

Actualités sur les machines de perfusion cardiaque



*Erwan Flécher, CHU Pontchaillou, Rennes
Ouest Transplant, Orléans, 15 novembre 2019.*

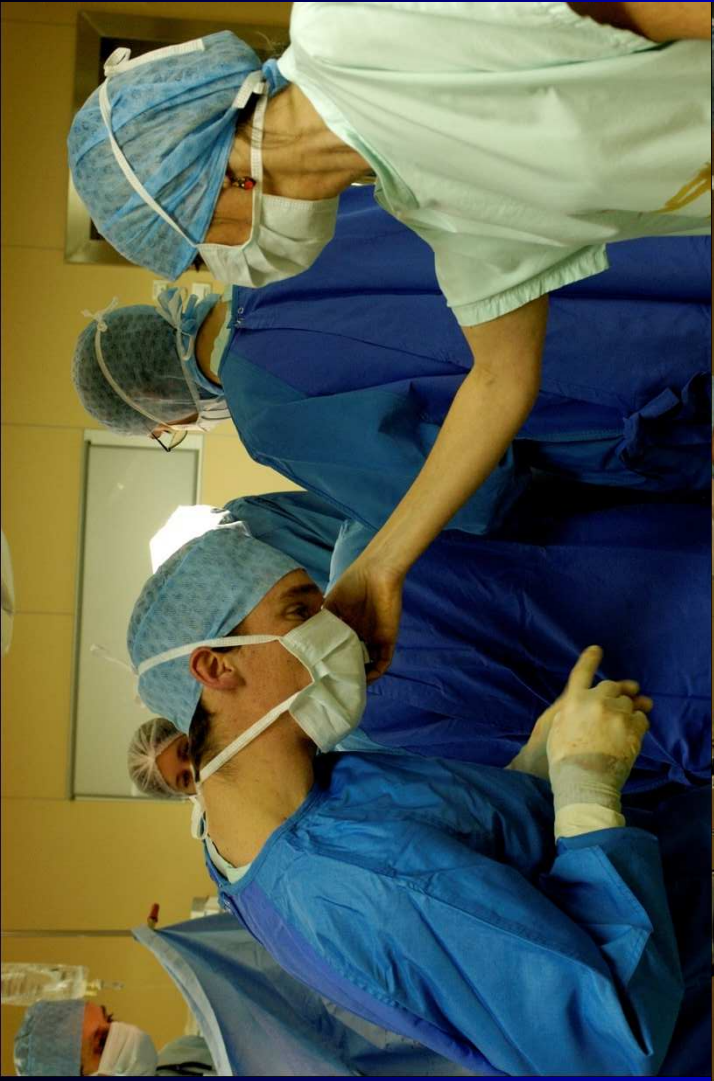
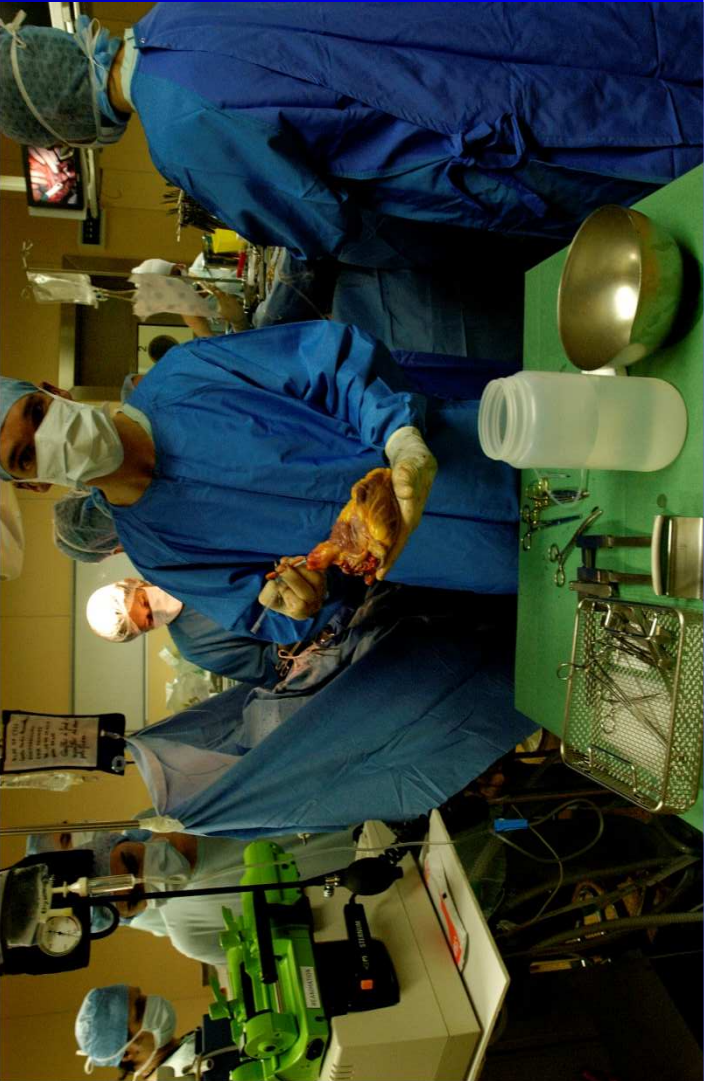
Déroulement de la Transplantation

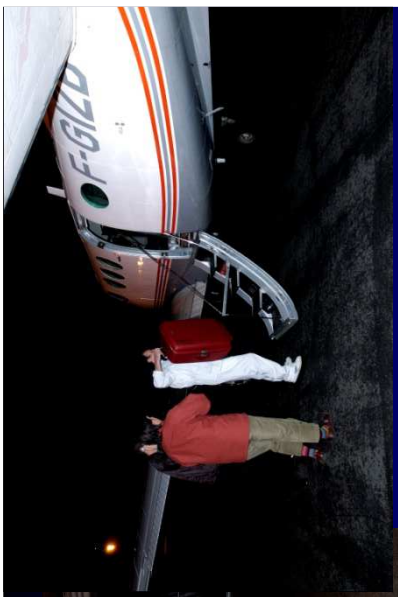
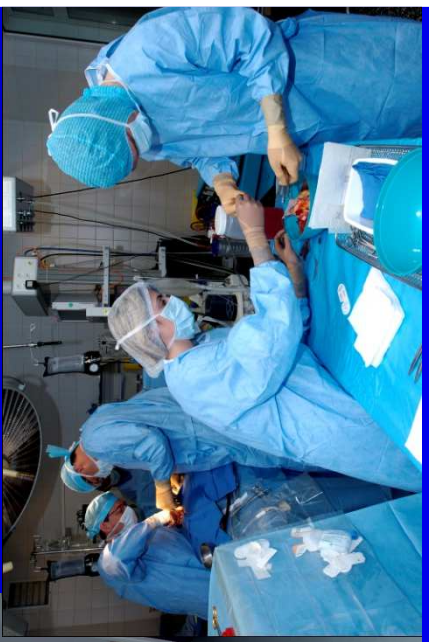
- ☞ Appel
- ☞ Acceptation du greffon: critères
- ☞ Organisation de la greffe:
plusieurs équipes à coordonner,
horaires, transports
- ☞ Prélèvement cardiaque: excision
du cœur, évaluation à thorax
ouvert+++ , transport dans liquide
conservation réfrigéré
- ☞ Transplantation



