JOURNÉES MEDITERRANÉENNES PRÉLÈVEMENT ET GREFFES D'ORGANS ET DE TISSUS
Nice, Octobre 14-15, 2015

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DISCLOSURE

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All presented images are used as essential references to illustrate this presentation.

Transpl Int. 2011 Apr;24(4):373-8

Critical pathways for organ donation*

POSSIBLE DECEASED ORGAN DONOR

A patient with a devastating brain injury or lesion OR a patient with circulatory failure
AND apparently medically suitable for organ donation

Treating physician
to identify/refer a potential donor

Donation after Circulatory Death (*DCD*)

POTENTIAL *DCD* DONOR

A. A person whose circulatory and respiratory functions have ceased and resuscitative measures are not to be attempted or continued.

or

B. A person in whom the cessation of circulatory and respiratory functions is anticipated to occur within a time frame that will enable organ recovery.

ELIGIBLE *DCD* DONOR

A **medically suitable** person who has been **declared dead** based on the irreversible absence of circulatory and respiratory functions as stipulated by the law of the relevant jurisdiction, within a time frame that enables organ recovery.

ACTUAL *DCD* DONOR

A consented eligible donor:

A. In whom an **operative incision** was made with the intent of organ recovery for the purpose of transplantation.

and/or

B. From whom at least **one organ was recovered** for the purpose of transplantation.

UTILIZED *DCD* DONOR

An actual donor from whom **at least one organ was transplanted**.

Reasons why a potential donor does not become a utilized donor

System

- *Failure to identify/refer a potential or eligible donor*
- *Brain death diagnosis could not be confirmed (e.g. does not fulfill criteria) or completed (e.g. lack of technical resources or clinician to make diagnosis or perform confirmatory tests)*
- *Circulatory death not declared within the appropriate time frame.*
- *Logistical problems (e.g. no recovery team)*
- *Lack of appropriate recipient (e.g. child, blood type, serology positive)*

Donor/Organ

- *Medical unsuitability (e.g. serology positive, neoplasia)*
- *Haemodynamic instability / unanticipated cardiac arrest*
- *Anatomical, histological and/or functional abnormalities of organs*
- *Organs damaged during recovery*
- *Inadequate perfusion of organs or thrombosis*

Permission

- *Expressed intent of deceased not to be donor*
- *Relative's refusal of permission for organ donation*
- *Refusal by coroner or other judicial officer to allow donation for forensic reasons*

Donation after BrainDeath (*DBD*)

POTENTIAL *DBD* DONOR

A person whose clinical condition is suspected to fulfill brain death criteria.

ELIGIBLE *DBD* DONOR

A **medically suitable** person who has been **declared dead** based on neurologic criteria as stipulated by the law of the relevant jurisdiction.

ACTUAL *DBD* DONOR

A consented eligible donor:

A. In whom an **operative incision** was made with the intent of organ recovery for the purpose of transplantation.

and/or

B. From whom at least **one organ was recovered** for the purpose of transplantation.

UTILIZED *DBD* DONOR

An actual donor from whom **at least one organ was transplanted.**

*The "dead donor rule" must be respected. That is, patients may only become donors after death, and the recovery of organs must not cause a donor's death.

Donation after Circulatory Death (*DCD*)

Critical Pathway for Organ Donation

POTENTIAL *DCD* DONOR

A. A person whose circulatory and respiratory functions have ceased and resuscitative measures are not to be attempted or continued or

B. A person in whom the cessation of circulatory and respiratory functions is anticipated to occur

POTENTIAL *DCD* DONOR

A.A person whose circulatory and respiratory functions have ceased and resuscitative measures are not to be attempted or continued . Uncontrolled

B.A person in whom the cessation of circulatory and respiratory functions is anticipated to occur within a time frame that will enable organ recovery. Controlled

B. From whom at least **one organ was recovered f**or the purpose of transplantation.

↓

UTILIZED *DCD* DONOR

An actual donor from whom **at least one organ was transplanted**.

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OPTING-OUT LEGISLATION

- Law 30/1979 de 27 de October
- R.D. 426/1980 de 26 de February
- 1995 First International Workshop on NHBD. Maastricht
- 1995 National Consensus Document (ONT)
- R.D. 2070/1999 30th December
- R.D. 1723/2012 29th December

"…it can be considered acceptable to start measures guided to preserve the organs with the possibility of a posterior transplant, while detecting relatives who can transmit the donation will of the death person…"

- Criteria for the diagnosis of cardiac death.
- Procedure after the diagnosis of cardiac death.

1. **Introduction**
2. **Glossary & classification of DCD**
3. **Determination of death by circulatory criteria**
4. **Uncontrolled DCD**
   a. Out-of-hospital logistics. Donor selection criteria
   b. In-hospital logistics. Donor selection criteria
   c. Preservation, recovery and organ viability
   d. Family approach
5. **Controlled DCD**
   a. Donor selection criteria
   b. WLST
   c. Family approach
   d. Extubation, cardiac arrest and death determination
   e. Preservation, recovery and organ viability
   f. Requisites for starting a controlled DCD programme
6. **Recipient selection criteria & peritransplant management. Information to the potential recipient**
7. **Communication with the media**
8. **Ethical & legal aspects**

DCD in Spain: state of the art and recommendations

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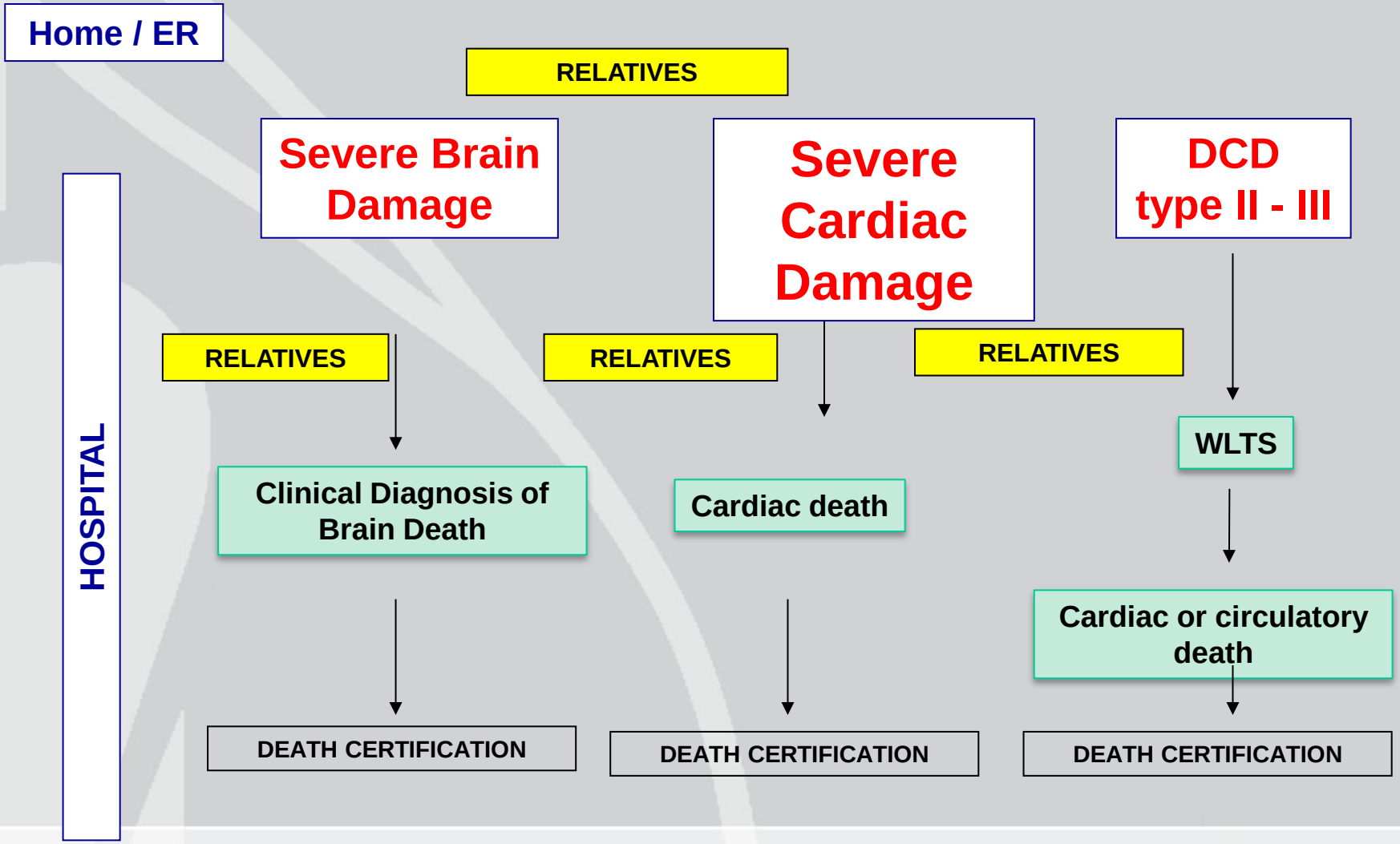
DCD Types

Classification of Maastricht			
Category	**Condition**	**Event**	**Frequency**
1	Uncontrolled	Death on arrival	Rare
2	Uncontrolled	CPR maneuvers unsuccessful	Very frequent
3	Controlled	Removal of ventilatory support followed by cardiac arrest	Less Frequent
4	Uncontrolled	Brain death followed by cardiac arrest	Rare

CPR, cardiopulmonary resuscitation

End of life process …



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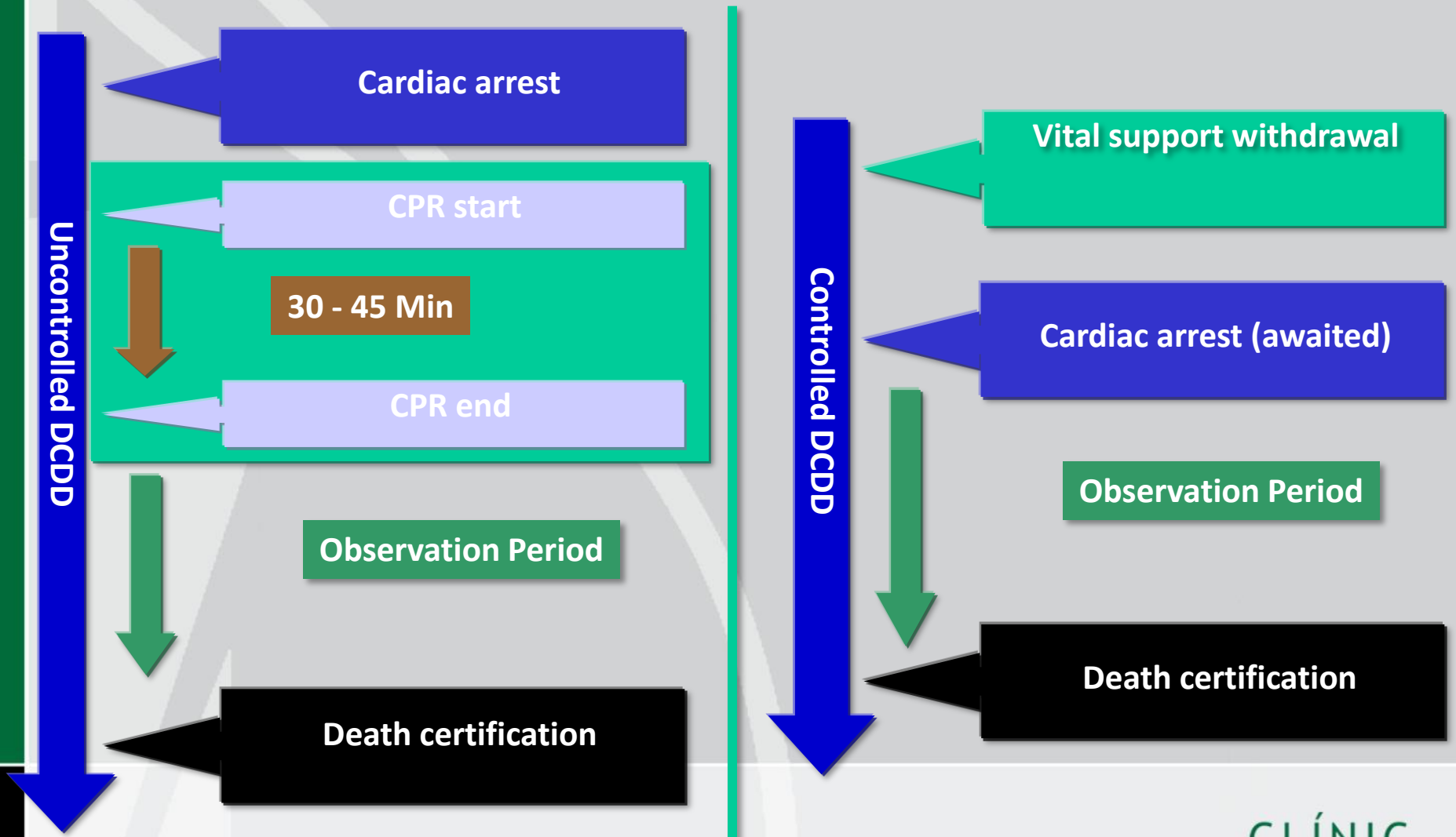
Determination of death

Controlled DCD vs. **UnControlled** DCD



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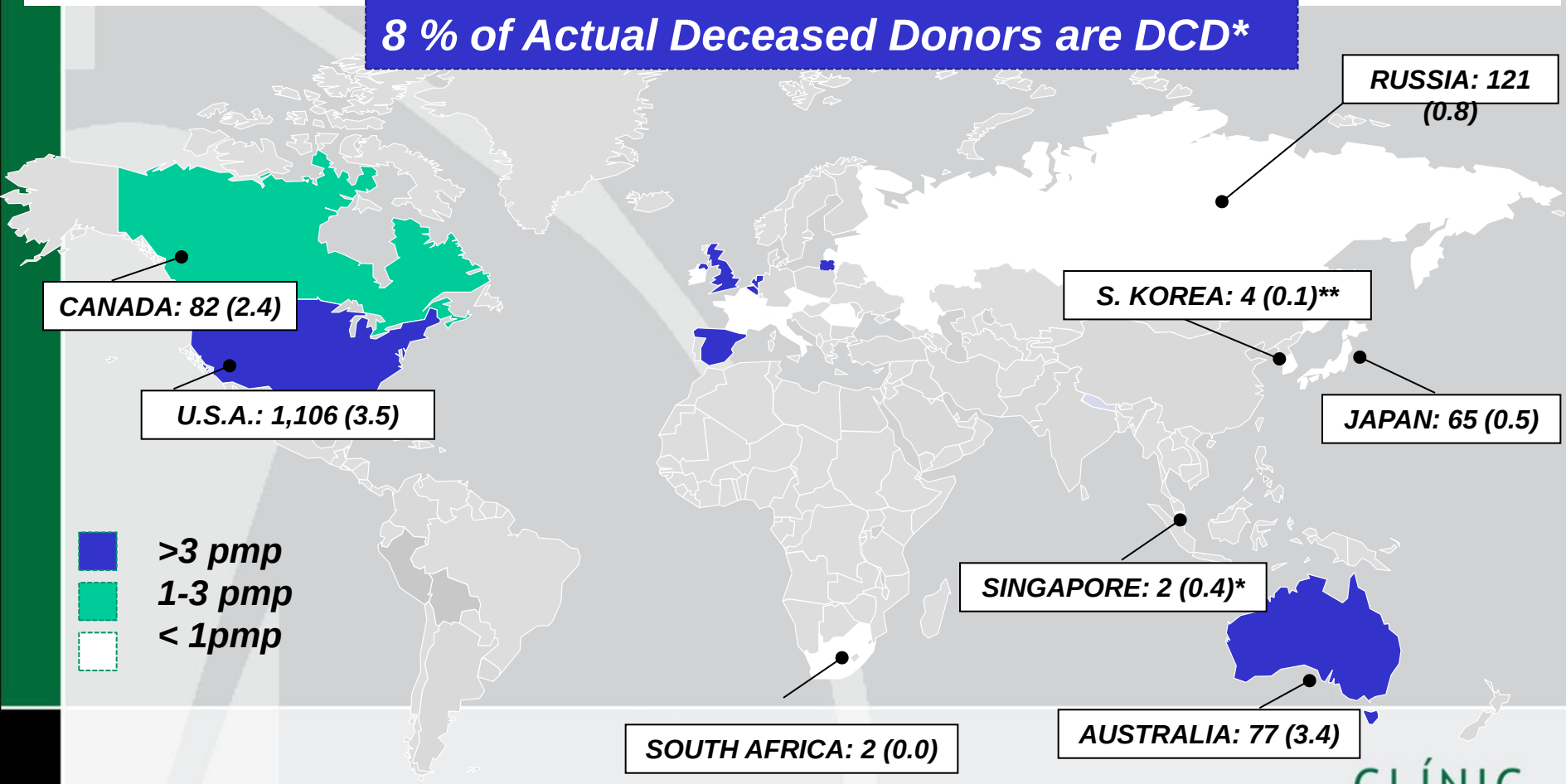
Actual DCD Donors *around the world*
Total number (pmp) - 2012

8 % of Actual Deceased Donors are DCD*



*2011 data; **2010 data

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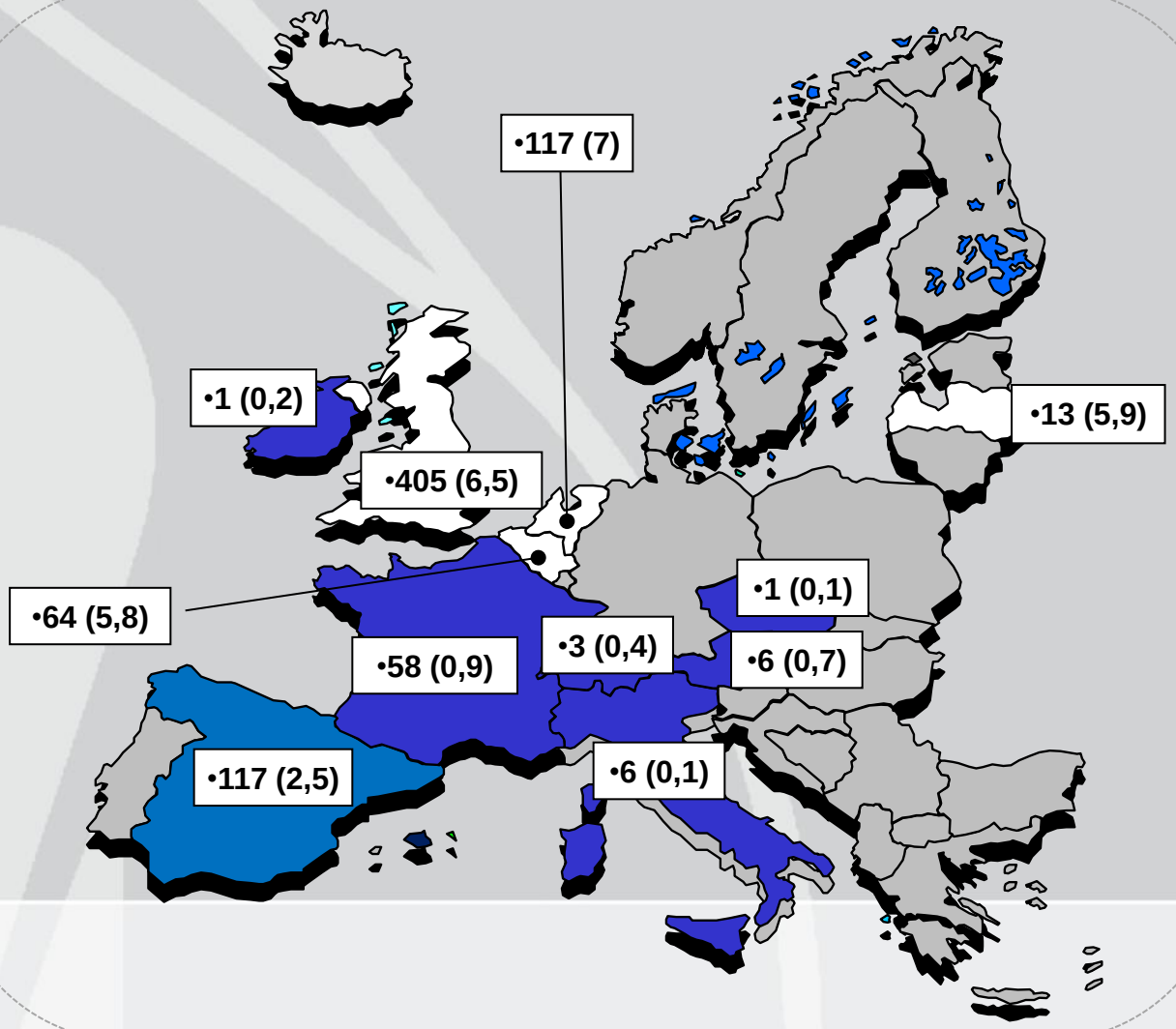
Europe: DCD Donation. Absolute pmp numbers 2011



- •>3 pmp
- •1-3 pmp
- •< 1pmp

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DBD changes in European Countries 2009 vs 2000

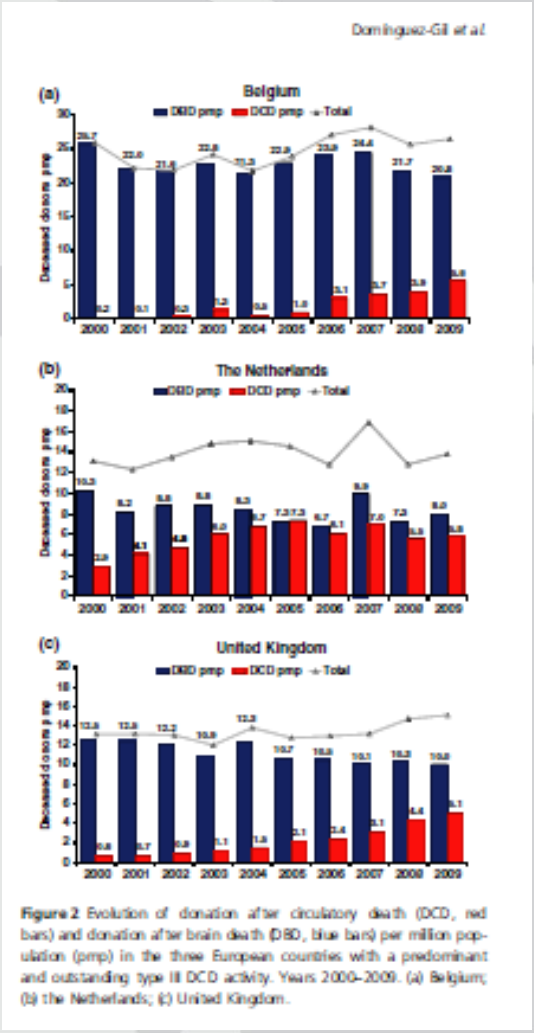
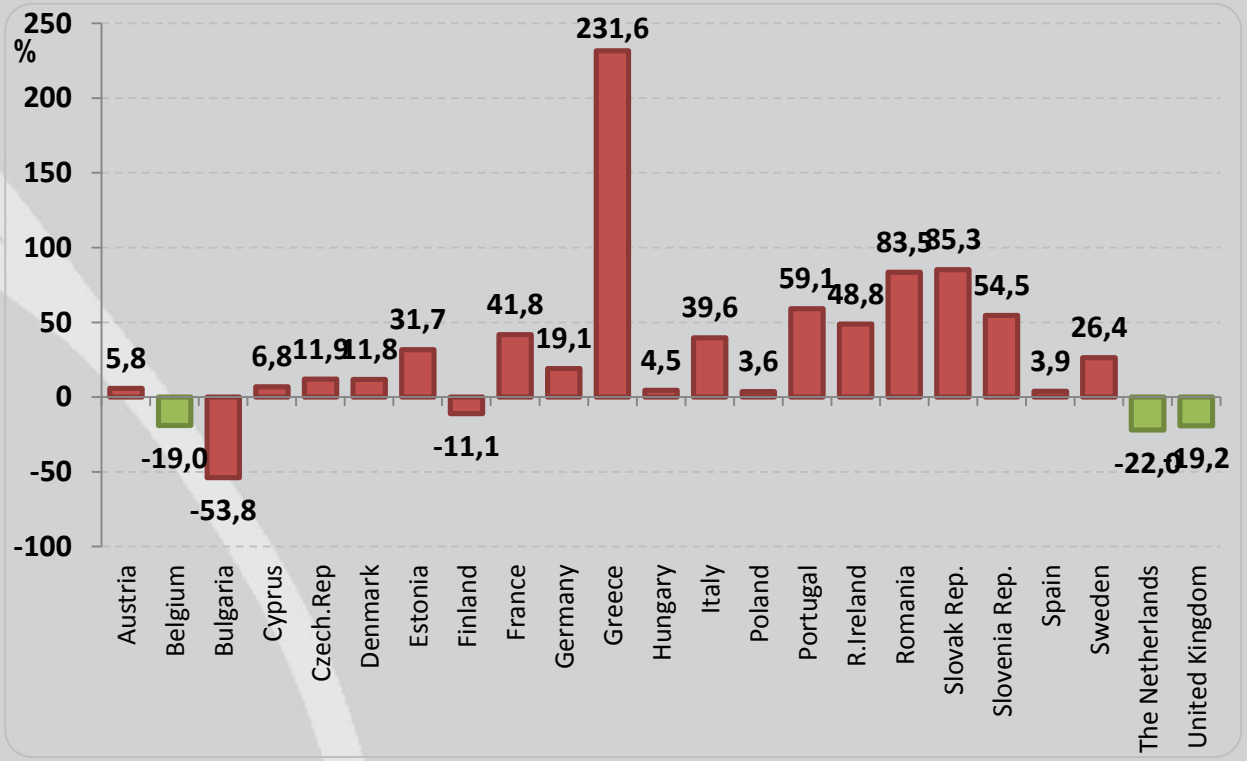


Figure 2 Evolution of donation after circulatory death (DCD, red bars) and donation after brain death (DBD, blue bars) per million population (pmp) in the three European countries with a predominant and outstanding type III DCD activity. Years 2000–2009. (a) Belgium; (b) the Netherlands; (c) United Kingdom.



