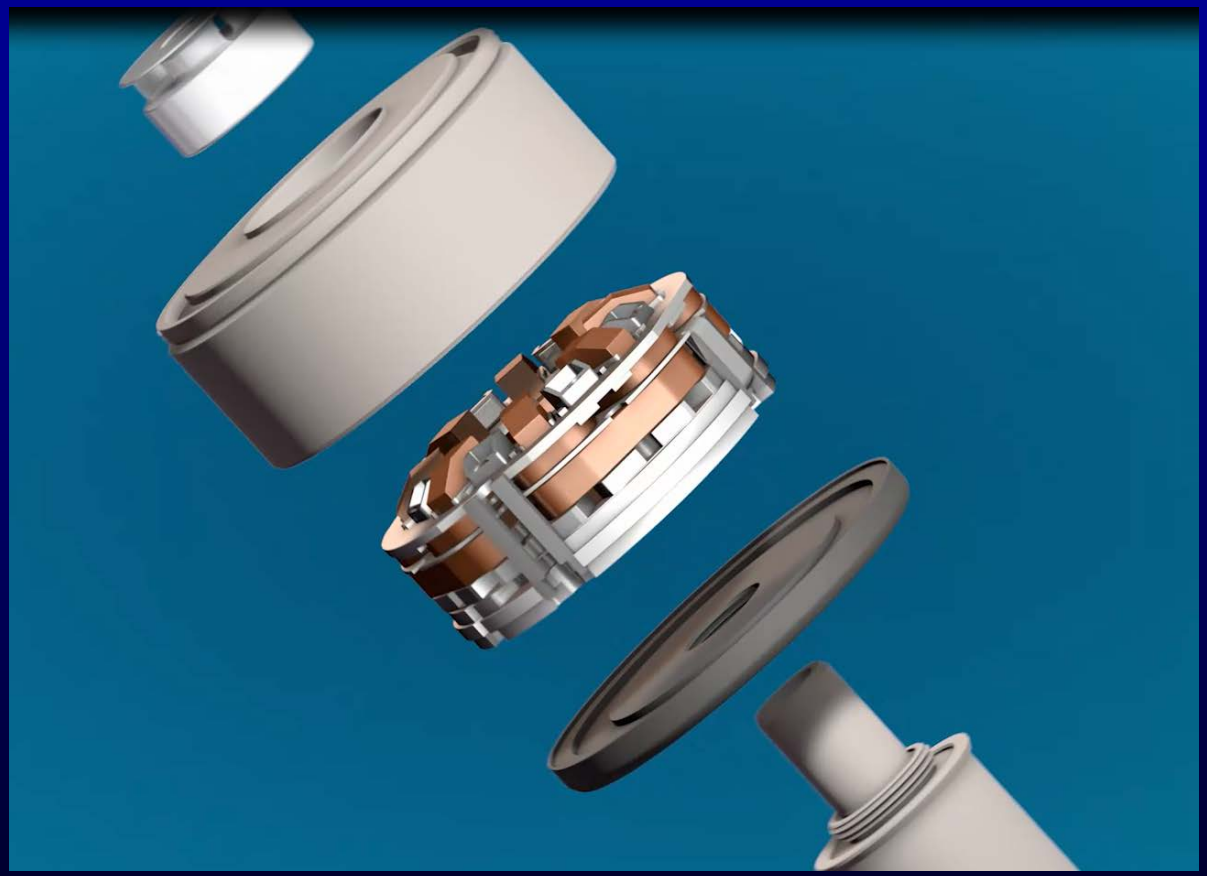
PREVENT Clinical Study

Conclusion

- Best to avoid LVAD Thrombosis is to prevent it
- Patient selection
- Better pump designs
- Better Blood – surface interfase
- Improved flow dinamics

New LVAD Trials

HM III



HeartMate III: Design Goals

- Build upon the highly successful HeartMate II LVAS
- Enhanced AE profile
- Increased surgical ease
- Elevate the patient experience

CAUTION: Investigational device. Limited by federal (U.S.) law to investigational use.

