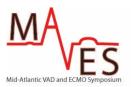




Welcome to the 12th Annual MAVES

3 May 2020



Thank YOU, 2020 vendors, for your support!!

During the breaks, please visit our supporting vendors in their breakout room through the CHAT function and be entered into a raffle for Amazon gift cards!





Caring for Lives through Innovation, Quality and Service

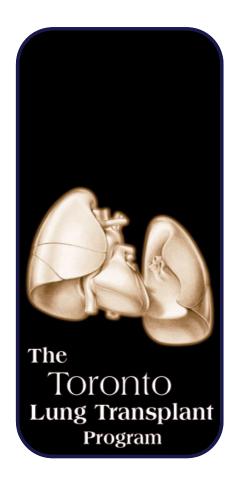






INVOSUITE SILVER SPONSORS









Update on Exvivo Perfusion

Cyril Serrick MSc, CPC, CCP

Manager – Perfusion Services and Exvivo Technologies University Health Network, Toronto General Hospital Toronto, Ontario, Canada





Major Obstacle for Transplantations

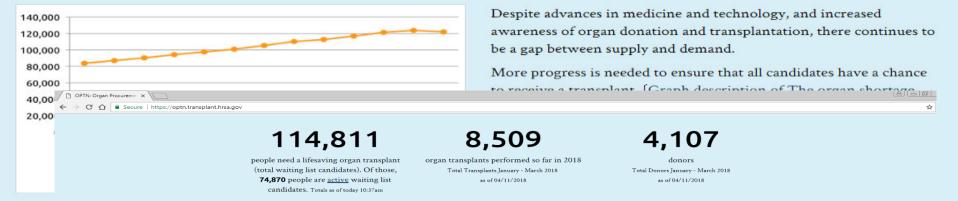
- Absence of sufficient organs to meet the growing demand
- Up to 30% patients die on wait lists
- Larger number of patients are not even listed



THE ORGAN SHORTAGE



The organ shortage continues



Organ donation and transplantation can save lives



1:8

Every ten minutes, someone is added to the national transplant waiting list. On average, 95 transplants take place each day in the U.S.

One organ donor can save eight lives. <u>Sign</u> <u>up to be a donor</u> in your state.

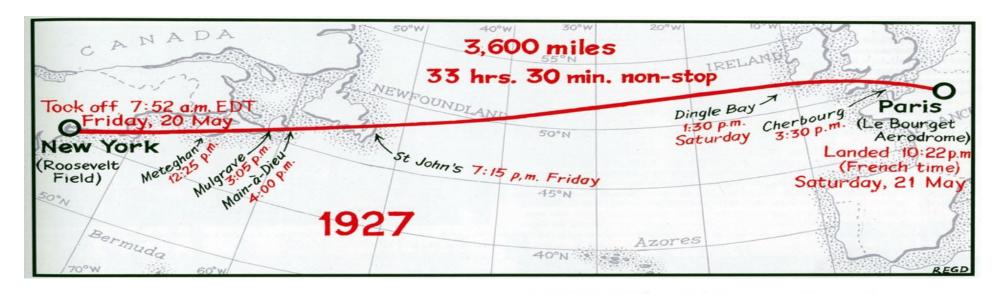


Charles Lindenburg









- May 20, 1927
- First nonstop flight from NY to Paris
- 200 miles across the Atlantic
- Total distance of 3600 miles
- Time 33.5 hours





SPECIAL ARTICLES

THE CULTURE OF WHOLE ORGANS

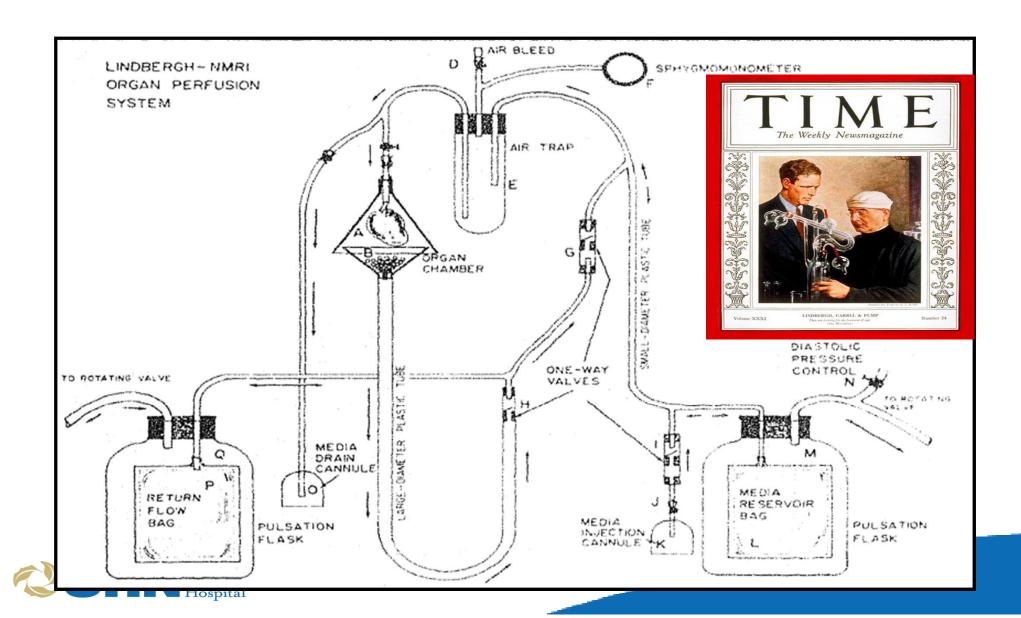
The method to be described consists of the transplantation of an organ or of any part of the body into a sterile chamber, and of its artificial feeding with a nutrient fluid through the arteries. It is not in any way a substitute for the method of tissue culture. Its techniques, as well as its purposes, are quite different. As is well known, tissues and blood cells grow like bacteria in flasks containing appropriate media. The techniques for the cultivation of tissues are somewhat analogous to bacteriological techniques, although far more delicate. But it is through the employment of complex mechanical and surgical procedures that

organs are enabled to live isolated from the body. Tissue culture deals with cells as units of bodily structures; the new method, with cellular societies as organic wholes. Its ultimate purposes are the manufacture in vitro of the secretions of endocrine glands, the isolation of the substances essential to the growth, differentiation and functional activity of those glands, the discovery of the laws of the association of organs, the production in vitro and the treatment of organic and arterial diseases, etc.

