



Ex vivo Lung Perfusion is an Essential Tool for Donor Optimization

Debate: Pro

AST CEOT Meeting
Phoenix, AZ, February 2018

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The
Toronto
Lung Transplant
Program



Disclosure

- Founding Partner:
 - Perfusix Canada Inc. (CSO)
 - Perfusix USA Inc. (Lung Bioengineering /UT)
 - XOR Labs Toronto Inc. (CSO)
- XVIVO Perfusion – Research support and clinical trial
- United Therapeutics – Research support and clinical trial
- Xenios/Fresenius – Research support and investor in XOR



Caution: All “EVLP” is not the same!

- Further disclosure and clarification
- EVLP with the **Toronto Technique** is a standard of practice at Toronto General Hospital
- The comments and claims that I will make are based on our research experience in the development of the **Toronto EVLP Technique** and on our CLINICAL experience of over 386 EVLP cases
- There are other systems and techniques out there that I cannot speak to as I have no experience with other than reported outcomes



The Problem

- Utilization of donor lungs in the USA is still only 20%
- Outcomes of lung transplantation are variable
- Many usable lungs are declined
- Varying levels of expertise and experience in decision makers regarding accept or not
- Donor Optimization = optimal utilization + optimal outcomes
- 10 reasons why EVLP is an essential tool for donor optimization

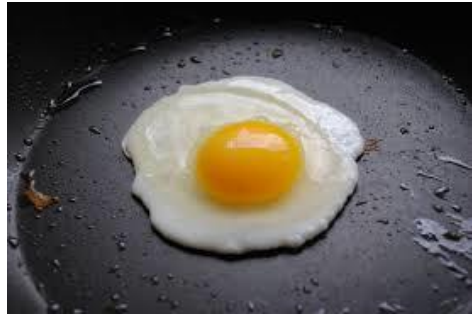


1. EVLP Provides the Opportunity to Test Questionable Organs

- Different thresholds of comfort to accept a “non-perfect” organ
- Retrieval by “unknown” retrieval surgeon
- If you are not sure/ not comfortable – check it out on EVLP
- Use more lungs SAFELY (the era of “adventures” with “marginal lungs” is over)
- A stable lung on EVLP will work after transplant



Decision Making - Experience



- Experienced team can make the decision together with the more junior team that went on recovery

You cannot make a chicken out of a fried egg!!





If you are not sure about a donor lung...

- Bring it home
- Put it on EVLP and check it out
- Easy!



2. EVLP Provides the Opportunity to Further Assess, Improve and Optimize Injured Donor Lungs

- Pulmonary edema
- Inflammation
- Infection
- Pulmonary embolism



Resolution of pulmonary edema during EVLP

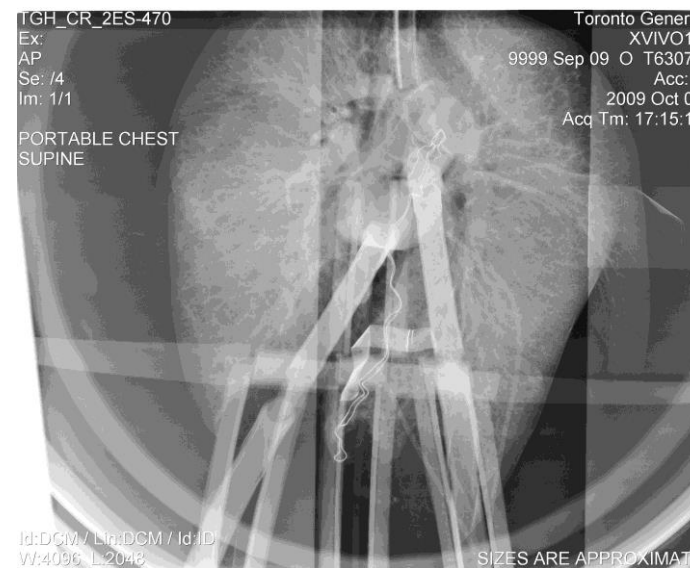
Donor P/F 230



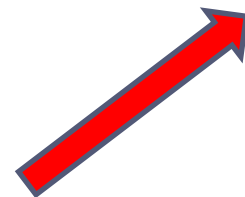
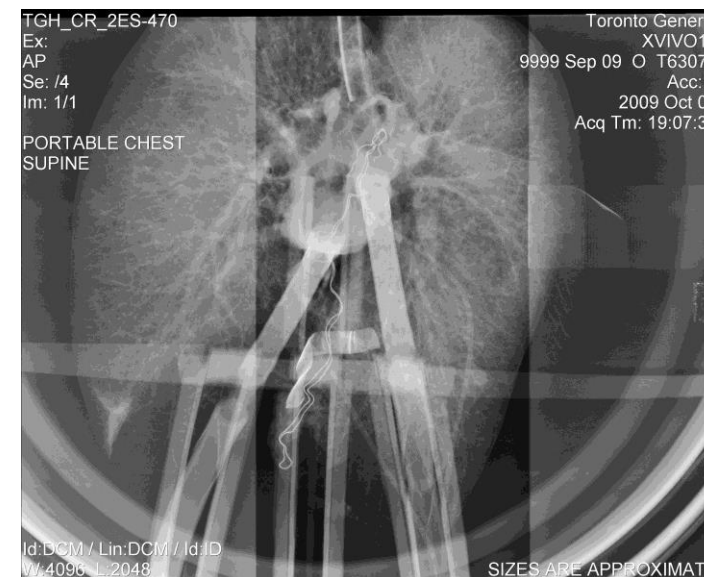
Recipient P/F 420



