



Pour votre santé, Foch s'engage

## Ex-Vivo Lung Perfusion

### EVLP

## Foch Hospital Experience



Foch Lung Transplant Group

Dr Julien De Wolf  
Service de Chirurgie Thoracique et Transplantation  
pulmonaire

# Conflict of interest

- . Organization of international workshop for XVIVO company

# Lungs Transplantation in France

## key data

400 lungs transplants in France per year

Average waiting time on lung transplantations list in France is 3 months.  
(Foch 3 weeks)

In the past 10 years: 16/30 patients dead on the waiting list

Lungs proposed in only 20% of all multiple organ donor.

50% survival at 5 years for all indications

PGD 3 : 50% mortality 1 year

Chronic rejection: 1st cause of mortality

The number of patients registered for lung transplants exceeds the number of organs available

Lack of organ donors

number of proposed lungs

< 20%

Increase of indications

+50% on 10 years

**EVLP**

Decrease waiting time

No deaths on waiting list

Improved matching

# EVLP in France



**2011:**

**1st Lung Transplantation from lung refused by all French TP teams and perfused in ex-vivo**

**2016:**

**1st lung transplantation from a cDCD (Maastricht III) donor**

**2018:**

**Groupe Poumon obtain reimbursement for ex-vivo procedures up to 31,343 euros per procedure**

# The different ex-vivo lung perfusion machines



# Organisation EVLP in France



## XPS:

Foch  
Bichat  
Bordeaux  
Toulouse  
Lyon

## OCS:

Strasbourg  
Marseille

## X-VIVO

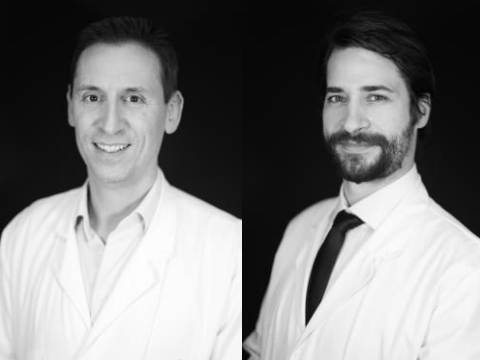
« home made »:

