28e congrès
OUEST TRANSPLANT

SYMPOSIUM :

28e congrès OUEST TRANSPLANT

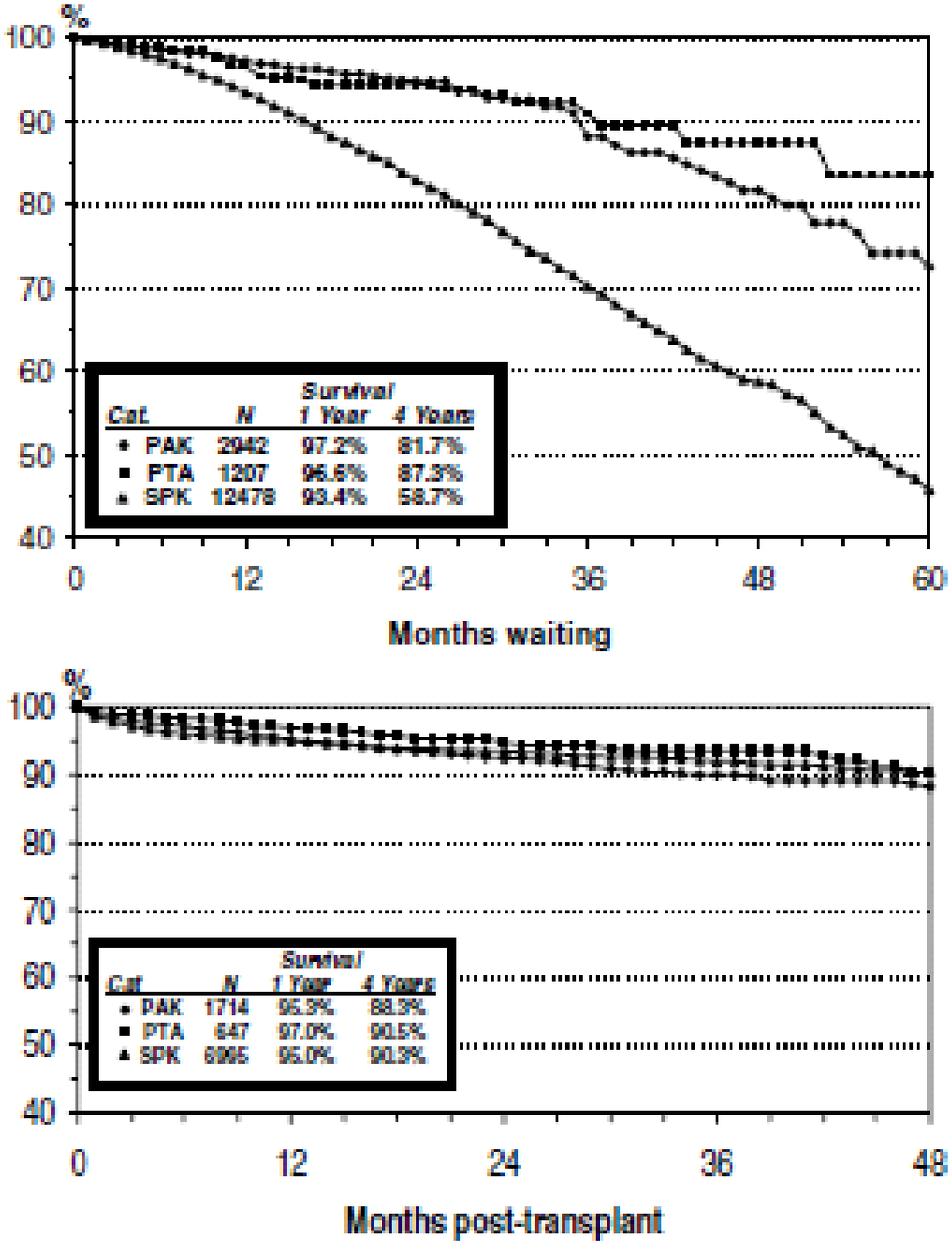
➡*Perfusion hépatique et rénale : Carlo Ceresa*
➡*Perfusion pulmonaire : Edouard Sage Phillipe Lacoste*
➡***Perfusion Pancreas : J Branchereau***

Chairs :
D. Cantarovich
A. Magnan

SYMPOSIUM :

IGL

Background : Pancreas Tx



Mortality on Tx waiting list

↓

Pancreas Tx

↓

Mortality after pancreas Tx

Clin Transplant 2005: 19: 433–455 DOI: 10.1111/j.1399-0012.2005.00378.x

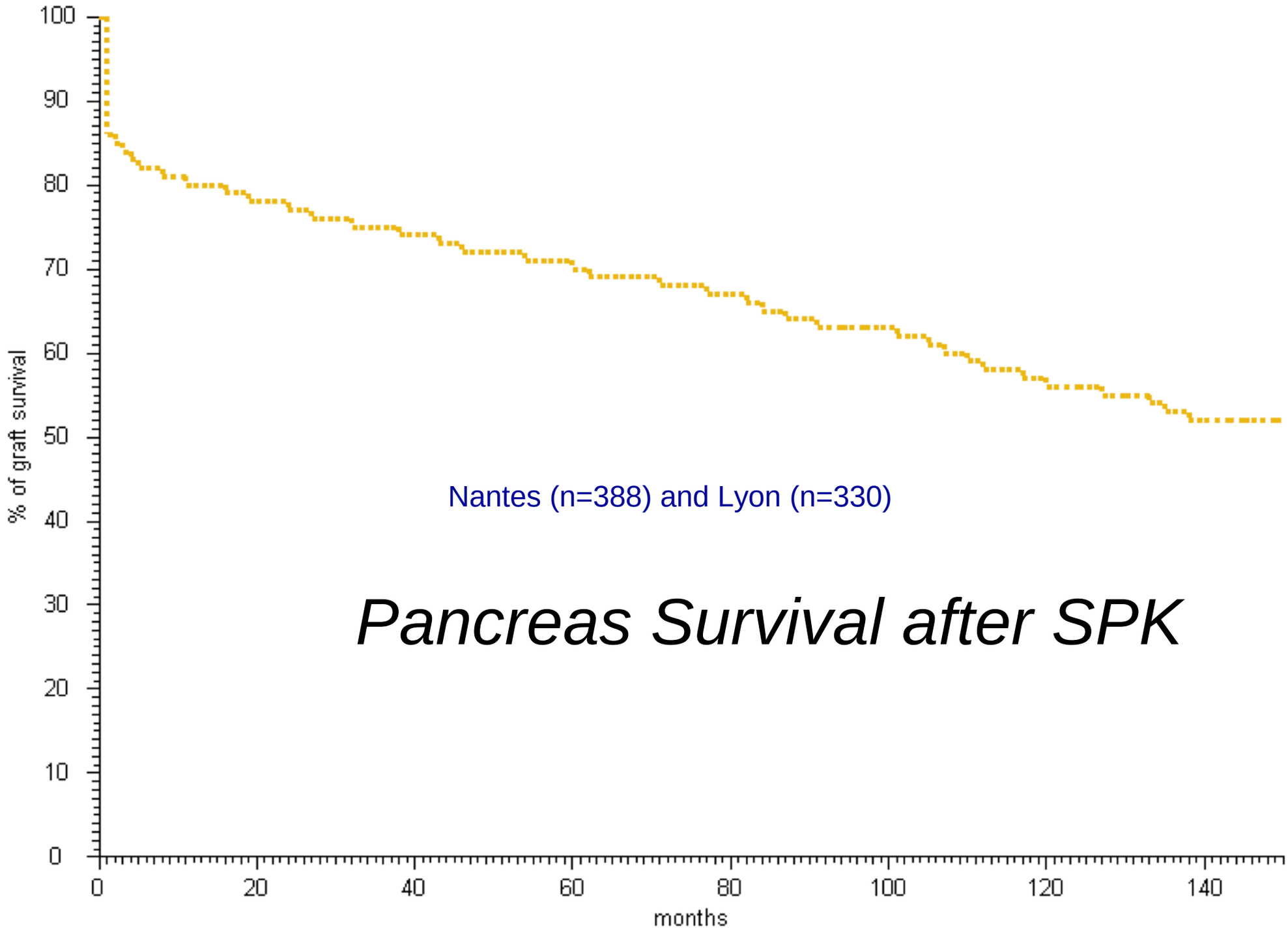
Clinical Transplantation

Review Article

Pancreas transplant outcomes for United States (US) and non-US cases as reported to the United Network for Organ Sharing (UNOS) and the International Pancreas Transplant Registry (IPTR) as of June 2004

IPTR, UNOS data Gruessner et al 2004

Ouest-Transplant

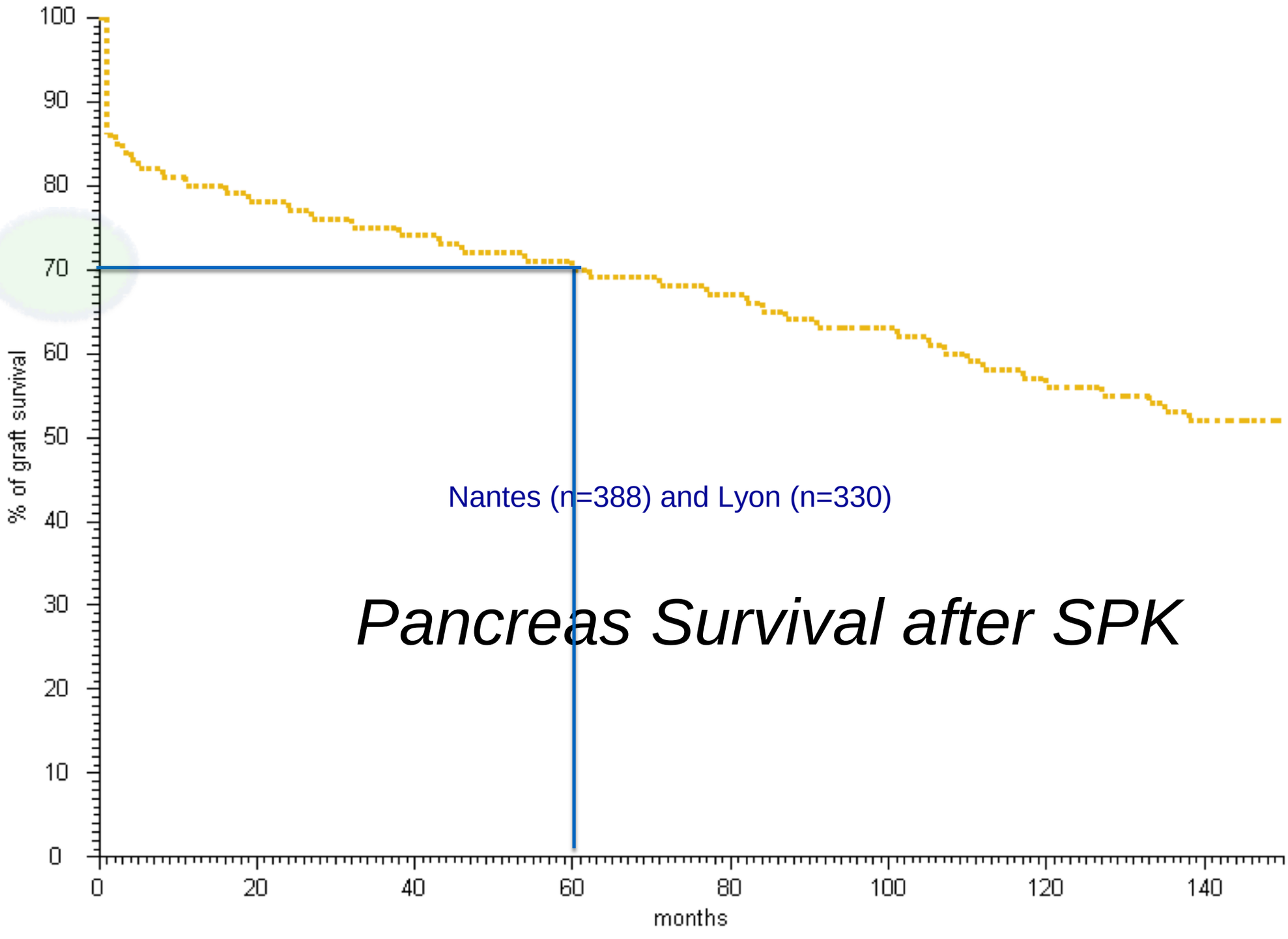


Nantes (n=388) and Lyon (n=330)