The idea of maintaining alive a portion of the body in order to study its functions is not new. In 1812, the physiologist Le Gallois¹ wrote that, "if one could sub-

Lindbergh, Science, 1935





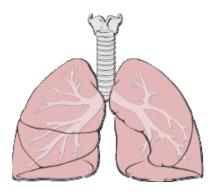
What is Normothermic Ex Vivo Perfusion





Chapter One

ExVivo Lung Perfusion (EVLP)







The lung transplant program - now the largest in the world - performed 167 transplants last year, with about one-third of them due to the innovative Toronto Ex Vivo Lung Perfusion System. This system for high-risk donor lungs, a world-first pioneered at TG in 2008, assesses, improves and treats donor lungs, making many more available for transplant.

This program is now expanding to other organs.

the top transplant program in the world," says Dr. Atul Humar, Medical Director of the transplants in 2011

"It is not just the experience we have in doing so many transplants, our outcomes are equal to or exceed





Conventional Cold Storage

Advantages:

Reduction of cell metabolism by 95%

Disadvantages:

- Normal physiological mechanisms and pathways are impaired
- No way to assess or improve function



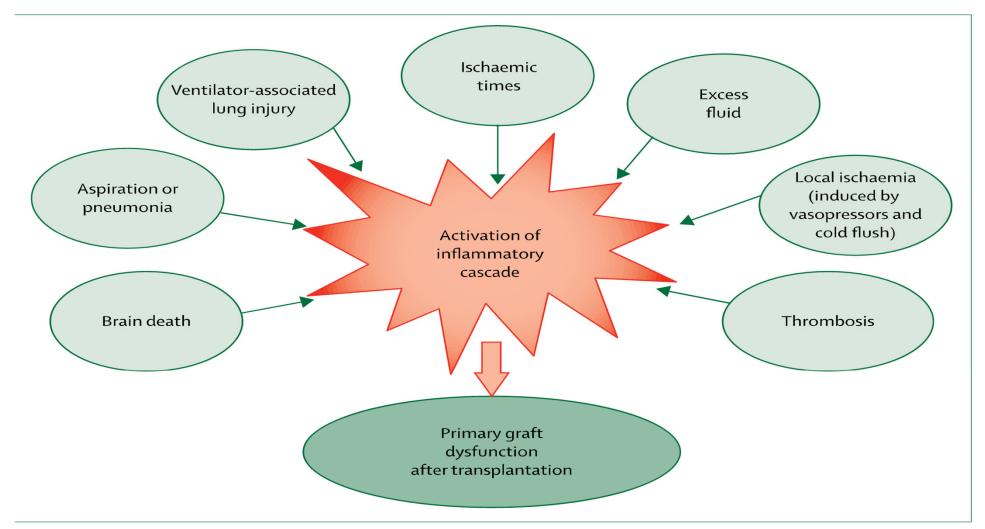


Figure 1: Injuries to donor lungs in potential multiorgan donors

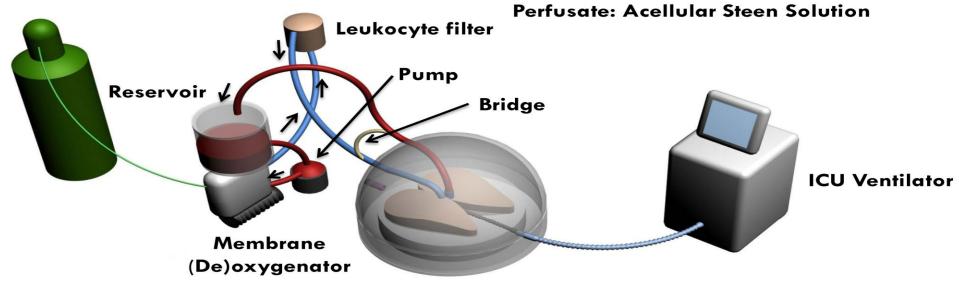




TORONTO EX VIVO LUNG PERFUSION (EVLP) SYSTEM

Gas for Deoxygenation $86\% N_2$, $8\% CO_2$, $6\% O_2$

Red: Venous (Oxygenated) perfusate Blue: Arterial (Deoxygenated) perfusate



XVIVO Chamber with Lungs

Perfusion: 40% CO, LAP 5mmHg, PAP 10-12mmHg

Ventilation: 7cc/kg, 7BPM, PEEP 5, FiO₂ = 21%

Health Network

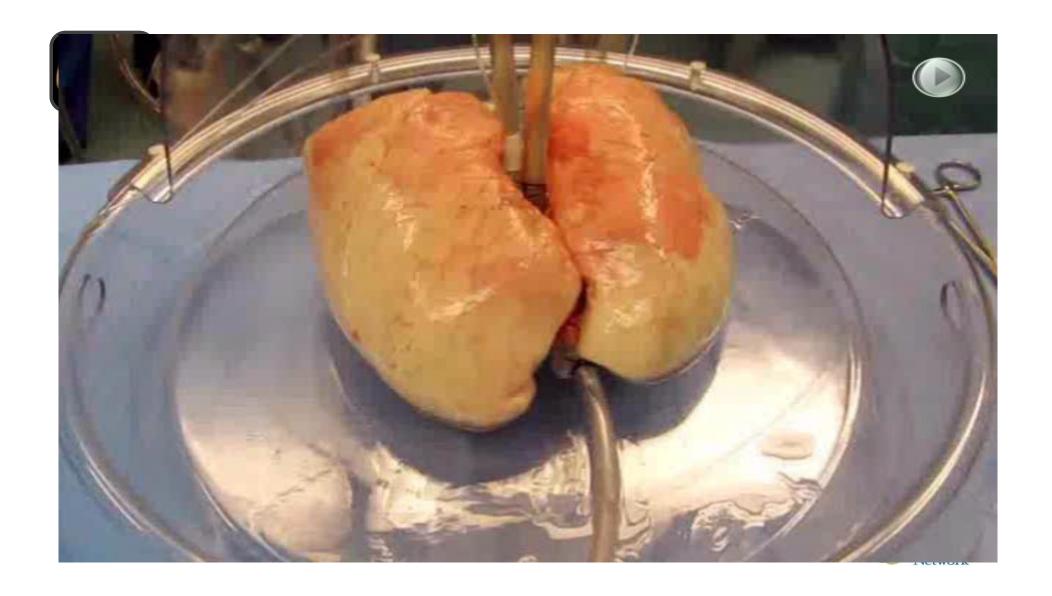
Cypel et al. J Heart Lung Transplant 2008; 27(12):1319-25.





