



THE CATALAN  
TRANSPLANTATION  
SOCIETY



SOCIETAT  
CATALANA DE  
TRASPLANTAMENT

# Will normothermic perfusion become the new standard for the maintenance of DCD donors?

## Abdominal normothermic perfusion

*Constantino Fondevila*

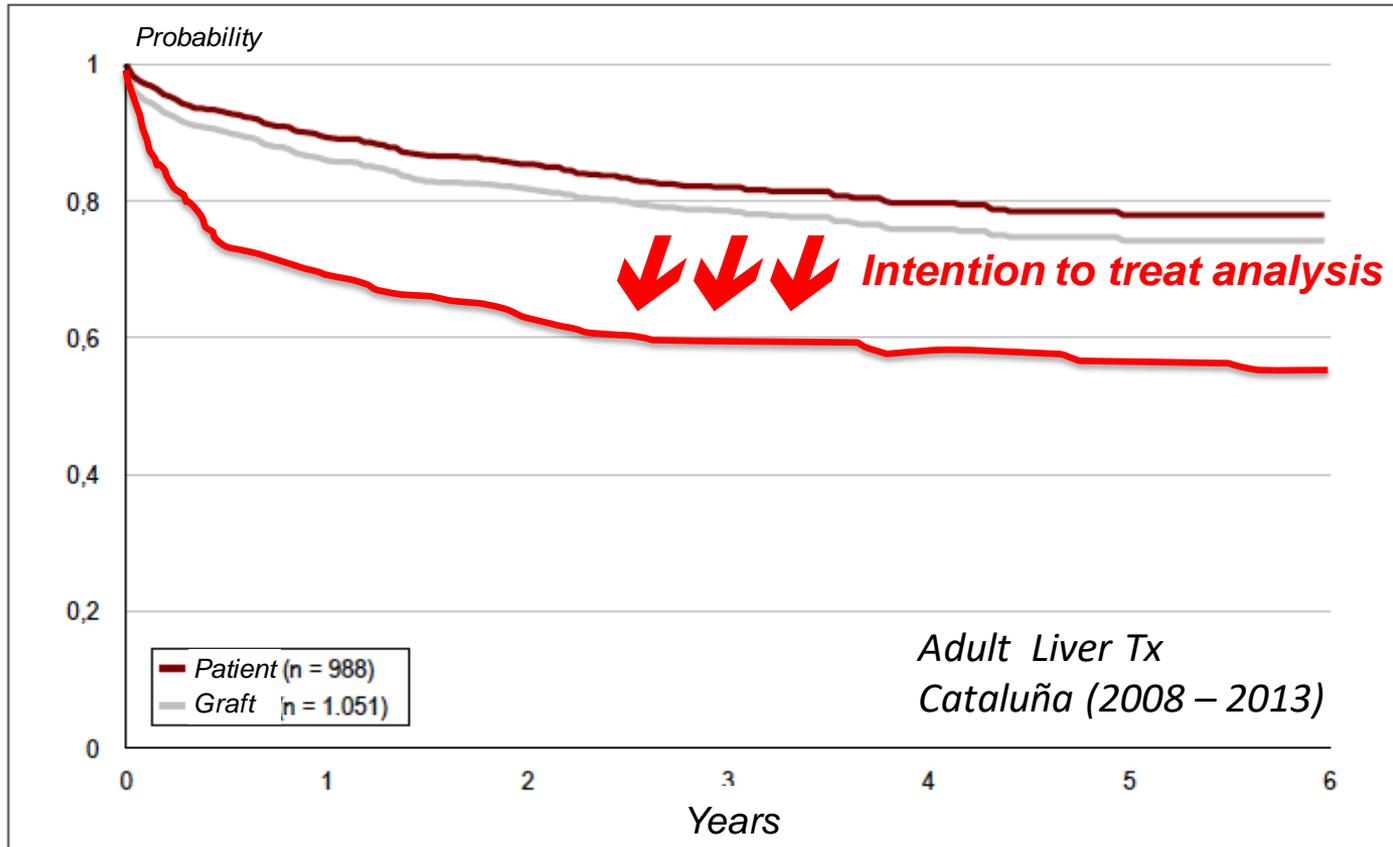
*Associate Professor of Surgery*

*Consultant in HPB & Liver Transplant Surgery*

*Hospital Clinic, University of Barcelona, Spain*



# Patient & Graft Survival



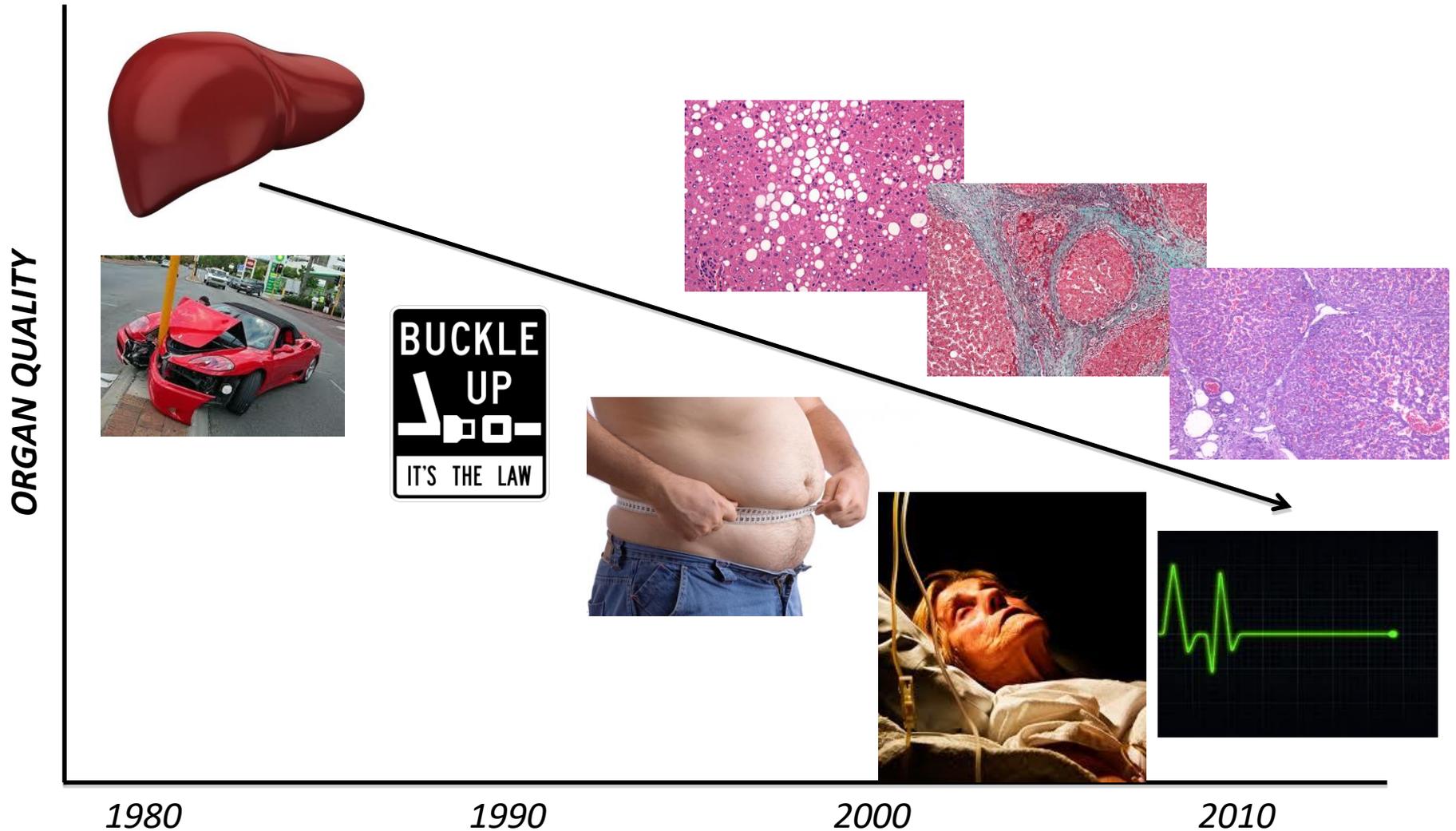
	1r mes	3r mes	6è mes	1r any	2n any	3r any	4rt any	5è any
Patient	0,97	0,95	0,93	0,89	0,85	0,82	0,80	0,78
Graft	0,95	0,92	0,90	0,86	0,82	0,79	0,76	0,74

# Liver Transplant Waiting List UK / Spain 2013



	<b>UK</b>	<b>SPAIN</b>
Population (millions):	63.1	46.9
Total number of patients ever active on the WL	1631	2095
Patients awaiting for a transplant (only active candidates) on 31/12/2013	525	667
Patients who died while on the WL during 2013	77	117

# Fewer and fewer "ideal" organs...



## ***“Extended criteria”***

- Livers:
  - Arising from older donors (>50-65 years)
  - With severe macrosteatosis
  - Recovered through the DCD process
  - That have been split
  - With positive infectious serology for hepatitis B or C virus

# “Extended criteria”

ORIGINAL ARTICLE

**Excellent long-term patient and graft survival are possible with appropriate use of livers from deceased septuagenarian and octogenarian donors**

Marcio F. Chedid, Charles B. Rosen, Scott L. Nyberg & Julie K. Heimbach

*American Journal of Transplantation* 2014; 14: 2072-2080  
Wiley Periodicals Inc.

© Copyright 2014 The American Society of Transplantation and the American Society of Transplant Surgeons

doi: 10.1111/ajt.12791

**Split Liver Transplantation Using Hemiliver Graft in the MELD Era: A Single Center Experience in the United States**

K. Hashimoto\*, C. Quintini, F. N. Aucejo, M. Fujiki, T. Diago, M. J. Watson, D. M. Kelly, C. G. Winans, B. Eghtesad, J. J. Fung and C. M. Miller

*American Journal of Transplantation* 2012; 12: 162-170  
Wiley Periodicals Inc.