Nantes  
CCML

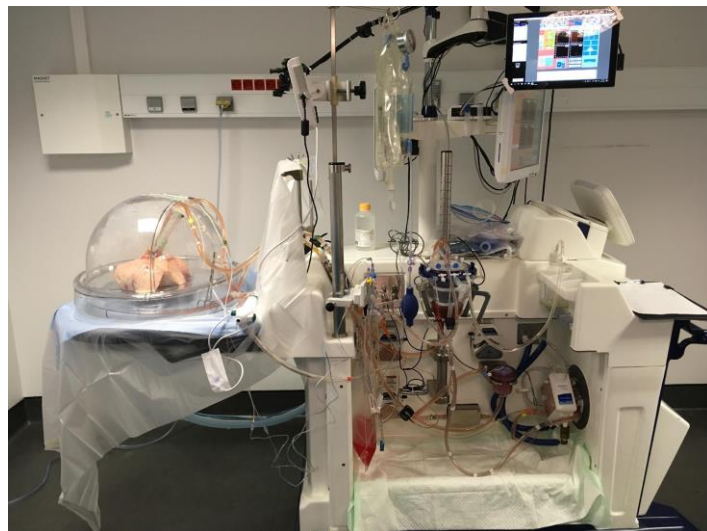
9 department equipped for EVLP

Only 1 department > 5 procedures / year





## Organisation EVLP - Foch



**Dedicated room for EVLP procedure**

**Senior Transplant Surgeon X 5**

**Perfusionist X 3**

**EVLP / XPS (XVIVO)**

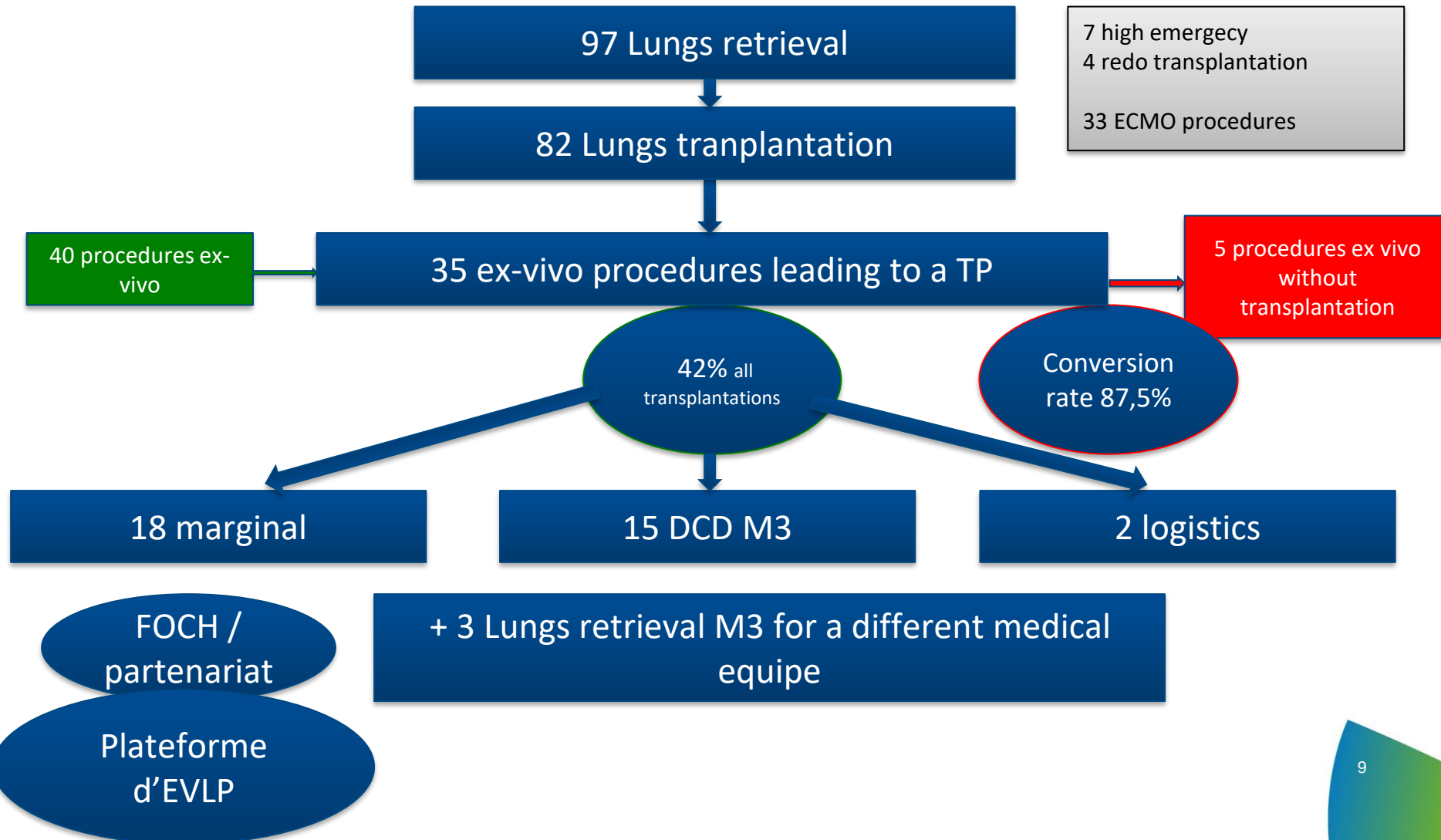
**Perfusate: Steen's liquid**

**Pneumoplegia: Perfadex Plus**

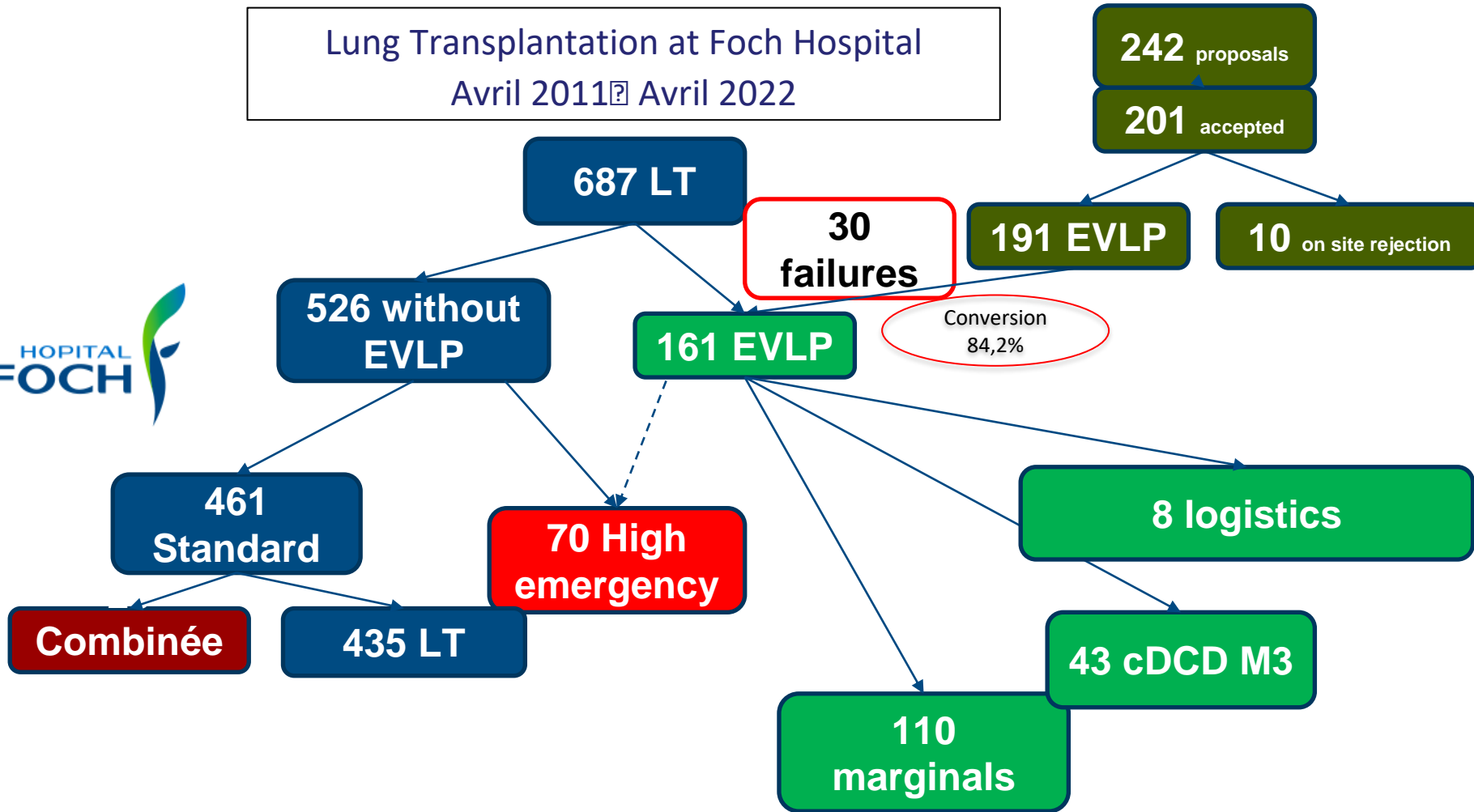




# Lung Transplantation- Hopital Foch 2019



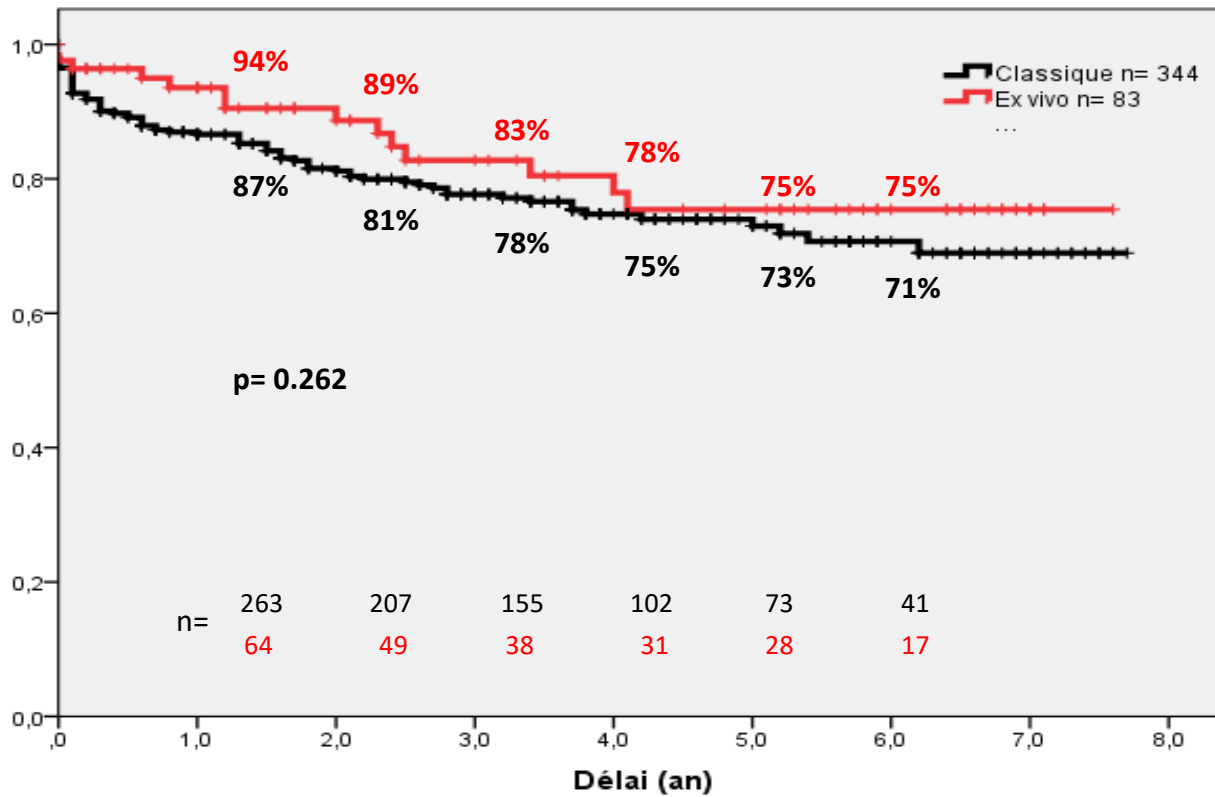
Lung Transplantation at Foch Hospital  
Avril 2011 à Avril 2022



# LUNG TRANSPLANTATION

Hôpital Foch: Ex vivo (2011 – 2021)

Survie actuarielle



# Indication in France

## Ex - vivo group of the SFCTCV



# Indication EVLP

## Indication validated by SFCTCV



3 procedures:

1. Optimisation and reconditioning of high-risk grafts,
2. Evaluation of lungs harvested after cardiac arrest (Maastricht III)
3. Dynamic preservation of selected lung grafts. (Logistic)

To be implantable: validate 3 groups of criteria

1. good clinical macroscopic assessment of the lung parenchyma through inspection, palpation and fibroscopy
2. validated oxygenation capacity with :  $PaO_2/FIO_2 > 350$
3. the pulmonary haemodynamic and aerodynamic component should be monitored, with PAP, RVP low and stable during the procedure

# Optimisation and reconditioning of high-risk grafts,

# Optimisation et reconditionnement des greffons à critères élargis

French donor categories

## Optimal:

Age < 56

P/F > 400

Chest X Ray: Normal  
No smoking history  
No gastric aspiration

## Extended criteria:

56 < Age < 70

200 < P/F < 400

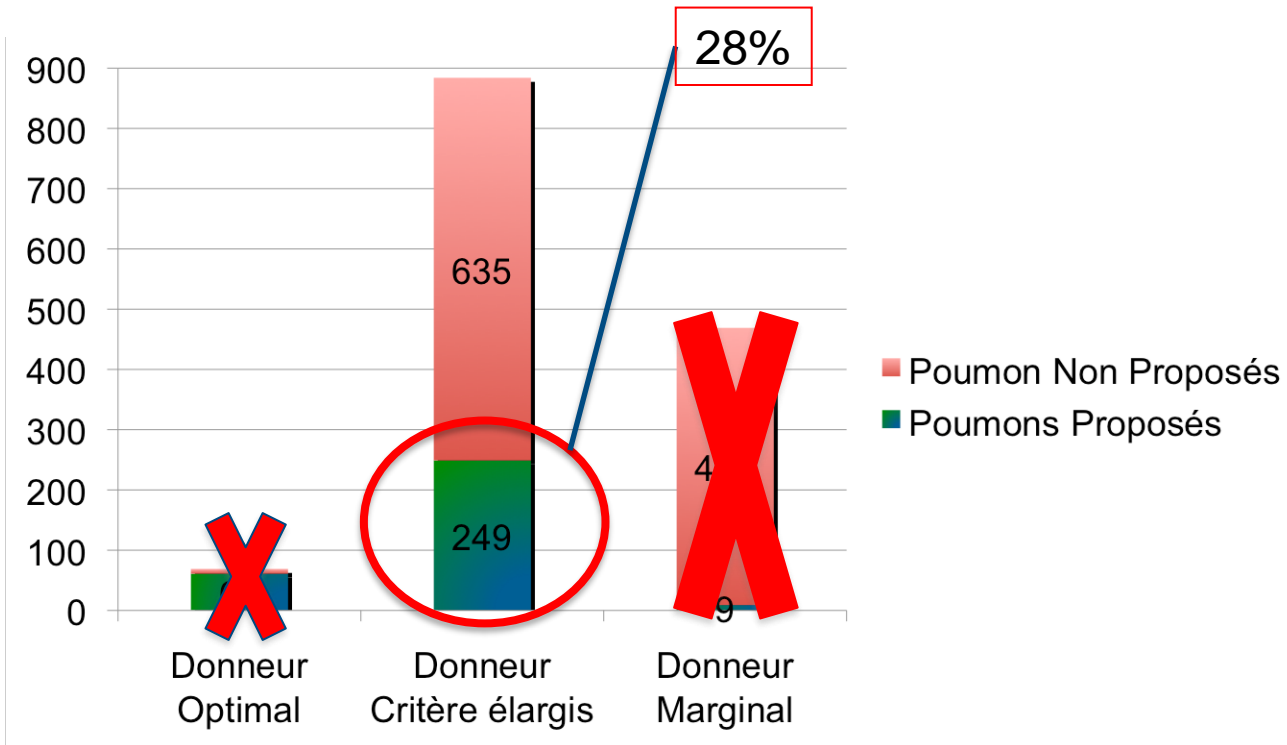
Chest X Ray :Anormal  
Smokin History  
Gastric aspiration