1h EVLP



3h EVLP

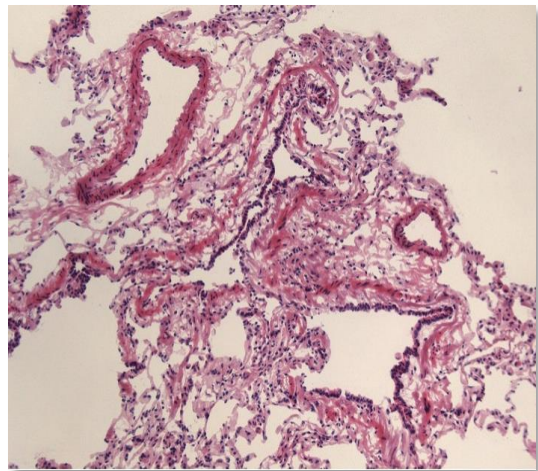
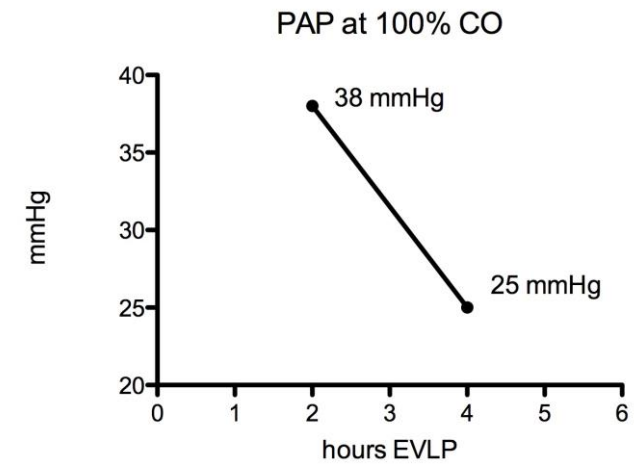
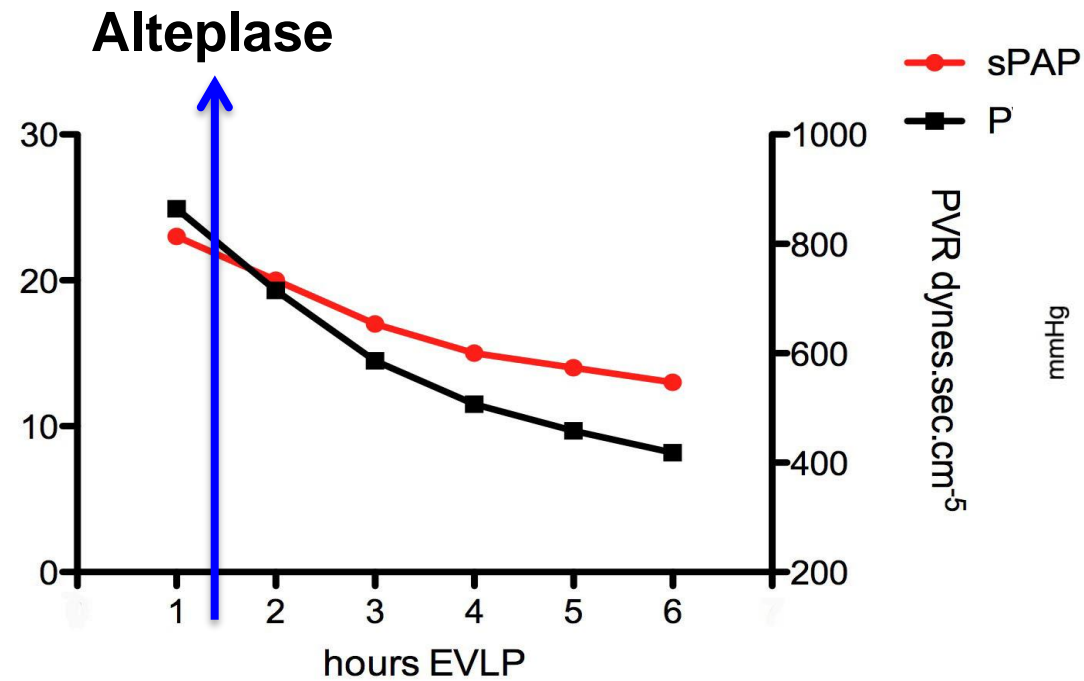




Donor with High PAP and PE: Significant Improvement of Pulmonary Hemodynamics after Treatment on EVLP



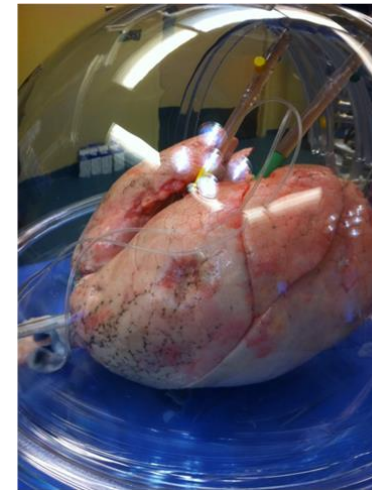
sPAP mmHg



diagnosis

treatment

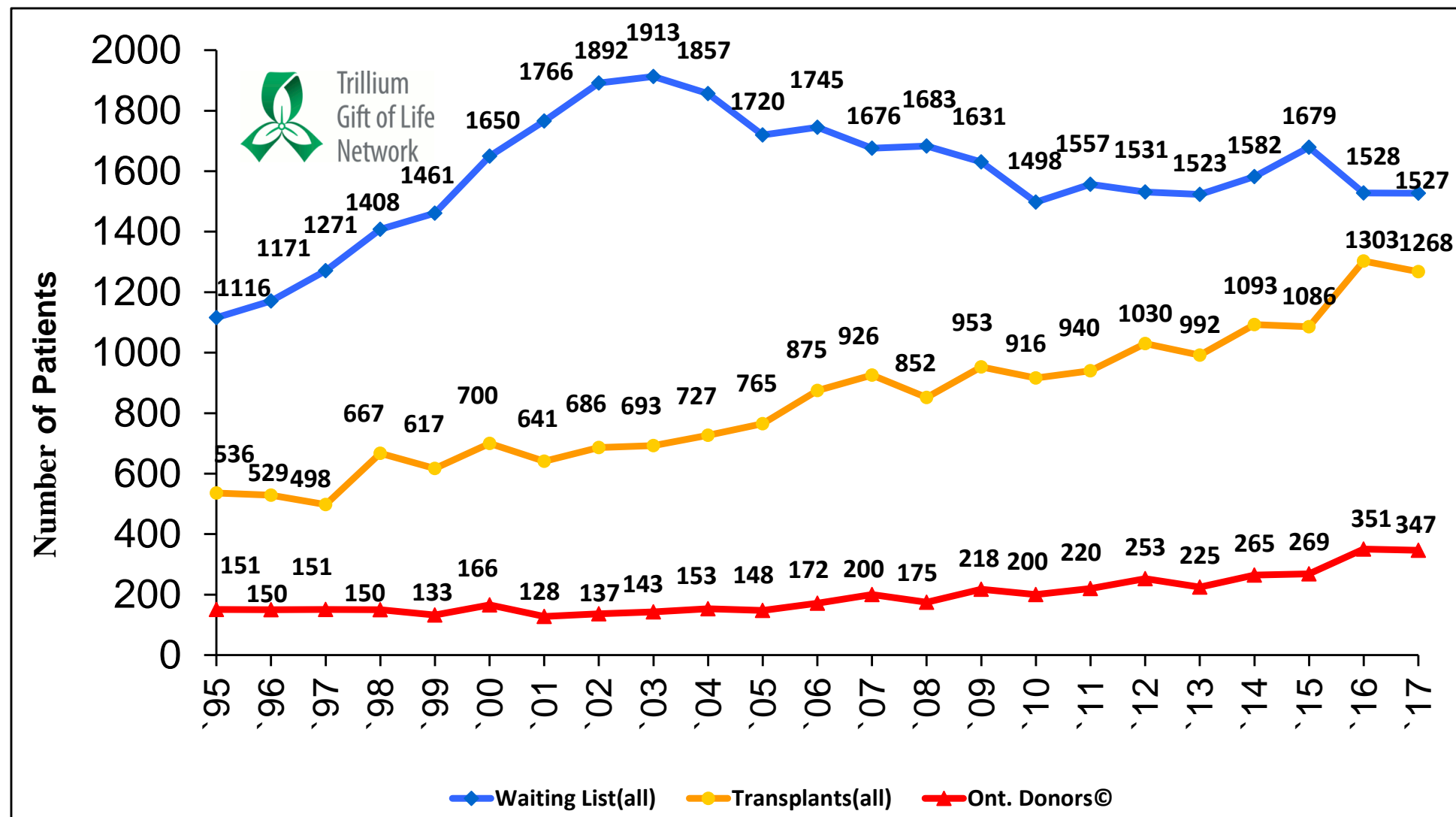
Response monitoring





Waiting List, Transplants and Donors (All Organs-Ontario)

