Mechanical Assist Devices: From Bridge to transplant to destination therapy

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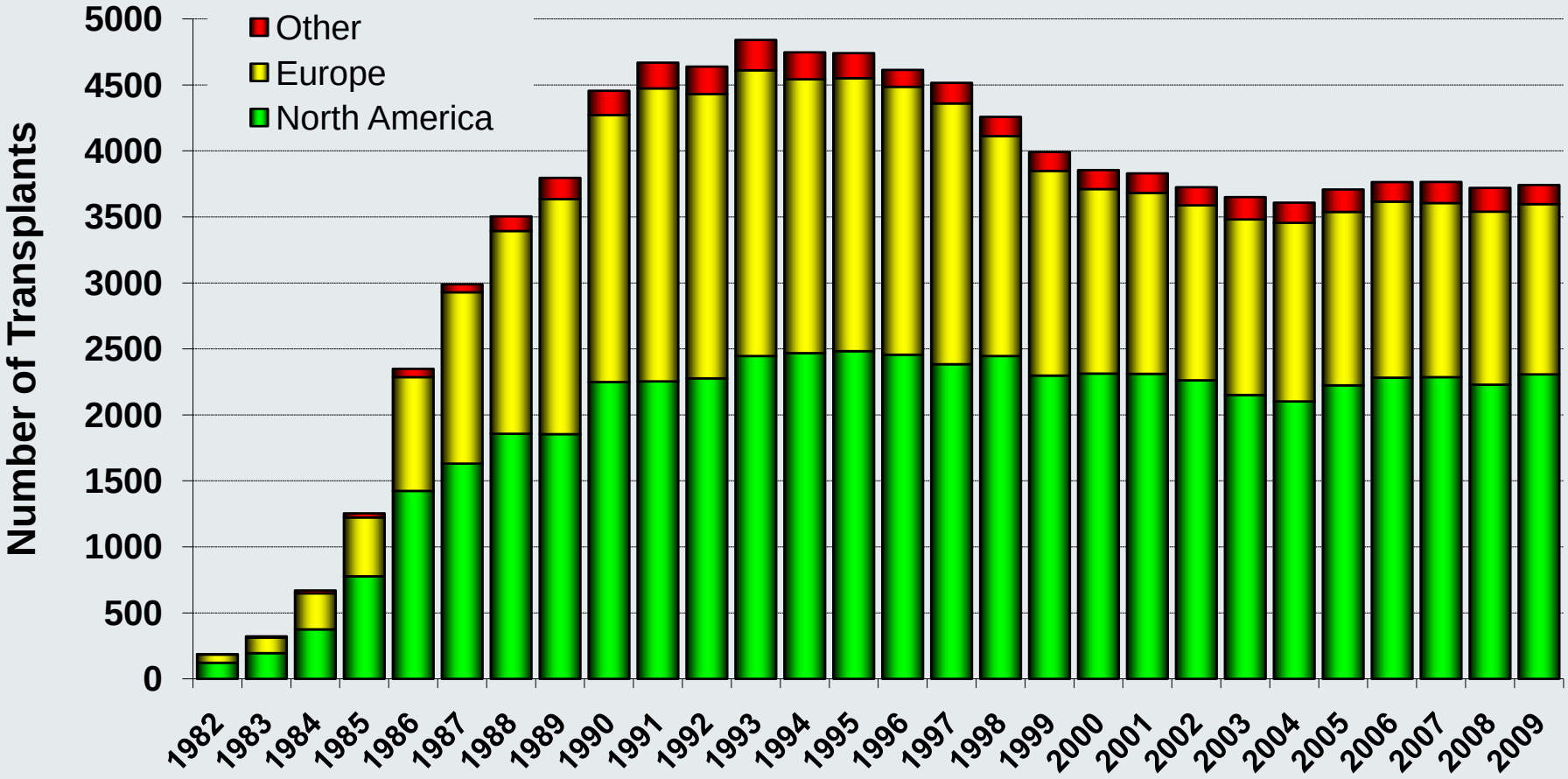
Nothing to disclose

NUMBER OF HEART TRANSPLANTS REPORTED BY YEAR



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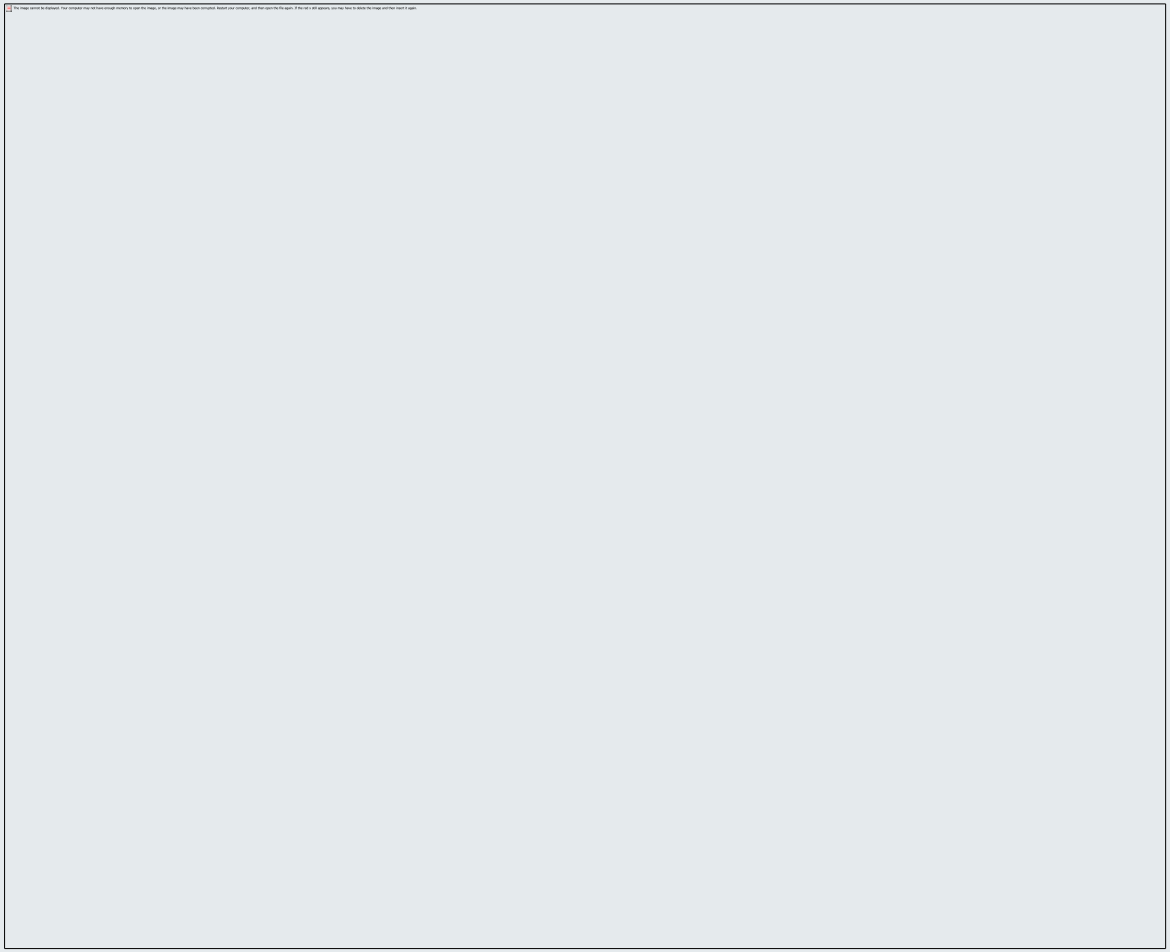
ISHLT 2011

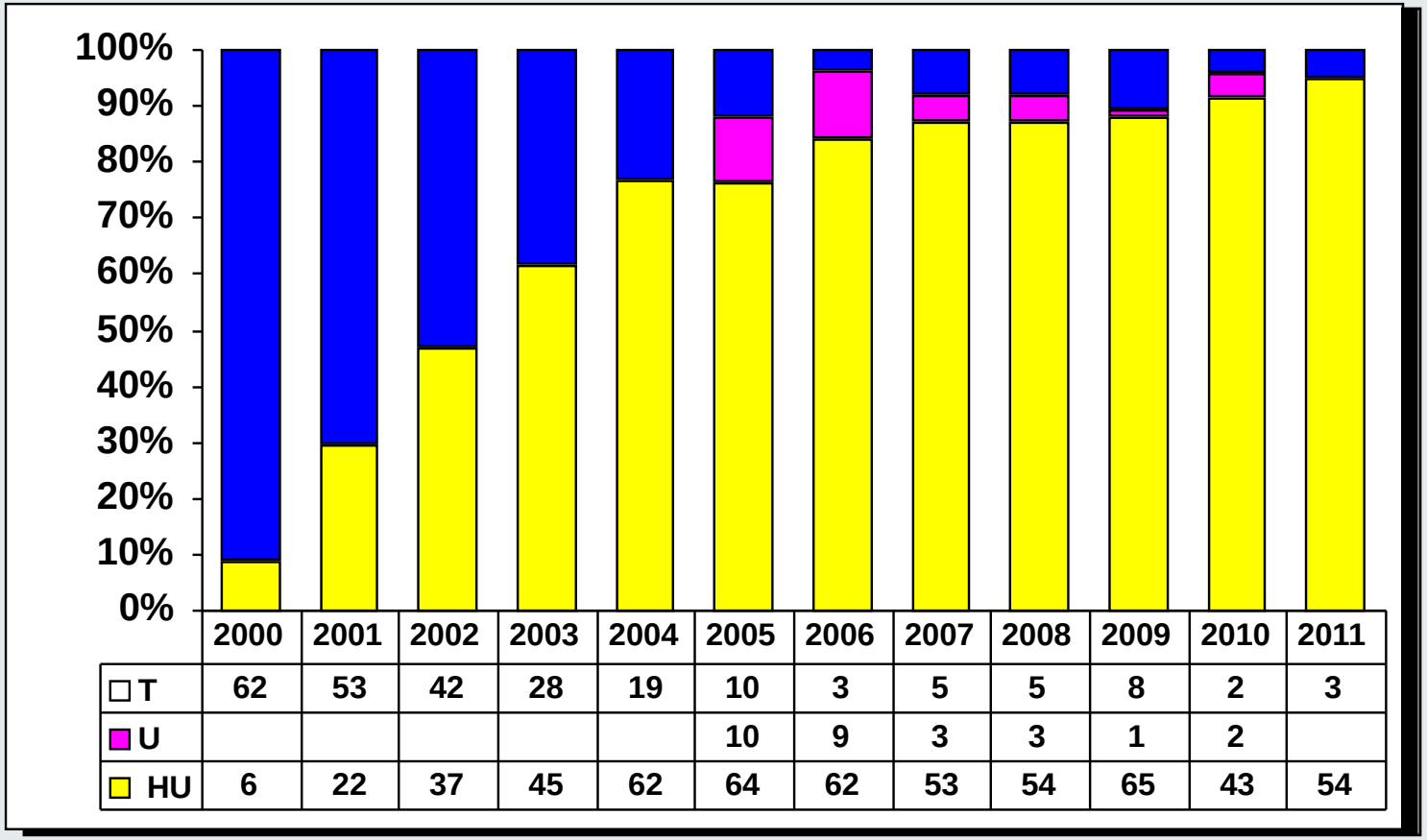
J Heart Lung Transplant. 2011 Oct; 30 (10): 1071-1132

Less organs – more listings result in growing waiting lists for HTx



Widening gap

High Urgency Transplantation exceeds elective Transplantation



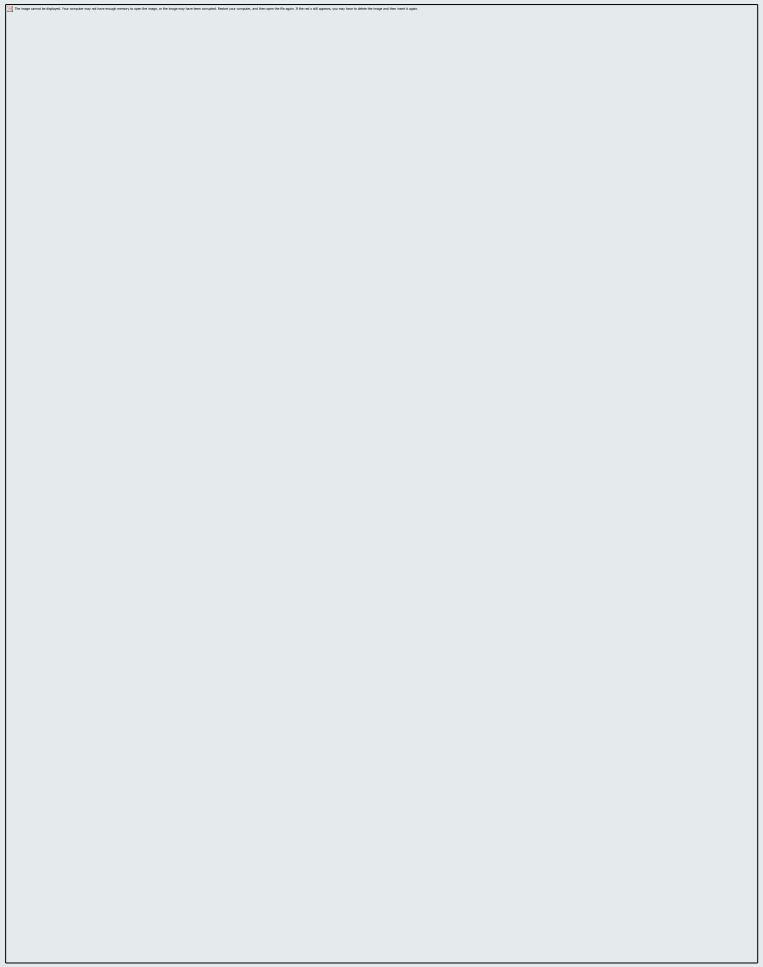
	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
T	62	53	42	28	19	10	3	5	5	8	2	3
U						10	9	3	3	1	2	
HU	6	22	37	45	62	64	62	53	54	65	43	54

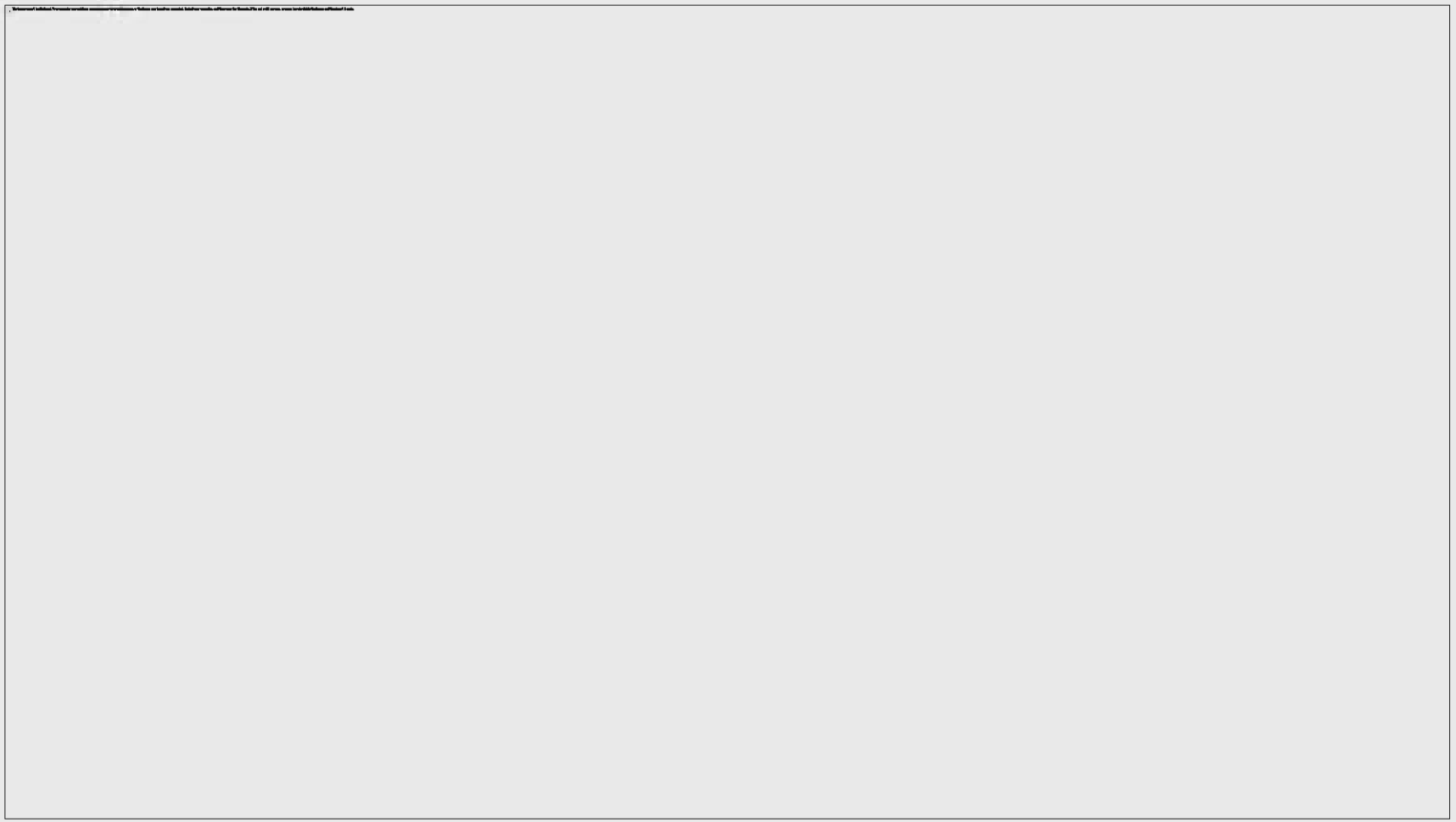
Courtesy J. Gummert, Bad Oyenhausen

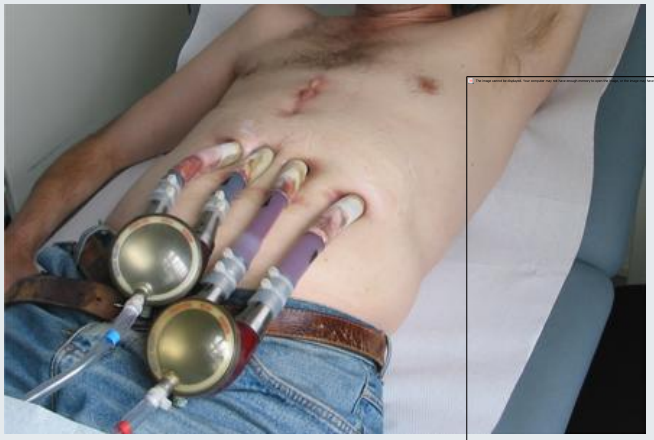
HTx issues – MCS a solution?