**Liver Transplantation Using Controlled Donation After Cardiac Death Donors: An Analysis of a Large Single-Center Experience**

Hani P. Grewal,<sup>1</sup> Darrin L. Willingham,<sup>1</sup> Justin Nguyen,<sup>1</sup> Winston R. Hewitt,<sup>1</sup> Bucin C. Taner,<sup>1</sup> Veny,<sup>1</sup> Jamie Aranda-Michel,<sup>1</sup> Raj Satyanarayana,<sup>1</sup> Mer,<sup>3</sup> and Christopher B. Hughes<sup>1</sup>  
ville, FL; <sup>2</sup>LifeQuest Organ Recovery Services, icine, Mayo Clinic, Jacksonville, FL

© Copyright 2011 The American Society of Transplantation and the American Society of Transplant Surgeons

doi: 10.1111/j.1600-6143.2011.03834.x

**Applicability and Results of Maastricht Type 2 Donation After Cardiac Death Liver Transplantation**

C. Fondevila<sup>a,\*</sup>, A. J. Hessheimer<sup>a</sup>, E. Flores<sup>a</sup>,

**Is It Time to Extend Liver Acceptance Criteria for Controlled Donors After Cardiac Death?**

Laura Taricotti,<sup>1</sup> Chiara Rocha,<sup>1</sup> M. Tamara PR Perera,<sup>1</sup> Bridget K. Gunson,<sup>1,2</sup> Simon R. Bramhall,<sup>1</sup> John Isaac,<sup>1</sup> John A. C. Buckels,<sup>1</sup> A. David Mayer,<sup>1</sup> Paolo Muiesan,<sup>1</sup> and Darius F. Mirza,<sup>1,3</sup>

The American Journal of Surgery 195 (2008) 214-220  
Clinical surgery—International

Effect of graft steatosis on liver function and organ survival after liver transplantation

Mar  
Benedikt W  
Department

**Utilization of Extended Donor Criteria Liver Allografts Maximizes Donor Use and Patient Access to Liver Transplantation**

John F. Renz, MD, PhD, Cindy Kin, BA, Milan Kinkhabwala, MD, Dominique Jan, MD, Rhaghu Varadarajan, MD, Michael Goldstein, MD, Robert Brown, Jr., MD, MPH, and Jean C. Emond, MD

**Use of Severely Steatotic Grafts in Liver Transplantation  
A Matched Case-Control Study**

Lucas McCormack, MD,\* Henrik Petrowsky, MD,\* Wolfram Jochum, MD,† Beat Mullhaupt, MD,‡ Markus Weber, MD,\* and Pierre-Alain Clavien, MD, PhD, FACS, FRCS (Eng), FRCS (Ed)\*

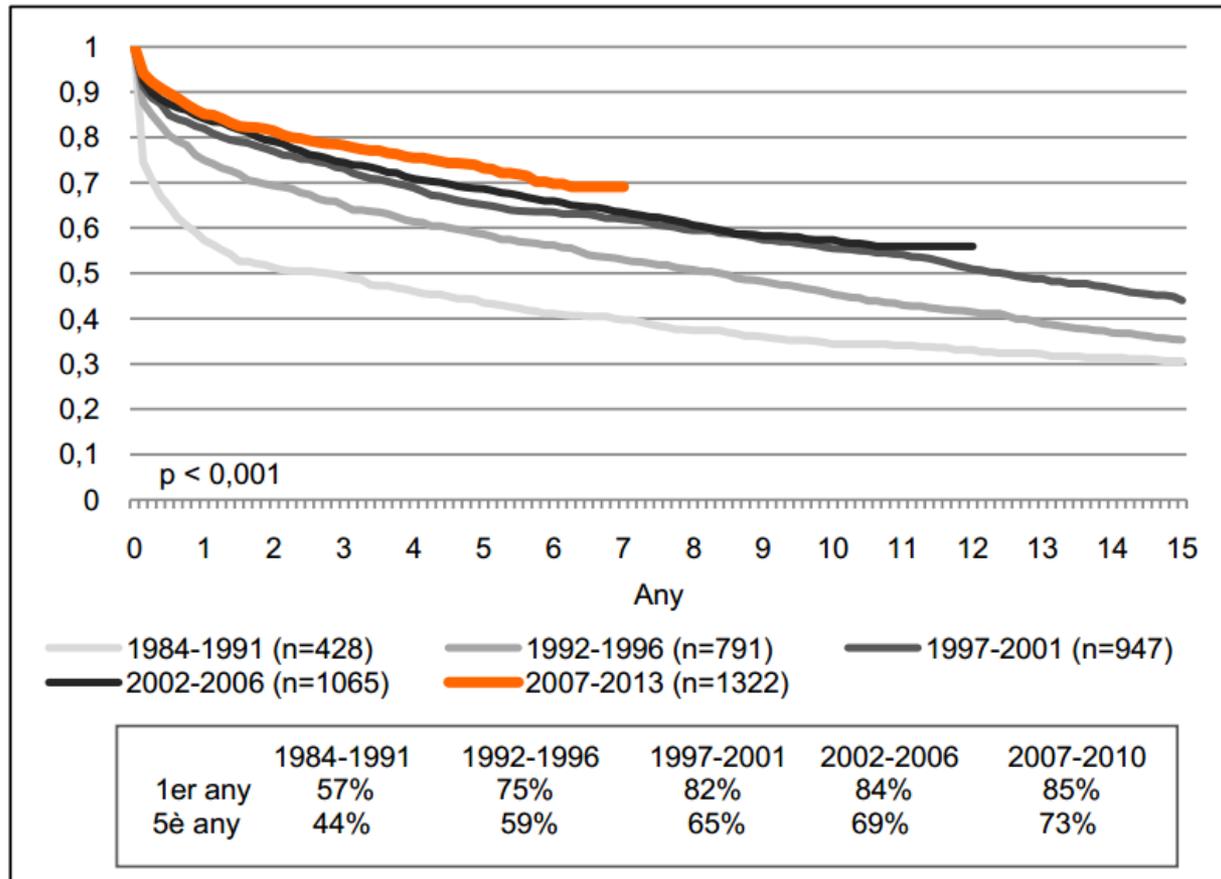
**Short- and Long-term Outcomes After Steatotic Liver Transplantation**

M. B. Maiella Doyle, MD; Neeta Vachharaiani, MD; Jason R. Wellen, MD; Christopher D. Anderson, MD;

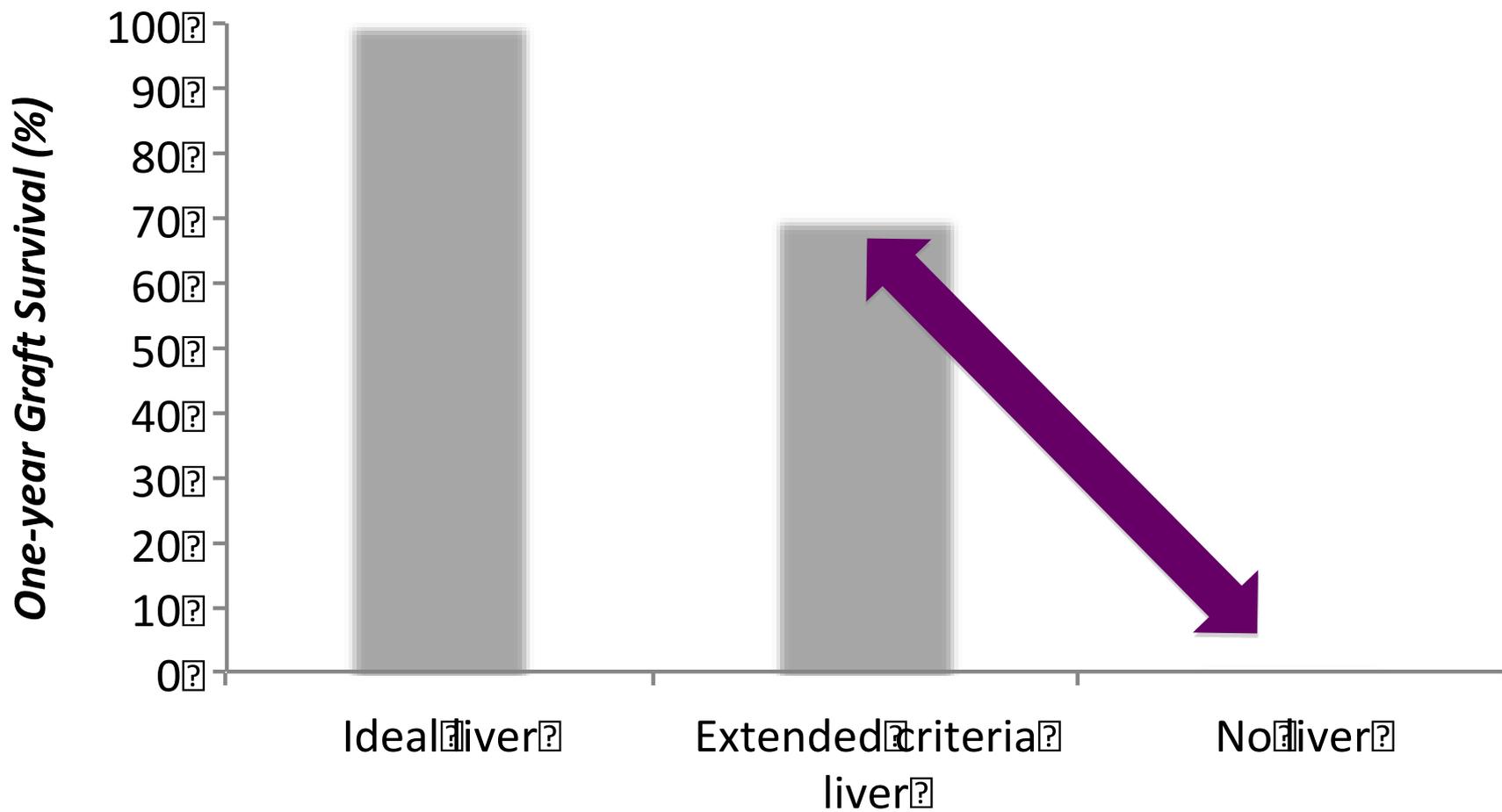
**Use of Extended Criteria Livers Decreases Wait Time for Liver Transplantation Without Adversely Impacting Posttransplant Survival**

A. Joseph Tector, MD, PhD,\* Richard S. Mangus, MD,\* Paul Chestovich, MD,\* Rodrigo Vianna, MD,\* Jonathan A. Fridell, MD,\* Martin L. Milgrom, MD, PhD,\* Carrie Sanders, BsN,\* and Paul Y. Kwo, MD†