Pancreas Survival after SPK

DIVAT PANCREAS, May 2012

Ouest-Transplant



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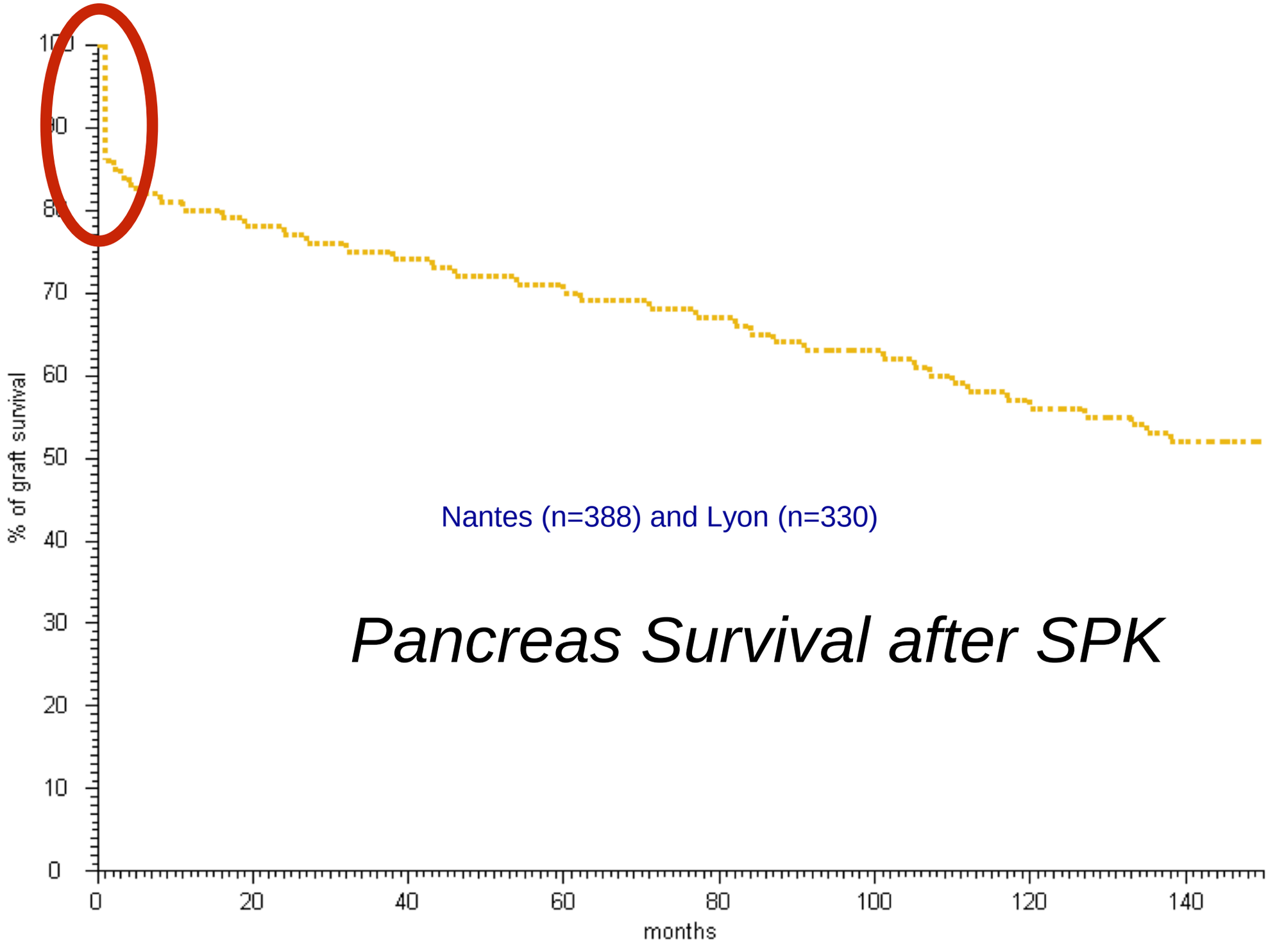
Ouest-Transplant



Nantes (n=388) and Lyon (n=330)

Pancreas Survival after SPK

DIVAT PANCREAS, May 2012

Ouest-Transplant

Nantes (n=388) and Lyon (n=330)

Pancreas Survival after SPK

Ouest-Transplant

Original Clinical Science—General

Outcomes From Pancreatic Transplant in Donation After Cardiac Death: A Review and Meta-Analysis

Sara Shahrestani, BSc [illegible]
Lawrence Yu[illegible]
and Wayne[illegible]

Extended pancreas donor program – the EXPAND study rationale and study protocol

Andrea Proneth[1], Andreas A Schnitzbauer[1,2], Florian Zeman[3], Johanna R Foerster[1], Ines Holub[1], Helmut Arbogast[4], Wolf O Bechstein[2], Thomas Becker[5], Carsten Dietz[6], Markus Guba[4], Michael Heise[7], Sven Jonas[8], Stephan Kersting[9], Jürgen Klempnauer[10], Steffen Manekeller[11], Volker Müller[12], Silvio Nadalin[13], Björn Nashan[14], Andreas Pascher[15], Falk Rauchfuss[16], Michael A Ströhlein[17], Peter Schemmer[18], Peter Schenker[19], Stefan Thorban[20], Thomas Vogel[21], Axel O Rahmel[22], Richard Viebahn[19], Bernhard Banas[23], Edward K Geissler[1], Hans J Schlitt[1] and Stefan A Farkas[1*]

Transplant International

REVIEW

Utilization of organs from donors after circulatory death for vascularized pancreas and islet of Langerhans transplantation: recommendations from an expert group

Thierry Berney[1], Catherine Boffa[2], Titus Augustine[3], Lionel Badet[4], Eelco de Koning[5], Johann Pratschke[6], Carlo Socci[7] & Peter Friend[2]

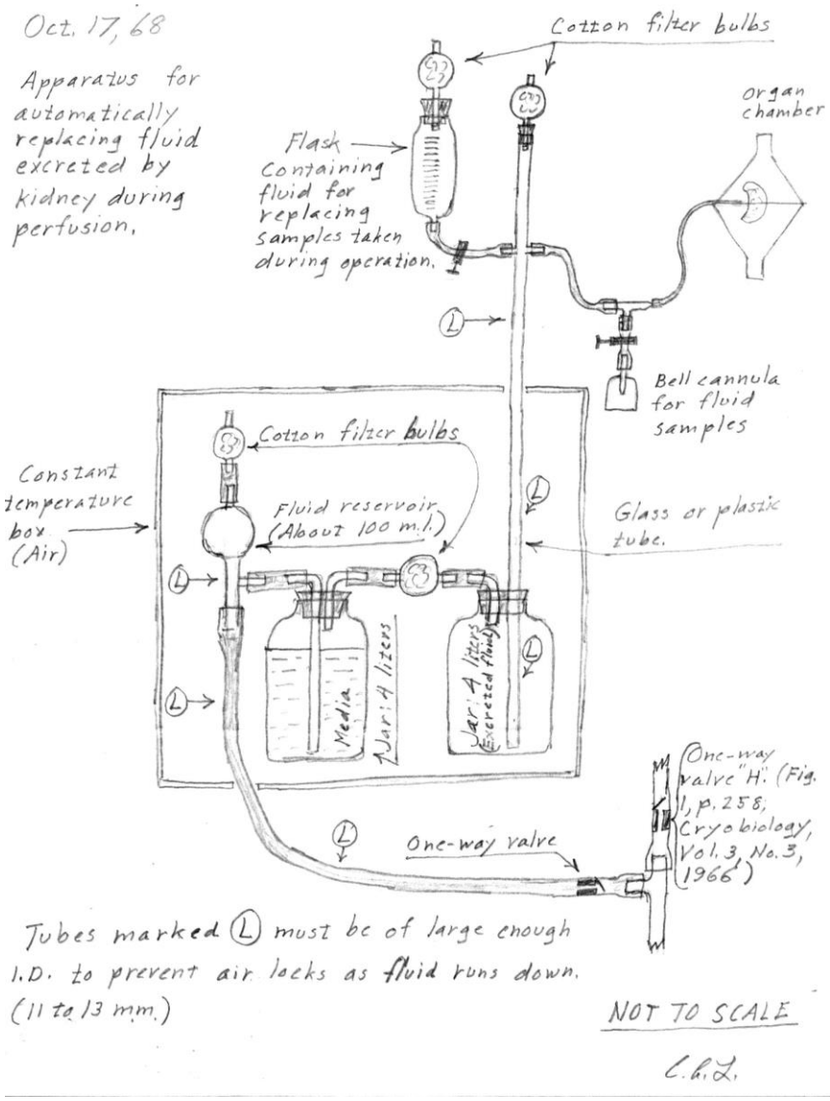
Extended pancreas : a solution to the shortage ?
few more veinous thrombosis

Machine de perfusion idéale

- **Evaluer** les greffons :
  - des paramètres de perfusion
  - de l'histologie en direct
- **Conserver** les greffons
- **Transporter** les greffons
- **Conditioner / « Soigner »**
  - oxygénation
  - nutriments
  - thérapie :
    - Cellulaire
    - Génétique
    - Médicamenteuse

Lindberg and Carrel

1935

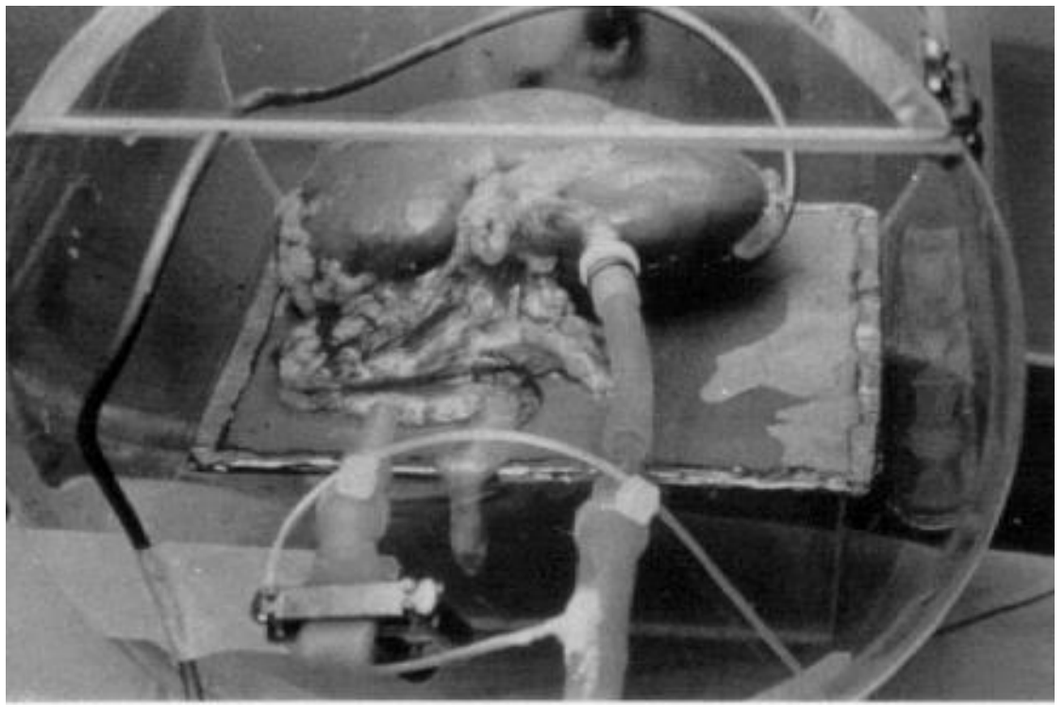


Ouest-Transplant

1964

O.Belzer

« hypothermic perfusion preservation of a human kidney had become a reality »



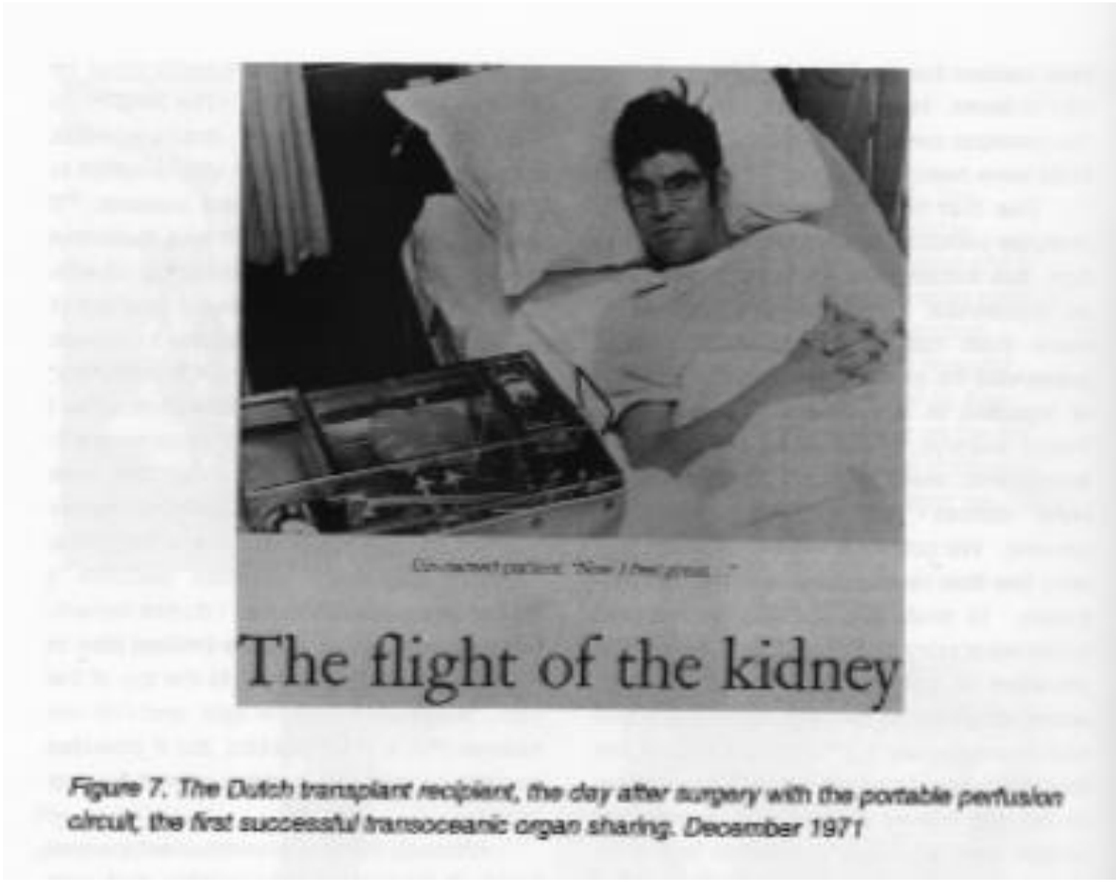


Figure 7. The Dutch transplant recipient, the day after surgery with the portable perfusion circuit, the first successful transoceanic organ sharing. December 1971