Domínguez-Gil et al. Transplant Int 2011

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Deceased donors in Spain (DBD + DCD)

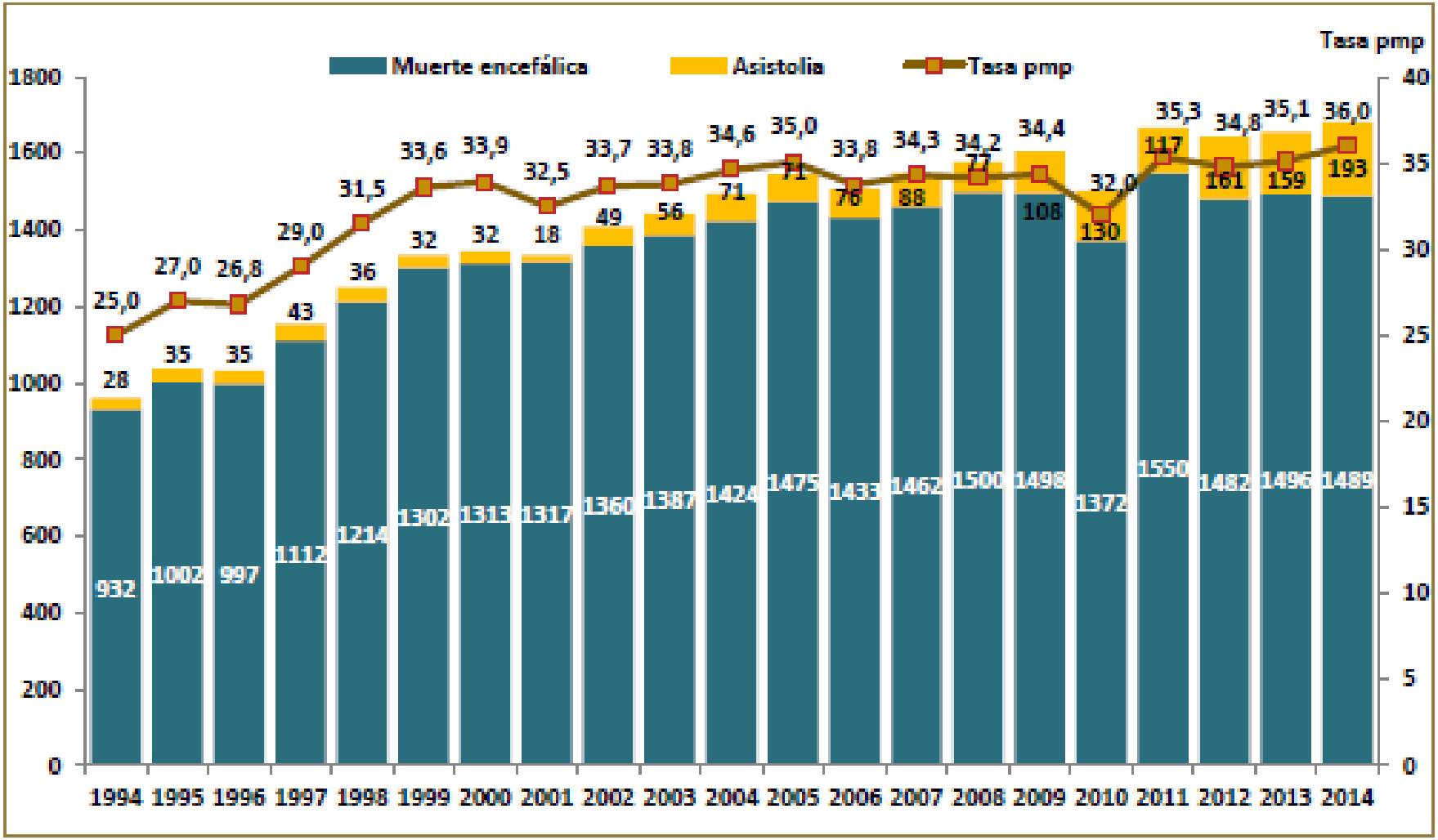

Figura 2.11. Porcentaje de donantes en asistolia sobre el total de donantes. España 1994-2014.

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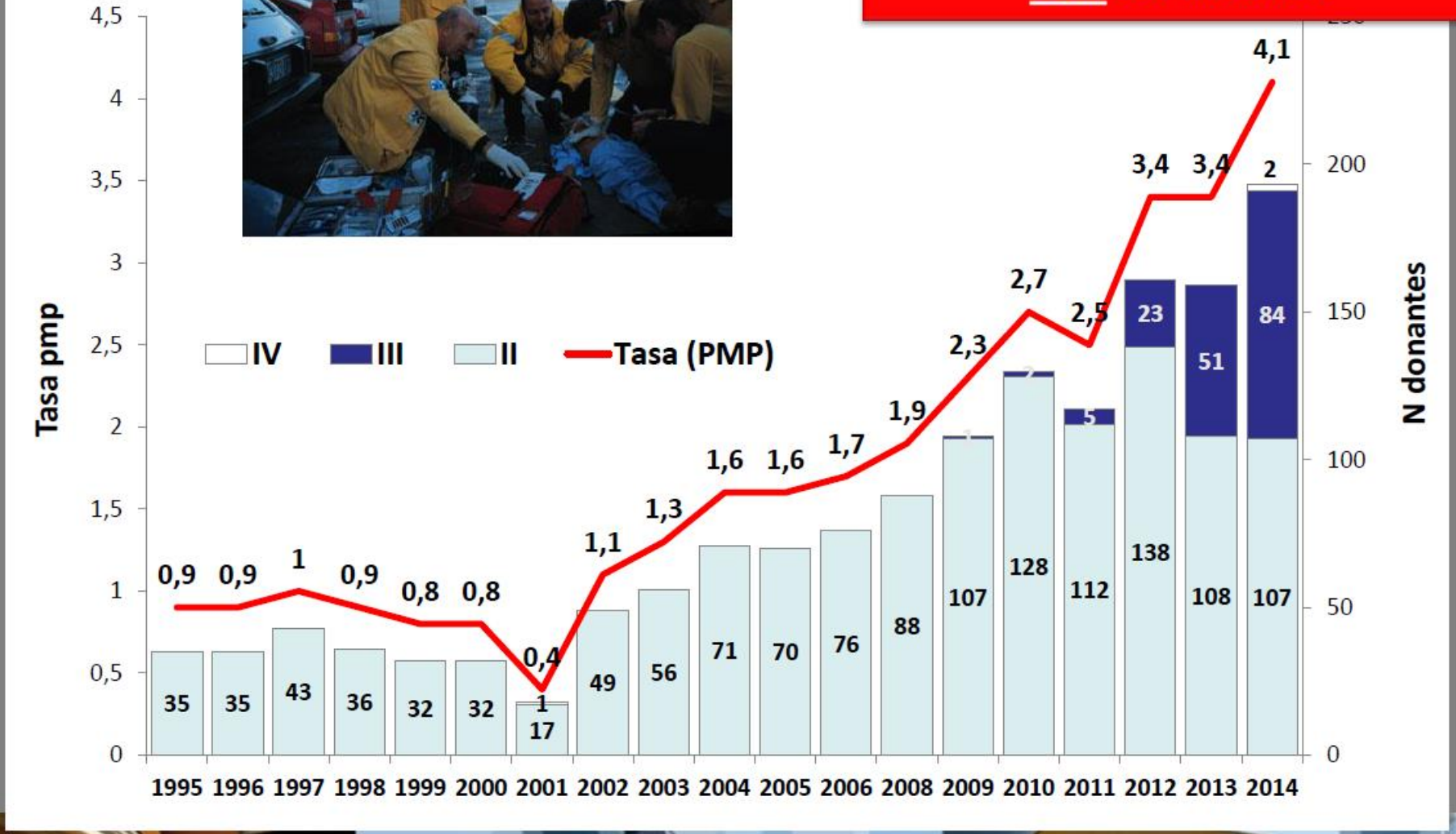
ONT

DONANTES EN PARADA CIRCULATORIA

11,5 % DE LOS DONANTES

32% EN MADRID



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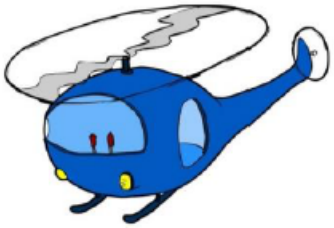
MINISTERIO DE SANIDAD, SERVICIOS SOCIALES E IGUALDAD
ONT

PROGRAMAS ESPAÑA DCD 2014

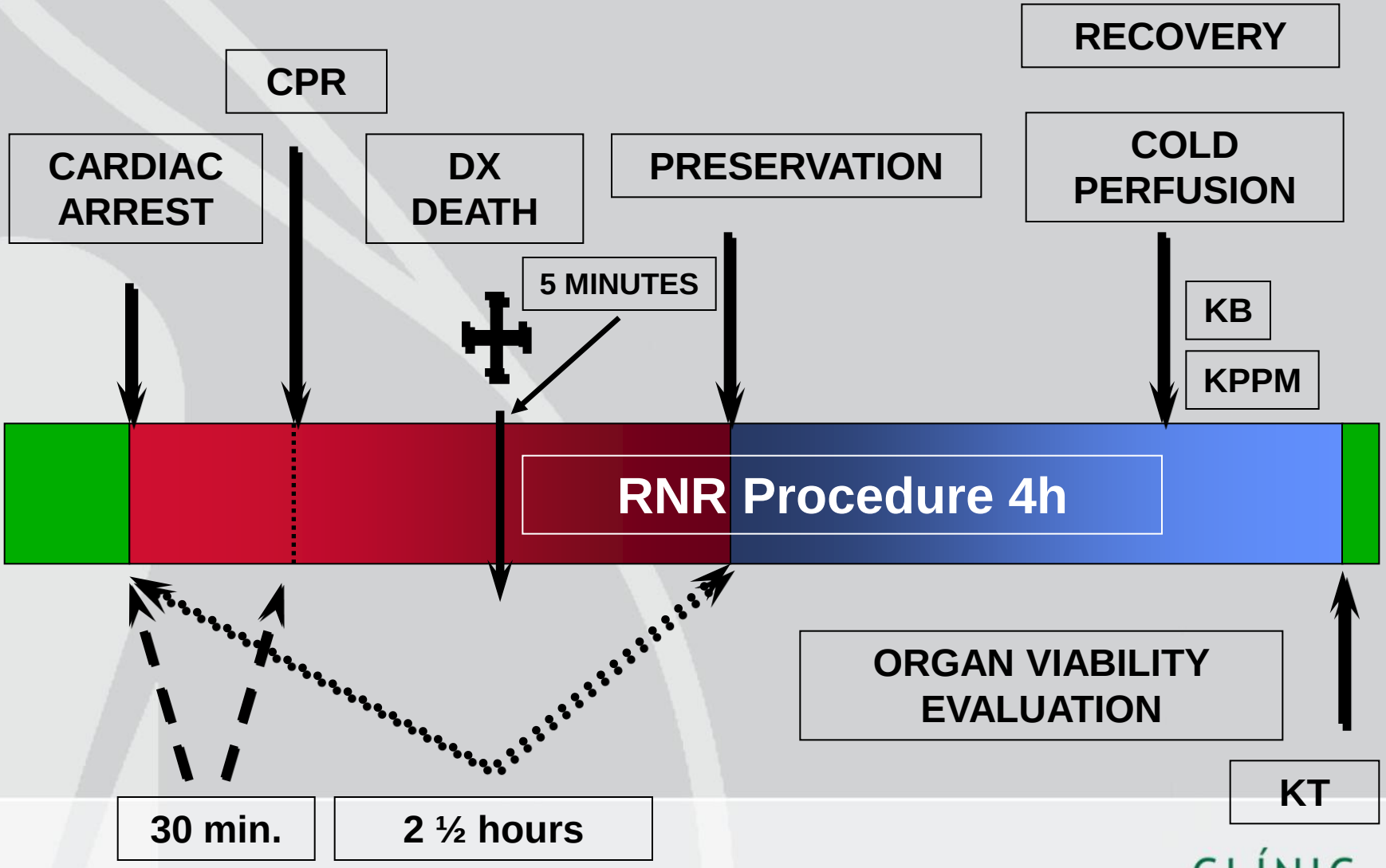


II
III
II + III

1
1
2
1
1
1
4
1
2
3
1
1
2
1
2
1
10
3
2

39 programas en 13 CCAA
12 DCD-II / 39 DCD-III

DONORS AFTER CARDIAC DEATH TYPE II



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Donantes a Corazón Parado. Ciudad de Barcelona.

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MÉTODOS DE DETECCIÓN

- Código 3.03

- Coordinación de Trasplantes
- Urgencias HCB

OCATT
Organització Catalana de Trasplantaments

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MÉTODOS DE DETECCIÓN

- BUSCA DE PAROS (EQUIPO Nº1)

- UNIDADES DE CUIDADOS INTENSIVOS
- AREA DE REANIMACIÓN

Donantes a Corazón Parado. PCR – RCP – Código 3.03

EVALUACIÓN
CRITERIOS DE ACTIVACIÓN
PROTOCOLO DCP
(COORDINADORES DE TRASPLANTES)

SÍ ← → **NO**

ACTIVACIÓN PROTOCOLO DCP

DESACTIVACIÓN PROTOCOLO DCP

ACTIVACIÓN DEL EQUIPO DE DCP →

2 CIRUJANOS GENERALES
1 ENFERMERA QUIRÚRGICA
1 ENFERMERA URGENCIAS

TRASLADO AL ÁREA DE CANULACIÓN

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Donors after Cardiac Death. Normothermic Recirculation (RNR)

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RCPa &
DIAGNÓSTICO DE MUERTE

PRESERVACIÓN DE LOS ÓRGANOS

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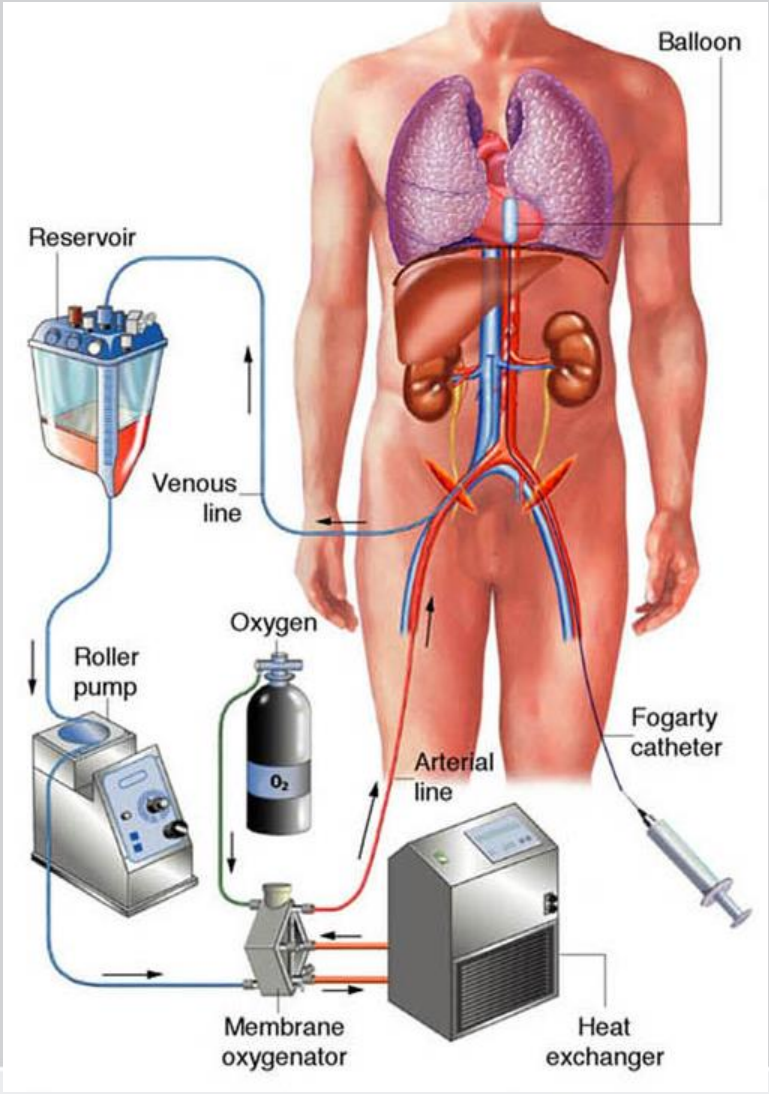
Donors after Cardiac Death. Normothermic Recirculation

- Normothermic Recirculation 1-4h (6h) with a pump maintenance > 1.2-1.7 L/m^2
- Continuous gasometric and ionic control (30 min)
- Biochemical renal & hepatic control
- Hemoglobin control
- Re-heparinization (1,5 mg/kg/90min)



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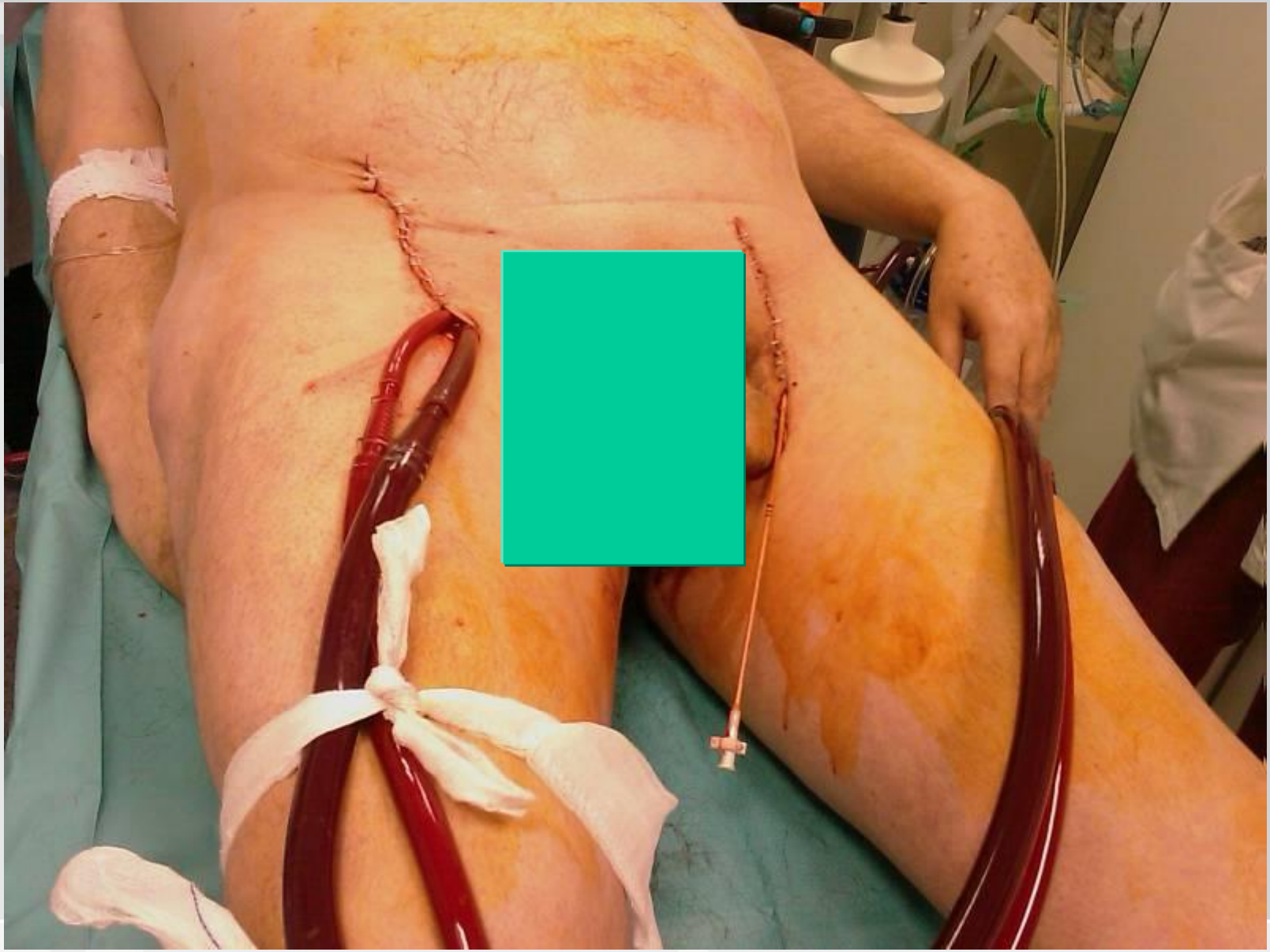

