Care of the DCD in ICU: the French experience

The National Steering Committee of donors after circulatory death

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No conflict of interest

2 challenges

Recent Legal Framework

- Léonetti Law – 22/04/2005 : outlining when and how to decide on withdrawing

  updated recommended investigations and having external 2d opinion

- Léonetti-Claeys Law – 2/02/16 : how to withdraw intensive treatment; right to continuous and deep sedation

Full compliance with the nationally agreed recommendations of Intensive Care Societies

- The decision to stop the treatment must be made strictly on medical judgement and be independent from the possibility of donation.
- OPO team should not be involved in the management of the potential donor
- The donation pathway must absolutely not cause or accelerate death

Authorized center : local protocol, consistent with national protocol defining the mandatory conditions to determine death and to realize procurement and transplantation

cDCD = Extended Criteria Donors

Warm ischemia : detrimental but unavoidable factor in situation of prolonged circulatory arrest

Donor Characteristics	LDRI
Age	
<40 years	
40-49 years	
50-59 years	
60-69 years	
>70 years	
Race: African American versus white	
Height (per 10-cm decrease)	
CVA as COD	
Other COD	
DCD	
Partial/split liver	

Donor Characteristics	KDRI
Age	
ars (applies to patients of all ages)	
ears (applies to patients < 18 years old)	
– 50 years (applies to patients > 50 years old)	
ican American versus white	
Creatinin	
SCR – 1 mg/dL (applies to all SCR values)	
SCR – 1.5 mg/dL (applies to SCR values > 1.5 mg/dL only)	
CVA as COD	
Height (per 10-cm increase)	
Weight (per 5-kg increase below 80 kg)	
DCD	
HCV	

➔ **National protocol with objectives to limit as much as possible the known risk factors of graft failure which worsen warm ischemia injuries**

National guidelines from USA, Canada, Australia and UK

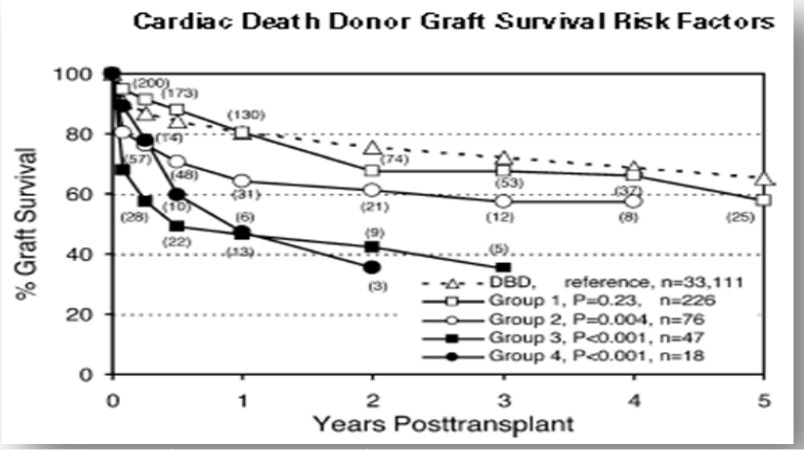
the 6th International Conference on Organ Donation after Circulatory Death organized in Paris in February 2013

1. Choice of donor and recipient selection criteria

- Donor age < 66 years
- No pre-existing injuries of the graft
  (liver biopsy with extemporaneous lecture)
- Clinical status of recipients :
  - Only adult
  - awaiting a 1st transplant,
  - UNOS IV
    (exclusion of patients that are too sick to cope with post-perfusion syndrome)
- No HLA incompatible recipients
  - Virtual crossmatch

DCD liver transplant can be improved by avoiding high-risk recipients

Matteo AJT 2006



Ref DBD	Recipients	grafts	
Group 1 ☐	Low risk	Low risk	IC < 10h FWIT< 30 mn
Group 2 ○	Low risk	High risk	IC > 10h or FWIT> 30 mn
Group 3 ■	High risk	Low risk	IF < 10h FWIT< 30 mn
Group 4 ●	High risk	High risk	IF > 10h or IFWIT> 30 mn

2. In situ abdominal organs perfusion performed by normothermia regional perfusion (NRP)

- To change the period of cardiac arrest into a period of pre-re-conditioning
  - Better prevention of IR injuries
- Strong experimental rationale to perfuse DCD organs by abdominal normothermic oxygenated recirculation (Spain, UK)
  - Lower risk of failure or better graft function at 1 year if NRP in French uDCD
- Possible organ **viability test** before retrieval (liver, pancreas)
- Logistic advantages (**in ICU**, **peaceful** goodbye from relatives)
- Femoral catheter (arterial and venous) placed before WLST
- **Post mortem** cannulation of femoral vessels + aortic occlusion balloon
  - Surgically or percutaneously or both)
- Optimal length : 2 hours (1h < NRP < 4h)
- **Lower cost** compared to ex vivo normothermic perfusion
- Lower **theater occupation**

