Actualités sur les machines de perfusion cardiaque

Erwan Flécher, CHU Pontchaillou, Rennes

Ouest Transplant, Orléans, 15 novembre 2019.

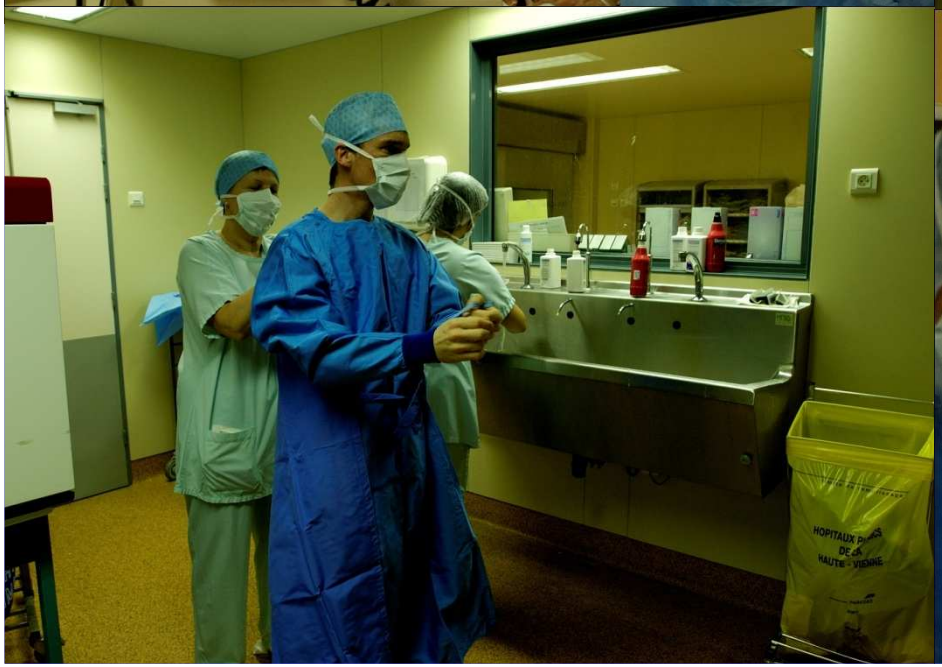
Déroulement de la Transplantation

- 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


870 AMS 35


LOC OPERATOIRE CENTRAL


TRANSFUSEURS
STERNUM


HOPITAUX
DE
HAUTE VIENNE





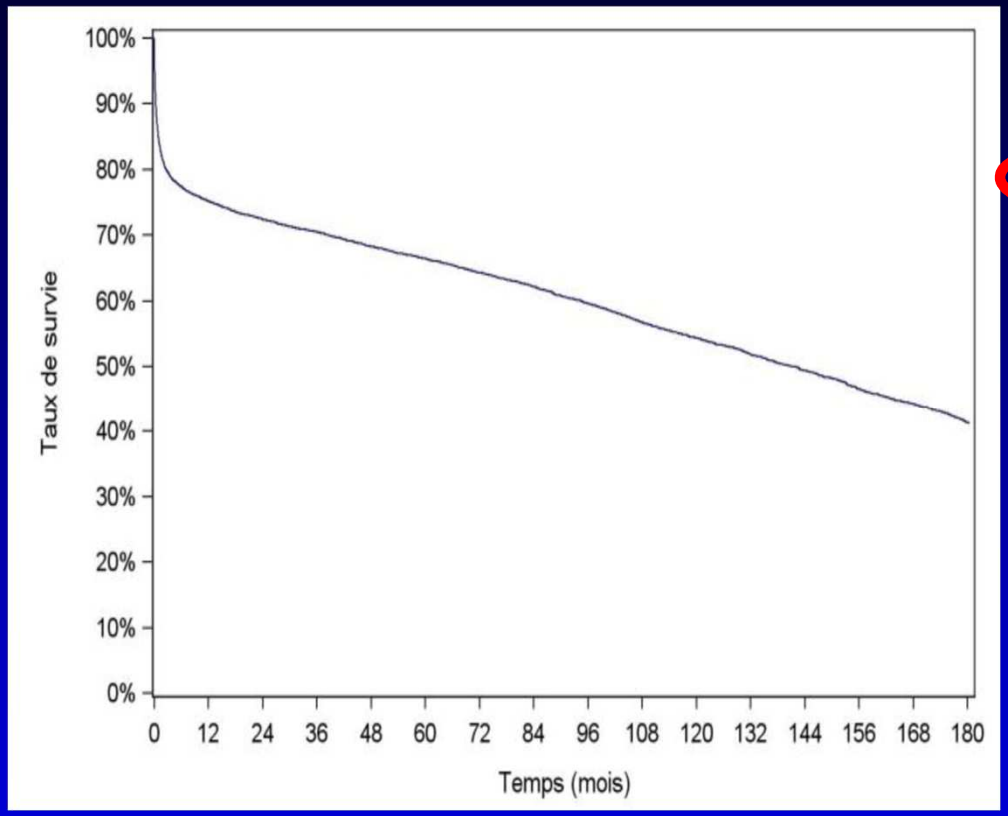
F-GIZD

F-GIZD


F-GIZD



Survie après 1ère 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?

ORIGINAL ARTICLE

Heart, Lung and Vessels. 2015; 7(3): 246-255

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

S.G. Michel[1,2], G.M. LaMuraglia II[1], M.L.L Madariaga[1], Lisa M. Anderson[3,4]