Ouest-Transplant

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 1, 2009 VOL. 360 NO. 1

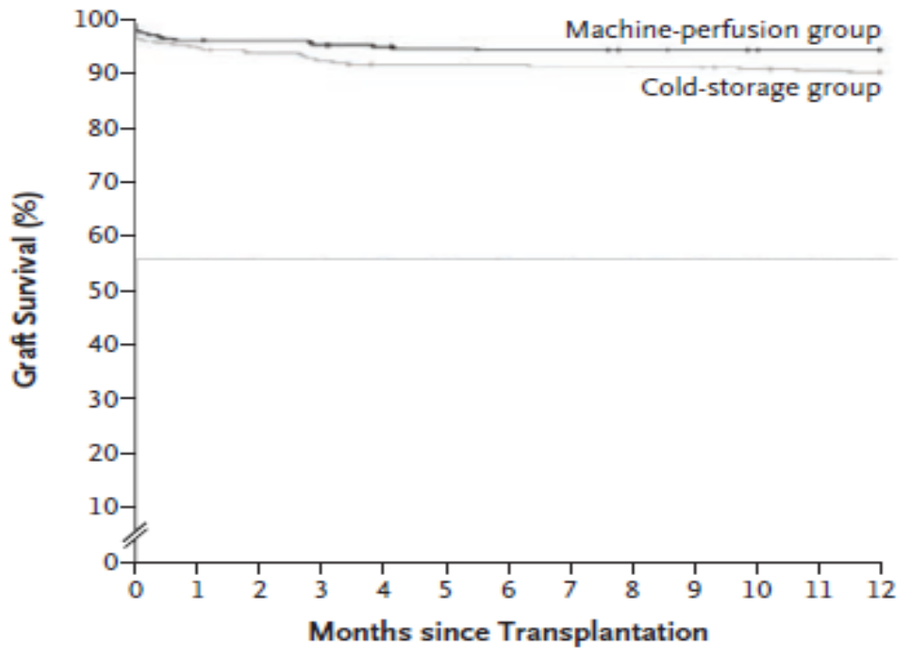
Machine Perfusion or Cold Storage in Deceased-Donor Kidney Transplantation

Cyril Moers, M.D., Jacqueline M. Smits, M.D., Ph.D., Mark-Hugo J. Maathuis, M.D., Ph.D., Jürgen Treckmann, M.D., Frank van Gelder, Bogdan P. Napieralski, Margitta van Kasterop-Kutz, Jaap J. Homan van der Heide, M.D., Ph.D., Jean-Paul Squifflet, M.D., Ph.D., Ernest van Heurn, M.D., Ph.D., Günter R. Kirste, M.D., Ph.D., Axel Rahmel, M.D., Ph.D., Henri G.D. Leuvenink, Ph.D., Andreas Paul, M.D., Ph.D., Jacques Pirenne, M.D., Ph.D., and Rutger J. Ploeg, M.D., Ph.D.*

Kidneys from DCD :

Better graft survival after 1year :

98 % vs 94 % (p=0,03)



No. at Risk													
Machine-perfusion group	336	323	322	319	317	315	314	314	312	311	310	309	309
Cold-storage group	336	318	313	308	304	304	304	303	302	302	299	299	296

Figure 3. Graft Survival after Transplantation.

The rate of graft survival at 1 year in the machine-perfusion group was significantly higher than the rate in the cold-storage group (94% vs. 90%, P=0.04). Data on graft survival were censored at the time of death in patients who died with a functioning allograft.

Ouest-Transplant

Demain …

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Successful Dual Kidney Transplantation After Hypothermic Oxygenated Perfusion of Discarded Human Kidneys

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ACDEF 1 **Matteo Ravaioli**
ABCDEF 1 **Vanessa De Pace**
DF 2 **Giorgia Comai**
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CDF 1 **Alessandro Cucchetti**
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1 Department of Medical and Surgical Sciences, S. Orsola-Malpighi Hospital, Alma Mater Studiorum, University of Bologna, Bologna, Italy
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Conflict of interest: None declared
Source of support: Funding sources were provided by "Fondazione del Monte" and University of Bologna

JOURNAL OF SURGICAL RESEARCH **34,** 493–504 (1983)

1983

Preservation of Canine Segmental Pancreatic Autografts: Cold Storage versus Pulsatile Machine Perfusion[1]

G. FLORACK, M.D.,[2] D. E. R. SUTHERLAND, M.D., PH.D.,[3] J. HEIL, B.S., J. P. SQUIFFLET, M.D., AND J. S. NAJARIAN, M.D.

Department of Surgery, University of Minnesota Health Sciences Center, Minneapolis, Minnesota

Presented at the Annual Meeting of the Association for Academic Surgery, San Diego, California, November 7–10, 1982

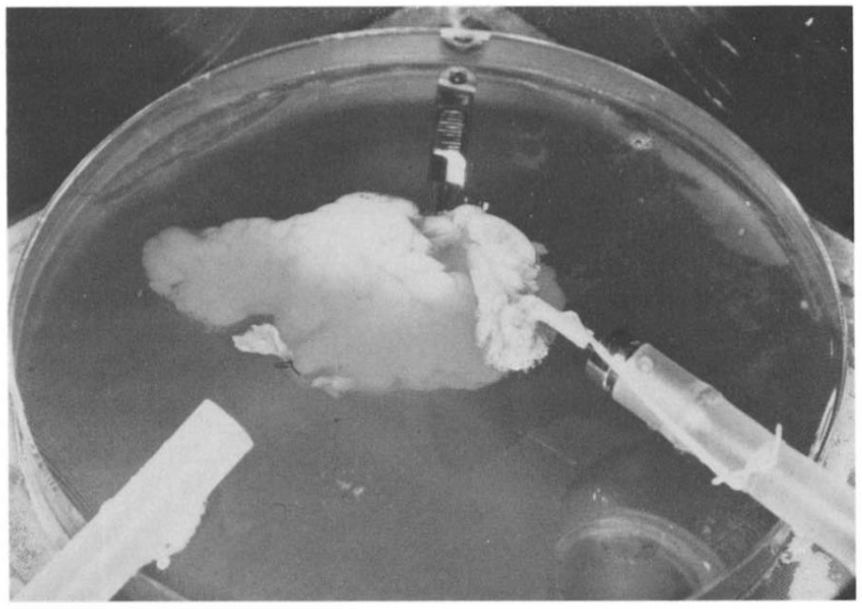

FIG. 1. Segmental pancreatic graft at the beginning of pulsatile perfusion on the Mox-100 machine.

- ***perfusion 30 mmHg***
- ***ringer solution***
- ***24 and up to 48h***

JOURNAL OF SURGICAL RESEARCH **34,** 493–504 (1983)

Preservation of Canine Segmental Pancreatic Autografts: Cold Storage versus Pulsatile Machine Perfusion[1]

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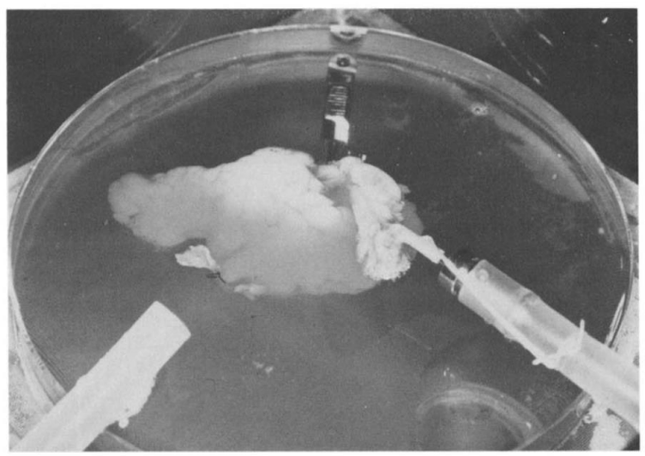


FIG. 1. Segmental pancreatic graft at the beginning of pulsatile perfusion on the Mox-100 machine.

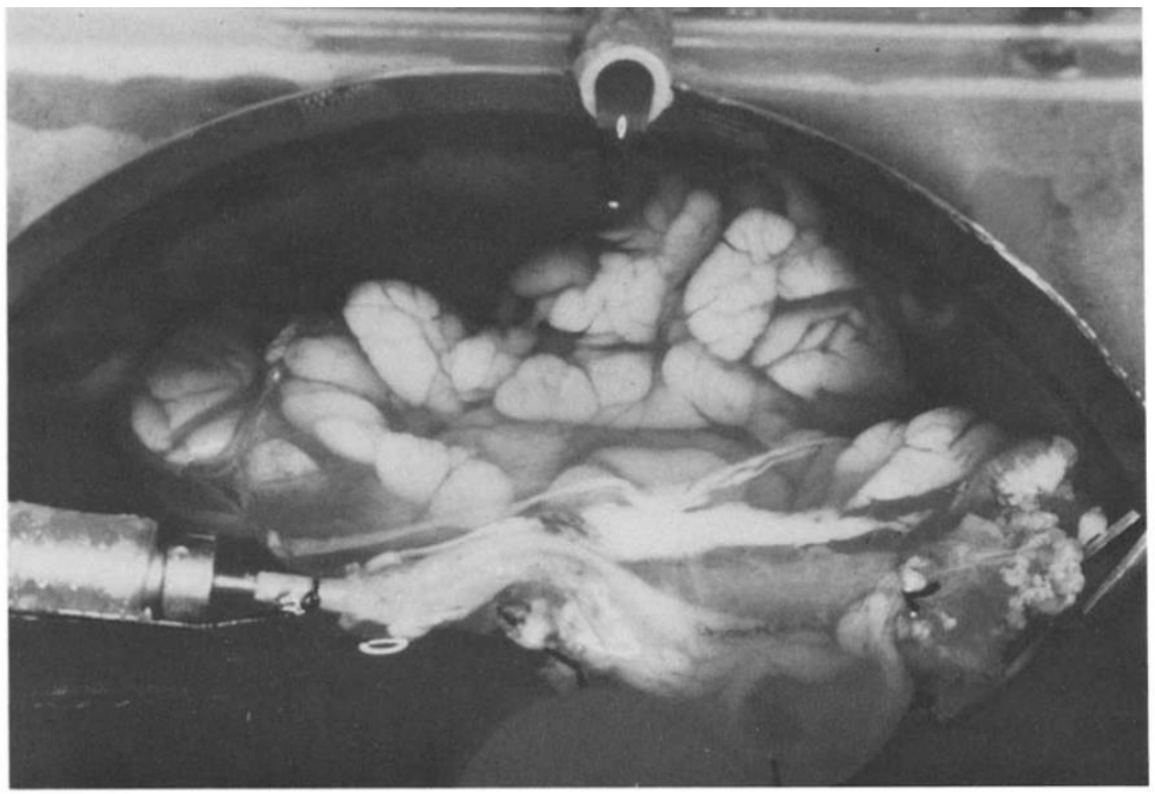


FIG. 2. Segmental pancreatic graft with severe interstitial edema developing after 48 hours of pulsatile machine perfusion.

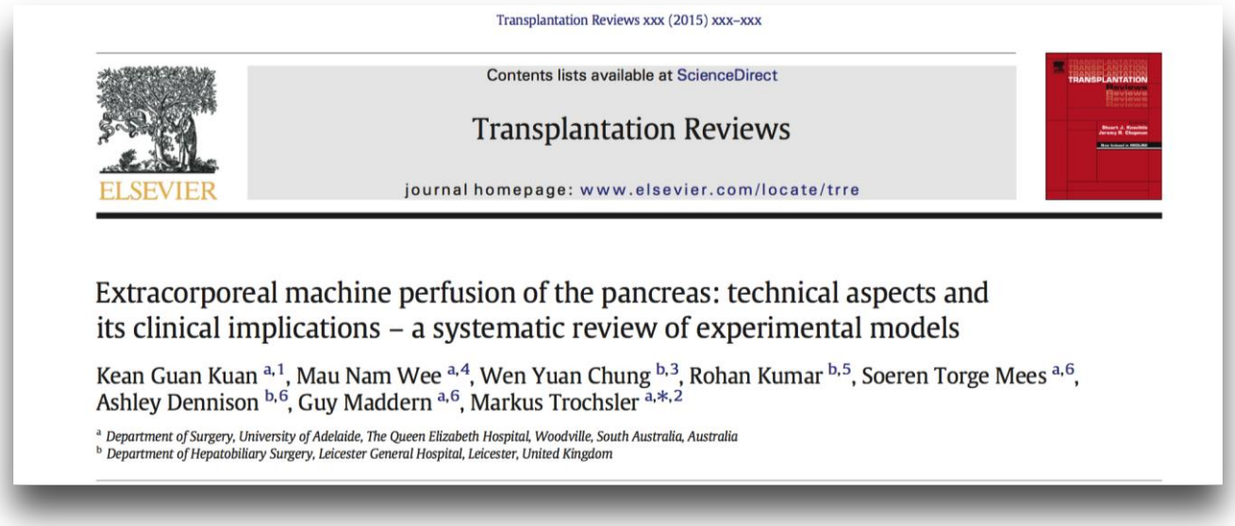
Severe interstitial edema

Nowadays still no clinical publication

- **Only few experimental series**

  - 8 normothermic

  - 13 hypothermic



Transplantation Reviews xxx (2015) xxx–xxx

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journal homepage: www.elsevier.com/locate/trre

Extracorporeal machine perfusion of the pancreas: technical aspects and its clinical implications – a systematic review of experimental models

Kean Guan Kuan [a,1], Mau Nam Wee [a,4], Wen Yuan Chung [b,3], Rohan Kumar [b,5], Soeren Torge Mees [a,6], Ashley Dennison [b,6], Guy Maddern [a,6], Markus Trochsler [a,*,2]

[a] Department of Surgery, University of Adelaide, The Queen Elizabeth Hospital, Woodville, South Australia, Australia
[b] Department of Hepatobiliary Surgery, Leicester General Hospital, Leicester, United Kingdom

- Pancreas perfusion: **fear of barotrauma injuries and edema**
  - endothelial lesions
  - platelet activation
  - thrombosis

Hypothermic Machine Perfusion Improves the Quality of Marginal Donor Pancreata

M. Leemkuil,[1] M. Engelse,[2] R. Ploeg,[3] E. de Koning,[2] C. Krikke,[1] H. Leuvenink.[1]

[1]Surgery, University Medical Center Groningen, Groningen, Netherlands
[2]Nephrology, Leiden University Medical Center, Leiden, Netherlands
[3]Transplant Biology, Oxford Transplant Center, Oxford, United Kingdom.

Meeting: 2015 American Transplant Congress

Abstract number: 853

Keywords: Donors, Islets, marginal, Pancreas transplantation, Preservation

one abstract : ISLET isolation

Introduction. Pancreas or islet transplantation is considered the most effective treatment for patients with type 1 diabetes mellitus. Due to the persistent organ shortage, pancreata from marginal donors are more frequently used for transplantation or islet isolation. These grafts are more vulnerable to ischemic damage. The traditional preservation method, cold storage (CS), might not be sufficient to completely prevent this damage. It is hypothesized that hypothermic machine perfusion (HMP) can improve the quality of the donor pancreas by an increase in viability and a reduction in injury compared to CS.