## Marginal:

Age > 70

P/F < 200

## Lung grafts in France - 2009



Extented  
criteria

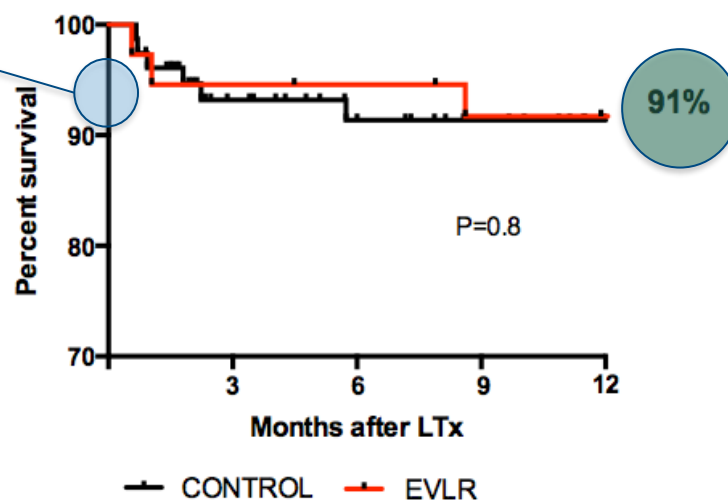


# Survival

Mortality at 90 days

Survival at 1 year

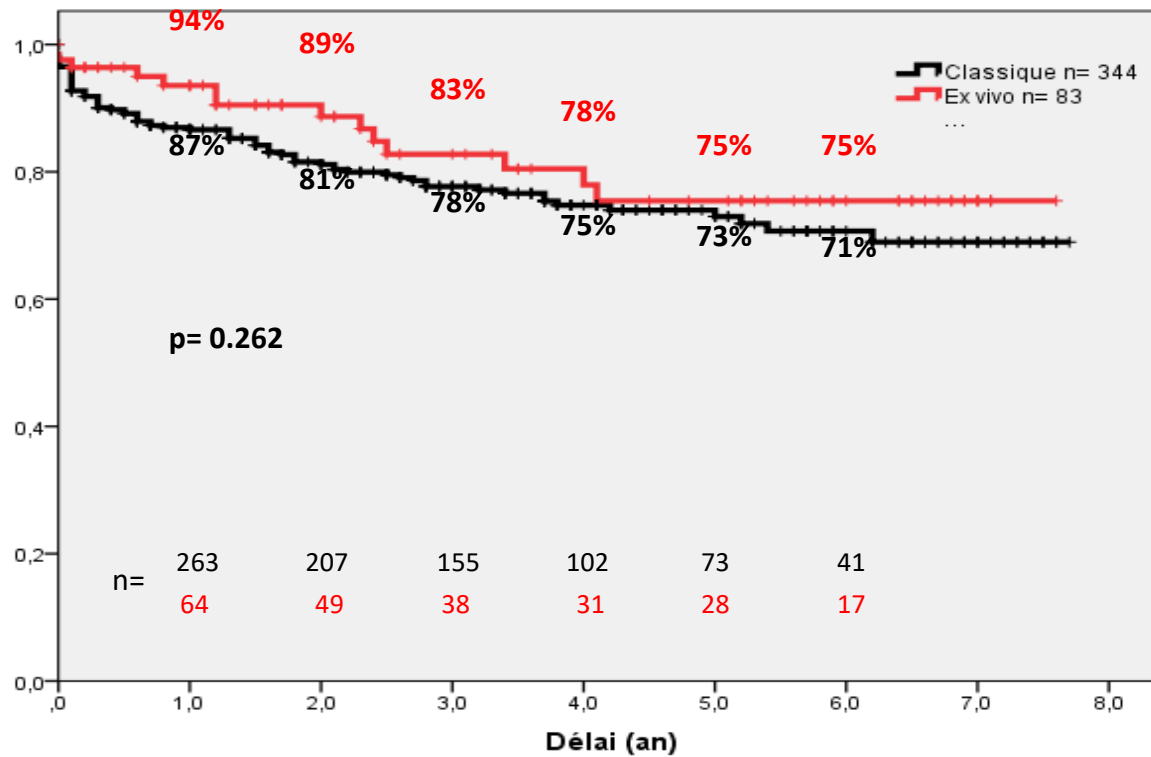
90 days mortality  
EVLP 3,1% (n=1)  
Control 3,7% (n=3)



# LUNG TRANSPLANTATION

## Hôpital Foch: Ex vivo (2011 – 2018)

Survie actuarielle



# cDCD

## Donation after circulatory death

### Maastricht III

**Controlled Donation after Circulatory Death Lung Transplantation: Results of the French Protocol Including In Situ Abdominal Normothermic Regional Perfusion and Ex Vivo Lung Perfusion.**

**De Wolf J.**, Fadel G, Olland A., Falcoz PE., Mordant P, Castier Y, Brioude G, Thomas PA., Lacoste P., Issard J, Antoine C., Fadel E., Chapelier A., Mercier O, Sage E. for the SFCTCV Lung Transplantation Group.  
JHLT-D-22-00538R1 accepted march 2023



# Maastricht III

Maastricht category	Definition
I	people who have cardiac arrest outside the context of medical care and who have died on arrival of qualified emergency personnel
II	people who have a cardiac arrest in the presence of trained paramedics, who are able to perform effective cardiac massage and mechanical ventilation, but whose resuscitation will not result in hemodynamic recovery
<b>III</b>	<b>people for whom a decision to stop therapeutic care or to limit therapeutic care is taken due to the prognosis of the pathologies and will require intensive care</b>
IV	brain-dead people who suffer an irreversible cardiac arrest during resuscitation
V	people who died by euthanasia (only in Belgium and the Netherlands)

First lung transplantation in France with cDCD M3  
May 2016



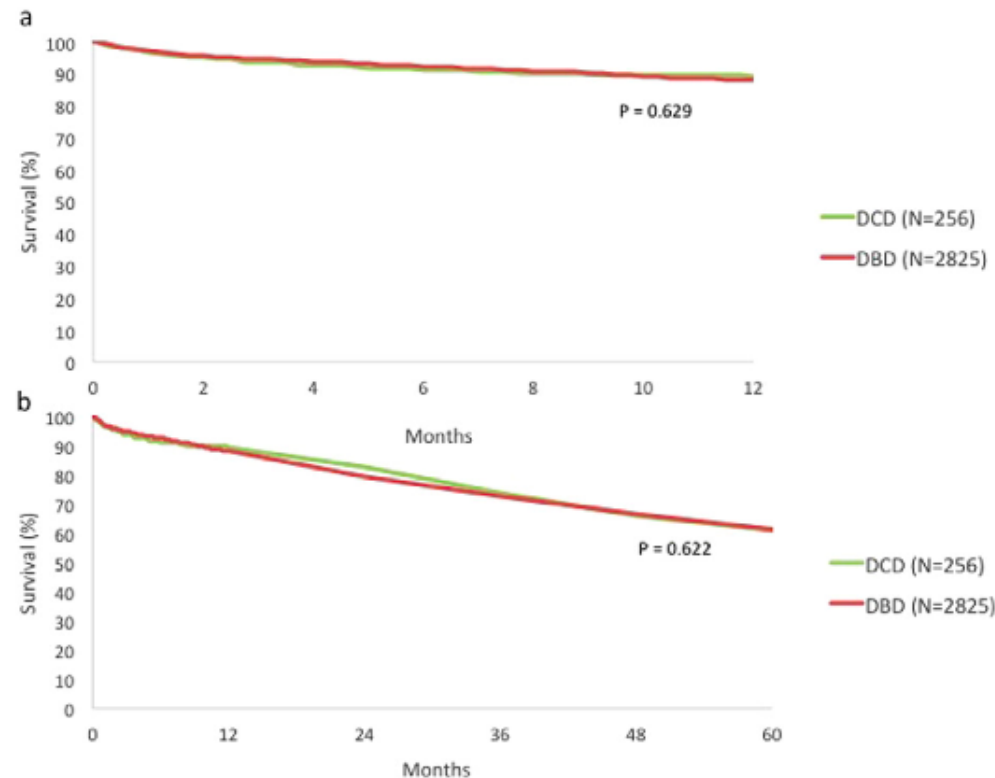
# International Society for Heart and Lung Transplantation Donation After Circulatory Death Registry Report

CYPEL J HeartLungTransplant2015;34:1278–1282

**Table 1** Characteristics of DCD Practices in Part

Center	Transplants 2012 to 2014 (n)	Percentage of Transplants from DCD (%)	Use of pr
Toronto	352	15	Ye
Sydney	139	23	No
Melbourne	214	23	Ye
Brisbane	93	15	No
Leuven	199	14	Ye
Groningen	112	32	No
Minnesota	126	7	Ye
St. Louis	191	<1	Ye
Cleveland	302	8	Ye

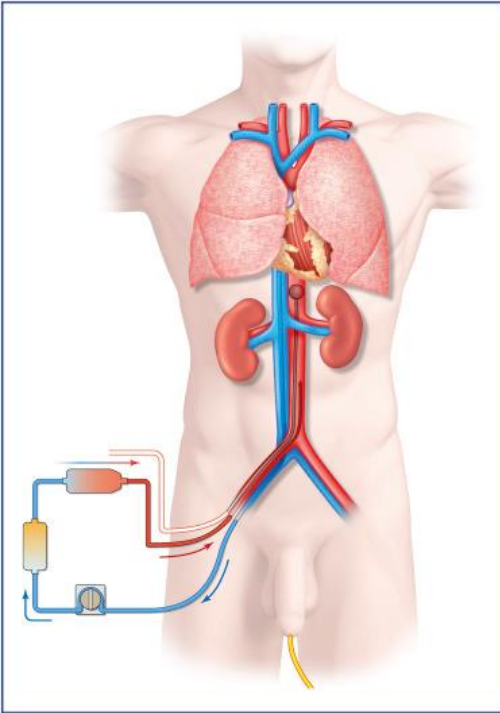
DCD, donation after circulatory death donor; EVLP, ex  
<sup>a</sup>When allowed by donor hospital.