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2. During NRP

Evaluate Thorax X-Ray: Fogarty placement, lung and heart

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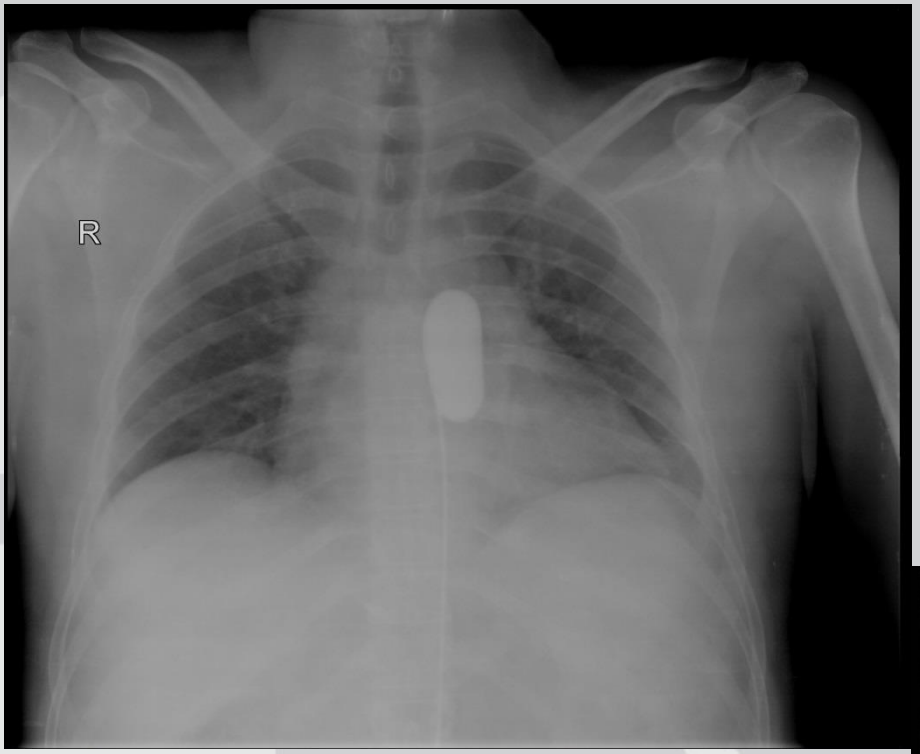

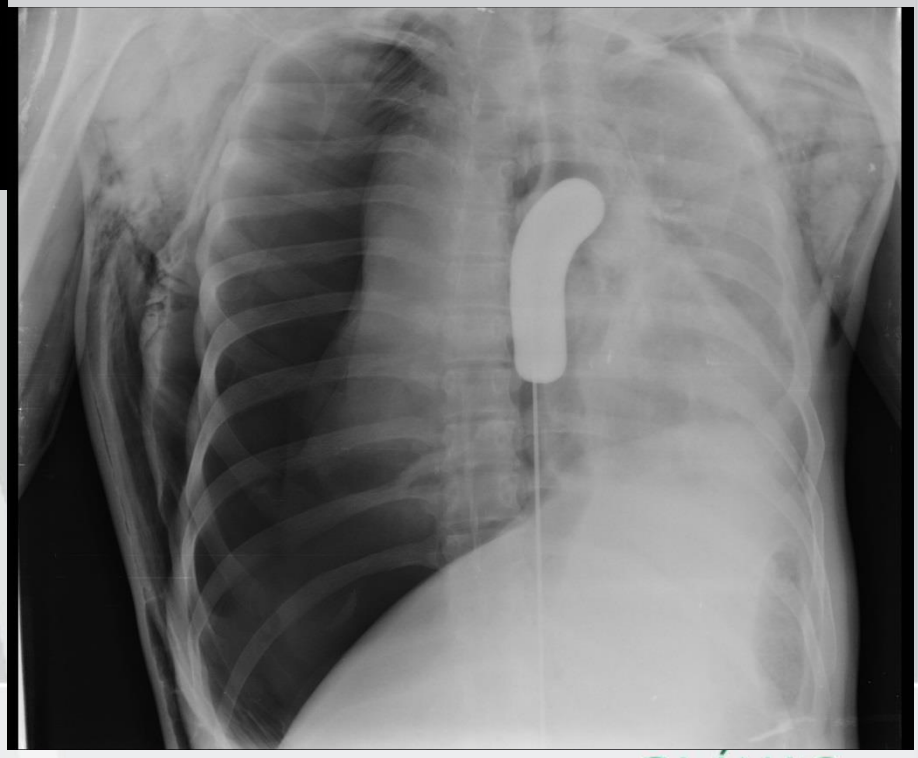

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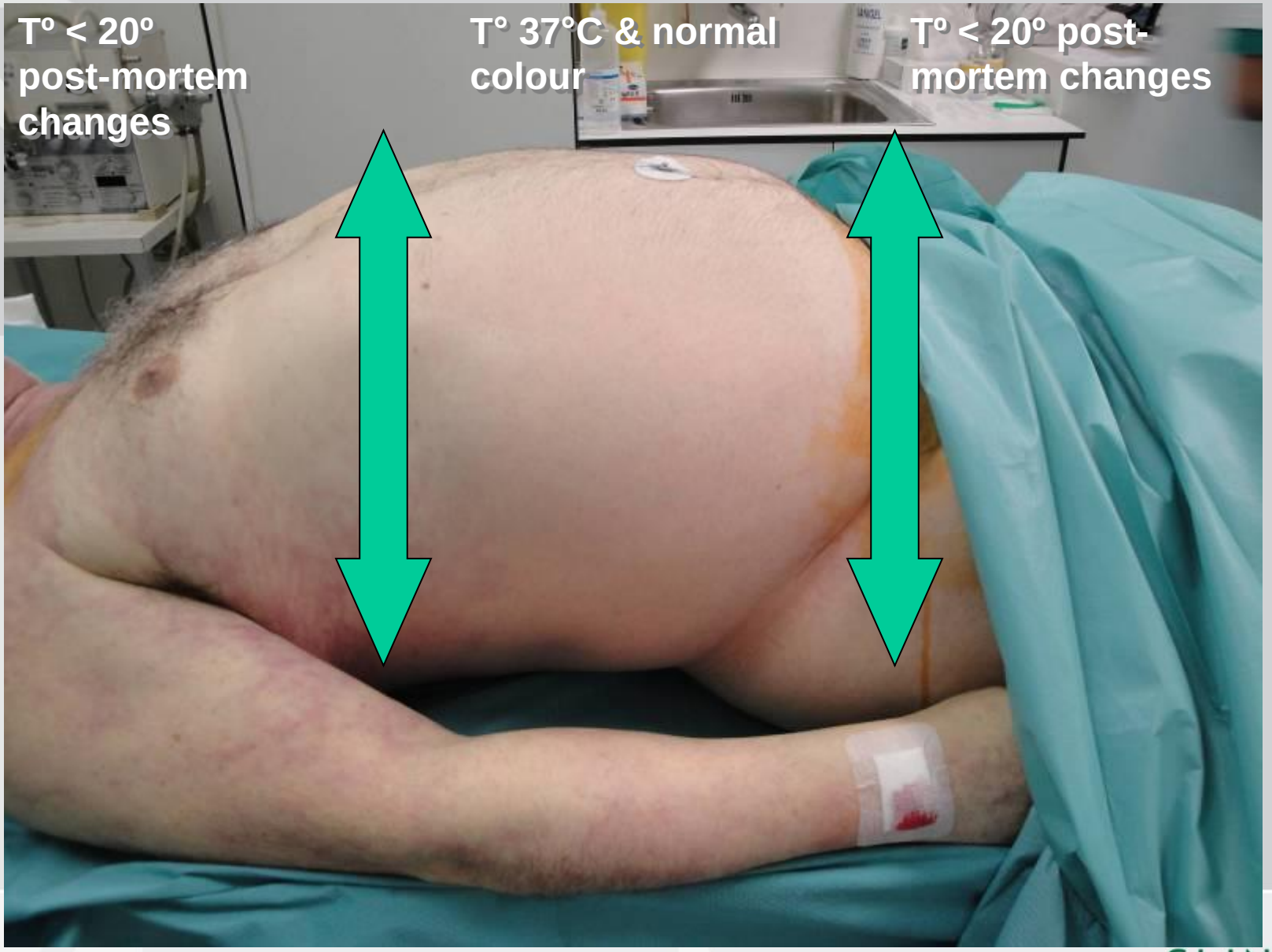

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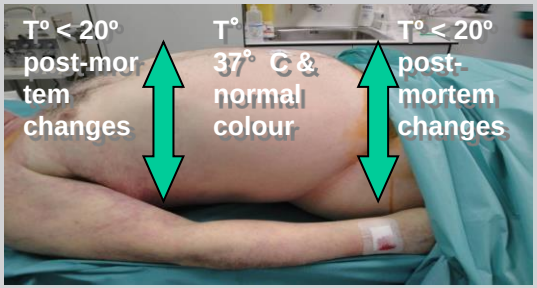
2. During NRP

Biochemical and hemodynamic goals:



- Blood temperature 37ºC
- Blood ph: 7.35 – 7.45 & Blood PaO2: 100-150 mmHg

- Haematocrit level > 20%

- Pump flow > 1.5-1.7 L/m^2

- Venous return, reservoir filling > 600 ml
  - Replace with Colloids vs crystalloids

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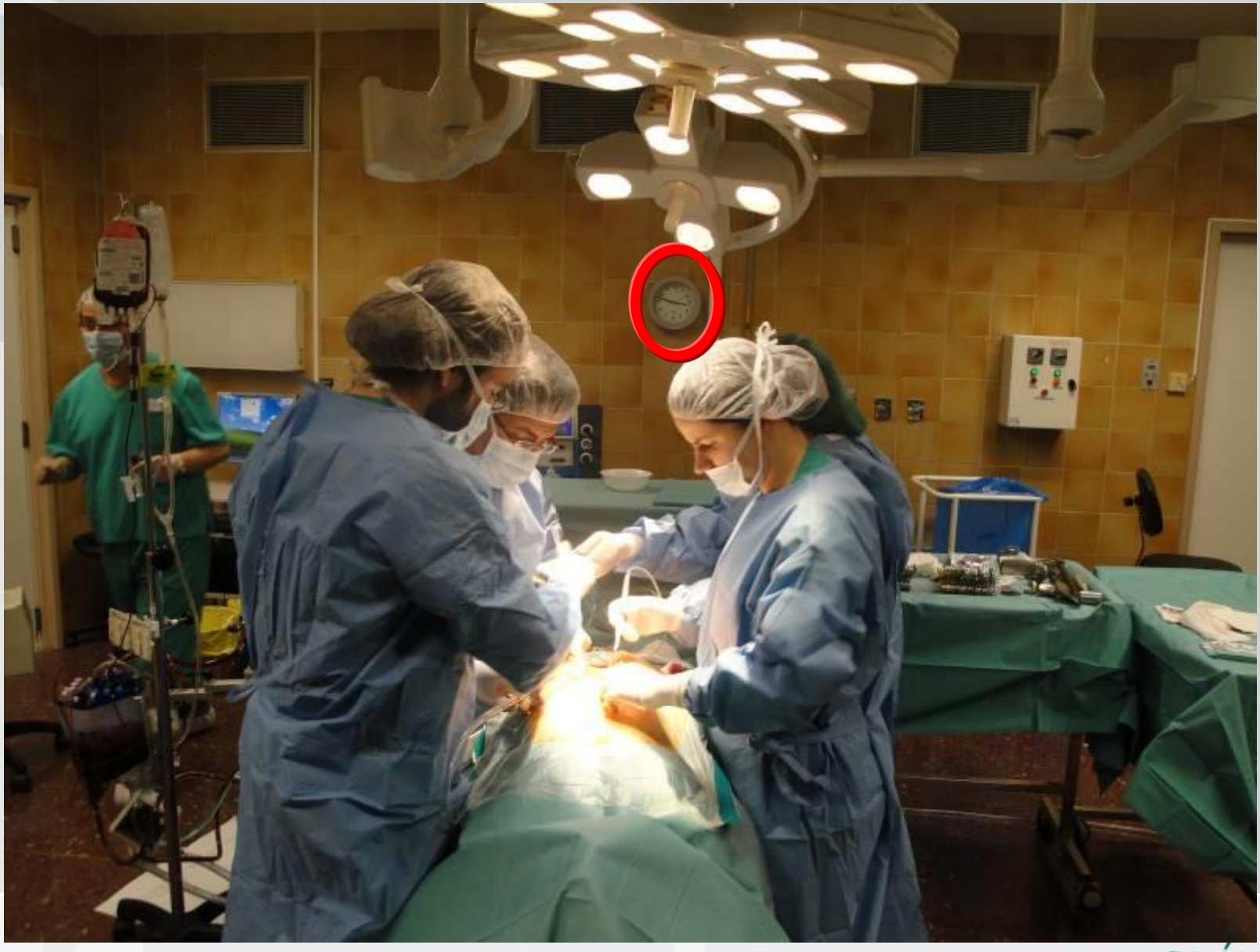

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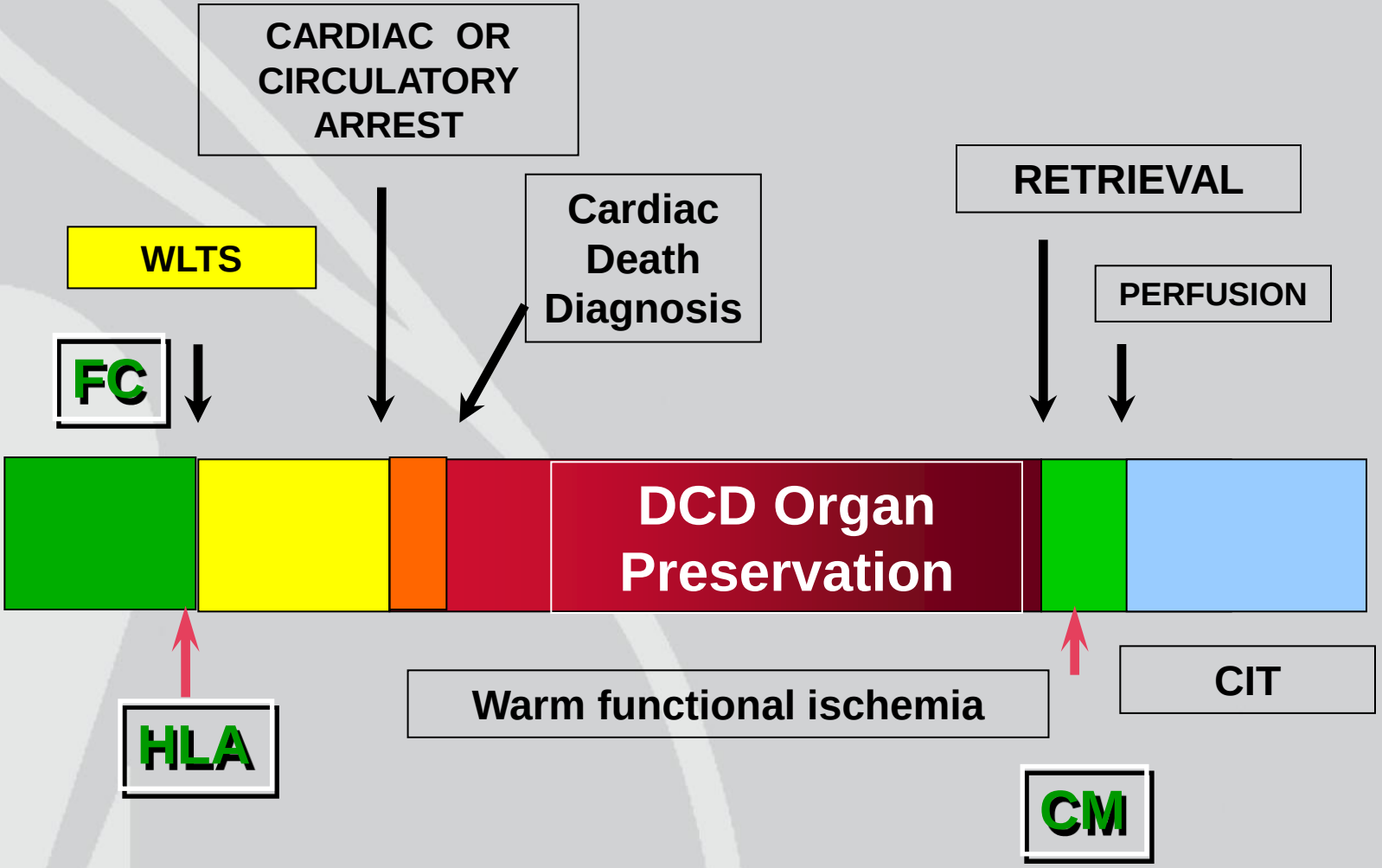
DONORS AFTER CARDIAC DEATH TYPE III + NRP



PROCEDIMIENTO DE LTSV – Hospital Clinic

- Protocolo hospitalario de LTSV. (Diferente en DAC)
- Sedoanalgesia según práctica habitual, dosis necesarias para evitar sufrimiento del paciente
- Evitar administración de relajantes musculares
- No extubación completa para evitar broncoaspiraciones
- Registro de hora de:
    - Inicio LTSV
    - Inicio Tiempo Isquemia verdadera
    - Diagnóstico de muerte

- Lugar de Realización: UCI
- Equipo médico asistencial

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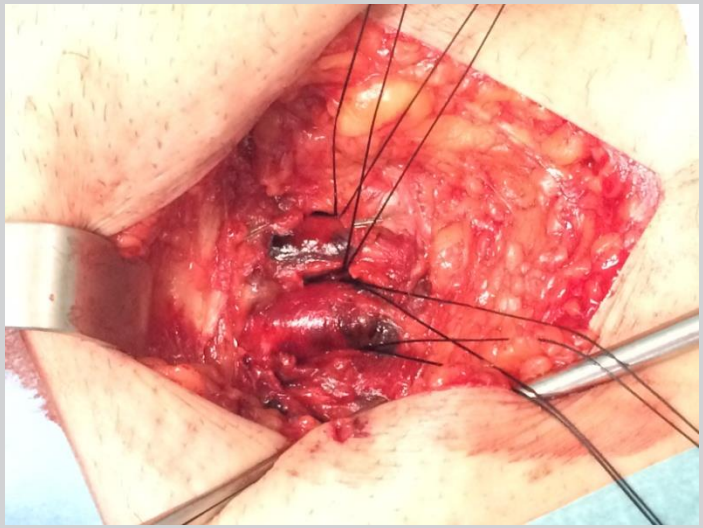

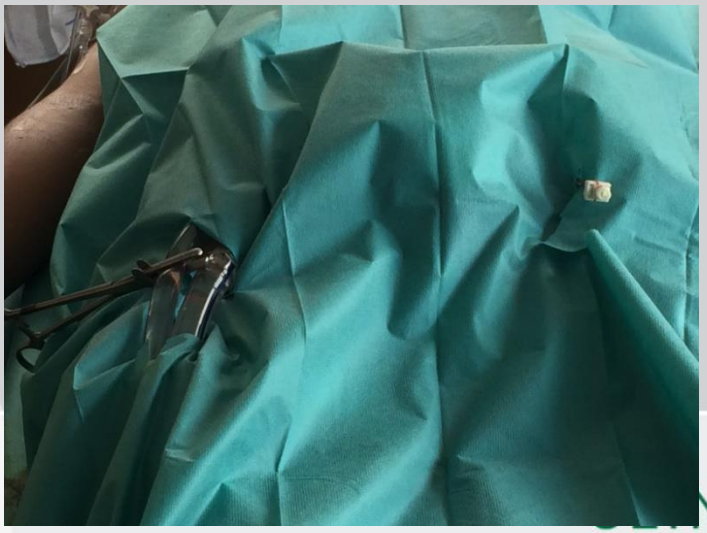

DIAGNÓSTICO DE MUERTE

c) La ausencia de circulación se demostrará mediante la presencia de al menos uno de los siguientes hallazgos:

1.º Asistolia en un trazado electrocardiográfico continuo.
2.º Ausencia de flujo sanguíneo en la monitorización invasiva de la presión arterial.
3.º Ausencia de flujo aórtico en un ecocardiograma.

Si así lo permiten los avances científicos y técnicos en la materia, podrá utilizarse cualquier otra prueba instrumental que acredite absoluta garantía diagnóstica.