Methods. In this study, 8 human pancreata (4 DCD and 4 DBD) were preserved by HMP and 8 (4 DCD and 4 DBD) by CS. HMP was performed for 6 hours with oxygenated Belzer UW-MPS® with dual perfusion of the mesenteric superior artery and the splenic artery. Tissue biopsies and samples of the preservation fluid were collected at baseline and after 6 hours of preservation by either HMP or CS.

Results. At baseline, the ATP content in the DCD group (8,2 +- 5,6 ¯o;mol/gram protein) was significantly lower than in the DBD group (43,5 +- 16,2 ¯o;mol/gram protein). After 6 hours of CS, the ATP content decreased to 4,2 +- 1,7 (DCD) and 25,6 +- 8,6 (DBD) ¯o;mol/gram protein. In the HMP preserved pancreata, the ATP content increased to 47,9 +- 25 (DCD) and 136,4 +- 144 (DBD) ¯o;mol/gram protein. In the DCD group, the ATP content after HMP was significant higher compared to CS and it was equivalent to the ATP content at baseline in the DBD group. During HMP, amylase, lipase and LDH levels in the preservation fluid increased. Lipase and LDH levels reached a plateau after 5 hours of HMP.

Conclusion. HMP seems to improve donor pancreata quality, demonstrated by the increased levels of ATP and potentially by washing out degrading enzymes. Therefore, we propose that DCD pancreata preserved by HMP could reach the quality of DBD pancreata and could be considered transplantable.

Hypothermic Pulsatile Perfusion of Human Pancreas

Is it feasible and safe for the whole organ?

First study of HPP of pancreas for **whole organ** transplantation

Julien Branchereau, Karine Renaudin, and Diego Cantarovich

institut transplantation urologie néphrologie
INSERM - UMR 643

CENTRE HOSPITALIER UNIVERSITAIRE DE NANTES

Study

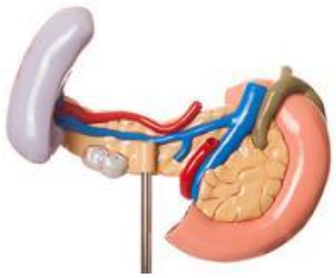
Primary endpoint : Is HPP feasible for pancreas?

Secondary EP : Is it safe ?

- **Pancreas discarded** for clinical Tx (WO or Islet)
- **Approved by ethics committee and National Biomedecine Agency** :*ref PFS08-017 amendement spécifique du 6/8/2014*

