



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

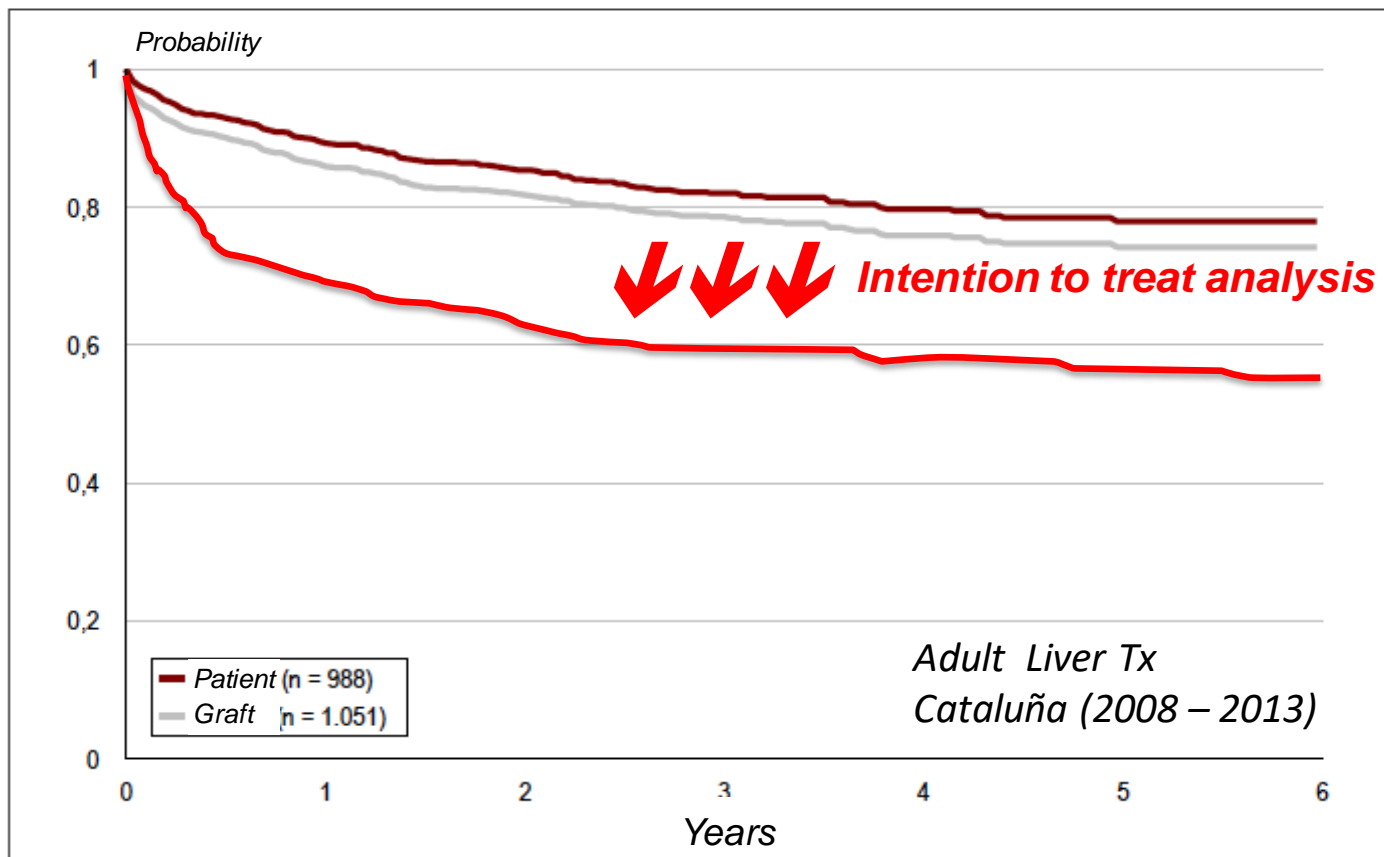
Associate Professor of Surgery

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Hospital Clinic, University of Barcelona, Spain



Patient & Graft Survival



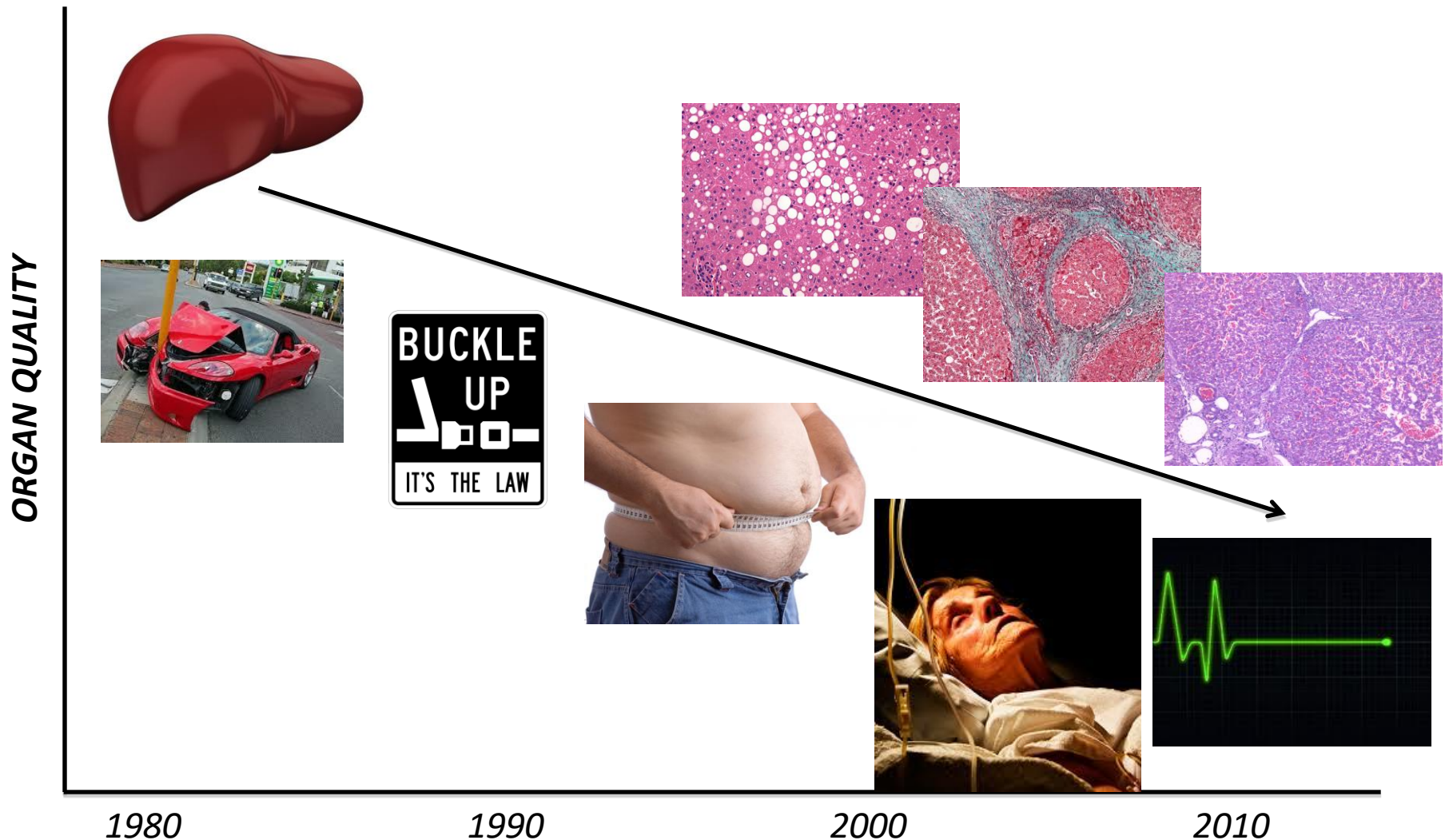
	1r mes	3r mes	6è mes	1r any	2n any	3r any	4rt any	5è any
Patient	0,97	0,95	0,93	0,89	0,85	0,82	0,80	0,78
Graft	0,95	0,92	0,90	0,86	0,82	0,79	0,76	0,74

Liver Transplant Waiting List UK / Spain 2013



	UK	SPAIN
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.

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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. Egtesad, 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,¹ Darrin L. Willingham,¹ Justin Nguyen,¹ Winston R. Hewitt,¹ Bucin C. Taner,¹ Veny,¹ Jamie Aranda-Michel,¹ Raj Satyanarayana,¹ mer,³ and Christopher B. Hughes¹
ville, FL; ²LifeQuest Organ Recovery Services, Medicine, Mayo Clinic, Jacksonville, FL

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doi: 10.1111/j.1600-6143.2011.03834.x

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

C. Fondevila^{a,*}, A. J. Hessheimer^a, E. Flores^a,

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

Laura Taricotti,¹ Chiara Rocha,¹ M. Thamara PR Perera,¹ Bridget K. Gunson,^{1,2} Simon R. Bramhall,¹ John Isaac,¹ John A. C. Buckels,¹ A. David Mayer,¹ Paolo Muiesan,¹ and Darius F. Mirza,^{1,3}