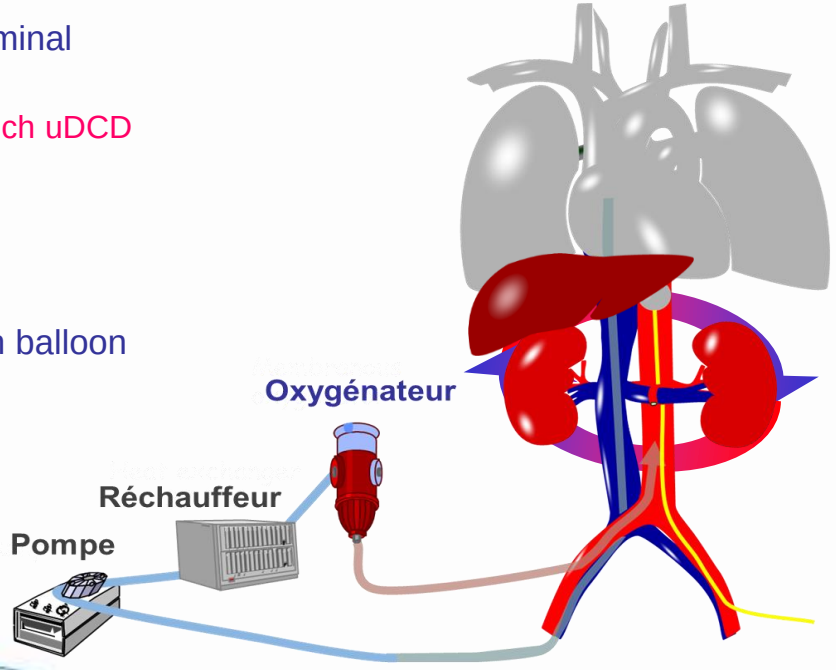
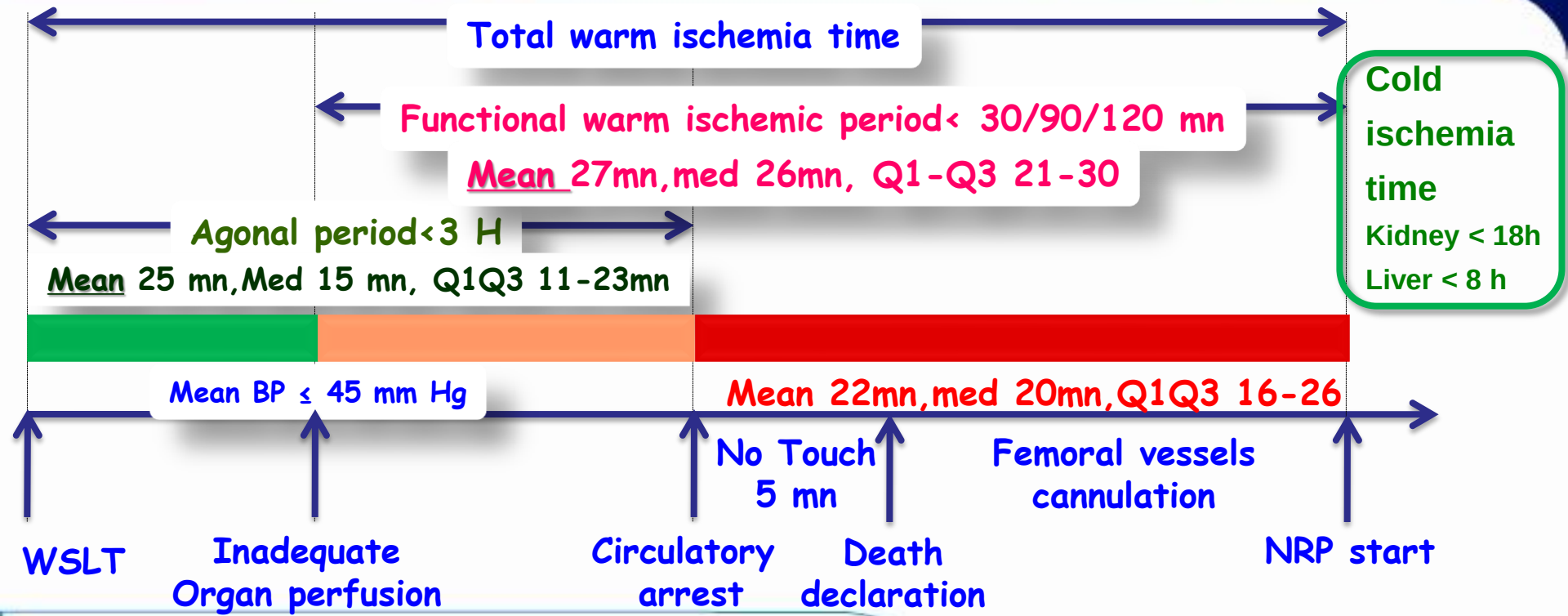