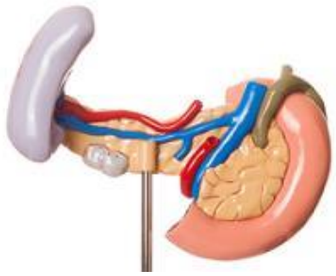
Study design : 3 groups

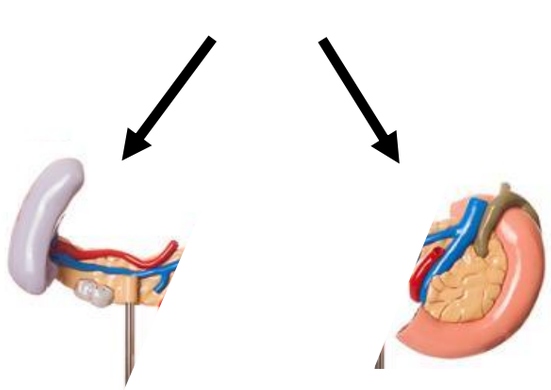
Control



n=2

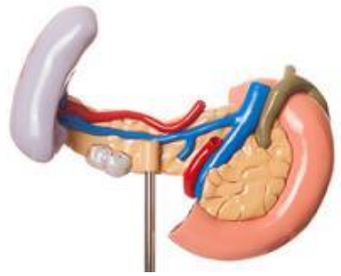
Splited





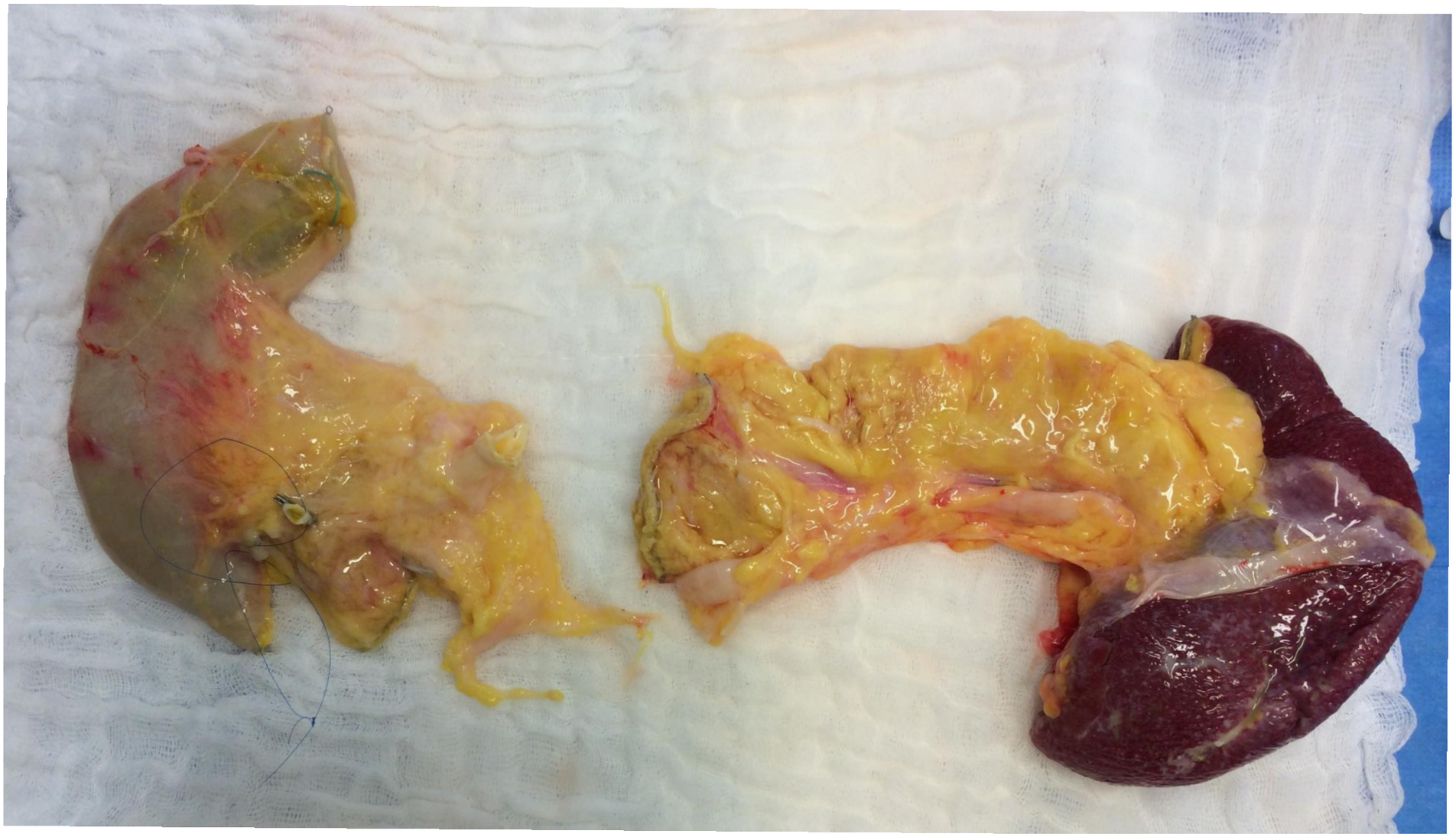
n=2

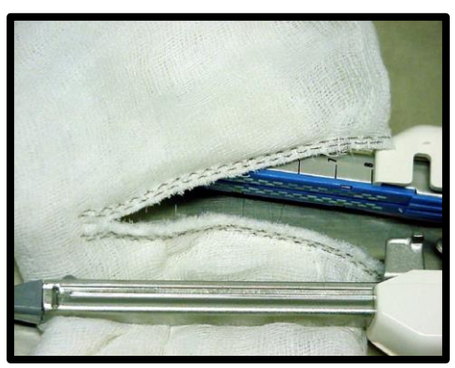
Whole



n=7

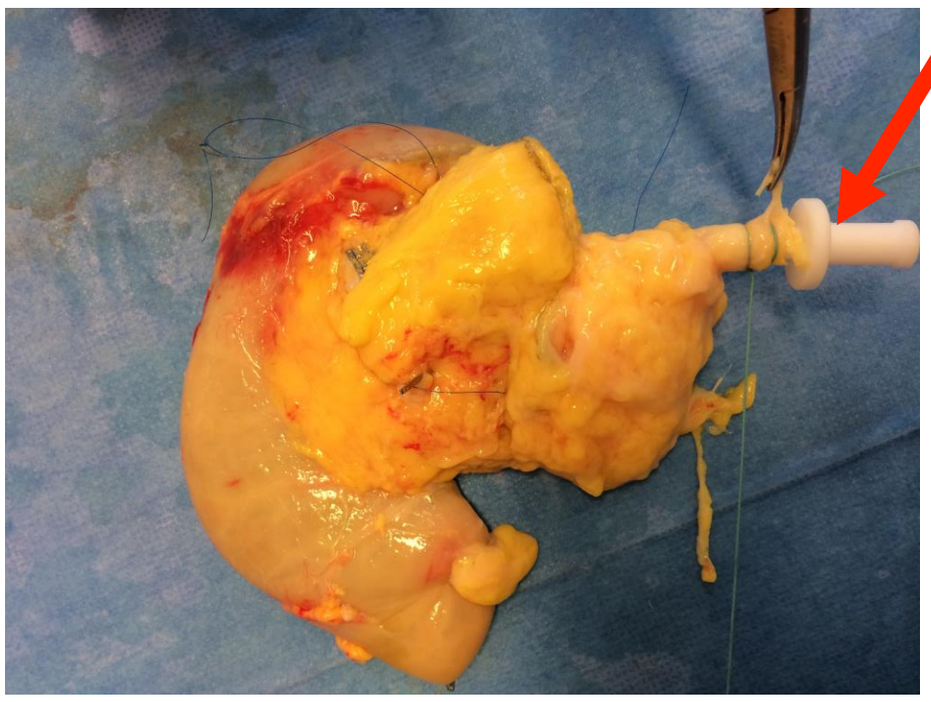
Group 2 : Splited *n*=2





GIA stapper 80 mm

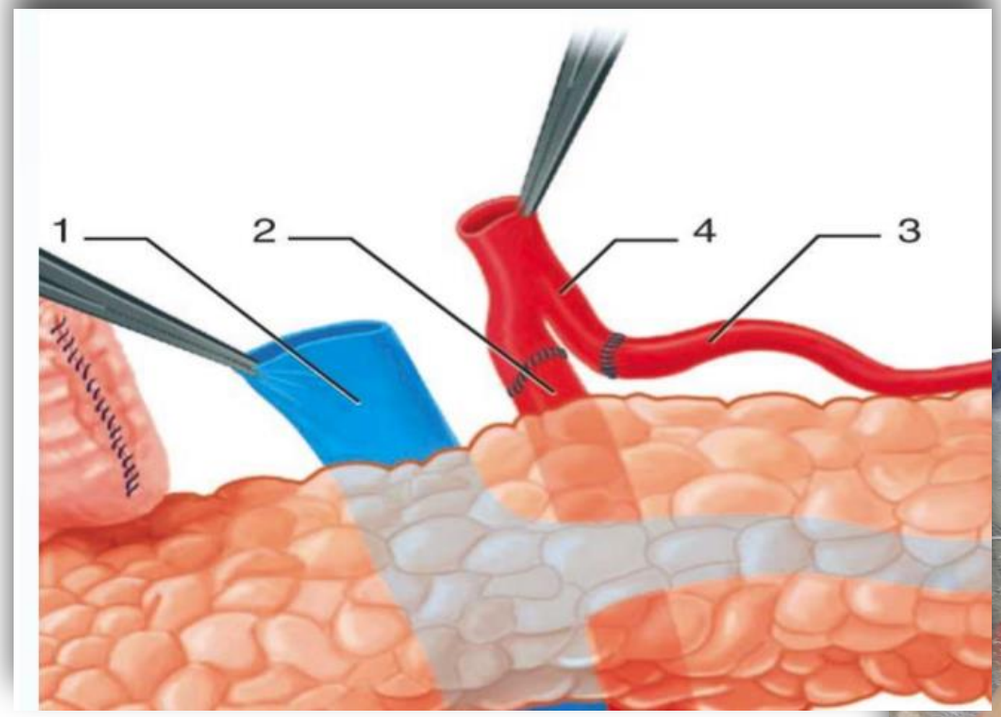
Group 2 : Splited *n=2*



HPP

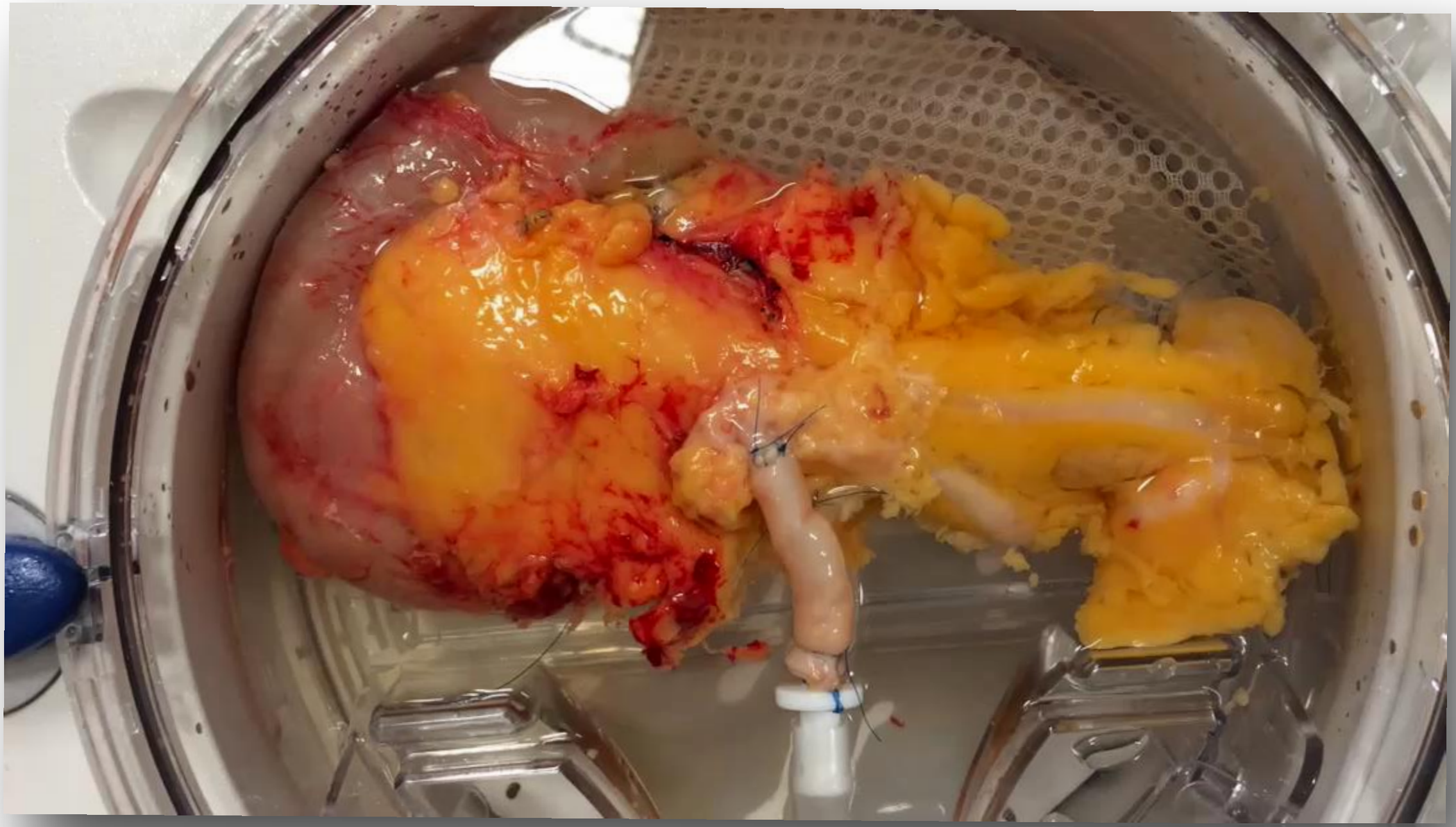
CS

Group 3 :Whole organ HPP *n*=7



Ouest-Transplant

Pulsatile perfusion

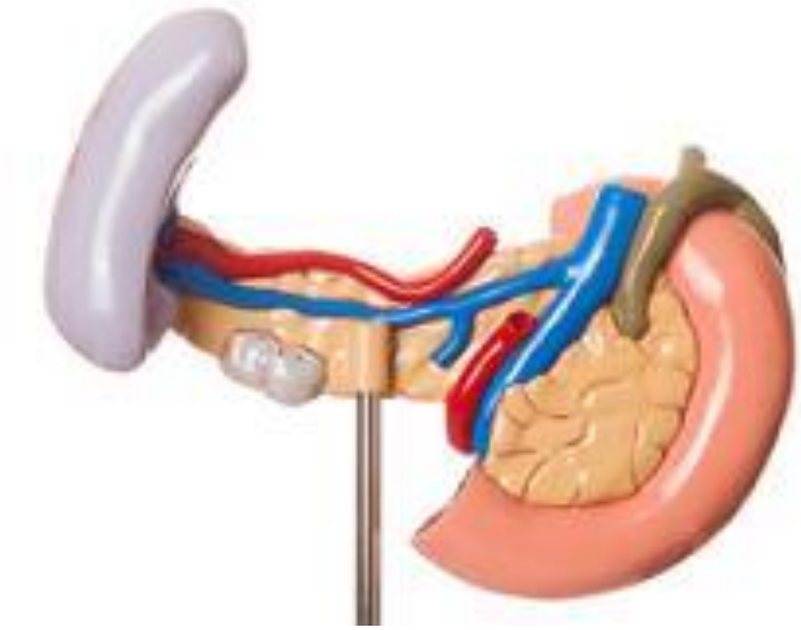


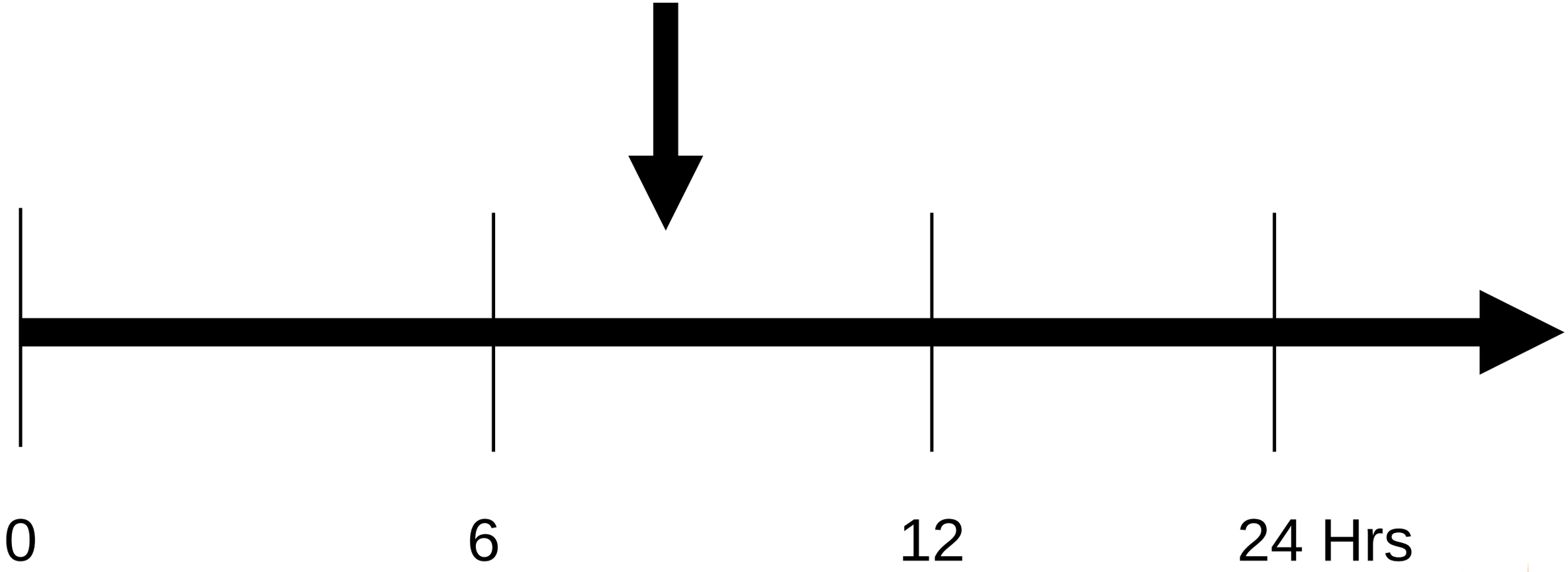
institut transplantation urologie nephrologie
INSERM - UMR 643

Pulsatile perfusion

- Waves **pulsatile machine**
- **Perf-Gen perfusat**: 1 liter
- Pressure: **25 mm HG**
- Temperature: **4/5 °C**

Histology at 0, 6, 12 and 24 hours





Ouest-Transplant

RESULTS

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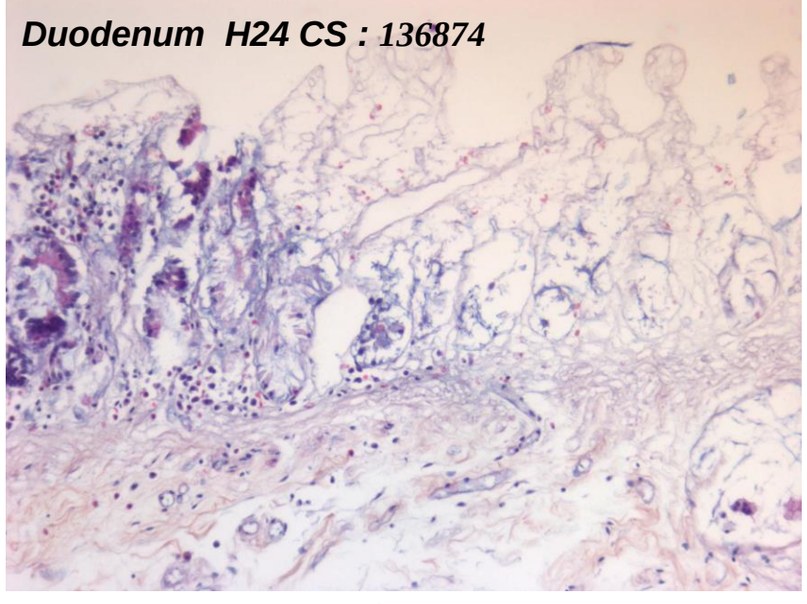
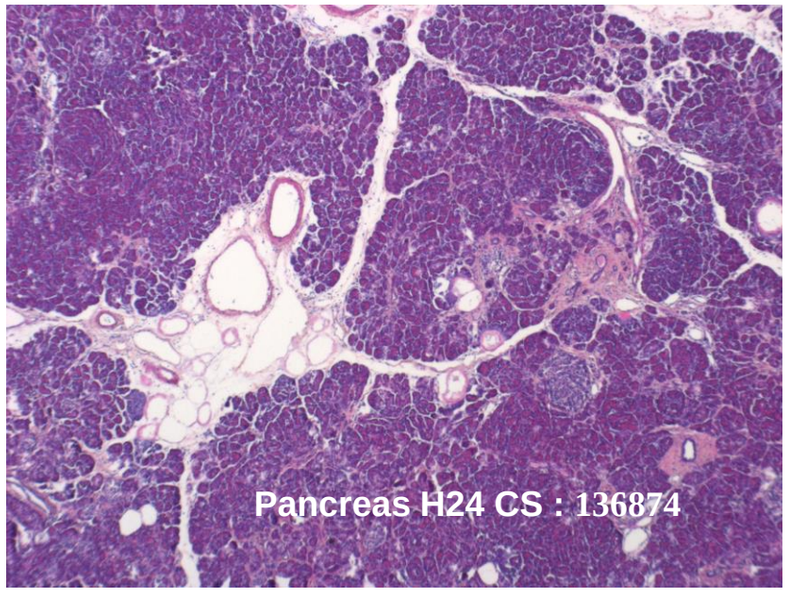
UNIVERSITAIRE DE NANTES

Control group

	n° CRSITAL	Conservation	T12		T24	
			exocrine tissue	ilset	exocrine tissue	ilset
8	133982	SCS	ischemic necrosis /steatonecrosis	ischemic necrosis	/	/
10	136874	SCS	no ischemic necrosis	no ischemic necrosis	ischemic necrosis /steatonecrosis	ischemic necrosis