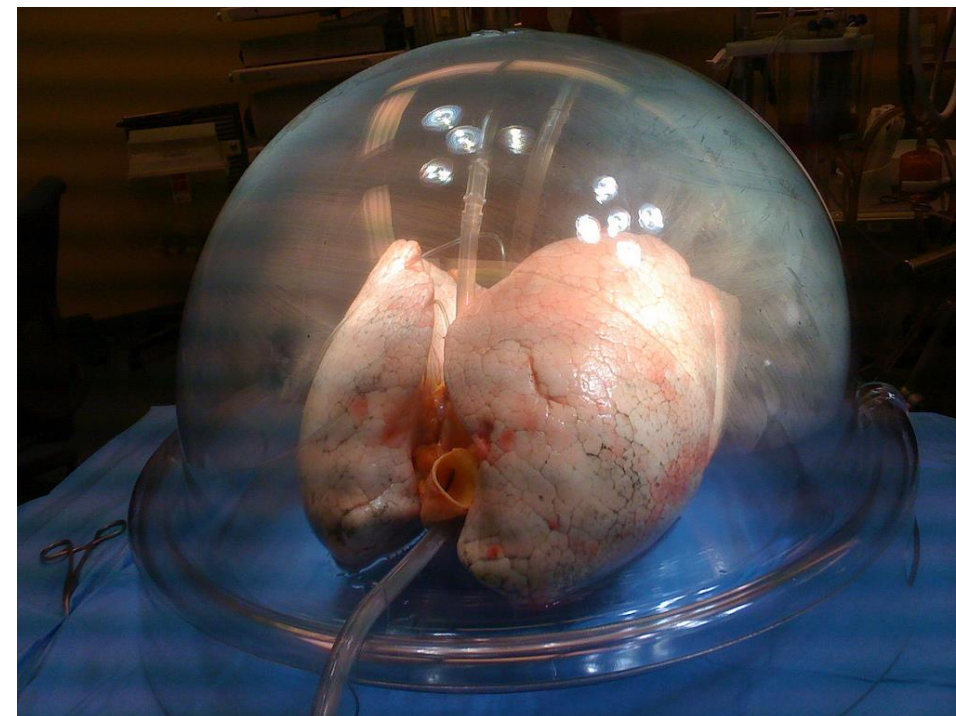
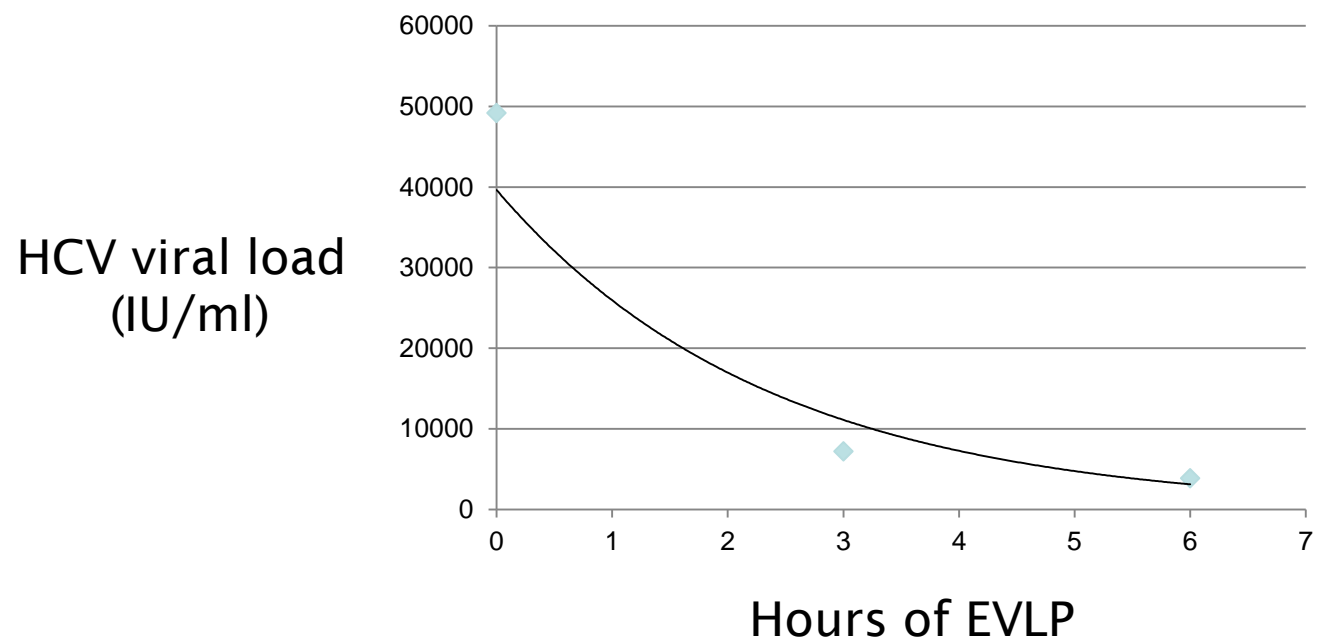
Source: TGLN 1995 - 2017





3. EVLP Creates the Opportunity to Develop New Sources of Organs

- DCD – donation after cardiac death
- Non- Perfused Organ Donors (NPODS)
- Hepatitis C infected organs





DCD Utilization Statistics

- DCD – source of many donor lungs
- DCD – has some potential increased risks:
 - Aspiration AFTER extubation
 - Shock lung with prolonged agonal hypotension
- DCD lungs are not being used in the US



Am J Transplant. 2016 April ; 16(4): 1207–1215. doi:10.1111/ajt.13599.

Lung Quality and Utilization in Controlled Donation after Circulatory Determination of Death Donors within the United States

Joshua J Mooney, MD¹, Haley Hedlin, PhD¹, Paul K Mohabir, MD¹, Rodrigo Vazquez, MD², John Nguyen, RN³, Richard Ha, MD⁴, Peter Chiu, MD⁴, Kapilkumar Patel, MD¹, Martin R. Zamora, MD⁵, David Weill, MD¹, Mark R Nicolls, MD¹, and Gundeep S Dhillon, MD¹

- SRTR data: DNDD utilization rate in USA is 21%
- DCDD utilization rate in USA is **2.1%**
- DCDD rate in Canada and Australia and Europe 28%

transplant recipients. Increasing lung transplant center expertise and commitment to cDCDD procurement along with minimizing the impact of aborted runs through the use of technologies such as EVLP are needed to improve U.S. cDCDD lung utilization.



Should All DCD Lungs be Treated with EVLP?

Avoid surprises...

DCD, rapid arrest after WLST, “no concerns” straight to transplant





DCD Lung Transplantation: Standard of Care

15-30% of transplants from DCDs

Table 1 Characteristics of DCD Practices in Participating Centers

Center	Transplants 2012 to 2014 (n)	Percentage of Transplants from DCD (%)	Use of heparin pre-mortem	Use of Bronchoscopy Pre-mortem	Selective use of EVLP	Stand-off period	Maximum time allowed for WLS T to arrest
Toronto	352	15	Yes	Yes	Yes	5 min	180 min
Sydney	139	23	No	No	Yes	2 min	90 min
Melbourne	214	23	Yes ^a	Yes	No	2 to 5 min	90 min
Brisbane	93	15	No	No	Yes	5 min	90 min
Leuven	199	14	Yes	No	Yes	5 min	120 min
Groningen	112	32	No	Yes	Yes	5 min	90 min
Minnesota	126	7	Yes	Yes	Yes	5 min	90 min
St. Louis	191	< 1	Yes	Yes	No	5 min	30 min
Cleveland	302	8	Yes	Yes	No	5 min	60 min

DCD, donation after circulatory death donor; EVLP, ex vivo lung perfusion; WLST, withdrawal of life support therapy.

^aWhen allowed by donor hospital.