# ***OCATT Liver Survival (Barcelona)***



***Graft survival in patients who received a liver transplant in Catalunya (1984-2013)***



# *History of Transplantation*



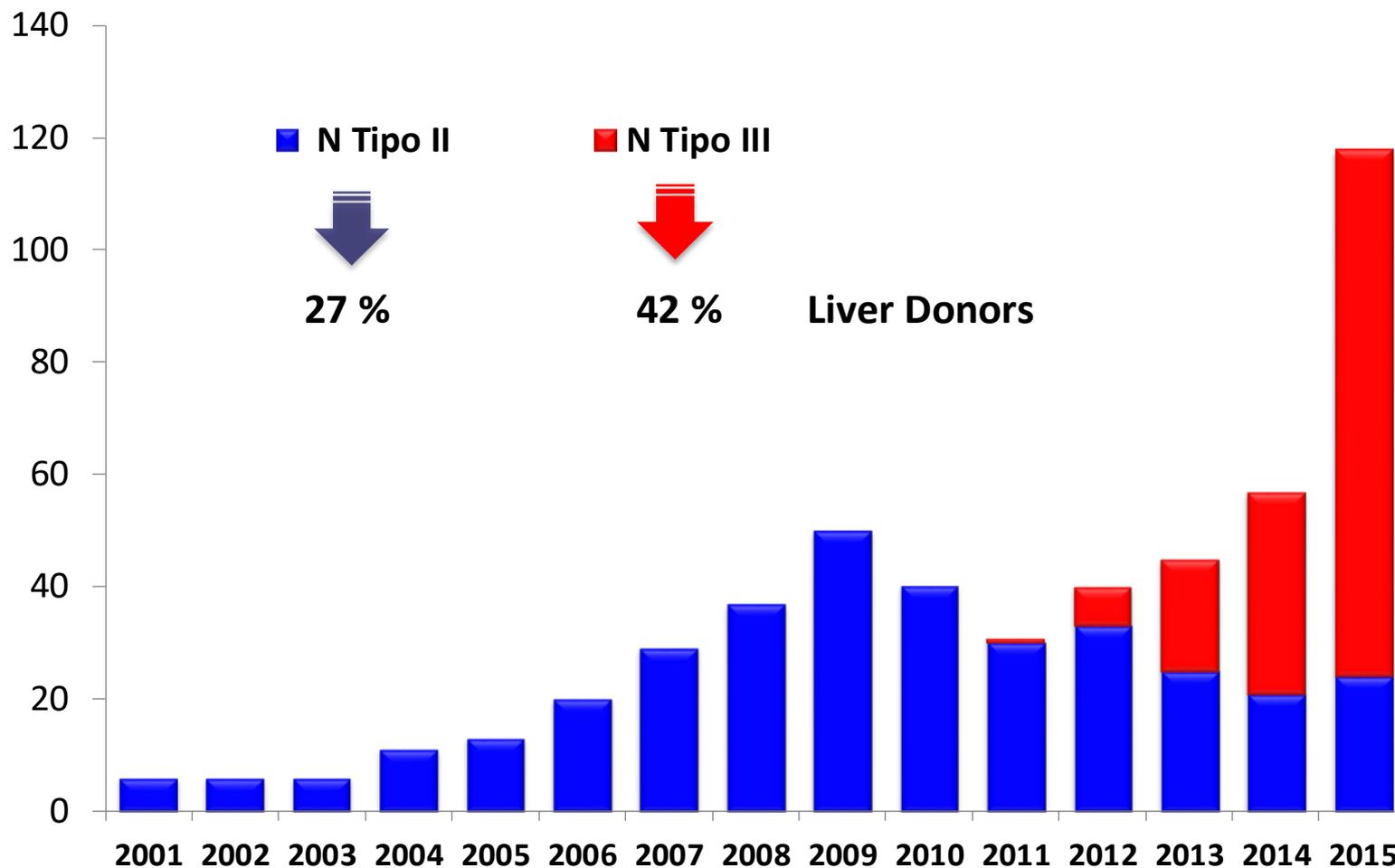
*"A problem might be achievable, but only with great risk to yourself, risk of failure and professional disgrace."*

*Thomas E. Starzl (1926 – 2017)*

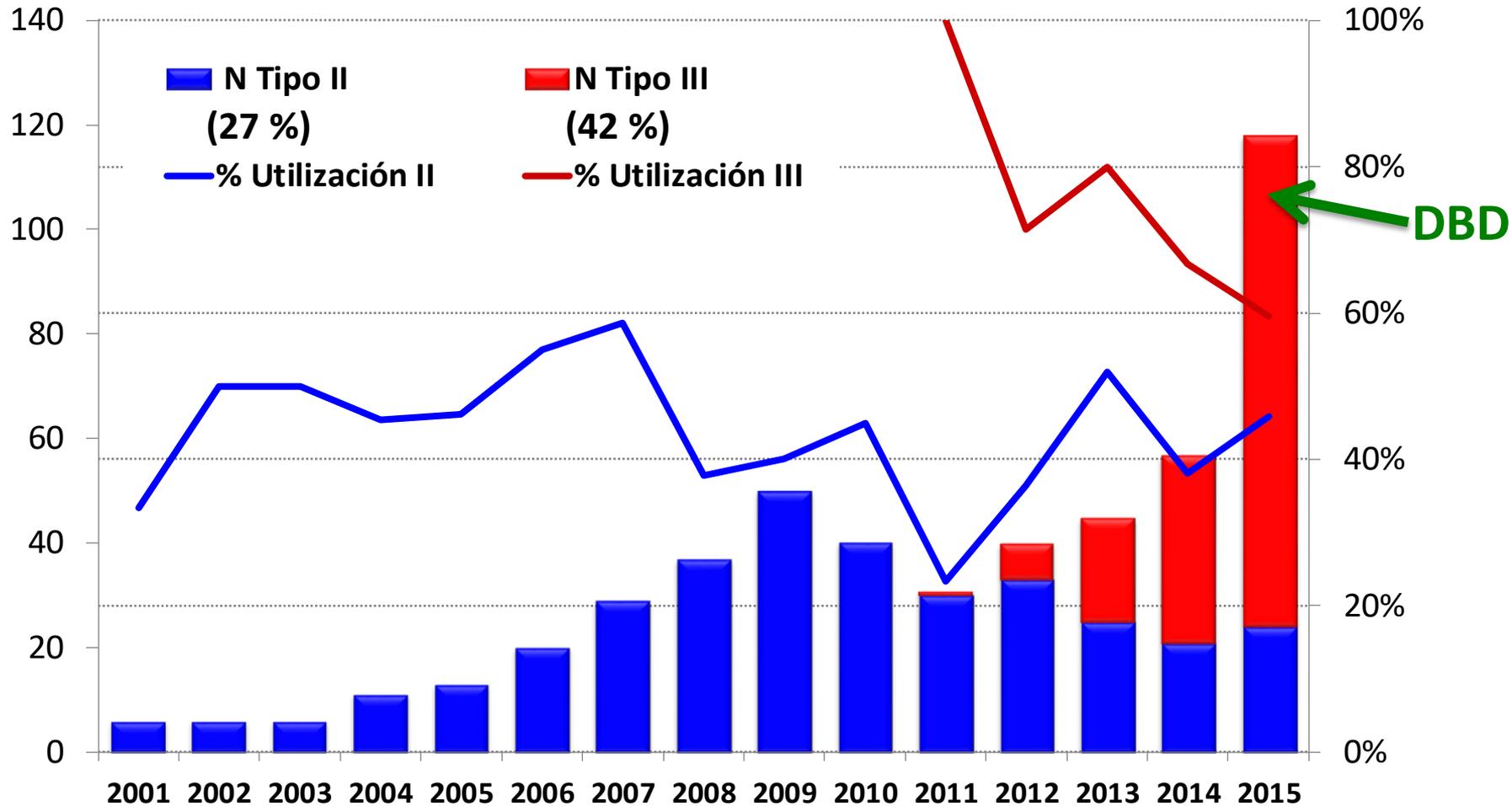
# Legal basis for DCD in Spain

- **General Law 30/1979**
- *National Consensus Statement on Donation in 1995 (including DCD type II)*
- **Royal Decree 2070/1999 (type II)**
- *National Consensus Statement on Donation in 2012 (including DCD type II & III)*
- **Royal Decree 1723/2012 (type II & III)**

# DCD liver donation



# DCD liver donation



**DBD**

# Single center experiences with DCD-LT

	University of Wisconsin, Wisconsin (n = 36)*	Albert Einstein Medical Center, Pennsylvania (n = 19)†	University of Pennsylvania, Pennsylvania (n = 30)‡	Kings College, London, United Kingdom (n = 32)§	Johns Hopkins University, Maryland (n = 20)
<b>Demographics</b>					
Donor age (years)		34	30	36	35
Recipient age (years)				38	53
WIT (minutes)	17	20	20	14	33
CIT (hours)	8.2	9.5	6.1	8.6	8.7
MELD score at orthotopic LT					19.6
Peak ALT (IU/mL)		141			1757
<b>Results</b>					
Follow-up time (months)¶	36 (1–80)	16 (1.5–37)	27 (1–46)	15 (1–40)	14 (1–73)
Patient survival	68% at 3 years	74%	79% at 3 years	89% at 1 year	78% at 1 year
Graft survival	50%		72% at 3 years	86% at 1 year	62% at 1 year
Retransplantation	19%	11%	6%	3%	20%
Biliary complications	37%	11%	33%	9%	55%
Hepatic artery complications	22%	16%	0	6%	30%
Primary nonfunction	5%	5%	6%	3%	5%

(Maheshwari A., *Liver Transplantation* 13,2007)

# DCD morbidity

	DCD	DBD	P
Number	51	334	
Recipient age (years)	54.8 ± 6.8	53.3 ± 9.4	NS
Recipient gender	M38/F13	M236/F98	NS
MELD	19.6 ± 6.9	18.8 ± 8.2	NS
Status 1	0	6	NS
Donor age (years)	37.7 ± 14.5	40 ± 16.4	NS
Donor gender	M37/F14	M206/F128	NS
Total ischemia time (minutes)	473 ± 130	463 ± 160	NS
Anastomosis time (minutes)	36.1 ± 11	34.8 ± 8.1	NS
Primary nonfunction	0	11	NS
Hepatic artery thrombosis	0	16	NS
Biliary anastomotic strictures	5	26	NS
Ischemic cholangiopathy	7 (14 %)	4 (1 %)	0.0001

(University of Washington, Seattle)

*Excluding donors that weighed >100 kg or those older than 50 years of age with >9h of total ischemia time, 6 out of 7 livers that did develop IC could have been avoided.*

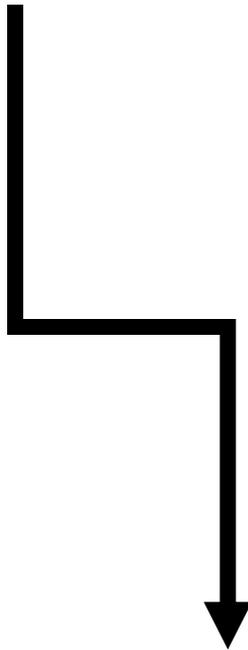
(Chan E Y., Liver Transplantation 14,2008)