Schéma de Benoit Barrou

3. Limit the warm and cold ischemia time

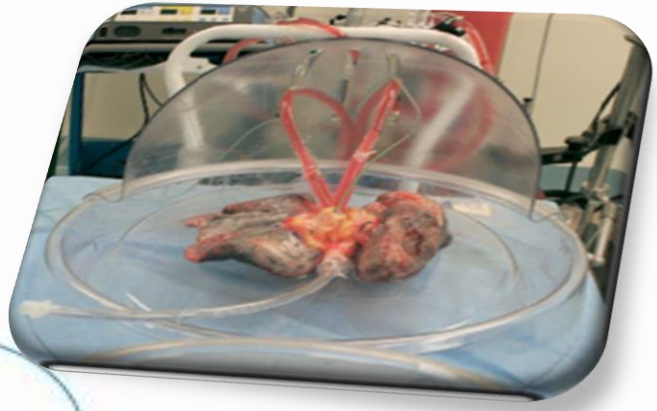


Time points in donation following circulatory death; 2015-2017; 99 actual cDCD donors

4. Ex vivo perfusion, after organ retrieval

- For kidney grafts
  - **Independent factor to decrease the rate of DGF**
  - **> 2 hours**
  - **Viability test (perfusion indexes)**

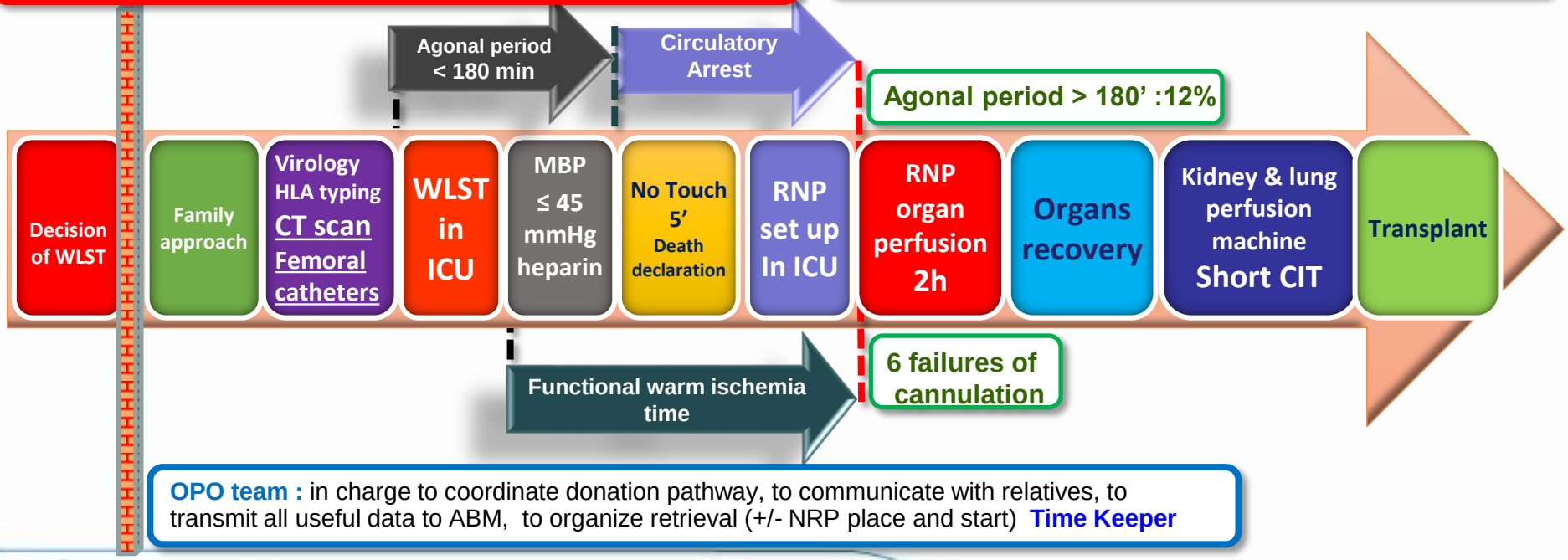
- For lung grafts
  - **Organ rehabilitation and viability criteria**
  - **Performed by ventilating the lungs and perfusing them with Steen Solution +/- red blood cells**
  - **Lung compliance, air way resistance & tidal volume via the ventilator**