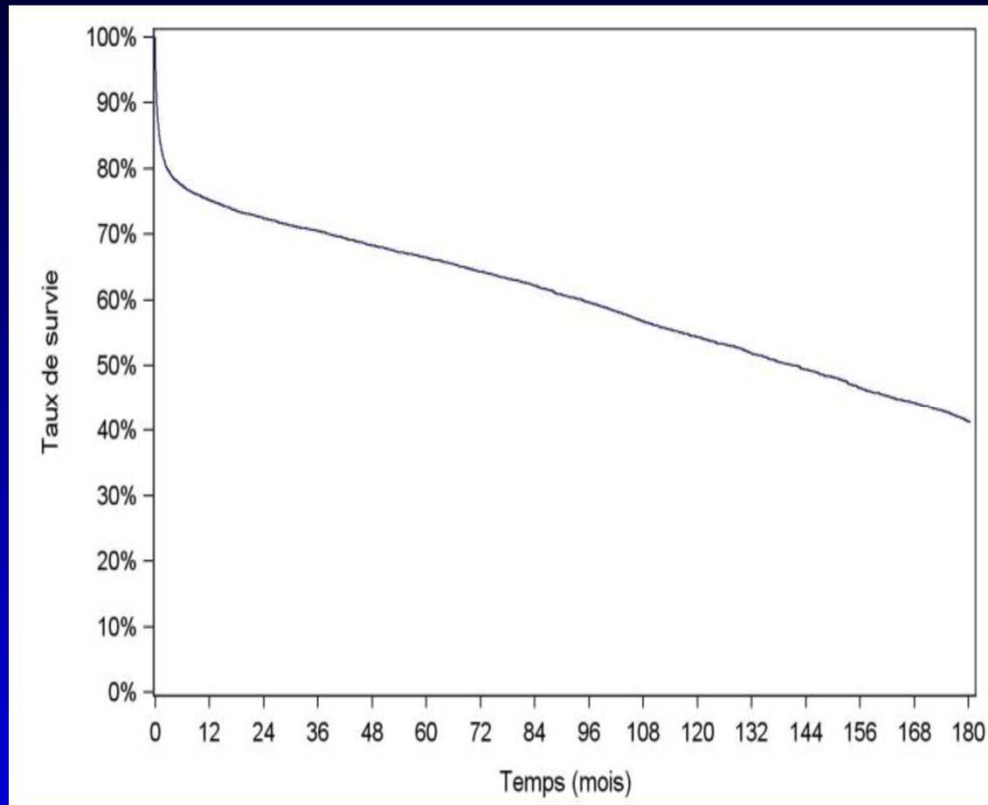








Survie après 1^{ère} greffe en France



Une survie (1 an) en
amélioration!

2013-2016: 79%

2009-2012: 77%

2005-2008: 72%



Une population grave!

2017: 53% sous inotropes, 23%
sous ECMO, 11% intubés, 25%
créat > 120, 16% bili > 35.

Période de greffe	N	Survie à 1 mois	Survie à 1 an	Survie à 5 ans	Survie à 10 ans	Survie à 15 ans	Médiane de survie (mois)
1993-juin 2016	8642	84,6% [83,8% - 85,4%]	75,2% [74,3% - 76,1%]	66,4% [65,4% - 67,5%]	54,3% [53,2% - 55,5%]	41,3% [40,0% - 42,7%]	141,2 [135,4 - 147,1]
nombre de sujets à risque*		7273	6367	4492	2648	1307	

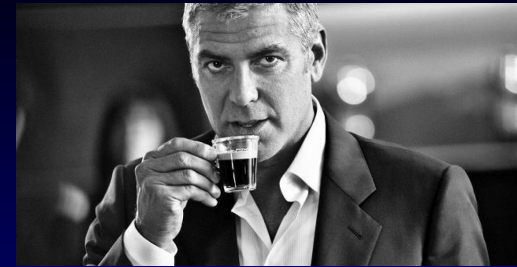
Gold standard

- ☞ Froid (4°C)
- ☞ Liquide préservation
- ☞ Economique (très)
- ☞ Bons résultats
- ☞ Historique



PARAGONIX®
Advancing Organ Preservation

What Else?



Innovative cold storage of donor organs using the Paragonix Sherpa Pak™ devices

S.G. Michel^{1,2}, G.M. LaMuraglia II¹, M.L.L. Madariaga¹, Lisa M. Anderson^{3,4}

¹Transplantation Biology Research Center, Department of Surgery, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA; ²Department of Cardiac Surgery, Ludwig-Maximilians-University, Munich, Germany;

³Paragonix Technologies, Inc., Braintree, MA, USA; ⁴Corresponding author: Lisa M. Anderson

Testing Conditions

Temperature profile
 “Hot” run: 1h @ 22°C, 1h @ 31°C, 15h @ 22°C, 1h @ 31°C, then 22°C until 30h
 “Cold” run: 1h @ 22°C, 1h @ -8°C, 15h @ 22°C, 1h @ -8°C, then 22°C until 30h

Individual Test Run Data

		Wetted probe					
Run#1	“Hot” Run #1	24 h	26 h	28 h	30 h		
Sample Size		8641	9361	10081	10801		
Range (°C)		4.2-5.7	4.2-5.9	4.2-6.5	4.2-7.2		
Mean ± St. dev.		4.65±0.41	4.74±0.49	4.84±0.60	4.97±0.77		
Run#2	“Hot” Run #2						
Sample Size		2881	121	3361	3601		
Range (°C)		6.6-7.5	6.6-8.0	6.6-8.6	6.6-9.2		
Mean ± St. dev.		6.96±0.29	7.02±0.35	7.11±0.47	7.23±0.64		
Run#3	“Cold” Run #1						
Sample Size		8641	9361	10081	10801		
Range (°C)		4.6-6.2	4.6-6.6	4.6-7.2	4.6-7.8		
Mean ± St. dev.		5.53±0.33	5.59±0.39	5.68±0.50	5.80±0.66		
Run#4	“Cold” Run #2						
Sample Size		2881	3121	3361	3601		
Range (°C)		4.6-6.7	4.6-7.3	4.6-7.8	4.6-8.6		
Mean ± St. dev.		5.93±0.33	6.01±0.43	6.12±0.57	6.26±0.76		
Major Finding	Maintenance of temperatures within a range of 4°C - 8°C for 24 h						

CONCLUSION

The Paragonix Sherpa Pak™ device may decrease cold injury of donor organs by maintaining the temperature consistently between 4°C and 8°C and therefore may decrease primary graft failure after organ transplantation.