# Liver transplant from DCD: complications

**PNF** ↓↓  
Up to 17%

**ARTERIAL** ↓↓  
Up to 50%

**BILIARY**  
Up to 60%



PRESERVATION INJURY



IR

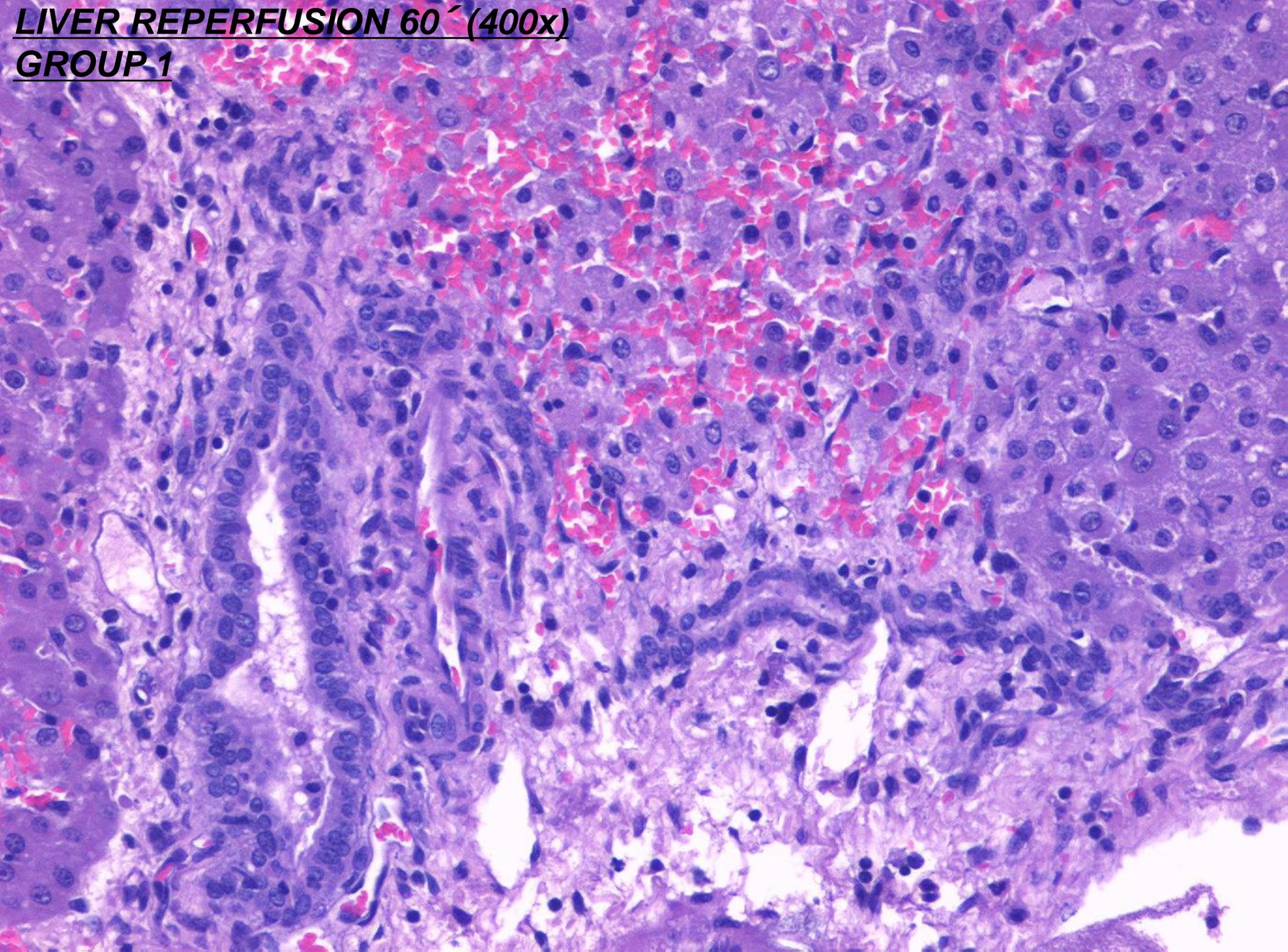
IBL



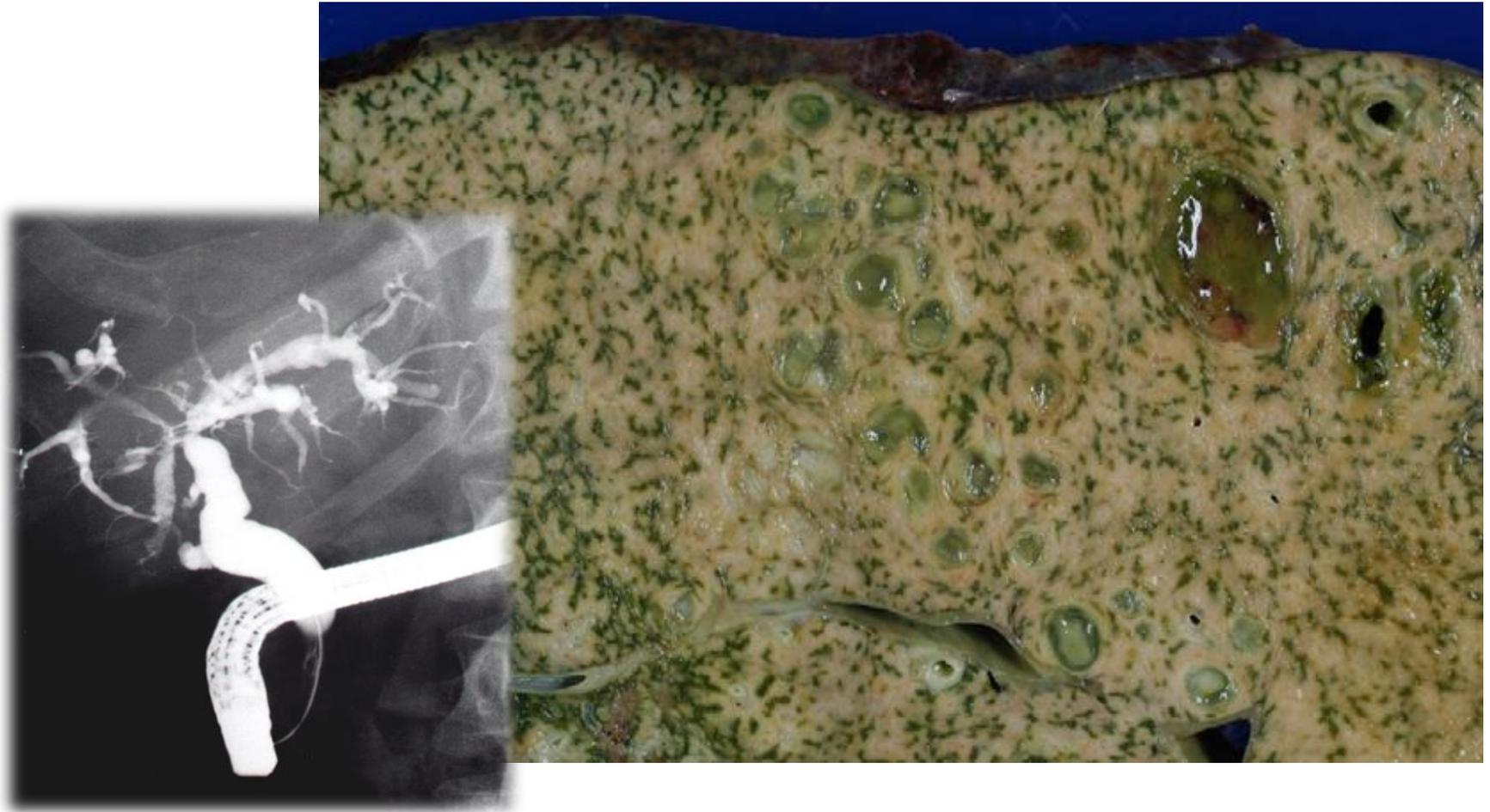
↑ **RETRANSPLANT**  
Up to 50%

LIVER REPERFUSION 60' (400x)

GROUP 1



# ***Ischemic Cholangiopathy***



# Organ Maintenance

Technique	Results
Perfusion <i>in situ</i>	Quick and easy. Inferior results (kidney).
Thoraco-abdominal compressions	Simultaneous chest (mechanical) and abdominal (manual) compressions with the aim of maintaining MAP $\geq 70$ mmHg and PaO <sub>2</sub> $\geq 100$ mmHg. <sup>1,2</sup>
Hypothermic recirculation	Primarily used to maintain Maastricht type III donors. Variable results, with high rates of DGF in some series (kidney). Little experience in Maastricht type II donors. <sup>1,2</sup>
Normothermic recirculation	Better immediate function, technique of choice for the preservation of abdominal organs. <sup>3,4</sup>

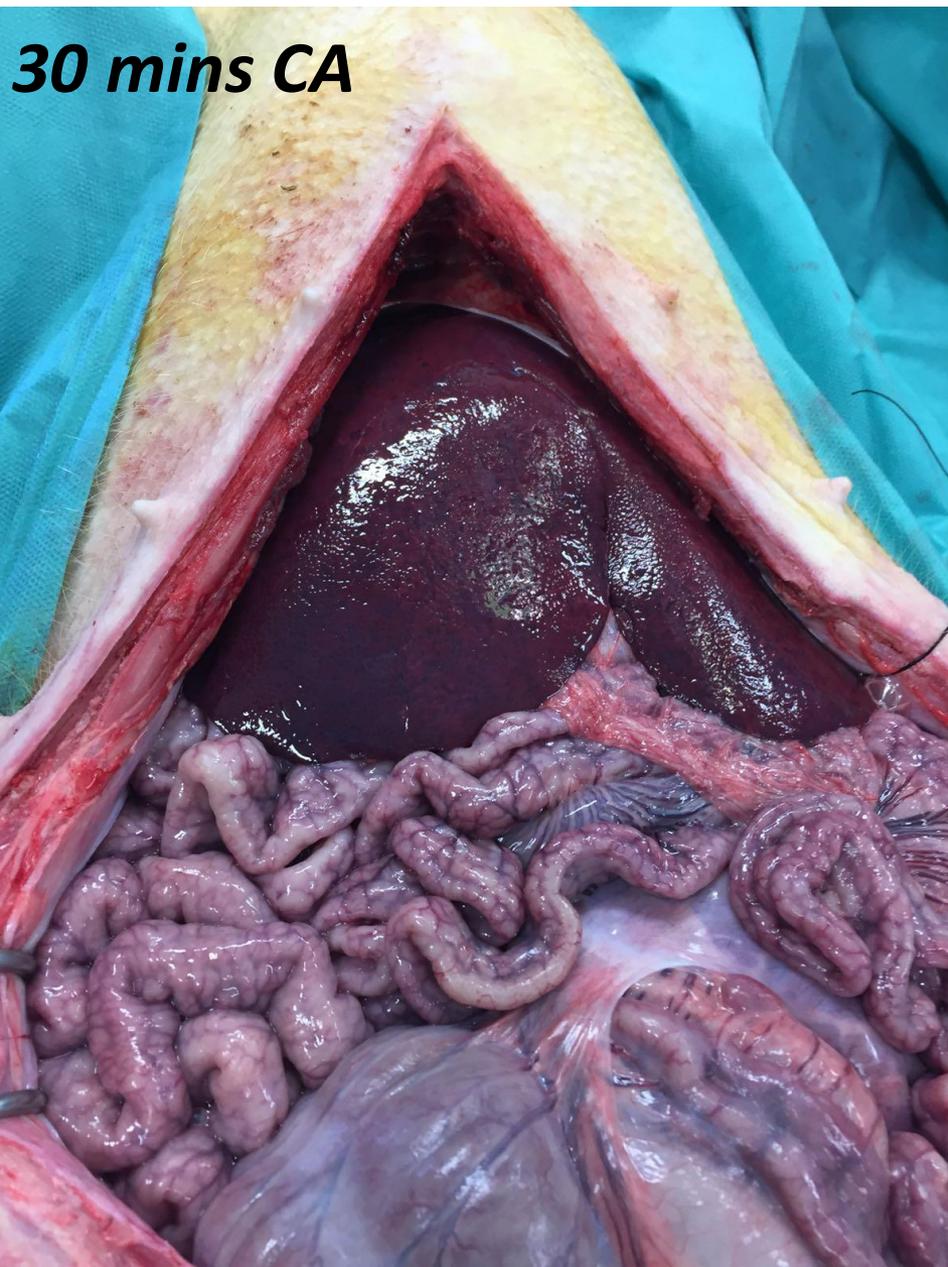
<sup>1</sup>Otero A. *Transplantation* 2003, <sup>2</sup>Suárez F. *Transplantation* 2008, <sup>3</sup>Fondevila C. *Am J Transplant* 2007., <sup>4</sup>Fondevila C. *Am J Transplant* 2012.