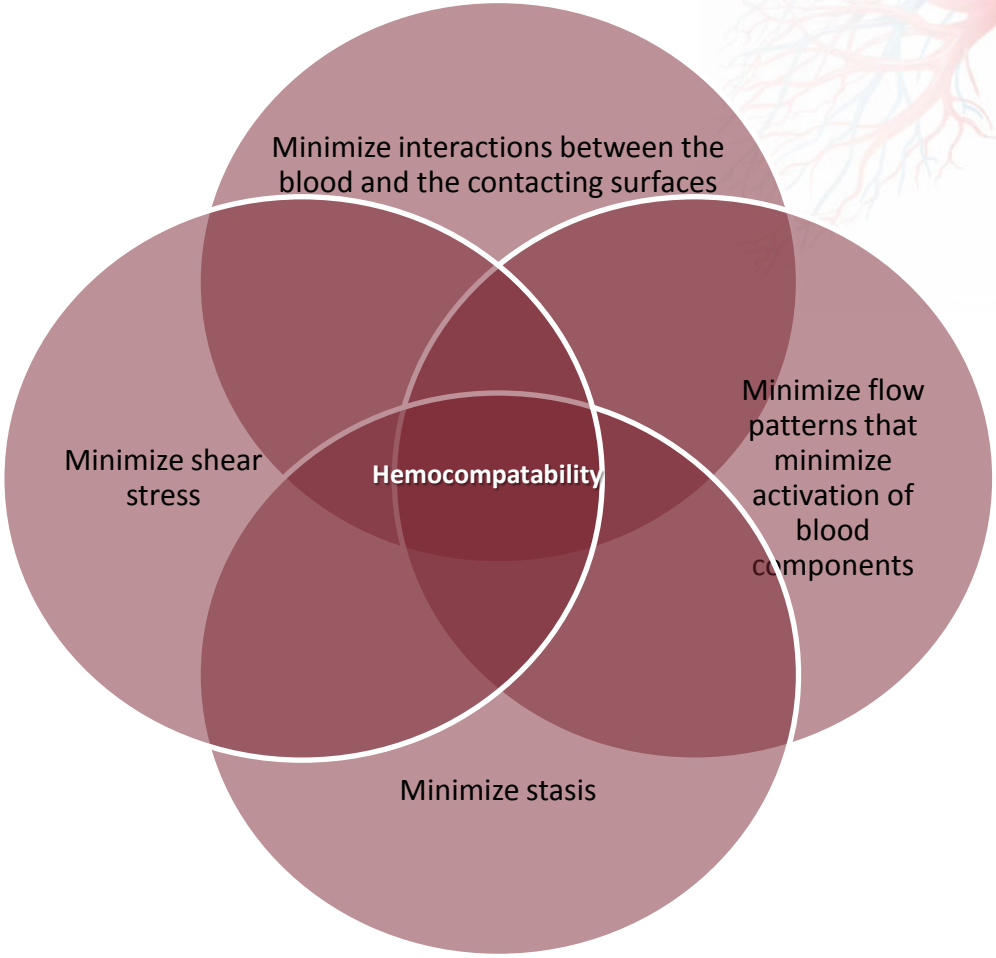
1011053 8/26/14

THORATEC® CORPORATION for Life

A Healthy Respect for the Blood

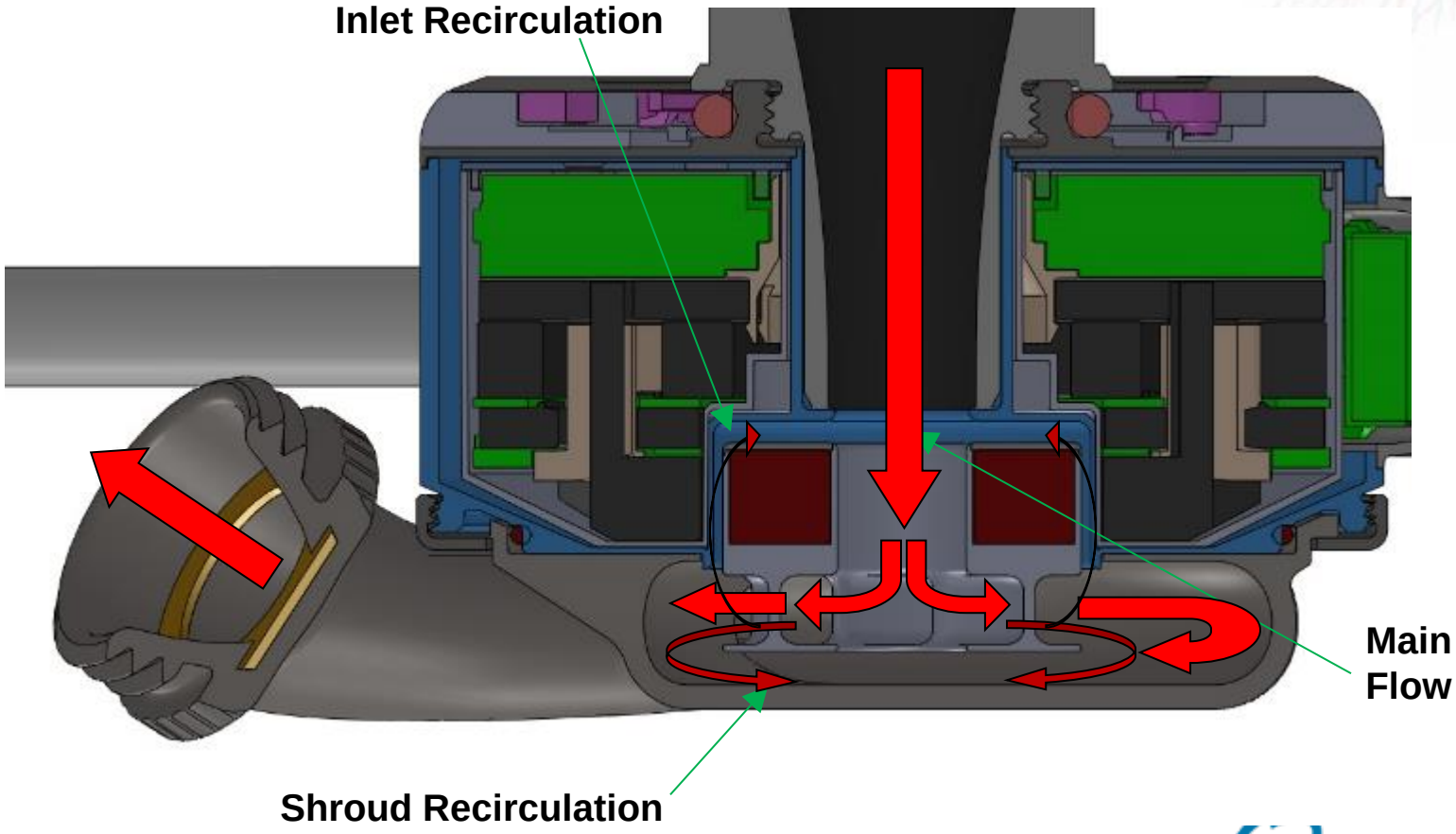
What influences hemocompatibility?

- **Hemocompatability[1]**
  - Minimize shear stress
  - Minimize stasis
  - Minimize flow patterns that minimize activation of blood components
  - Minimize interactions between the blood and the contacting surfaces