- Organ shortage
- In some countries already 90% of transplants are HU
  - worse outcomes, no hearts for elective patients
- Short-term support for BTT no realistic option for many patients
- BTT effectively means DT in many cases
- MCS an alternative to HTx?

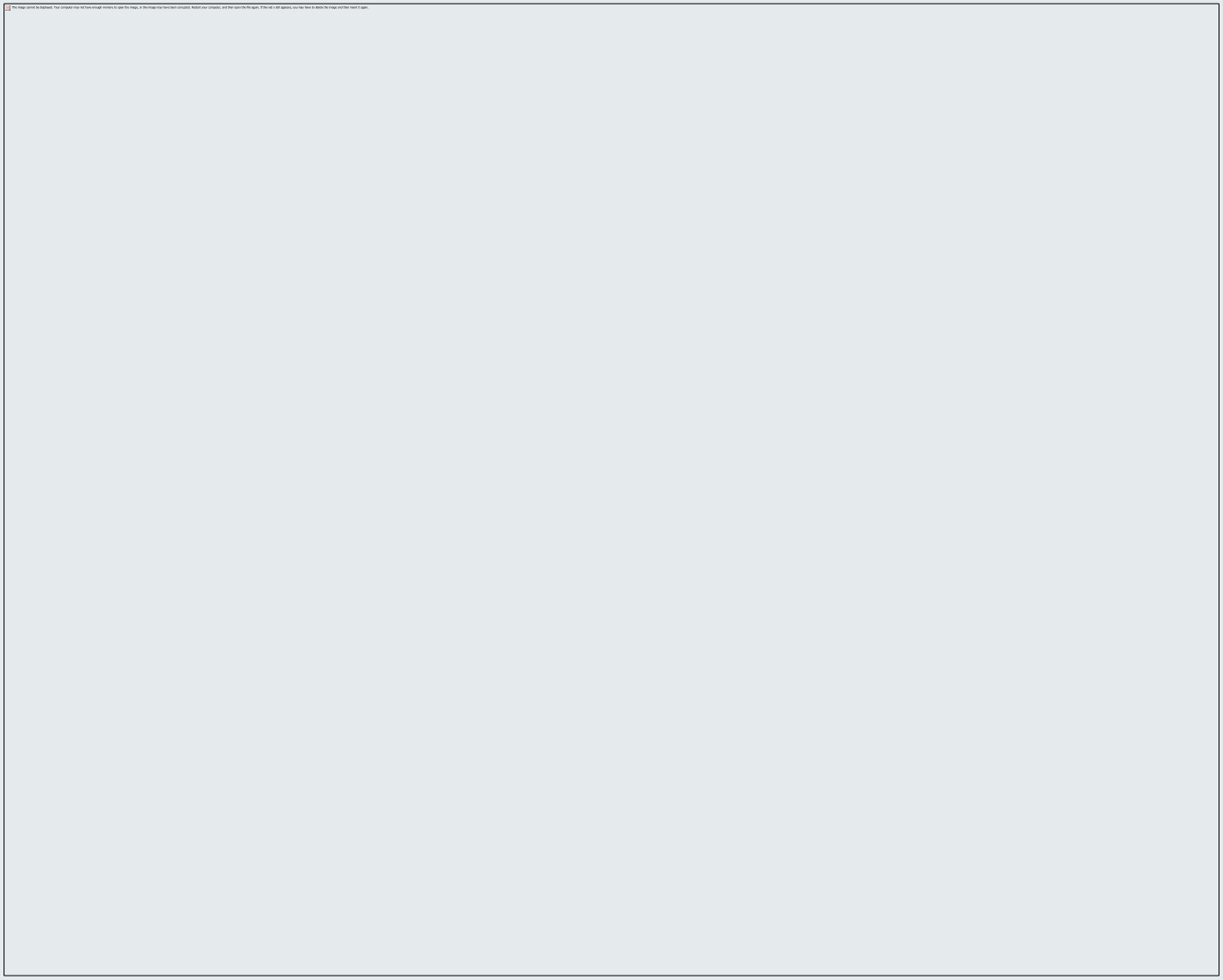
First generation pulsatile devices







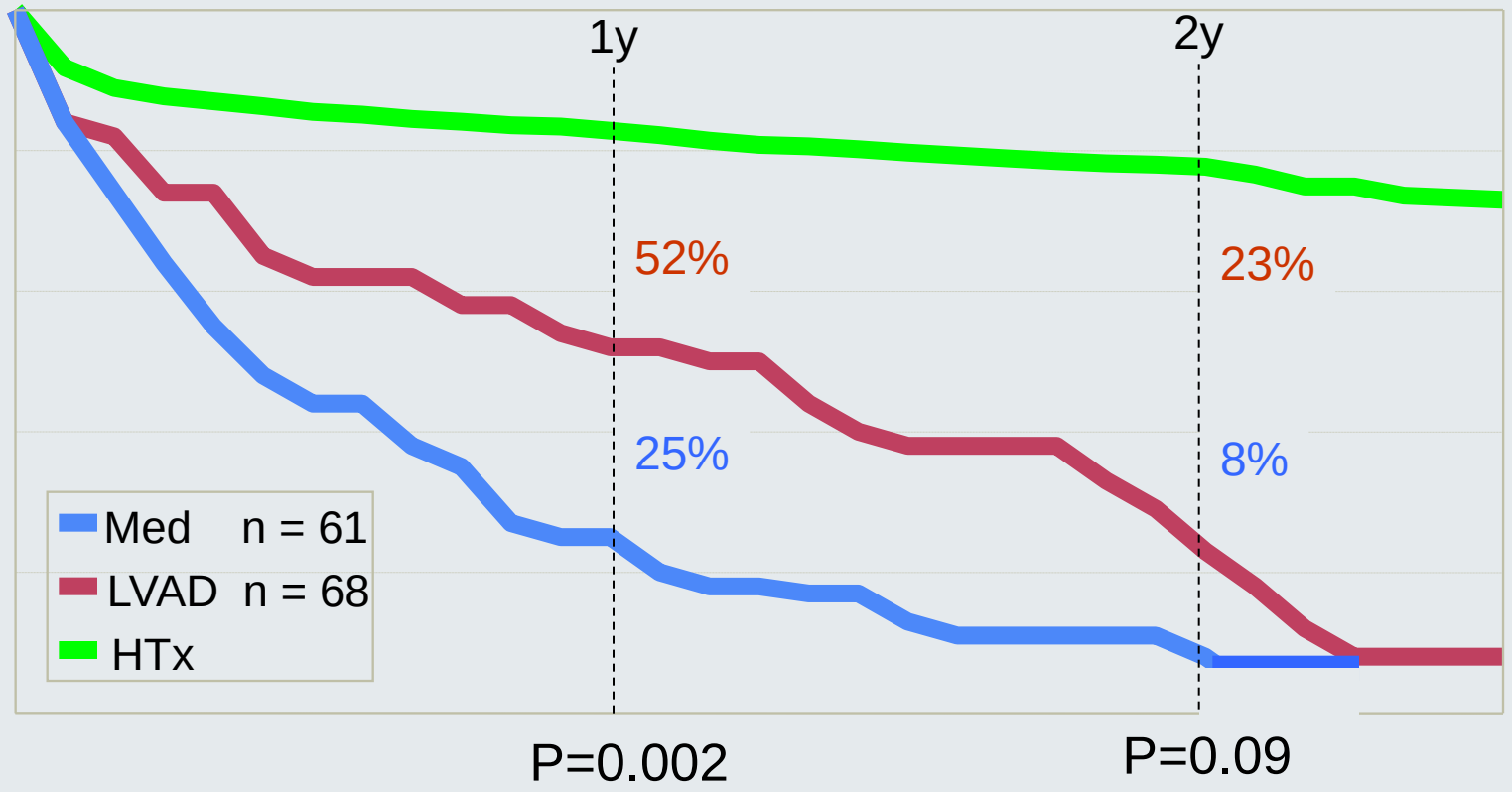
Züricher Patienten mit Berlin Heart



Courtesy E. Henning DHZB

REMATCH-Trial (Heartmate I)

129 pts. randomized to LVAD (68) or medical therapy (61)
1998 – 2001; all pts. NYHA 4 non eligible for HTx



Rose NEJM 2001

REMATCH
Complications (n/Patient - year)

	Contr.	LVAD	Rate Ratio
all	2.75	6.45	2.35
Bleeding	0.06	0.56	9.47
Neurologic dysfunction	0.09	0.39	4.35
Supraventricular Arrhythmia	0.03	0.12	3.92
Peripheral emboli	0.06	0.14	2.29
Sepsis	0.30	0.60	2.03
Local infection	0.24	0.39	1.63
Cardiac arrest	0.18	0.12	0.65
Myocardial infarct	0.03	0.02	0.65
Ventricular arrhythmia	0.56	0.25	0.45

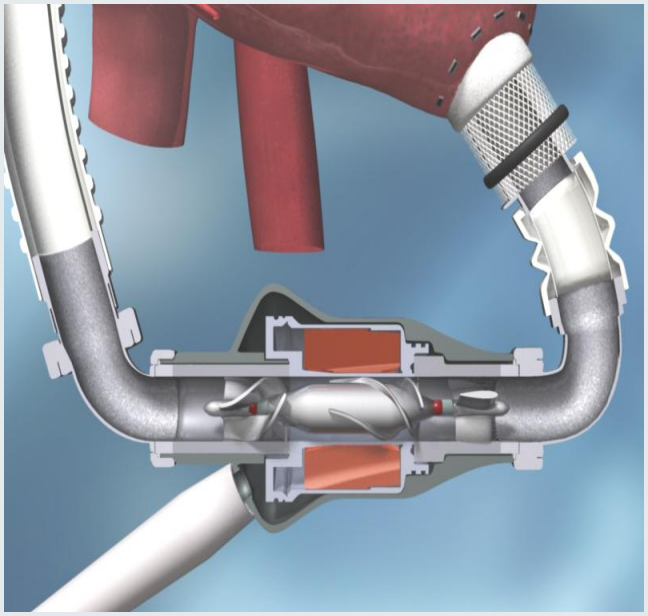
Complications

- Mechanical wear
- Valve dysfunction
- Thrombembolic complications

Non pulsatile Devices

Advantages

- No valves
- No membranes
- Smaller housing
- Less moving parts
- Ease of implant

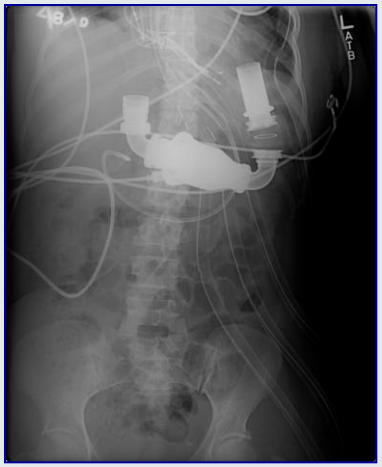


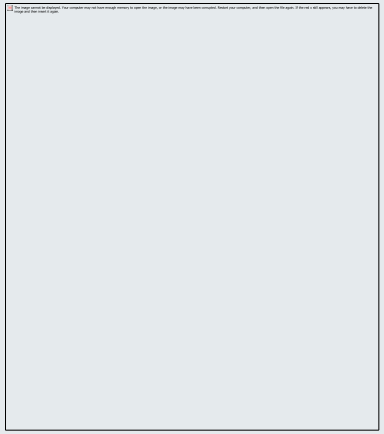
Disadvantages

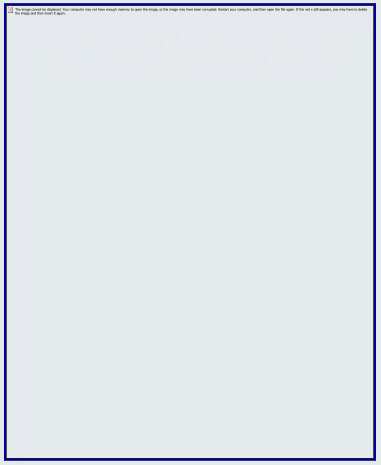
- Non pulsatile ?
- AI in pump failure
- Afterload dependent

Improved patient comfort

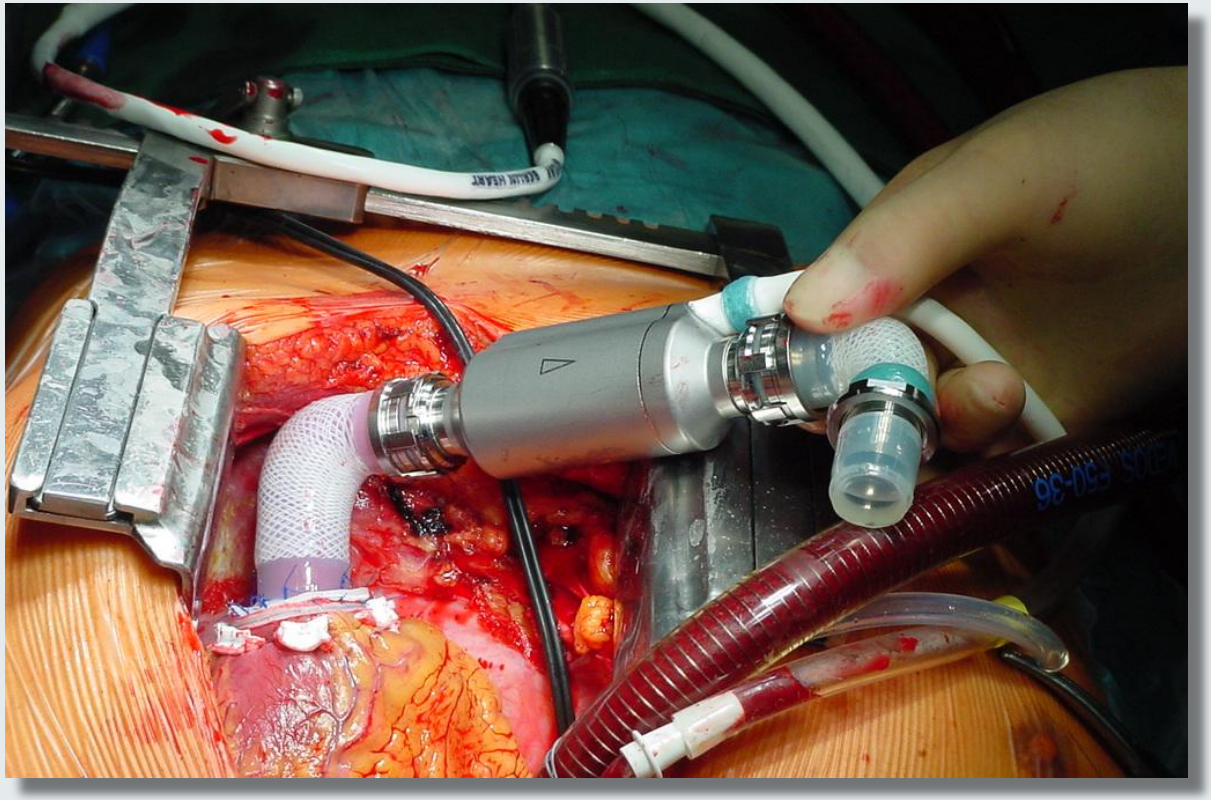
- Less Trauma
- Less noise
- Smaller
- Longer battery charge