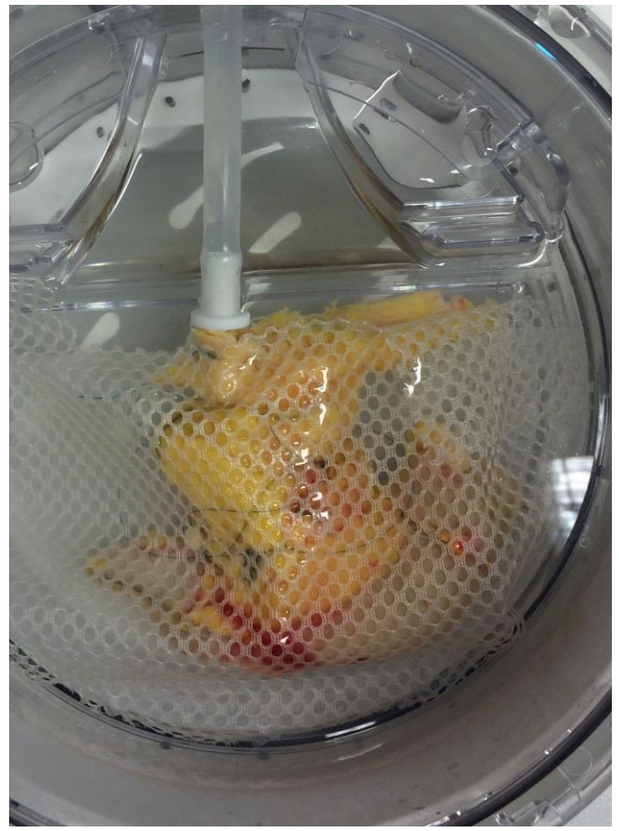
Control n=2

Macroscopic aspect unchanged

BUT Ischemic & necrosis lesions at 24 H

Split group : Macroscopic aspect

HPP (splited) HEAD
115035
H0



HPP (splited) HEAD
115035 H24

Split group n =2

No difference between Head and Tail

No difference after 24 H

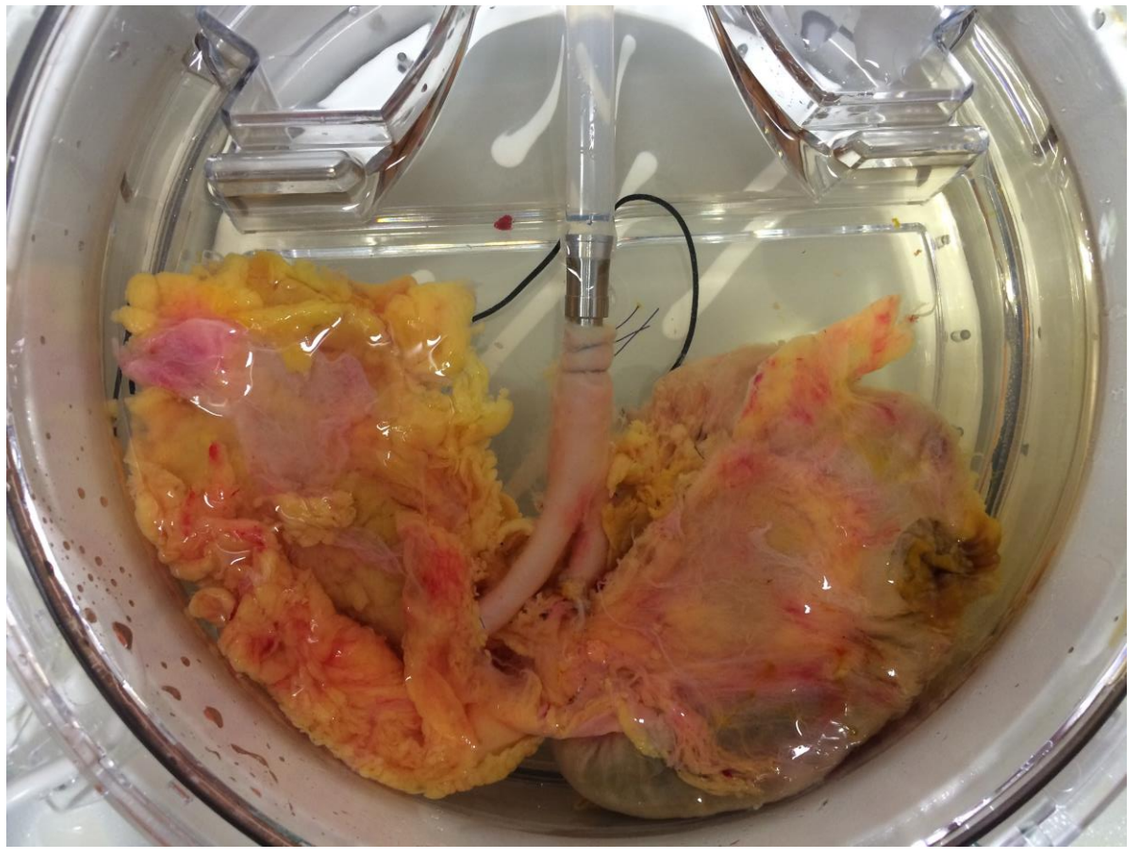
Split group : Histologic aspect

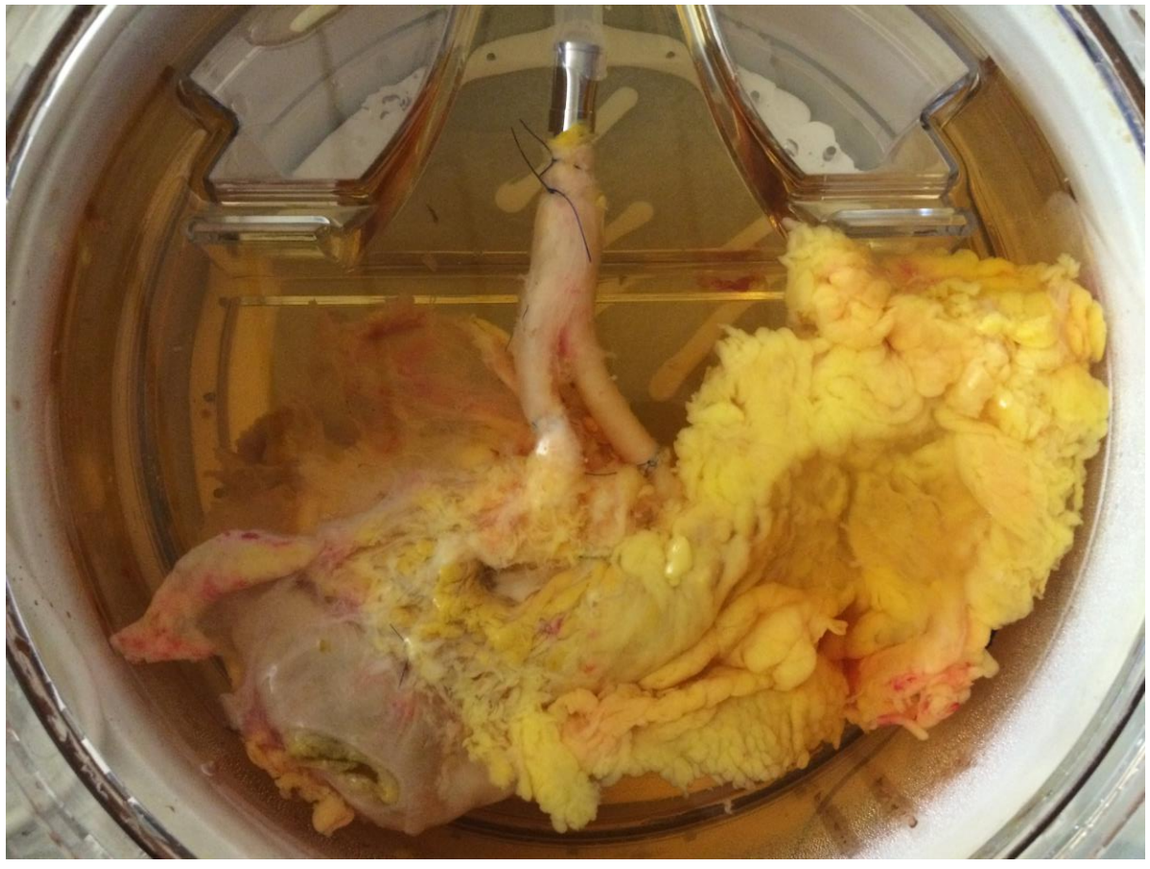
n°	CRSITAL	Conservation	T12		T24	
			exocrine tissue	ilset	exocrine tissue	ilset
1	115035	HPP (splited) HEAD	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis
		CS (splited) TAIL	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis
2	116232	HPP (splited) HEAD	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis
		CS (splited) TAIL	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis

Split group n =2

No difference between Head and Tail

Whole organ HPP: Macroscopic aspect





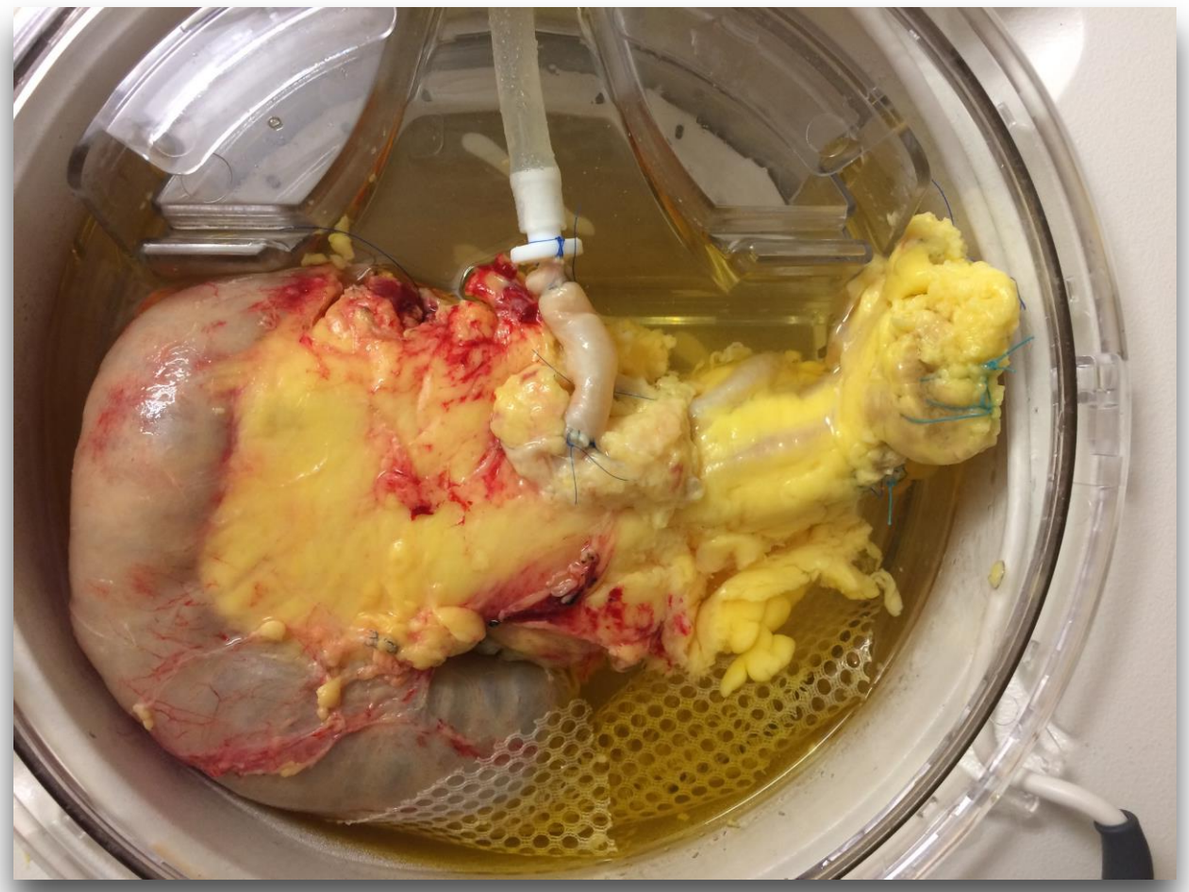
0h

- **female**
- **57 years**
- **alcohol**
- **57 kg /155 cm**
- **BMI 24.7**

24hrs

Macroscopic aspect unchanged

Whole organ HPP: Macroscopic aspect



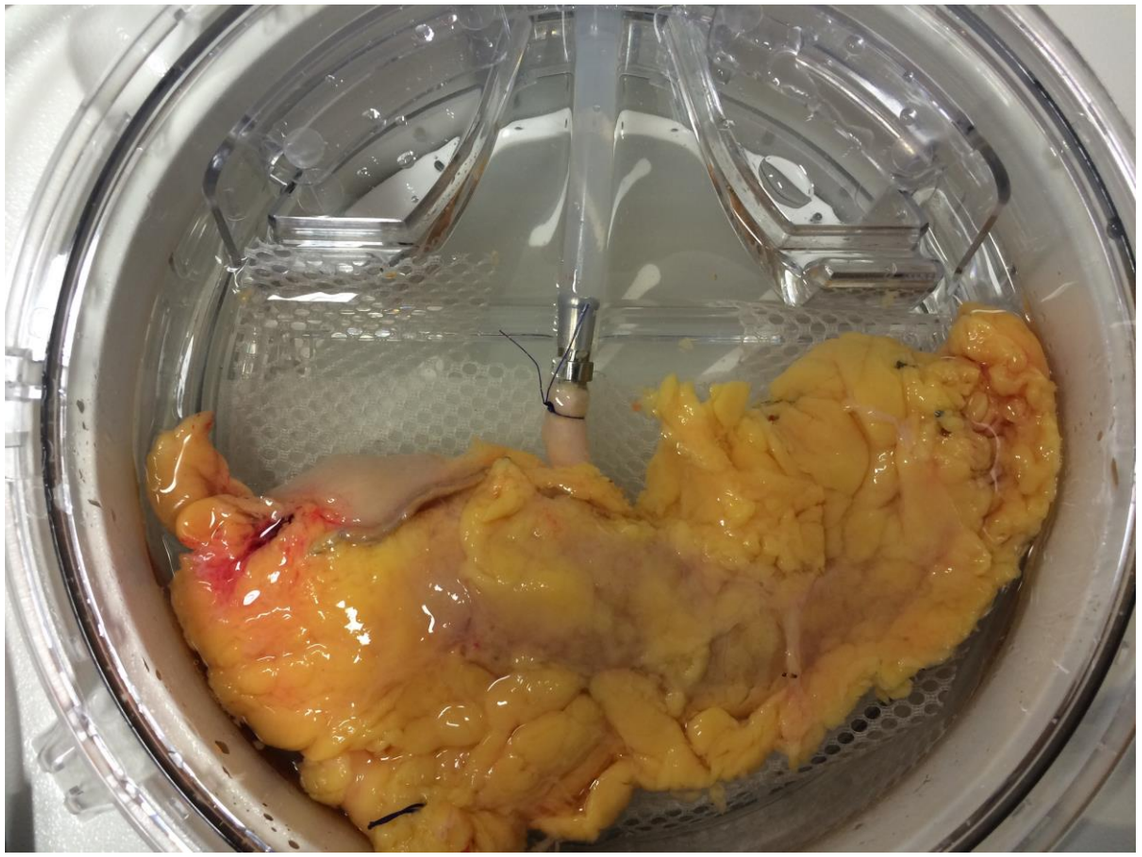
0h

- male
- 47 years
- 82 kg /173cm
- BMI 27.4
- alcohol

24hrs

Macroscopic aspect unchanged

Whole organ HPP: Macroscopic aspect



0h

- **male**
- **64 years**
- **89 kg /168 cm**
- **BMI 31.5**

24hrs

Macroscopic aspect unchanged

Whole organ HPP : Histologic aspect

n°	CRSITAL	Conservation	T12		T24	
			exocrine tissue	ilset	exocrine tissue	ilset
3	118879	HPP (whole organ)	ischemic necrosis /steatonecrosis	ischemic necrosis	ischemic necrosis /steatonecrosis	ischemic necrosis
4	119785	HPP (whole organ)	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis
5	121505	HPP (whole organ)	ischemic necrosis /steatonecrosis	ischemic necrosis	no ischemic necrosis	ischemic necrosis
6	128826	HPP (whole organ)	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis	ischemic necrosis
7	130280	HPP (whole organ)	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis	ischemic necrosis
9	134002	HPP (whole organ)	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis
11	137101	HPP (whole organ)	no ischemic necrosis	no ischemic necrosis	ischemic necrosis /steatonecrosis	ischemic necrosis

Whole organ HPP : Histologic aspect

n°	CRSITAL	Conservation	T12		T24	
			exocrine tissue	ilset	exocrine tissue	ilset
3	**118879**	**HPP (whole organ)**	**ischemic necrosis /steatonecrosis**	**ischemic necrosis**	**ischemic necrosis /steatonecrosis**	**ischemic necrosis**
4	119785	HPP (whole organ)	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis
5	121505	HPP (whole organ)	ischemic necrosis /steatonecrosis	ischemic necrosis	ischemic necrosis	ischemic necrosis
6	128826	HPP (whole organ)	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis	ischemic necrosis
7	130280	HPP (whole organ)	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis	ischemic necrosis
9	134002	HPP (whole organ)	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis
11	137101	HPP (whole organ)	no ischemic necrosis	no ischemic necrosis	ischemic necrosis /steatonecrosis	ischemic necrosis