Método de elección

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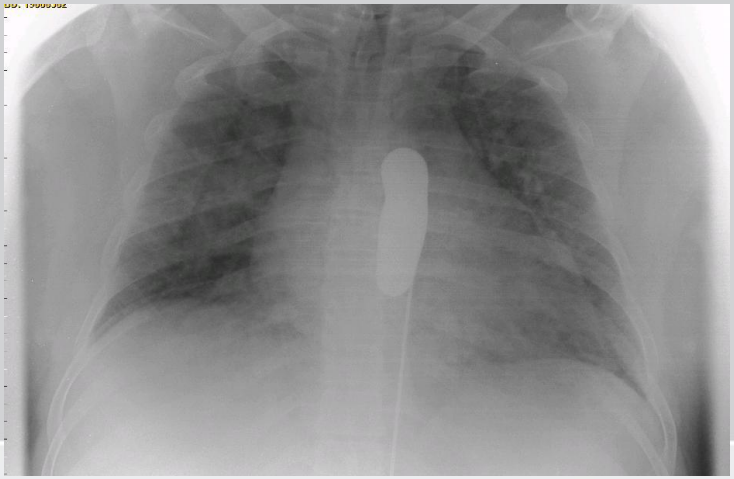
DONORS AFTER CARDIAC DEATH TYPE III + NRP



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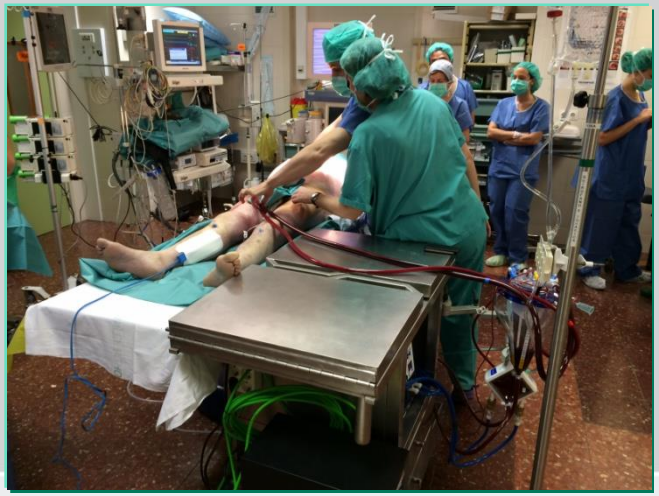
DONORS AFTER CARDIAC DEATH TYPE III + NRP



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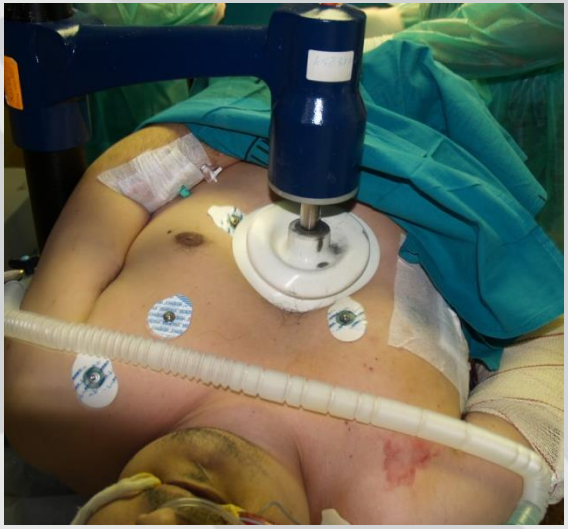
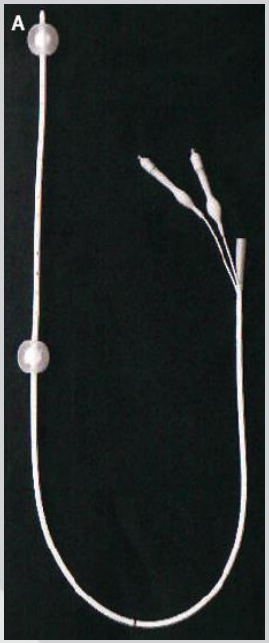
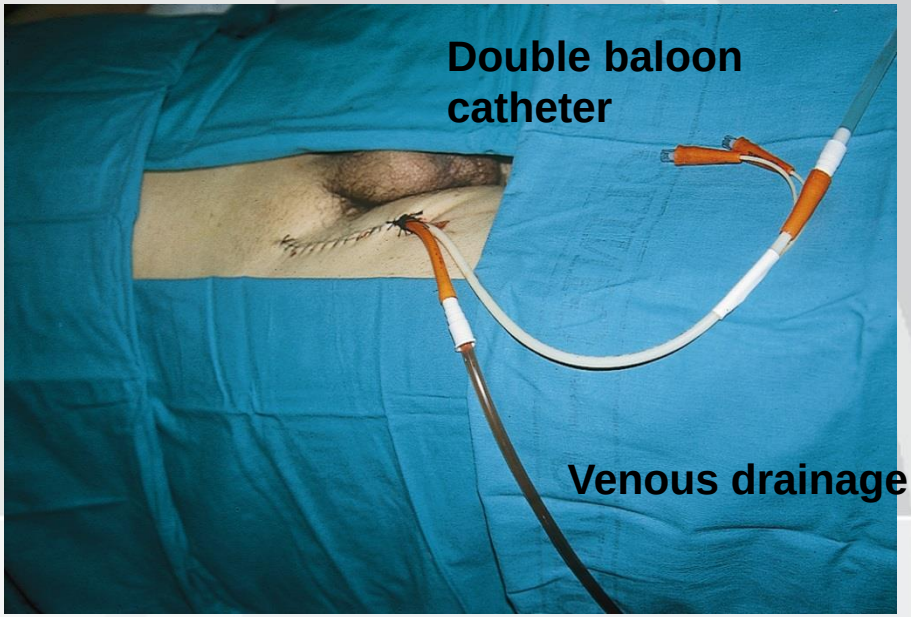
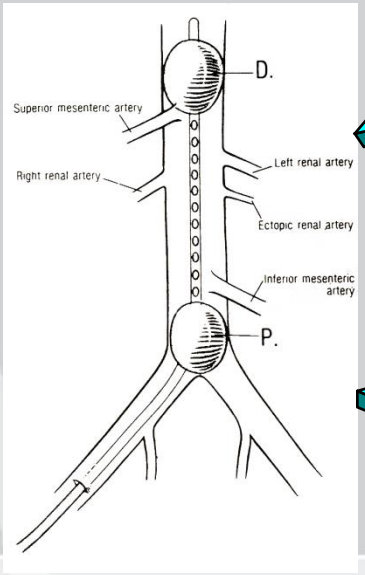
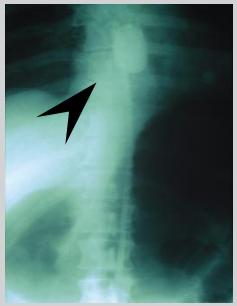
Técnicas Preservación Órganos
IN SITU PERFUSION











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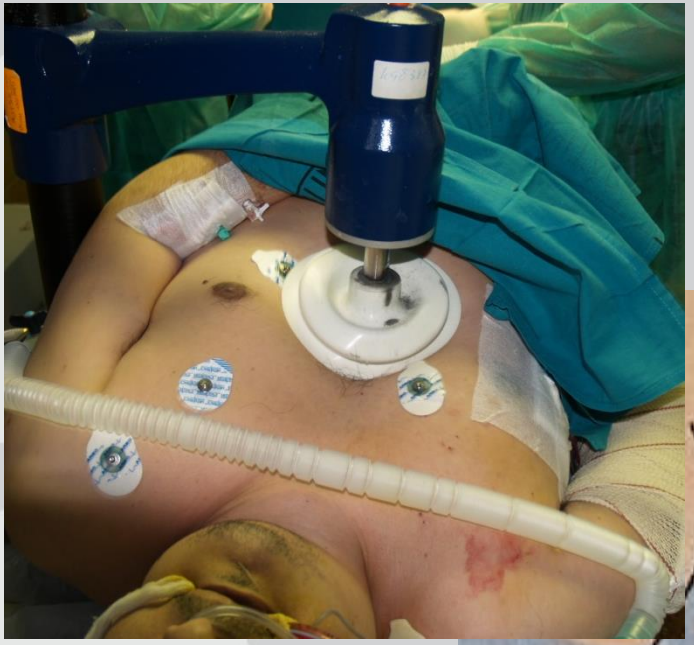
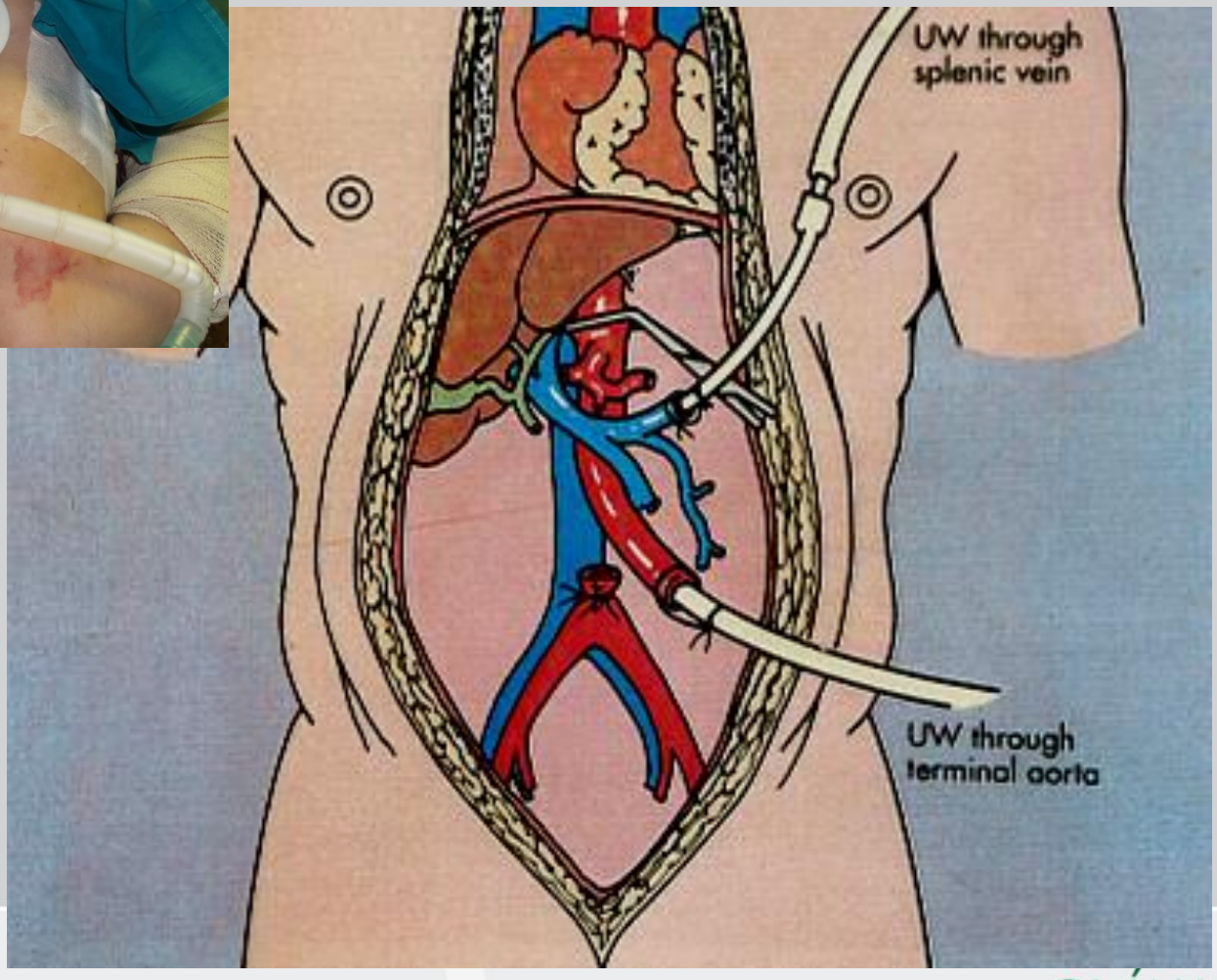
Técnicas Preservación Órganos
Super rapid retrieval





DONORS AFTER CARDIAC DEATH TYPE III + FAST ORGAN RETRIEVAL + In situ Perfusion

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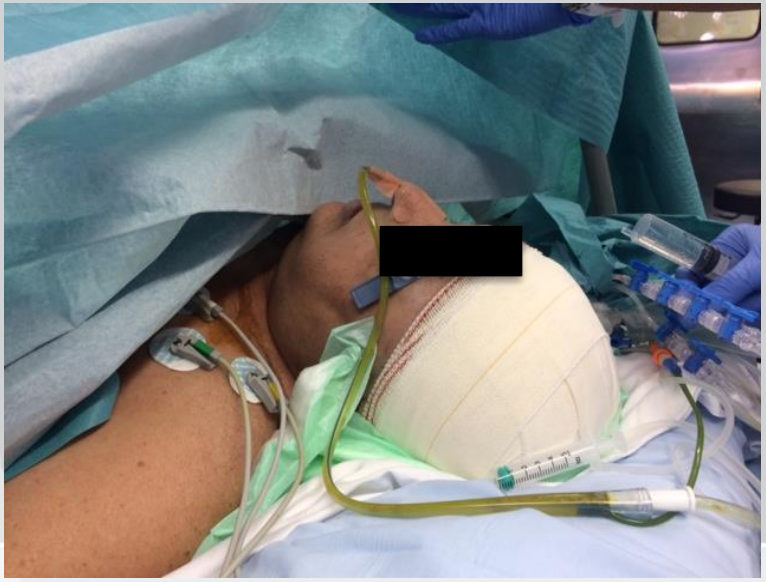

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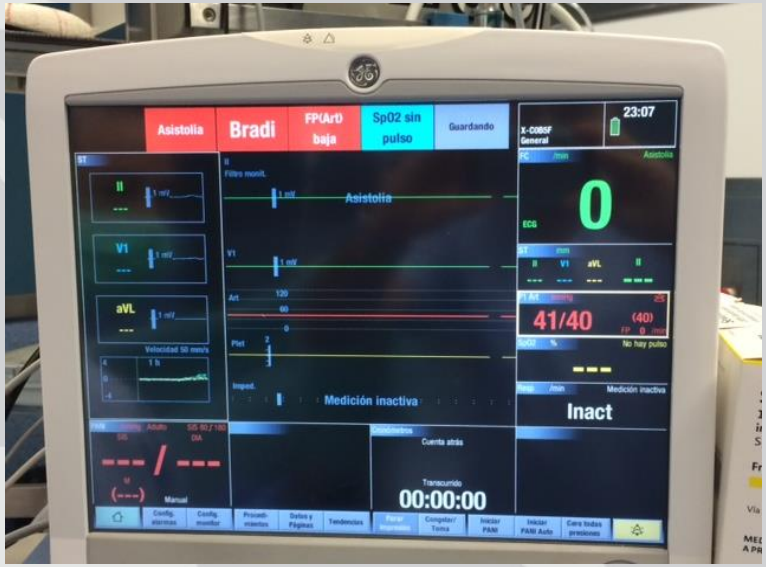

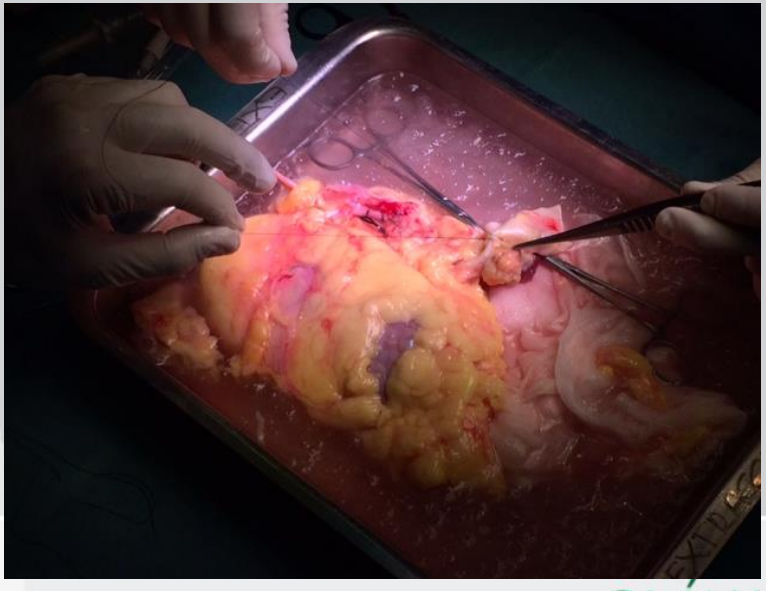

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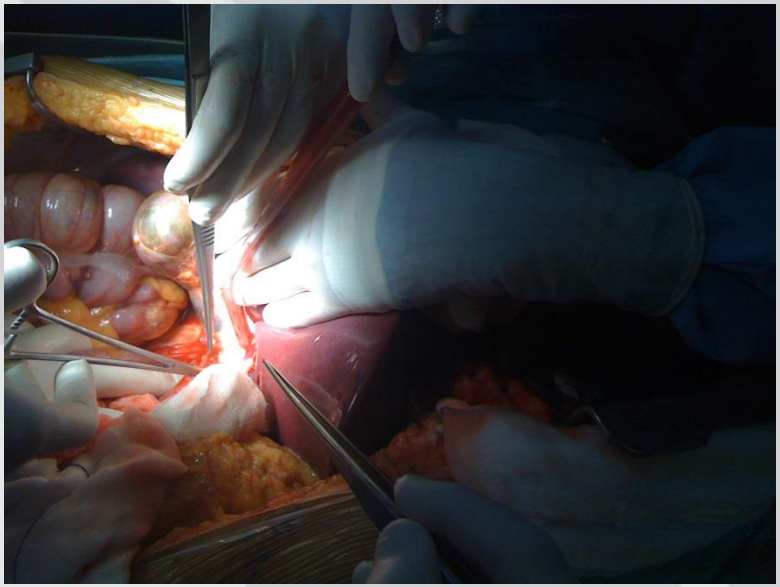
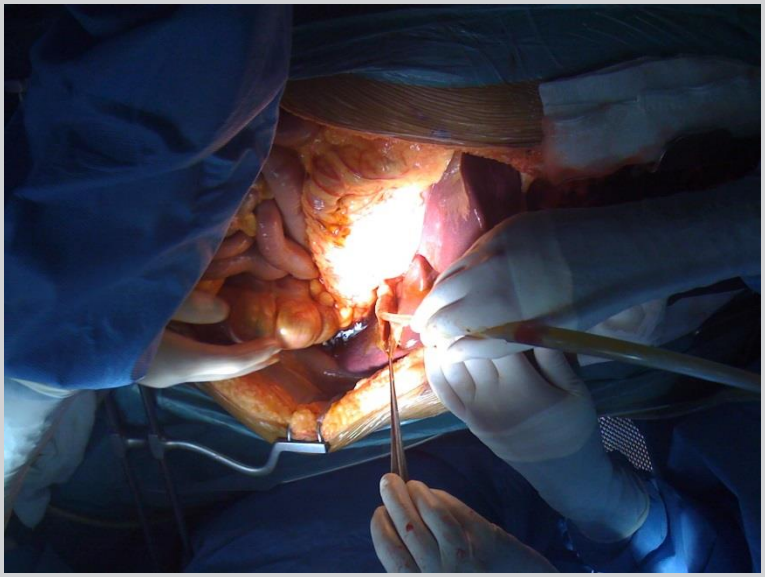
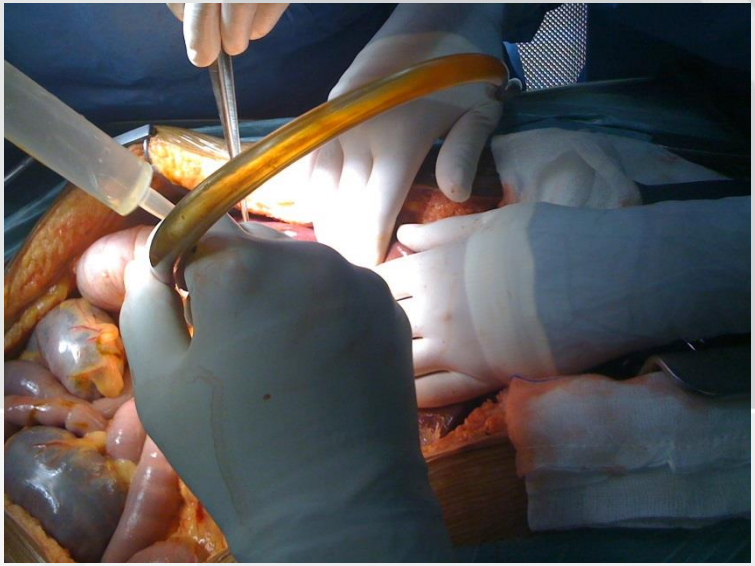
3. During organ retrieval

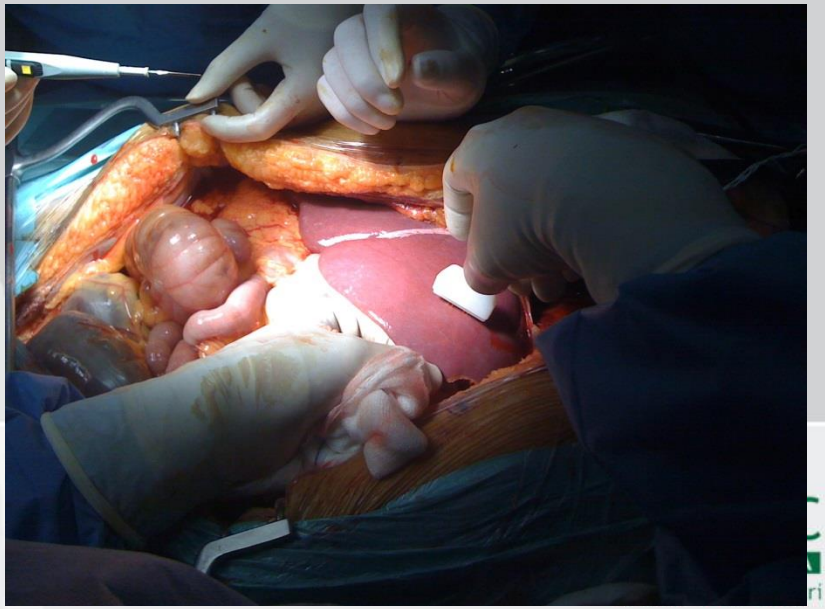
Explore abdominal cavity (if coroner permission: chest)
In case of trauma evaluate integrity
Macroscopic organ evaluation
Vascular evaluation
Rule-out incidental tumors, infections, bowel necrosis
Lymph nodes & spleen (CM typing)