**+15%**

# Specificities of the French protocol

## NRP / Ex-Vivo lung perfusion evaluation



**NRP**

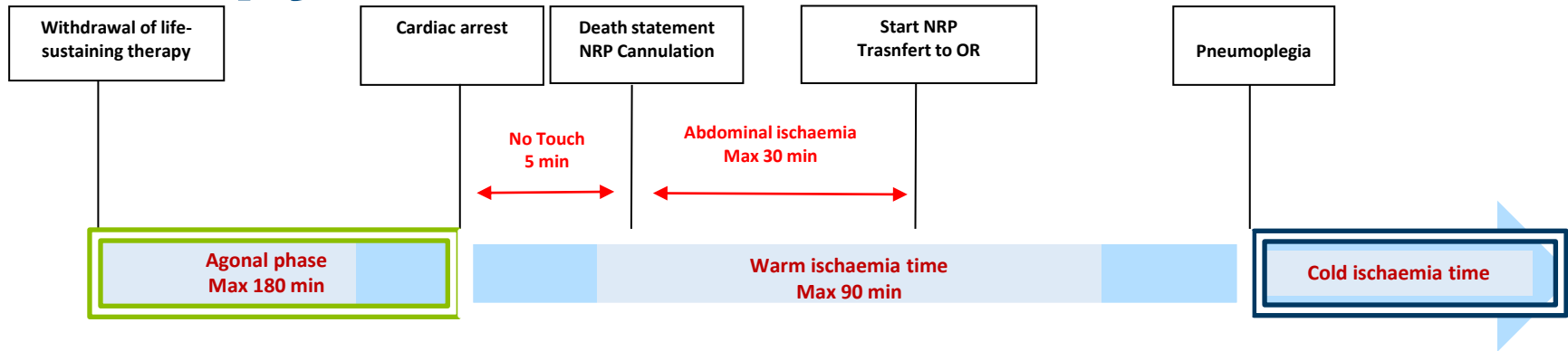
*Deceased donation in renal transplantation  
Thuret Progrès en Urologie  
Volume 26, Issue 15, November 2016, Pages  
909-939*

Two particularities

- **NRP** (Normothermic Regional perfusion) recommended in case of abdominal organs removal : **Duration 1 to 4h**
- **EVLP** (Ex-vivo lung perfusion) **mandatory, minimum duration 2h**



# French Protocol of withdrawal of life-sustaining therapy



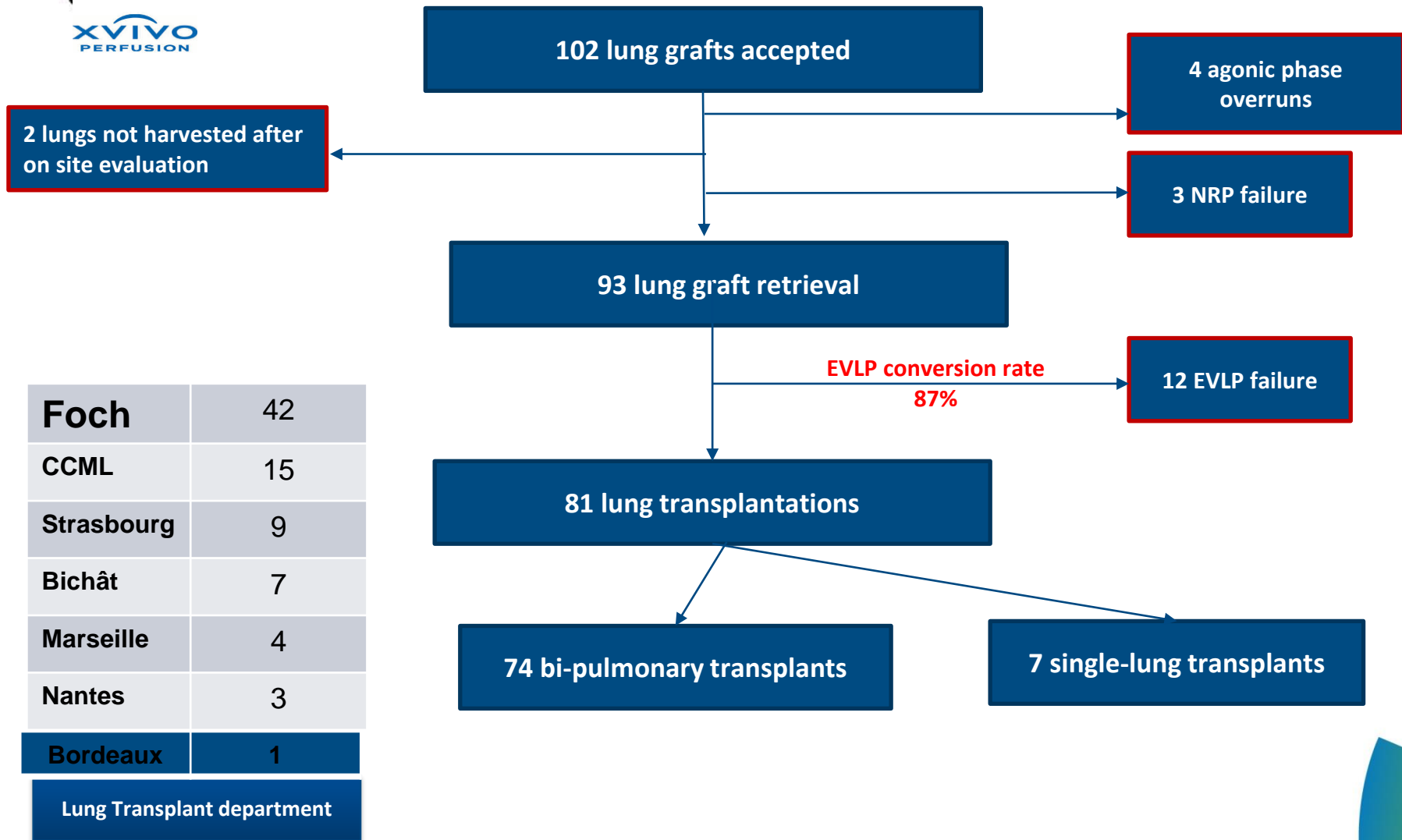
In case of **NRP** placement failure or abdominal ischaemia time is exceeded: lung sampling always possible!

No limit in the duration of cold ischemia



XVIVO  
PERFUSION

# French national cohort 2016-2021



<b>Foch</b>	42
CCML	15
Strasbourg	9
Bichât	7
Marseille	4
Nantes	3
<b>Bordeaux</b>	<b>1</b>

Lung Transplant department



# Population DATA

## Donors

<b>Age (years)</b>	49,5 (19-66)
<b>Length of stay in intensive care (days)</b>	10 (4-97)
<b>Duration of mechanical ventilation(days)</b>	10 (4-97)
<b>Last P/F ratio</b>	405 (219-555)
<b>Smoking History</b>	53 %
<b>Abnormal chest x-ray</b>	41,5 %
<b>Dirty Tracheobronchial secretion</b>	43,4 %

**Marginal grafts +++**

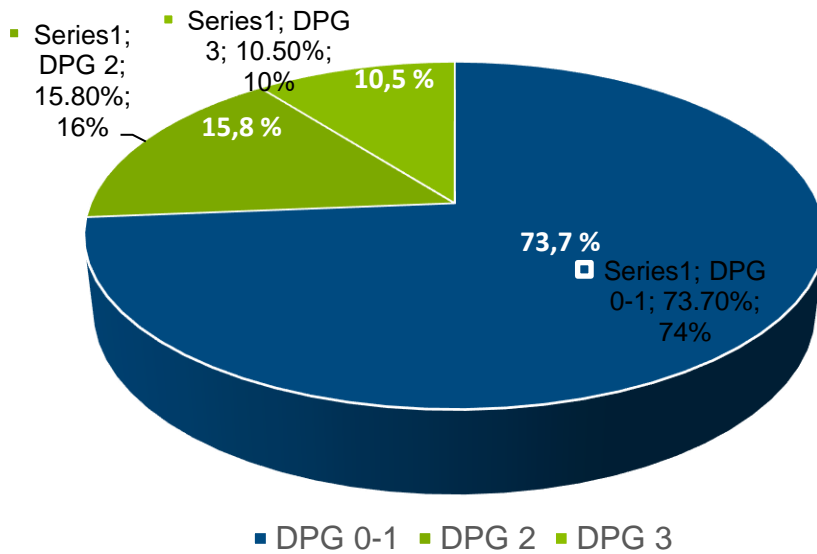
## Recipients

<b>Age (years)</b>	55 (18 – 70 )
<b>Sex</b>	60% Male 40% Female
<b>Indications</b>	COPD 39,6%
	Cystic fibrosis 26,4%
	Fibrosis 20,8%
	Pulmonary Hpertension 9,4%
	Groth Versus Host 1,9%
	Bilateral lepidic adenocarcinoma 1,9%
<b>High emergency list</b>	1