Ex Vivo Lung Perfusion in Lung Transplantation

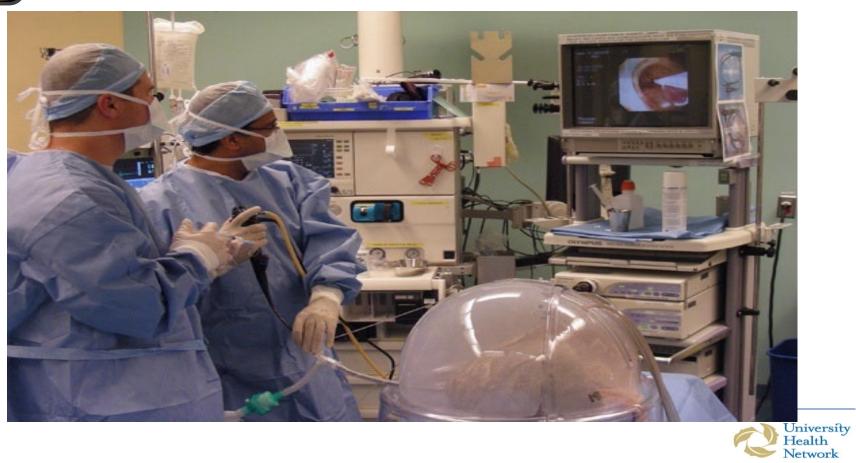








Bronchoscopy



Lung X-ray







The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

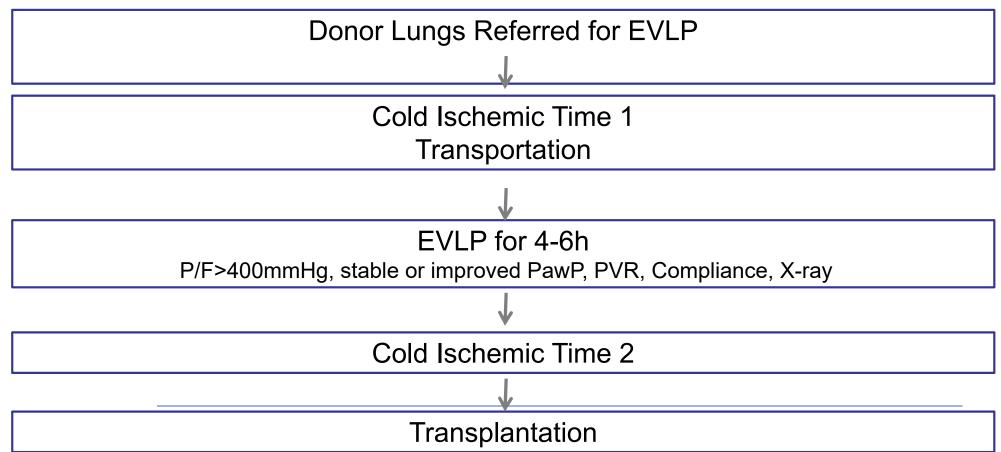
Normothermic Ex Vivo Lung Perfusion in Clinical Lung Transplantation

Marcelo Cypel, M.D., Jonathan C. Yeung, M.D., Mingyao Liu, M.D., Masaki Anraku, M.D., Fengshi Chen, M.D., Ph.D., Wojtek Karolak, M.D., Masaaki Sato, M.D., Ph.D., Jane Laratta, R.N., Sassan Azad, C.R.A., Mindy Madonik, C.C.P., Chung-Wai Chow, M.D., Cecilia Chaparro, M.D., Michael Hutcheon, M.D., Lianne G. Singer, M.D., Arthur S. Slutsky, M.D., Kazuhiro Yasufuku, M.D., Ph.D., Marc de Perrot, M.D., Andrew F. Pierre, M.D., Thomas K. Waddell, M.D., Ph.D., and Shaf Keshavjee, M.D.





Study Design





Early outcomes similar in both groups

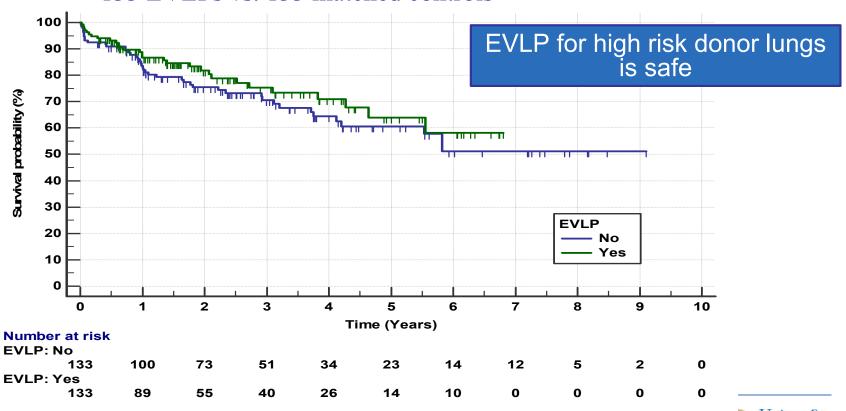
End Point		EVLP Lungs (N = 20)		Control Lungs (N=116)	Absolute Difference†	P Value;
	Donors without a Heartbeat (N=9)	Brain-Dead Donors (N=11)	Total (N = 20)			
					percentage points (95% ⊂I)	
Primary end point §						
PGD grade 2 or 3 at 72 hr (%)	11	18	15	30	15 (-3 to 33)	0.11
Secondary end points∫						
PGD grade 2 or 3 at ICU arrival (%)	33	18	25	30	5 (-15 to 26)	0.30
PGD grade 2 or 3 at 24 hr (%)	11	18	15	36	21 (3 to 39)	0.07
PGD grade 2 or 3 at 48 hr (%)	33	27	30	35	5 (-17 to 27)	0.46
ECMO (%)	0	0	0	4		0.37
PaO ₂ :F1O ₂ on arrival in ICU (mm Hg)						0.51
Median	420	423	422	372		
Range	85-518	86-538	85-538	49-591		
Mechanical ventilation after transplan- tation (days)						0.15
Median	2	2	2	2		
Range	1–27	1-101	1-101	1-43		
ICU stay after transplantation (days)						0.68
Median	4	5	4	4		
Range	1-34	1-101	1-101	1-103		
Hospital stay after transplantation (days)						0.39
Median	19	34	23	27		
Range	7-54	11-101	7-101	9–156		