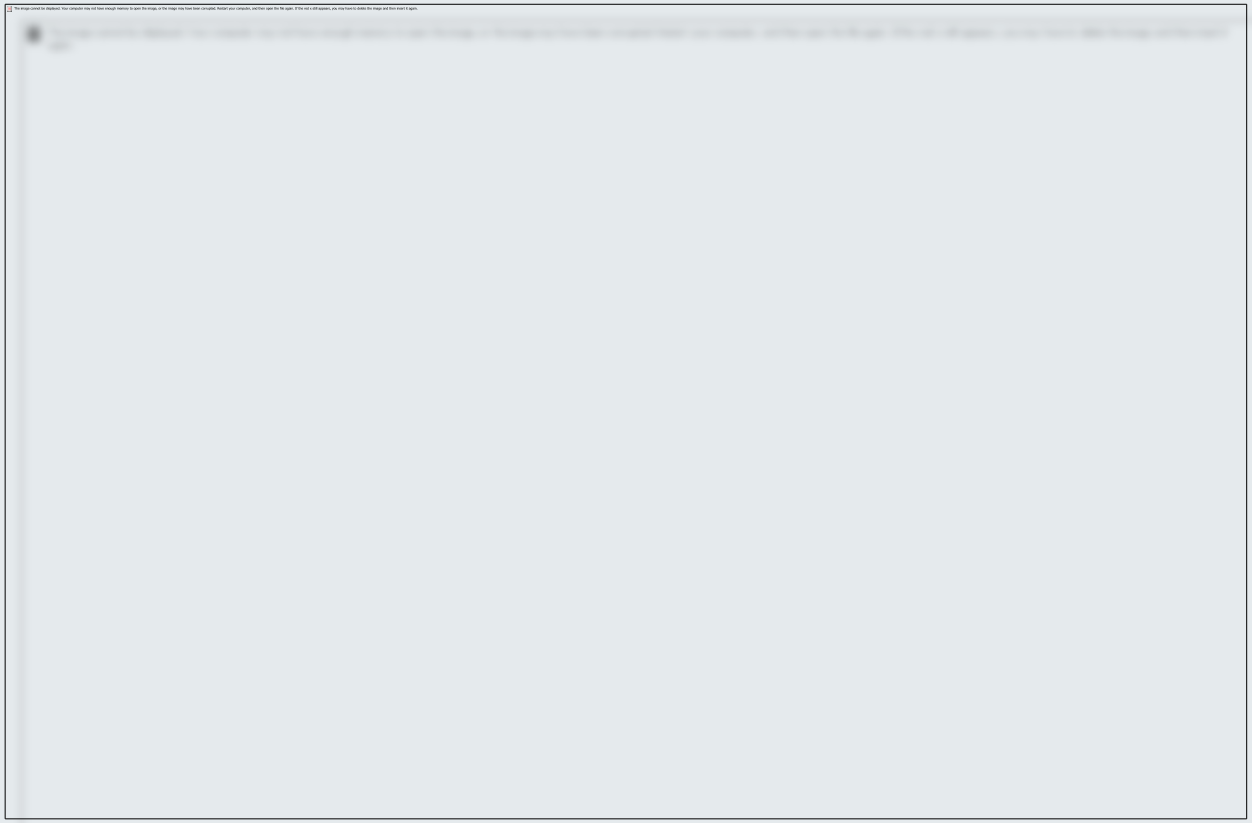




Inflow- Canula and LVAD

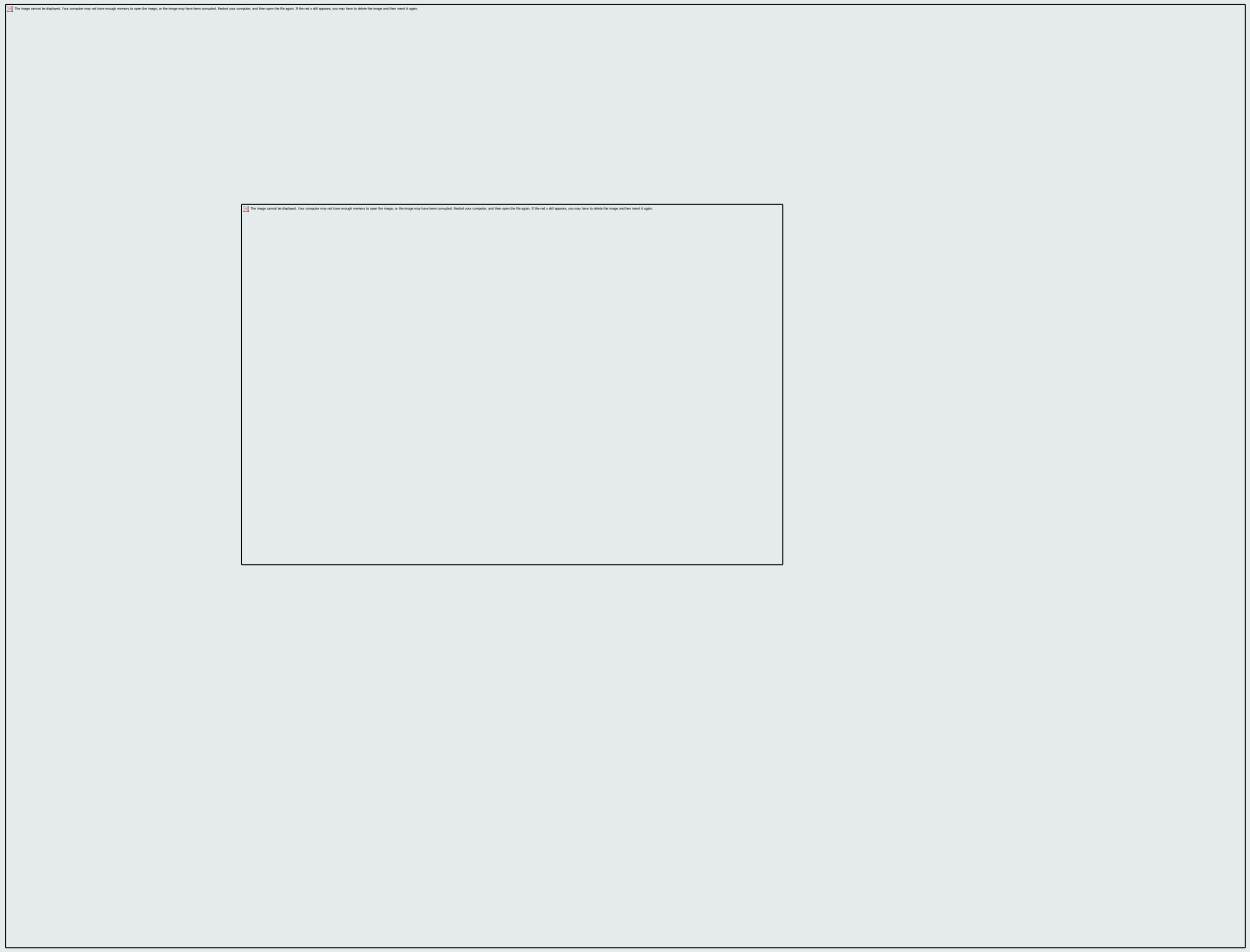


Implanted LVAD



Heartmate II vs. Heartmate I – Adverse Events

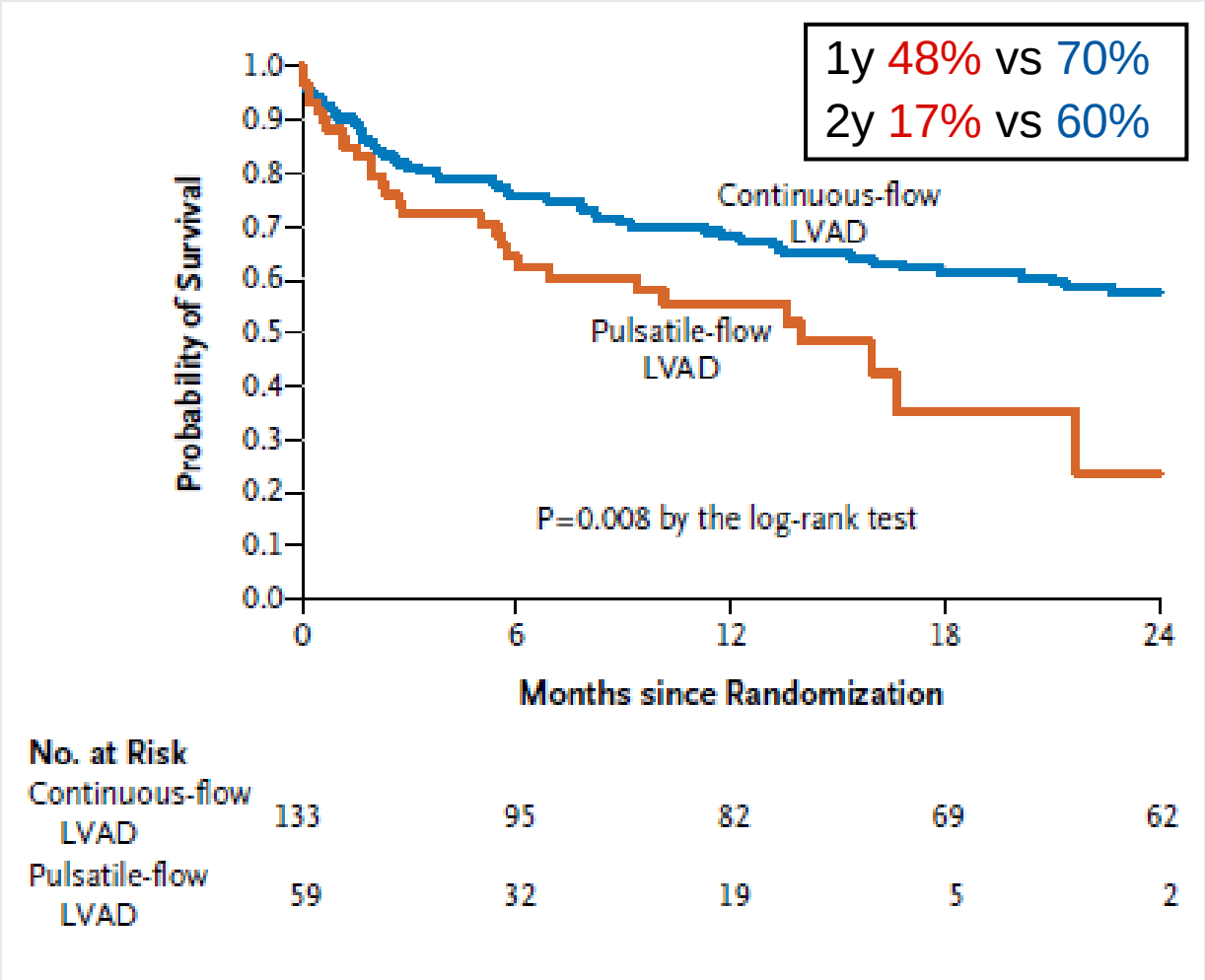
(US – Multicenter trial – Chronic Implant)



Slaughter NEJM 2010

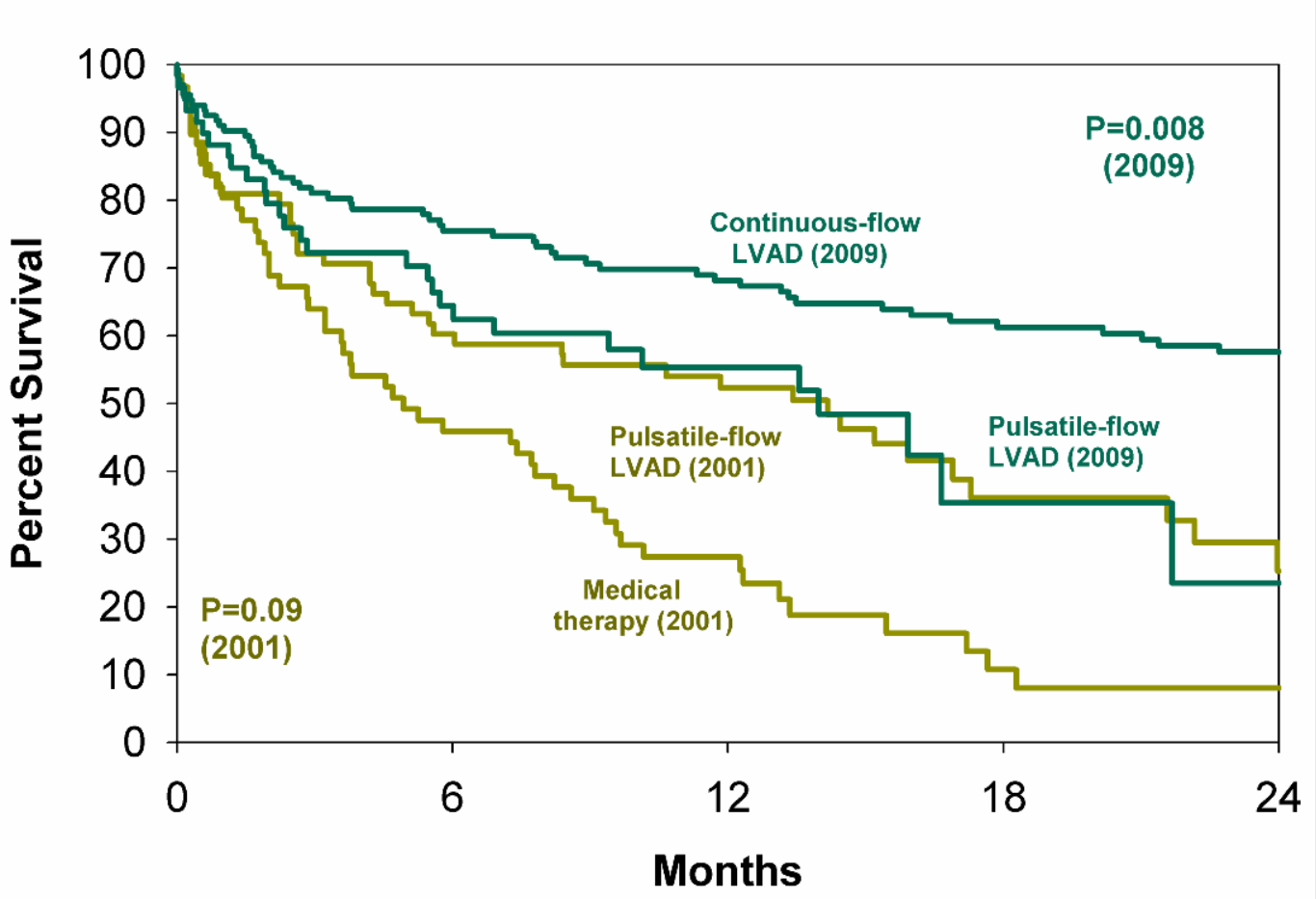
Heartmate II vs. Heartmate I - Survival

(US – Multicenter trial – Chronic Implant)