[1]Transplantation Biology Research Center, Department of Surgery, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA; [2]Department of Cardiac Surgery, Ludwig-Maximilians-University, Munich, Germany; [3]Paragonix Technologies, Inc., Braintree, MA, USA; [4]Corresponding 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
	"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
- Monitorage et enregistrement
- Température homogène
- Greffon immergé
- Facilité de mise en œuvre
- Sans énergie électrique
- Design, manipulation
- Surcout

Une glacière « active »?

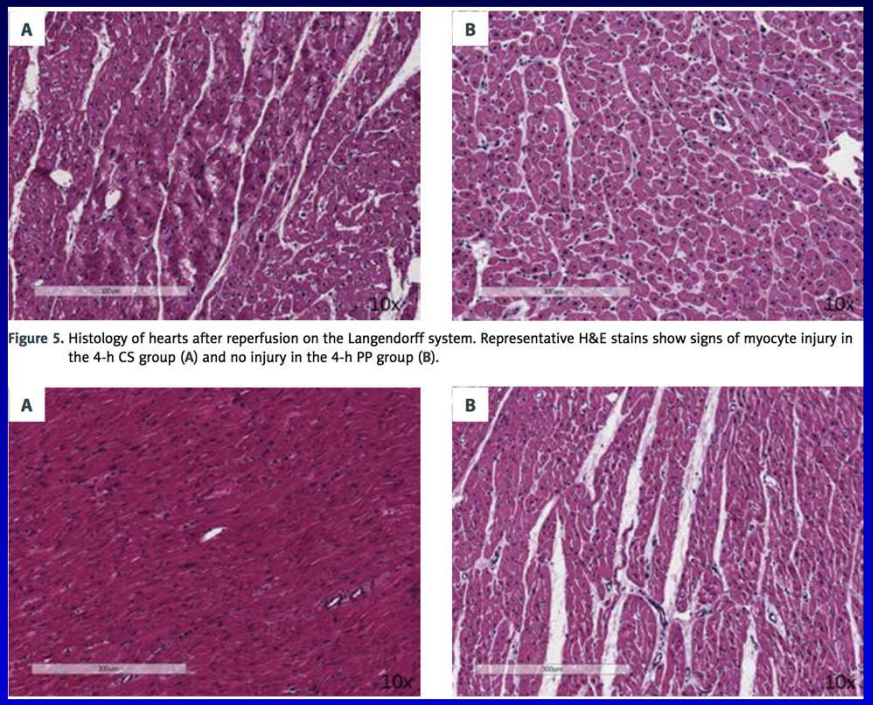


Figure 5. Histology of hearts after reperfusion on the Langendorff system. Representative H&E stains show signs of myocyte injury in the 4-h CS group (A) and no injury in the 4-h PP group (B).