Survival Probability

133 EVLPs vs. 133 matched controls



Yeung, J. JHLT 2016





Clinical Problem - PGD







EVLP is associated with decreased rates of PGD

Category	/	No EVLP (n=133)	EVLP (n=133)	р
Hospital IQR)	LOS (Median,	23 (16.5-43)	21 (16-34)	0.21
ICU LOS	(Median, IQR)	4 (2-14.5)	4 (2-10.5)	0.83
ISHLT P	GD at 72h			0.02
0		82 (61.7%)	92 (69.2%)	
1		8 (6.0%)	18 (13.5%)	
2		30 (22.6%)	14 (10.5%)	
3		12 (9.0%)	9 (6.8%)	

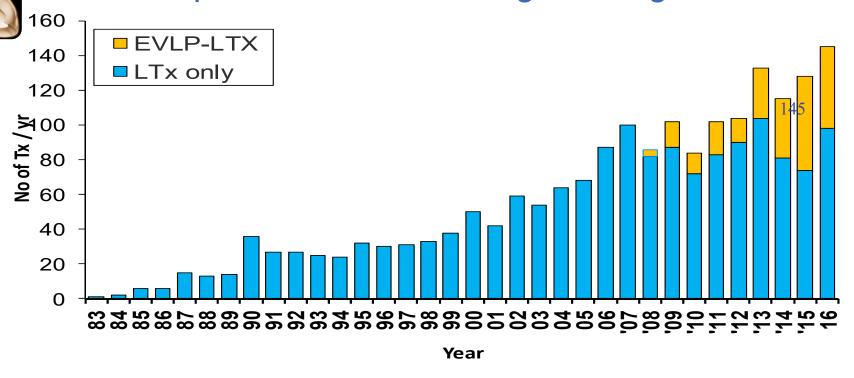
Yeung. J, JHLT 2016

Table 1.3: ISHLT PGD Grading⁸⁷

Grade	P/F ratio	Chest x-ray	
0	> 300	Normal	_
1	> 300	Diffuse allograft infiltrates	ers
2	200-300	Diffuse allograft infiltrates	th
3	₹200	Diffuse allograft infiltrates	orl

ersity th ork

Impact of EVLP on Lung Tx Program

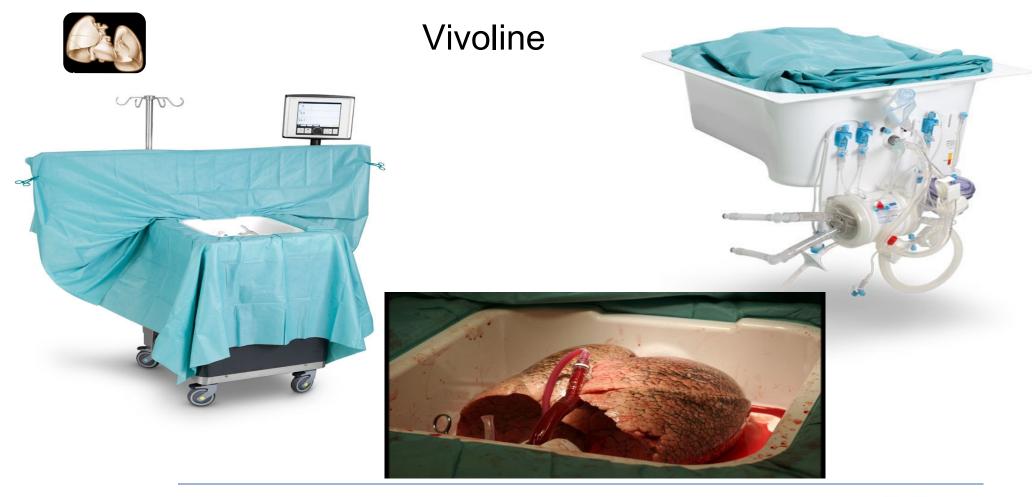


Year	Cases	Used	%	% Lung Tx	
2018-19	127	86	68%	38%	
2019-20	123	77	61%	30%	Iniversity Tealth
					Health Network



EVLP Industry









XVIVO Perfusion Inc.

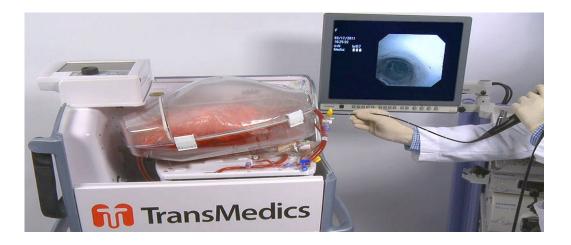






TransMedics









Perfusion Protocols

	Toronto	Lund (Vivoline)	Organ Care System
Perfusion			
Target total	40% cardiac output (1 h)	100% cardiac output (1 h)	2·5 L (15-30 min)
Start rate	150 mL/min	100 mL/min	200 mL/min
Pulmonary arterial pressure	<15 mm Hg	<20 mm Hg*	<20 mm Hg
Left atrial pressure	3-5 mm Hg	0 mm Hg	0 mm Hg
Pump	Centrifugal	Roller	Pulsatile
Perfusate	2 L Steen solution	2 L Steen solution plus red blood cells (haematocrit 10%)	1-5 L Steen solution plus red blood cells (haematocrit 20%)
/entilation			
Mode	Volume controlled	Volume controlled	Volume controlled
Tidal volume	7 mL/kg	5-7 mL/kg	6 mL/kg
Frequency	7 bpm	20 bpm	10 bpm
Positive end-expiratory pressure	5 cm H ₂ O	5 cm H ₂ O	5 cm H ₂ O
Fraction of inspired oxygen	21%	50%	21%
[emperature			
Start ventilation	32°C	32°C	32°C
Start perfusion	25°C	25°C	32°C
Start evaluation	37°€	3/°C	37°€
Perfusion time	12 h	2 h	Duration of transpor
Pulmonary arterial pressure of <1	5 mm Hg used in pigs.	+Mehn time of 5 h in pilet study (ra	inge 3–10).78
able 2: Ex-vivo lung perfusion	protocols		

Munshi L, Keshavjee S, Cypel M **Donor management and lung preservation for lung transplantation** The Lancet Respiratory Medicine, 2013, 1(4);318 - 328,