ORGAN MACROSCOPIC EVALUATION

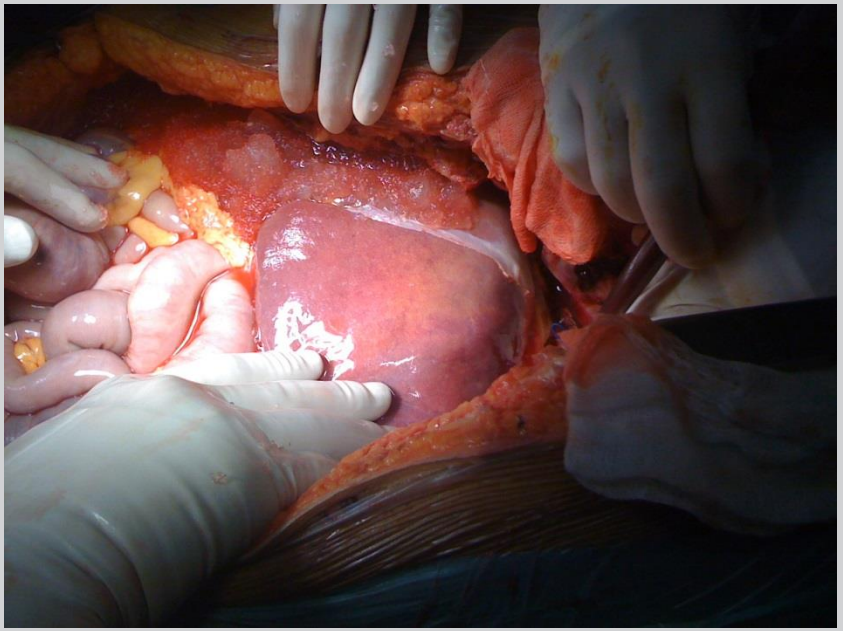


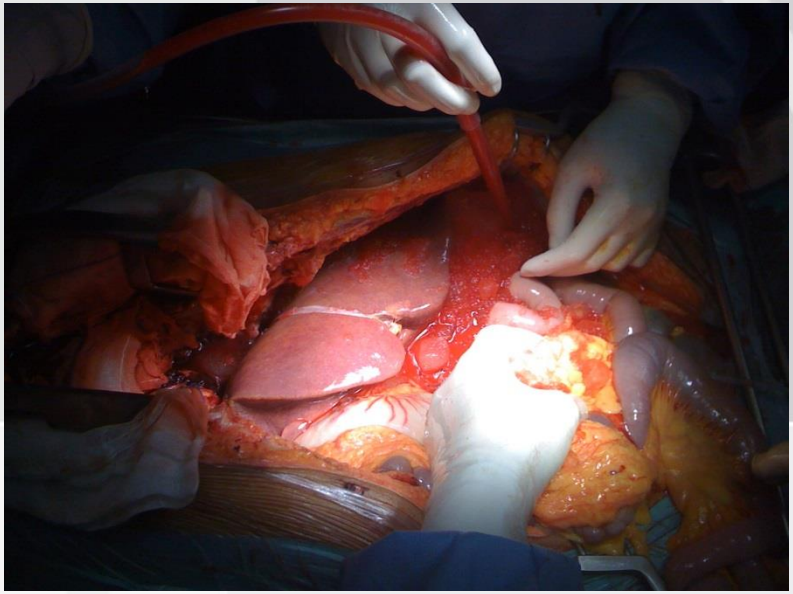


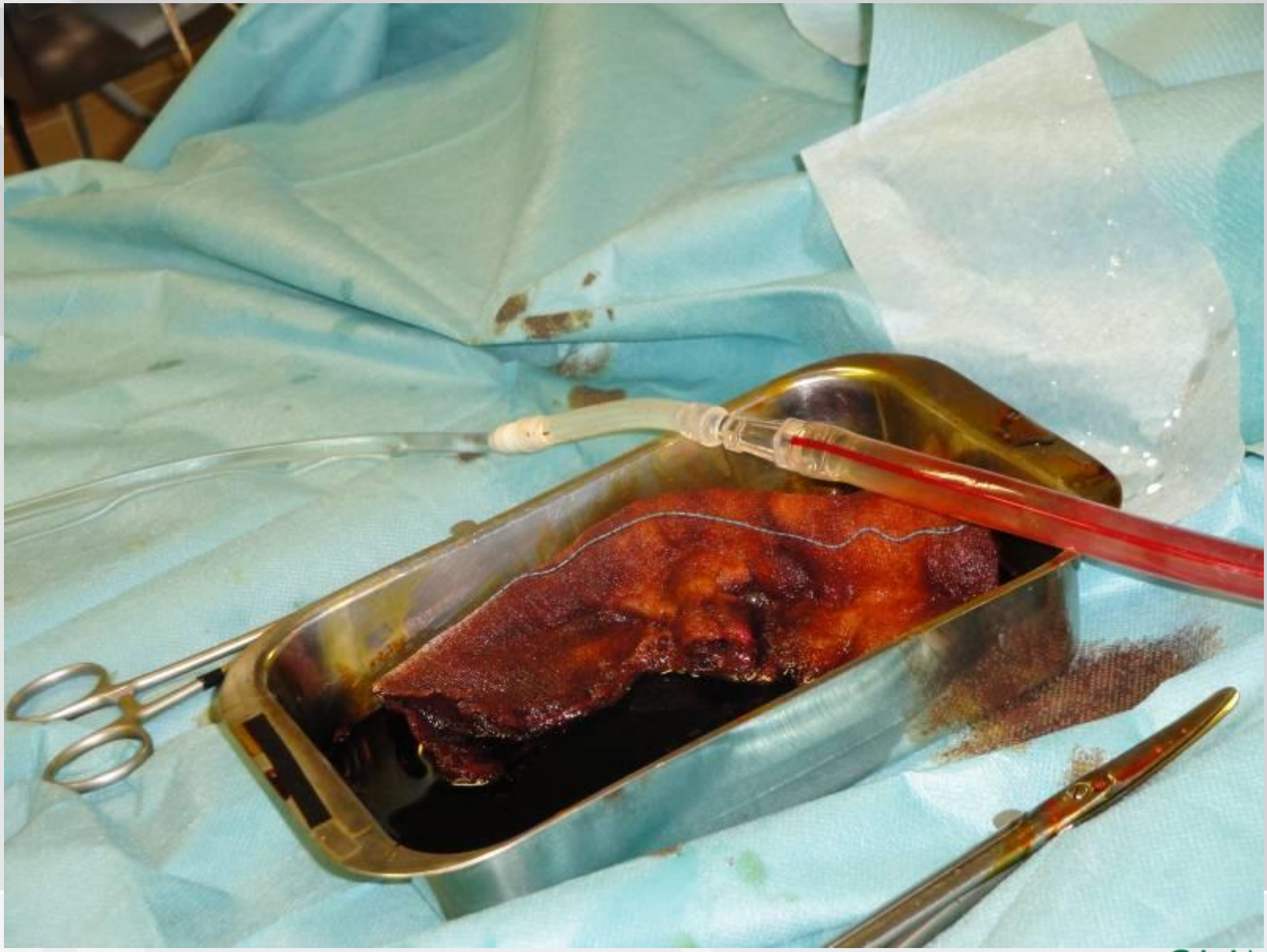


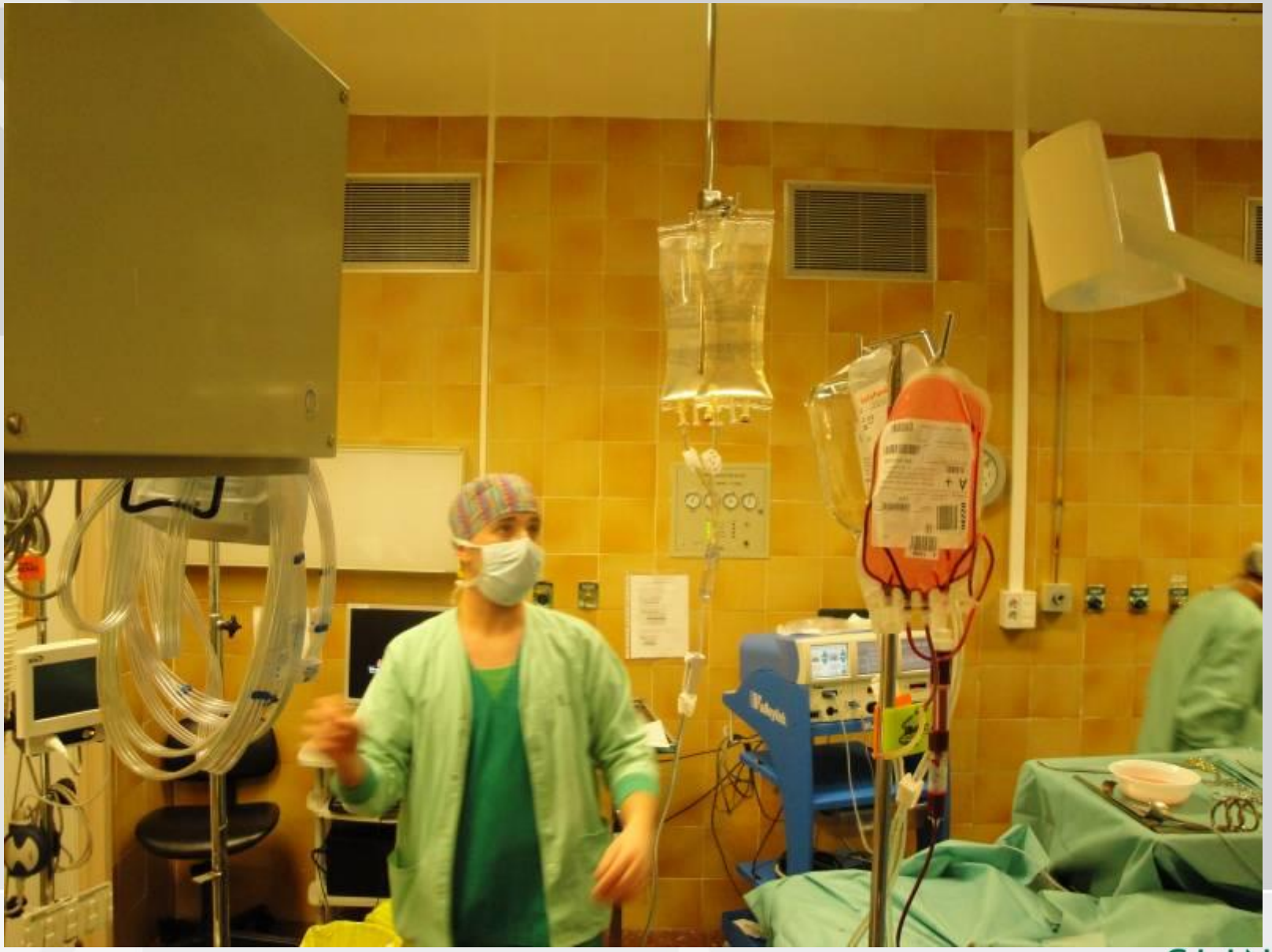


ORGAN MACROSCOPIC EVALUATION









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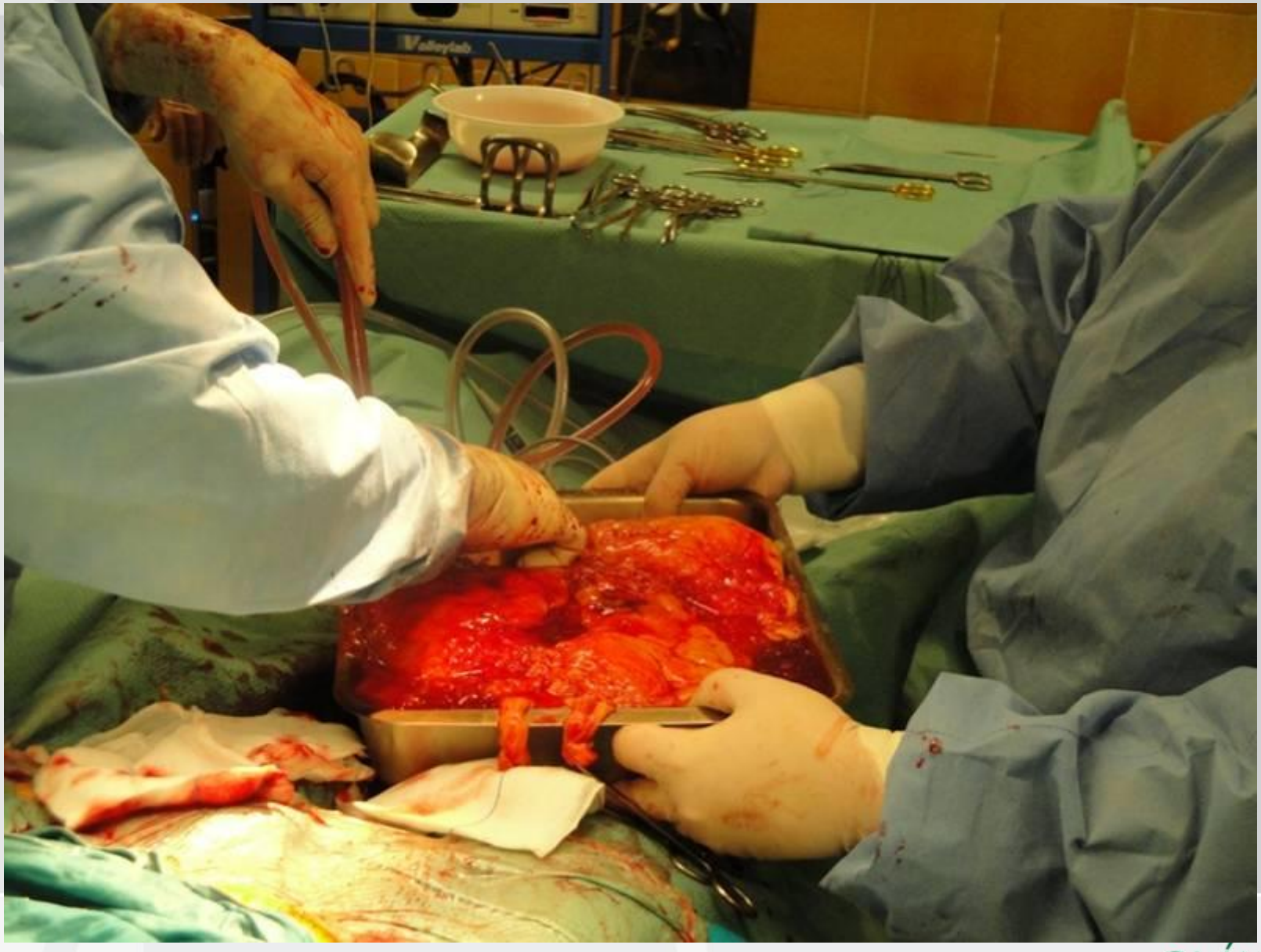

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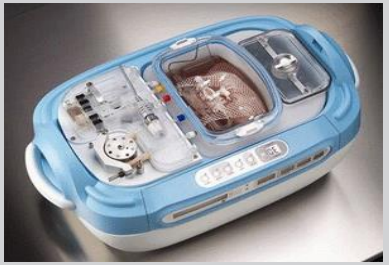
4. Post retrieval

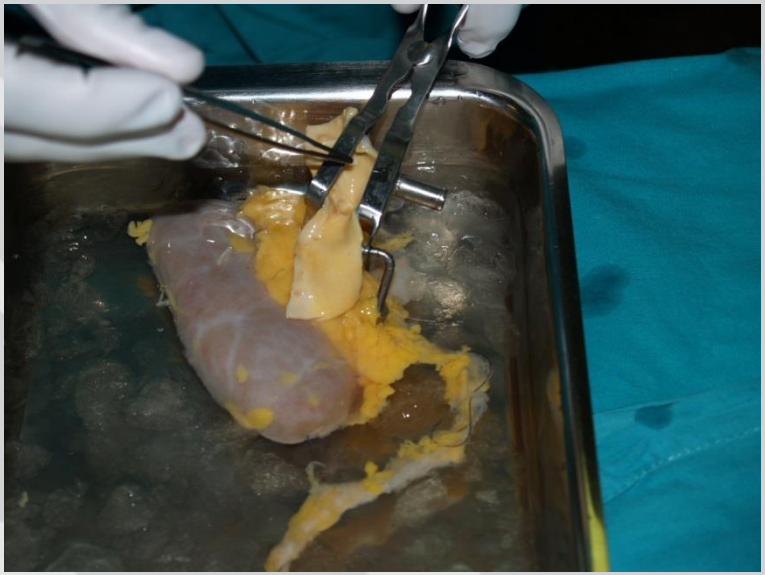
RM3 (Waters IGL)

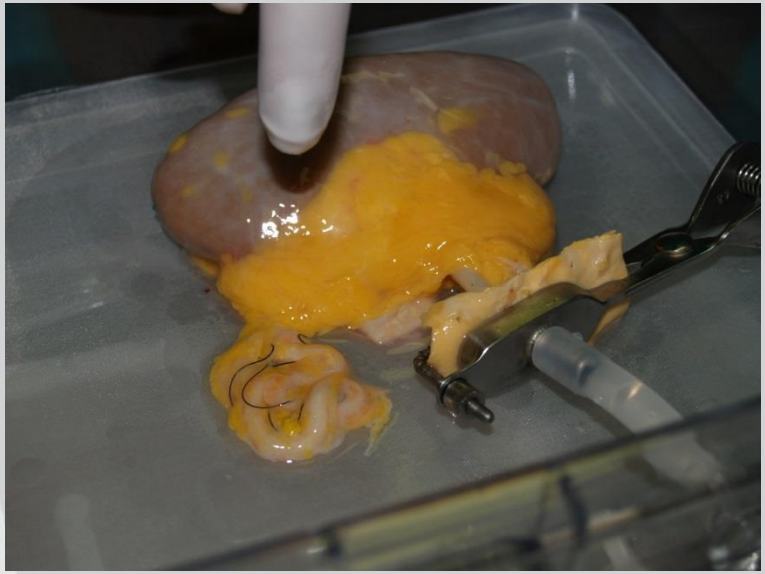


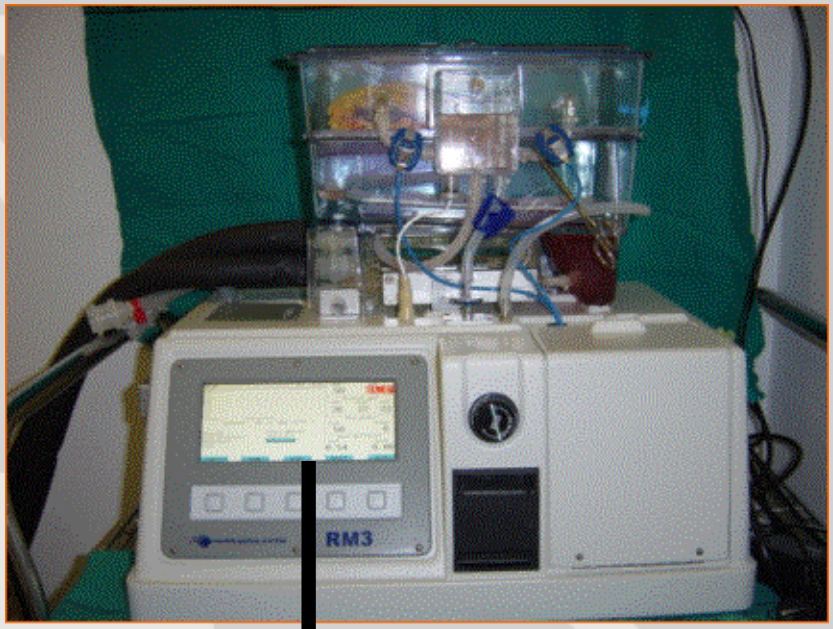
Lifeport (ORS)

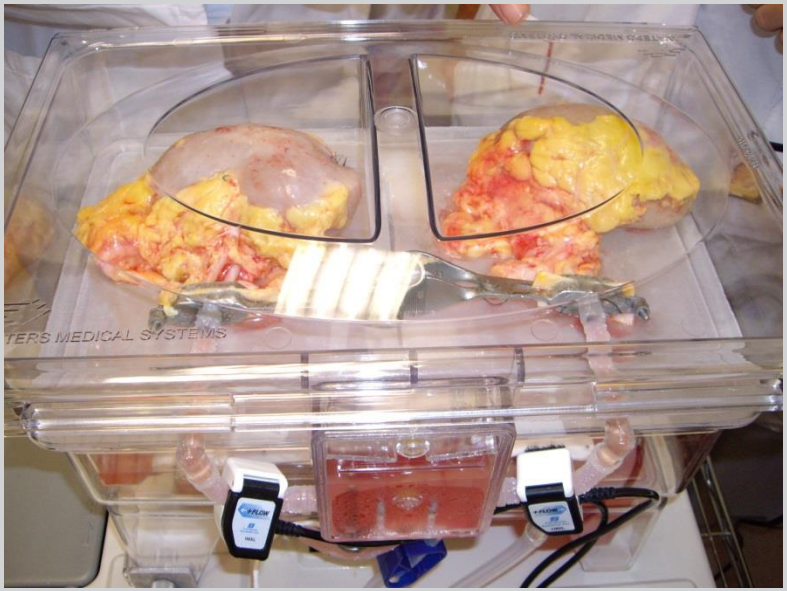
Kidney – liver biopsy
Ex-situ machine perfusion: kidney – liver

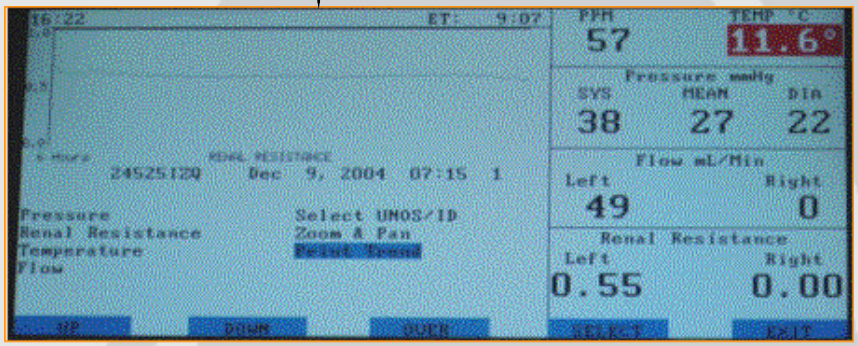
Necropsy or Autopsy: Clinical or Coroner diagnostic to confirm cause of death
Blood cultures
Post-retrieval blood serology