ANNALS OF TRANSPLANTATION

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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

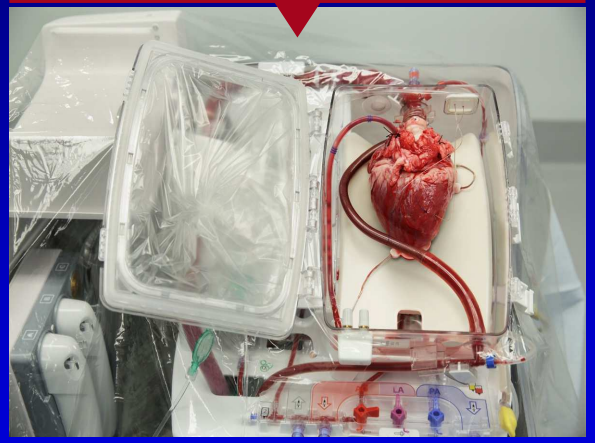
A sterile, protective, biocompatible chamber that houses the heart and circulating perfusate

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

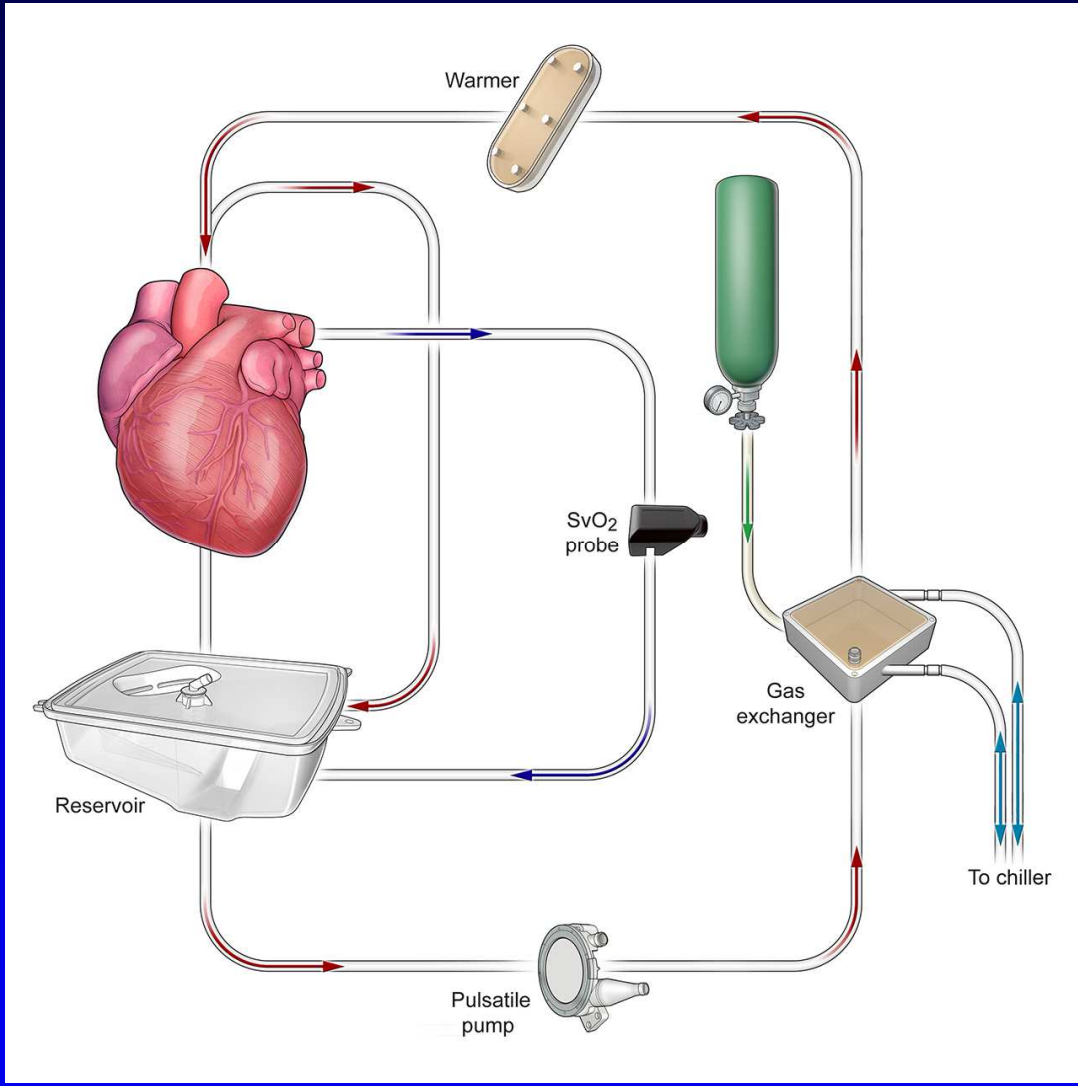
OPTIMIZE ORGAN CONDITION

Optimize O_2 Delivery Replenish Substrates & Hormones

EX-VIVO ASSESSMENT

Metabolic Assessment & Perfusion Parameters

Une CEC portative et transportable…



CAUTION HEAVY

Un monitorage du greffon « Wifi »

Coronary Blood Flow