Avantages/inconvénients

- Régulation permanente de la température souhaitée
- Monitoring et enregistrement
- Température homogène
- Greffon immergé
- Facilité de mise en œuvre
- Sans énergie électrique
- Design, manipulation

➤ Surcout



Une glacière « active »?

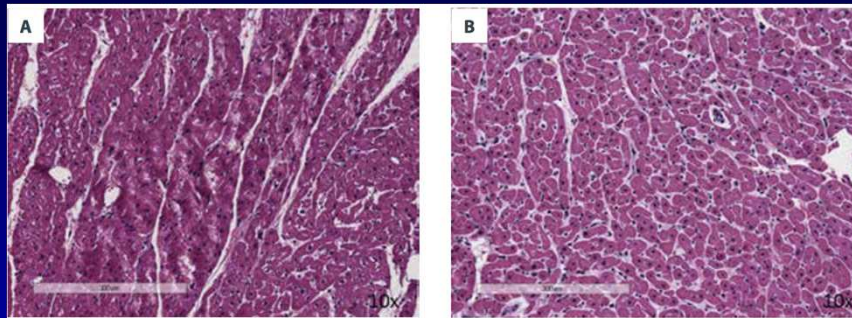
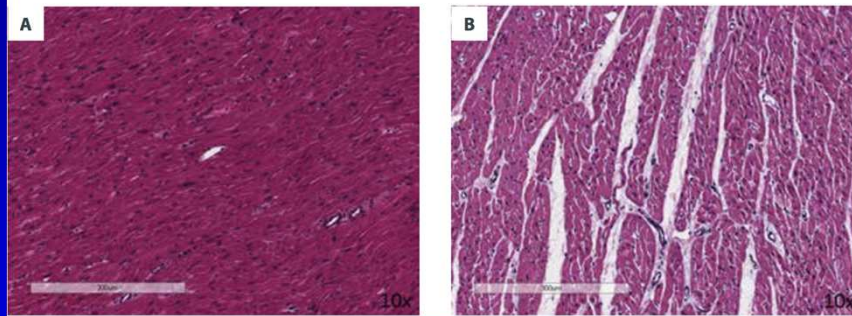


Figure 5. Histology of hearts after reperfusion on the Langendorff system. Representative H&E stains show signs of myocyte injury in the 4-h CS group (A) and no injury in the 4-h PP group (B).



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Preservation of Donor Hearts Using Hypothermic Oxygenated Perfusion



Conclusions

Hypothermic pulsatile perfusion of donor hearts during the storage interval is a simple technique that leads to a better-preserved cell structure compared to the conventional cold storage method. This may lead to less risk of primary graft failure

Mais faut-il rester à l'Age de glace?



The OCS Heart

The world's only portable ex-vivo heart perfusion system



Organ Care System Console

Portable, integrated perfusion & assessment system, fits in all standard modes of transportation for donor organs



Wireless Monitor

Controls and displays physiologic and functional parameters of the heart



Perfusion Module

A sterile, protective, biocompatible chamber that houses the heart and circulating perfusate

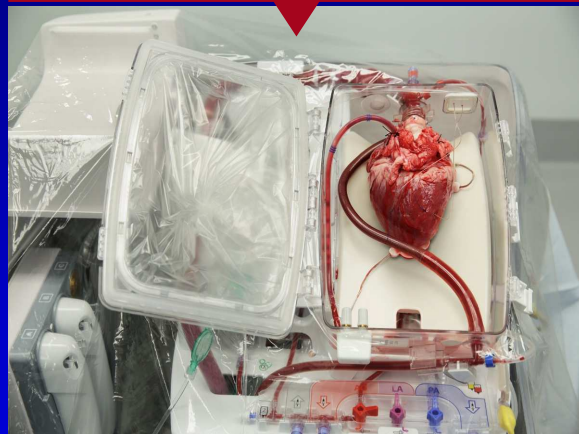


Heart Solution Set

Infused into blood circulation; provides nutrients and substrates

OCS System Designed to Address Limitations of Cold Storage

REDUCE ISCHEMIC INJURY



Warm Oxygenated
Blood Perfusion – Heart is
Beating

OPTIMIZE ORGAN CONDITION



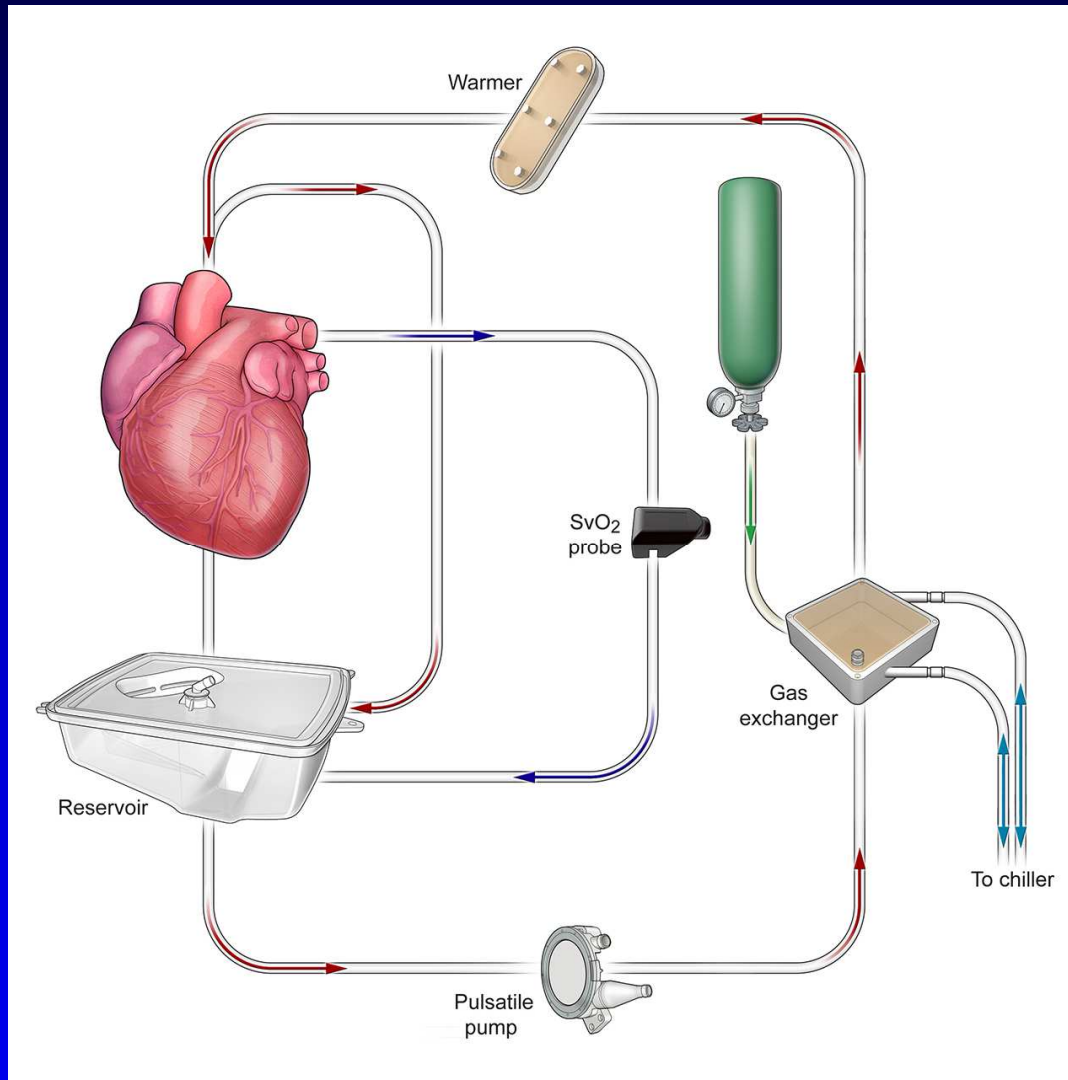
Optimize O₂ Delivery
Replenish Substrates &
Hormones