PROS

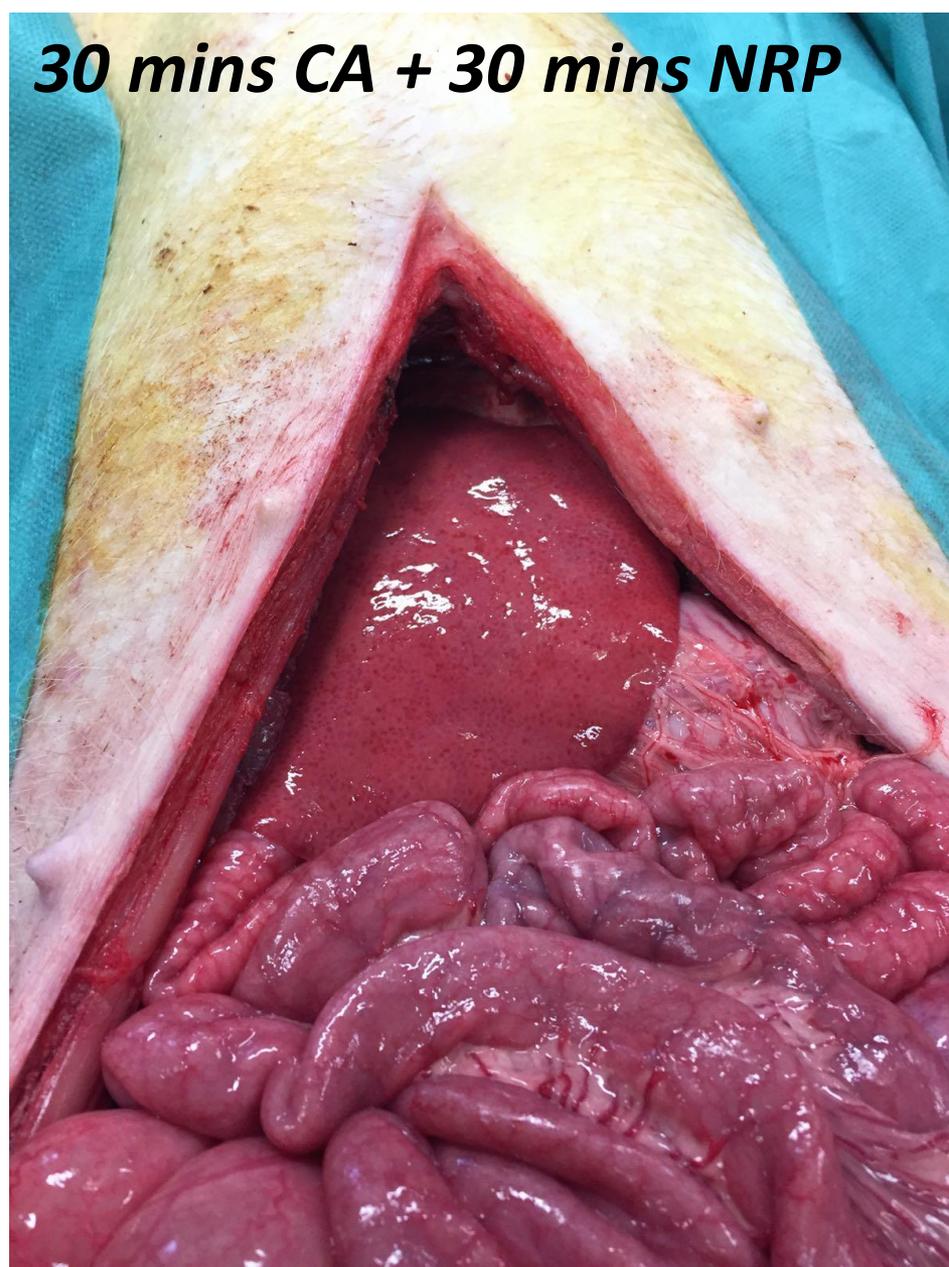
CONS



**30 mins CA**



**30 mins CA + 30 mins NRP**



# DCD Selection Criteria

		Hospital Clínic Barcelona <sup>1,2</sup>
Normothermic regional perfusion	T <sup>o</sup>	37 °C
	pH	7.35-7.45
	PaO <sub>2</sub>	100-150 mmHg
	Hct	>20%
	Initial AST, ALT	<3 x ULN
	Final AST, ALT	<4 x ULN
	Pump flow	>1.7 L/min with Fogarty in supraceliac aorta
	Heparinization	1.5 mg/kg every 90 min.
	Time	<4 hours

# First Experience of Liver Transplantation With Type 2 Donation After Cardiac Death in France

Eric Savier,<sup>1,4</sup> Federica Dondero,<sup>5</sup> Eric Vibert,<sup>6</sup> Daniel Eyraud,<sup>7</sup> H el ene Brisson,<sup>2</sup> Bruno Riou,<sup>3</sup> Fabienne Fieux,<sup>8</sup> Salima Naili-Kortaia,<sup>9</sup> Denis Castaing,<sup>6</sup> Jean-Jacques Rouby,<sup>2</sup> Olivier Langeron,<sup>2,3</sup> Safi Dokmak,<sup>5</sup> Laurent Hannoun,<sup>1</sup> Jean-Christophe Vaillant,<sup>1</sup> and the Donation After Cardiac Death Study Group

		IC	ReTx	1-y Graft Survival	1-y Patient Survival
Barcelona, 2012	34 uDCD 538 DBD	3 (9%)	3 (9%)	70 vs 87% (p=0.01)	82 vs 90% (p=0.14)
Paris/Clichy/ Villejuif, 2014	13 uDCD 41 DBD	1(7.6%)	3 (23%)	69 vs 93% (p=0.03)	85 vs 93% (p=0.39)

# Single-Center Experiences with Controlled DCD Liver Transplant

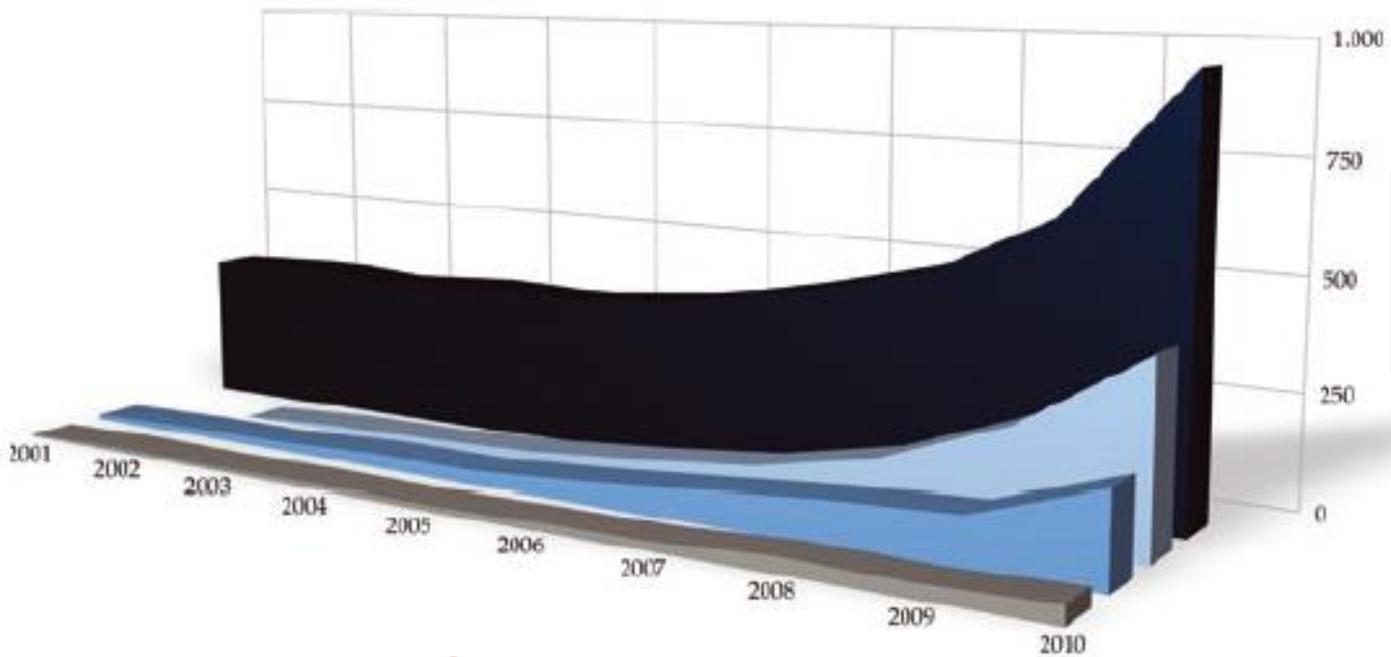
	N	Source	1-yr graft survival	1-yr patient survival	IC	All biliary complications
Abt 2003	15	UPenn	72%	79%	27%	33%
Chan 2008	52	UWash	~80%	~84%	14%	--
de Vera 2007	141	Pitt	69%	79%	16%	25%
Dezza 2007	13	Ghent	54%	62%	23%	--
Foley 2011	87	Wisconsin	69%	84%	34%	47%
Fujita 2007	24	Florida	69%	87%	13%	--
Grewal 2009	108	Mayo (FL)	79%	92%	8%*	--
Kaczmarek 2007	11	Newcastle	73%	82%	27%	45%
Maheshwari 2007	20	Hopkins	55%	75%	50%	60%
Manzarbeitia 2004	19	Albert Einstein	--	90%	--	11%
Pine 2009	39	St. James (UK)	80%	80%	21%	33%
Skaro 2009	32	Northwestern	61%	74%	38%	53%
DeOliveira 2011	167	King's College	90%	90%	2.5%	15%

\*Only cases leading to graft loss.

Fondevila 2011 ★	34	Barcelona	70%	82%	8%	12%
------------------	----	-----------	-----	-----	----	-----

★ Uncontrolled

# Year-to-year evolution of controlled DCD activity:



**Stringent criteria**

DCDD USED GRAFTS	5	10	8	13	12	18	21	35	32	41
DCDD ACCEPTED OFFERS	11	18	19	30	31	49	72	95	110	201
DCDD DECLINED OFFERS	0	0	14	18	27	48	75	130	235	412
TOTAL DONATION OFFERS	347	358	342	357	349	375	429	494	531	951

Figure 3: King's College Hospital annual evolution since the start of the DCDD programme (2001–2010) of total donation offers and DCDD accepted, declined offers and used grafts.