Cypel et al. *J Heart Lung Transplant* 2015 Oct;34(10):1278-82

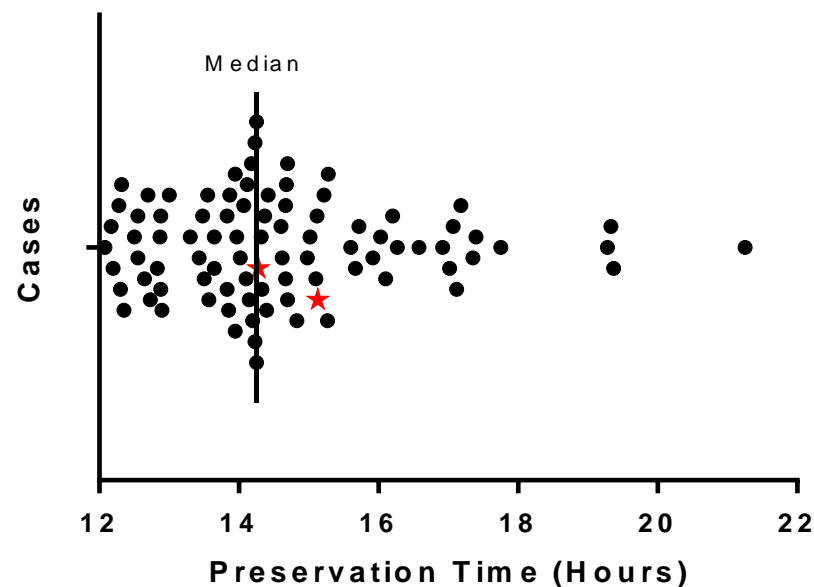


4. EVLP Allows Significant Prolongation of Preservation Time

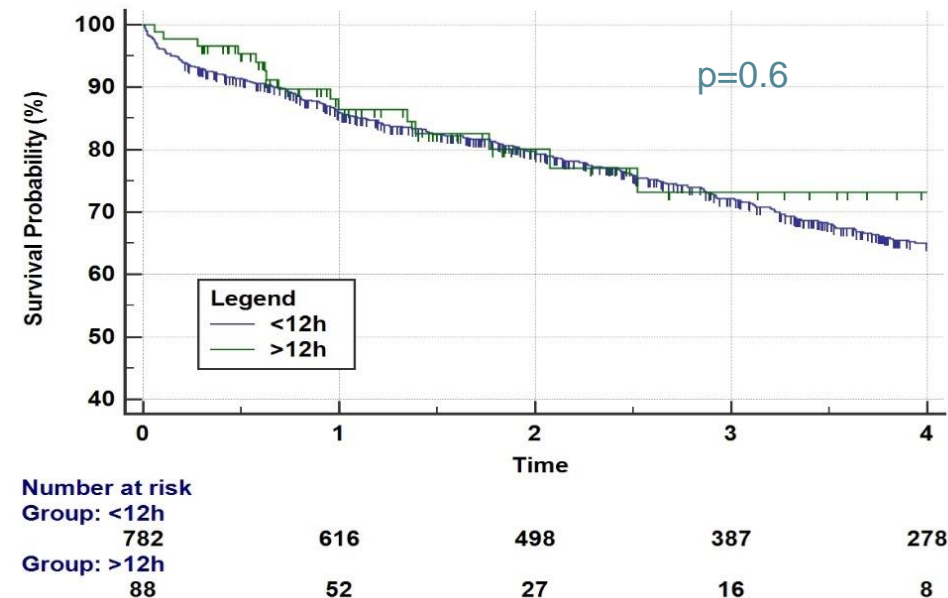
- At TGH we routinely transplant lungs over 12h preservation time
- Patients can remain at home – further distances
- Don't need to call in patient until donor assessment is complete (even more important in DCD as 40-50% don't arrest)
- No need to rush in difficult cases worrying about ischemic time
- More transplants can occur in the daytime – teams can sleep → better performance, lower costs, allow program volume escalation without team burnout



Towards Elective Lung Transplantation: Outcome of Transplantation of Lungs Preserved More Than 12h



★ 90-day Mortality



THE LANCET
Respiratory Medicine

Yeung J, Krueger, Yasufuku K, de Perrot M, Pierre A, Waddell T, Singer L, Keshavjee S, Cypel M. Nov 17, 2016



TGH OR

THURS. June 11, 2015

HOUSEKEEPING
416-790-9684

RT TECH
416-790-8828

OR 13 B-Wei - laparotomy + washout - 9ES
Donor # 259828

OR 9 A-Greig - Kidney/Pancreas Tx - 7M @ 0700
Donor # 260015

A-Selzner - Kidney Tx - 7M - June 11 @ 2000
Donor 259939 Donor start time 2000 tonight

A-Keshavjee - Double Lung Tx [Plasma] - 7M

70600 June 12 A-Selzner - Kidney Tx - 7M
Donor 260027 - DCD WD @ 1200

OR 18 @ 1400 A-EXVIVO Double Lungs June 11 ?
A-Keshavjee - Double lung [Plasma] - 7M Afternoon
Donor 260009 DCD

A-Hickey - Heart Tx [Rodo] CCU June 11 AM?
OR 3 @ ? * lines to be done in O.R. by J. Heggie

A-Keshavjee - Lung Tx -
Donor 260154

A-EXVIVO DBL Lung

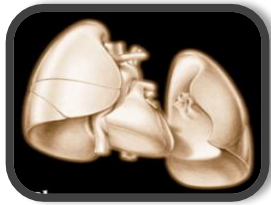
A-Keshavjee - DBL Lung Tx [Plasma] 7M @ 20:00
Donor 260139