EX-VIVO ASSESSMENT



Metabolic Assessment &
Perfusion Parameters

Une CEC portative et transportable...



**CAUTION
HEAVY**

Un monitoring du greffon « Wifi »



The OCS™ Heart in Clinical Practice

☞ Sur Site PMO

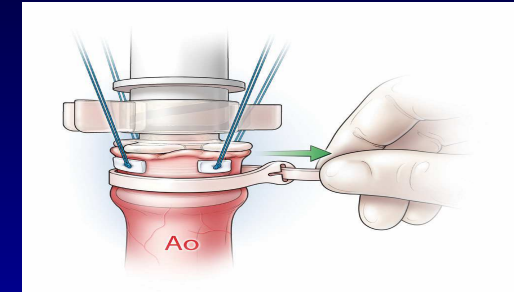
- Optimisation donneur
- Prélèvement sang (1,5L) et cardioplégie
- Cannulation Ao et AP
- Démarrage
- Stabilisation

☞ Transport

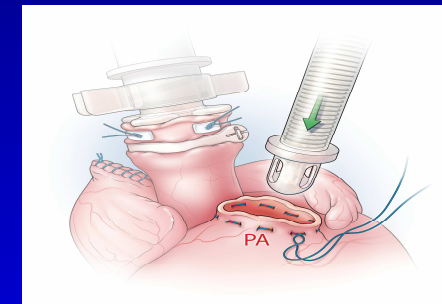
- Monitoring continu du greffon
- Ajustement paramètres de perfusion

☞ A la maison:

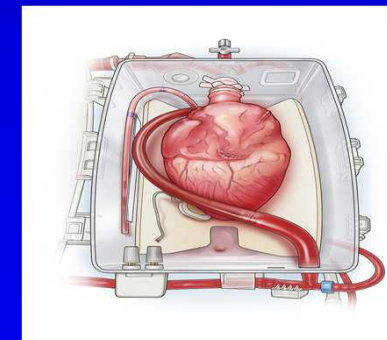
- Echo? Coro?
- Nouvelle cardioplégie
- Greffe