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

**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;

Jeffrey ARCH

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

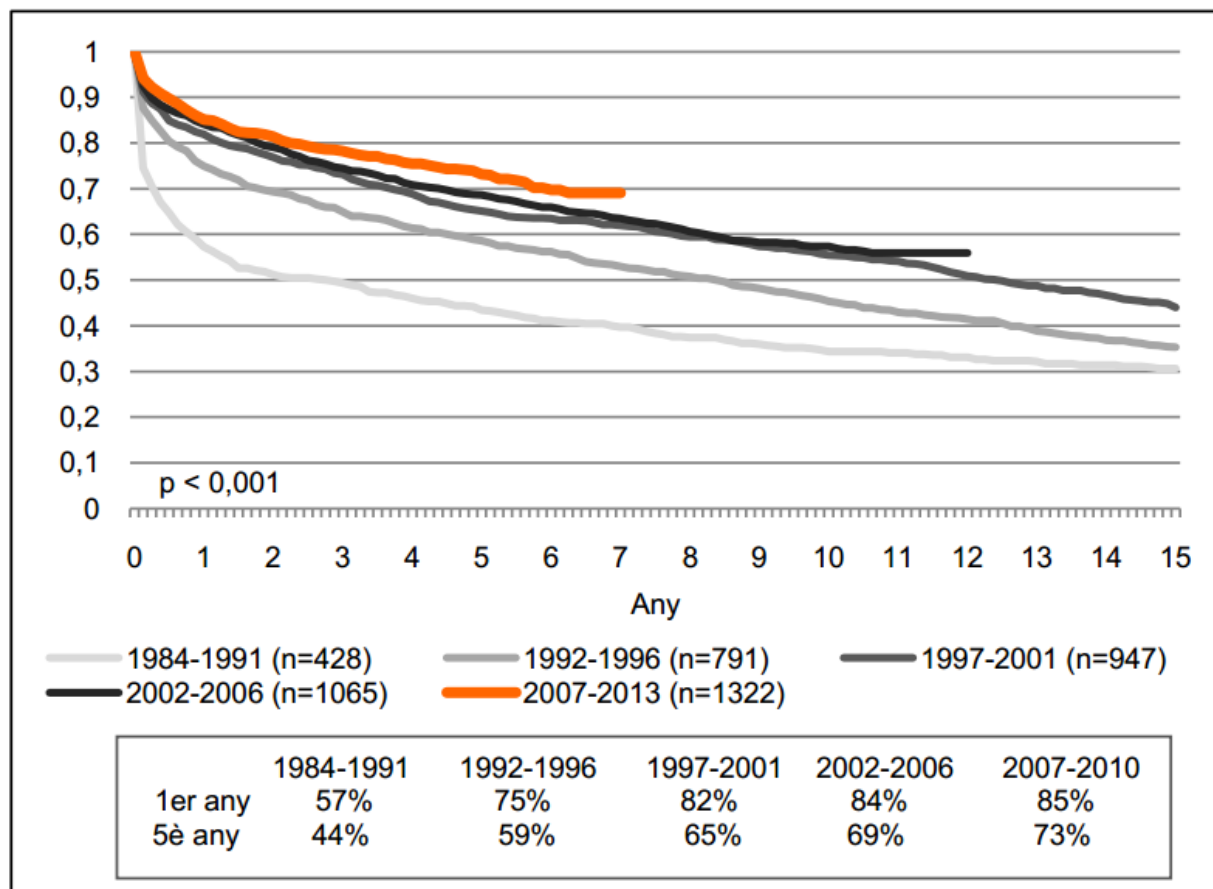
A. Joseph Tector, MD, PhD,* Richard S. Mangus, MD,* Paul Chestovich, MD,* Rodrigo Vianna, MD,* Jonathan A. Fridell, MD,* Martin L. Milgrom, MD, PhD,* Carrie Sanders, BsN,* and Paul Y. Kwo, MD†

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

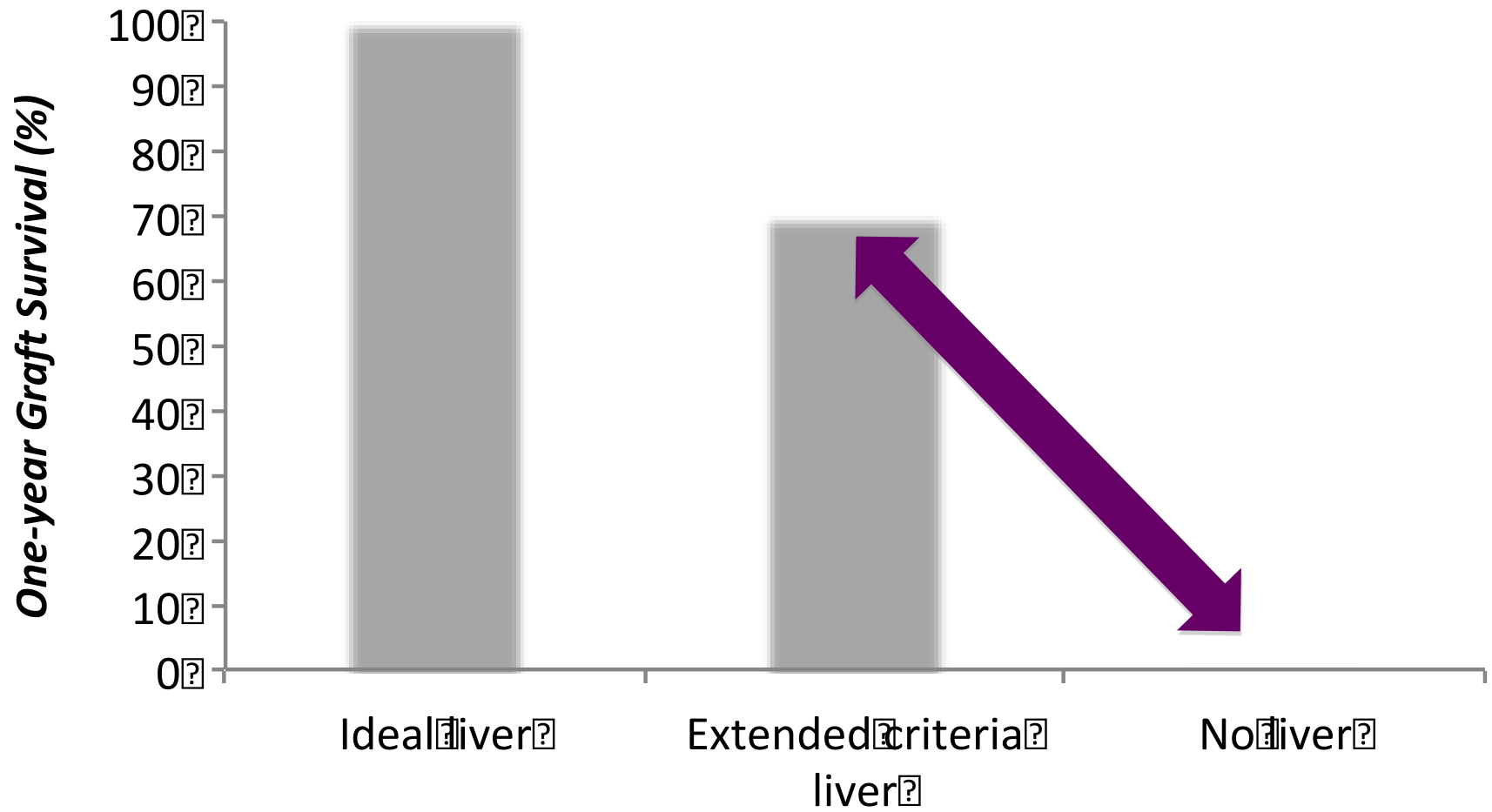
John F. Renz, MD, PhD, Cindy Kin, BA, Milan Kinkhabwala, MD, Dominique Jan, MD, Rhaghu Varadarajan, MD, Michael Goldstein, MD, Robert Brown, Jr., MD, MPH, and Jean C. Emond, MD

Mar
Benedikt W
Department

OCAAT Liver Survival (Barcelona)



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



History of Transplantation



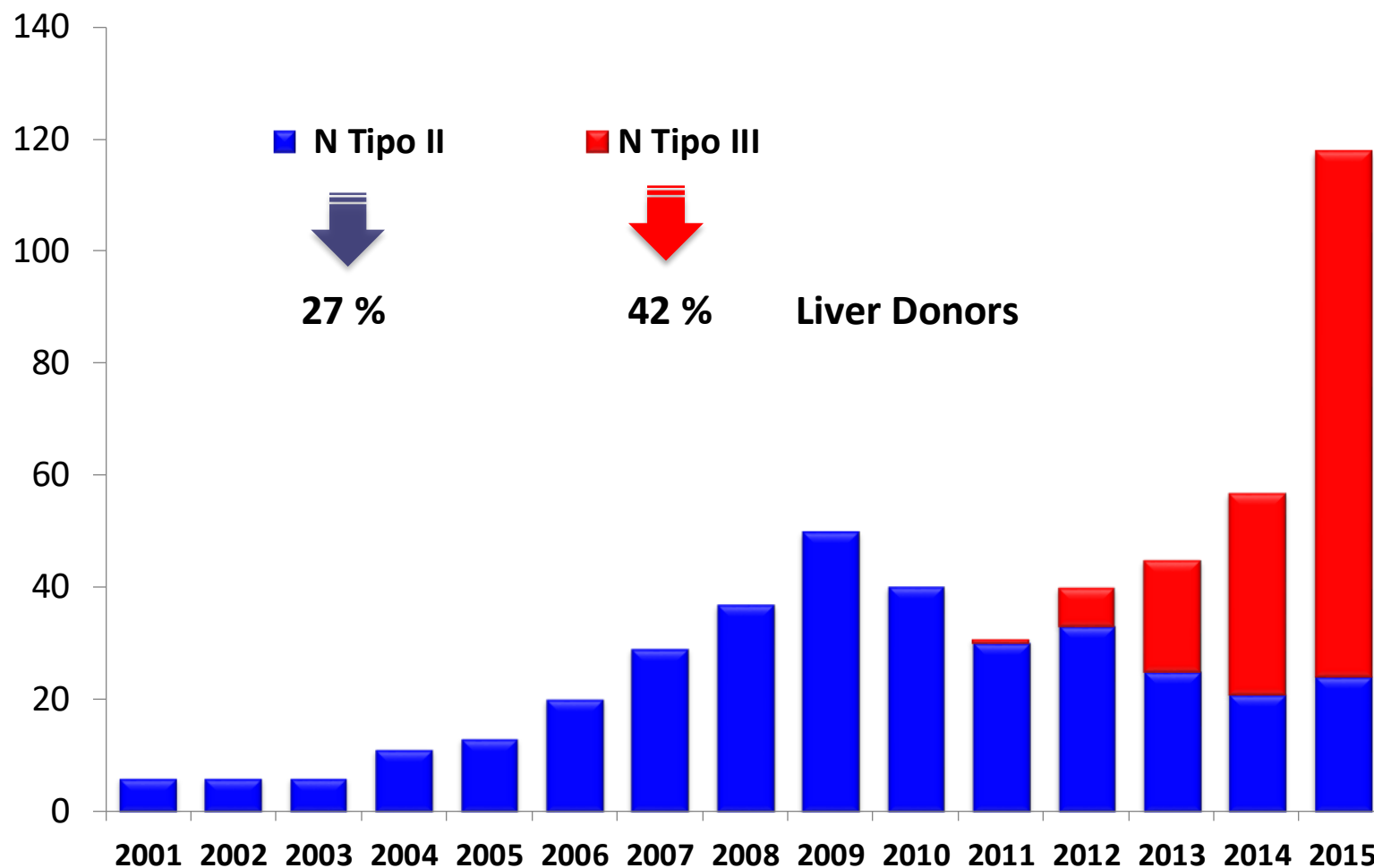
"A problem might be achievable, but only with great risk to yourself, risk of failure and professional disgrace."