1. Moazami N, et al. Ann Thorac Surg. 2014;98(2):54-7.

Design Configuration

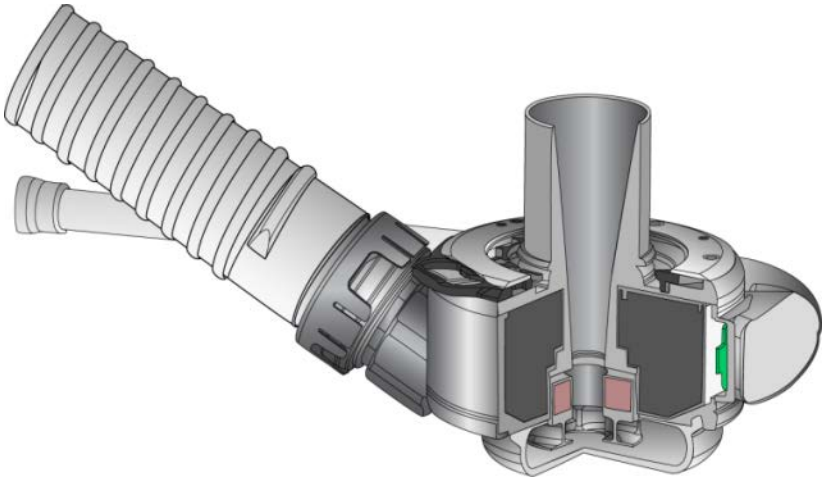


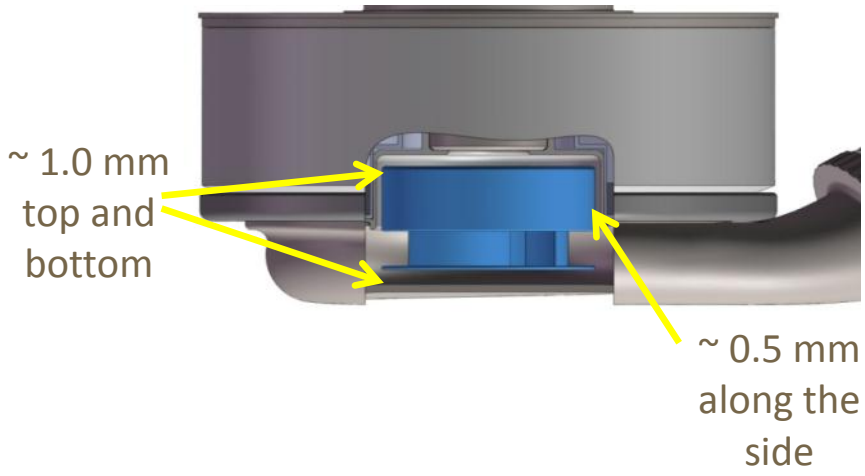
THORATEC CORPORATION for Life

HeartMate III: Full MagLev Technology

Key Design Benefits: Optimized Geometry

- HeartMate III secondary flow paths are ~0.5 mm along the side, and ~1.0 mm pump above and below the rotor.
- HeartMate III pump surfaces are flat and flow is undisturbed.





CAUTION: Investigational device. Limited by federal (U.S.) law to investigational use.

1011053 8/26/14

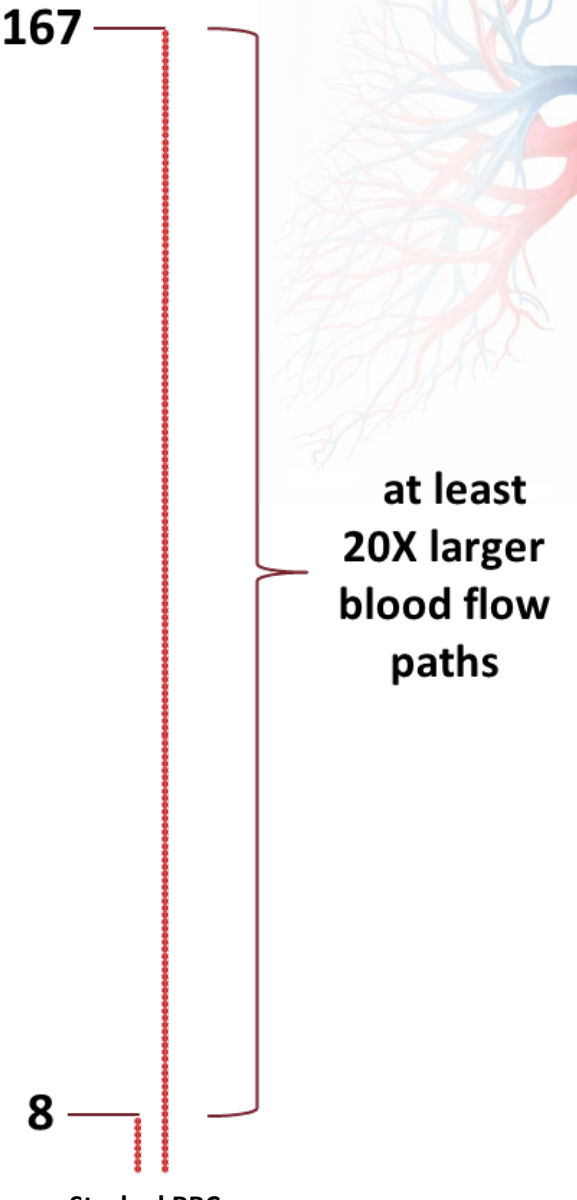
THORATEC CORPORATION for Life

How much difference is there?

From a Red Blood Cell's Point of View

6-8 µm

	Gap Size	# of Red Blood Cells
Full MagLev	1,000µm	167
Hydrodynamic Bearing	50µm	8