A-Cattral - liver TX - 7M

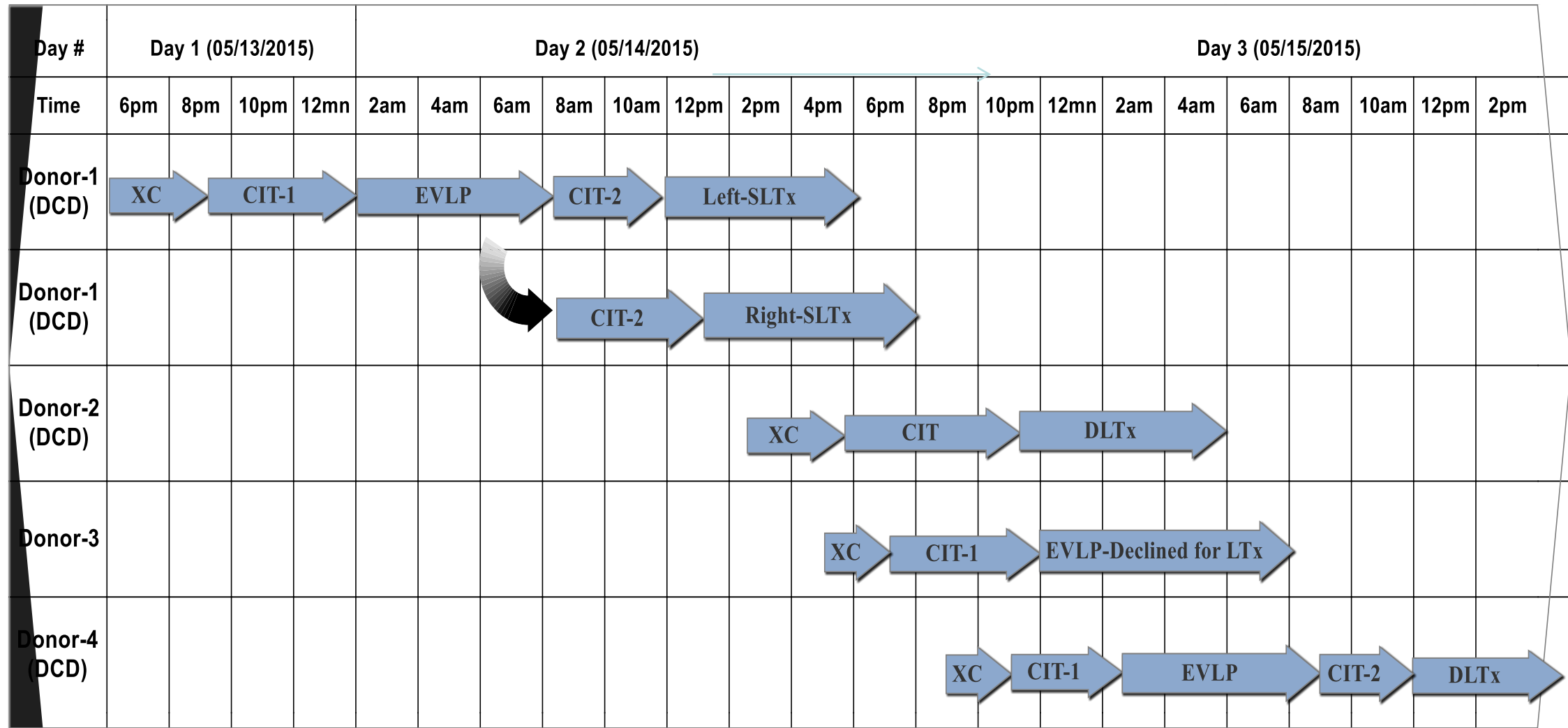
A-Keshavjee - DBL Lung Tx - 7M

5. EVLP Improves transplant logistics

Time for manpower and operating room logistical planning (for lung and other organs as well as other OR activity)



Improving Transplant Logistics





6. EVLP Provides Time for Improved Allocation

- Allows time for organ allocation when decline occurs at the last minute by original accepting team
- Will allow time for advanced organ matching: epitope based HLA matching



So, I've told you that EVLP is essential for donor lung optimization and utilization....

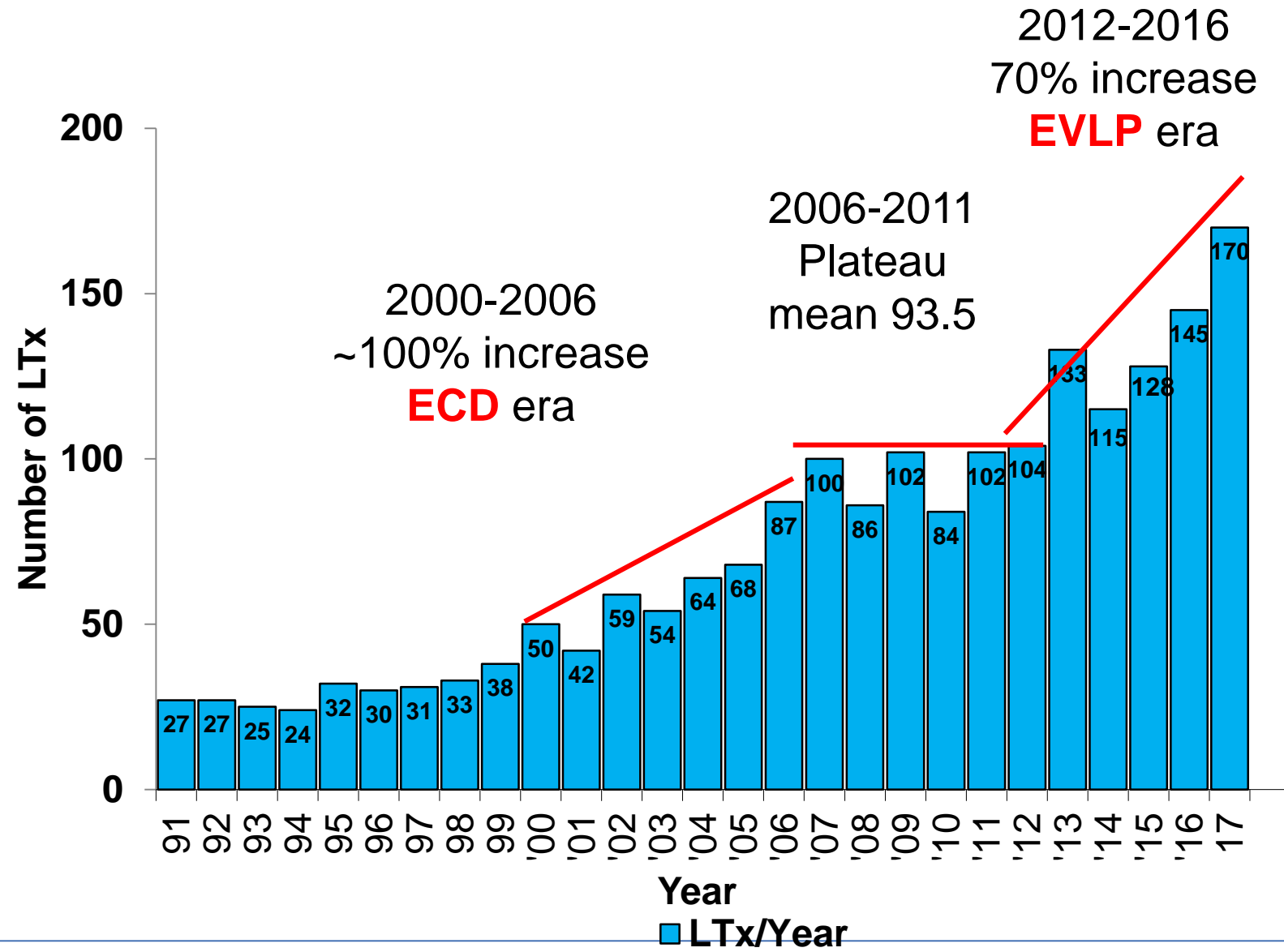


Where is the proof?