Thomas E. Starzl (1926 – 2017)

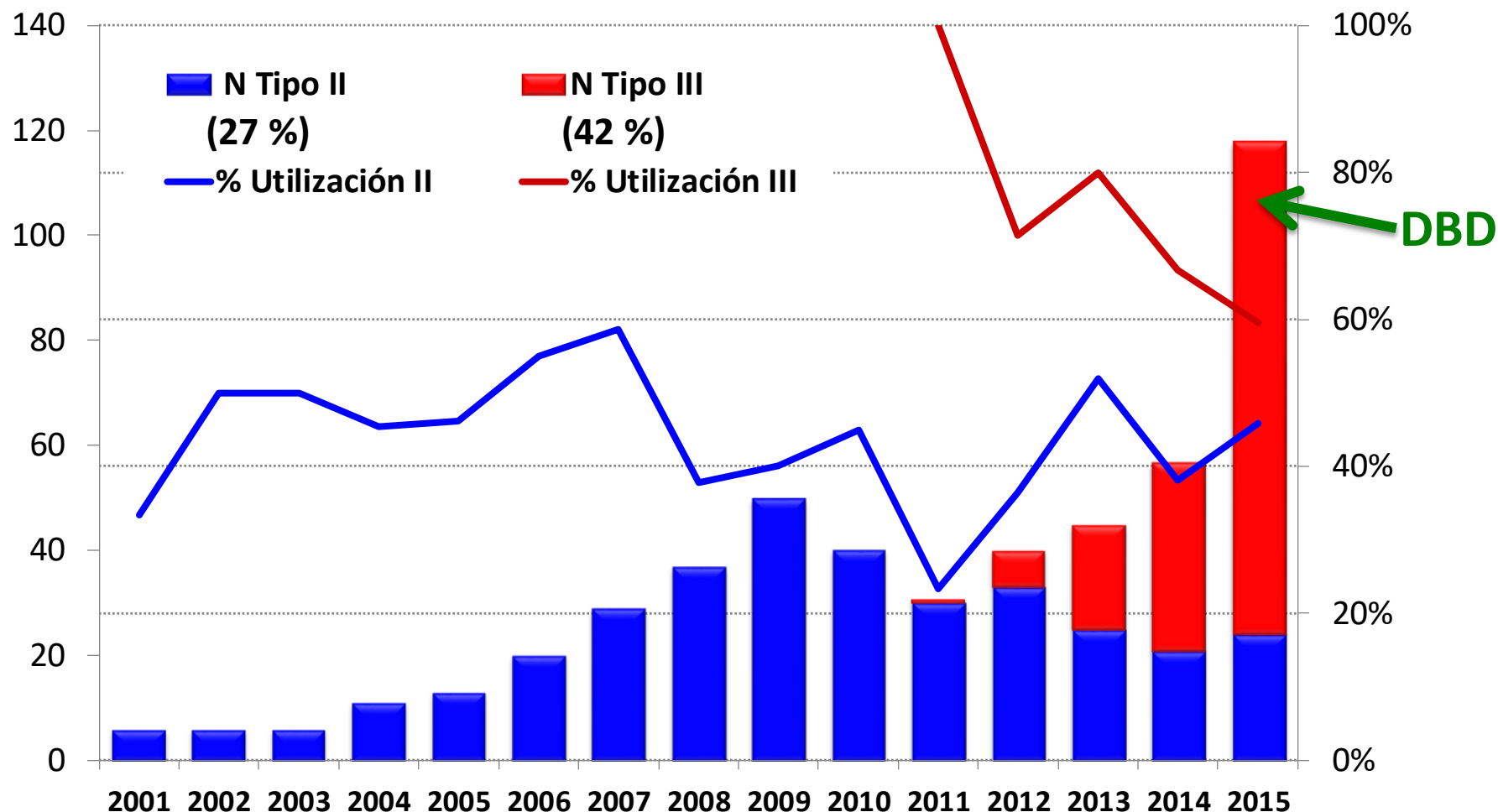
Legal basis for DCD in Spain

- **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



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)
Demographics					
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
Results					
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

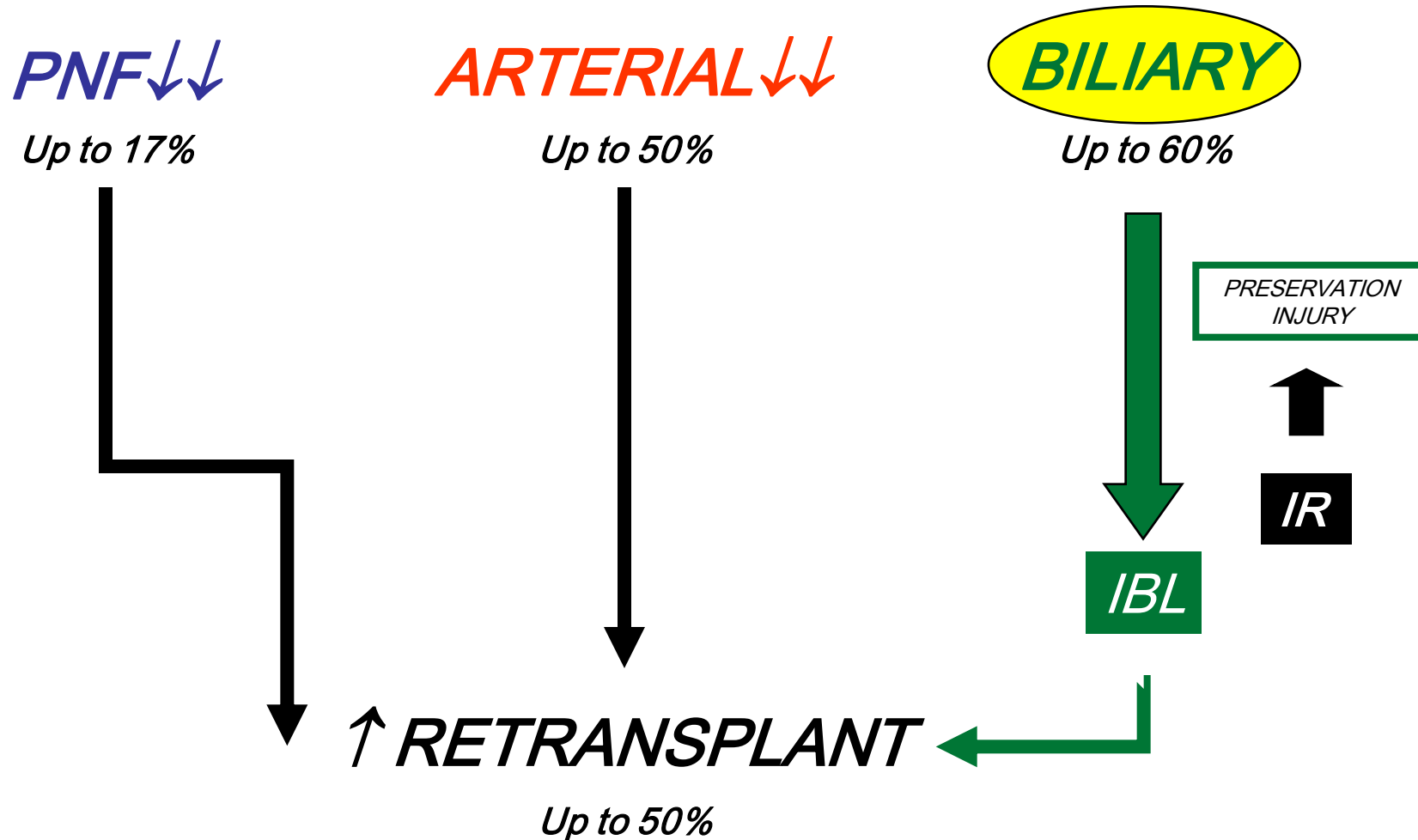
	DCD	DBD	P
Number	51	334	
Recipient age (years)	54.8 ± 6.8	53.3 ± 9.4	NS
Recipient gender	M38/F13	M236/F98	NS
MELD	19.6 ± 6.9	18.8 ± 8.2	NS
Status 1	0	6	NS
Donor age (years)	37.7 ± 14.5	40 ± 16.4	NS
Donor gender	M37/F14	M206/F128	NS
Total ischemia time (minutes)	473 ± 130	463 ± 160	NS
Anastomosis time (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.