Slaughter NEJM 2010

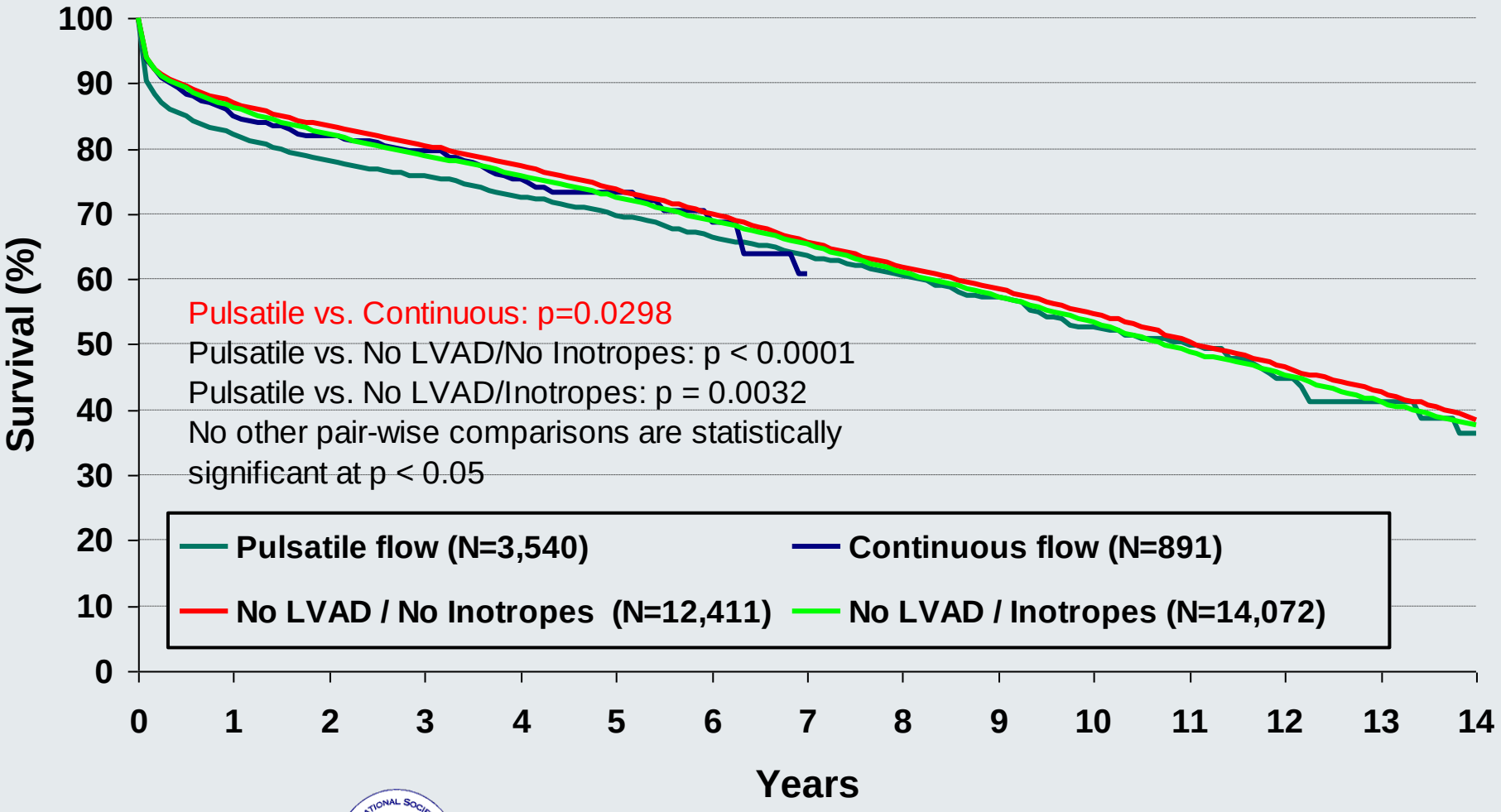
Improving Survival in DT trials



N Engl J Med 2009;361:2282-85

ADULT HEART TRANSPLANTATION

Kaplan-Meier Survival by VAD usage (Transplants: 4/1994-6/2009)



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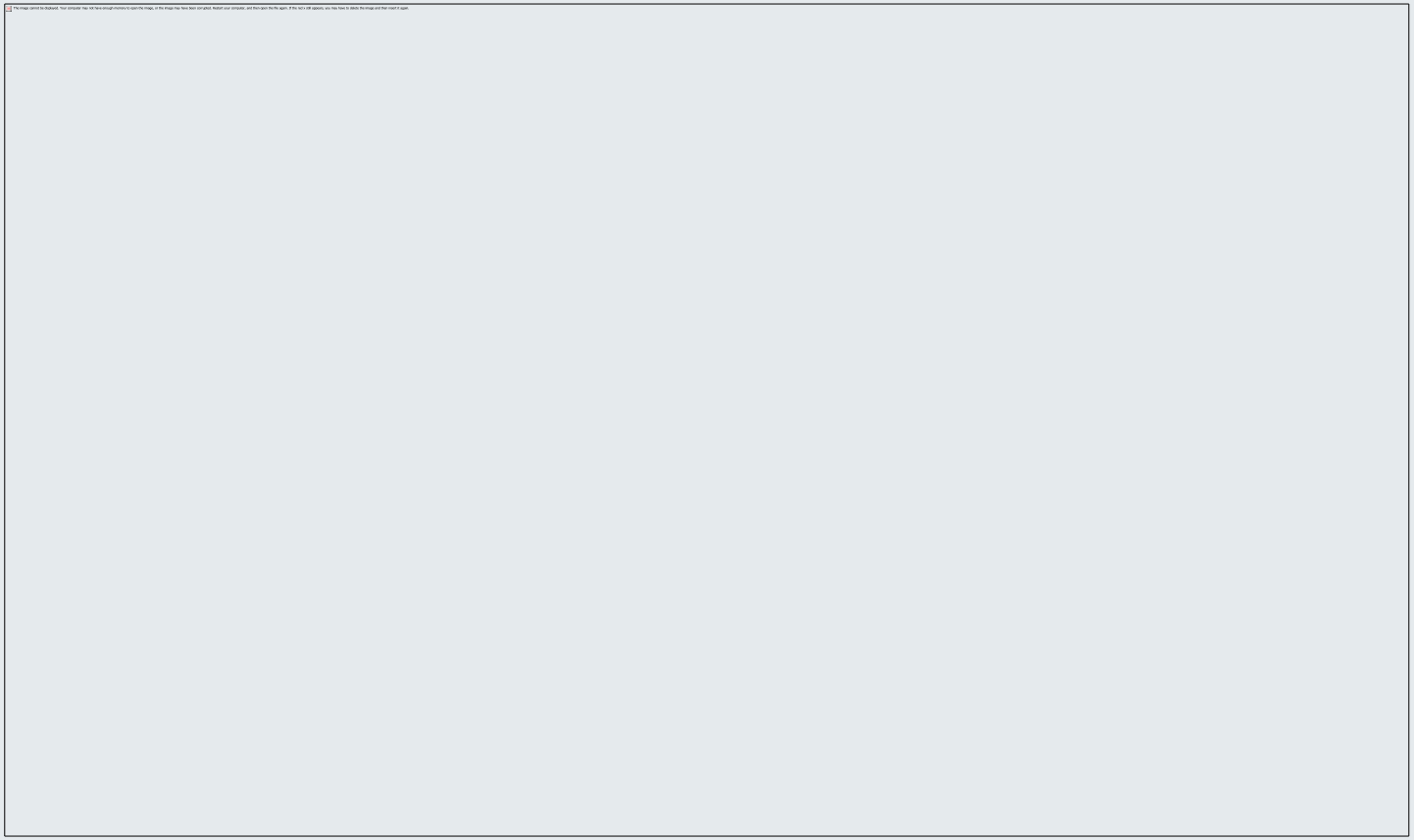
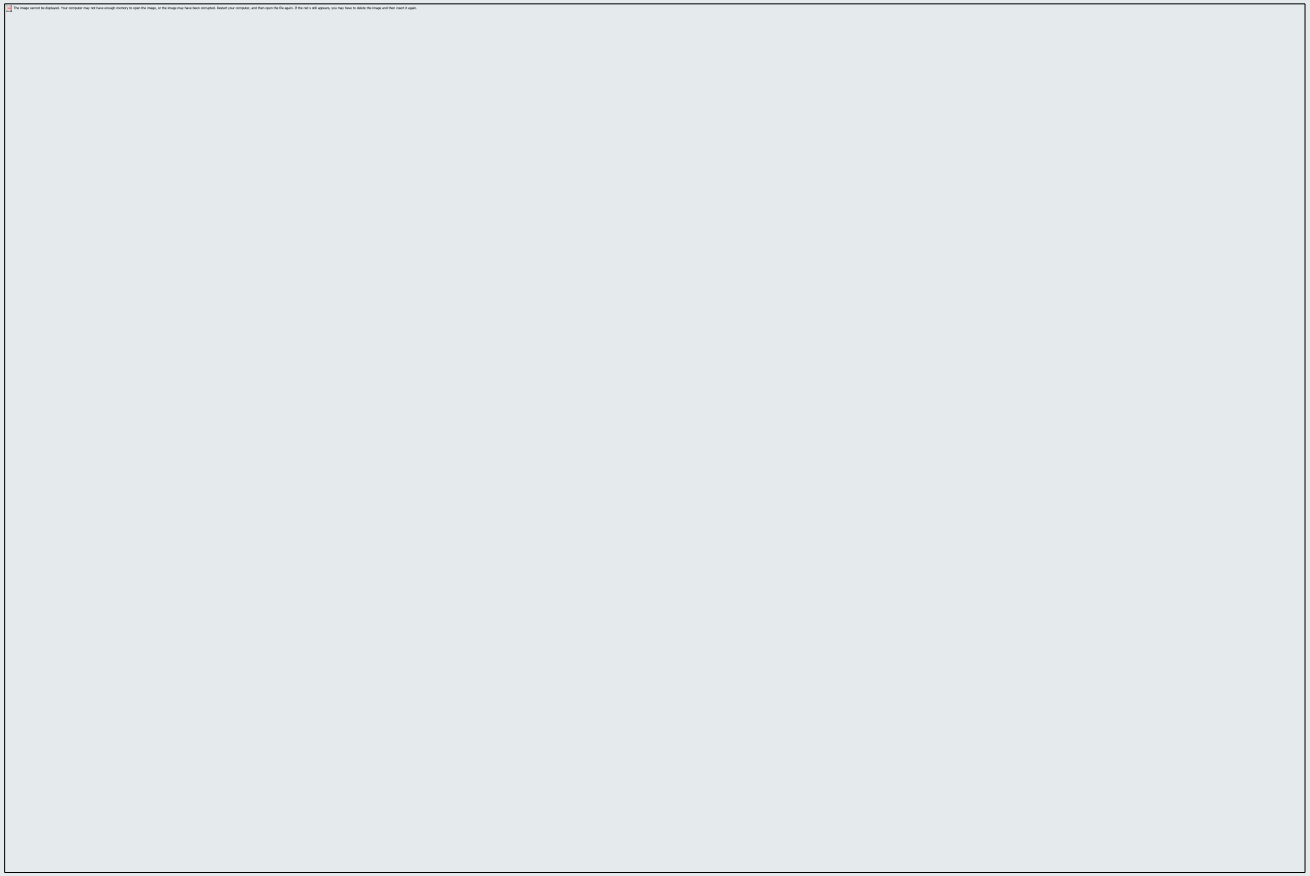
Rapid growth in LVAD therapy



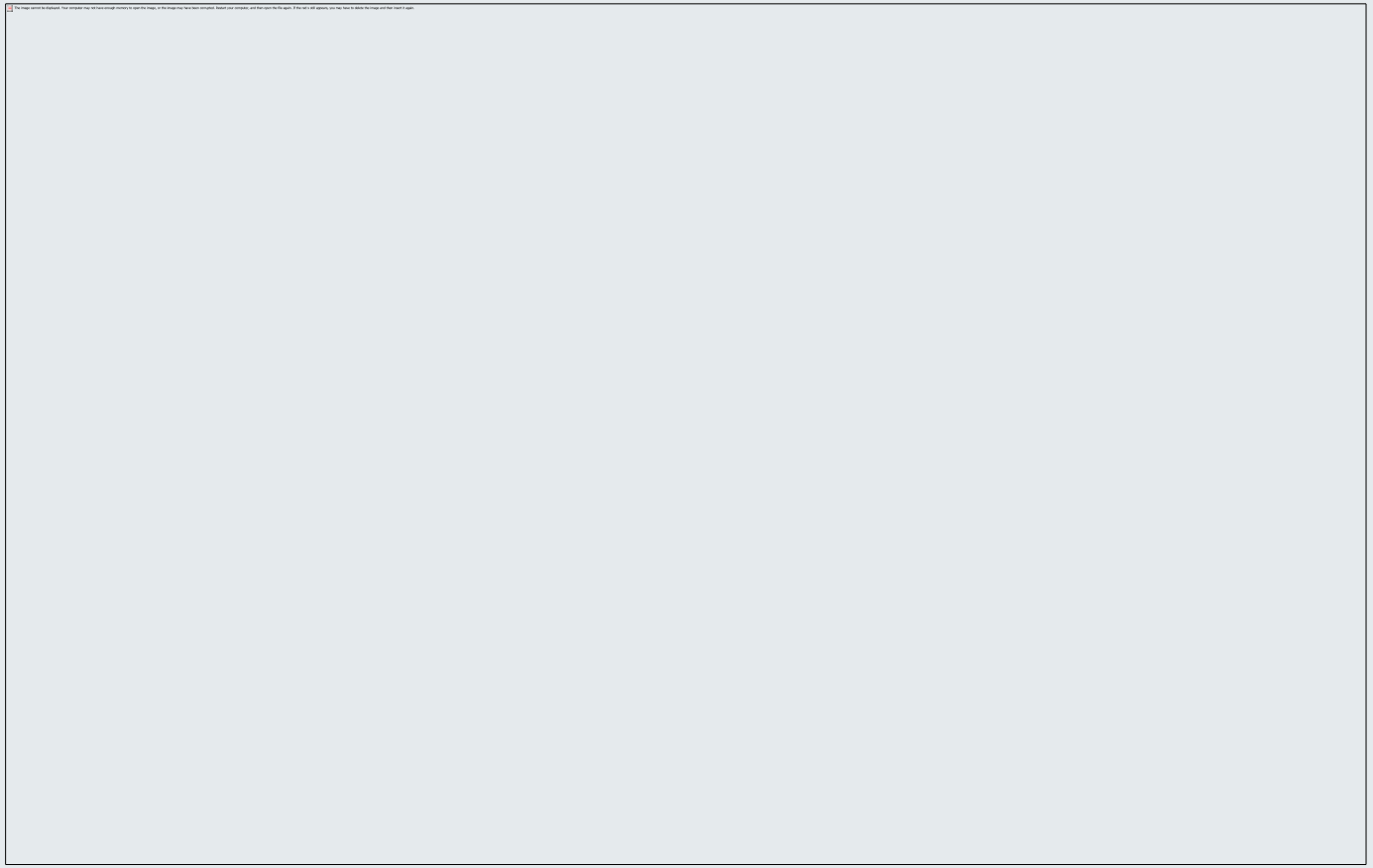
Kirklin JK 4th Intermacs report JHLT 2012

The rise of continuous flow pumps



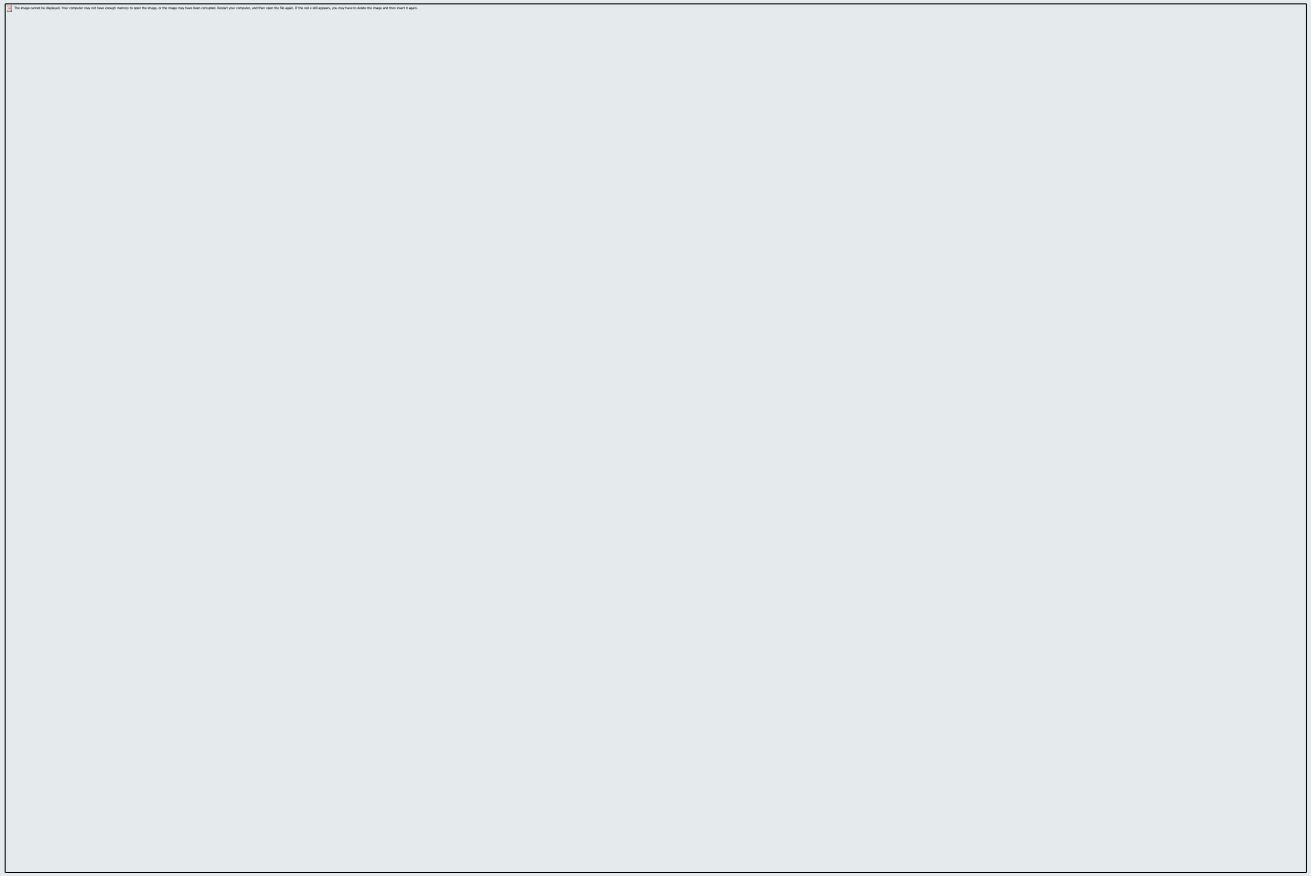
Kirklin JK 4th Intermacs report JHLT 2012