Toronto Lung Transplant Program Annual Growth

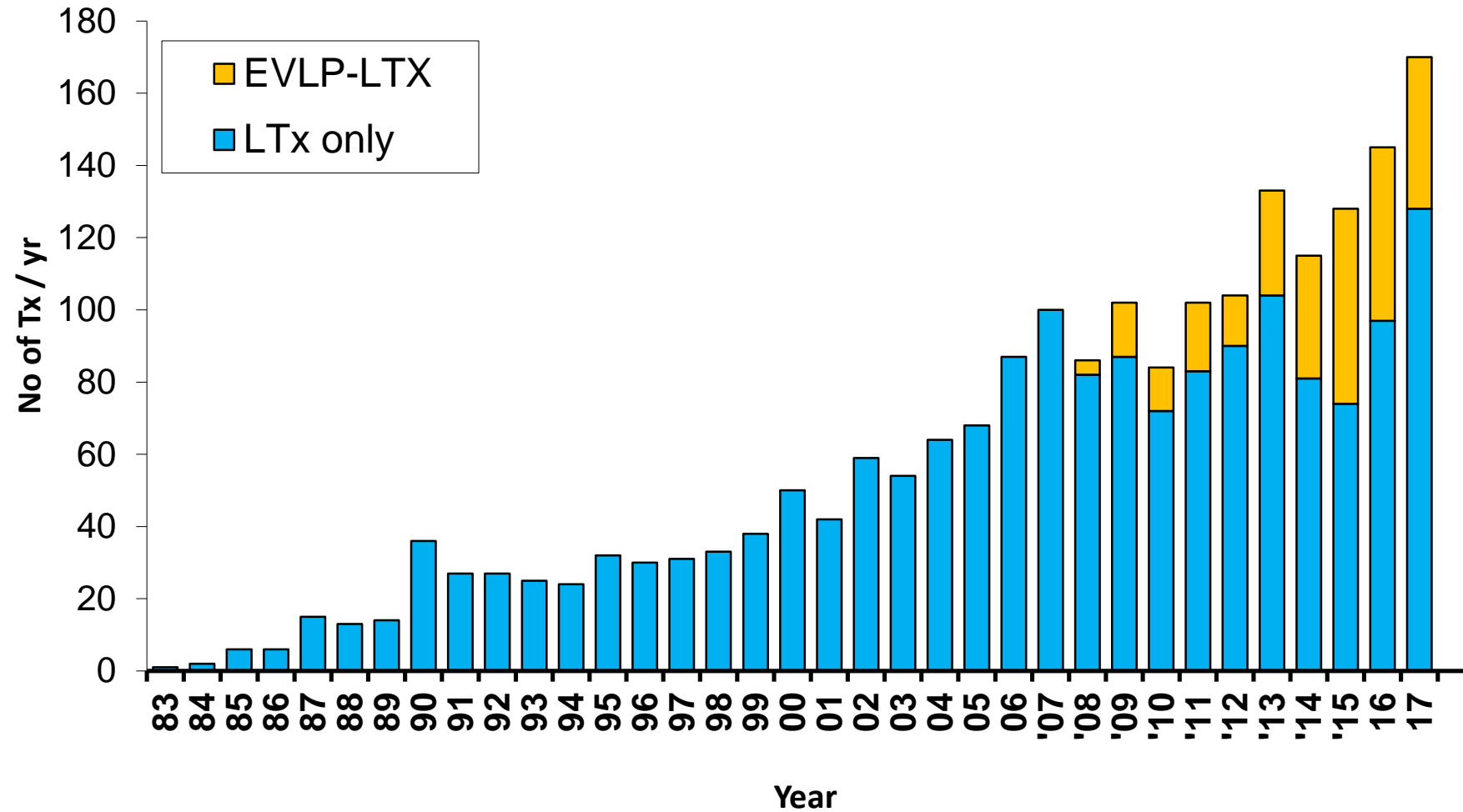
1991-2017





EVLP & Lung Transplant Activity / Year

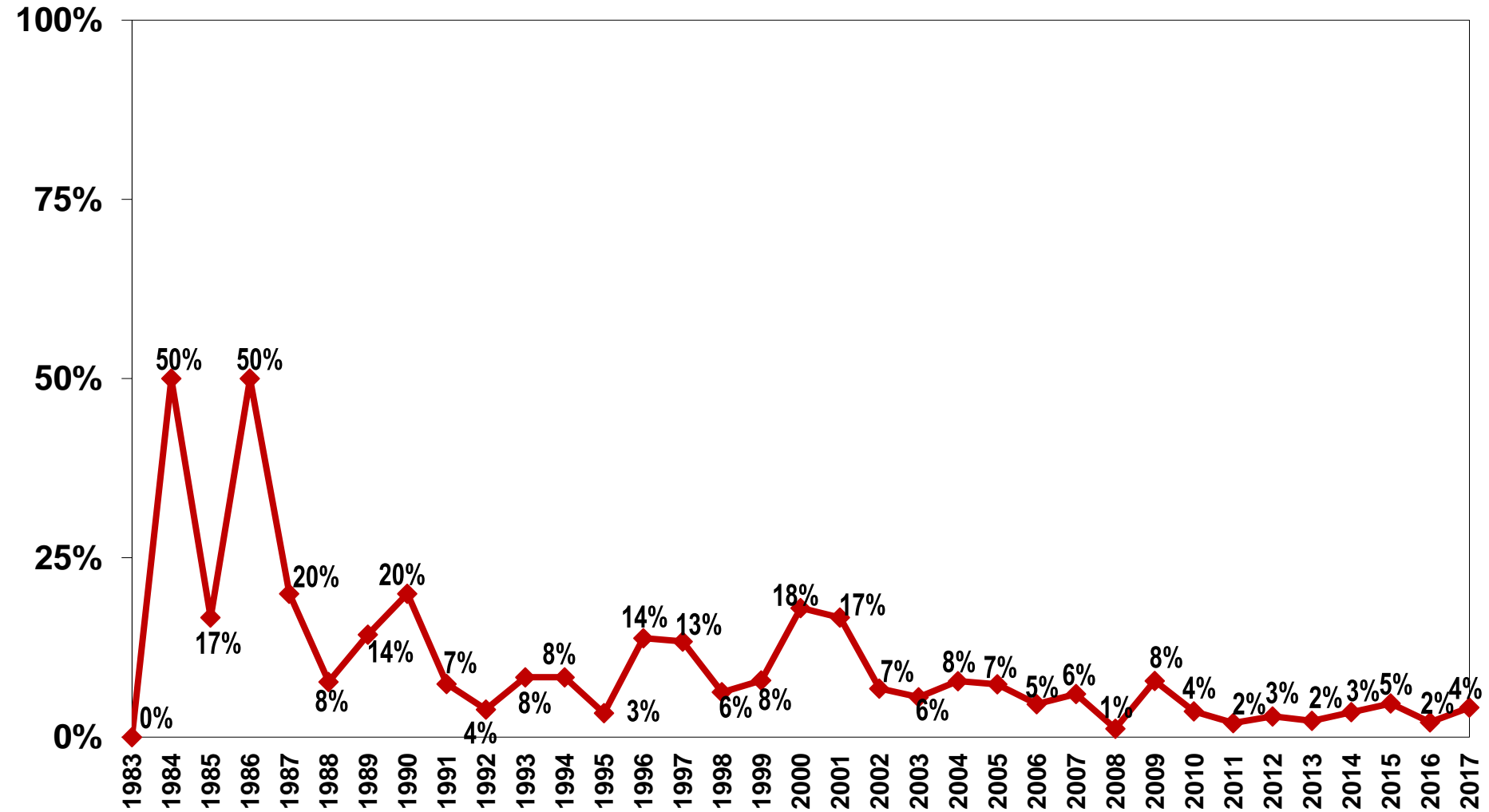
1983 - 2017



Total EVLP performed to-date(N=252)