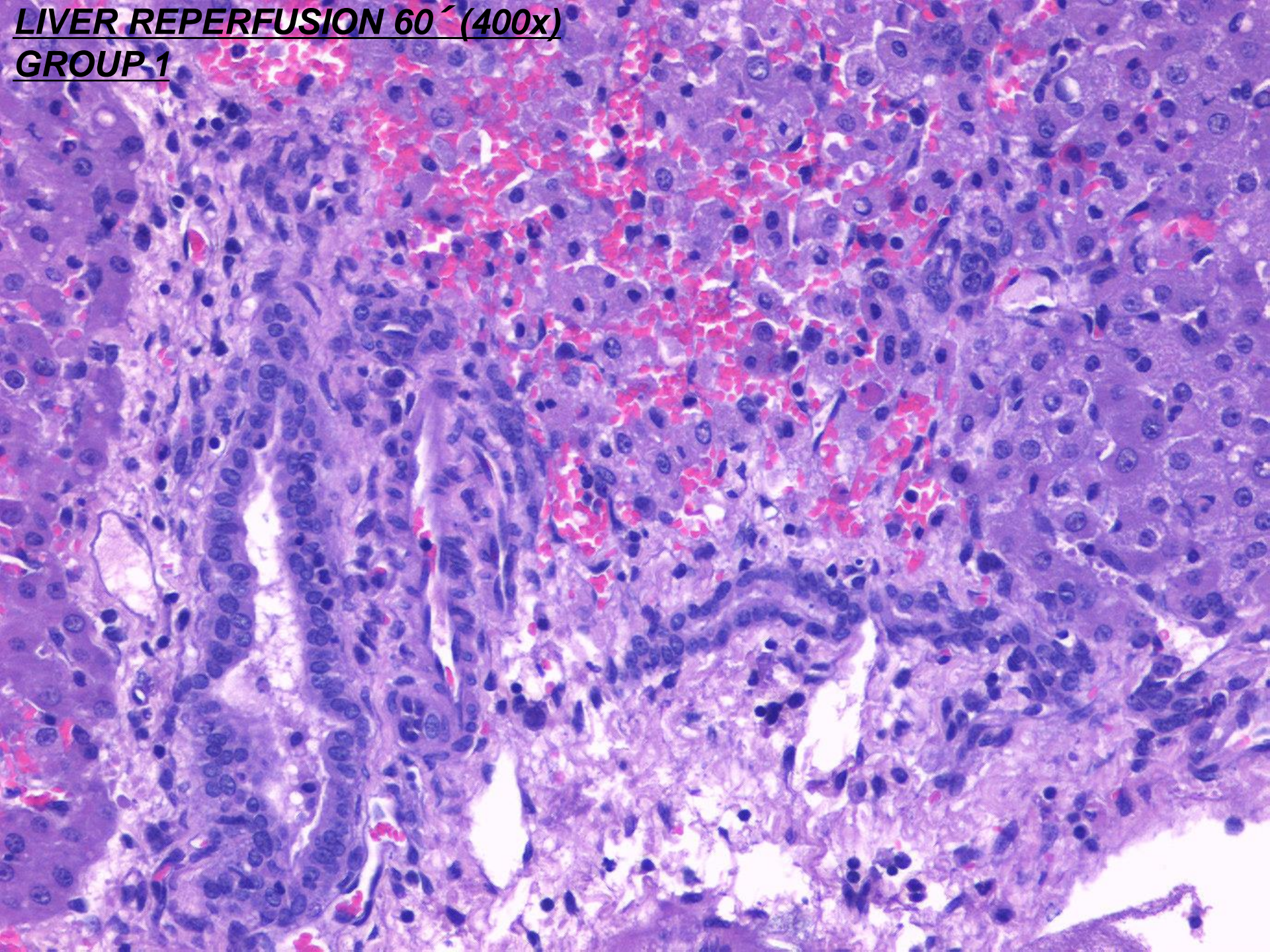
(Chan E Y., Liver Transplantation 14,2008)

Liver transplant from DCD: complications

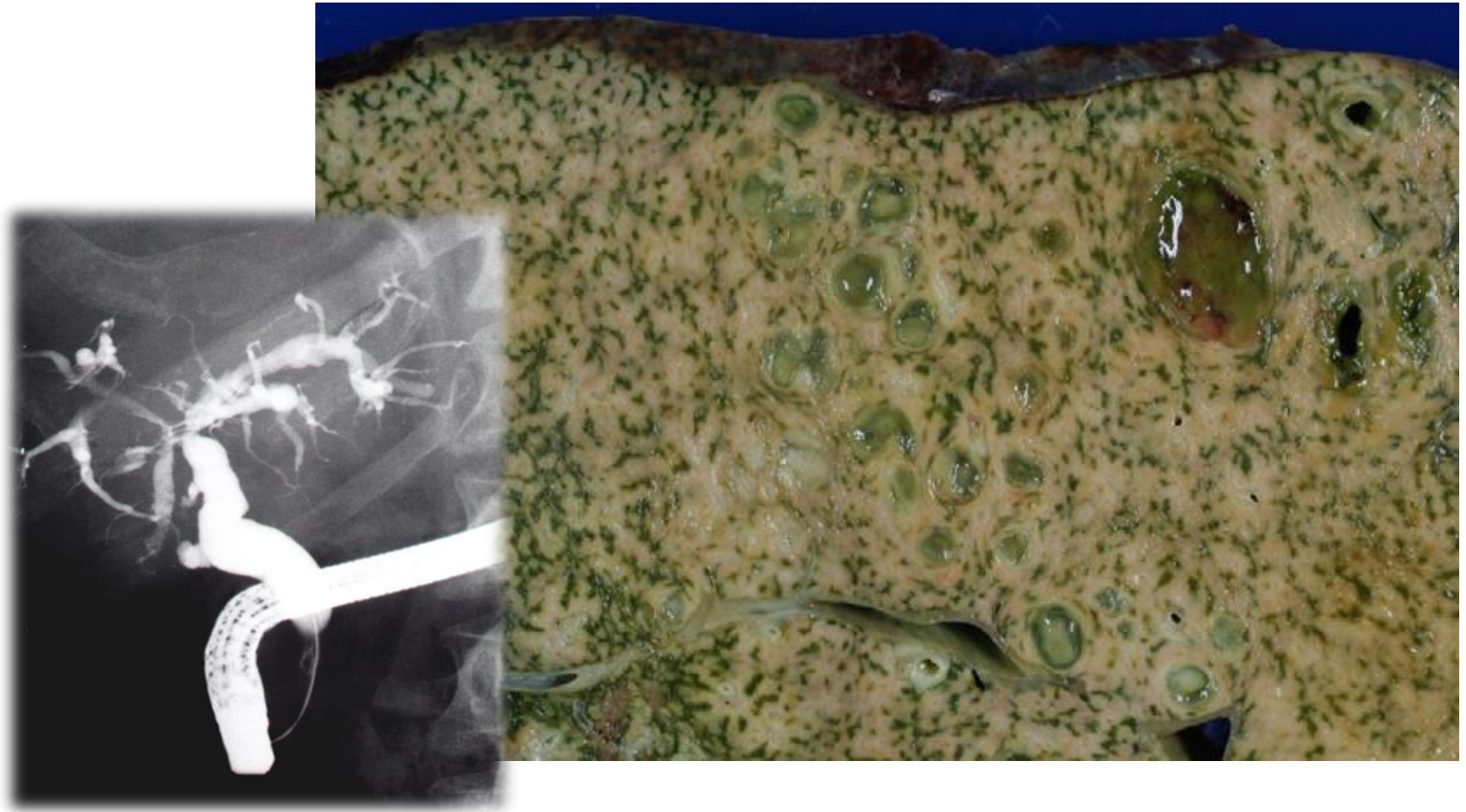


LIVER REPERFUSION 60' (400x)