Increase of LVAD vs BVAD support



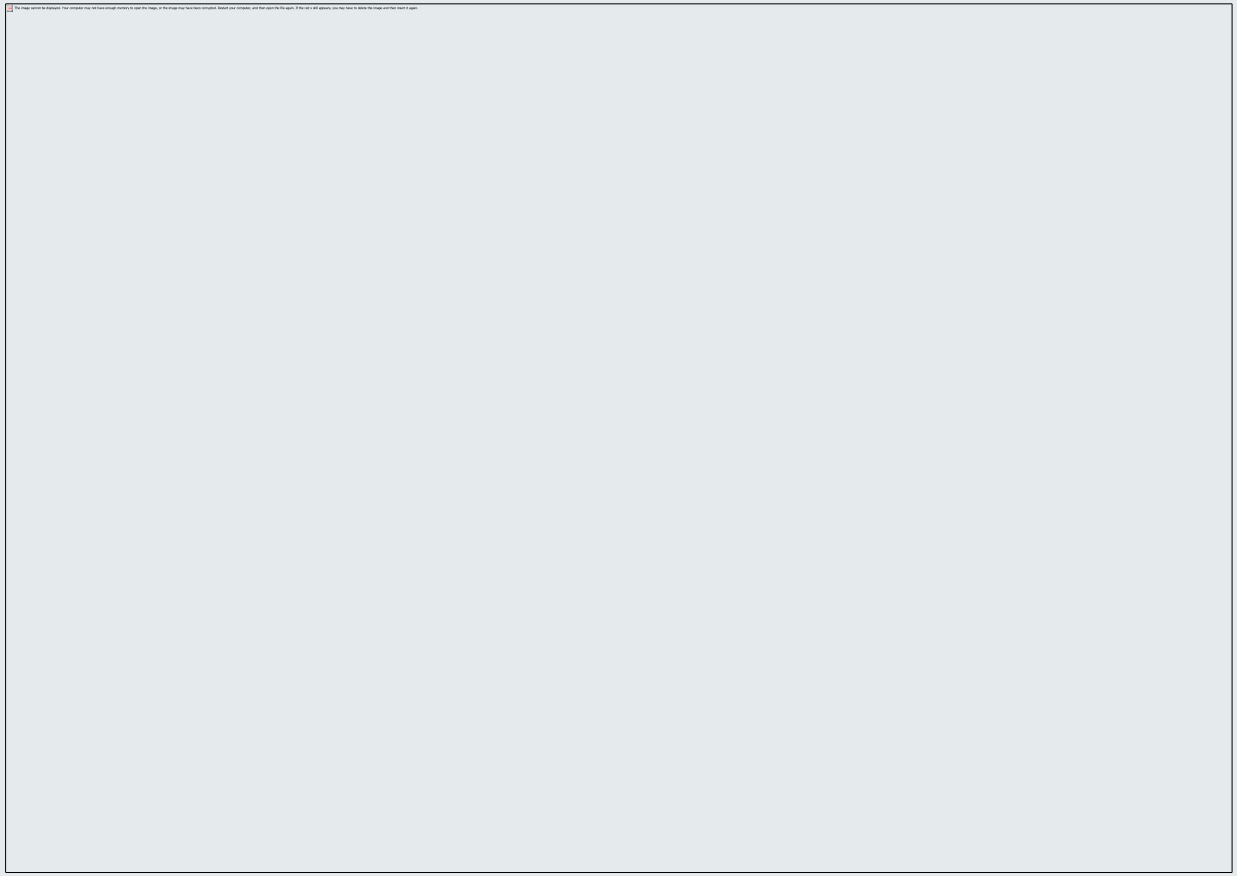
Kirklin JK 4th Intermacs report JHLT 2012

Improved Survival by Implantation period



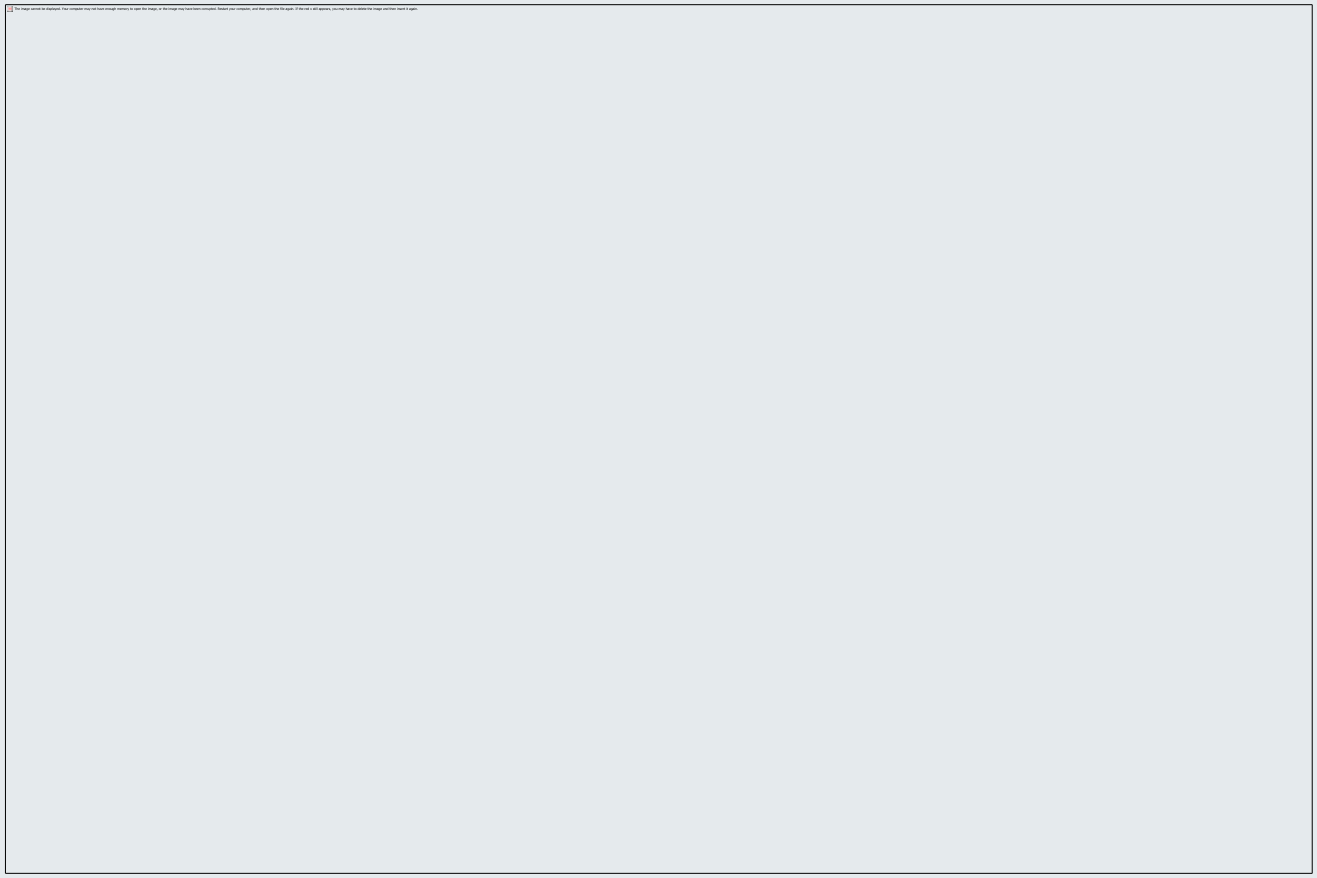
Kirklin JK 4th Intermacs report JHLT 2012

Improved Survival with Continuous Flow Pumps



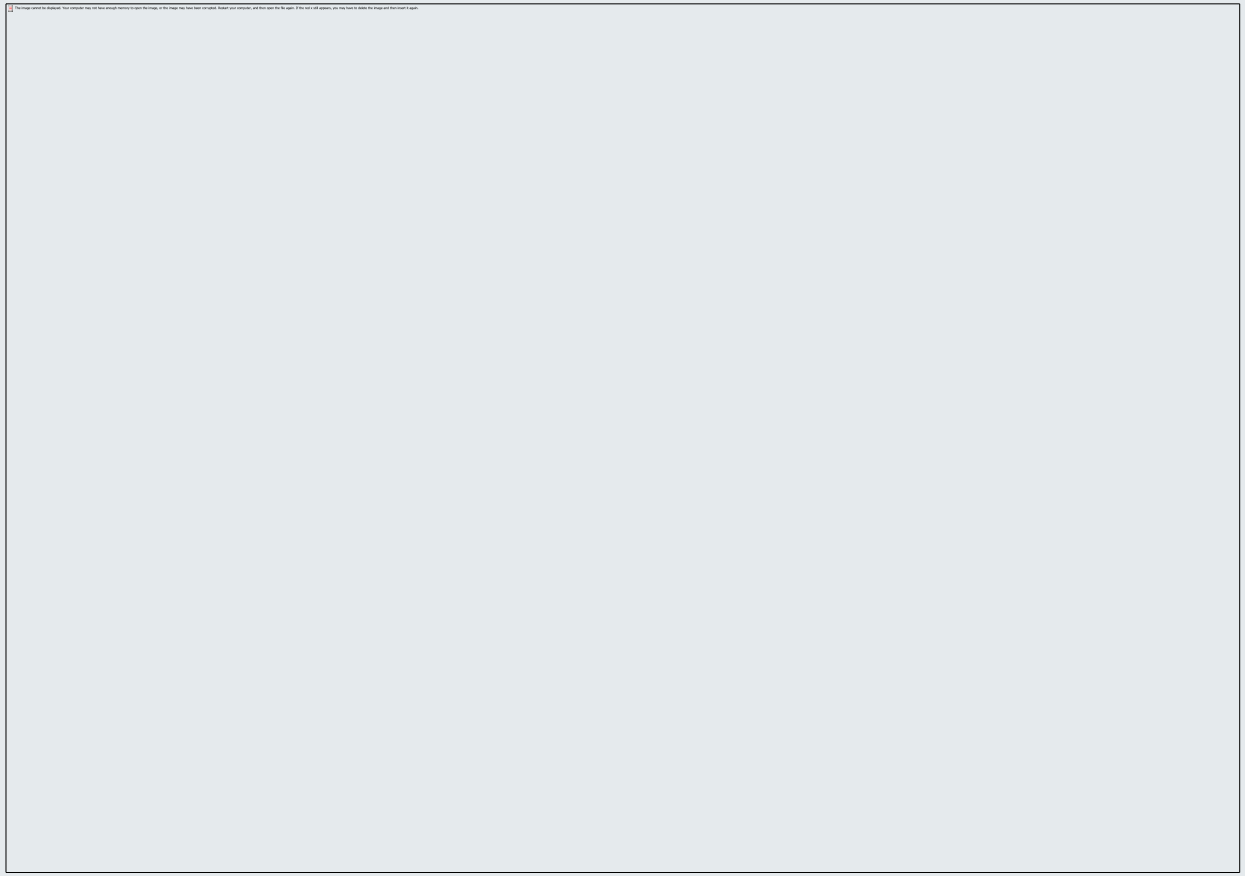
Kirklin JK 4th Intermacs report JHLT 2012

Bridge to Candidacy with CF Devices



Kirklin JK 4th Intermacs report JHLT 2012

Destination Therapy with CF Devices



Kirklin JK 4th Intermacs report JHLT 2012

Outcomes of DT according to preoperative risk

INTERMACS Data 6/2006-3/2011 from 106 US institutions

Identification of risk factors for increased mortality (p<0.05)

- Older age
- Larger BMI
- Diabetes
- History of CABG
- INTERMACS level I / cardiogenic shock
- Lower sodium
- Increased bilirubin
- Use of pulsatile flow devices

	continuous	pulsatile	overall
1 year survival	79%	61%	75%
2 year survival	78%	35%	51%

Kirklin JK presented at AATS 2012

DT competitive with HTx in current era

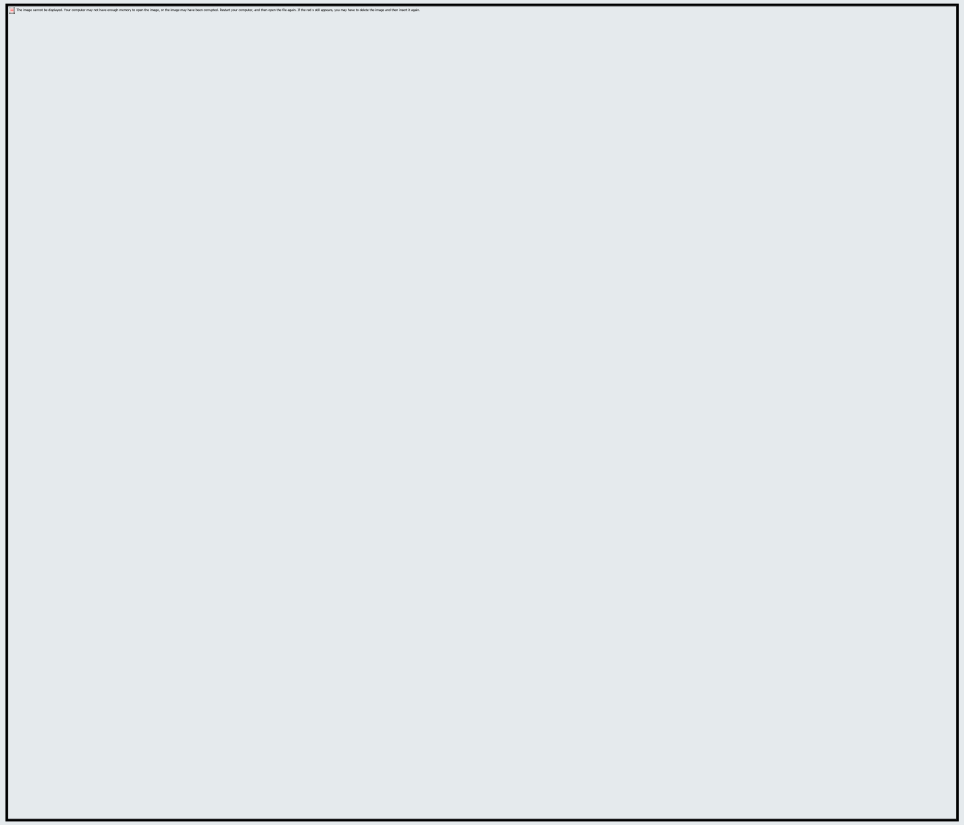
- DT accounts for 33% of implants in recent years
- Risk factors play a major role for survival outcome
  (DT therapy not appropriate for rapidly deterioating patients or patients in shock)
- Mechanical circulatory provides competitive survival to heart transplantation in selected subsets:

  Continuous flow LVAD / no diabetes / no cardiogenic shock / BUN <50

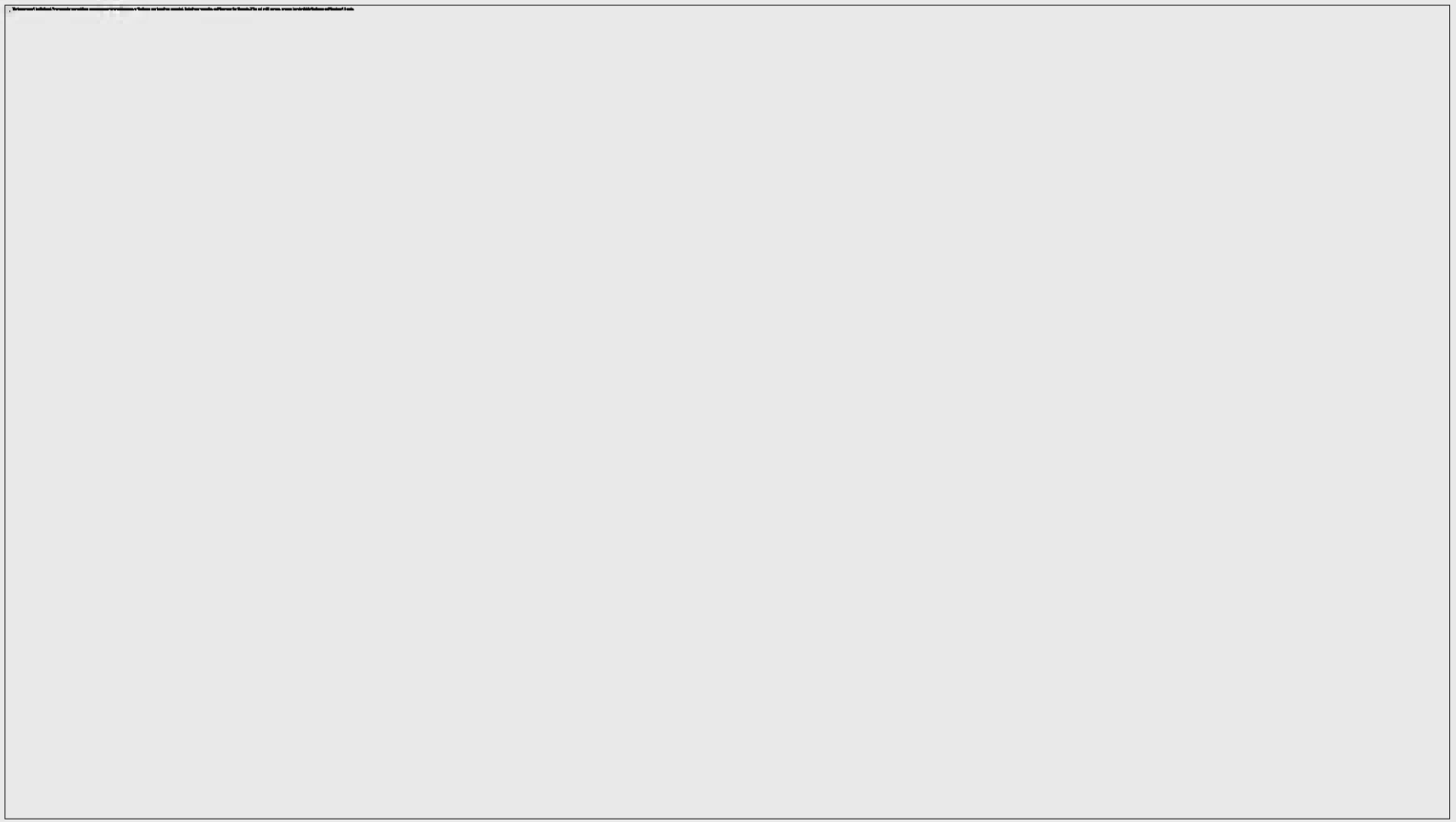
  1 & 2 year survival with LVAD 85%
  comparable to 1 year survival after HTx 85-87%

Kirklin JK presented at AATS 2012

Second generation non pulsatile devices

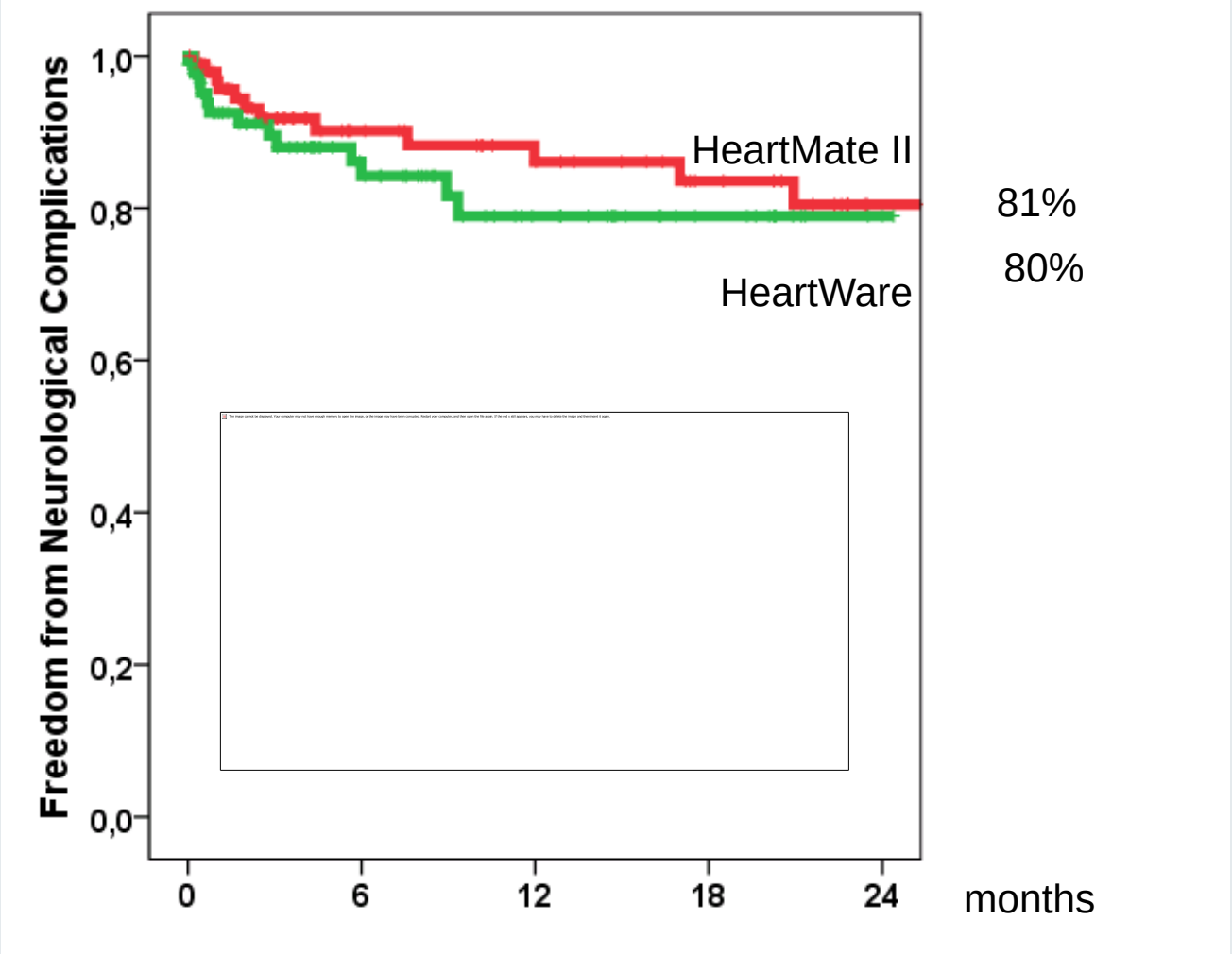


- Simplified Implantation Technique
- Electromagnetic bearing
- Less blood trauma



Freedom from Stroke or (Bleeding or embolic)

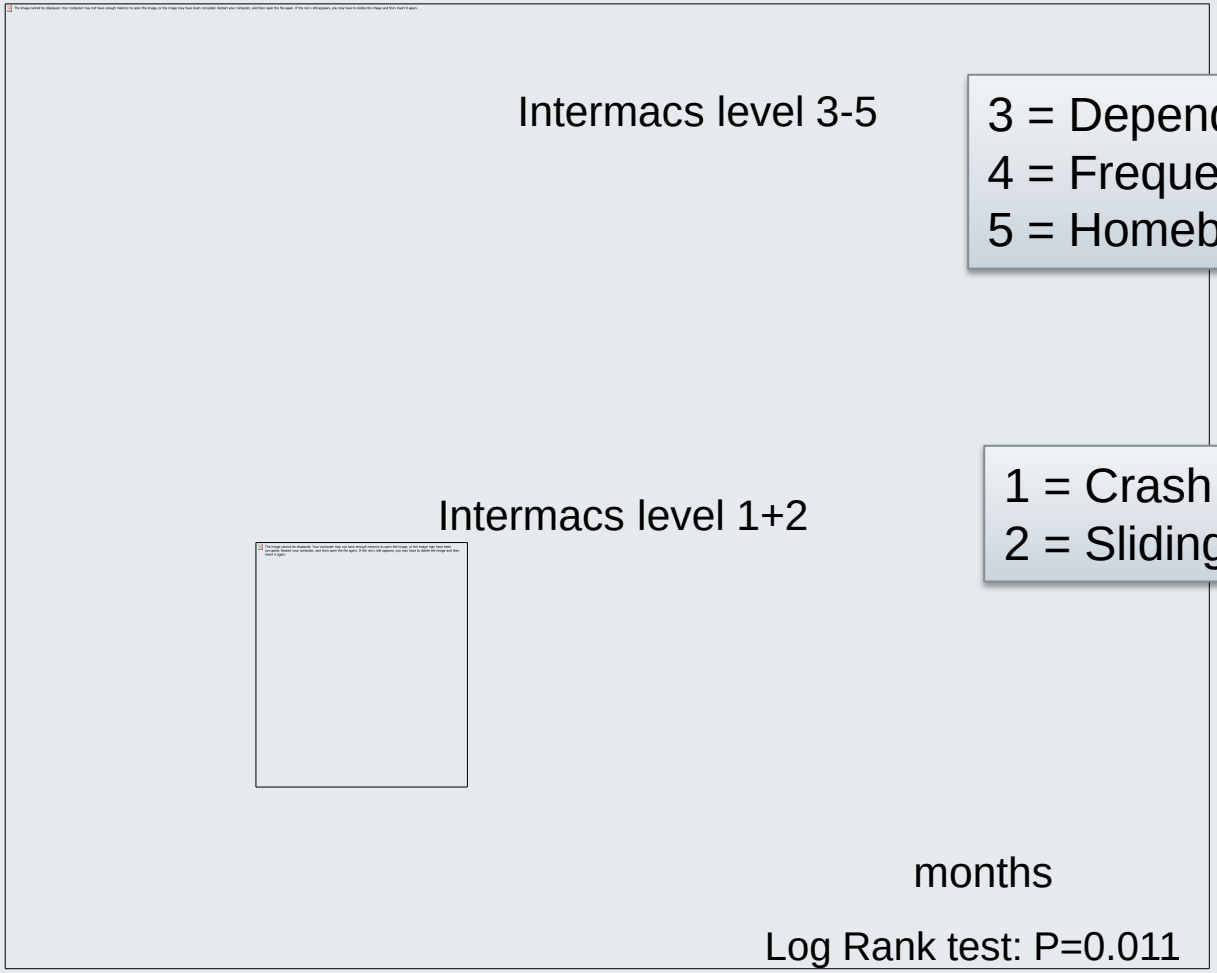
Implantationen Bad Oyenhausen: 9/2006 – 8/2011; n = 187



Courtesy J. Gummert, Bad Oyenhausen

Survival and preoperative Intermacs-Level

Heartware – Implantationen Bad Oyenhausen: Aug. 2009 – Aug. 2011; n = 88



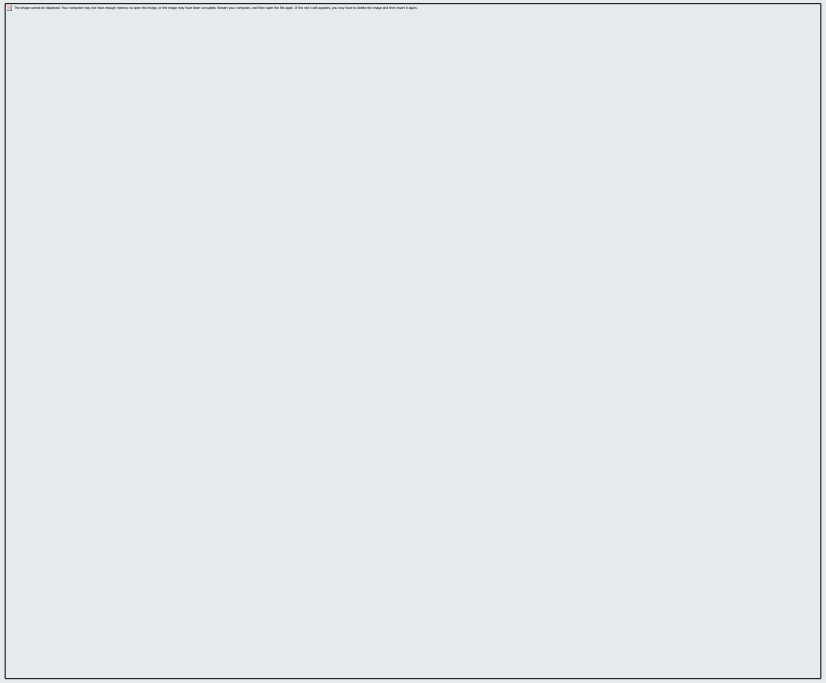
Courtesy J. Gummert, Bad Oyenhausen

New pumps / HeartMate

Project Objectives

- Develop a full-support, blood pump with full magnetic rotor levitation and wide gaps for optimized blood flow
  - **Reduced adverse event profile**
- Incorporate textured surfaces
  - **Potential for reduced or no anticoagulation**
- Capable of producing an artificial pulse
  - Physiologic blood flow with potential to help address late bleeding
- Operate at **lower power consumption**, allowing miniaturization of external components

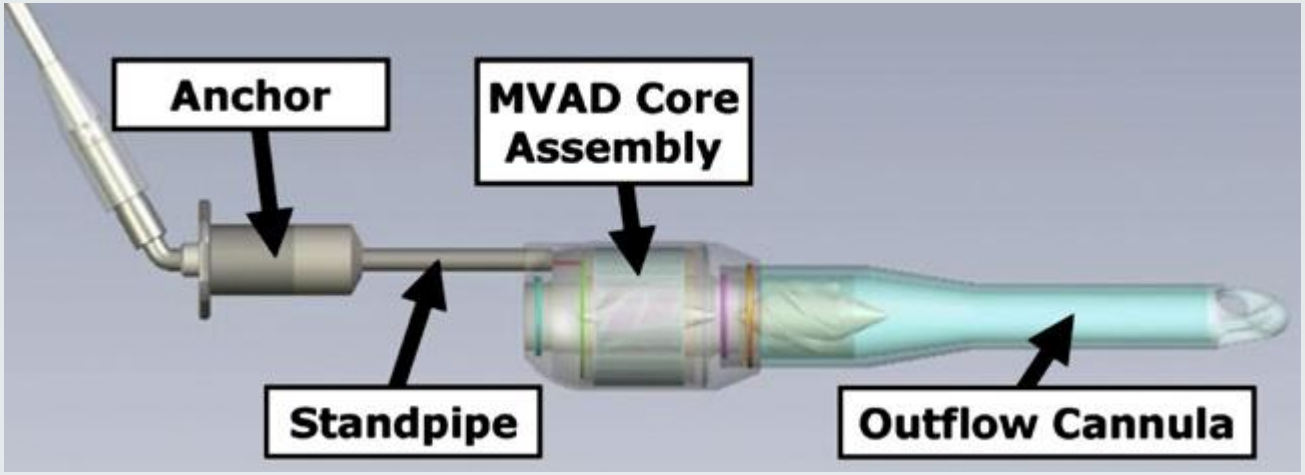
Miniaturized VAD Design / MVAD



Project Objectives

- Three MVADS designs all showing strong results in preclinical studies.
- Wide bladed, axial flow technology allows significant **miniaturization.**
- **Partial or full support** attainable in all designs.
- All versions can **eliminate full sternotomy.**
- Wear-less impeller suspension.
- **Versatile, configurable and scalable.**

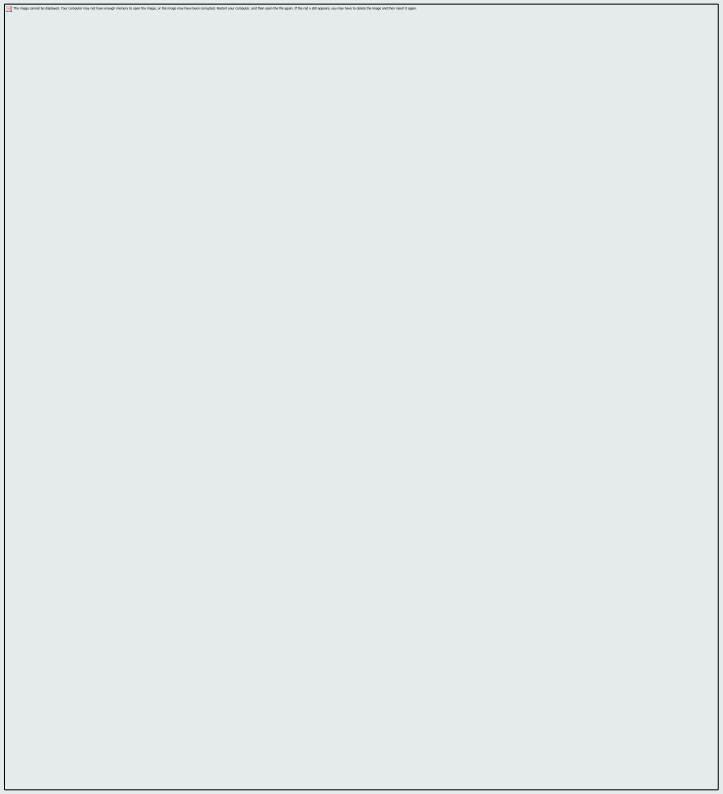
Miniaturized ventricular assist device (MVAD)