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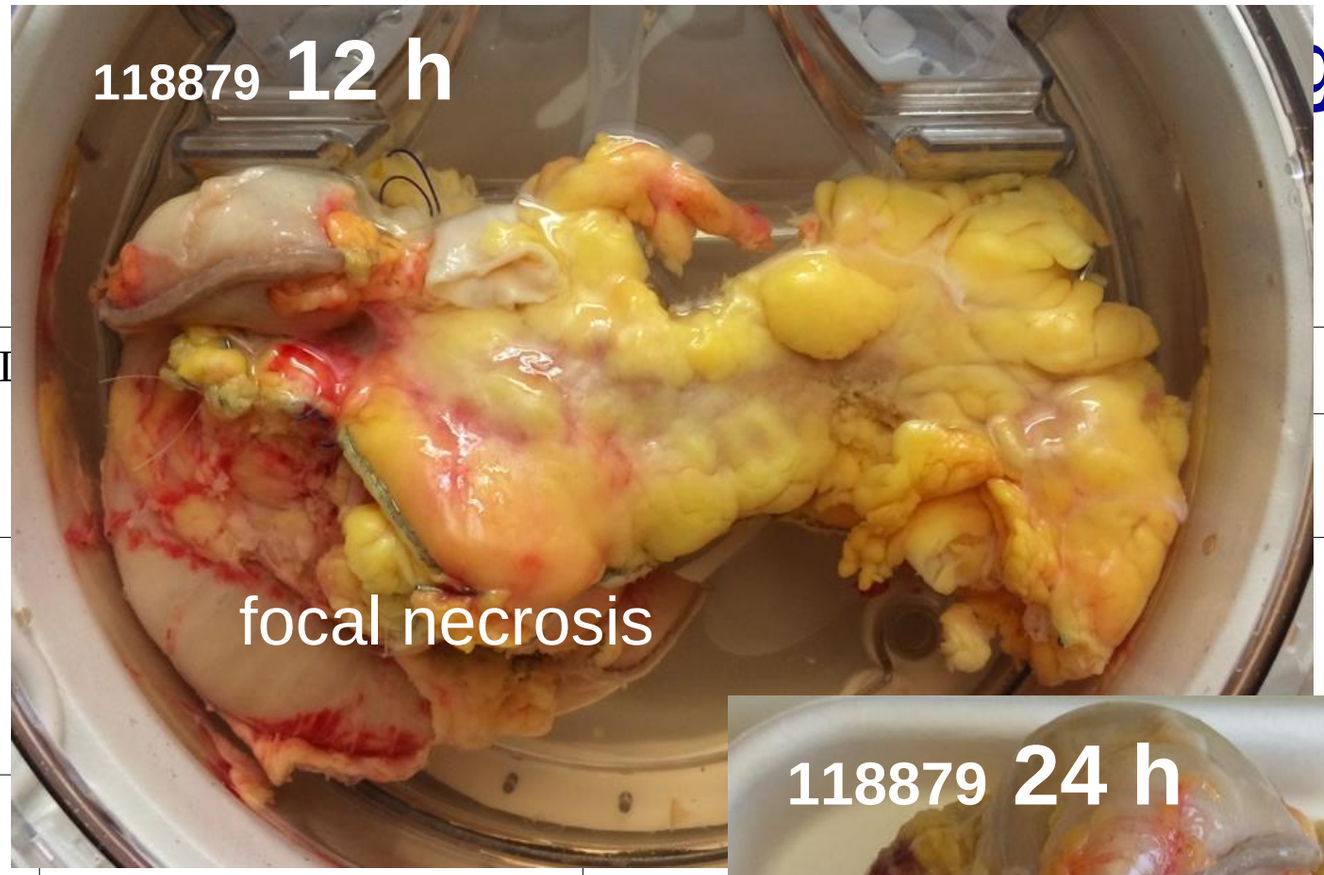
gic aspect



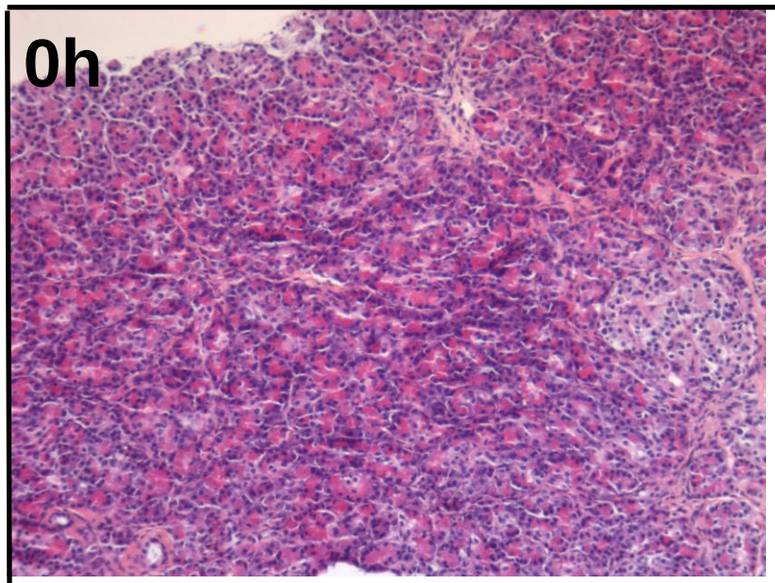
n°	CRSITAL			T24	
				exocrine tissue	ilset
3	**118879**			**ischemic necrosis /steatonecrosi**	**ischemic necrosis**
4	119785				
5	121505	HPP (whole organ)	ischem /steato		
6	128826	HPP (whole organ)	no isch		
7	130280	HPP (whole organ)	no isch		
9	134002	HPP (whole organ)	no isch		
11	137101	HPP (whole organ)	no isch		

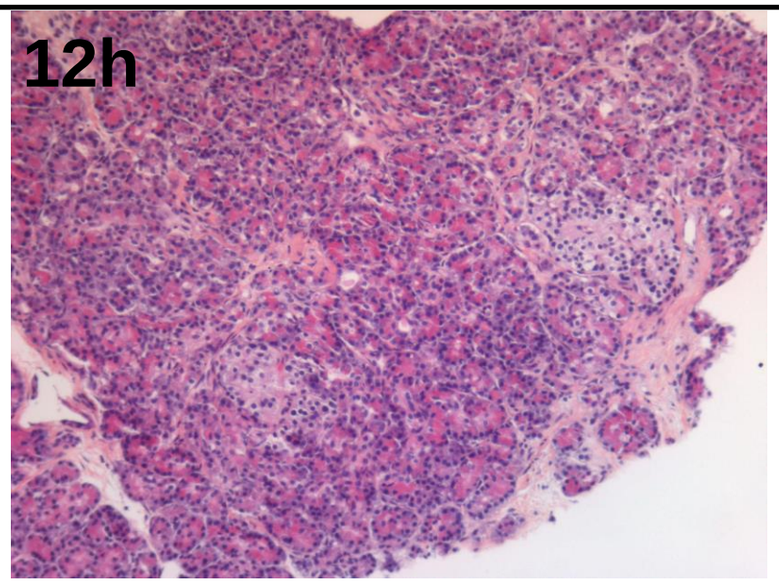
Whole organ HPP : Histologic aspect

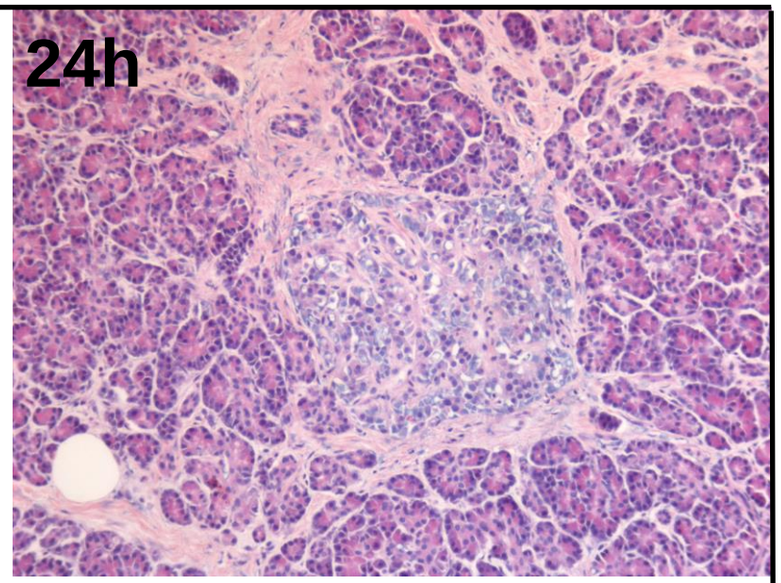
n°	CRSITAL	Conservation	T12		T24	
			exocrine tissue	ilset	exocrine tissue	ilset
3	118879	HPP (whole organ)	ischemic necrosis /steatonecrosis	ischemic necrosis	ischemic necrosis /steatonecrosis	ischemic necrosis
4	119785	HPP (whole organ)	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis
5	121505	HPP (whole organ)	ischemic necrosis /steatonecrosis	ischemic necrosis	no ischemic necrosis	ischemic necrosis
6	128826	HPP (whole organ)	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis	ischemic necrosis
7	130280	HPP (whole organ)	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis	ischemic necrosis
9	134002	HPP (whole organ)	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis	no ischemic necrosis
11	137101	HPP (whole organ)	no ischemic necrosis	no ischemic necrosis	ischemic necrosis /steatonecrosis	ischemic necrosis

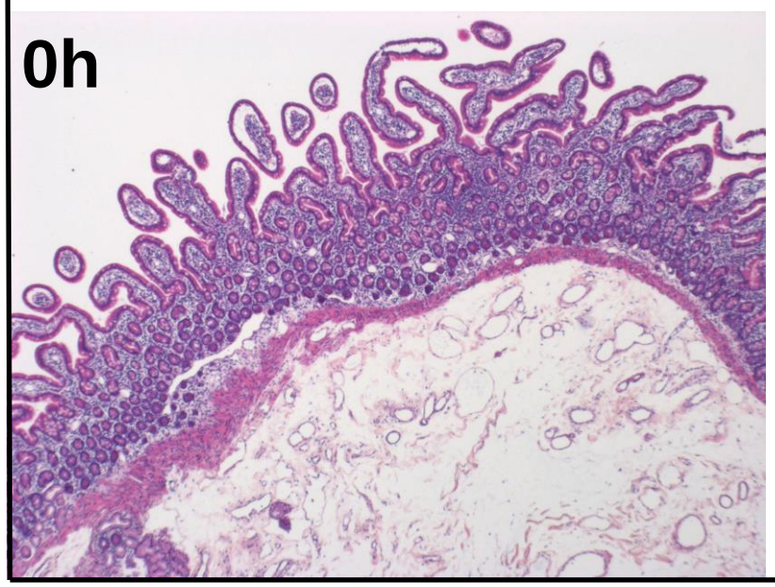
Pancreas after 24 H of HPP *n = 9*
no damage