GROUP 1



Ischemic Cholangiopathy



Organ Maintenance

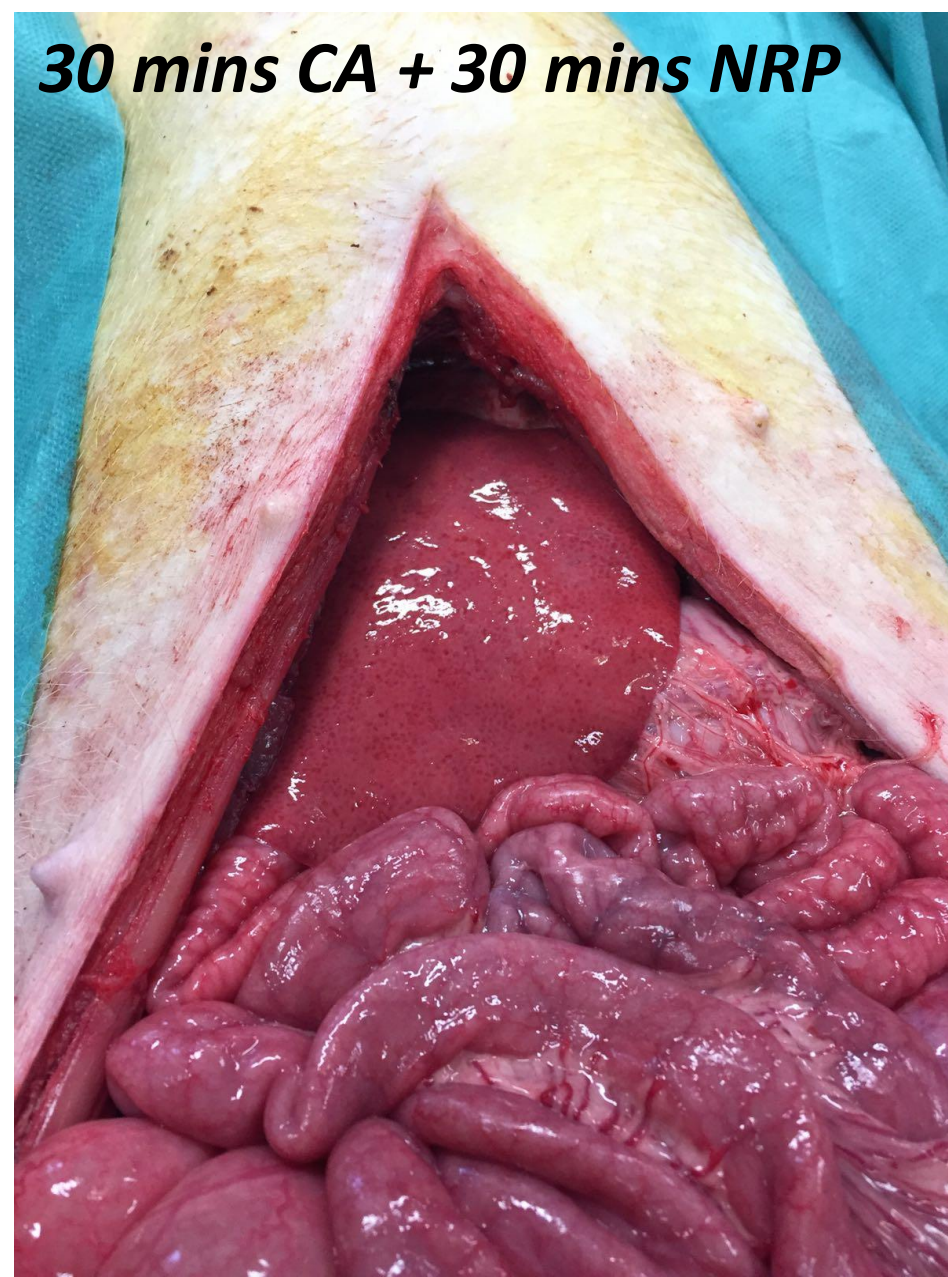
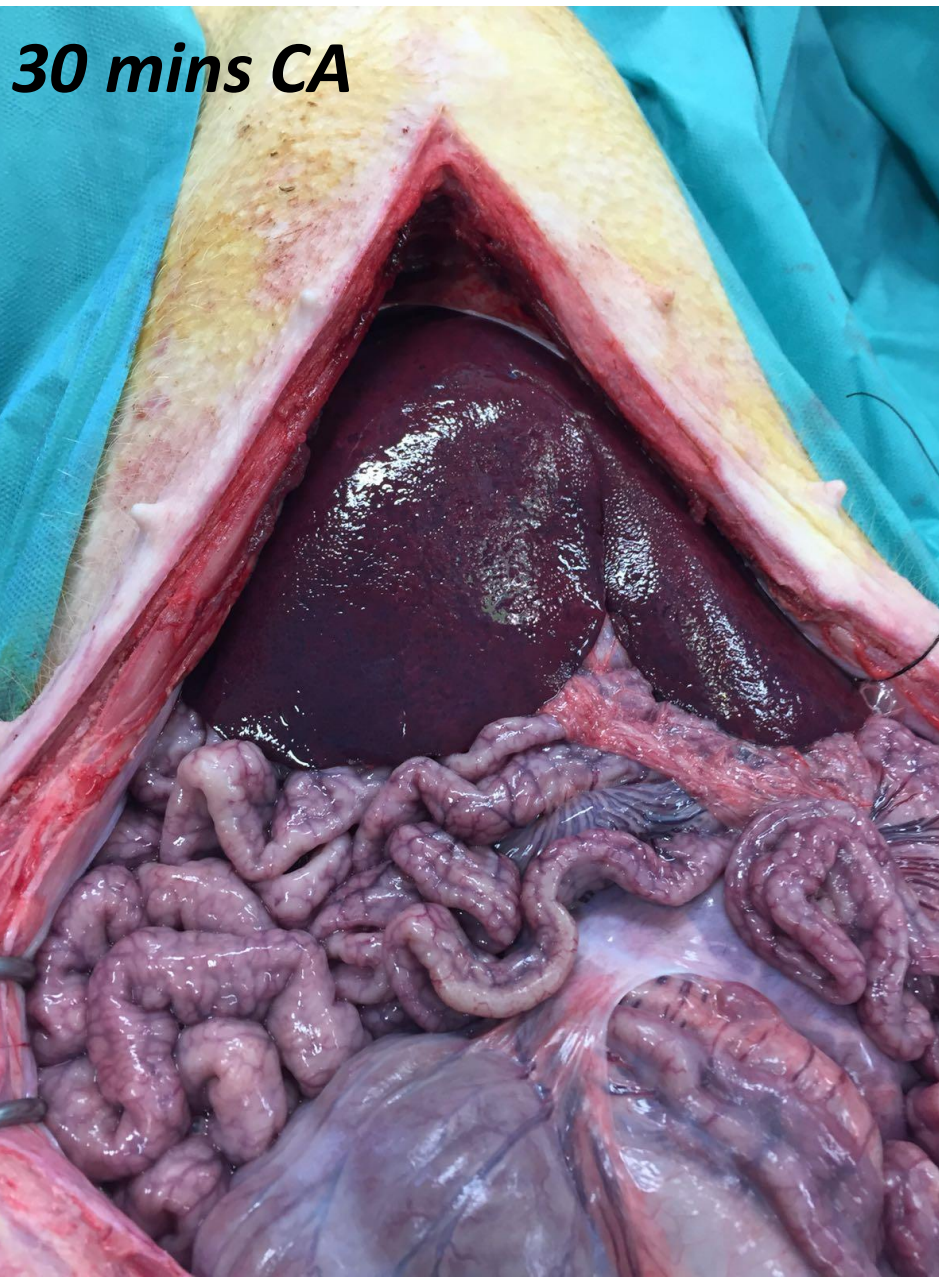
Technique	Results
Perfusion <i>in situ</i>	Quick and easy. Inferior results (kidney).
Thoraco-abdominal compressions	Simultaneous chest (mechanical) and abdominal (manual) compressions with the aim of maintaining MAP ≥ 70 mmHg and PaO ₂ ≥ 100 mmHg. ^{1,2}
Hypothermic recirculation	Primarily used to maintain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

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

PROS

CONS





DCD Selection Criteria

		Hospital Clínic Barcelona ^{1,2}
Normothermic regional perfusion	T ^o	37 °C
	pH	7.35-7.45
	PaO ₂	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,^{1,4} Federica Dondero,⁵ Eric Vibert,⁶ Daniel Eyraud,⁷ Hélène Brisson,² Bruno Riou,³ Fabienne Fieux,⁸ Salima Naili-Kortaia,⁹ Denis Castaing,⁶ Jean-Jacques Rouby,² Olivier Langeron,^{2,3} Safi Dokmak,⁵ Laurent Hannoun,¹ Jean-Christophe Vaillant,¹ 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

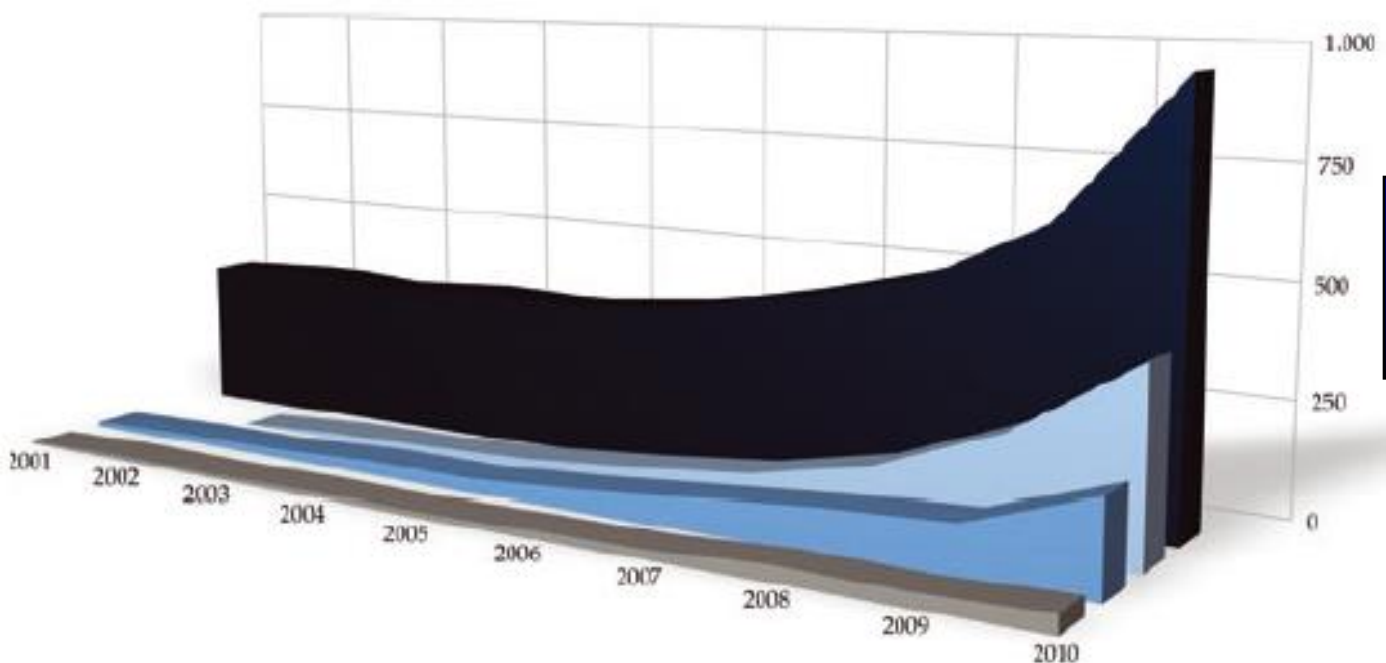
	N	Source	1-yr graft survival	1-yr patient survival	IC	All biliary complications
Abt 2003	15	UPenn	72%	79%	27%	33%
Chan 2008	52	UWash	~80%	~84%	14%	--
de Vera 2007	141	Pitt	69%	79%	16%	25%
Dezza 2007	13	Ghent	54%	62%	23%	--
Foley 2011	87	Wisconsin	69%	84%	34%	47%
Fujita 2007	24	Florida	69%	87%	13%	--
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%
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★ Uncontrolled

Year-to-year evolution of controlled DCD activity:



**Stringent
criteria**

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.