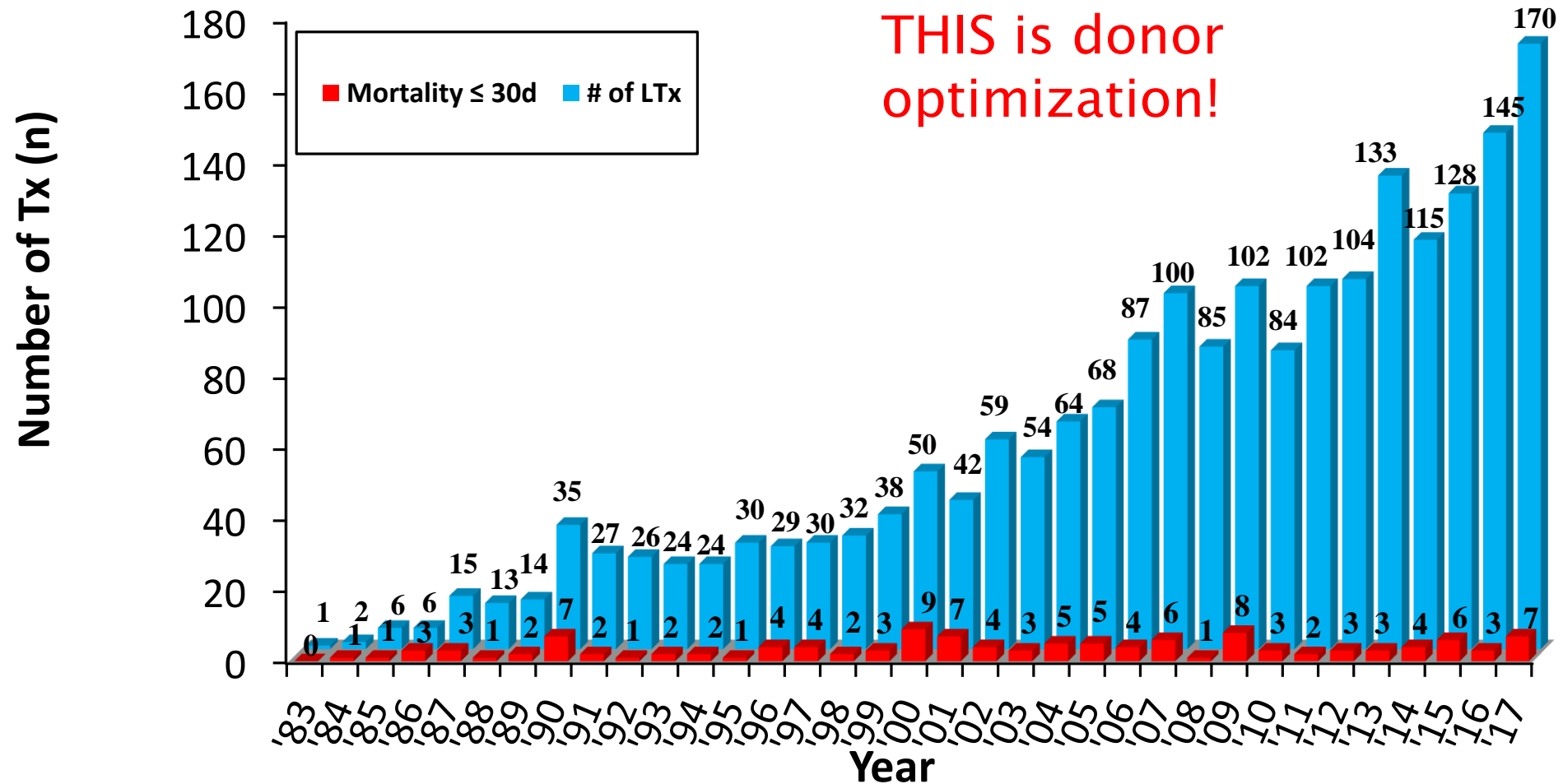
Operative (30d) Mortality Rate (Avg 3% past 5 yr)