Aortic Blood Flow

Coronary Sinus Saturation

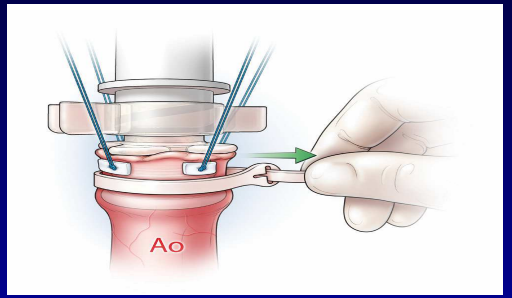
Aortic Pressure

Heart Rate

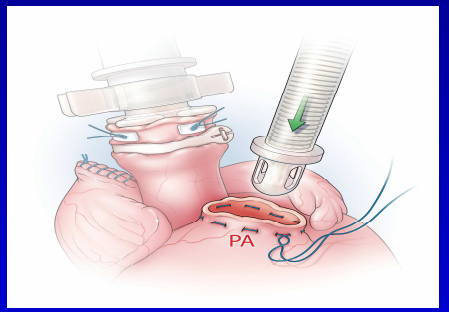
Serial Lactate Levels
Arterial & Venous
Lactate Differential and Trend

The OCS ™ Heart in Clinical Practice

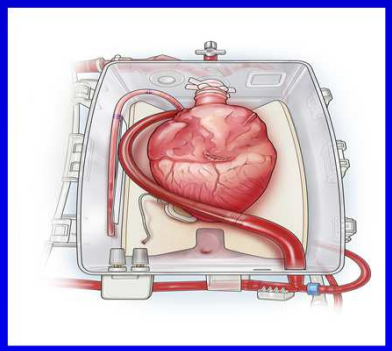
- **Sur Site PMO**
  - Optimisation donneur
  - Prélèvement sang (1,5L) et cardioplégie
  - Cannulation Ao et AP
  - Démarrage
  - Stabilisation
- **Transport**
  - Monitorage continu du greffon
  - Ajustement paramètres de perfusion
- **A la maison:**
  - Echo? Coro?
  - Nouvelle cardioplégie
  - Greffe