Graft used for all types of indications

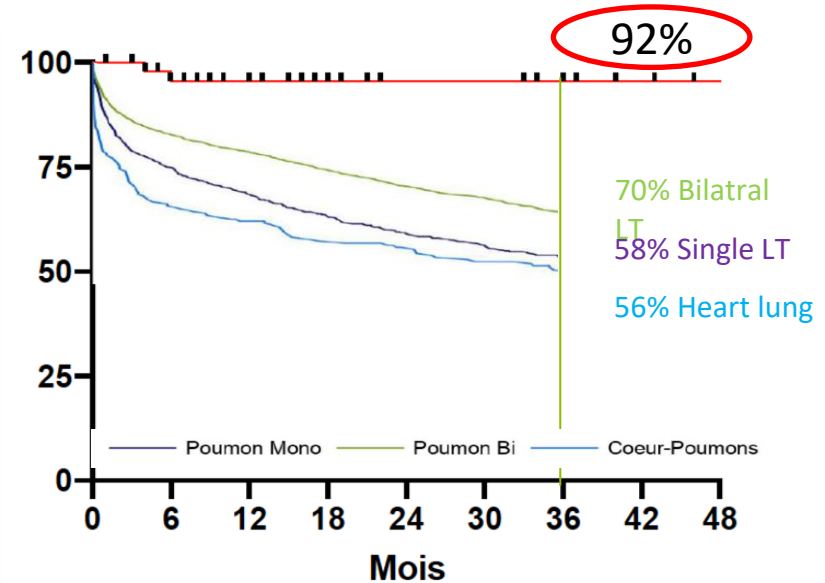
# Results

## Primary graft dysfunction at 72h



## 3 years survival

Data from the french registry ABM



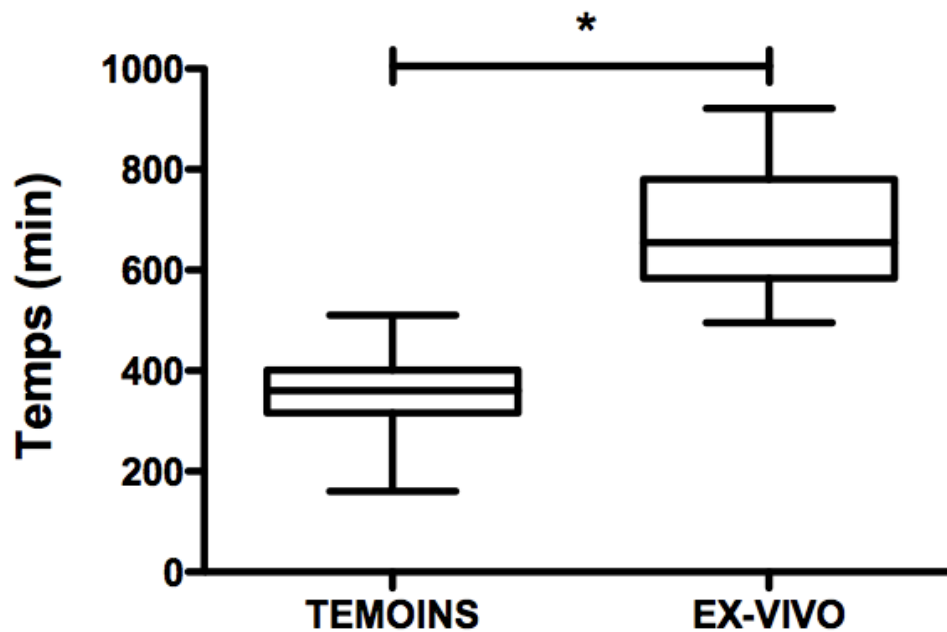
T0	1 year	2 years	3 years
N= 56	N=44	N=31	N=23



# Logistical Use

# Ex-vivo lung perfusion: Logistics ?

Ischemia 2nd side



Control: 350 min (160-510)  
or 5H50  
Ex-Vivo: 678 min (495-921)  
or 11H18

$p < 0,0001$

+ 5H30 with ex-vivo  
Equivalent long term result

*Lung transplantation from initially rejected donors after ex vivo lung reconditioning: the French experience.  
Sage E. et al. Eur J Cardiothorac Surg. 2014*

## 1. Use to buy time for potentially difficult surgery

a. Difficult dissection+++.

Patients with lung destruction, history of thoracic surgery (pleural talcage)

b. Redo transplantation

## 2. Use to increase the surgical activity

## 3. Extending the indications

**Lung transplantation for Hyperimmunized patients**

## Hyperimmunized patients

Hyperimmunized patients: cPRA>80%.  
Anti-HLA antibody is central to the rejection process

HLA sensitisation:

- acute rejection
- chronic rejection
- decreased survival

Graft/recipient matching: virtual crossmatch

Systematic prospective crossmatch in renal transplantation

***Cross match = 4H of additional ischemia***

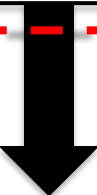
# Schéma décisionnel



Acceptance of a lung graft



Call of the hyperimmunised patient and a 2nd "backup" patient



EVLP

Crossmatch prospective



Transplantation of the hyperimmunized patient

Transplantation of the 2nd patient

# Patients and methods

April 2012 October 2013

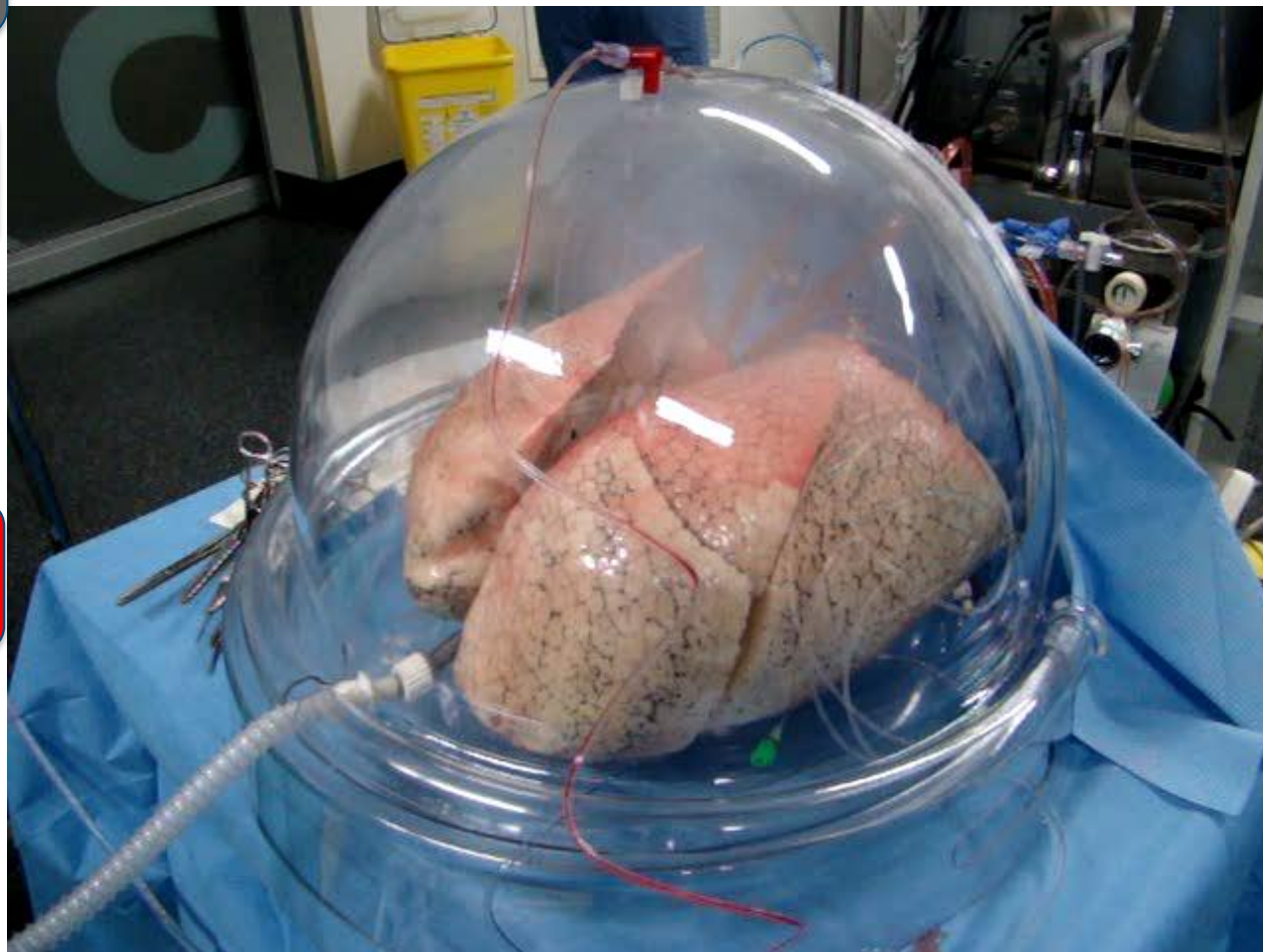
95 Transplants

"Logistics" EVLP



**3 patients  
Hyperimmunized.**

**3 patients alive at 5 years  
with no rejection**



*Logistic ex-vivo lung perfusion for hyperimmunized patient.  
De Wolf et al. Annals of thoracic surgery 2016*