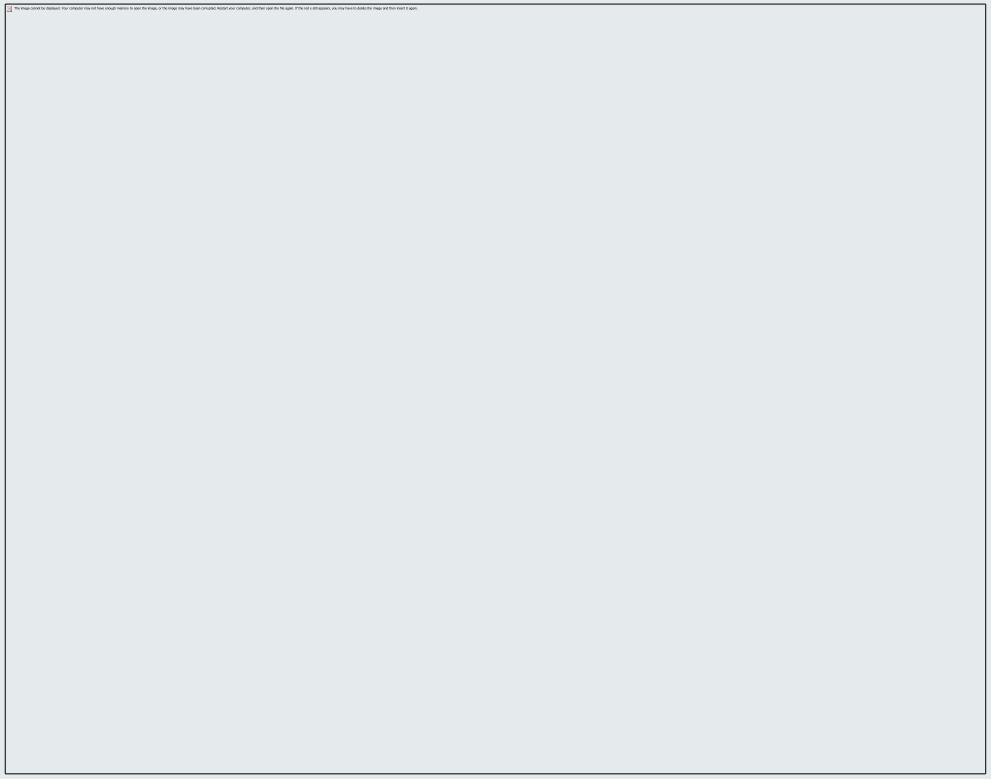


- Continuous axial flow pump
- Transapical implantation, Transaortic outflow
- 10 animals: 100% successful implantation, 100% normal end-organ perfusion, no significant hemolysis, no pump failures, no device-related complications

Slaughter MS JTCVS 2011

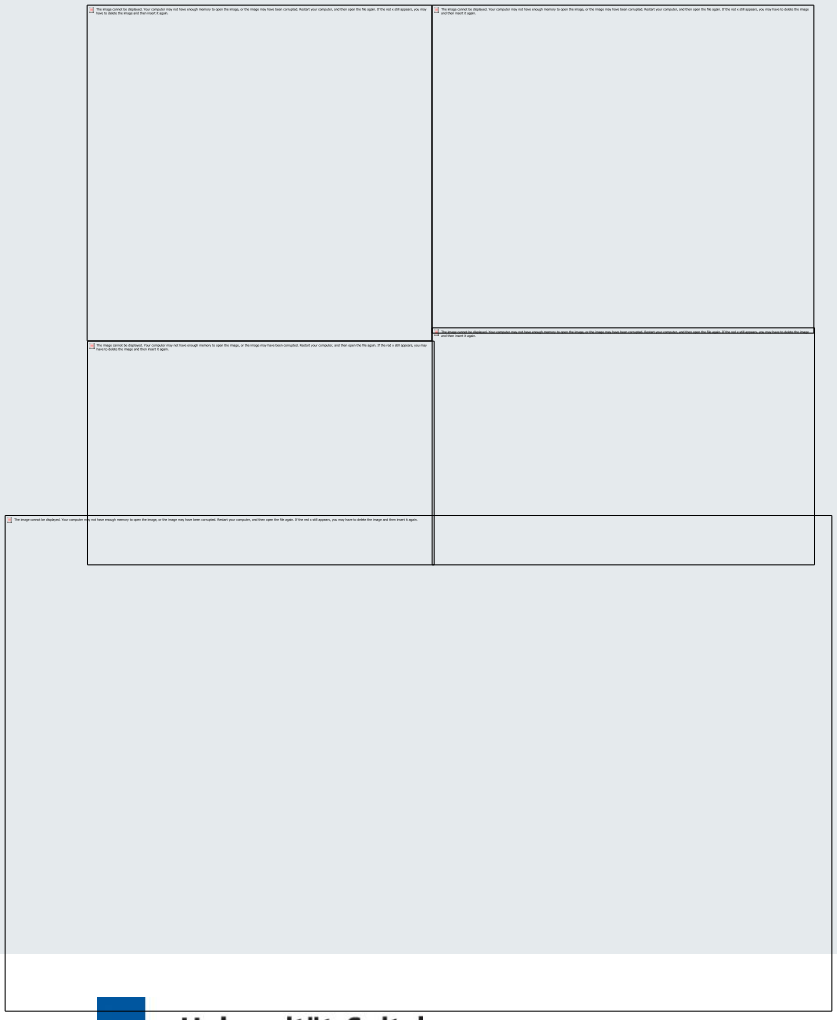
Miniaturized ventricular assist device (MVAD)





Slaughter MS JTCVS 2011

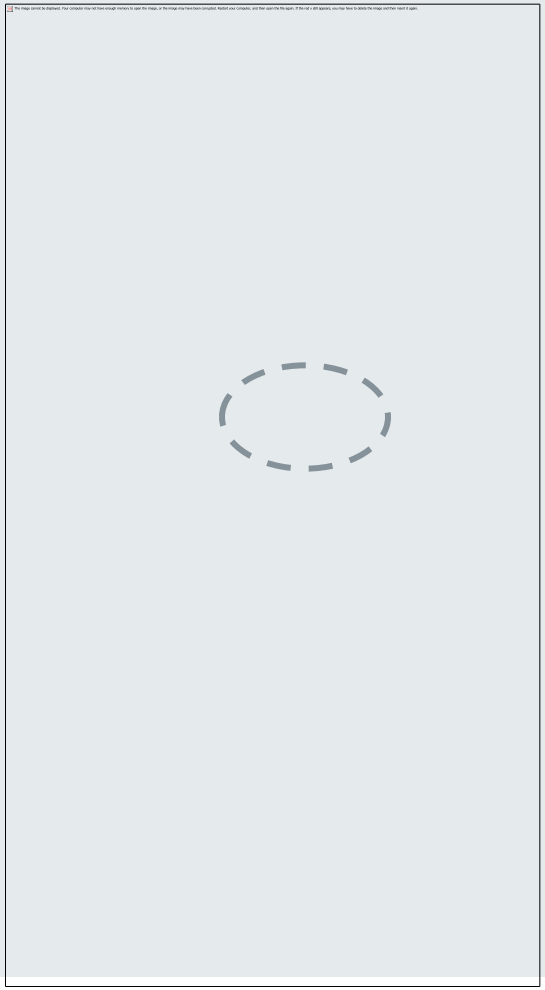
Infection Reduction Technology

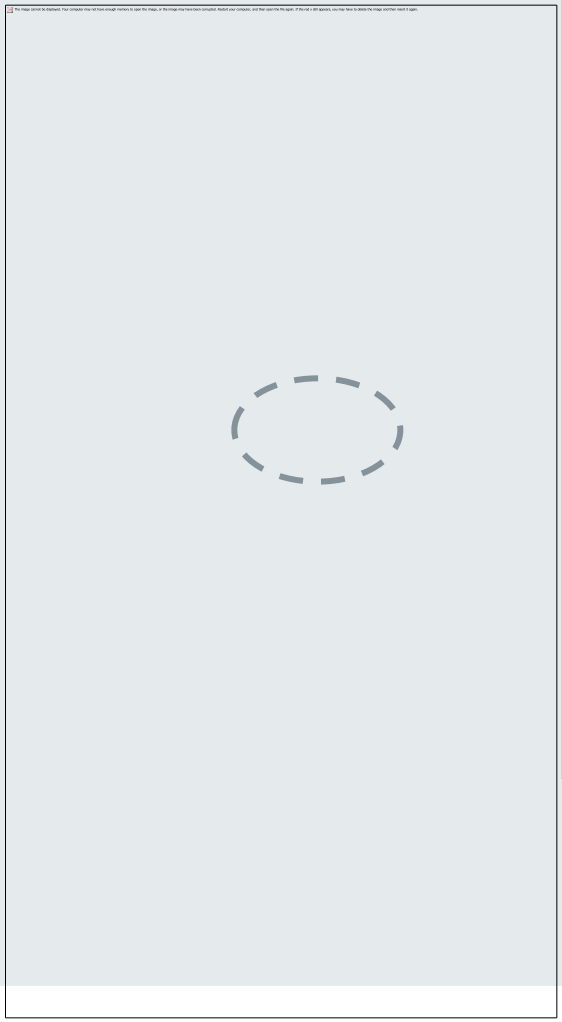


Project Objectives

- Develop stabilization and exit site improvement technologies to significantly **reduce percutaneous lead (driveline) infection.**
- Pursuing device-based internal mechanical stability anchoring technologies
  - Focus on trauma-induced late-onset infection
- Advanced exit site material morphology and chemistry for improved tissue / percutaneous lead interface

Fully-Implantable LVAS (FILVAS)





Project Objectives

- LVAD incorporating **implantable battery and control system** enabling patients to have some duration of **“un-tethered time” without external components.**
- Mitigate the need for a standard **percutaneous “driveline”**, reducing infection.
- Minimize need for external components, enhancing quality of life.

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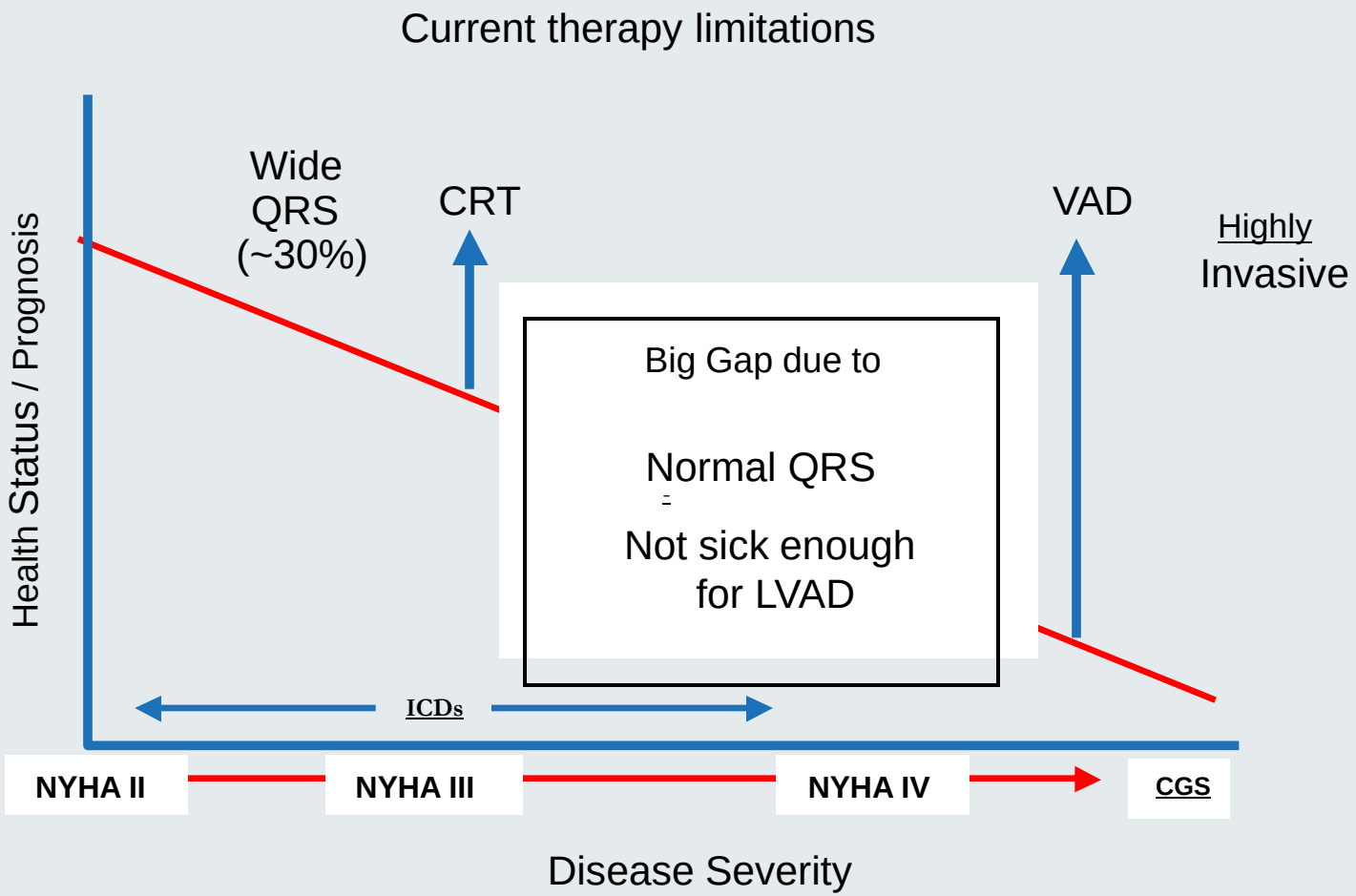
Partial ventricular support
New philosophy and indications

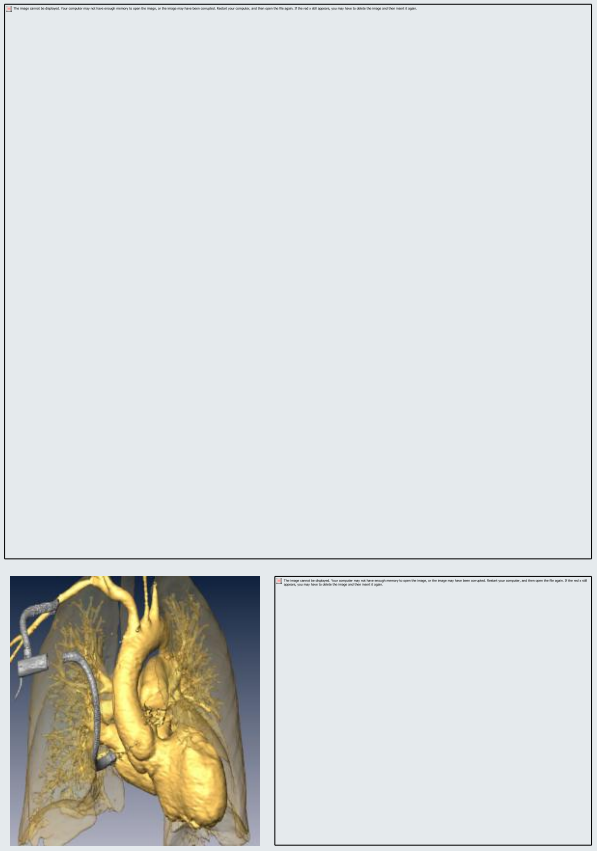


Partial ventricular support (CircuLite)

	CircuLite	Current VADs
Patient	• Class IIIb and early Class IV • Cardiac Output: 2-3L/minute • Ambulatory, **home-bound (INTERMACS Level >4)**	• Late Class IV and Shock • Cardiac Output: 1-2L/minute • Hospitalized, bed-bound
Design	• Partial Support, 2-3L/minute • **Supplements** native function	• Full Support, 5-6L/minute • Replaces native function
Procedure	• **Limited Access** procedure • **Off-pump** mini-thoracotomy	• Urgent, open heart procedure • Sternotomy and bypass