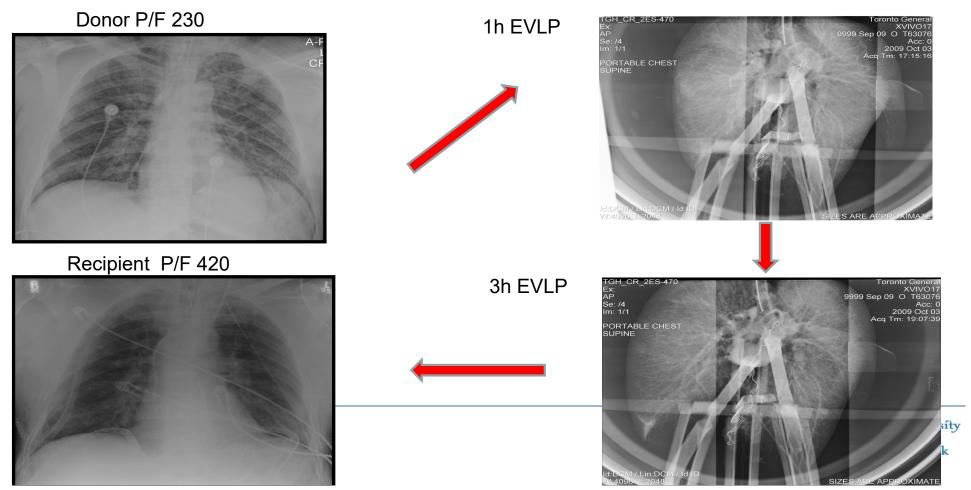
Exvivo treatment opportunities

- 1- Pulmonary Edema
- 2- Brain death associated inflammation
- 3- Infection, Pneumonia
- 4- Aspiration
- 5- Pulmonary emboli
- 6- Ischemia-reperfusion injury
- 7- Immunologic preparation





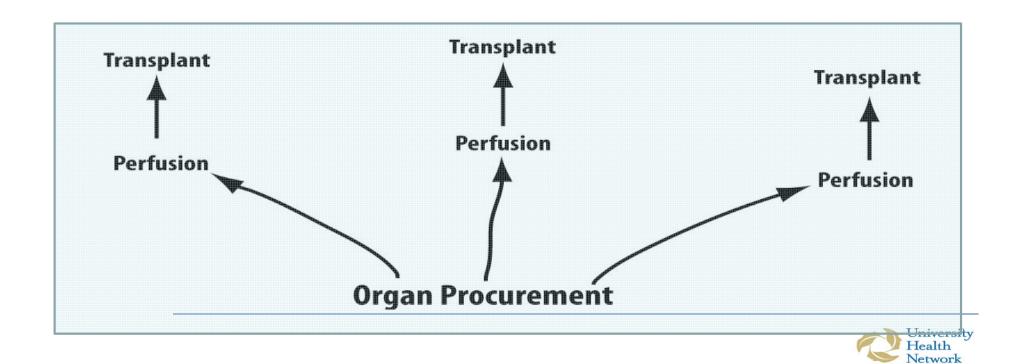
Resolution of pulmonary edema



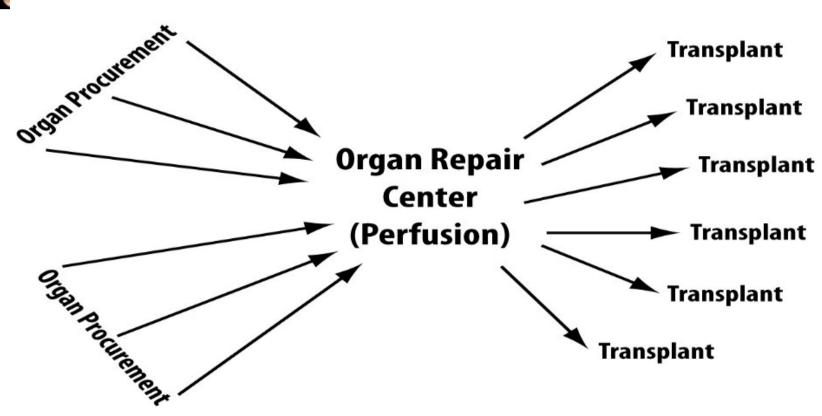


Conventional Model of Organ Procurement

• Transplant Center - Centric Model







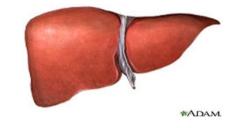






Chapter Two

EXVIVO LIVER PERFUSION SYSTEM





UHN Experience: July 8, 2015





Search

News Article

Jul 28, 2015

UHN Toronto General Hospital perform first liver transplant with the OrganOx metra

UHN Toronto General Hospital, Dr David Grant and Dr Markus Selzner have announced the first liver transplant at UHN using the OrganOx *metra*



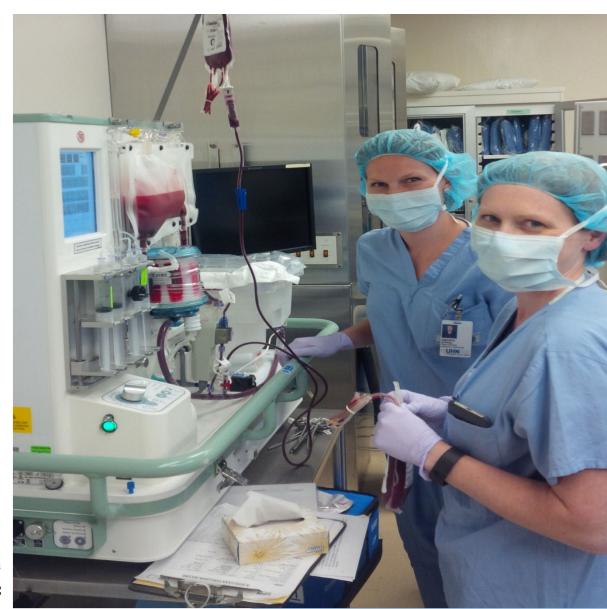
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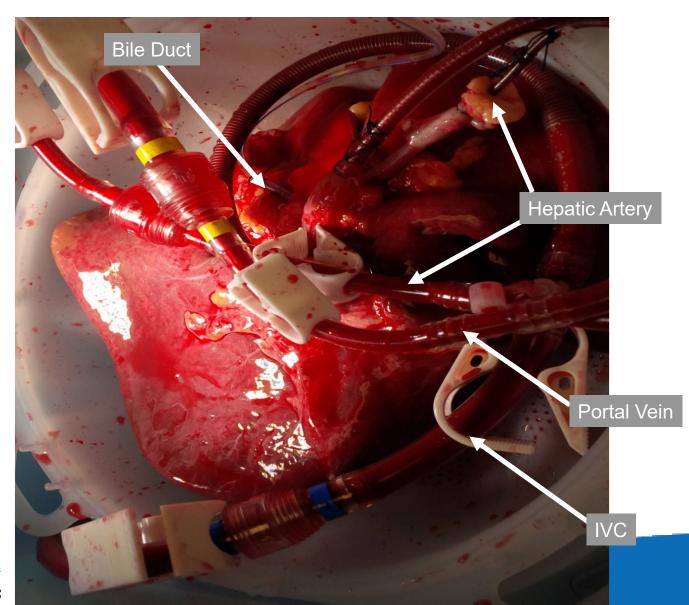