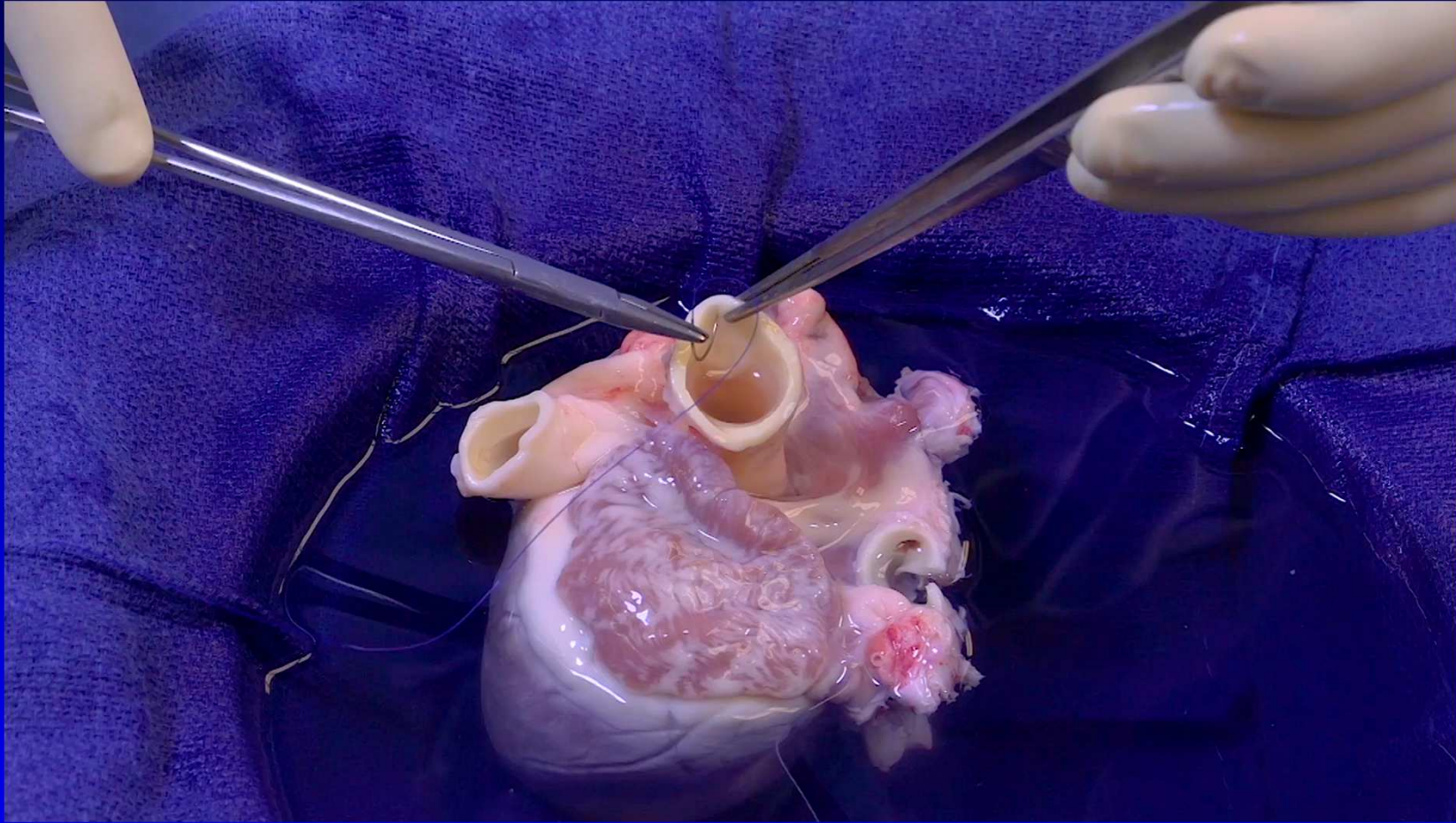
AO Cannulation



PA Cannulation



Cannulation Process



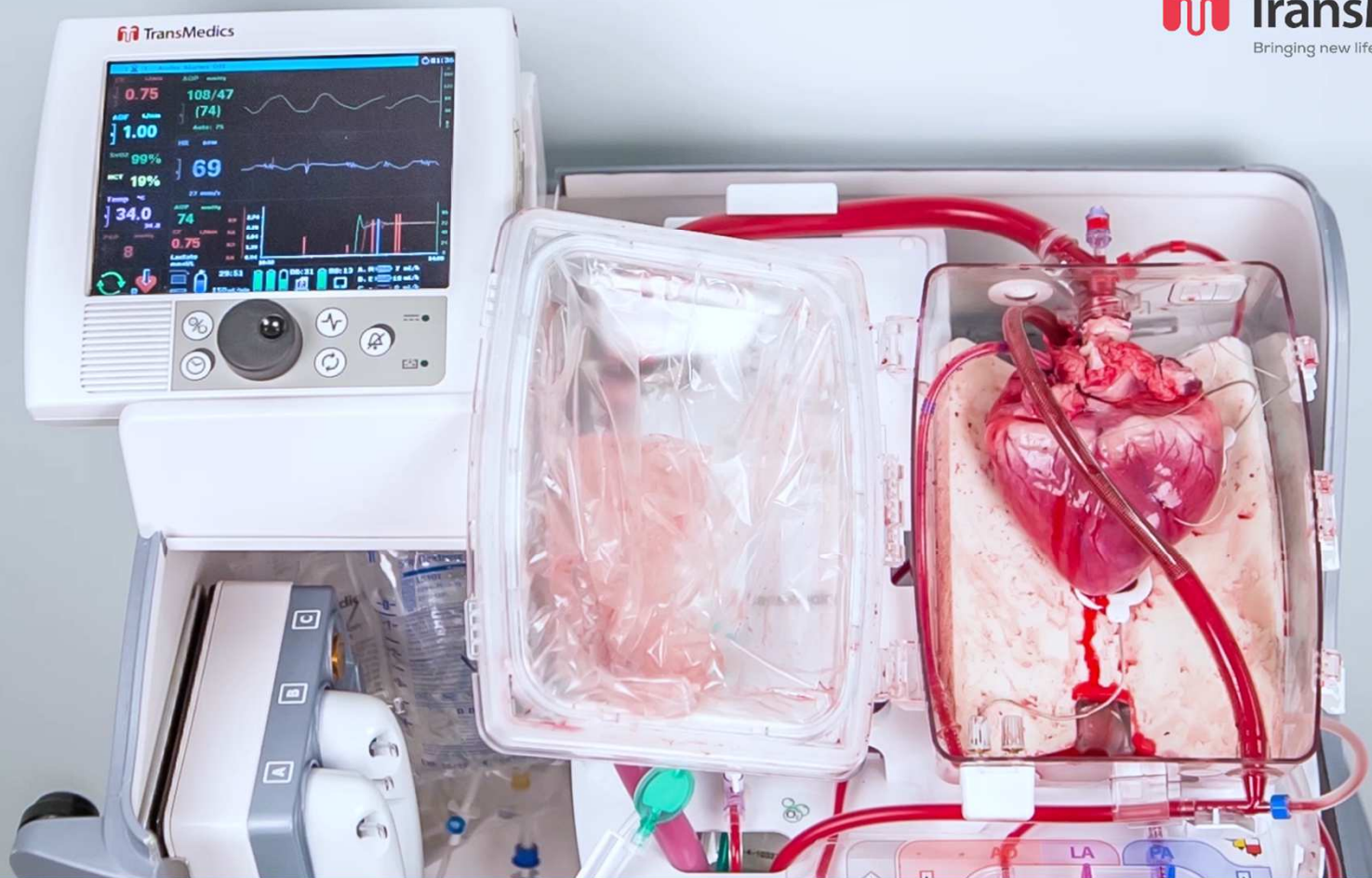
Instrumentation Process



The OCS™ Heart

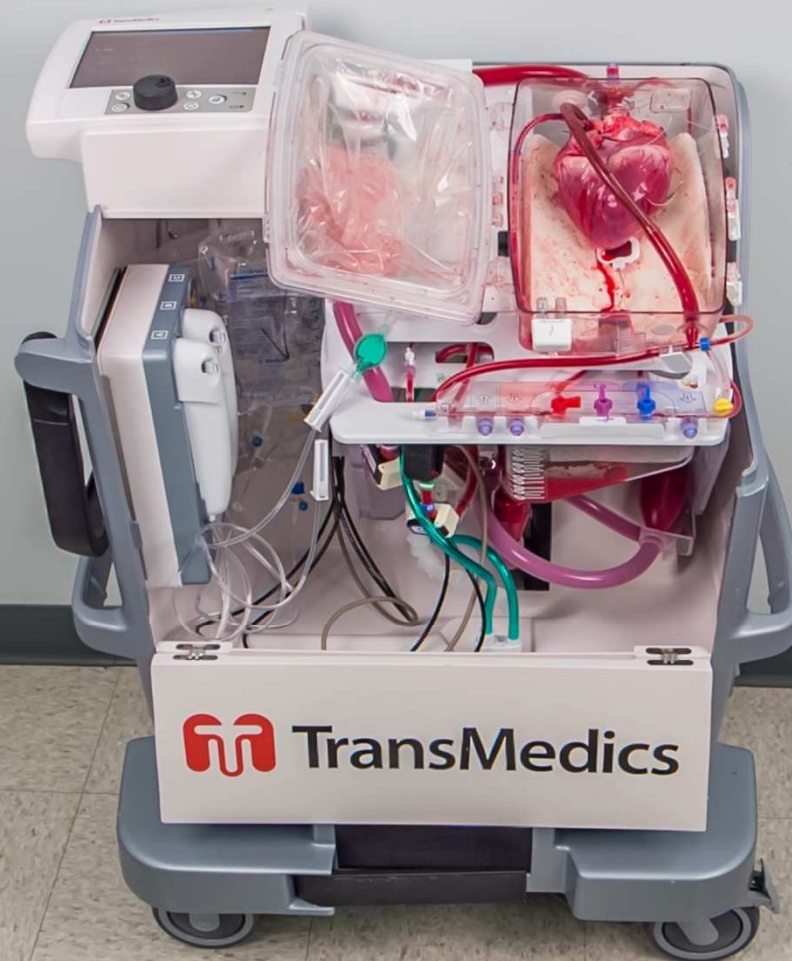
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 **TransMedics**
Bringing new life to organ transplant



The OCS™ Heart

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Inconvénients

- ➡ Cout: 30 à 35 000 euros/greffon !!!!!!!!!!!!!
- ➡ Encombrement, poids, ergonomie
- ➡ PMO plus compliqué, plus de personnel impliqué
- ➡ Working mode non fonctionnel à ce jour...
- ➡ Non inférieur, mais est ce supérieur?