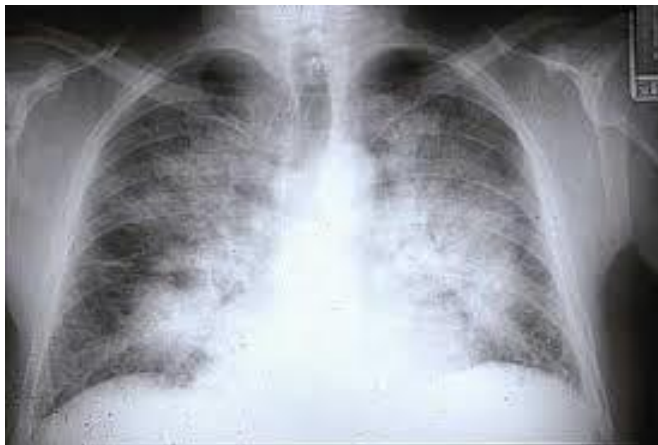
# Clinical Research Platform

# Lung parenchyma evaluation by O-Arm during ex-vivo lung reconditioning: an advantage for graft selection

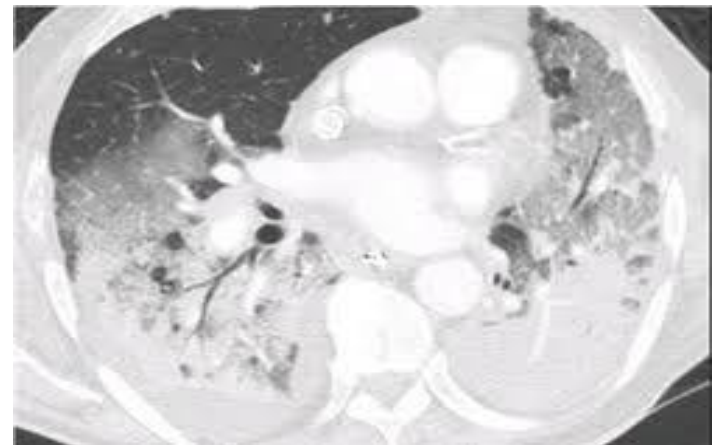
**Lung edema:**  
increased fluid in interstitial and then alveolar areas

**Chest X-ray**

**More detailed CT scan**

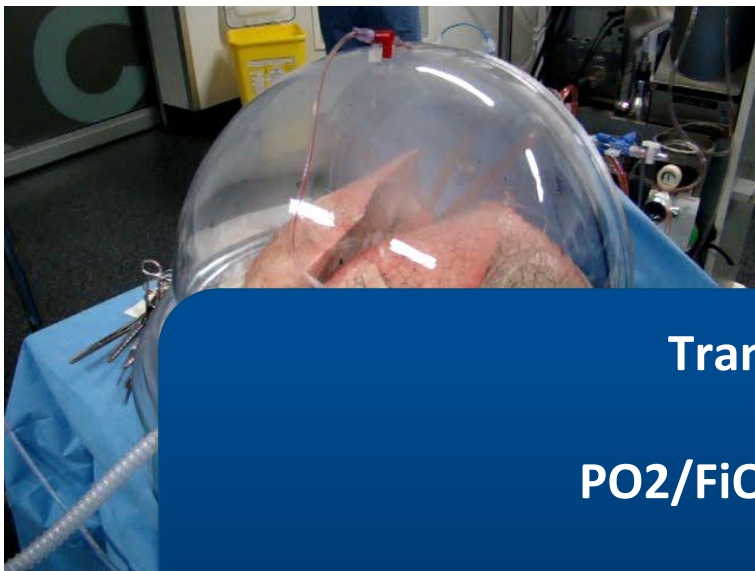


**Chest X ray  
Vs  
CT-scan**



# Methods

## EVLP : Toronto protocol



## Functional evaluation : every 1H

- Arterial PO<sub>2</sub>/FiO<sub>2</sub>
- Dynamic compliance of the lung parenchyma
- Peak ventilatory pressure
- Vascular resistance pulmonaire

## Transplant decision

PO<sub>2</sub>/FiO<sub>2</sub> ratio > 400 mmHg

+

Improvement or stability of all functional parameters



# Reconditioning

**Graft 3**  
**First cold ischemia (min)**  
**168**  
**EVLN time (min)**  
**240**



## Conclusion

**The use of O-Arm has allowed us to safely and accurately evaluate lung parenchyma progression for ex-vivo reconditioned expanded criteria grafts**

# Research Platform Animal Model

# Stabilisation of electrolyte balance by continuous dialysis during EVLP in a pig model

- No correction of the hydroelectrolytic disorders of Steen
- Turnover of 500 ml of STEEN every 2 hours
- Deterioration of lung grafts after 12 hours of EVLP
- No prolonged procedures in clinical routine

**Challenging the Ex Vivo Lung Perfusion Procedure With Continuous Dialysis in a Pig Model .**

Transplantation 2022 May 1;106(5):979-987.

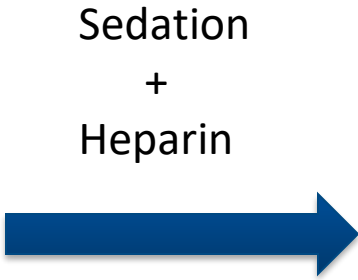
Julien De Wolf , Matthieu Glorion , Luc Jouneau , Jérôme Estephan , Jean-Jacques Leplat , Fany Blanc , Christophe Richard , Céline Urien , Antoine Roux , Morgan Le Guen , Didier Journois , Isabelle Schwartz-Cornil , Edouard Sage