Rate %: # death within 30-d post-op / # Tx within Calendar year

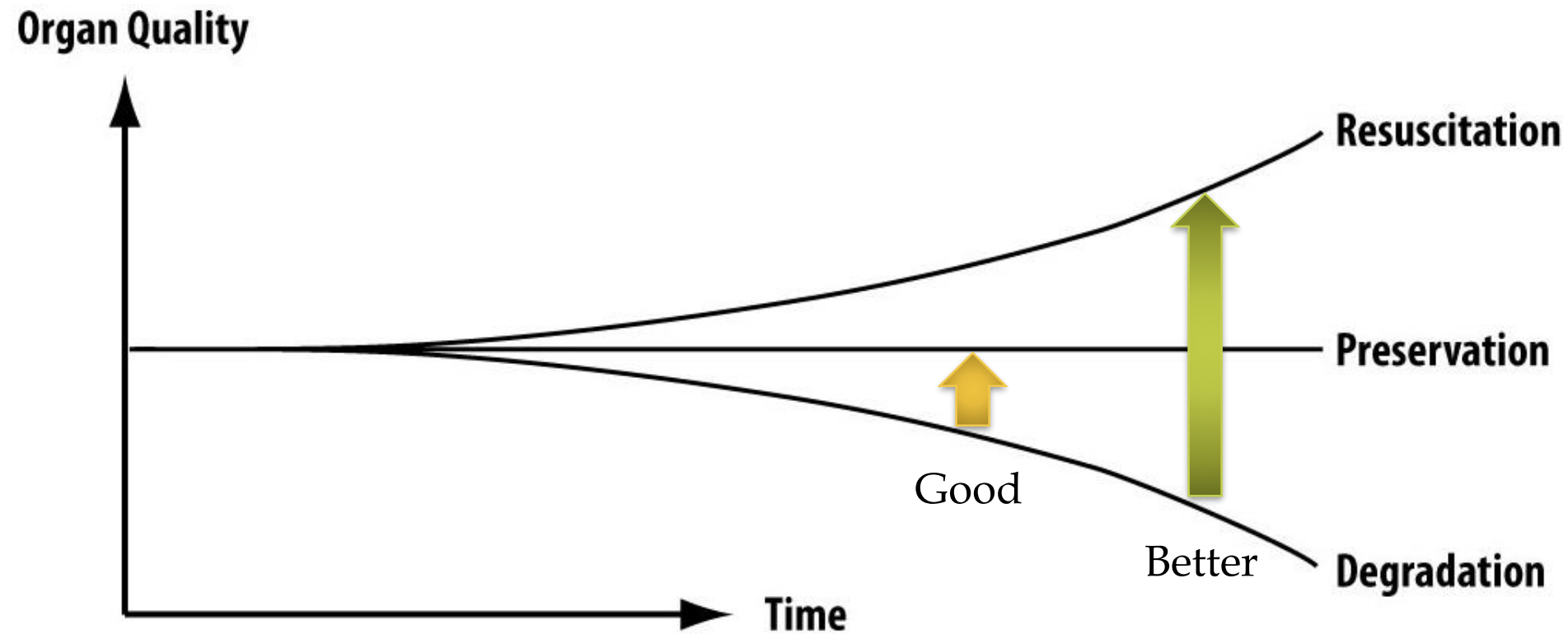


Operative (30d) Mortality by Year 1983 – 2017





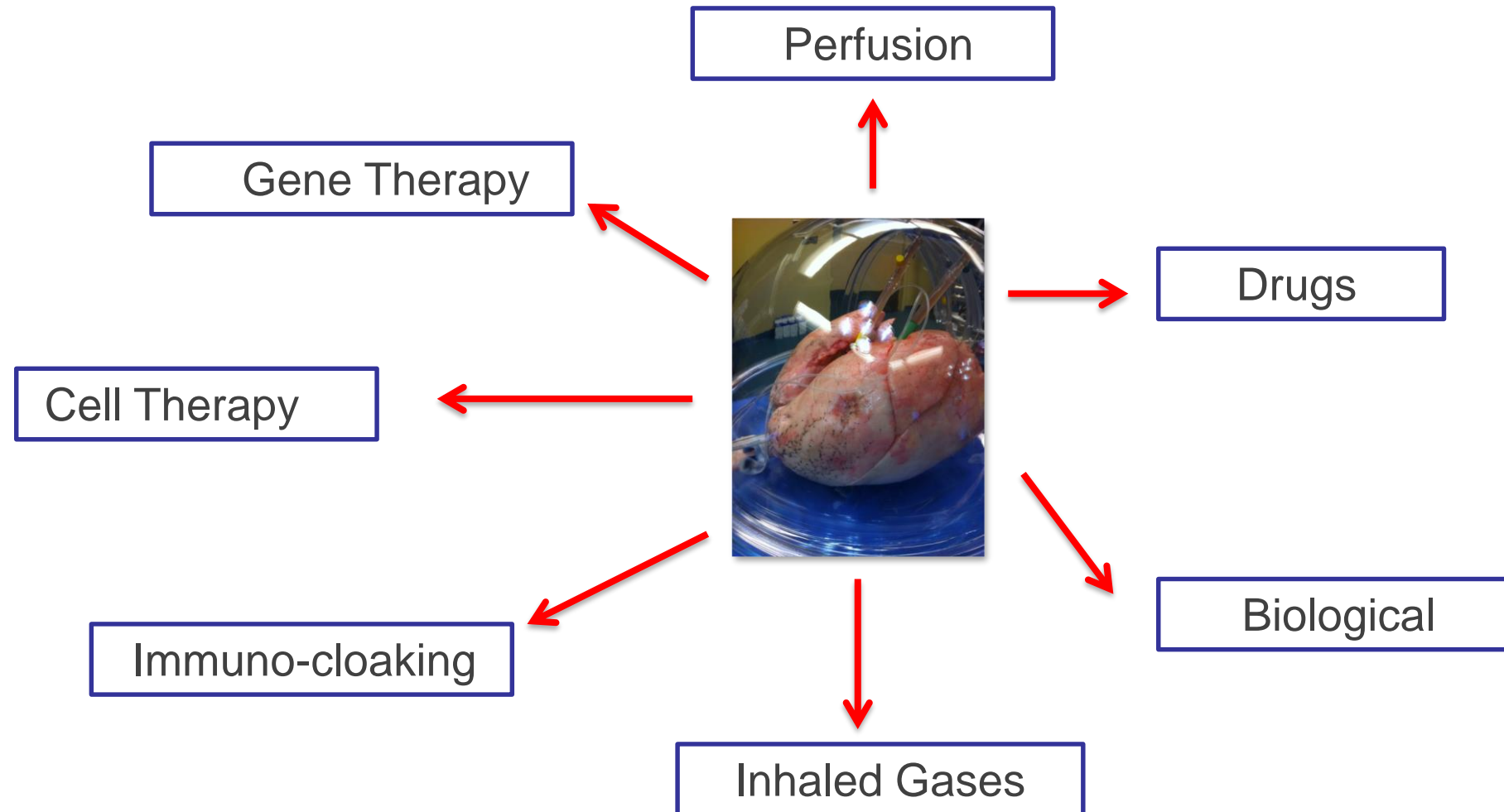
We should aspire to creating organs that are **BETTER** than the state in which we found them...





7. EVLP Provides the Opportunity to Repair Donor Lungs

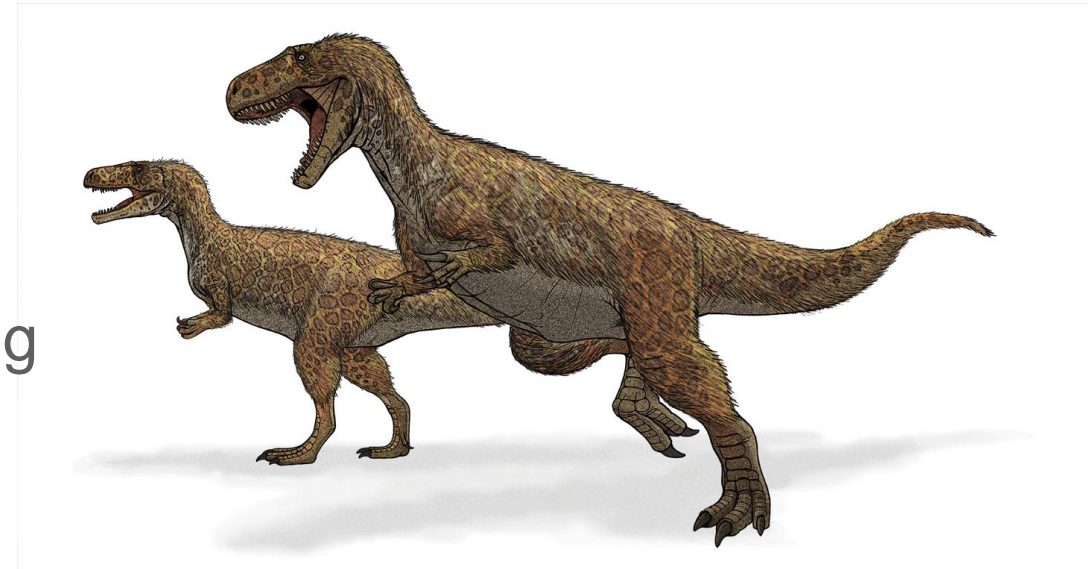
EVLP Treatment Strategies





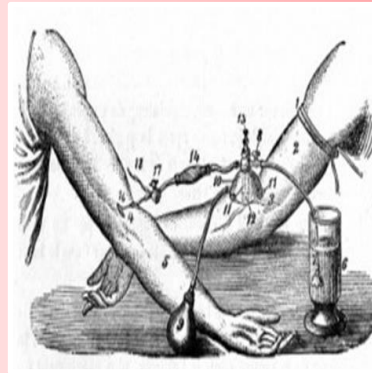
8. EVLP Will Prepare You for The Future

- Management of donor organs today has essentially not changed since the inception of transplant
- Processes are highly inefficient
- Assessment - imprecise
- Allocation systems - inefficient, ineffective and challenging
- Significant logistical challenges
- Resource intense - inefficient and expensive use of transportation, people and ORs etc.
- We need to accelerate evolution of processes of organ management and transplantation as a whole...

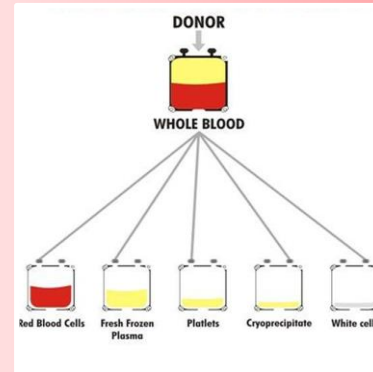




9. EVLP will enable specialization of organ management in specialized centers: a lesson from the history of blood transfusion



Unprocessed whole blood transfusion in the battlefield

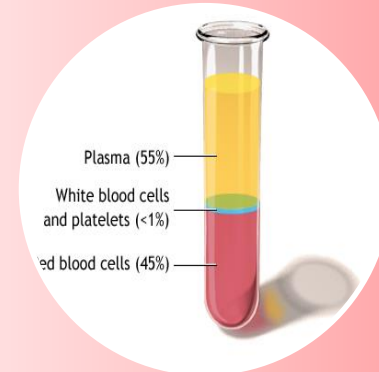


Processed blood transfusion in individual hospitals



Standardized, centralized collection, processing, storage, distribution

Control quality - SOP's, infection control, shelf life, inventory, distribution, tracking, safety standards



Optimized utilization

Separation of components for specific patient needs (RBC, platelets, plasma, cryo etc.)

Management of Blood Products – The Evolutionary Path

Ability to scale up, achieve cost and utilization efficiencies



10 Key Reasons Why EVLP is an Essential Tool for Donor Optimization

1. EVLP provides the opportunity to test questionable organs, improve utilization
2. EVLP provides the opportunity to further assess, improve and optimize injured donor lungs, improve outcomes
3. EVLP creates the opportunity to develop new sources of organs
4. EVLP allows significant prolongation of preservation time
5. EVLP improves transplant logistics – performance and cost



10 Key Reasons Why EVLP is an Essential Tool for Donor Optimization

6. EVLP provides time for improved allocation
7. EVLP provides the opportunity to repair donor lungs
8. EVLP will prepare you for the future - engineered organs with superior, predictable function and outcomes
9. EVLP will enable specialization and scaling of organ management processes in specialized organ repair centers
10. I have just shown you it's possible!



The
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