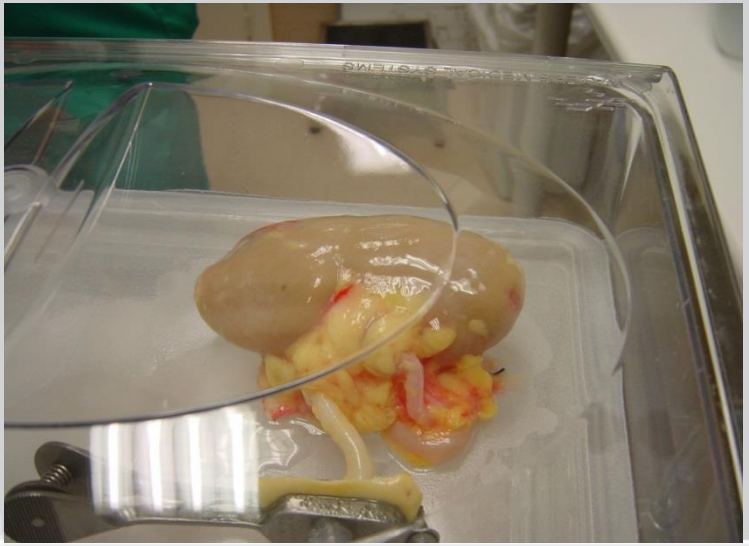












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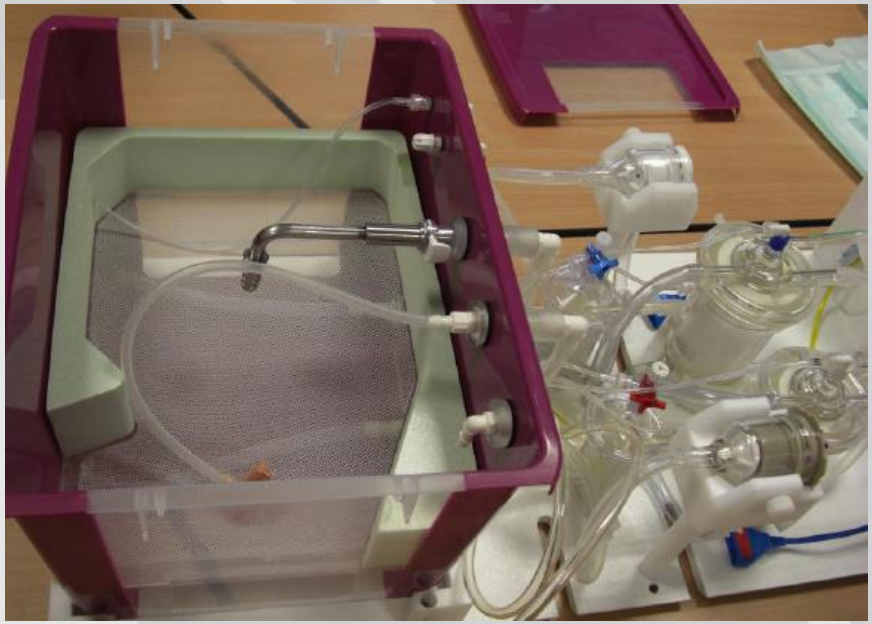
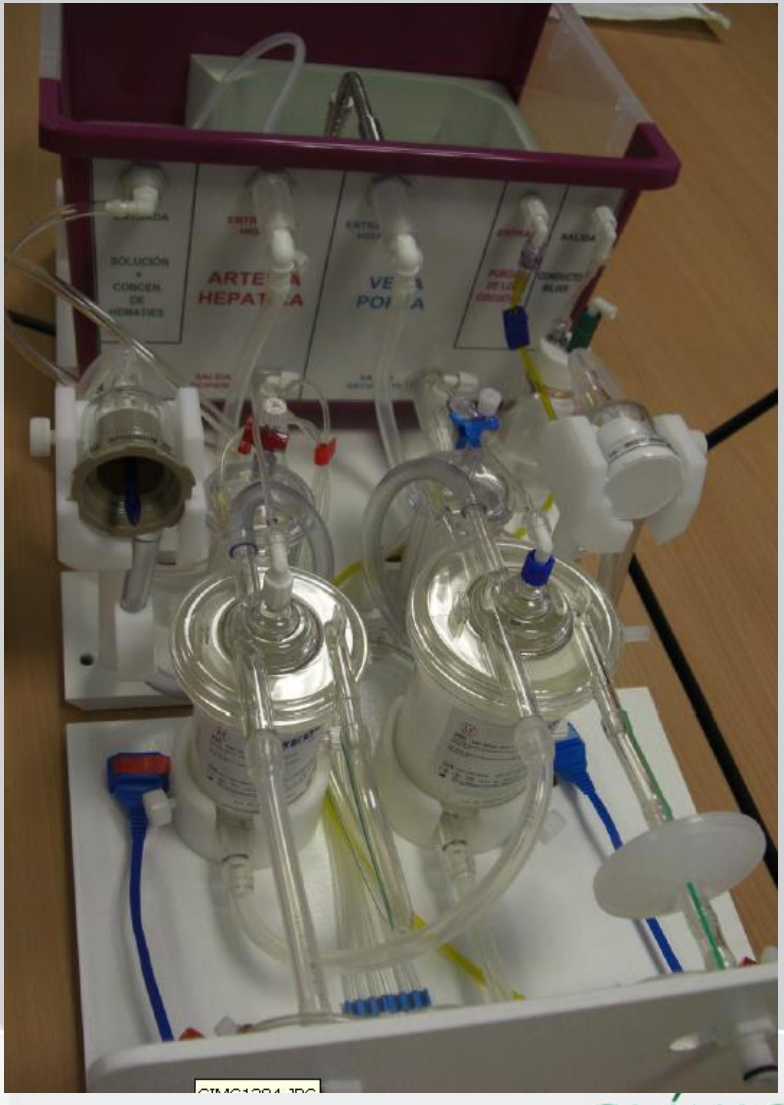
BARCELONA NMP MODEL

BARCELONA LIVER NMP MODEL





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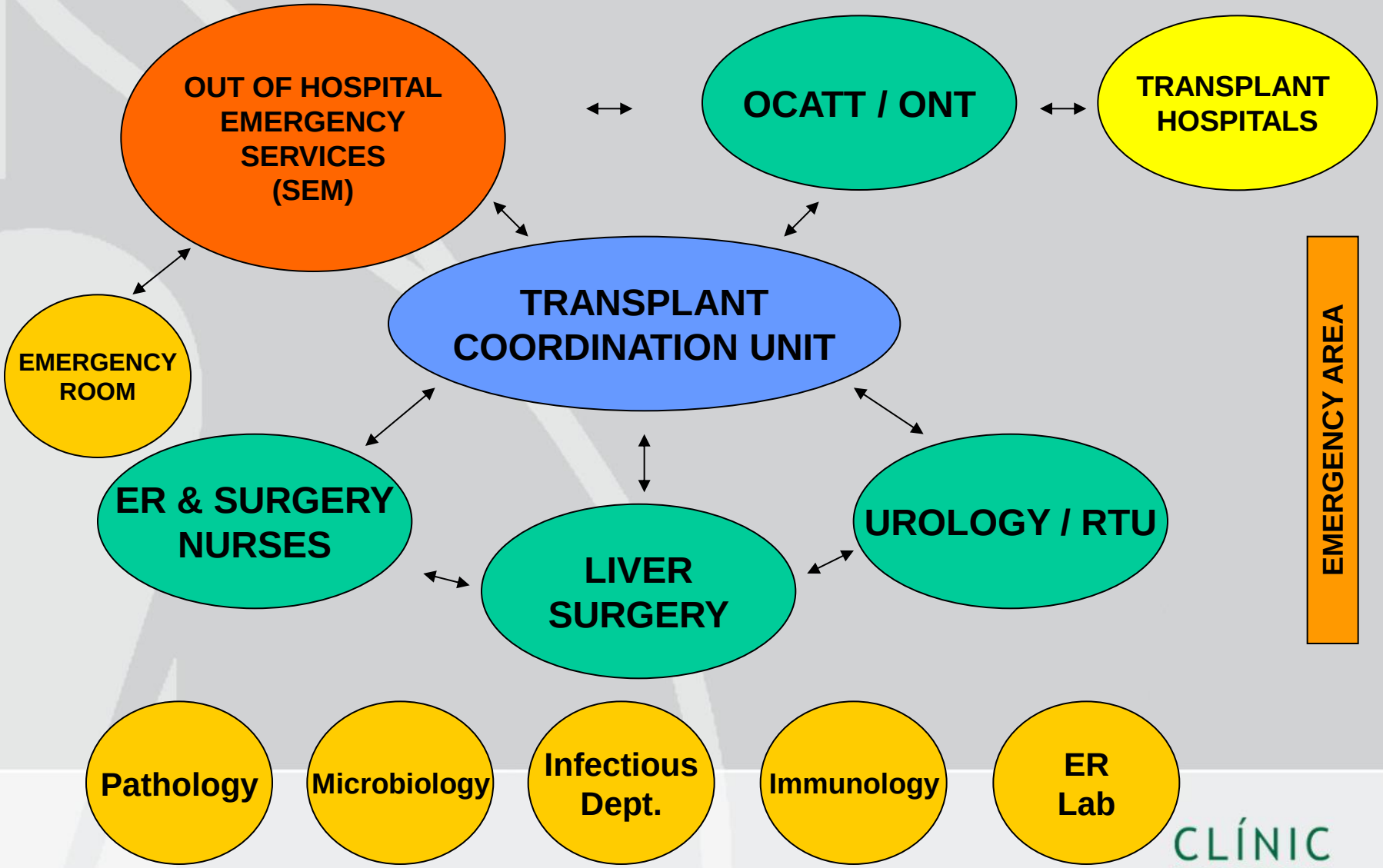
MULTIDISCIPLINARY PROGRAM



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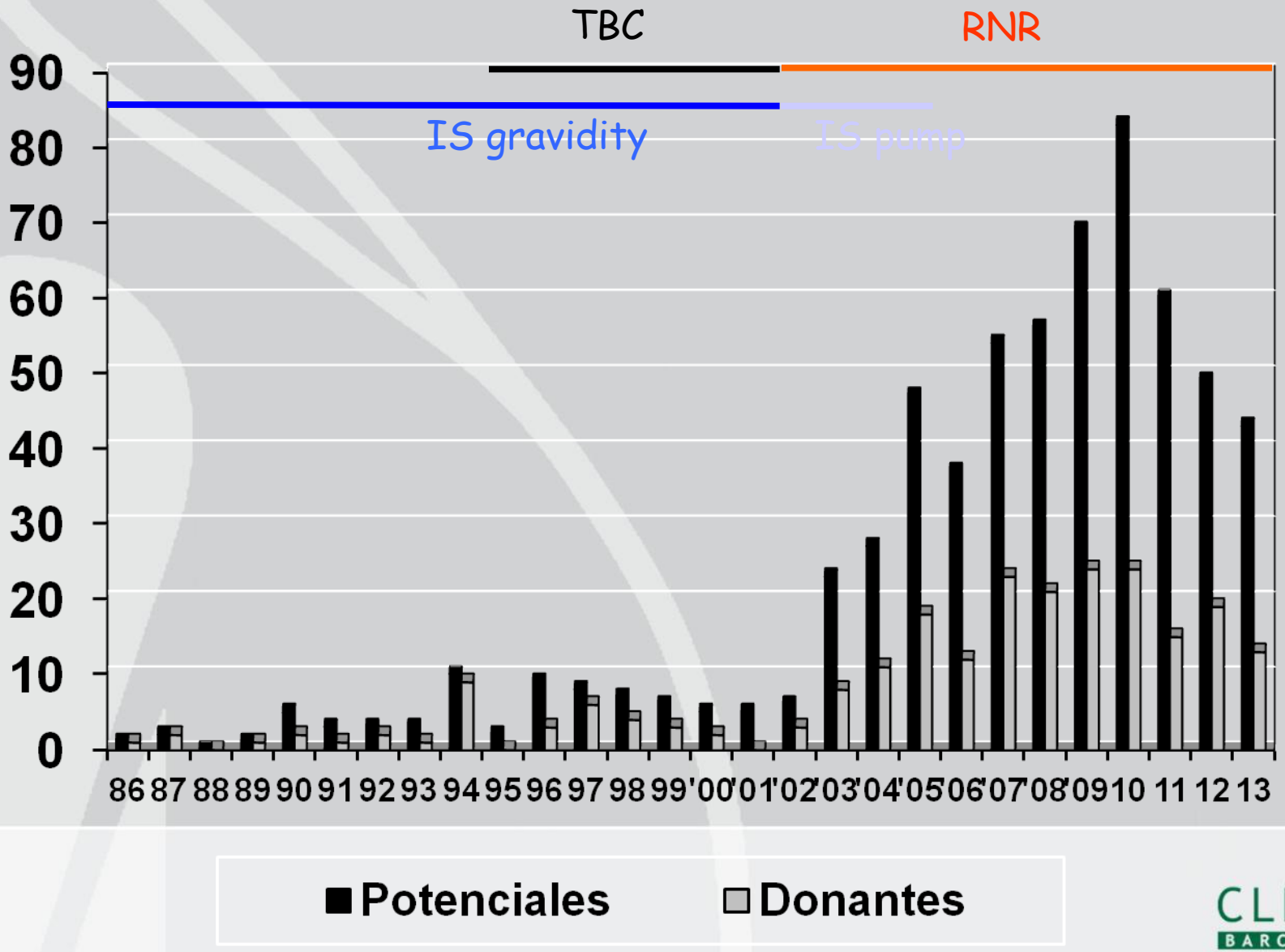
ACTIVIDAD PROGRAMA DE DCP 1986 - 2013



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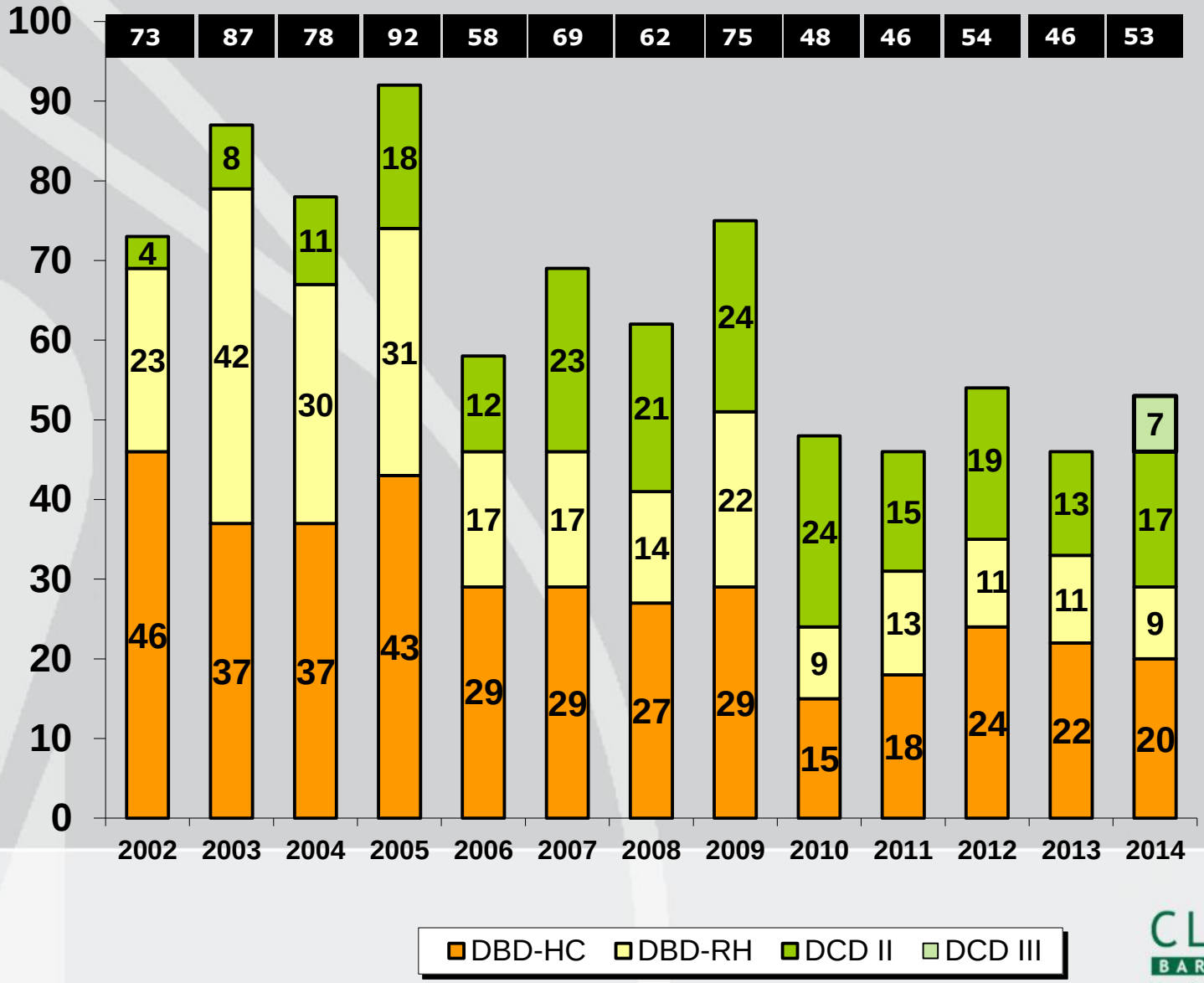
Origen del Donant HC 2002 - 2014



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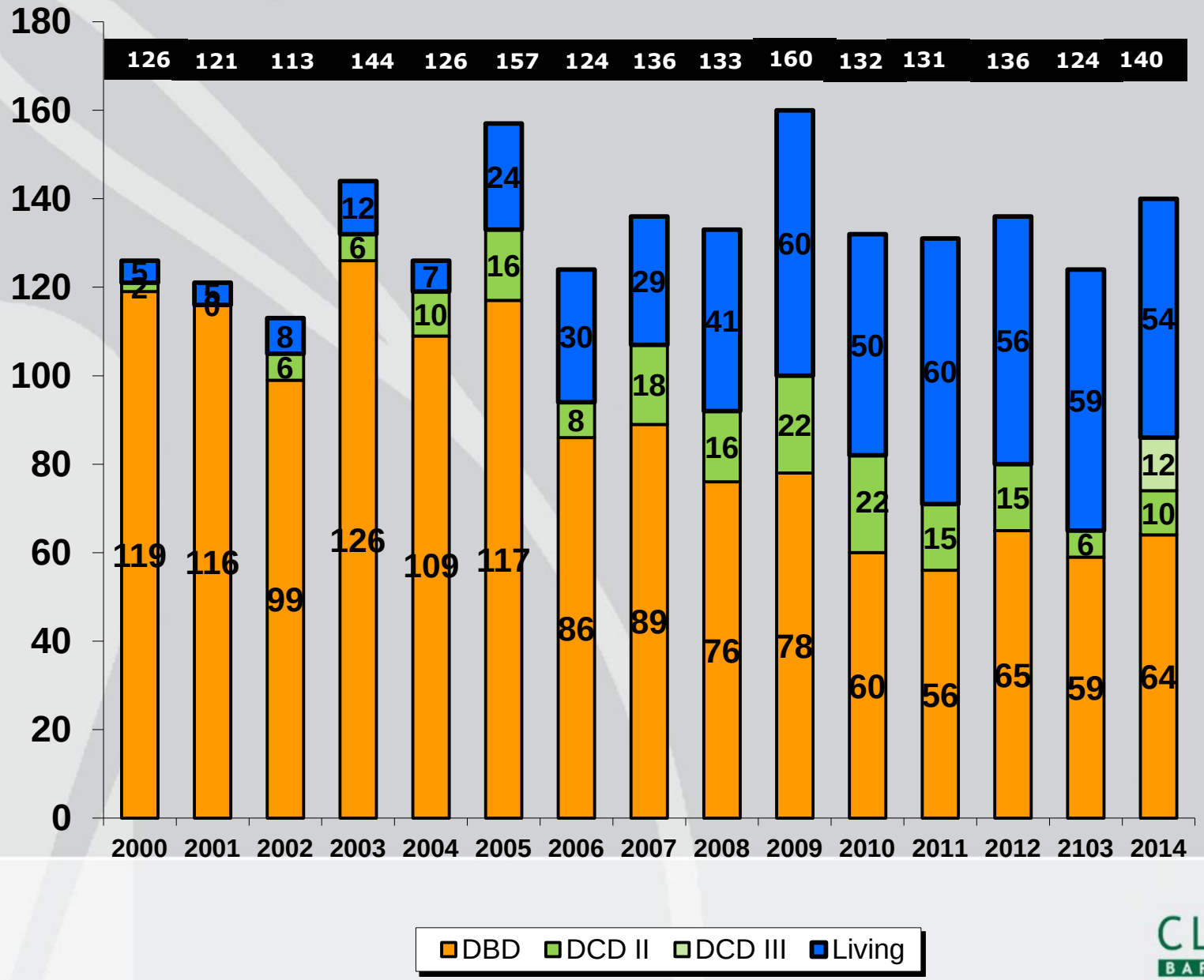
Trasplantament Renal HC 2000-2014



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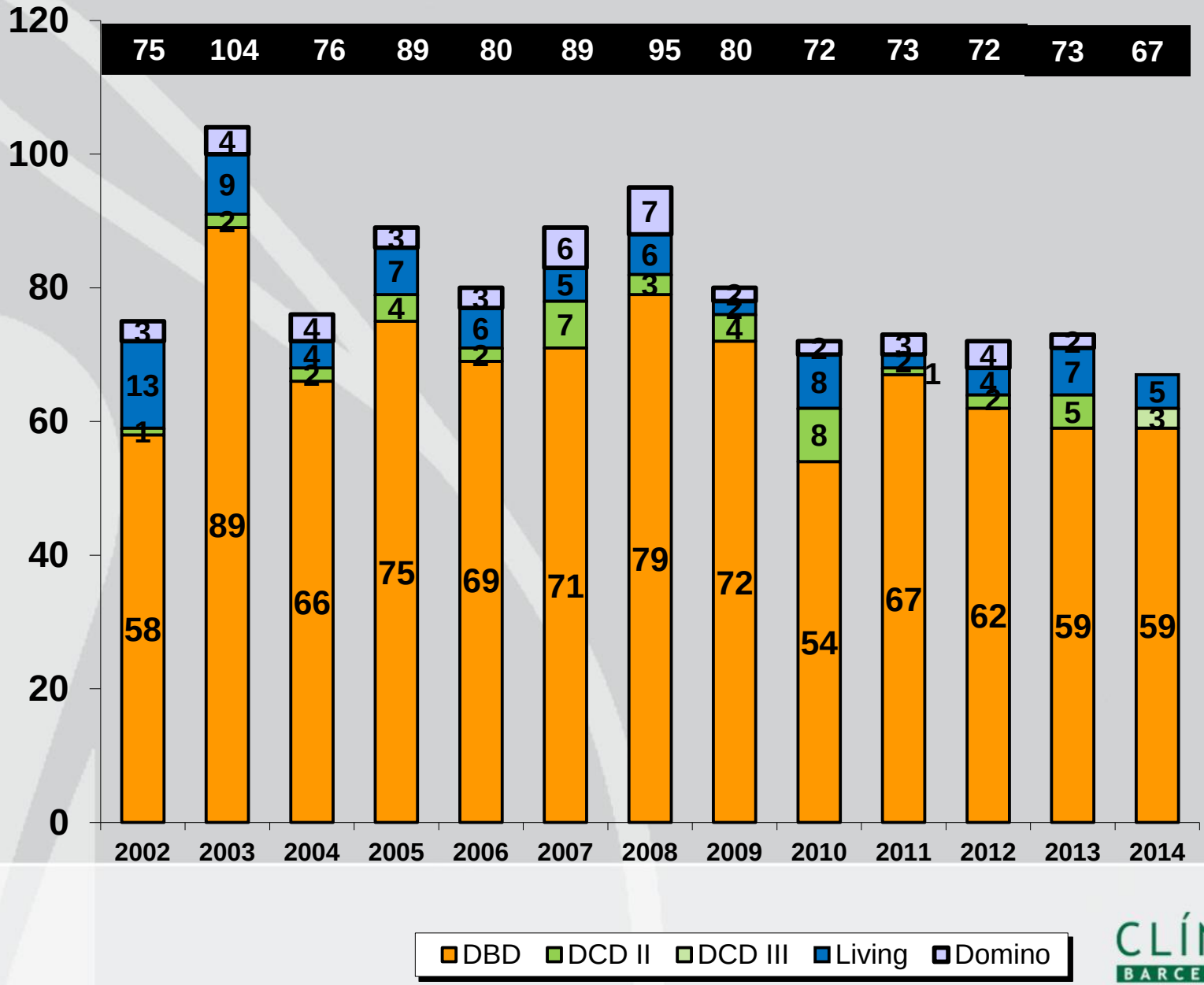
Trasplantament Hepàtic HC 2002 – 2014



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ANÁLISIS DE ACTIVIDAD DEL PROGRAMA DA II NC 1986-2014

Activaciones Código 3.03	
Posibles DA II	75
Contraindicaciones Clínicas	17 (22,6%)
Negativas Familiares	11 (14,6%)
Negativas Judiciales	5 (6,6%)
Donantes Reales de Órganos	42 (56%)
Donantes de Tejidos	8 (10,6%)

*16 años

Activaciones Código 3.03	642
Posibles DA II	596
Contraindicaciones Clínicas	285 (47,8%)
Negativas Familiares	65 (10,9%)
Negativas Judiciales	37 (6,2%)
Donantes Reales de Órganos	209 (35%)
Donantes de Tejidos	165 (27,7%)

*13 años

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CARACTERÍSTICAS DE LOS DONANTES DA II