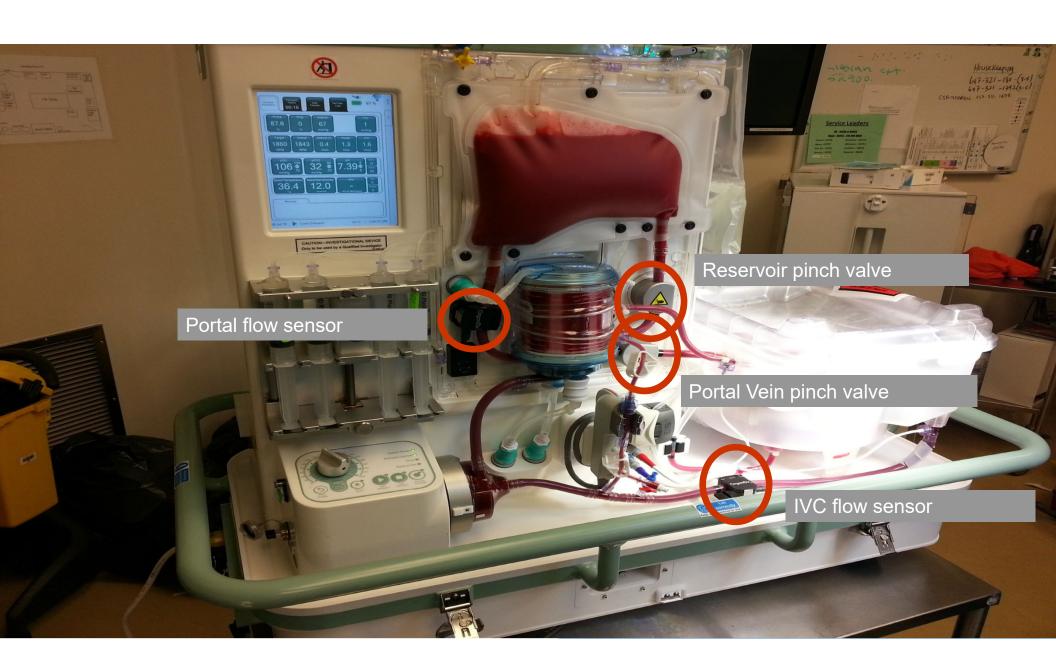












Clinical Trial Normothermic Ex Vivo Liver Perfusion in Toronto

ORIGINAL ARTICLE

SELZNER ET AL.

Normothermic Ex Vivo Liver Perfusion Using Steen Solution as Perfusate for Human Liver Transplantation: First North American Results

Markus Selzner, ¹ Nicolas Goldaracena, ¹ Juan Echeverri, ¹ Johan M. Kaths, ¹ Ivan Linares, ¹ Nazia Selzner, ² Cyril Serrick, ³ Max Marquez, ¹ Gonzalo Sapisochin, ¹ Eberhard L. Renner, ² Mamatha Bhat, ² Ian D. McGilvray, ¹ Leslie Lilly, ² Paul D. Greig, ¹ Cynthia Tsien, ² Mark S. Cattral, ¹ Anand Ghanekar, ¹ and David R. Grant

Departments of Surgery; ²Medicine, and ³Perfusion Services, Multi-Organ Transplant Program, Toronto General Hospital, Toronto, Ontario, Canada

The European trial investigating normothermic ex vivo liver perfusion (NEVLP) as a preservation technique for liver transplantation (LT) uses gelofusine, a non–US Food and Drug Administration–approved, bovine-derived, gelatin-based perfusion solution. We report a safety and feasibility clinical NEVLP trial with human albumin-based Steen solution. Transplant outcomes of 10 human liver grafts that were perfused on the Metra device at 37 °C with Steen solution, plus 3 units of erythrocytes were compared with a matched historical control group of 30 grafts using cold storage (CS) as the preservation technique. Ten liver grafts were perfused for 480 minutes (340-580 minutes). All livers cleared lactate (final lactate 1.46 mmol/L; 0.56-1.74 mmol/L) and produced bile (61 mL; 14-146 mL) during perfusion. No technical problems occurred during perfusion, and all NEVLP-preserved grafts functioned well after LT. NEVLP versus CS had lower aspartate aminotransferase and alanine aminotransferase values on postoperative days 1-3 without reaching significance. No difference in postoperative graft function between NEVLP and CS grafts was detected as measured by day 7 international normalized ratio (1.1 [1-1.56] versus 1.1 [1-1.3]; P = 0.5) and bilirubin (1.5; 1-7.7 mg/dL versus 2.78; 0.4-15 mg/dL; P = 0.5). No difference was found in the duration of intensive care unit stay (median, 1 versus 2 days; range, 0-8 versus 0-23 days; P = 0.5) and Diodo-Clusion, 3 3th occurred to 1.1 versus 1.3 days; range, 8-17 versus 7-89 days; P = 0.23). Major complications P = 0.5 and P = 0.5 on the NEVLP grades P = 0.5 of the position of the

Methods

Match control study design 1:3

Liver transplants with NEVLP as preservation method (n=10)

NEVLP Transplantation

Control group:
Liver transplants with CS as preservation method (n=30)

CS Transplantation

- Matched for
 - donor type (DCD vs BDD)
 - medical MELD (severity of liver disease)
 - donor and recipient age
 - preservation time
- 3 months follow-up
- Exclusion: fulminant liver failure, multiorgan transplant