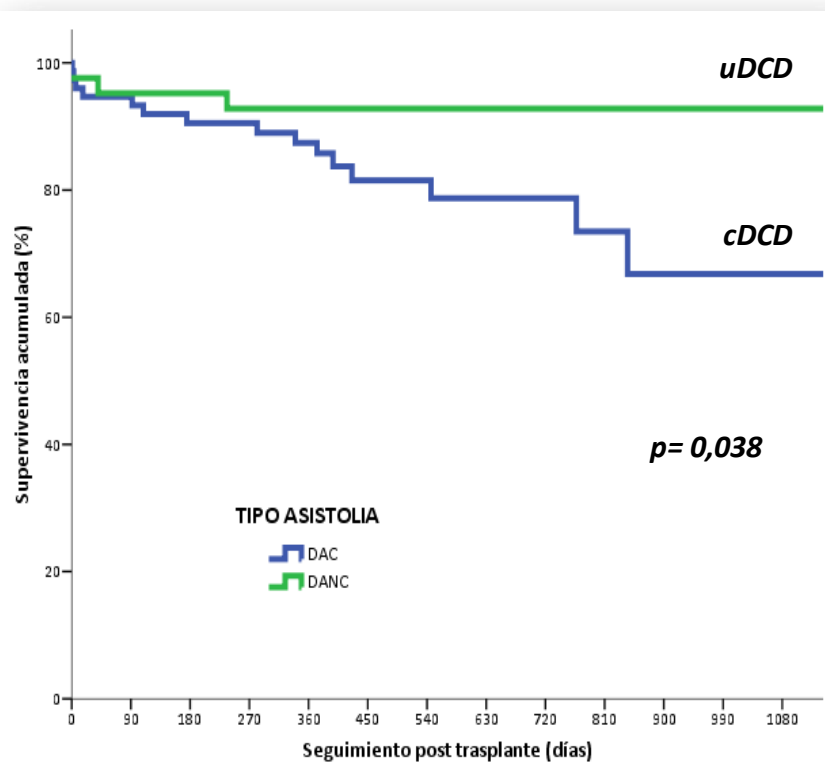
Table 2: Individual center normothermic regional perfusion retrieval and organ transplant activity