# ***Blood and Transplant***

## *Novel Technologies for Organ Transplantation Working Group*

*To identify and evaluate new techniques and technologies for the preservation/reconditioning of retrieved organs with a view to increase organ utilisation.*

*In-situ normothermic perfusion in category II DCD donation and applicability to DCD III.*

# ***In Situ* Normothermic Regional Perfusion for Controlled Donation After Circulatory Death—The United Kingdom Experience**

**Table 1:** Donor demographics and timings for withdrawal and normothermic perfusion

N = 21 (36 attended)	Donor data median (range)
Age (years)	46 (16–74)
Cause of death	
Cerebrovascular accident	9
Hypoxic brain damage	8
Trauma	3
Respiratory failure	1
Withdrawal to asystole	13 min (6 min–249 min)
Asystole to NRP	16 min (10 min–23 min)
Functional warm ischemia time	26 min (13 min–48 min)
NRP duration	2 h (34 min–2 h 36 min)

NRP, normothermic regional perfusion.

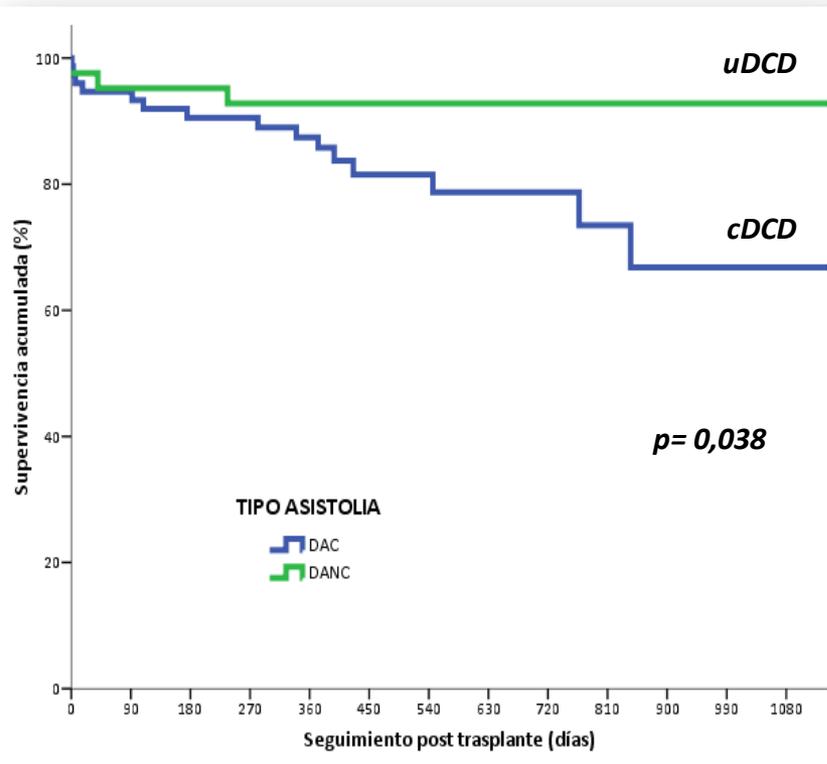
**Table 2:** Individual center normothermic regional perfusion retrieval and organ transplant activity

Transplant center	Donors	Number of		
		Livers	Kidneys	Pancreata
Birmingham	3	2	5 <sup>1</sup>	–
Cambridge	9	4	16 <sup>2</sup>	2
Edinburgh	9	5	17 <sup>3</sup>	1 <sup>4</sup>
All	21	11	38	3

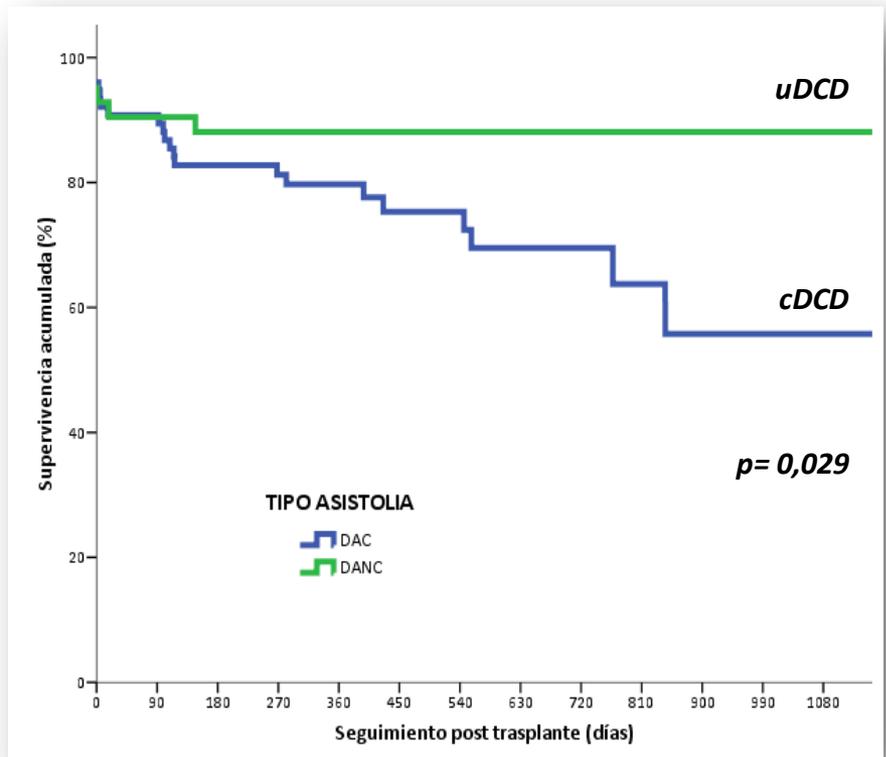
# Liver Transplant from DCD - Spain

118 transplants: 42 uDCD & 75 cDCD  
(2012 – 2015)