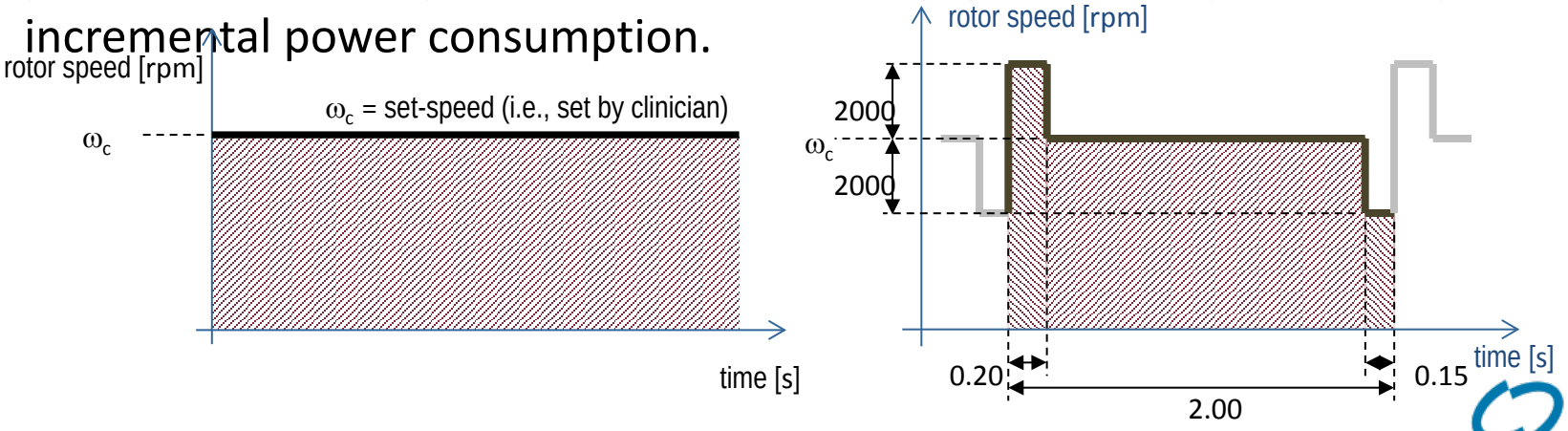
CAUTION: Investigational device. Limited by federal (U.S.) law to investigational use.

1011053 8/26/14

THORATEC CORPORATION for Life

HeartMate III: Artificial Pulse

- Rotary pumps have been used chronically with constant rotor speed in more than seventeen thousand patients, confirming that a pulse is not needed for survival.
- However, we hypothesize that augmenting the pulsatility that is generally diminished in rotary pump patients may have **benefit for some patients** or **in certain circumstances**, perhaps in part addressing adverse events such as aortic insufficiency, bleeding, and thrombogenesis.
- The HeartMate III centrifugal blood pump is intrinsically capable of very sharp speed changes. We have produced an **"artificial pulse"** feature that has so far in pre-clinical studies proved to contribute negligible hemolysis and require low incremental power consumption.



CAUTION: Investigational device. Limited by federal (U.S.) law to investigational use.