Et en France?



3 hôpitaux
Financements...



OCS Heart Published Data

THE LANCET

Ex-vivo perfusion of donor hearts for heart transplantation (PROCEED II): a prospective multicentre, randomised non-inferiority trial

Alban Arshady, Ihabul Madihi, Alan Cheng, Yoon Jang, et al. *Lancet* 2014; 384: 1621-31

www.thelancet.com Published online April 12, 2014

Summary Background The Organ Care System is the only clinical platform for ex-vivo perfused donor hearts to be used for heart transplantation. We aimed to assess the clinical outcomes of the Organ Care System compared with hearts donated after circulatory death.

Methods We did this prospective, open-label, multicentre, randomised non-inferiority trial in the USA and Europe. Eligible heart-transplant candidates aged >18 yr and medical staff were not randomised into the Organ Care System or standard cold storage. We did analyses in the primary endpoint (1 yr survival) and in a secondary endpoint (3 yr survival).

Results Between June 25, 2006, and Sept 18, 2013, we randomly assigned 100 patients (50 in the Organ Care System group and 50 in the standard cold storage group) to the Organ Care System or standard cold storage. In the primary endpoint, 1 yr survival was similar in the Organ Care System group (92%) and the standard cold storage group (90%).

Conclusion Ex-vivo perfusion of donor hearts using the Organ Care System is not inferior to standard cold storage. This trial is registered with ClinicalTrials.gov, number NCT00485712.

Introduction Heart transplantation is the treatment of choice for many patients with end-stage heart disease. Despite substantial progress in many aspects of heart transplantation (eg, donor management, organ preservation, immunosuppression regimen), the technique for preservation of donor hearts is still cold ischemic. Cold storage leads to non-perfused donor hearts, which can impair heart function after transplantation. Prolonged cold ischemia time in the donor heart and death of the recipient, a limitation of cold ischemic storage, can also adversely affect use of donor hearts and possible organ sharing. In the past several decades there has been scientific and clinical interest in ex-vivo heart perfusion with oxygenated and normoxic perfusion to reduce ischemic injury to the donor heart and potentially enable ex-vivo assessment of heart function. Several ex-vivo perfusion systems have been developed, but none have been shown to be superior to standard cold storage for preservation of donor hearts for transplantation.

Summary Background The Organ Care System is the only clinical platform for ex-vivo perfused donor hearts to be used for heart transplantation. We aimed to assess the clinical outcomes of the Organ Care System compared with hearts donated after circulatory death.

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THE LANCET

Adult heart transplantation with distant procure ex-vivo preservation of donor hearts after circulatory death: a case series

Samuel Elvik, Arjan van Dieen, et al. *Lancet* 2014; 384: 1632-35

www.thelancet.com Published online April 12, 2014

Summary Background Orthotopic heart transplantation is the gold standard long-term treatment for a single heart failure. However, suitable cardiac donors are scarce. Although donation after circulatory death (DCD) is used for heart transplantation, it is not used for heart transplantation from donors after circulatory death.

Methods The recipients were patients at St Vincent's Hospital, Sydney, Australia. They received hearts donated after circulatory death from people younger than 40 years and with a 10% non-inferiority margin. We did analyses in the primary endpoint (1 yr survival) and in a secondary endpoint (3 yr survival).

Results Between June 25, 2006, and Sept 18, 2013, we randomly assigned 100 patients (50 in the Organ Care System group and 50 in the standard cold storage group) to the Organ Care System or standard cold storage. In the primary endpoint, 1 yr survival was similar in the Organ Care System group (92%) and the standard cold storage group (90%).

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THE ANNALS OF THORACIC SURGERY

Official Journal of The Society of Thoracic Surgeons and the Southern Thoracic Society

Evaluation of the Organ Care System in Heart Transplantation With an Adverse Donor/Recipient Profile

Diana Garcia Saez, MD, Bartłomiej Zych, MD, Anton Sabashnikov, MD, et al. *Ann Thorac Surg* 2014; 97: 162-70

www.annals.org Published online April 12, 2014

Background A severe shortage of available donor hearts has created an impetus to use extended criteria for heart transplantation. Although such attempts increase donor availability, they may result in adverse donor/recipient risk profile. The TransMedics Organ Care System (OCS) (TransMedics, Inc, Boulder, CO) allows preservation of the donor heart by perfusing the donor heart at 37°C in a heating state, potentially reducing the detrimental effect of cold storage and providing additional support. We describe a single-center experience with the OCS in high-risk heart transplant recipients.

Methods Thirty hearts were procured using the OCS between February 2013 and January 2014. 24 of which were transplanted. Procedures were classified as high risk based on 10 donor factors. In 18 of these cases, the donor heart was procured using the OCS. In 6 of these cases, left ventricular hypertrophy (LVH), donor

Conclusion Ex-vivo perfusion of donor hearts using the Organ Care System is not inferior to standard cold storage. This trial is registered with ClinicalTrials.gov, number NCT00485712.

Heart Lung and Circulation

Applied Cardiopulmonary Pathophysiology

Successful Heart Transplant after Hours Out-of-body Time using TransMedics Organ Care System

Nikki L. Stamp, MBBS (Hons)*, Amit Shah, FRACP^b, Vij Brian Wright^b, Clare Wood, NP^b, Warren Pavey^c, Chris G Sharron Chih, FRACP^b, Lawrence Dembo, FRACP^b, Rob Larbalestier, FRACS*

*Department of Cardiothoracic Surgery, Royal Perth Hospital, Perth, WA

^bAdvanced Heart Failure and Cardiac Transplantation Service, Department of Cardiology, Royal Perth Hospital, Perth, WA

^cDepartment of Anesthetics, Clinical Pathology, Royal Perth Hospital, Perth, WA

Received 23 September 2013; received in revised form 31 December 2013; accepted 19 January 2014; online published April 12, 2014

Objective We report the successful transplantation of a heart following an recipient with dilated cardiomyopathy and left ventricular assist device (LVAD) support. Our patient was urgently awaiting a cardiac transplant while receiving LVAD support. We report our experience with the Organ Care System (OCS) in this patient.

Patients Our patient was urgently awaiting a cardiac transplant while receiving LVAD support. We report our experience with the Organ Care System (OCS) in this patient.

Results Although requiring ECMO and inotropic support in the first 171 hours after hospital on day 15 post-transplant with normal cardiac function.

Conclusion We report some of the salient points of the process and discuss the use of the OCS in high-risk heart transplant recipients.