Whole organ HPP : Histologic aspect









NA

128826

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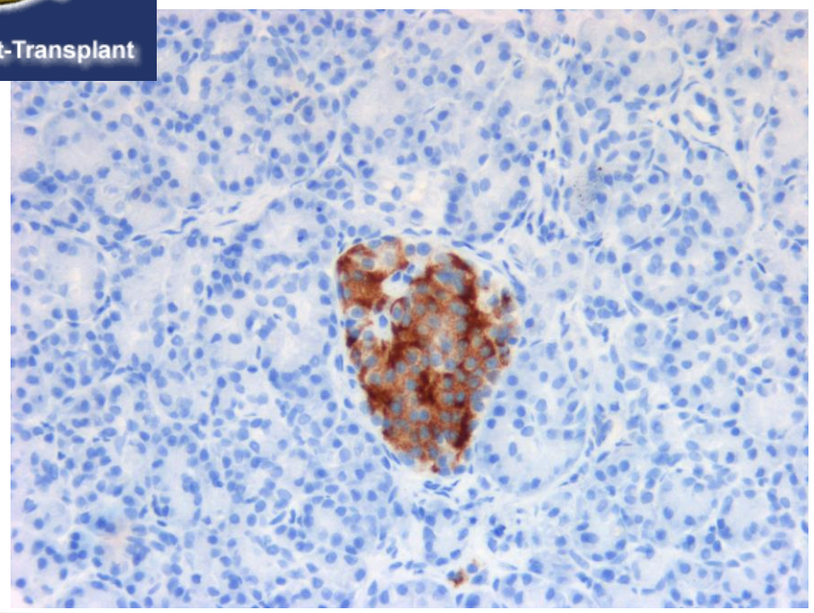
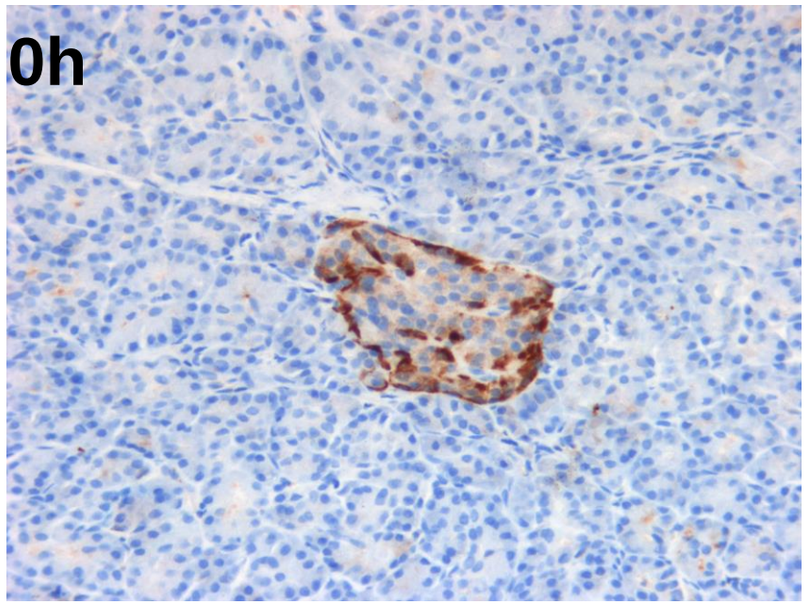
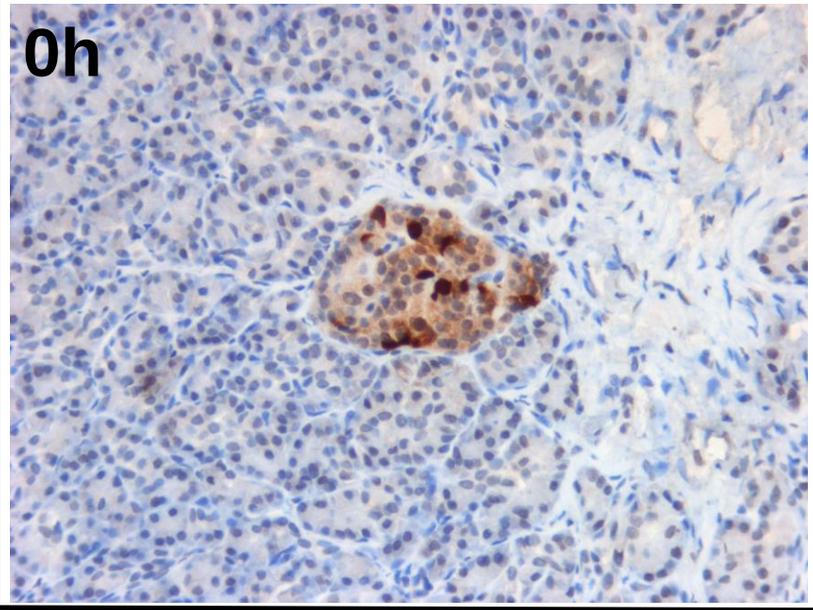
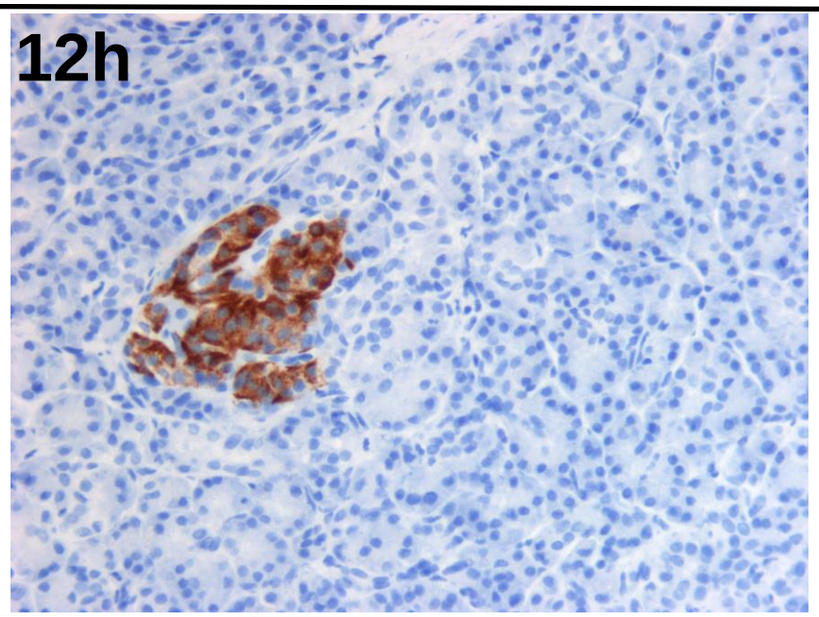
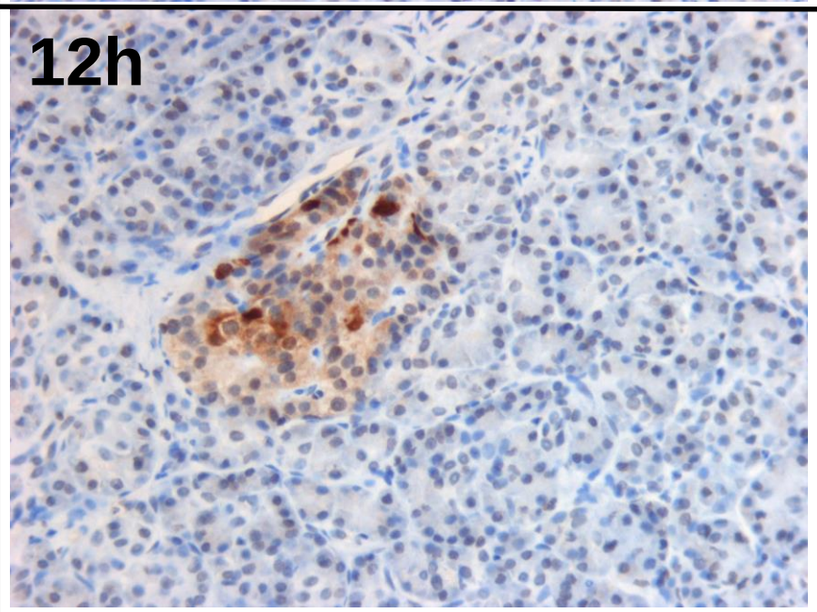
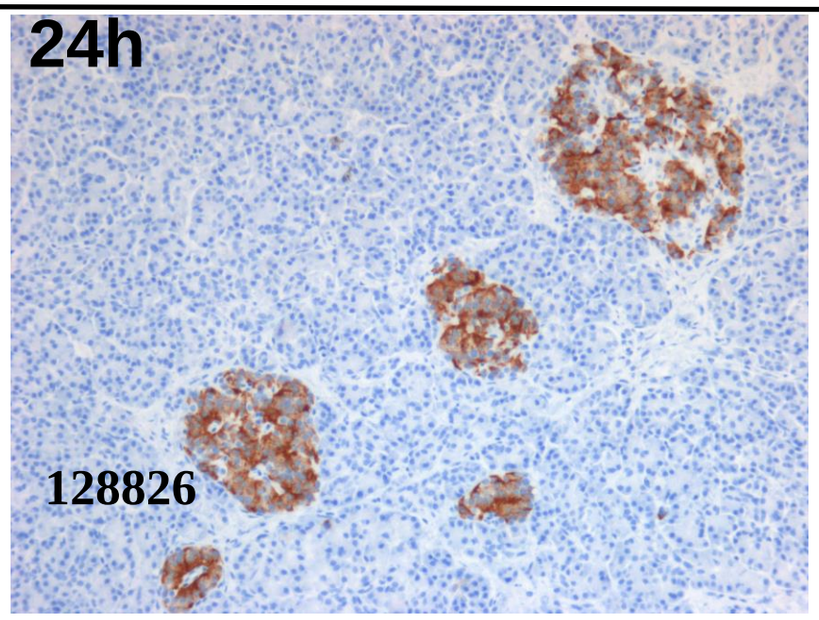
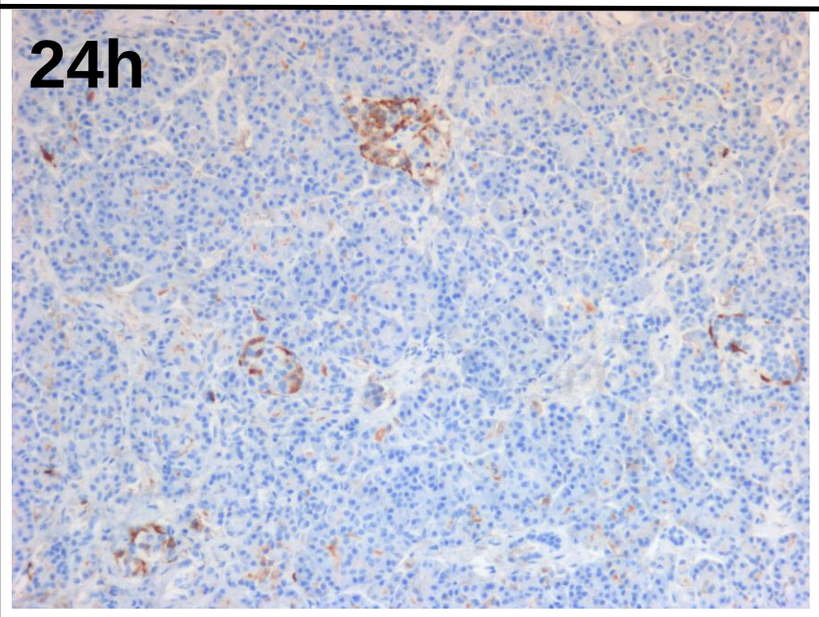
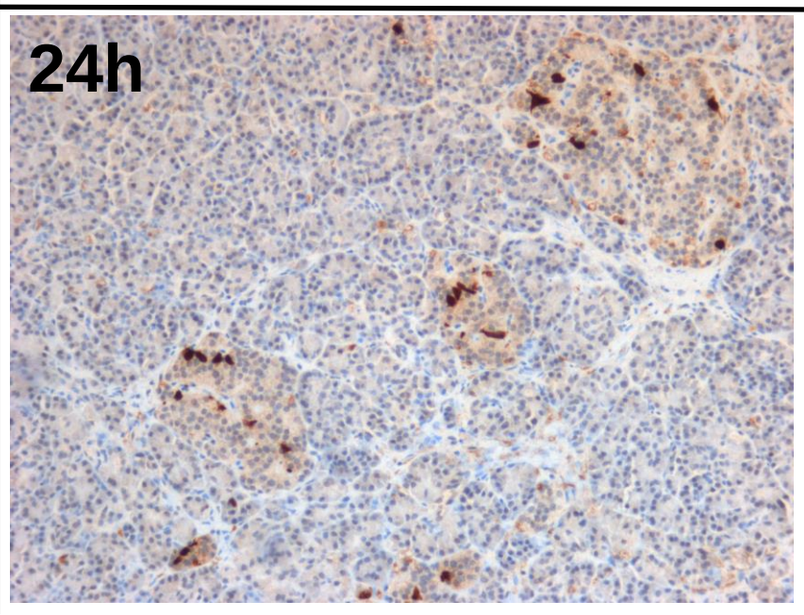
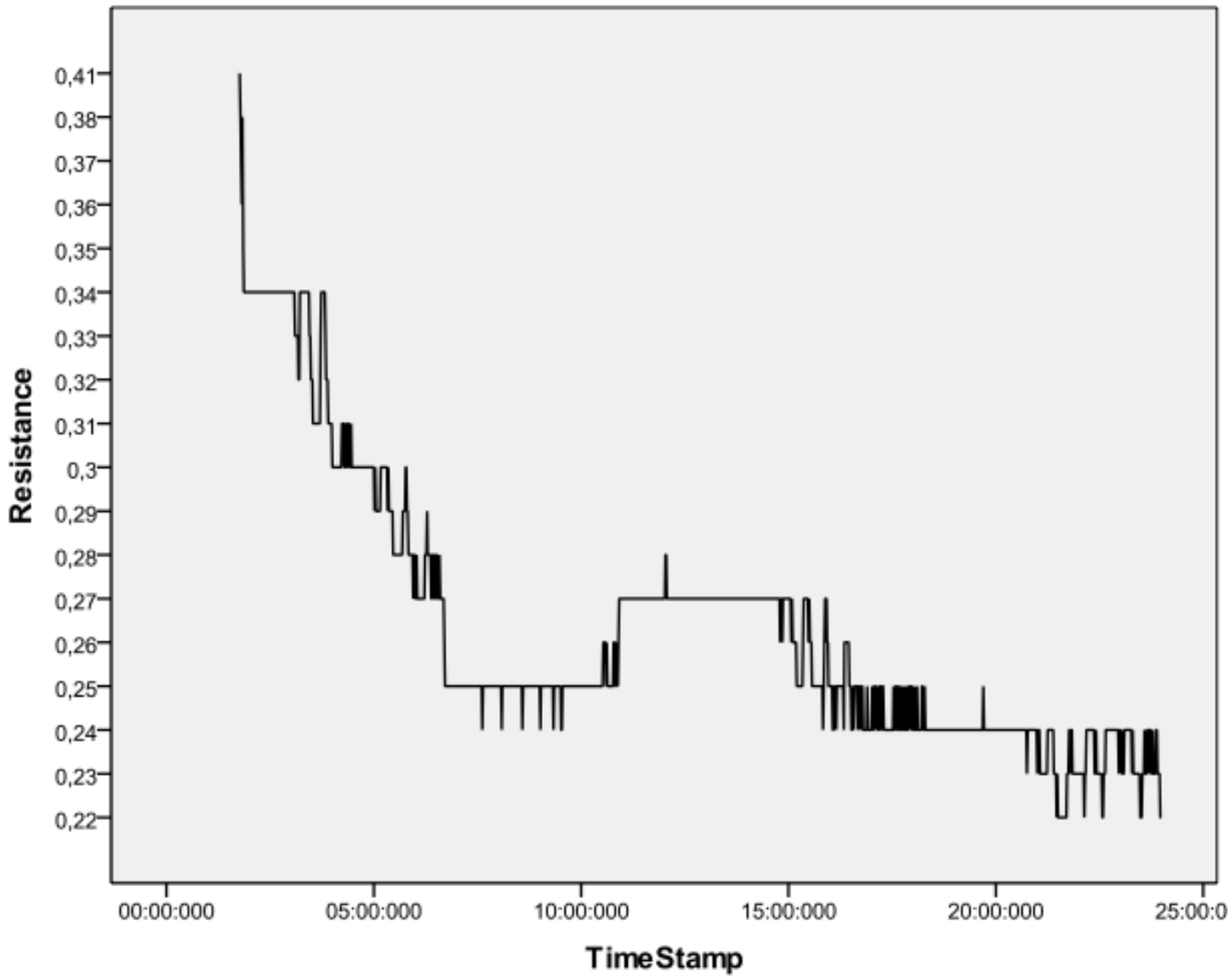
insulin	glucagon	somatostatin
		
	NA	
		

Pancreas Resistance Index



Resistance index decline up to 12 Hours

Take home message:

Hypothermic pulsatile perfusion of human pancreas is :

- **technically feasible**
- **safe :**
  - **no pancreas edema**
  - **unaltered duodenum villi**

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