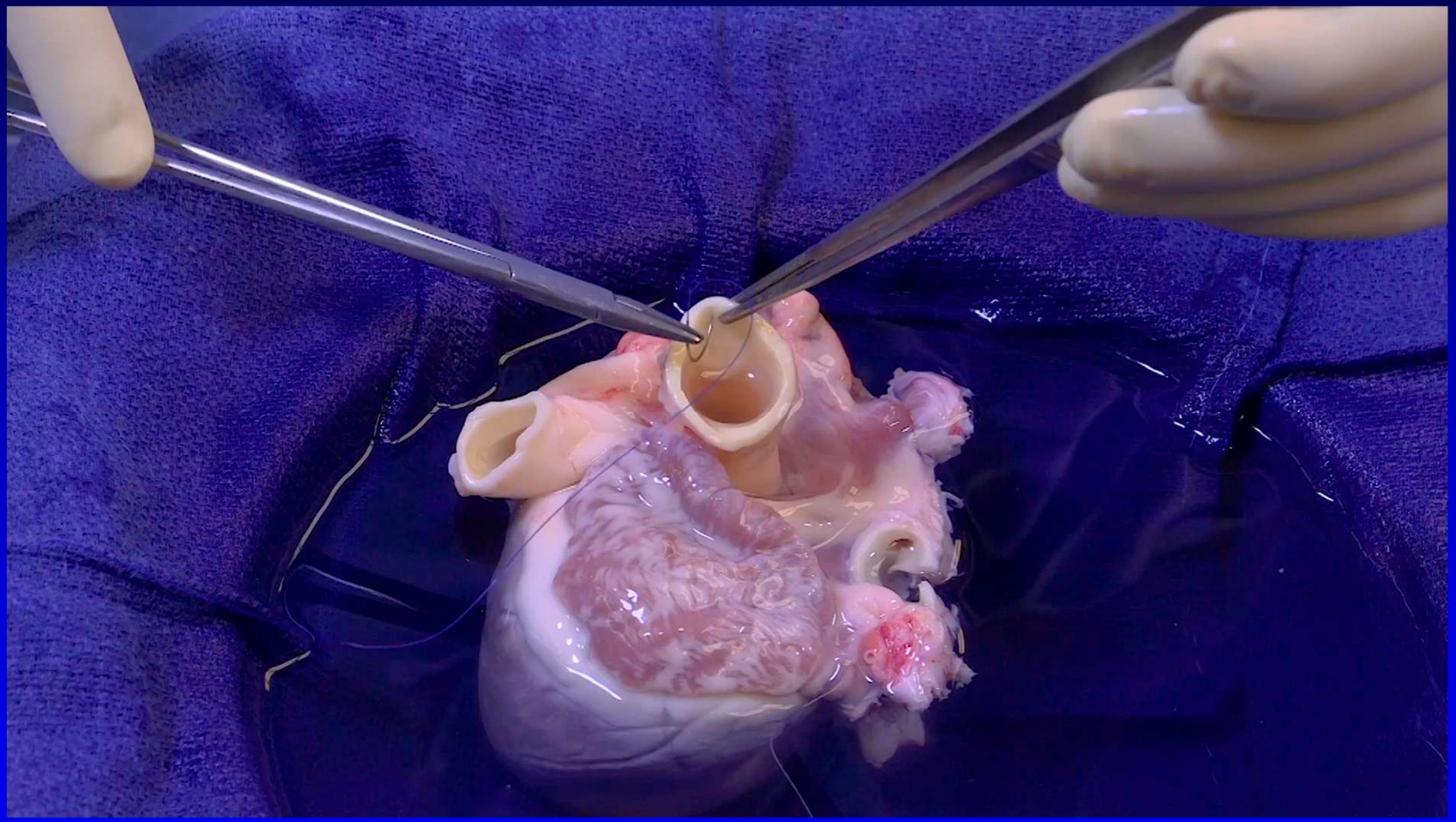
AO Cannulation



PA Cannulation

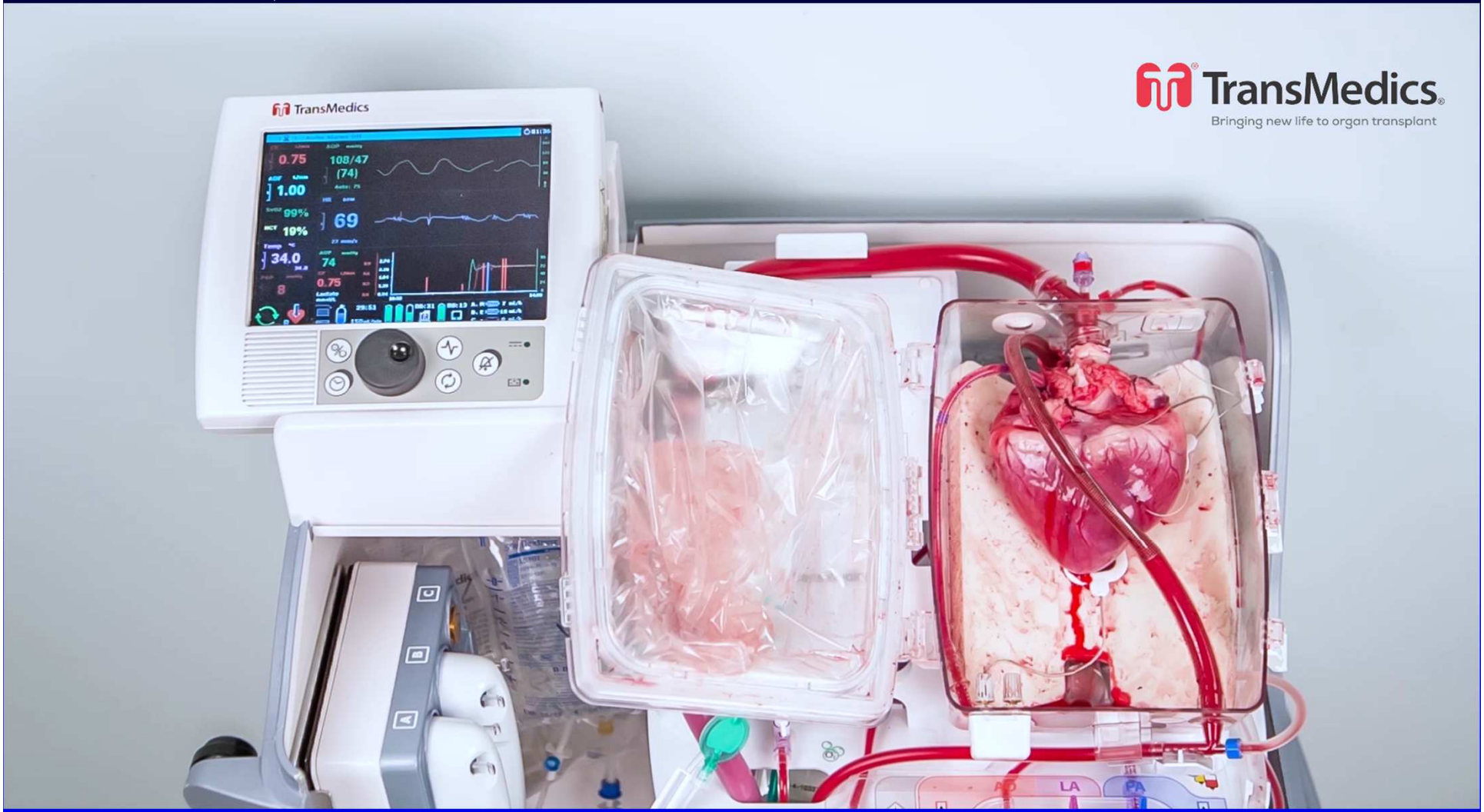


Cannulation Process



Instrumentation Process

The OCS ™ Heart



The OCS ™ Heart

Inconvénients

- **<u>Cout: 30 à 35 000 euros/greffon !!!!!!!!!!</u>**
- 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?

Hôpital
Marie Lannelongue

3 hôpitaux
Financements…

CHU
Rennes

OCS Heart Published Data

THE LAN

Ex-vivo perfusion of donor hearts for hum transplantation (PROCEED II): a prospectiv multicentre, randomised non-inferiority t

THE LANCI

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

THE ANNALS OF THORACIC SURGERY

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

Evaluation of the Organ Care System in Hear Transplantation With an Adverse Donor/Reci Profile

Heart Lung and Circulation

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

applied cardiopulmonary pathophysiology

Organ preservation with the organ care system

Applied Cardiopulmonary Pathophysiology 15: 207-212, 2011

Organ preservation with the organ care system

Ruhi Yeter, Michael Hübler, Miralem Pasic, Roland Hetzer, Christoph Knosalla

Department of Cardiothoracic and Vascular Surgery, Deutsches Herzzentrum Berlin

Abstract

Introduction

Cold hypostatic organ preservation

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	Transplanted
Alcohol abuse, cardiac arrest	Declined
Electrocardiographic ischemia	Transplanted
Cardiac arrest, estimated ischemic time > 4 h	Transplanted
Cardiac arrest, LVH (diastolic interventricular septum 16 mm), Estimated ischemic time > 4 h	Declined
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