Keywords Transplantation • Heart transplantation • Organ preservation • Cardiomyopathy

applied cardiopulmonary pathophysiology

Applied Cardiopulmonary Pathophysiology 15: 207-212, 2011

Organ preservation with the organ care system
Ruhf Yeter, Michael Hübler, Miralem Pasic, Roland Hetzer, Christoph Knossalla
Department of Cardiothoracic and Vascular Surgery, Deutsches Herzzentrum Berlin

Abstract

Clinical heart transplantation is limited by the shortage of donor organs. The recent development of new donor organ maintenance systems may help to increase the utilization of adult preservation.

Keywords: organ preservation, warm preservation, heart donor, heart transplantation

Introduction

Heart transplantation presents the most efficient therapy for end stage heart disease. Until today orthotopic heart transplantation has been performed in 89,000 patients worldwide (1). With the success of heart transplantation the criteria for acceptance of donor hearts have been continuously evolved by the shortage of suitable donor organs. Especially donor age and length of ischemic time are limiting factors (1). Utilization of marginal donor hearts that result in significant impaired function as a consequence of brain dead environment are currently not used due to the lack of a reliable method to predict the functional recovery of the graft after procurement.

Cold hypostatic organ preservation

The standard method of organ preservation in this context is cold hypostatic static preservation. The heart is perfused with a cold preservative solution, then explanted and stored at 4°C in a solution for transportation to the recipient hospital. There are two cellular solutions such as Bretschneider solution, University of Wisconsin (UW), EuroCollins and Starved solution and the extracellular solutions Colson, St. Thomas Hospital, Lyon Preservation and modified University of Wisconsin solution (2). The preference for a specific cardioplegic solution often depends on the individual experience of each transplant center. A whole arsenal of different preservation solutions are used today and this fact may suggest that there is no 'superior' one available. Despite the large number of different solutions there are limitations for cold preservation. The generally accepted ischemic time for cold preservation lies within 4 hours. Data from the ISHLT registry sug-

Evaluation of the Organ Care System in Heart Transplantation With an Adverse Donor/Recipient Profile

Conclusions. Use of the OCS is associated with markedly improved short-term outcomes and transplant activity by allowing use of organs previously not considered suitable for transplantation or selection of higher risk recipients, or both.

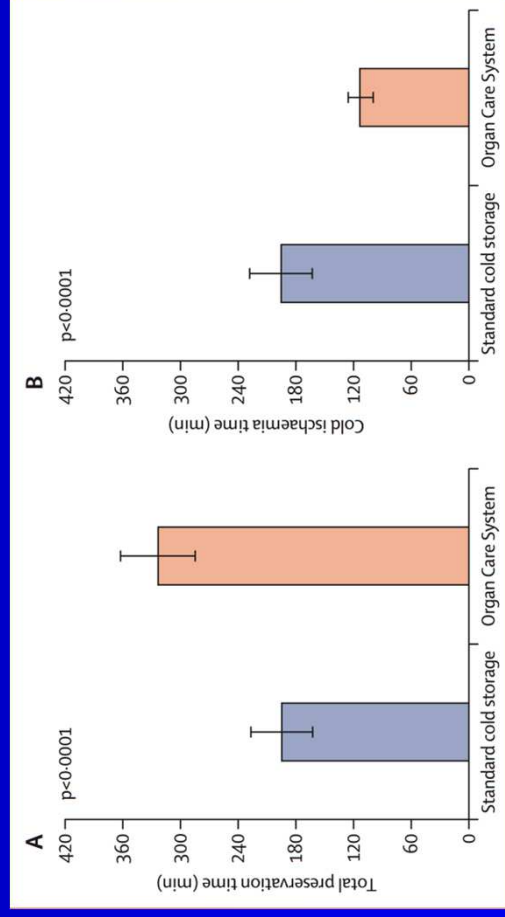
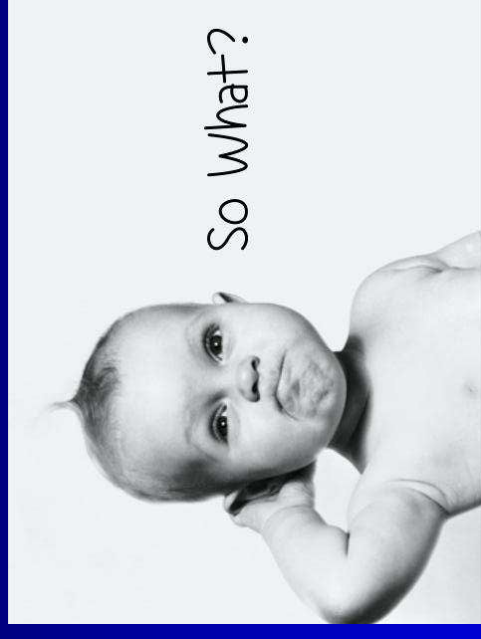
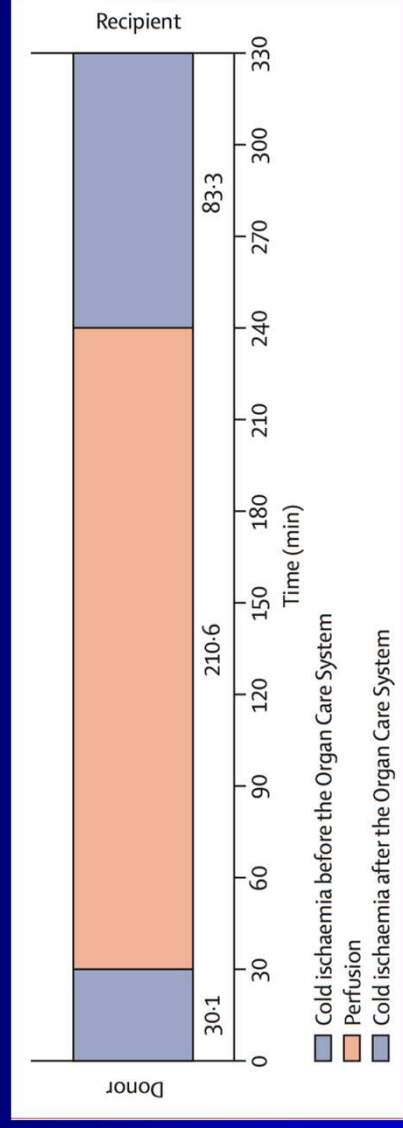
Risk Factors	Outcome
Estimated ischemic time > 4 h	Transplanted
Cardiac arrest, diabetes mellitus	Transplanted
Estimated ischemic time > 4 h	Transplanted
Obesity, alcohol abuse, palpable coronary artery disease	Transplanted
...	Transplanted
Cocaine-alcohol overdose, cardiac arrest	Transplanted
Obesity, palpable coronary artery disease	Transplanted
LVH (diastolic interventricular septum 15 mm)	Transplanted
Estimated ischemic time > 4 h	Transplanted
Estimated ischemic time > 4 h, LVH (diastolic interventricular septum 15 mm)	Transplanted
...	Transplanted
Estimated ischemic time > 4 h	Transplanted
Reduced LVEF, cardiac arrest	Declined
Estimated ischemic time > 4 h	Transplanted
LVH (diastolic interventricular septum 16 mm)	Transplanted
Estimated ischemic time > 4 h, reduced LVEF	Transplanted
LVH (diastolic interventricular septum 14 mm), alcohol abuse	Transplanted
Estimated ischemic time > 4 h	Transplanted
Estimated ischemic time > 4 h	Transplanted
Palpable coronary artery disease	Declined
Alcohol abuse, cardiac arrest	Transplanted
Electrocardiographic ischemia	Transplanted
Cardiac arrest, estimated ischemic time > 4 h	Declined
Cardiac arrest, LVH (diastolic interventricular septum 16 mm), Estimated ischemic time > 4 h	Transplanted
Reduced LVEF, palpable coronary artery disease	Transplanted
Estimated ischemic time > 4 h, palpable coronary artery disease	Transplanted
Cocaine overdose, estimated ischemic time > 4 h, right ventricular dysfunction	Transplanted
Cardiac arrest, estimated ischemic time > 4 h	Declined
Cardiac arrest, reduced LVEF, LVH (diastolic interventricular septum 15 mm)	Transplanted
Cardiac arrest	Transplanted