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

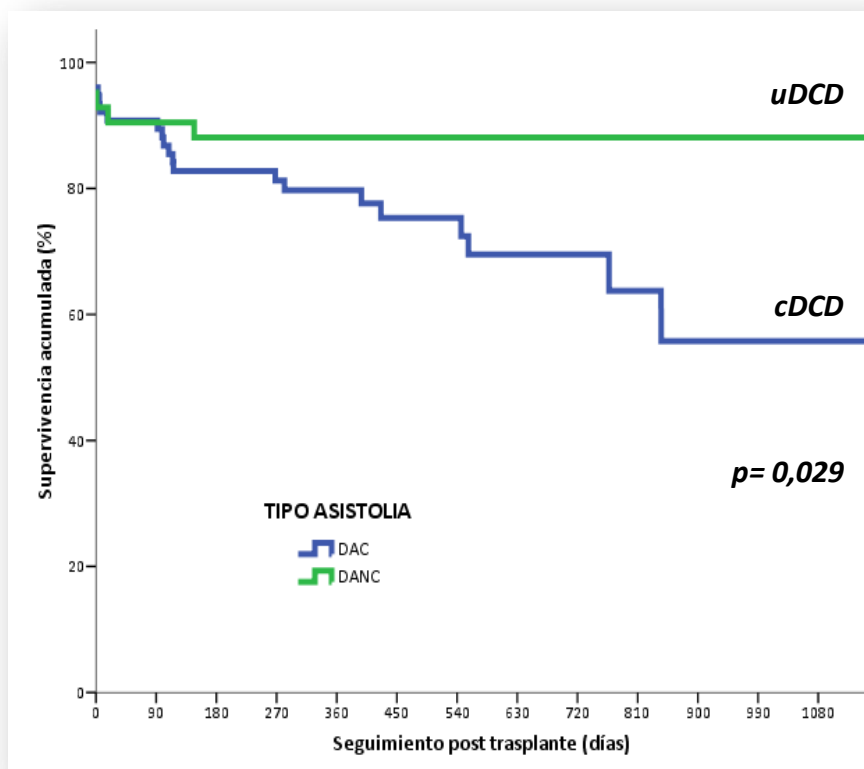
Liver Transplant from DCD - Spain

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

Patient Survival

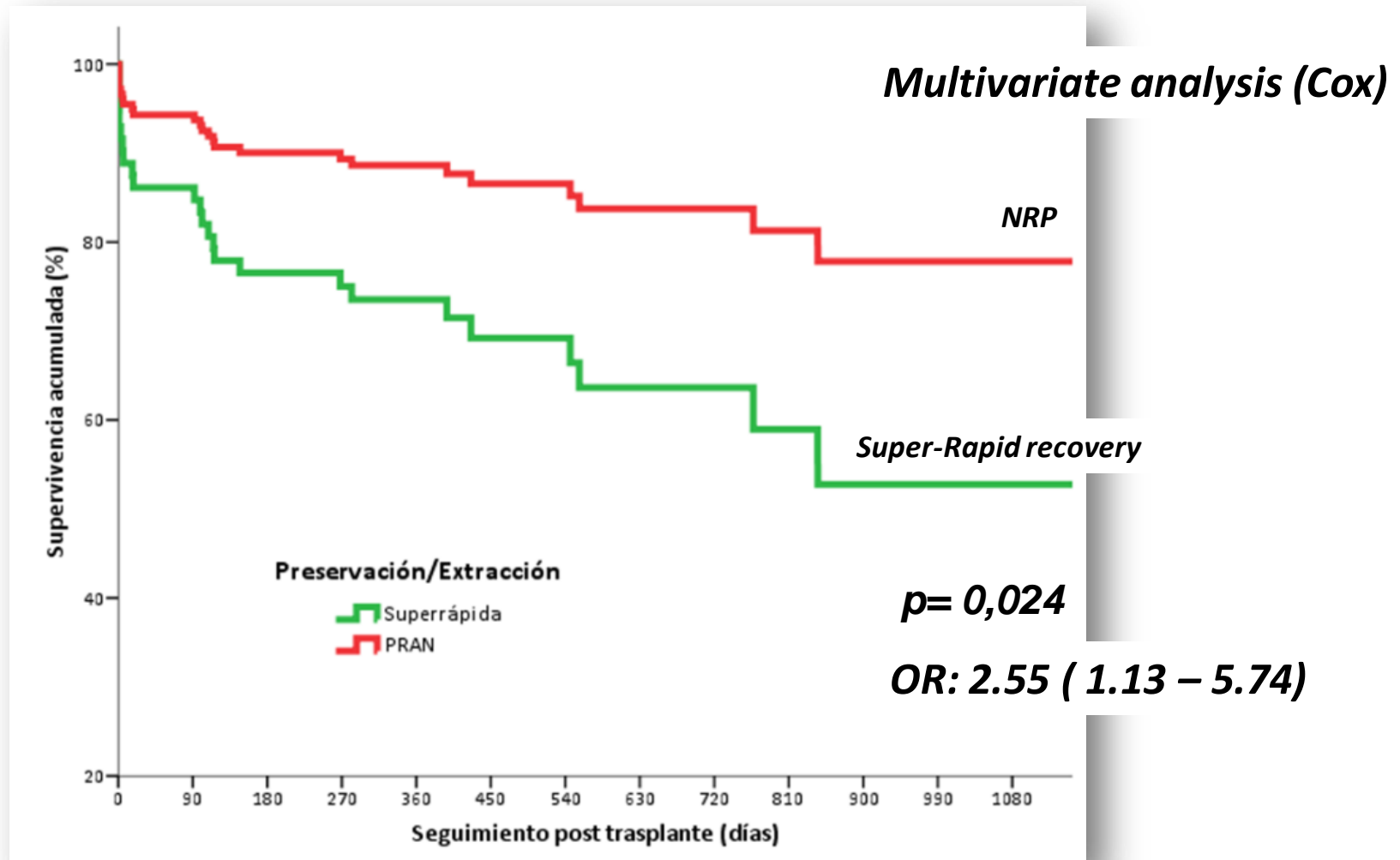


Graft Survival

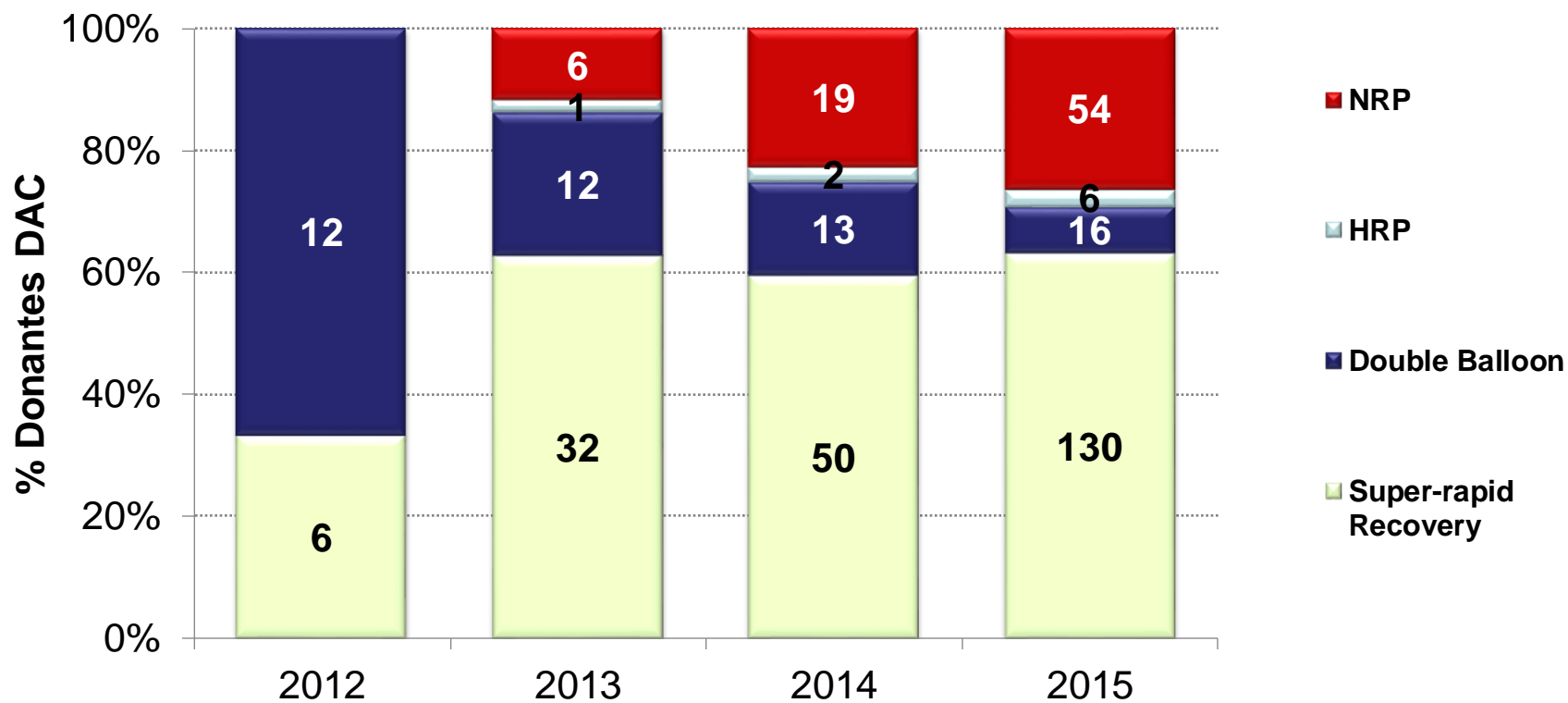


Liver Transplant from DCD - Spain

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



Preservation technique in cDCD



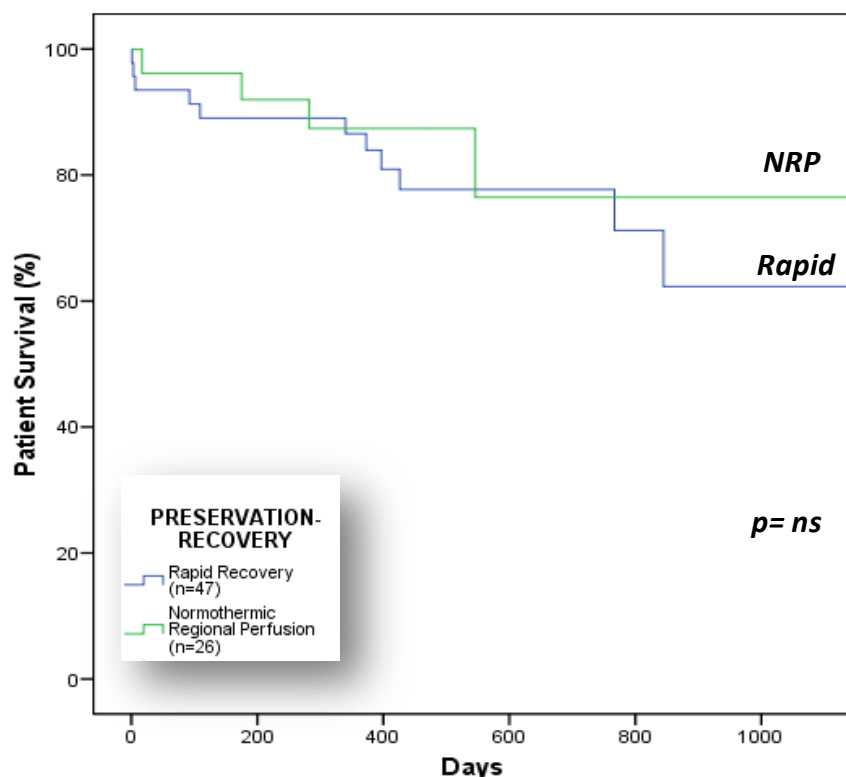
LIVER DONORS	
Double balloon	6%
Super-rapid	44%
NRP	71%

Liver Transplant from DCD - Spain

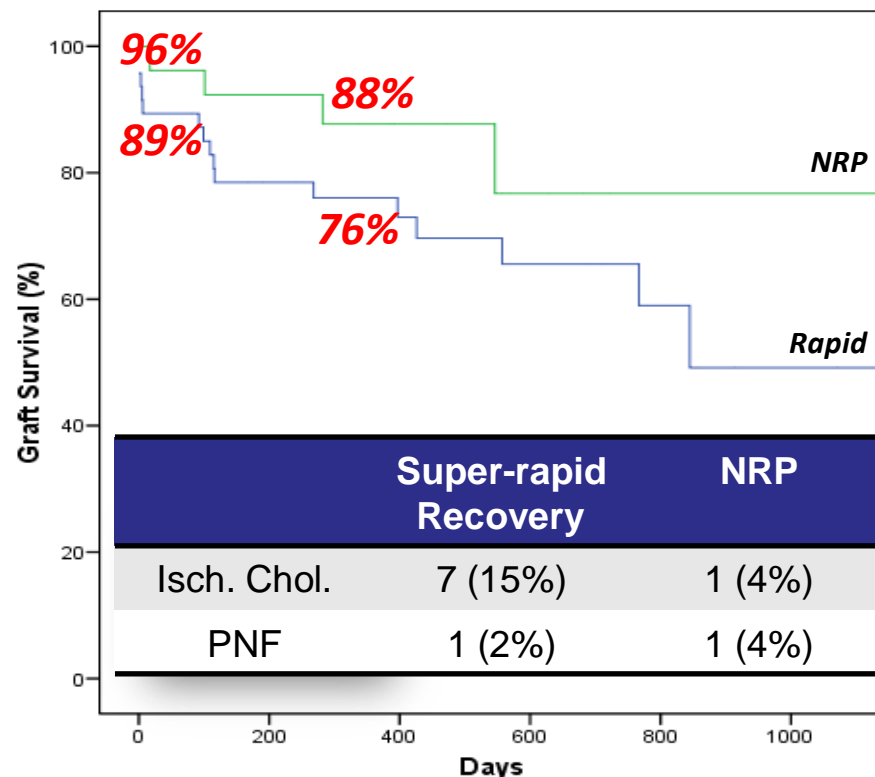
75 cDCD (2012 – 2015)

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

Patient Survival



Graft Survival



When to cannulate?

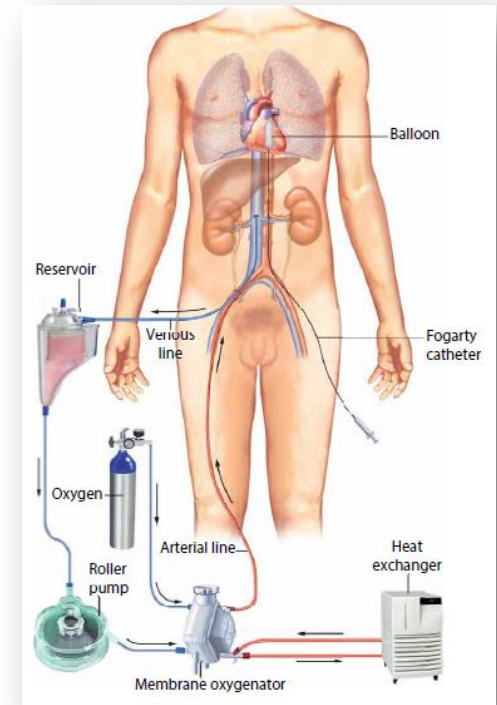
Pre and post-mortem interventions in DCD in Spain

PRE-MORTEM INTERVENTIONS (cDCD)

Heparin	Specific authorization required
Cannulation	Specific authorization required

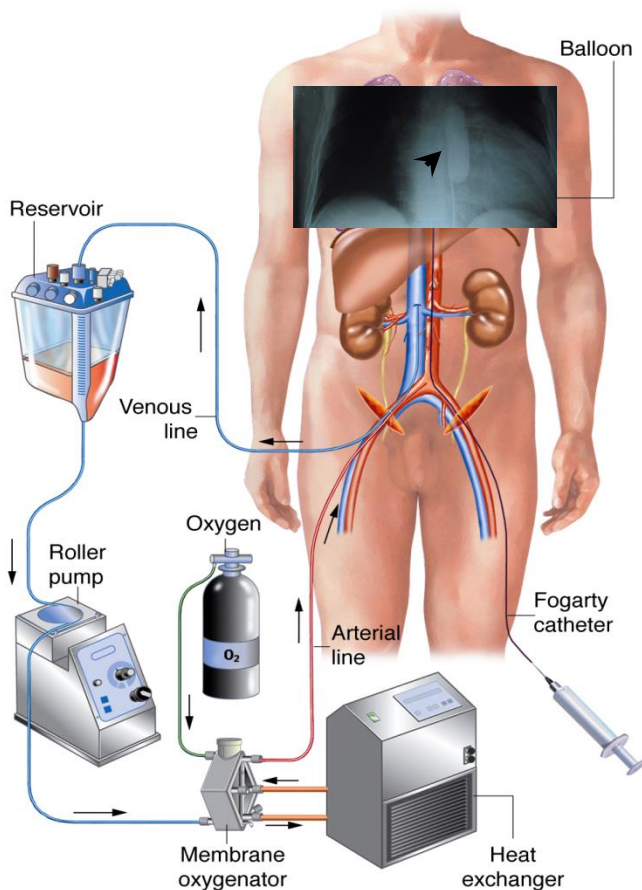
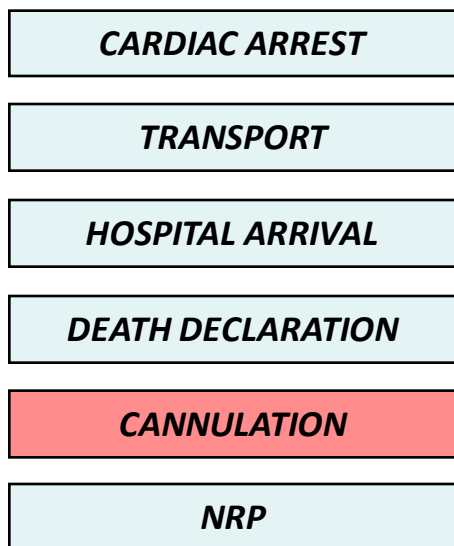
POST-MORTEM INTERVENTIONS