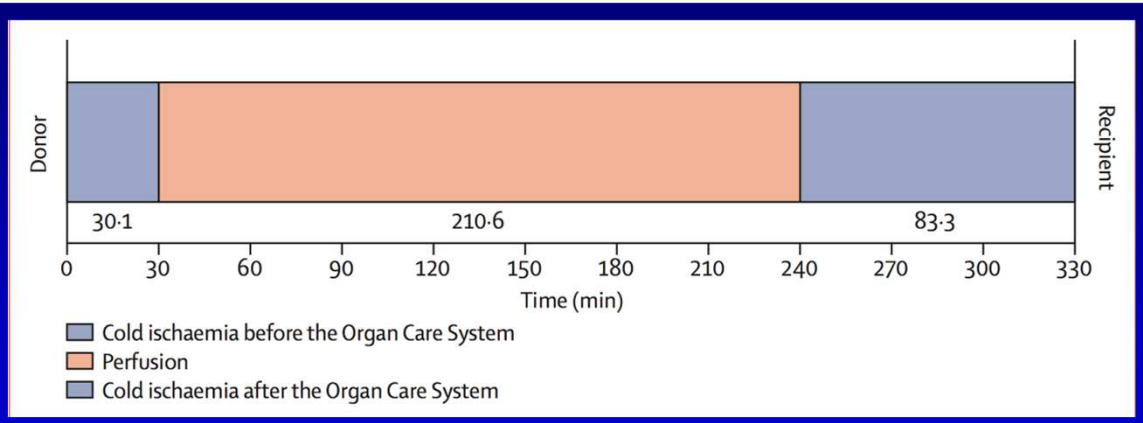
Table 2. Recipient Characteristics[a]

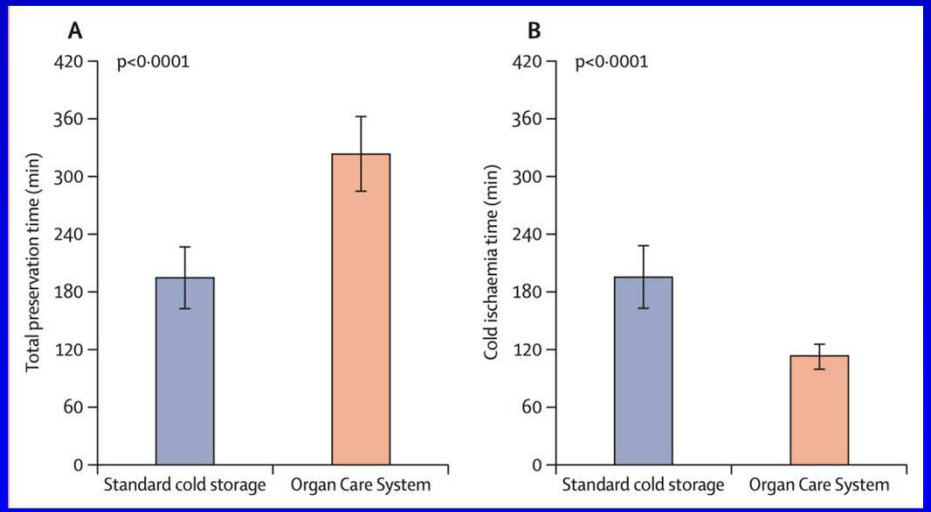
Donor Number	Diagnosis	Age (y)	Sex	LVAD	Risk Factors
1	Dilated cardiomyopathy	39	Male	No	PVR > 4 WU
2	Ischemic cardiomyopathy	58	Male	HVAD	LVAD, 5 sternotomies, moderate renal impairment
3	Dilated cardiomyopathy	29	Male	No	Moderate renal impairment
4	Ischemic cardiomyopathy	61	Male	No	Previous sternotomy, 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

(Ann Thorac Surg 2014;98:2099–106)

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 Hsich, 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