**Patient Survival**

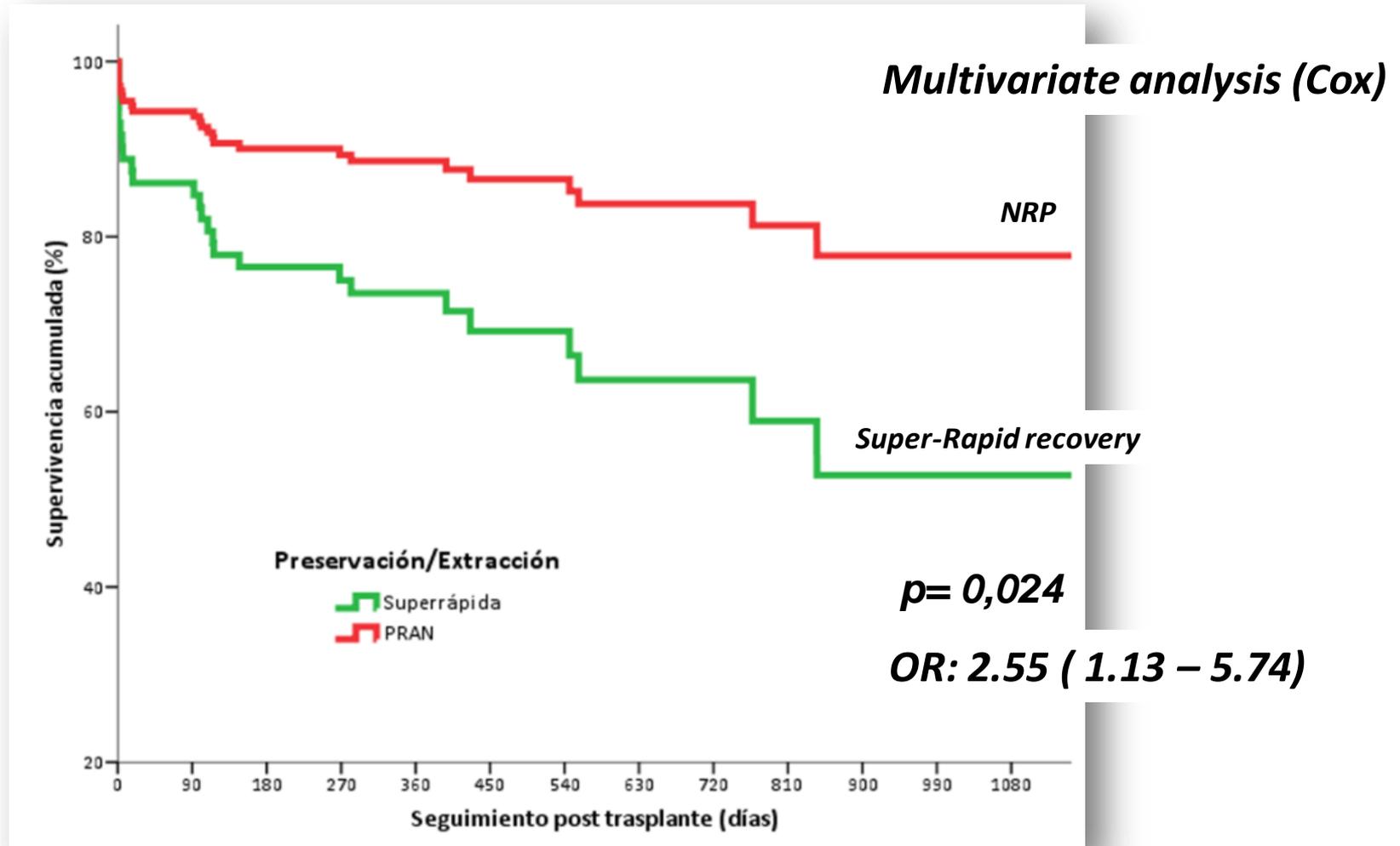


**Graft Survival**

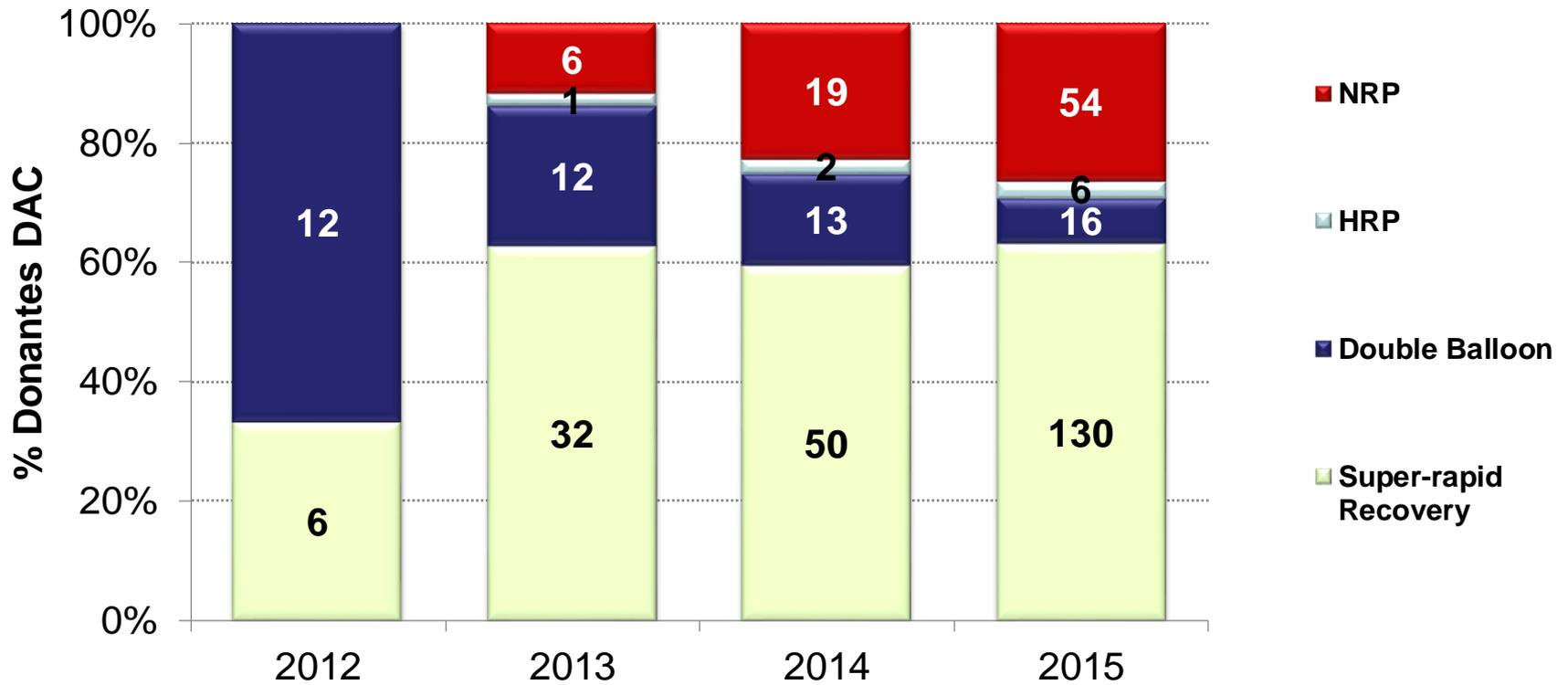


# Liver Transplant from DCD - Spain

107 transplants: 34 uDCD & 73 cDCD (2012 – 2015)



# Preservation technique in cDCD



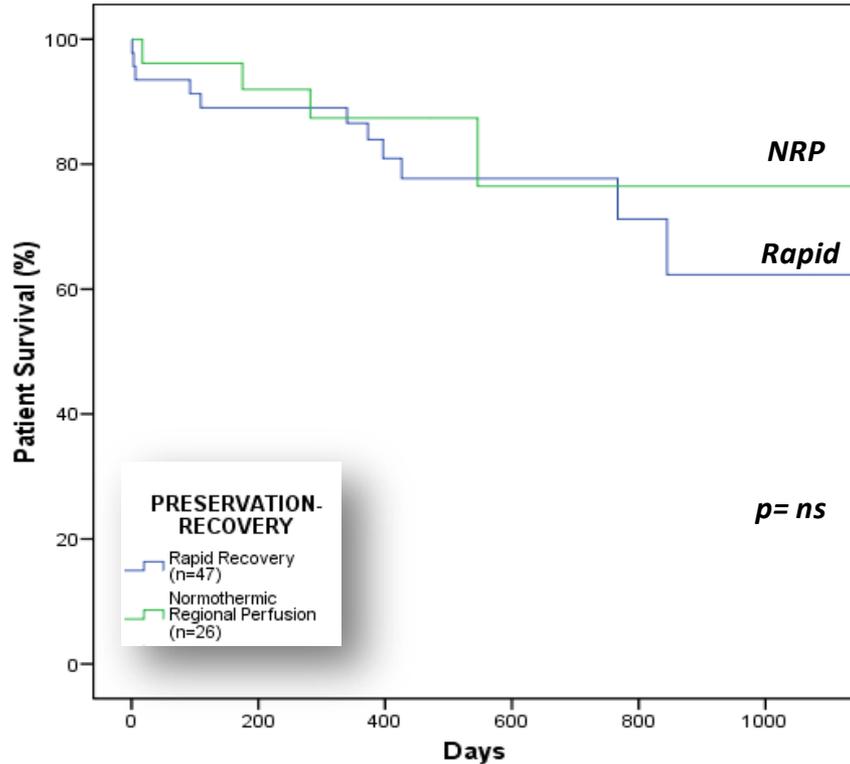
LIVER DONORS	
Double balloon	6%
Super-rapid	44%
NRP	71%

# Liver Transplant from DCD - Spain

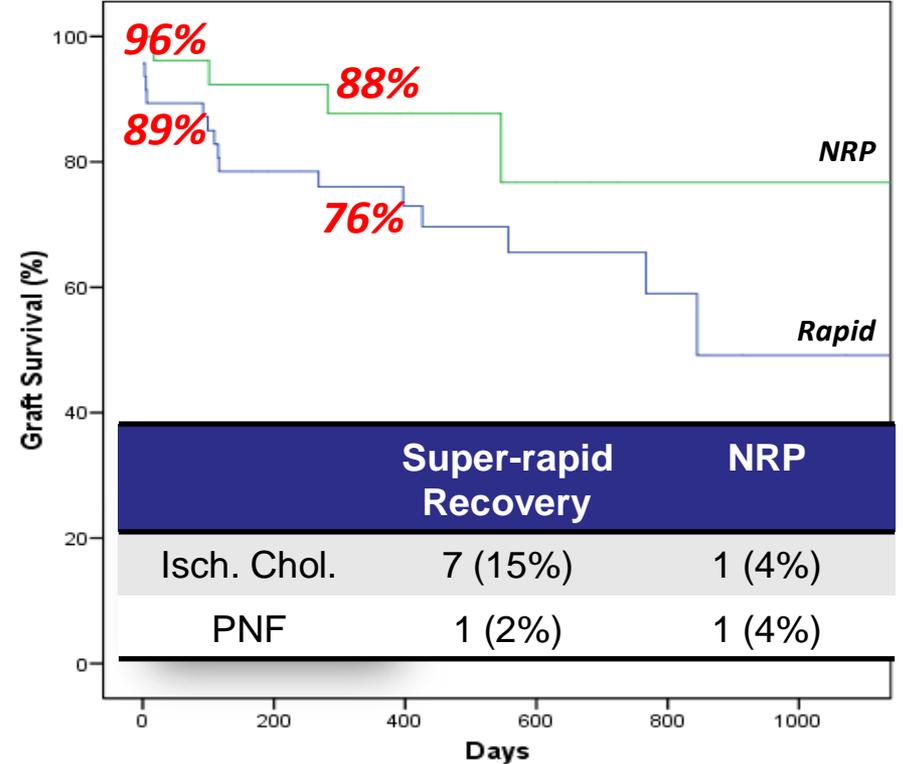
75 cDCD (2012 – 2015)

47 super-rapid recovery / 26 NRP / ~~2 double balloon~~

**Patient Survival**



**Graft Survival**



# ***When to cannulate?***

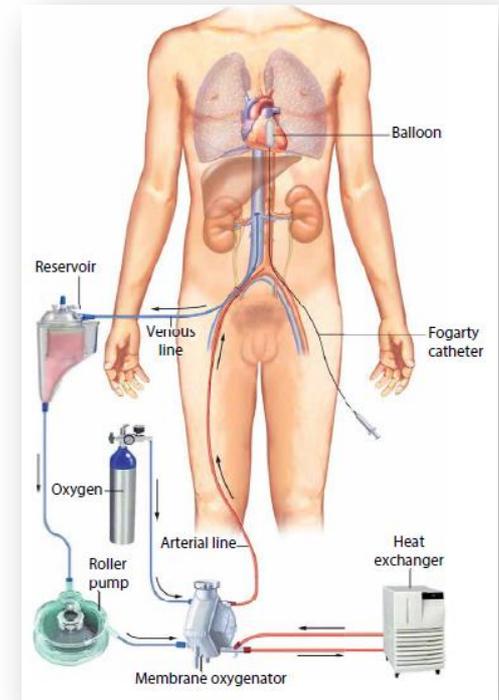
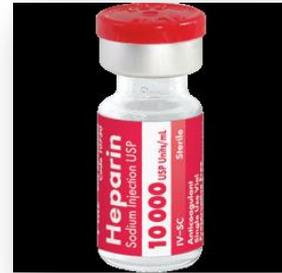
# Pre and post-mortem interventions in DCD in Spain

## PRE-MORTEM INTERVENTIONS (cDCD)

<b>Heparin</b>	Specific authorization required
<b>Cannulation</b>	Specific authorization required

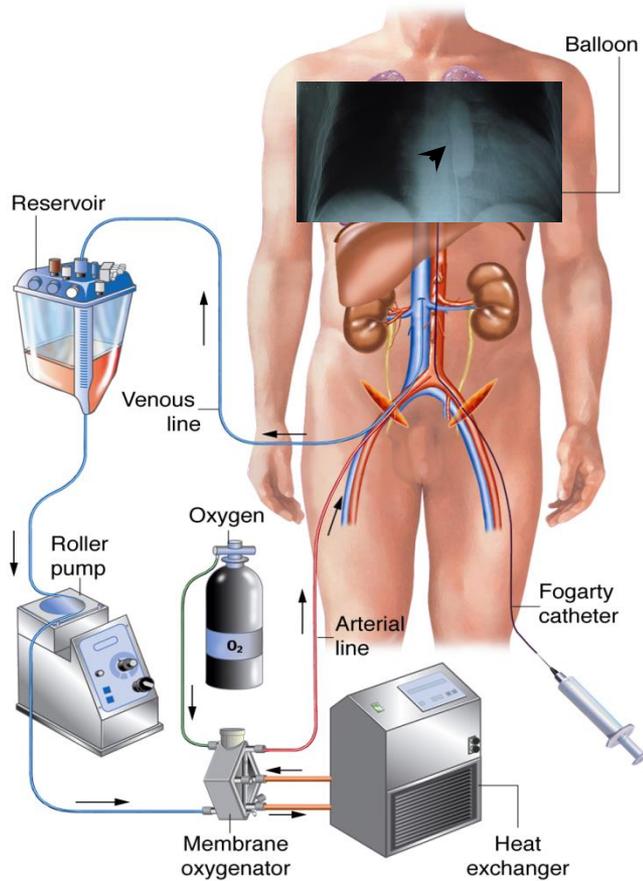
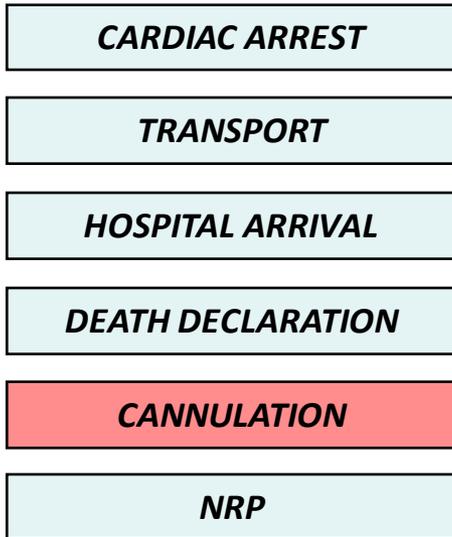
## POST-MORTEM INTERVENTIONS