CircuLite – Clinical experience

- 27 pts. awaiting HTx (EF 21±6%)
- Duration of support 6 to 281 days
- significant hemodynamic improvement:
  - increase in CI from 2.0±0.4 to 2.8±0.6 l min^{-1} m^{-2} ($p < 0.001$)
  - reduction in PCWP from 28±6 to 18±7 mm Hg ($p = 0.002$)



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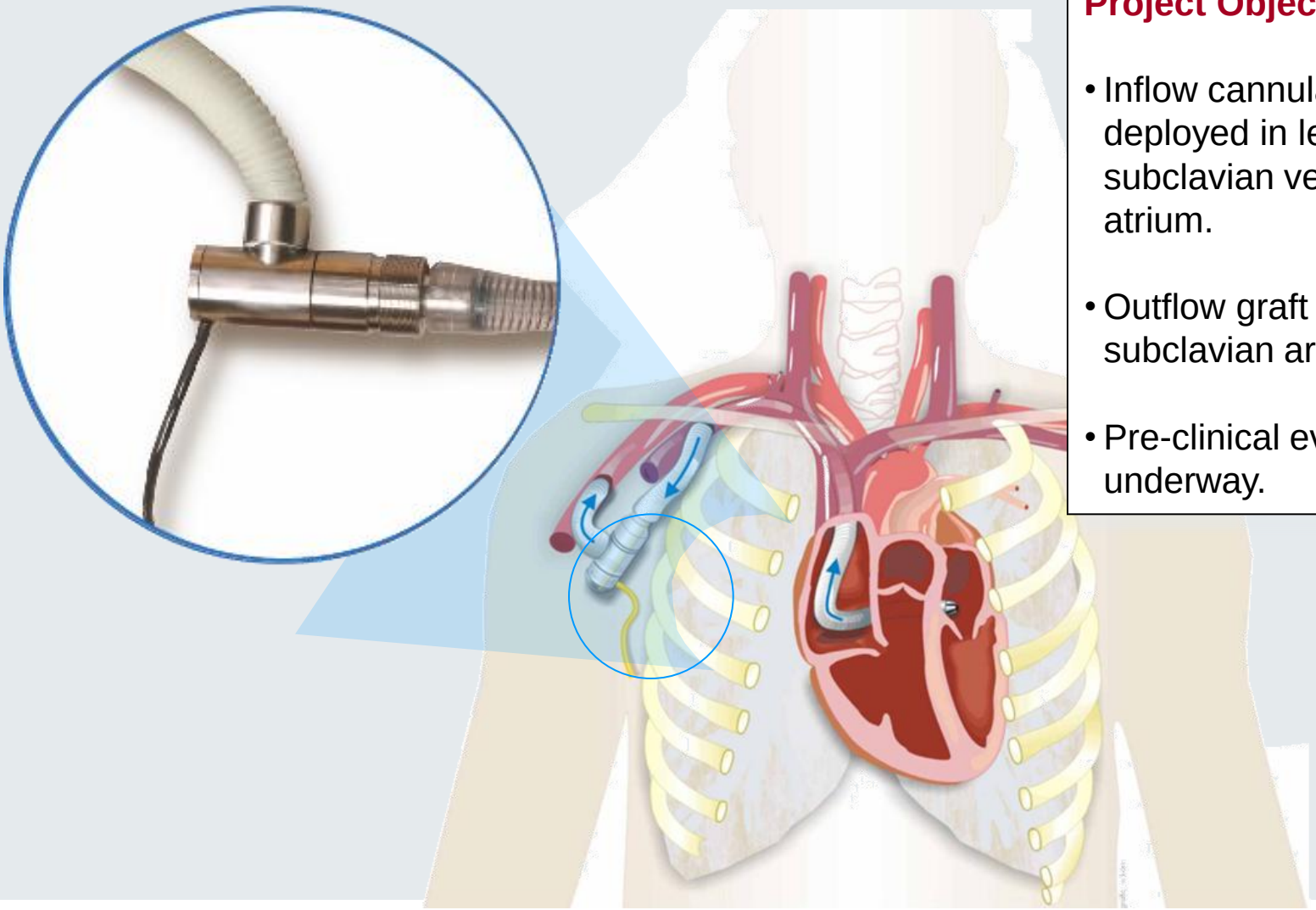
Meyns BP EJCTS 2011

Endovascular VAD Implantation



Project Objectives

- Inflow cannula transeptally deployed in left atrium, via the subclavian vein and right atrium.
- Outflow graft attached to the subclavian artery.
- Pre-clinical evaluation underway.

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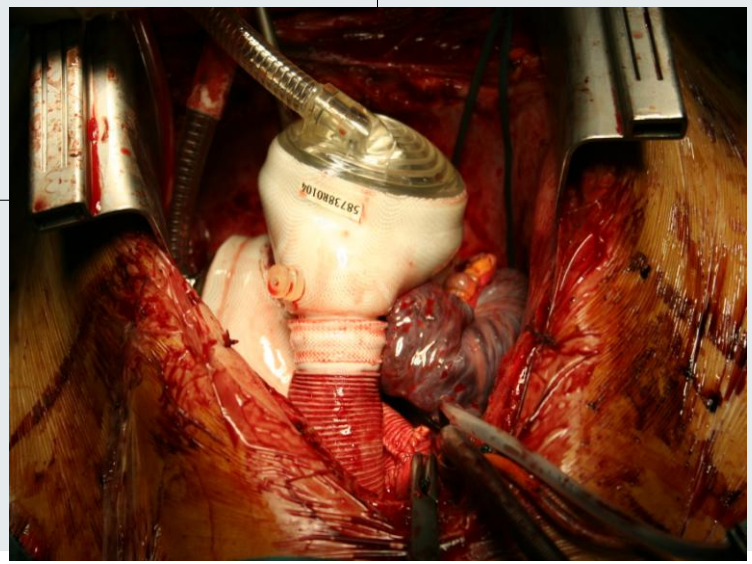
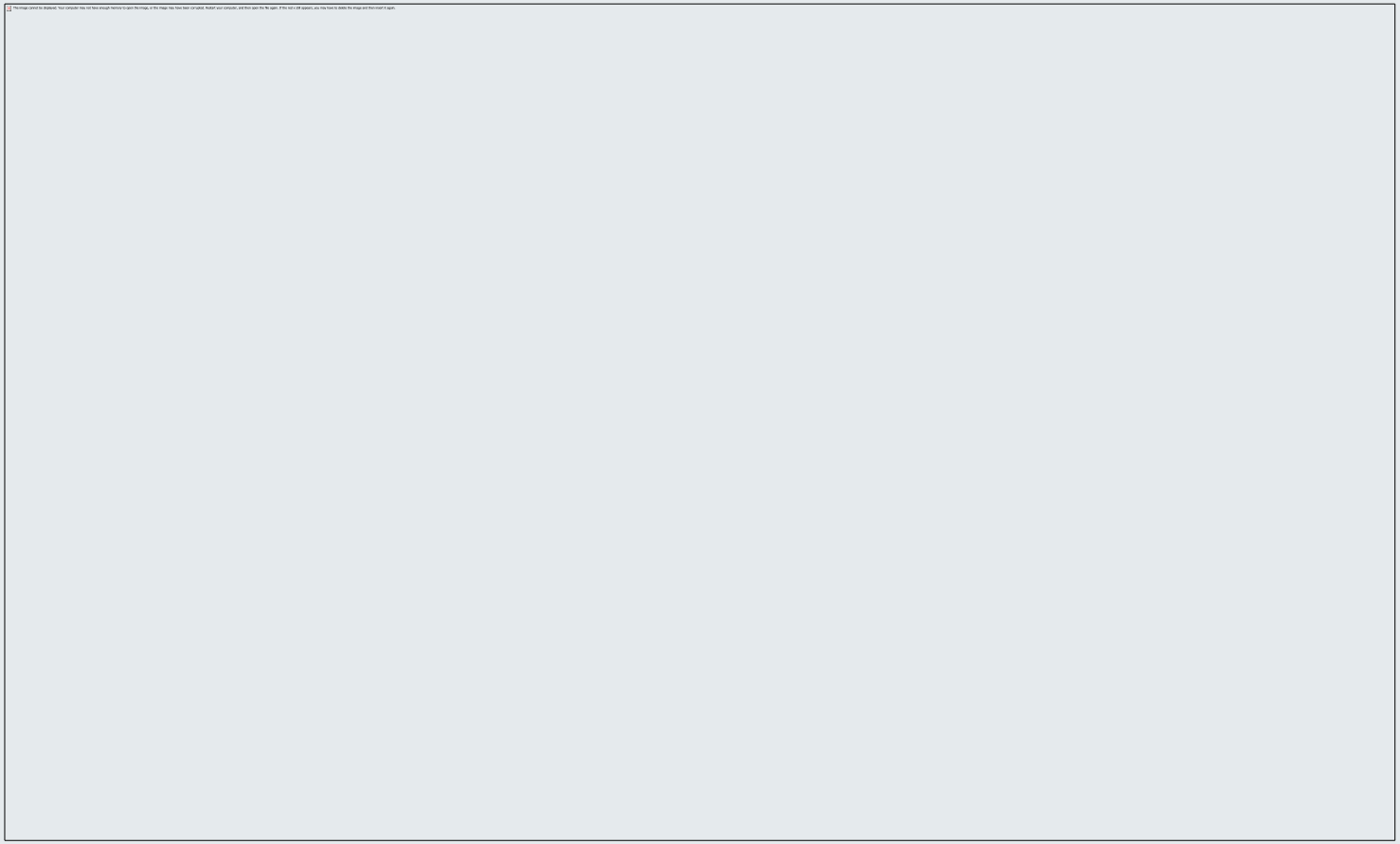
With permission of CircuLite

Total Artificial Heart – Syncardia Cardiowest



Bridge to Transplant results

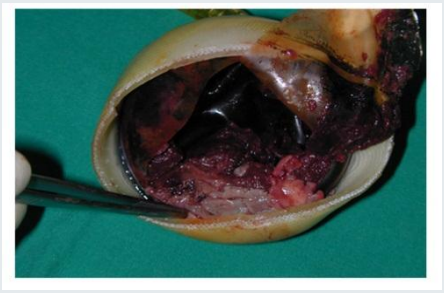
Non randomised US five center trial with historical controls



Copeland - NEJM 2004

CardioWest: Survival rate

Bad Oyenhausen 2/2001 – 8/ 2011; n = 150



12 months

5 year

months

Worldwide: 1020 pts (as of 12/13/2011)

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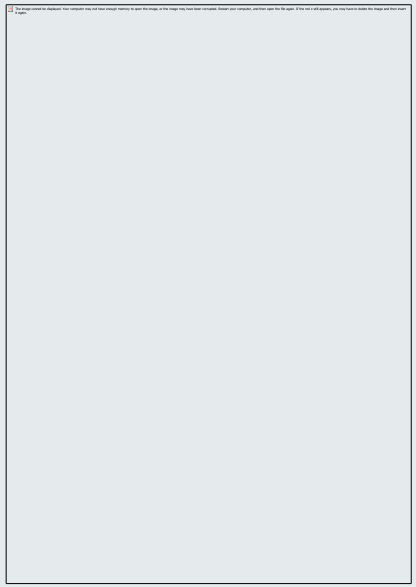
Courtesy J. Gummert, Bad Oyenhausen

TAH: Long-Term Experience

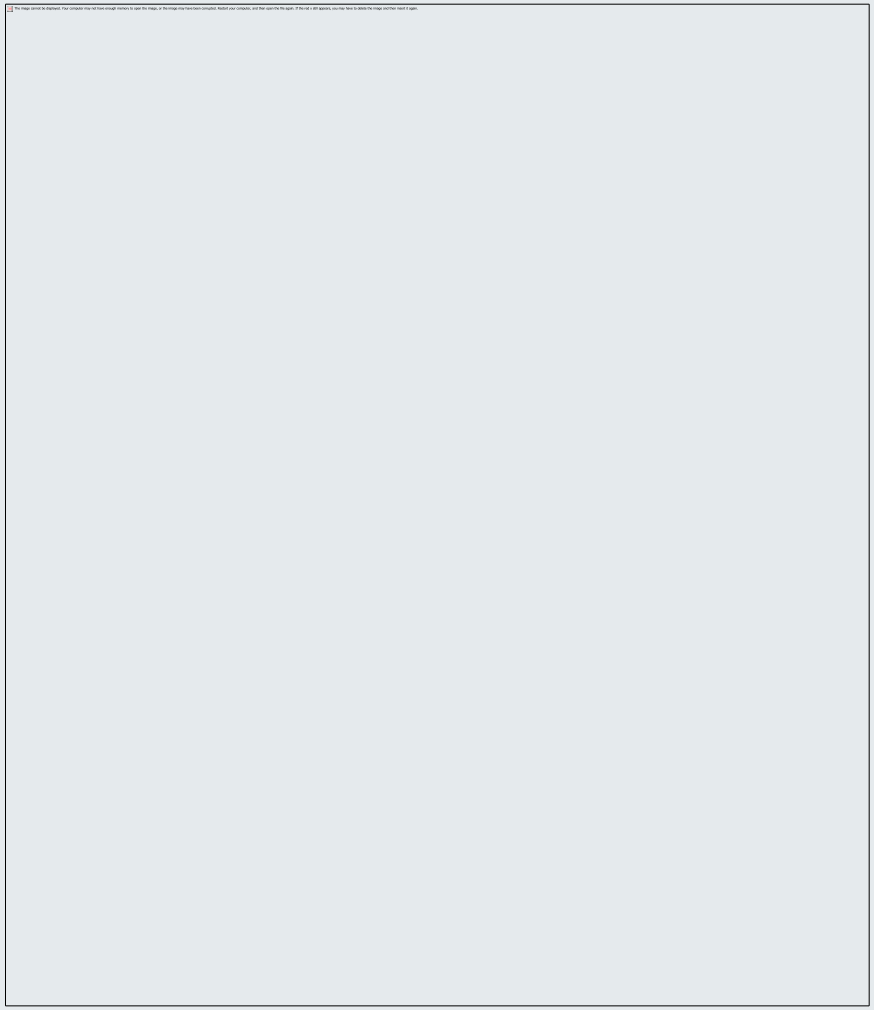
Patient Duration Over 6 Months			
Time (Yrs)	**US**	**OUS**	**Total**
>.5	37	101	138
> 1	8	44	52
>1.5	2	23	25
>2	1	8	9
>2.5	0	3	3
>3	0	1	1
>3.5	0	1	1

82.4% survival

113 alive on device or transplanted



ESC GL HF 2012: Indications for MCS



- Upgrade of LVAD indication for destination therapy

Pts. Eligible for LVAD or BiVAD implantation:

Patients with >2 months of severe symptoms despite optimal medical and device therapy and more than one of the following:
• LVEF <25% and, if measured, peak VO_2 < 12 mL/kg/min
• ≥3 HF hospitalizations in previous 12 months without an obvious precipitating cause
• Dependence on i.v. inotropic therapy
• Progressive end-organ dysfunction (worsening renal and/or hepatic function) due to reduced perfusion and not to inadequate ventricular filling pressure (PCWP ≥20 mm Hg and SBP ≤80–90 mmHg or CI ≤2 L/min/m^2)
• Deteriorating right ventricular function

Conclusions

- Destination Therapy is an established therapy (>30% of implants)
- Results match HTx in selected subsets
- Organ shortage and growing heart failure population will increase need for LVADs
- Earlier implantation in pts. without end-organ failure yields better results
- Partial assist/smaller devices upcoming

ENDURANCE is a randomized, controlled, unblinded, multi-center clinical trial to evaluate the use of the HeartWare Destination Therapy

The non-inferiority study 450 patients with end-stage heart failure ineligible for cardiac transplantation.

Patients randomized to LVAD HeartWare LVAD against control group of any alternative LVAD approved by the FDA for DT in a 2:1 ratio.

Primary endpoint at two years, with a subsequent follow-up period extending to five years post implant.

- Secondary endpoint of survival was 94% at six months; 91% projected survival at one-year for investigational device -

- Conference call today at 6:30 p.m. U.S. Central Time -

FRAMINGHAM, Mass. and SYDNEY, Nov. 14, 2010 /PRNewswire-FirstCall/ -- HeartWare International, Inc. (Nasdaq: HTWR) (ASX: HIN), a leading innovator of less invasive, miniaturized circulatory support technologies that are revolutionizing the treatment of advanced heart failure, today announced that data from its pivotal bridge to heart transplantation (BTT) study, ADVANCE, showed that 92% of the investigational device patients met the per protocol primary endpoint of the trial, which was defined as alive on the originally implanted