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

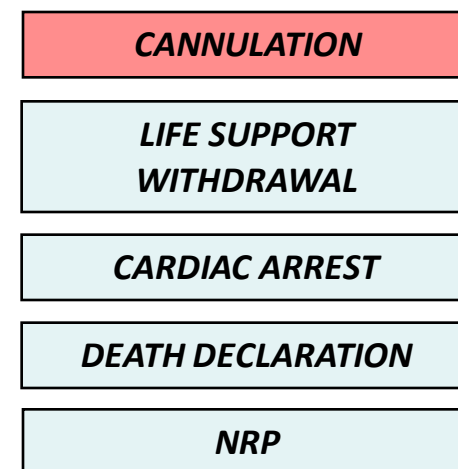


Abdominal NRP in DCD OLT

uDCD



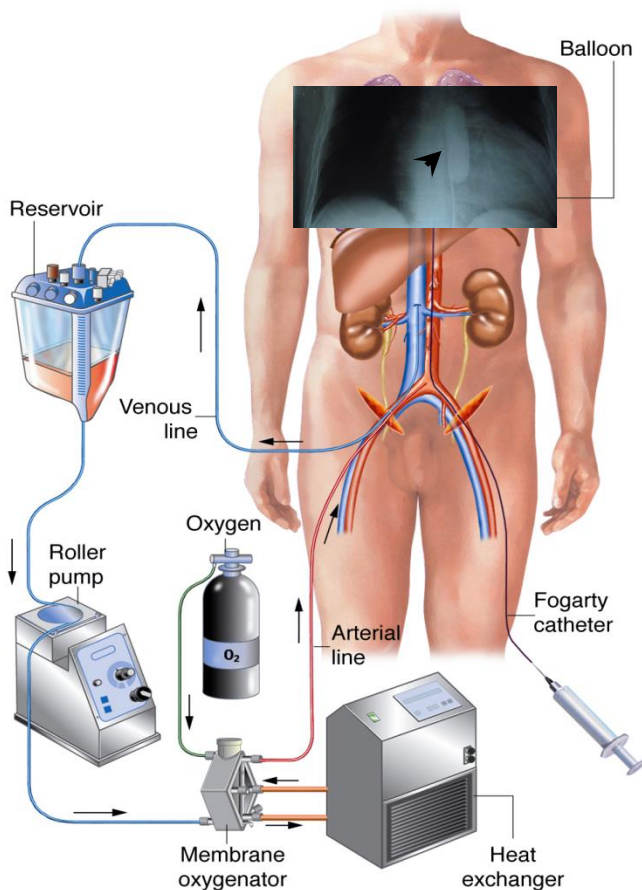
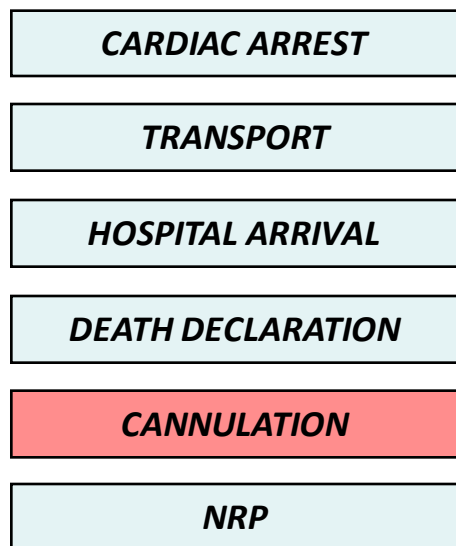
*cDCD**



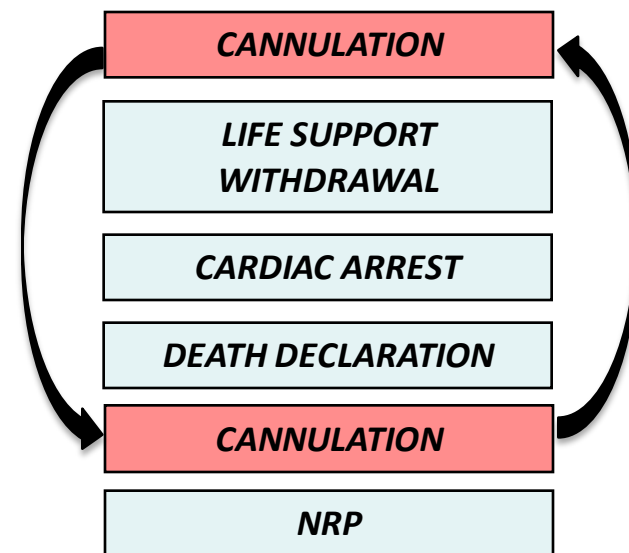
*Spanish Royal Decree 1723/2012

Abdominal NRP in DCD OLT

uDCD



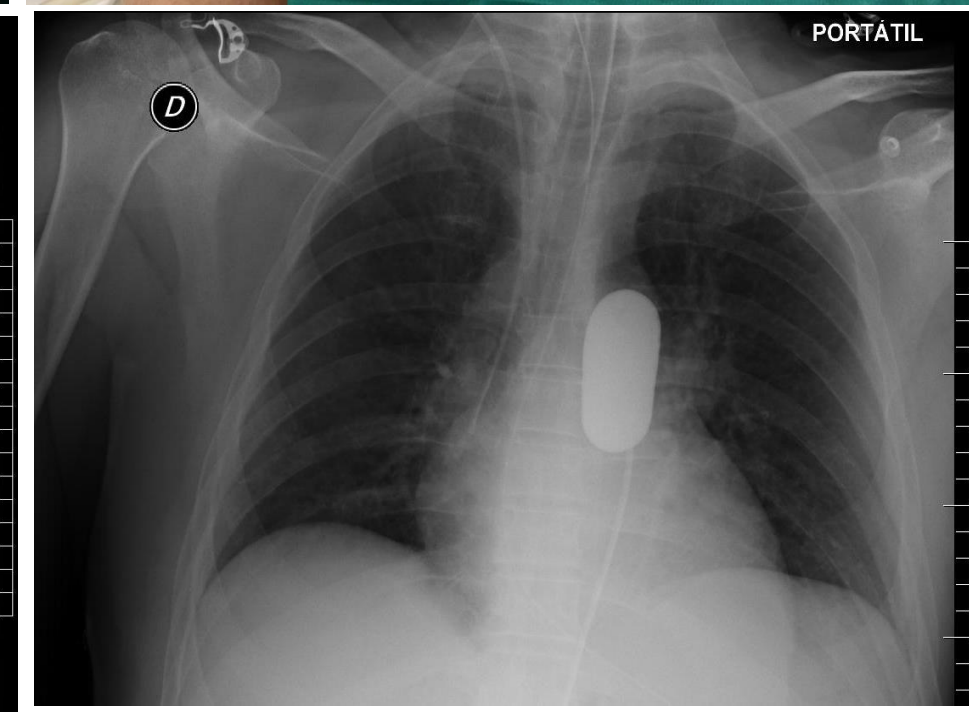
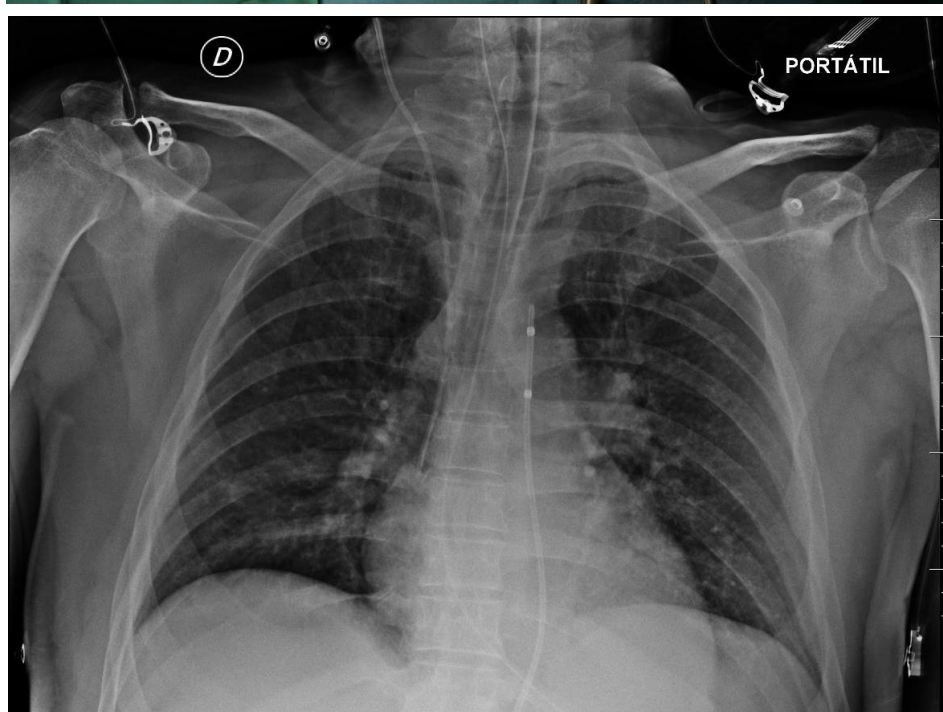
*cDCD**



*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