<b>Cardiac compression + mechanical ventilation</b>	Allowed in uDCD
<b>Normothermic regional perfusion</b>	<p>Allowed in both cDCD &amp; uDCD</p> <ul style="list-style-type: none"> <li>▪ Fogarty balloon catheter placed via femoral artery</li> <li>▪ Radiologic control before WLST</li> <li>▪ Invasive monitoring of arterial pressure in radial artery during NRP</li> </ul> <p>OR</p> <ul style="list-style-type: none"> <li>▪ Supraceliac aortic clamp after rapid laparotomy following the determination of death</li> </ul>

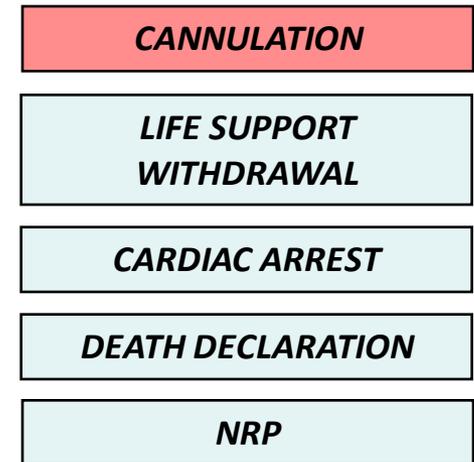


# Abdominal NRP in DCD OLT

## uDCD



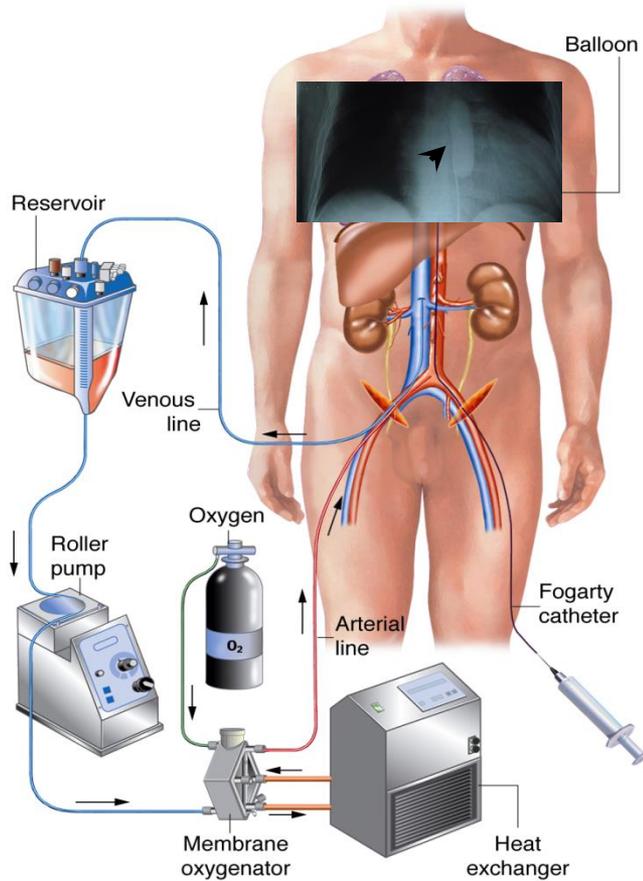
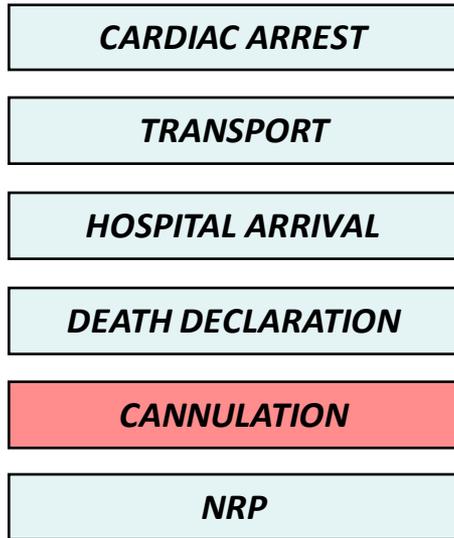
## cDCD\*



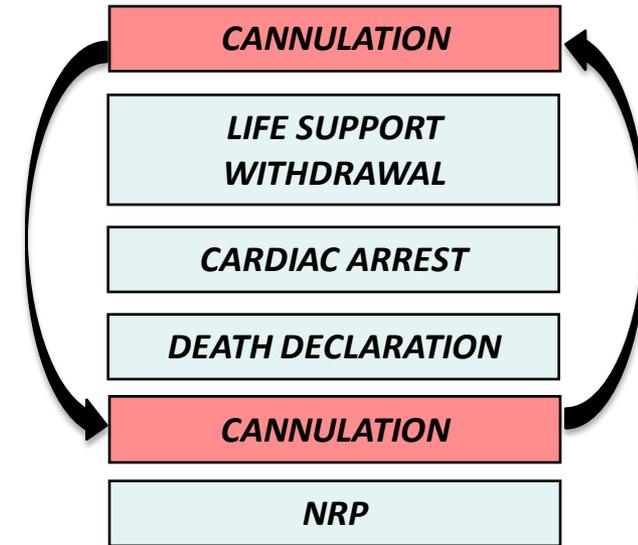
\*Spanish Royal Decree 1723/2012

# Abdominal NRP in DCD OLT

## uDCD



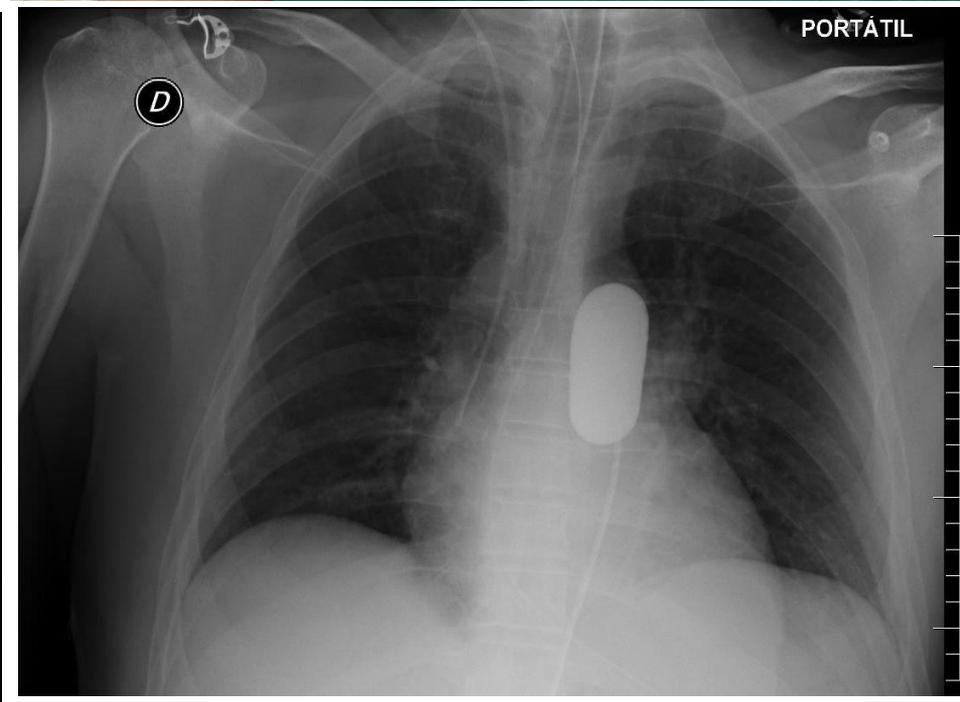
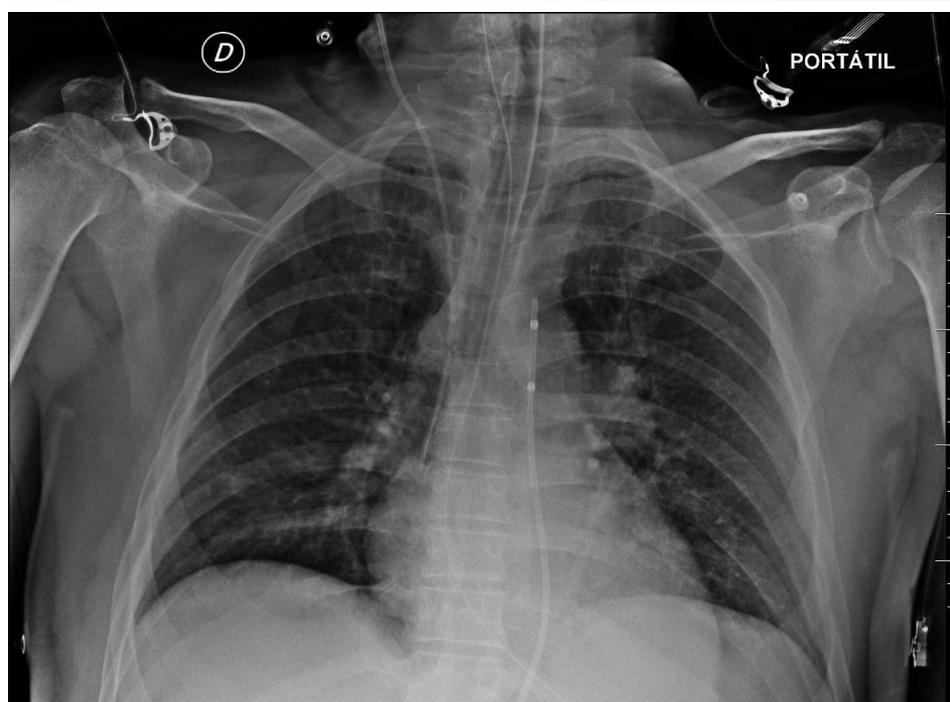
## cDCD\*



\*Spanish Royal Decree 1723/2012

# ***How to cannulate?***





# ***Organ Maintenance (controlled DCD)***



***NRP***

# Abdominal NRP in cDCD

- When to cannulate:
  - If possible, pre-mortem, with next-of-kin consent
- Where:
  - ICU or OR, in accordance with patient's family's wishes
- How:
  - Percutaneously if possible, depending on material available and technical expertise

# ***Cost of Abdominal NRP?***



***DCD:***

- Canulation*
- NRP*

***TOTAL 2800€***



# ***Abdominal NRP in DCD***

- ***Pros:***

- More organs (livers, pancreata, in particular)
- Better quality organs (even kidneys...)
- With pre-mortem cannulation, becomes a “standard” donation (less graft *AND* surgeon injury)

- ***Cons:***

- ~~Local legislation~~
- ~~Logistics & Cost~~
- Fogarty balloon catheter placement in pre-mortem cannulation has to be perfect (*must not* reperfuse arch vessels)

# ***Abdominal NRP in DCD***