# Swine non-heart-beating donor model



Large White  
50-55 kg



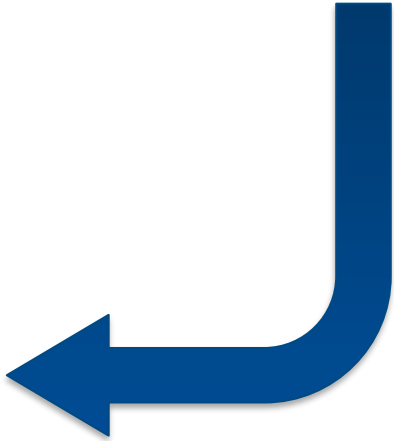
10 min  
no Touch



Pneumoplegia  
Perfadex Plus



Heart-Lung Monobloc



1H  
Warm Ischaemia

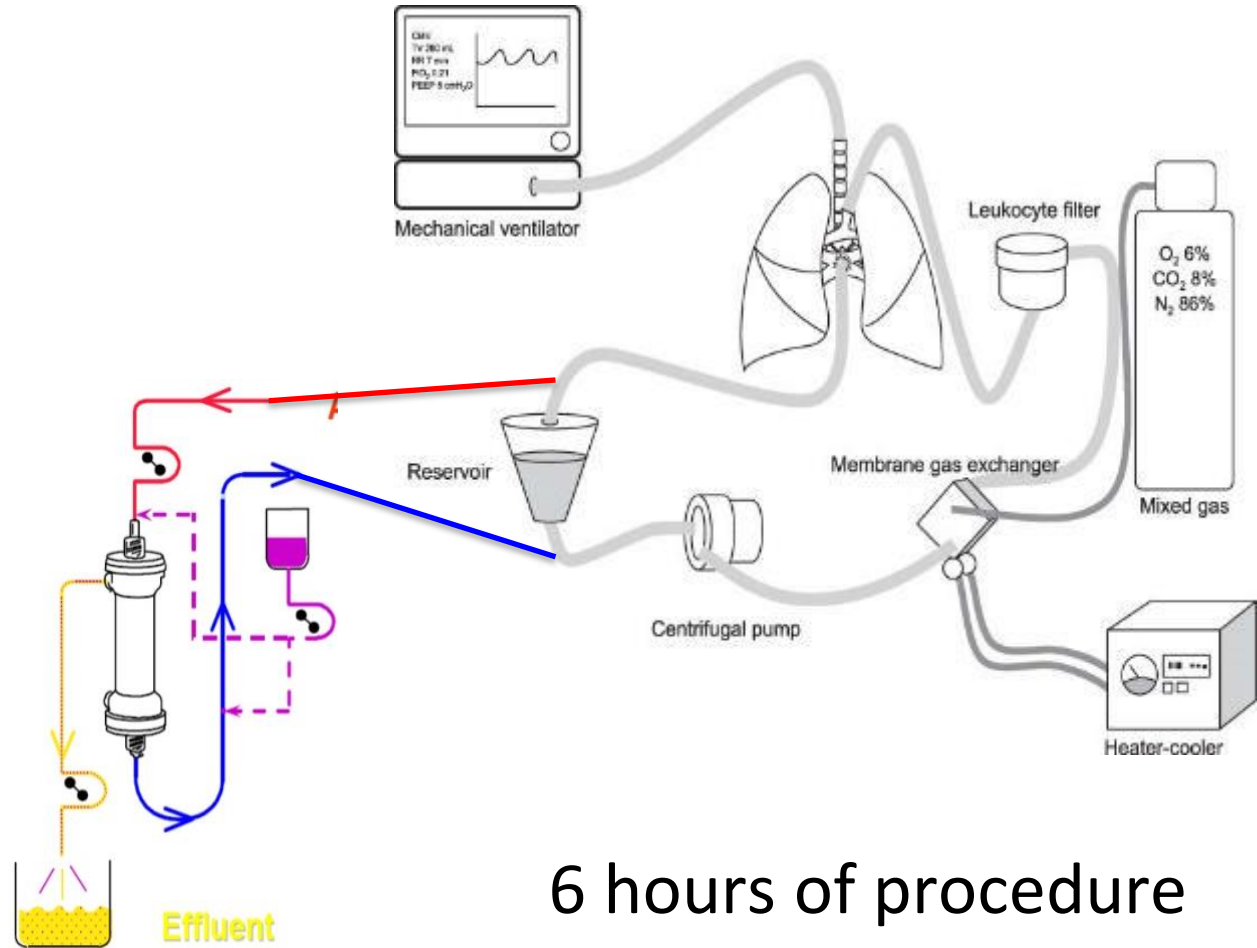




# EVLP-Dialysis



Fresenius Multifiltrate  
CCVHD mode



# Study Design



Large white pig / DCD donor model  
N=16

Adult Dialysis  
N=4



Pediatric Dialysis  
N=4



No Steen Change  
N=4



No modification

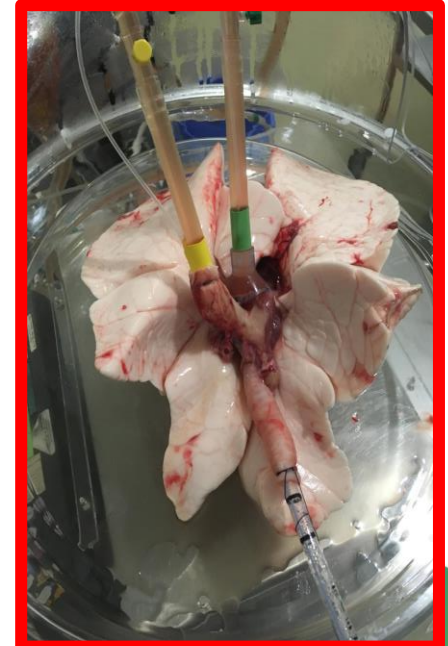
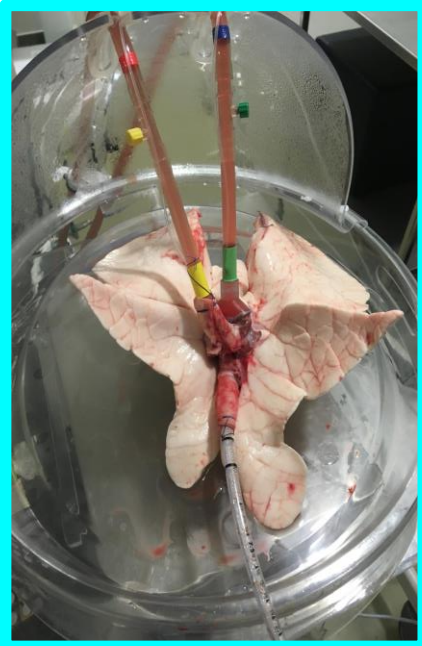
Gold standard  
N=4



Replacement  
100mL/ 1H

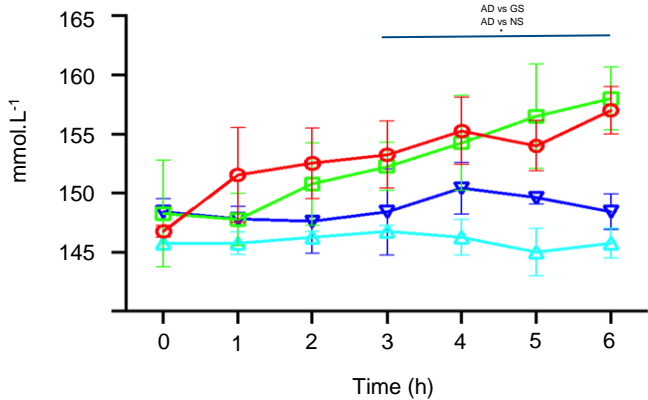
# Results

- Every procedures were completed without technical issues
- No differences regarding physiological parameters
- Dialysis grafts did not show any macroscopic difference

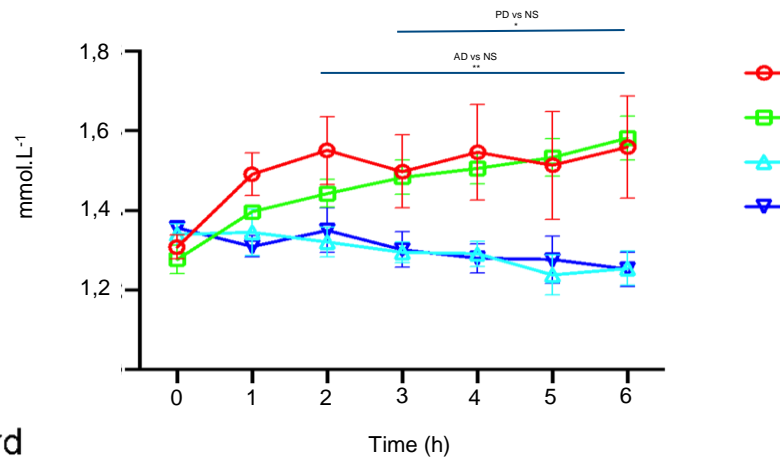


# Electrolytes

Na<sup>+</sup>

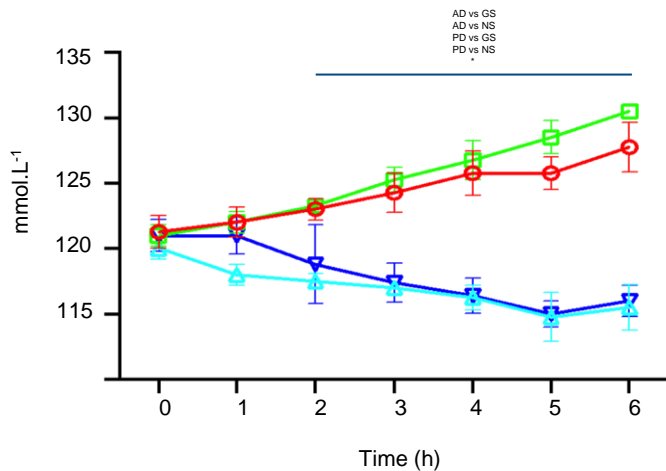


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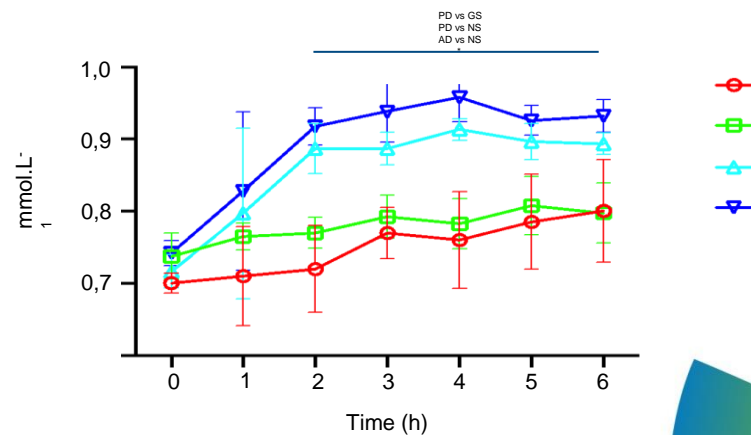