Results

TABLE 3. Graft Function and Injury After Transplantation

	NEVLP (n = 10)	CS (n = 30)	<i>P</i> Value
ALT peak 48 hours, U/L	619 (55-2858)	949 (233-3073)	0.55
INR peak	2.6 (2-4.4)	2.7 (1.7-5.8)	0.61
INR 1 week	1.1 (1-1.56)	1.1 (1-1.3)	0.47
INR 3 month	1 (1-2)	1 (1-2)	0.91
Bilirubin 1 week, mg/dL	1.5 (1.0-7.7)	2.78 (0.4-15)	0.49
Bilirubin 3 month, mg/dL	0.4 (0.2-0.8)	0.6 (0.2-18)	0.21
ALP 1 week, U/L	202 (96-452)	147 (87-456)	0.21
ALP 3 month, U/L	111 (101-136)	132 (54-657)	0.33
Creatinine 1 week, mg/dL	1.0 (0.5-2.0)	0.9 (0.5-2.3)	0.76
Creatinine 3 month, mg/dL	1.1 (0.9-2.4)	1.1 (0.3-1.8)	0.53

NOTE: Data are provided as median and range.



First randomized clinical trial for NEVLP

- Peter Friend et al. presented outcomes of 121 NEVLP vs 101 CS transplants.
- Primary outcome was difference in peak AST within 7 days after transplantation
- Secondary outcomes were organ utilization, preservation time, post-reperfusion syndrome, EAD and graft and patient survival

Peter Friend et al. 2017 at International Liver Transplantation Society conference





Primary outcome

DBD	NEVLP (n=87)	SCS(n=80)	Reduction	p-value
Peak AST (DBD)	526.2 (424.9- 651.5)	880.2 (795.2- 1192.3)	40.2%	p<0.001

DCD	NEVLP (n=33)	SCS (n=20)	Reduction	p-value
Peak AST (DCD)	389.7 (286.7- 529.9)	1458.1 (913.4- 2327.6)	73.3%	p<0.001

Peter Friend et al. 2017 at International Liver Transplantation Society conference





Secondary outcomes

	NEVLP	scs	P-value
Transplanted	121	101	
Discarded	16 (11.7%)	32 (24.1%)	p=0.008
Grafts with moderate or severe steatosis	29 (24%)	12 (11.9%)	p=0.019
Total preservation time	11hrs 20mins	7hrs 9mins	p<0.0001
Machine perfusion time	10hrs 8mins		
Post-reperfusion syndrome	15 (12.4%)	29 (33%)	p=0.0002
Early Allograft Dysfunction (EAD)	12 (10.1%)	29 (29.9%)	p=0.0002

Peter Friend et al. 2017 at International Liver Transplantation Society conference

Clinical Trials: Normothermic Ex Vivo Liver Perfusion

Organox/ Metra







LiverAssist







Chapter Three

Normothermic Exvivo Kidney Perfusion





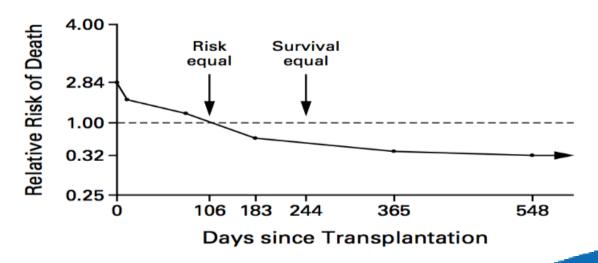


Kidney Transplantation

Kidney transplantation vs. dialysis

- Longer patient survival
- Reduced patient morbidity
- Better quality of life (freedom from dialysis, increased energy, less diet restrictions)
- Improved cost-effectiveness

Kidney transplantation is the treatment of choice for end-stage renal disease (ESRD)



Wolfe, R. A. et al. (1999) NEJM, *341*(23), 1725–1730. Meier-Kriesche et al. (2000) *Kidney Int*, *58*(3), 1311–1317.

PROBLEM: OUTCOME DCD

Effect of donor age and cold storage time on outcome in recipients of kidneys donated after circulatory death in the UK: a cohort study



Dominic M Summers, Rachel J Johnson, Alex Hudson, David Collett, Christopher J Watson, J Andrew Bradley

Outcome

- 3 year graft survival not different between DCD and DBD (HR 1.14, p = 0.16)
- Donor age older than 60 years associated with increased risk of graft loss for both groups (HR 2.35, p < 0.0001) (no difference between the groups)
- Prolonged cold ischemic time (>24h vs. <12h) associated with poorer graft survival for kidneys from DCD donors compared to DBD donors (HR 2.36, p = 0.004)
- Higher delayed graft function rate (DGF) in DCD transplants compared to DBD transplants (OR 3.08, p < 0.0001)





Public Affairs Toolkit Updates from CEO CEO Reports

UHN Purpose & Values Strategy & Planning

About UHN Committees Templates

Courage to Lead
Accreditation
Advance Care Planning
eLearning
IP Education & Care
Patient Experience
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UHN Corporate Intranet UHN Public Web Site

UHN NEWS Device keeps donor kidneys healthy outside the body until transplant



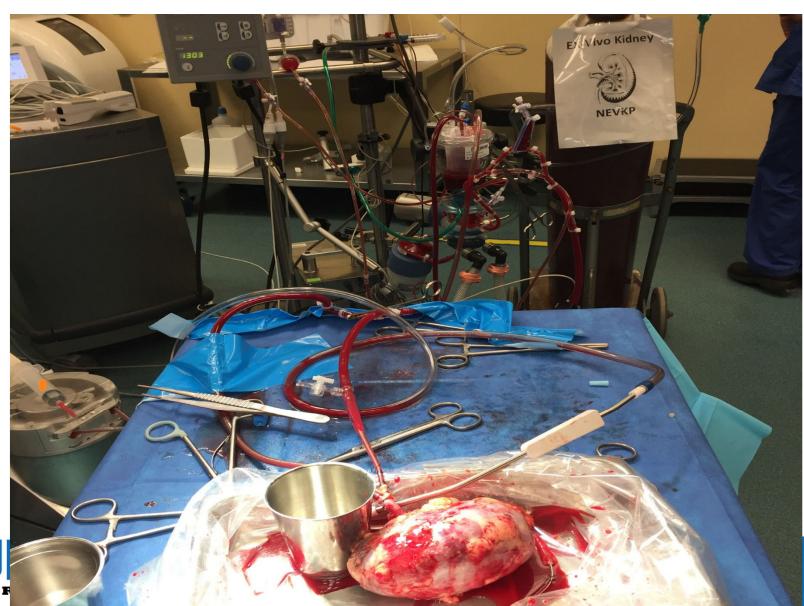
Dr. Markus Selzner, transplant surgeon at UHN, prepares the ex vivo organ perfusion system which allows a donor kidney to improve and repair itself, potentially leading to better outcomes for patients. November 2017 was the first time it has been used successfully in North America on a kidney from a deceased donor. (Photo: UHN)

A deceased donor kidney has been preserved and kept healthy outside the body in a device that mimics the body's physiological functions and successfully transplanted into a human, for the first time in North America.