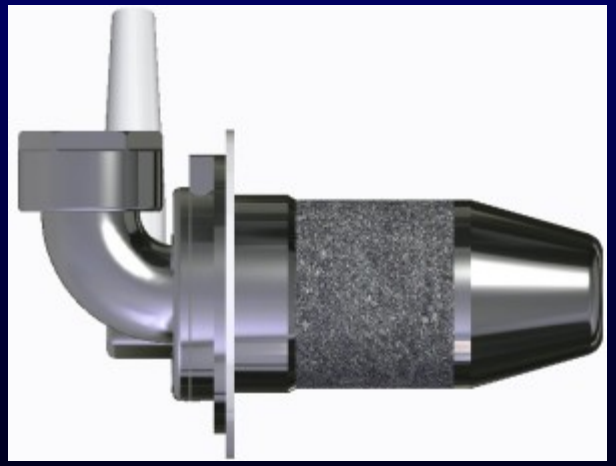
1011053 8/26/14

THORATEC CORPORATION for Life

Future

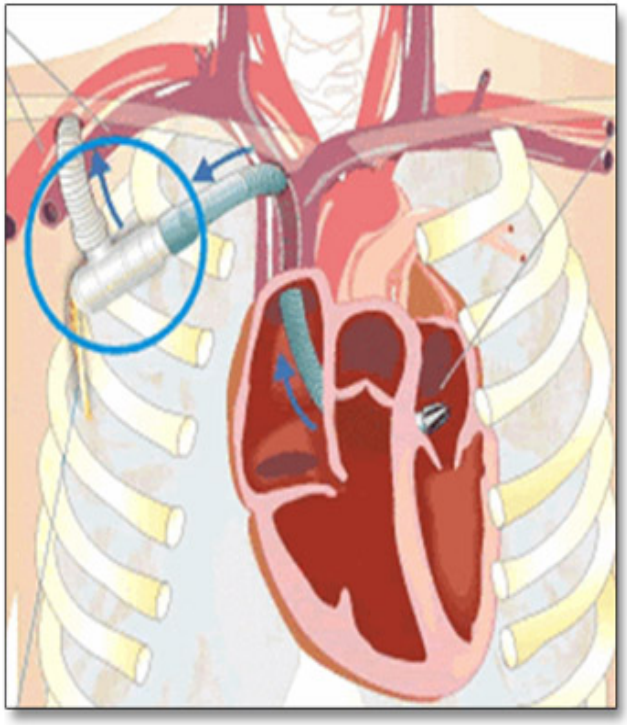
- M - VAD

- A - VAD

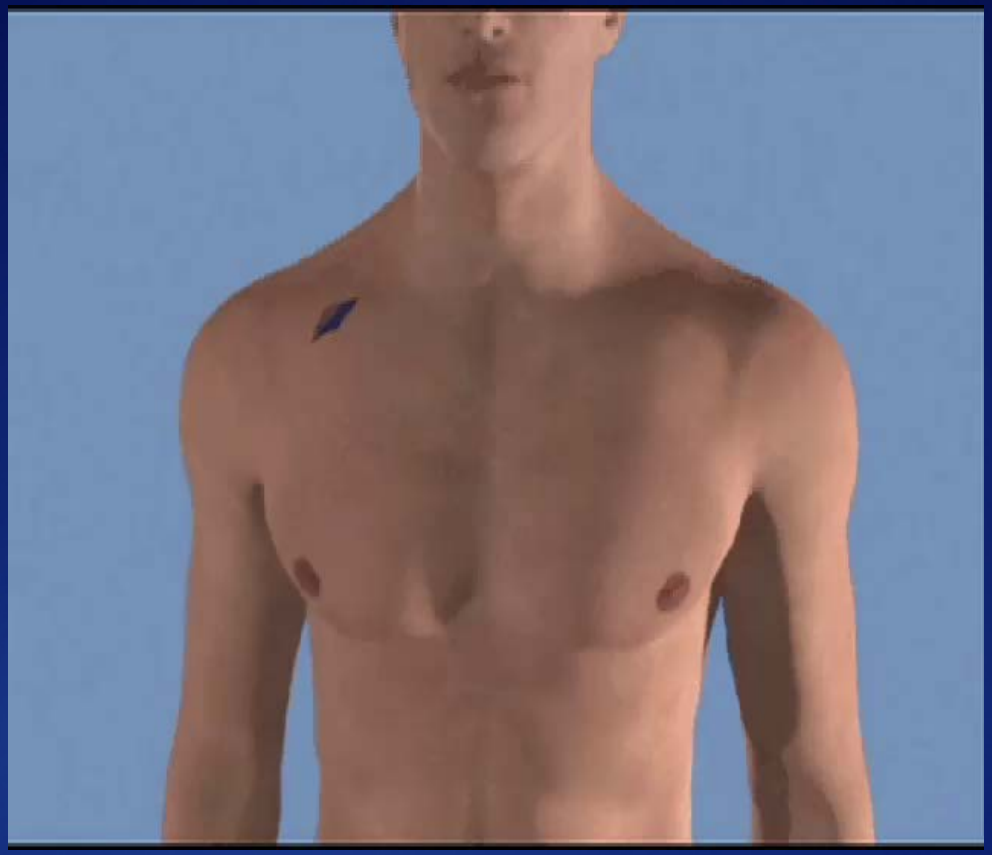


MINIATURE VAD Development
- for Adults

Circulite



Future LVADs



Center for Advanced Heart Failure
Research Division

IRB approved protocols:

INTERMACS
LAPTOP-HF
PROACT (On-X Valve)
SynCardia TAH Postmarket Surveillance
SynCardia Freedom driver
PARTNER II TRIAL
ROADMAP
Amplatzer Cardiac Plug Trail
ABSORB III Randomized Trial
TEG monitoring in LVADs
PARACHUTE IV
TRIS
Portico TAVR
Sepian III PARTNER II Version 4.5
Transfusions in LVADs and HT
PREVENT
Recover Right study (Impella RP)
RELIANTHEART
Von Willebrand Syndrome in LVADs
Pathological assessment of explanted hearts
Heart Mate III

Protocols in submission:

Aortic annulus measurement
Outcomes in AHF patients who require MCS or HT
Left Atrial Pressure Monitoring - Millar catheter
Milrinone therapy in advanced heart failure
Clopidogrel in Cardiogenic Shock
TandemHeart and ECMO; transfusion threshhold
Advanced ECG to Identify non-ST Elevation


THANK
YOU

END