- Gold Standard
- No Steen change
- △ Adult dialysis
- ▽ Pediatric dialysis

Cl<sup>-</sup>

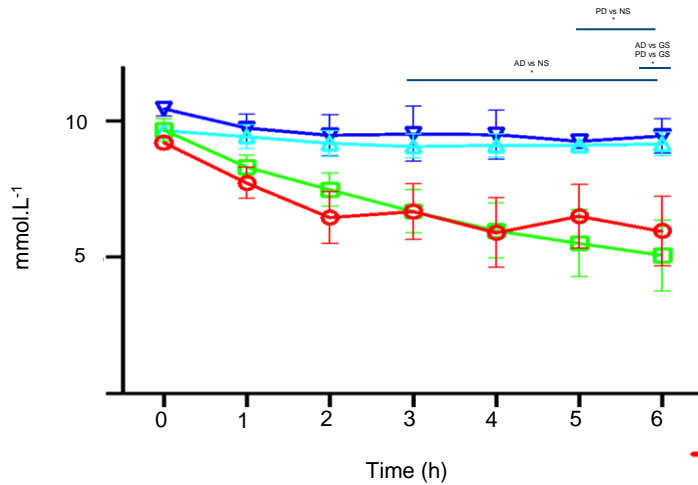


Ca<sup>2+</sup> ionisé

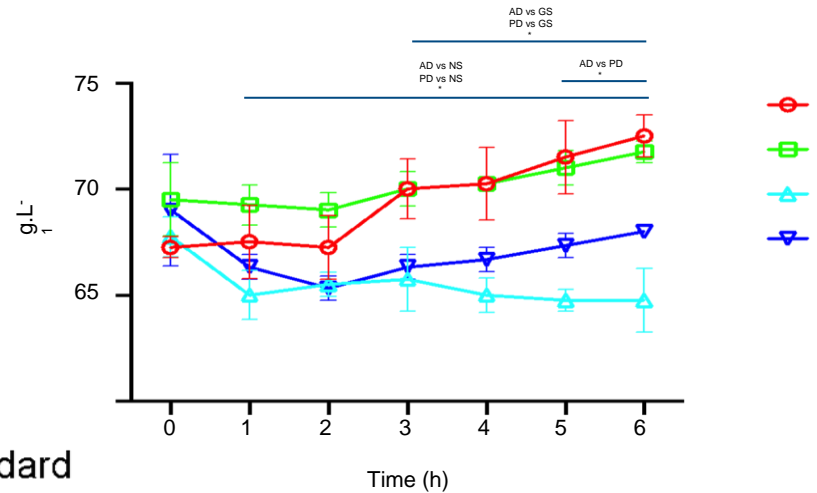


# Metabolism

## Glucose

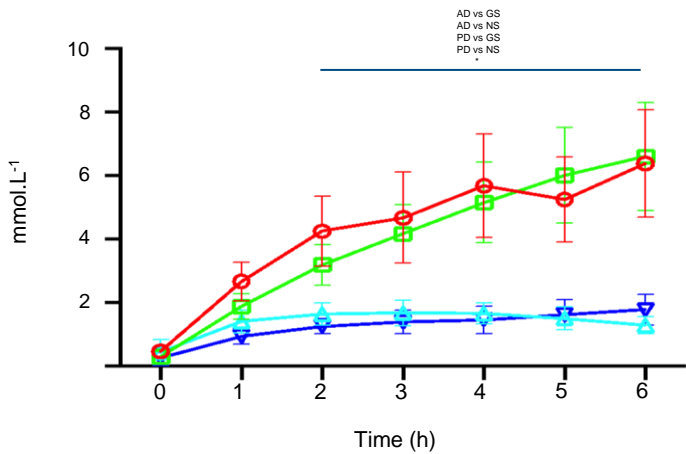


## Protide

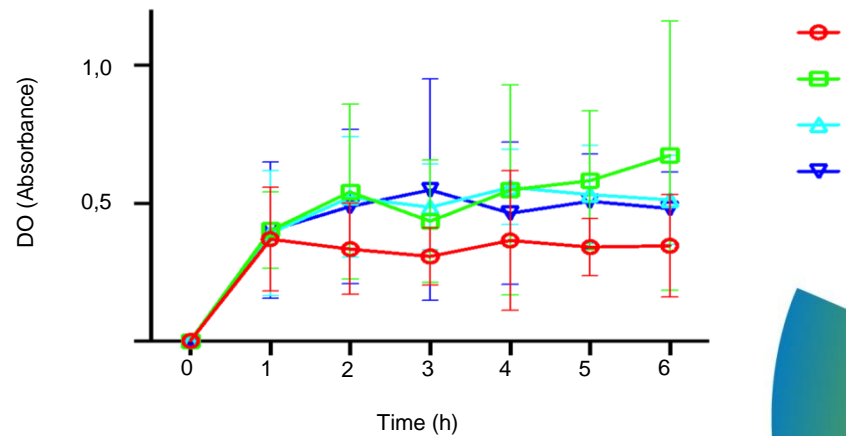


- Gold Standard
- No Steen change
- △ Adult dialysis
- ▽ Pediatric dialysis

## Lactates



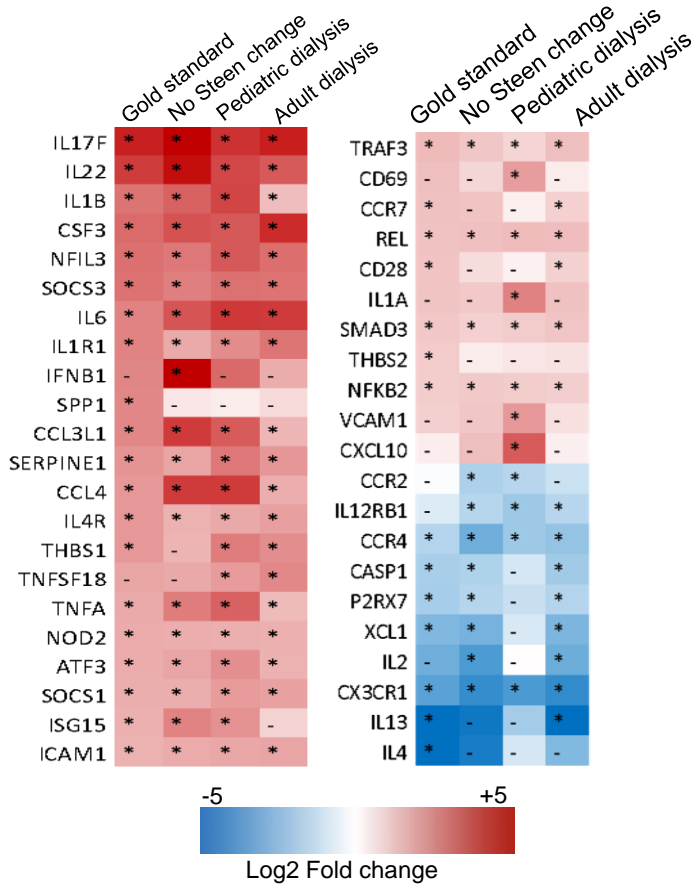
## LDH



# Genomic

## Inflammatory responses

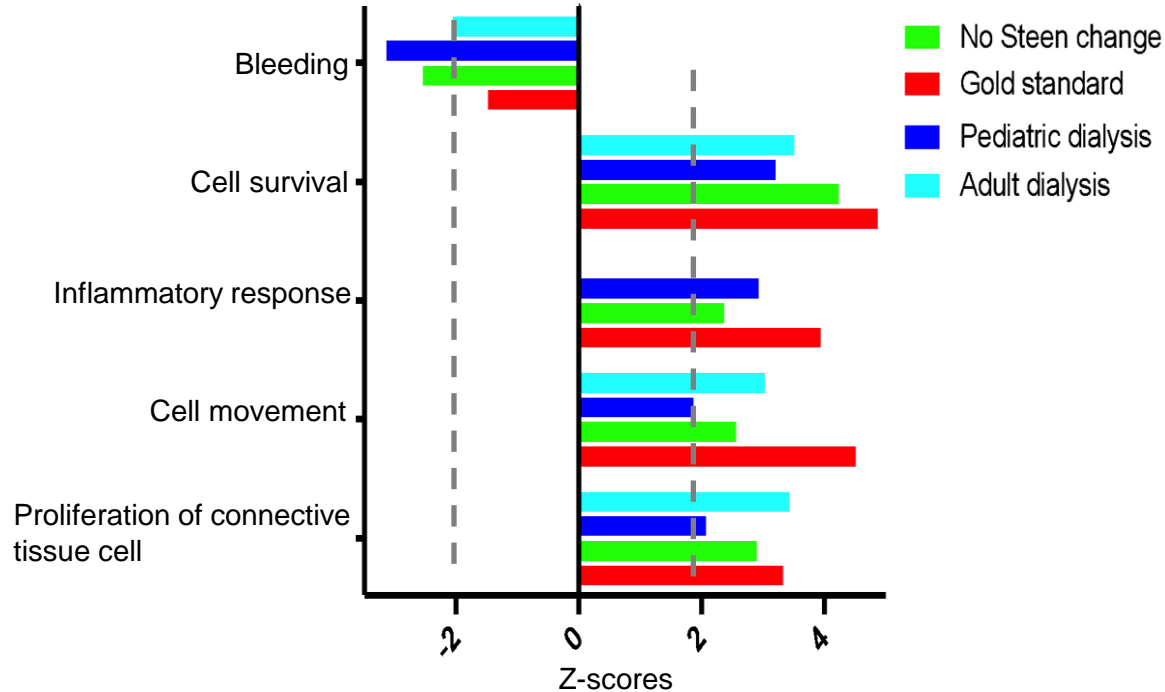
Gene expression (mean) T6H vs T0H



\* corrected p-value < 0.01

## Modulated functions predicted by gene expression

T6H vs T0H



# Conclusion

- **Perfusate management by dialysis corrected the electrolyte and metabolite concentrations**
- **Dialysis did not reduce the acute inflammatory response**
- **Perfusate replacement does not modify the gene expression in lung tissue**



Official Journal of  
The Transplantation Society  
International Liver Transplantation Society



# Transplantation®

# Advantages / Disadvantages?



# Advantages

## RECIPIENTS:

Increase of the graft pool

Expansion of indications (hyperimmune, risk of long and bleeding surgery...)

## OPERATING ROOM:

To fluidify the activity in a common block

Anticipation and adaptation

## FINANCIAL:

Reimbursement of the technique effective since 2019 (taking into account 20% of failures: 31 143 euros)

# Disadvantages

## TEAMS:

Extension of the global LT procedure time + 4H

"On anticipation"! cancellation of programmed block

## cDCD :

If WLST in the afternoon, nocturnal LT+++ (100% of cases)

Incision midnight, End of LT 6am

## FINANCIAL:

Under-use of the consumable expiry procedure



EVLP allows in France:  
Increase of the graft pool: with extended criteria  
Access to M3

Need to have a "habit/knowledge" of these extended criteria grafts

Intraoperative ECMO  
Protective post-operative support  
Prolonged resuscitation time

Thank You...  
To our  
perfusionist