Table 2. Recipient Characteristics^a

Donor Number	Diagnosis	Age (y)	Sex	LVAD	Risk Factors
1	Dilated cardiomyopathy	39	Male	No	PVR > 4 WU
2	Ischemic cardiomyopathy	58	Male	HVAD	LVAD, 5 sternotomies, moderate renal impairment
3	Dilated cardiomyopathy	29	Male	No	Moderate renal impairment
4	Ischemic cardiomyopathy	61	Male	No	Previous sternotomy, liver function impairment
5	Dilated cardiomyopathy	25	Male	HVAD	LVAD
6	Dilated cardiomyopathy	36	Male	Synergy	LVAD
7	Dilated cardiomyopathy	37	Female	No	...
8	Dilated cardiomyopathy	24	Male	HVAD	LVAD, moderate renal impairment
9	Dilated cardiomyopathy	44	Female	No	IABP, moderate renal impairment
10	Dilated cardiomyopathy	56	Male	HeartMate II	LVAD, pump pocket infection, PVR > 4, moderate renal impairment
11	Dilated cardiomyopathy	61	Male	HeartMate II	LVAD, pump pocket infection, moderate renal impairment
12	Dilated cardiomyopathy	48	Male	No	PVR > 4 WU
14	Dilated cardiomyopathy	22	Male	No	IABP, moderate renal impairment
15	Dilated cardiomyopathy	57	Male	No	PVR > 4 WU
16	Dilated cardiomyopathy	26	Female	No	PVR > 4 WU, moderate renal impairment
17	Dilated cardiomyopathy	33	Male	HVAD	LVAD
18	Ischemic cardiomyopathy	48	Male	No	...
19	Ischemic cardiomyopathy	33	Male	HeartMate II	LVAD, pump pocket infection
20	Dilated cardiomyopathy	48	Male	HeartMate II	LVAD, pump pocket infection, 4 previous sternotomies
22	Dilated cardiomyopathy	56	Male	No	...
23	Dilated cardiomyopathy	58	Male	HVAD	LVAD + RVAD Levitronix, severe renal impairment
25	Dilated cardiomyopathy	34	Male	No	-
26	Dilated cardiomyopathy	59	Female	HVAD	LVAD, PVR > 4 WU
27	Dilated cardiomyopathy	30	Male	No	IABP
29	Dilated cardiomyopathy	57	Male	No	PVR > 4 WU
30	Dilated cardiomyopathy	56	Female	No	Moderate renal impairment

Ex-vivo perfusion of donor hearts for human heart transplantation (PROCEED II): a prospective, open-label, multicentre, randomised non-inferiority trial

Abbas Ardehali, Fardad Esmailian, Mario Deng, Edward Soltesz, Eileen Hsieh, Yoshifumi Naka, Donna Mancini, Margarita Camacho, Mark Zucker, Pascal Leprince, Robert Padera, Jon Kobashigawa, for the PROCEED II trial investigators*



In conclusion, our findings show that the clinical outcomes of donor hearts adequately preserved with the Organ Care System platform are non-inferior to the outcomes of those preserved with standard cold storage. Evaluation of the metabolic assessment capability of the Organ Care System requires further study.

Pour favoriser le M 3 cœur?

Lancet 2015; 385: 2585-91

Adult heart transplantation with distant procurement and ex-vivo preservation of donor hearts after circulatory death: a case series



To our knowledge, this report describes the first successful clinical heart transplantations after circulatory death with donor organs procured at a distance necessitating reanimation, resuscitation, and transportation with use of an ex-vivo cardiac perfusion device. Our findings confirm that human hearts donated after circulatory death can be adequately preserved and their function assessed in a physiological ex-vivo platform before safe clinical transplantation with excellent outcome. A broader adoption



	Donor 1	Donor 2	Donor 3
Withdrawal parameters			
Location of withdrawal	Operating theatre	Intensive care unit	Anaesthetic bay
Withdrawal to systolic blood pressure <50 mm Hg (min)	7	5	11
Withdrawal to SaO ₂ <50% (min)	8	2	1
Withdrawal to cessation of circulation (min)	16	10	11
Observation period (min)	2	2	5
Warm ischaemic time (min)*	28	25	22
OCS parameters			
Pacing	Yes	Yes	No
Adrenaline infusion (µg/h)	5	5	5-7
Adenosine infusion (mg/h)	0-21	0-21	0-21
Total OCS perfusion time (min)	257	260	245
Total ischaemic time (min)†	90	96	107
A-V lactate at start of perfusion (mmol/L)	8.30-8.10	6.79-6.48	7.60-7.40
A-V lactate at end of perfusion (mmol/L)	3.60-3.60	2.80-2.30	2.69-2.54

OCS=Organ Care System. A-V=arteriovenous. *Time from withdrawal of support to cardioplegia delivery. †Composite of the time from cessation of circulation to instrumentation on the OCS apparatus plus the time from cardioplegia delivery at the end of OCS perfusion to post-transplant reperfusion.

Table 2: Donor heart management

DCD donors with OCS procurement



>100+ successful DCD heart transplants

- ☞ Australia – St. Vincent's, Sydney
- ☞ UK – Papworth Hospital
- ☞ UK - Harefield Hospital
- ☞ UK - Whythenshawe Hospital

Conclusions



- Glacière: Gold standard (en tout cas pour les greffes standards...)
- Intérêt des machines de perfusion +++
- Evaluation à poursuivre : quelles indications préférentielles? Quelle machine? (registre?)
- Surcout notable, quel financement?

Merci de votre attention