Edad de los Donantes (años)	48,7 ± 12,5 (15 – 65)	
Sexo (% Masc)	87,5	
Grupo Sanguíneo (A - 0 - B - AB) (%)	47,8 - 40,6 - 7,5 - 3,1	
Características antropométricas	Peso(Kg)	80,75 ± 13,47
	Talla (m)	1,73 ± 0,07
	IMC (Kg/m^2)	26,8 ± 3,8
Causa de Muerte (%)	IAM	52,8
	Arritmia Cardiaca	21,4
	Trauma	8,8
	AVC	5,7
	Otras	11,3
Presencia de Factores de riesgo CV(%)	67,3	
Uso LUCAS® (%)	68,8	

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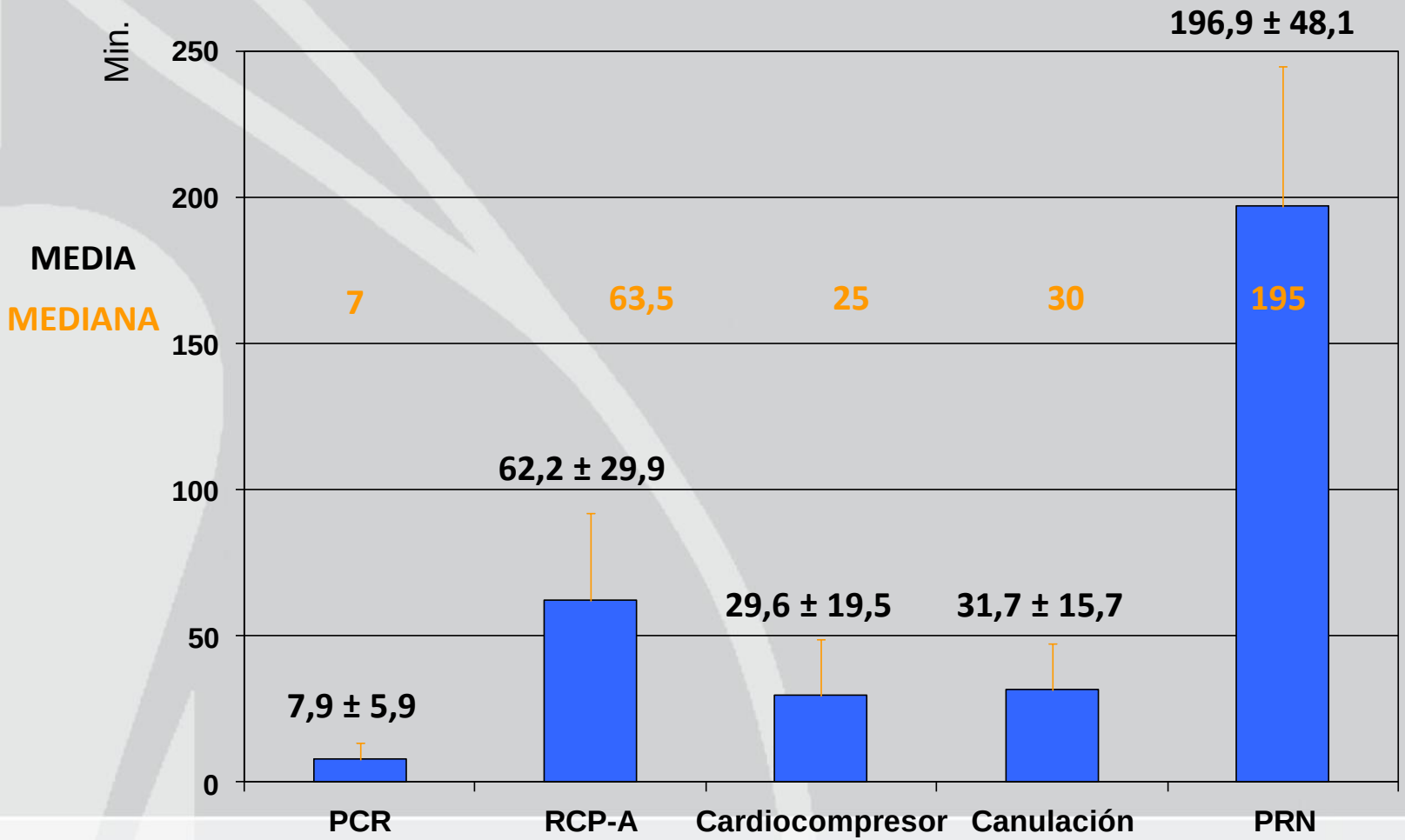
CARACTERÍSTICAS DE LOS DONANTES DA II



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ANÁLISIS DE ACTIVIDAD DEL PROGRAMA DA II

	Total
DA II Reales	209
DA II Efectivos	143 68,4%

	Total
Riñones	408
Riñones Tx	254 62,2%

	Total
Hígados	132
Hígados Tx	42 31,8%

RIÑÓN:

H. CLÍNIC DE BARCELONA → 165

FUNDACIÓ PUIGVERT → 35

H. DEL MAR → 27

H. VALL D'HEBRÓ → 19

H. BELLVITGE → 5

H. CAN RUTI → 2

H. JUAN CANALEJO → 1

HÍGADO:

H. CLÍNIC DE BARCELONA → 41

H. DE BELLVITGE → 1 (Grupo B)

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RESULTADOS TRASPLANTE RENAL DA II

N° (Periodo 2002-2011)	134
Edad del Donante (años)	44.3 ± 13.9 (15 – 65)
Sexo (% Masc)	92,7
Tiempo de Isquemia fria (h)	13.6 ± 3.5 (6 – 23)
PNF (Primary non function)	No función 5 (5.1%) Trombosis 2 (2%)
DGF n (%) - intérvalo (días)	63 (64.9%) - 18.8 ± 9.9 (1–44)
Creatinina sérica (mg/dl) a 1 año	1.57 ± 0.55 (0,78 – 4,02) (n=67)
a 5 años	1.60 ± 0.59 (0,82 – 3.20) (n=24)
Proteinuria a 1 año (gr/24hr)	0.53 ± 0.81 (0.06 – 4.7) (n=67)
Proteinuria > 1 gr/24hr a 1 año	10%
Proteinuria a 5 años (gr/24hr)	0.99 ± 1.47 (0.06 – 5.9) (n=23)
Proteinuria > 1 gr/24hr a 5 años	26%

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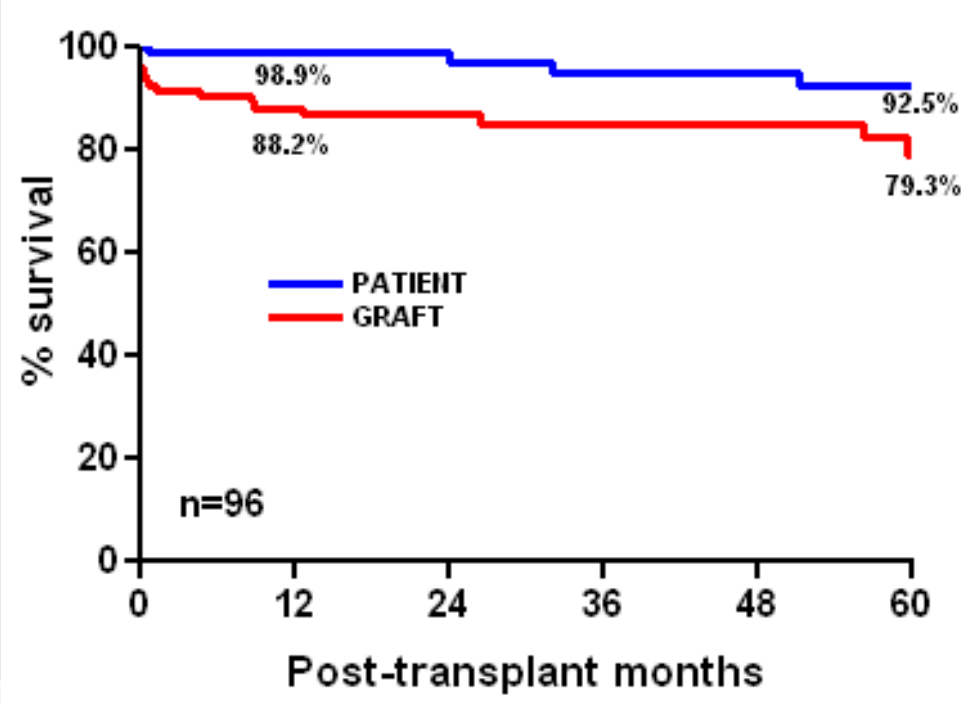
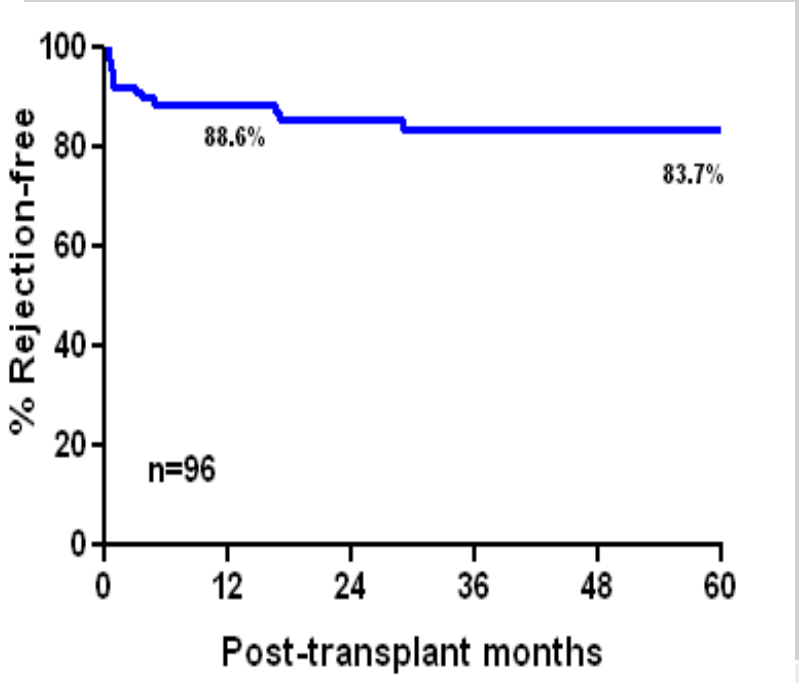
Edad (años)	48.4 ± 11.8 (24 – 71)
Sexo (%Masc.)	55,2%
Retrasplante	7 (7.3%)
HLA-PRA > 10%	15 (15.6%)





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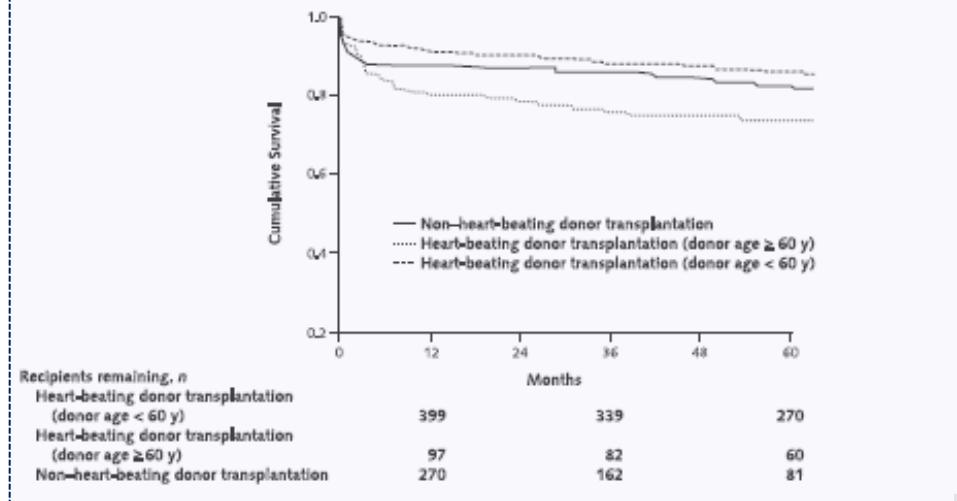
Kidney transplantation from Uncontrolled DCD –preservation approaches and outcomes

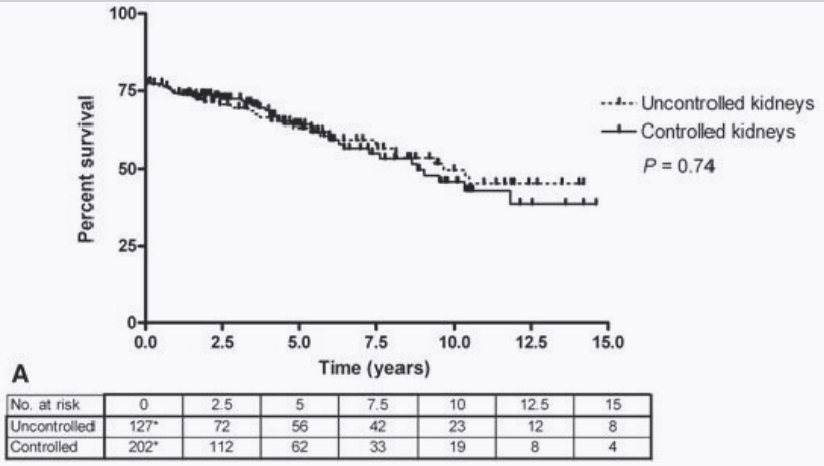
DGF: 69%
PNF: 4%

Fructuoso, Ann Intern Med 2006
N=320



Hoogland, Am J Transplant 2011
N=128

DGF: 61%
PNF: 22%



No. at risk	0	2.5	5	7.5	10	12.5	15
Uncontrolled	127*	72	56	42	23	12	8
Controlled	202*	112	62	33	19	8	4

Re-establishment of cardiac compression and mechanical ventilation + Normothermic Regional Preservation

In situ cooling preservation

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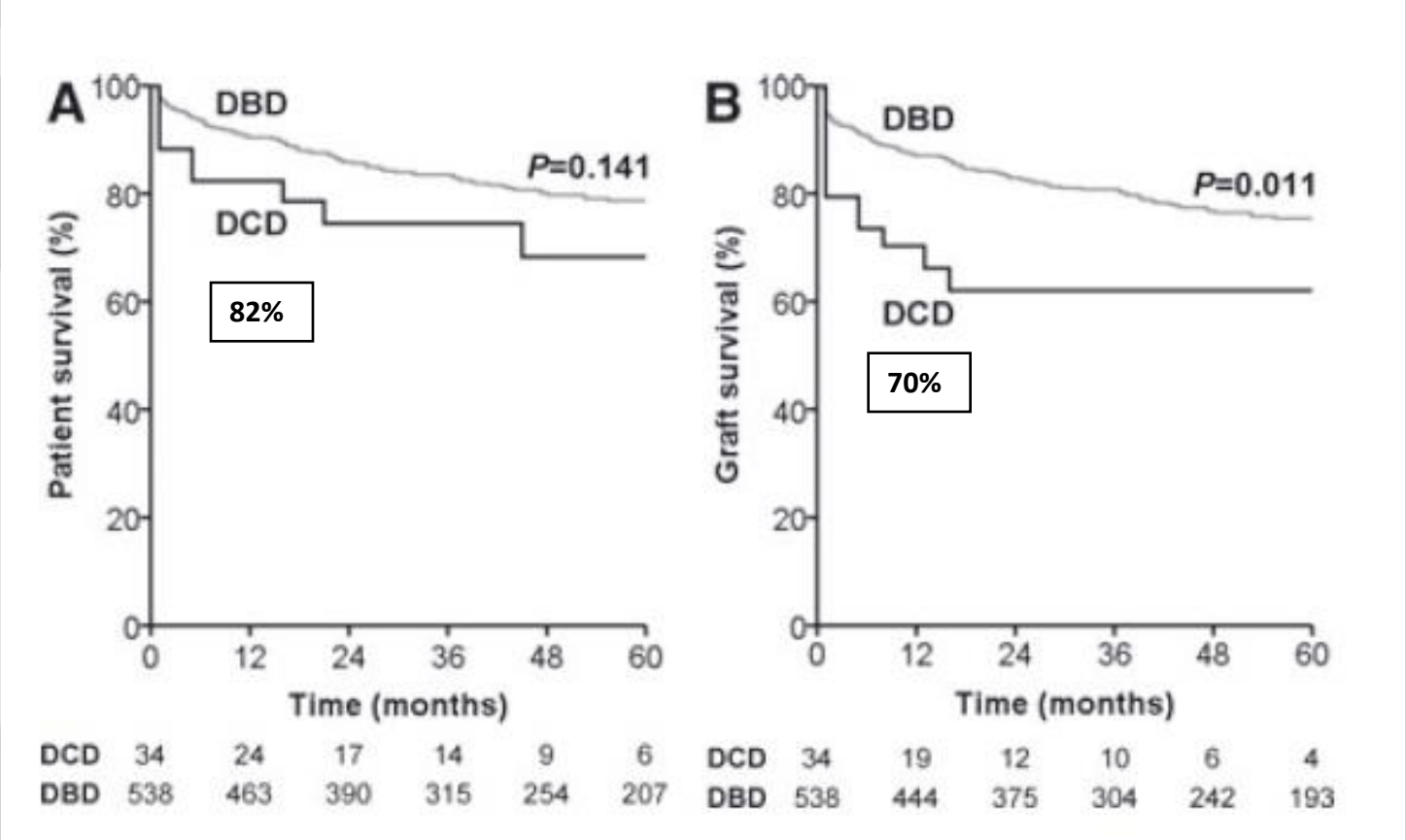
RESULTADOS TRASPLANTE HEPÁTICO DA II



Mitjana seguiment: 24 mesos (r= 0-111)

(Match de variables: sexo, edad, MELD score, IMC)

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RESULTADOS 2014 DA III

- N = 7 (6 UCI-Quirúrgica / 1 UCI-Coronaria)
- Casos No Judiciales: 100%
- 5 ♂ : 2 ♀
- Edad Media: 48,4 años (21-65)
- Grupo sanguíneo: 6 A+ / 1 O+

- Peso: 83,8 ± 14,2 (60-100) Kg
- Talla: 1,79 ± 0,09 (1,60-1,92) cm
- IMC: 26,30 ± 3,3 (22,3-31,6) Kg/m^2

- Días de UCI: 9 ± 3,8 (4-14) días

- Causa de muerte:
  - Encefalopatía anóxica (2)
  - HSA (2)
  - HSA + Encefalopatía anóxica post-PCR (2)
  - Tumor Cerebral Primario

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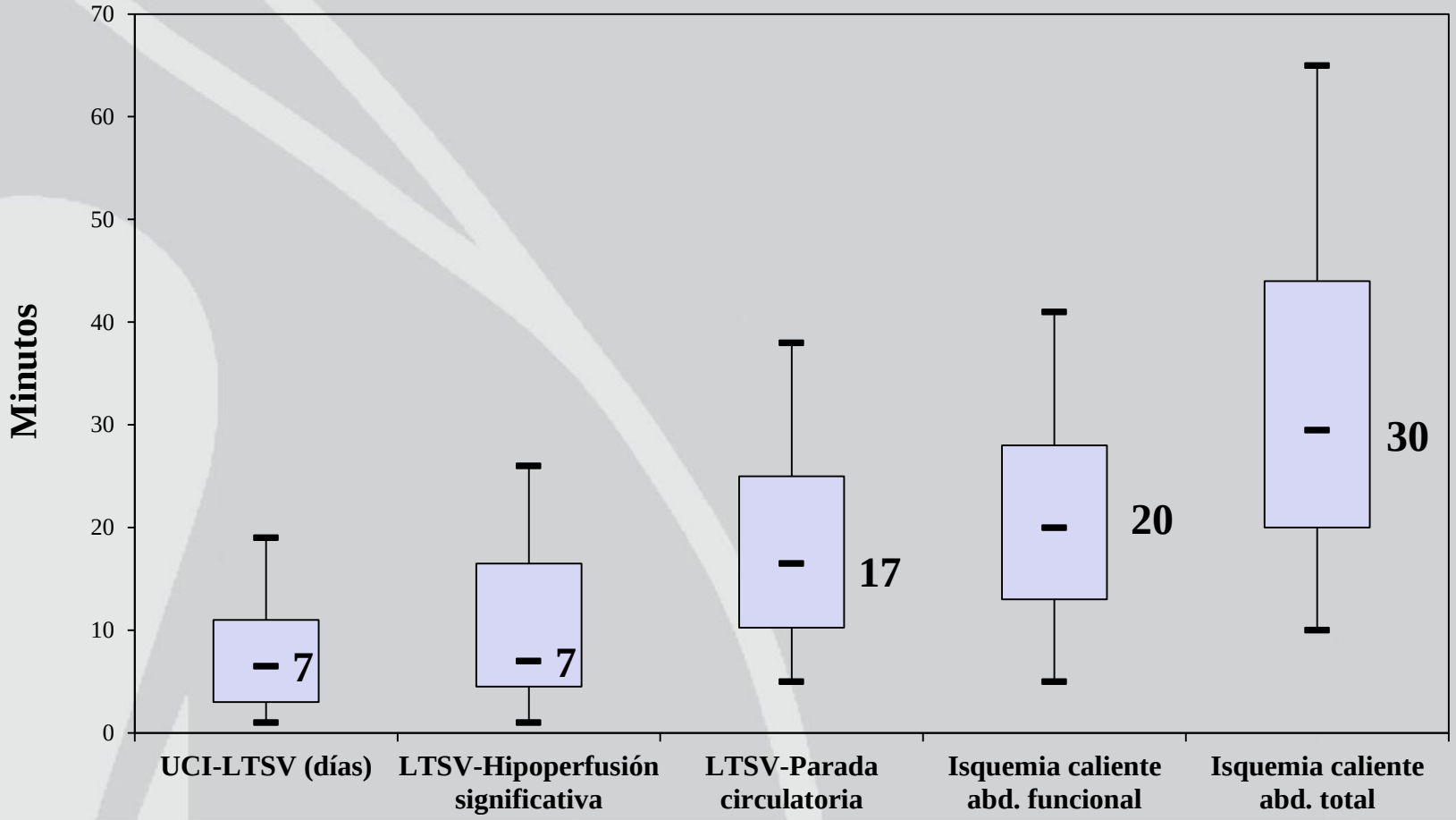
Tiempos (minutos) del proceso de donación en asistolia tipo III de Maastricht. Diagramas de caja (Mediana y Percentiles 25 – 75). España 2013 (N=51).



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RESULTADOS 2014 DA III Hospital Clinic

N Donantes (7)

- Órganos Generados: 6 Hígados – 14 Riñones
- Órganos trasplantados: 3 Hígados – 13 Riñones.

- Donantes Eficaces: 100%
- Tasa de Trasplante Renal: 93% (1 Mala perfusión)
- Tasa de Trasplante Hepático: 50% (3 Esteatosis + Aspecto Macrosc.)
- 6 Corneas , 6 Hueso, 5 Arterias, 5 Válvulas, 4 piel.