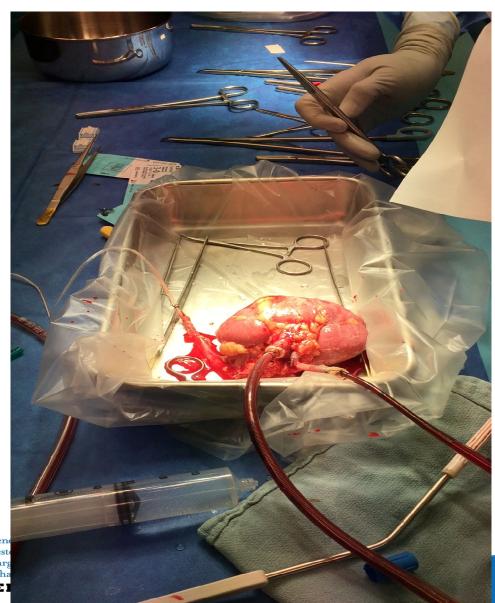
The technique, unique solution, and device are part of a Phase I clinical trial at Toronto General Hospital (TG), University Health Network (UHN), assessing the safety of the device, with subsequent phases examining its efficacy.

Kidneys are the most frequently transplanted solid organ, but a continuing shortage of donor kidneys











First in Man Renal Transplantation After Ex Vivo Normothermic Perfusion

Sarah A. Hosgood and Michael L. Nicholson

Results:

- Left NP kidney transplanted into a 55-year-old female recipient:
 - Slow graft function but remained dialysis independent
 - Serum creatinine 3 months post KTx: 132 μmol/L
- Right SCS kidney transplanted into a 52-year-old male recipient:
 - Delayed graft function period of 26 days requiring dialysis
 - Serum creatinine 3 months post KTx: 218 µmol/L

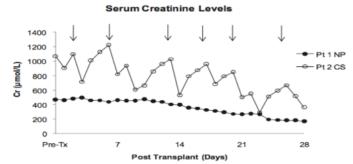


FIGURE 1. Serum creatinine levels of patient 1; normothermic perfusion (NP) and patient 2; cold storage (CS) from pretransplant (Pre-Tx) to 28 days posttransplant. The arrows indicate the episodes of dialysis therapy in patient 2 on days 2, 6, 13, 17, 20, and 26 posttransplant.



Renal Transplantation After *Ex Vivo* Normothermic Perfusion: The First Clinical Study

M. L. Nicholson* and S. A. Hosgood

Methods:

- 18 ECD kidneys underwent static cold storage and <u>1 additional hour</u> of normothermic perfusion at 34.6 ° C immediately before transplantation
- 47 ECD kidneys underwent static cold storage (control group)
 (matched for donor and recipient age, CIT, first transplant only)



Renal Transplantation After *Ex Vivo* Normothermic Perfusion: The First Clinical Study

M. L. Nicholson* and S. A. Hosgood

Results:

- Delayed graft function (defined as need for dialysis within first 7 days)
 - 1/18 patients in NEVKP group (5.6%)
 - 17/47 patients in SCS only group (36.2%) (p = 0.014)
- No difference in graft (p = 0.510) or patient survival (p = 1.000)







Chapter Four

Exvivo Heart Perfusion



TransMedics OCS (Organ Care System)



OCS Heart

- Monitor Cardiac Output, temperature, coronary flow, blood pressure
- Allows direct continuous visual and ECG surveillance
- Low percentage (2%) of primary graft failure with warm perfusion times up to 6 hours
- Very low rate of early incidence of rejection



TransMedics OCS



COURAGE LIVES HERE

DCD Heart

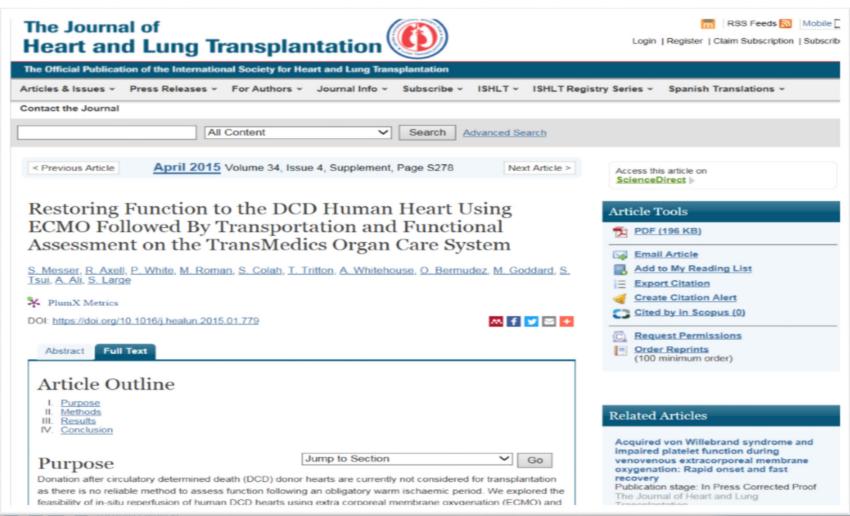




DCD Heart Protocol

- Following declaring of death, the donor transferred to OR.
- Rapid sternotomy is performed and the pericardium is opened.
- The right atrium is opened and 1.2 to 1.5L of blood is rapidly drained from the donor immediately prior to the flush of the abdominal organs.
- The donor blood is mixed together with 500cc of OCS solution that is used to prime the perfusion circuit.
- The heart is then excised and placed on the TransMedics OCS device.
- Normothermic machine perfusion is then started.
- A detachable device monitor with control capability continuously displays the ECG, aortic
 pressure, pump flow, coronary flow and haematocrit.
- Serial arterial and venous lactate measurements are made to optimize preservation of the organ.







To be continued...









Thank You