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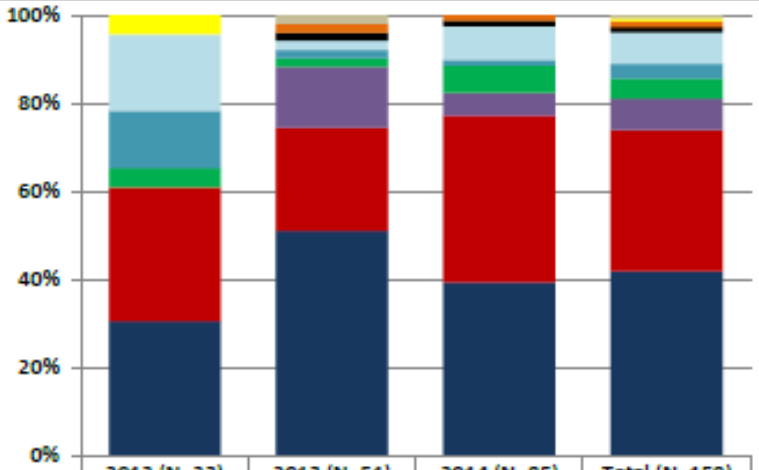
RESULTADOS 2014 DA III
Espagne



	2012 (N=23)	2013 (N=51)	2014 (N=85)	Total (N=159)
Otras		1		1
Intoxicación	1			1
Tumor SNC		1	1	2
Enf. Deg. Neuromuscular		1	1	2
TCE no tráfico	4	1	6	11
TCE tráfico	3	1	1	5
Patología Pulmonar	1	1	5	7
ACVi	0	7	4	11
ACVh	7	12	30	49
Encefalopatía anóxica (PCR/PR)	7	26	31	64

ACVh: Accidente cerebrovascular hemorrágico; ACVi: Accidente cerebrovascular isquémico; Enf. Deg.: Enfermedad degenerativa; PCR/PR: Parada cardiorespiratoria/Parada respiratoria; SNC: Sistema Nervioso Central; TCE:

Figura 19. Causa de fallecimiento de los donantes en asistolia tipo III de Maastricht. España 2012-2014.

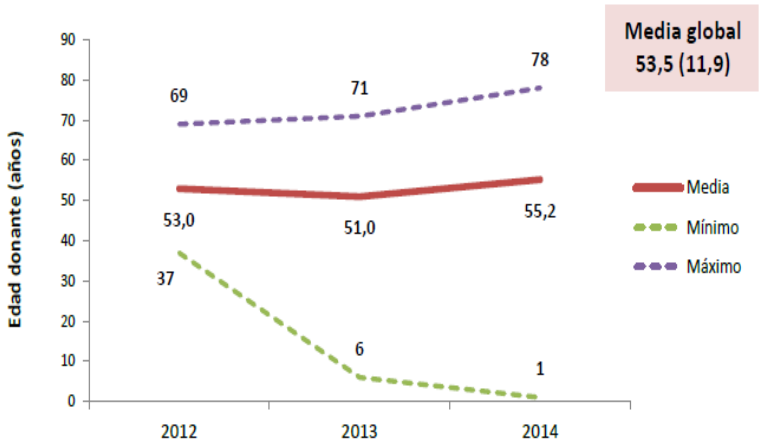


Figura 16. Evolución de la edad de los donantes en asistolia tipo III. España 2012-2014.

RESULTADOS 2014 DA III
Espagne

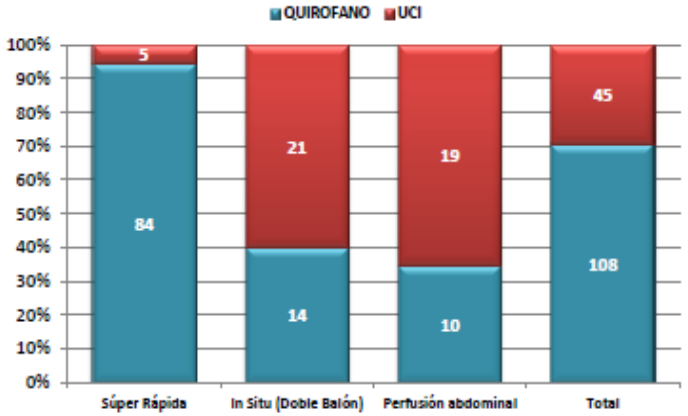


Figura 20. Lugar de retirada de soporte ventilatorio de los donantes en asistolia tipo III de Maastricht, total y por tipo de preservación-in situ y extracción. España 2012-2014.

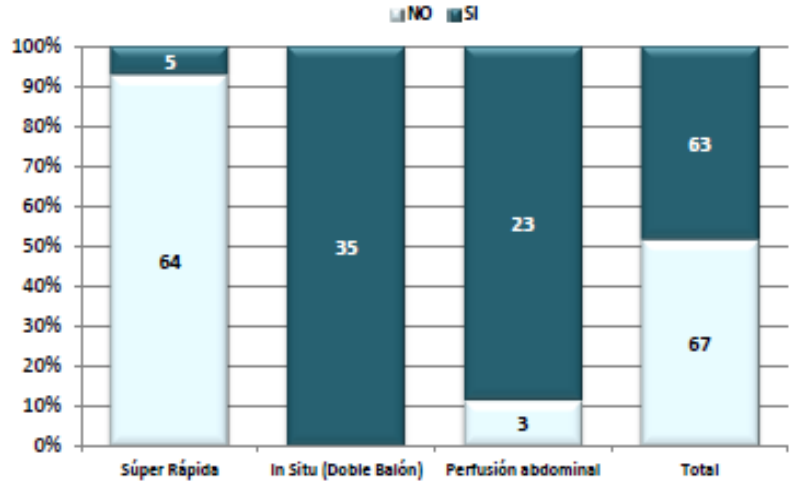


Figura 21. Canulación pre-mortem de los donantes en asistolia tipo III de Maastricht. España 2012-2014.

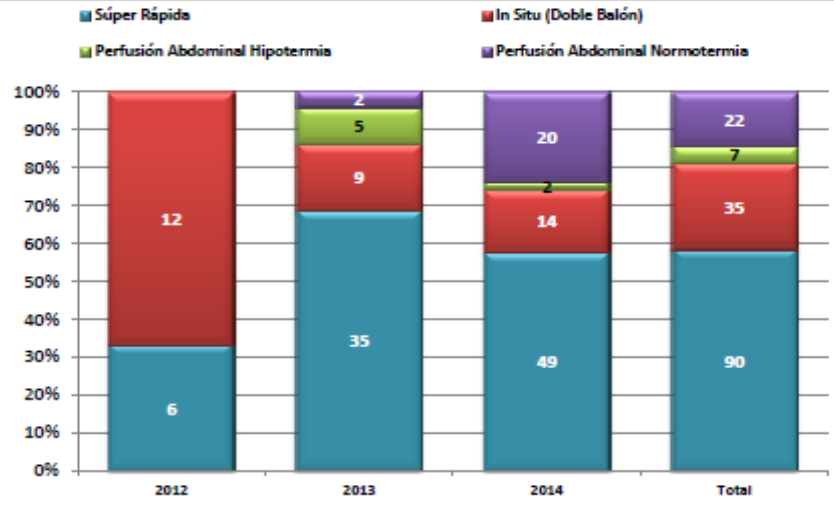


Figura 23. Tipo de técnica de preservación regional abdominal-extracción. Donantes en asistolia tipo III. España 2012-2014.

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RESULTADOS 2014 DA III
Espagne

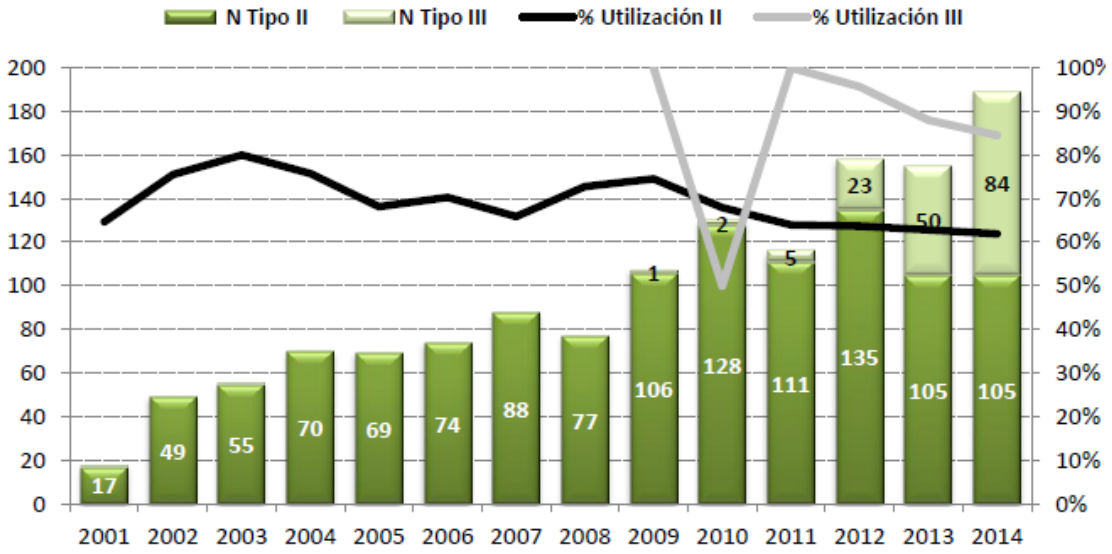

Figura 31. Número de donantes renales y porcentaie de utilización (donantes utilizados/ donantes renales) en función del tip

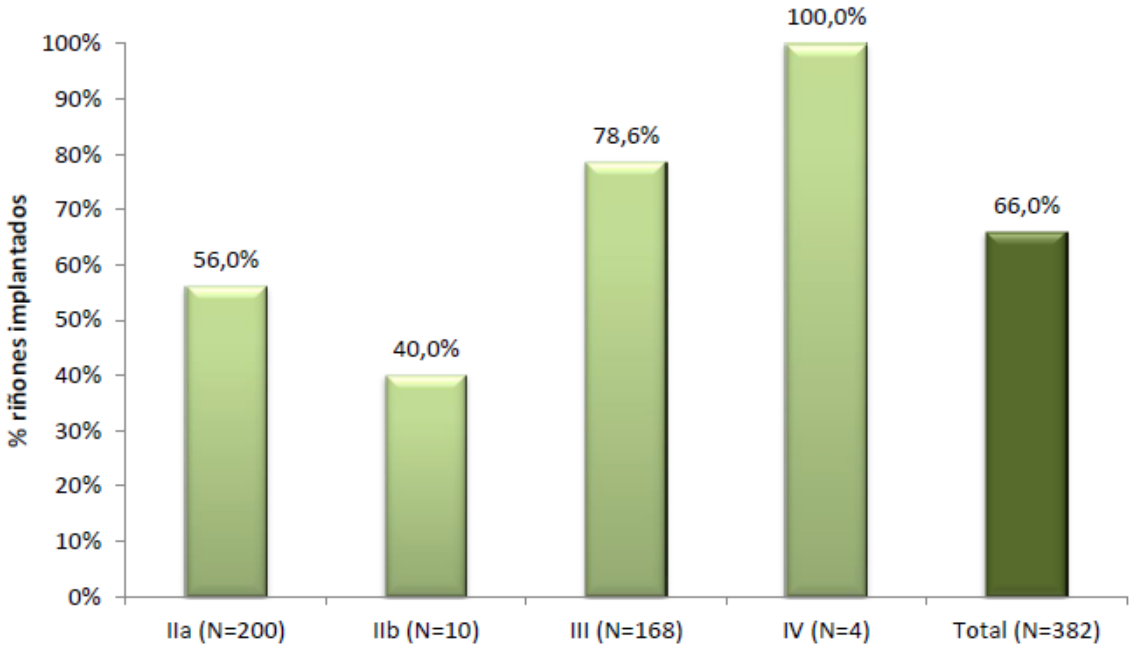

Figura 33. Efectividad de los riñones extraídos de los donantes en asistolia. España 2014.

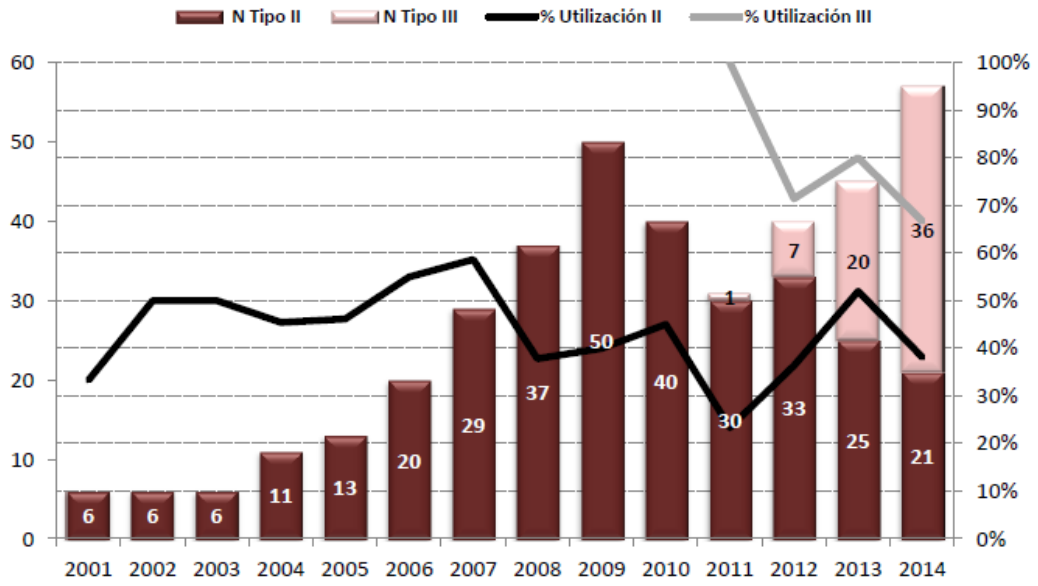

Figura 35. Número de donantes hepáticos y porcentaje de utilización en función del tipo de Maastricht. España 2001-2014.

RESULTADOS 2014 DA III
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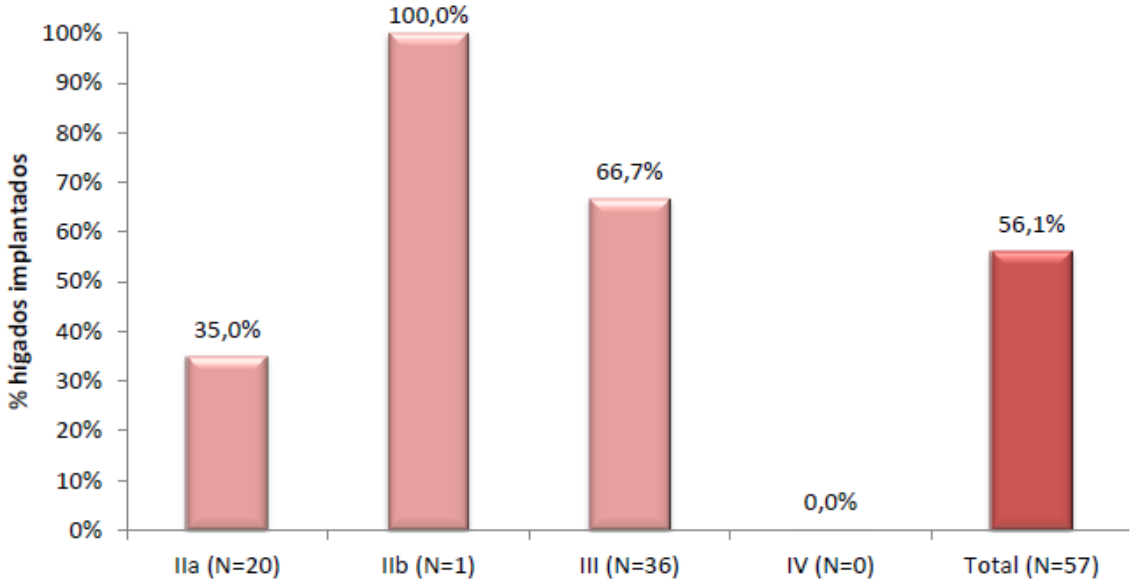

Figura 37. Efectividad de los hígados extraídos de los donantes en asistolia. España 2014.

Efectividad de los donantes eficaces en asistolia. Total y por tipo de Maastricht . España 2013.

		TOTAL	IIa	IIb	III
Donantes eficaces	**N**	**159**	**104**	**4**	**51**
Org. extraídos	N	391	255	8	128
Org.extraidos por donante eficaz	N	2,5	2,5	2,0	2,5
Donantes utilizados	**N**	**119**	**70**	**3**	**46**
(% sobre donantes eficaces)		**(74,8%)**	**(67,3%)**	**(75,0%)**	**(90,2%)**
Órganos implantados	N	246	136	4	106
Org. implantados por donante eficaz	N	1,5	1,3	1,0	2,1
Org. implantados por donante utilizado	N	2,1	1,9	1,3	2,3

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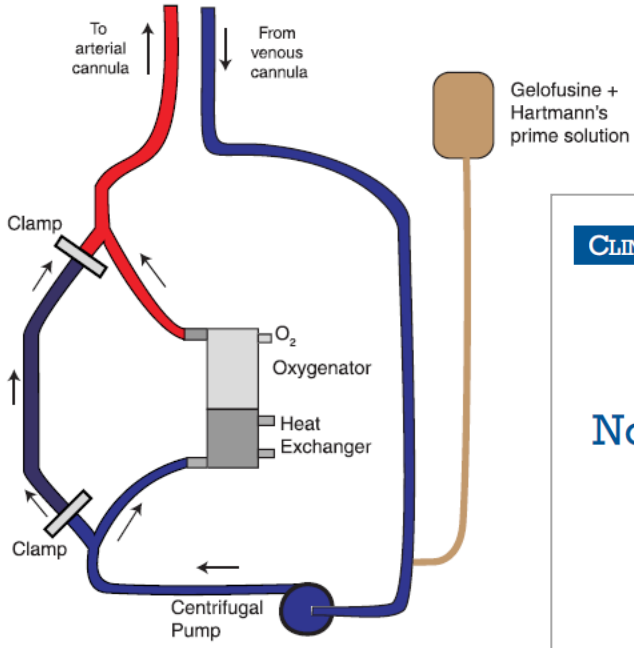
Normothermic Regional Perfusion – a Role in Controlled DCD?



CLINICAL AND TRANSLATIONAL RESEARCH

Normothermic Regional Perfusion for Donation After Circulatory Death Without Prior Heparinization

Andrew J. Butler,[1] Lucy V. Randle,[1] and Christopher JE Watson[1,2]

Background. Over 40% of deceased donors in the UK donate after circulatory death (DCD). Normothermic regional perfusion has been reported to improve outcomes in such donors in Europe and the United States. Unlike the United States, legal and professional requirements in the UK prevent cannulation and heparinization before verification of death, which must be a minimum of 5 min after circulatory arrest. We developed a novel protocol for in situ normothermic regional perfusion (NRP) which complied with these requirements.

Methods. NRP was achieved by cannulating the aorta and vena cava after death. Donor blood was then warmed and oxygenated using a bespoke extracorporeal membrane oxygenator circuit before return to the donor. A shunt was incorporated into the extracorporeal circuit to permit heparin mixing before oxygenation and warming was commenced to prevent thrombosis of the oxygenator. Normothermic perfusion was continued for 2 hr before in situ cold perfusion with preservation fluid. All organs were subject to static cold storage after recovery.

Results. Eight controlled DCD donors underwent NRP from which 3 livers, 2 pancreases, and 14 kidneys were transplanted. Four livers were not used because of biochemical evidence of hepatocellular damage and one because of cirrhosis. Two kidneys were lost from venous thrombosis before function returned and two developed delayed graft function; all transplanted livers and pancreases had primary function.

Conclusions. Cannulation and heparinization after circulatory arrest does not prevent successful normothermic regional perfusion. The technique permits evaluation of donor organs before implantation and may improve short-term outcomes.

Keywords: Donation after circulatory death, Normothermic regional perfusion, Extracorporeal membrane oxygenation, Liver transplantation, Kidney transplantation, Pancreas transplantation.

(*Transplantation* 2014;00: 00–00)

PRESENTATION

Currently, donation after circulatory death (DCD) donors are a focus of intense interest in the transplant community, based on the incredible potential they have to increase the number of organ donors. In spite of its estimated potential, the actual use of organs from DCD donors for transplant is scarce. While many transplant groups across the globe are interested in initiating DCD programs, they lack the experience necessary to appropriately manage these donors during organ maintenance, recovery, and transplantation, in order to be able to achieve posttransplant outcomes similar to conventional donors.

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DATES June 19 & 20, 2014

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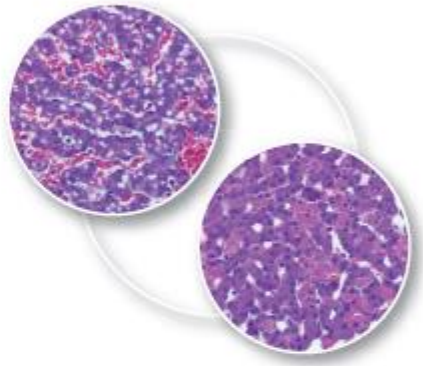

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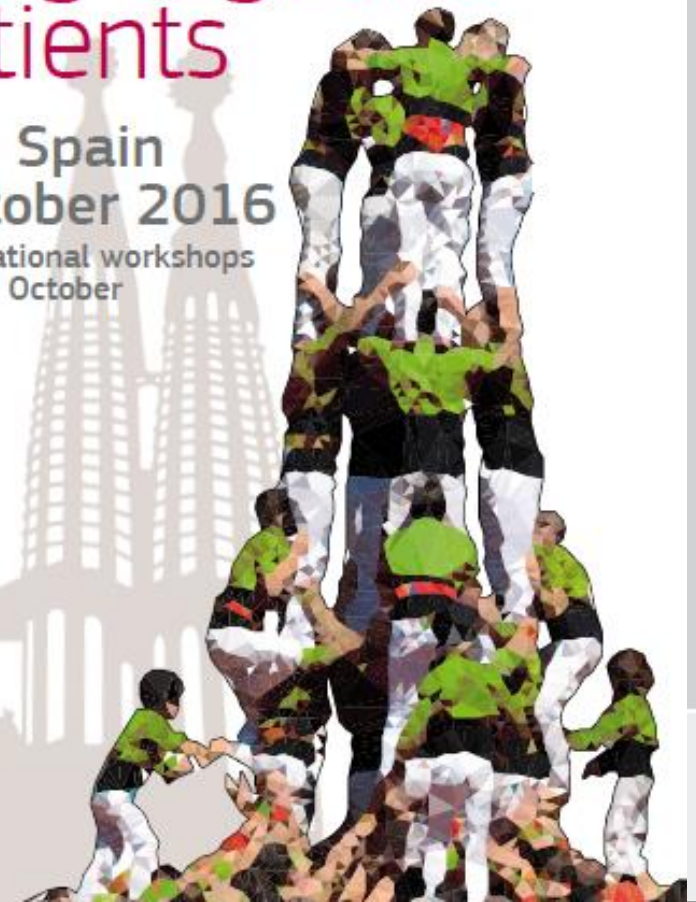

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