The limitation or the banning of other risk factors known to result in graft loss

Intensive care team : fully responsible for deciding & achieving of WLST (withdrawal of ventilatory support and discontinuation of inotropic drugs) , monitor dying process, observe no-touch interval, death determination

Surgical teams: in charge of vessels cannulation, organs retrieval, ex vivo organ perfusion



OPO team : in charge to coordinate donation pathway, to communicate with relatives, to transmit all useful data to ABM, to organize retrieval (+/- NRP place and start) **Time Keeper**

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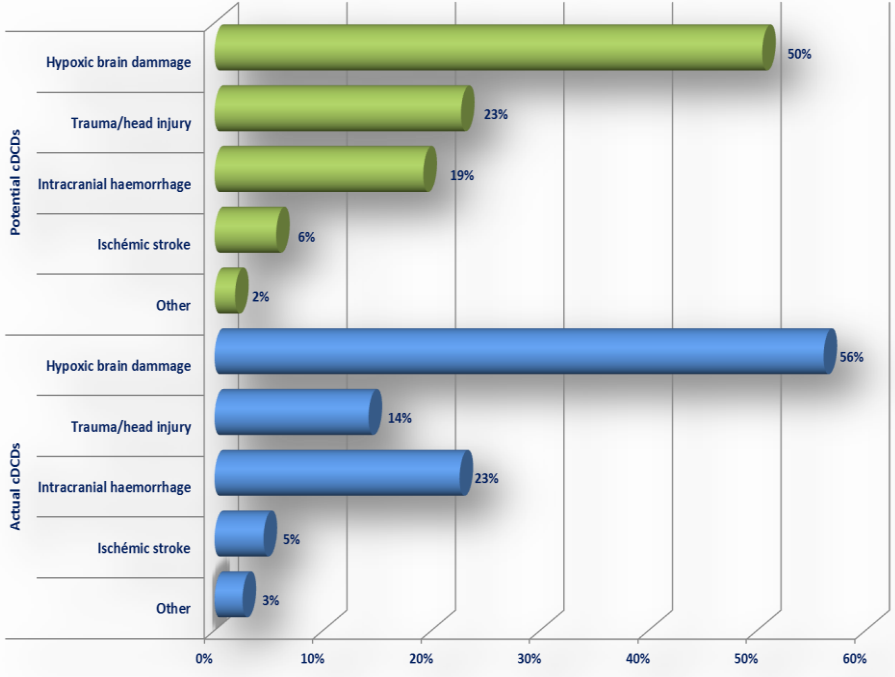
How France launched its donation after cardiac death program, Antoine C, et al. AnnFrAn 2014

Diagnostic categories of patients
317 cDCD potential donors/ 155 actual cDCD donors



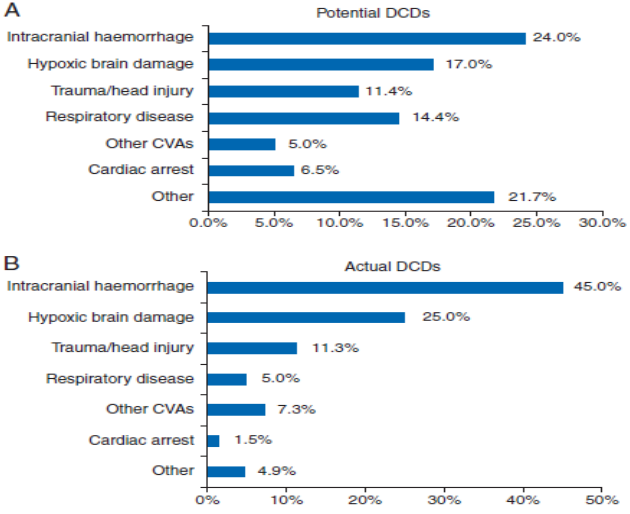


Fig 2 Diagnostic categories of (A) the 3825 patients referred as potential controlled DCDs and (B) the 397 patients who went on to became actual controlled DCDs in the UK between October 2009 and December 2010 (data courtesy of NHSBT).

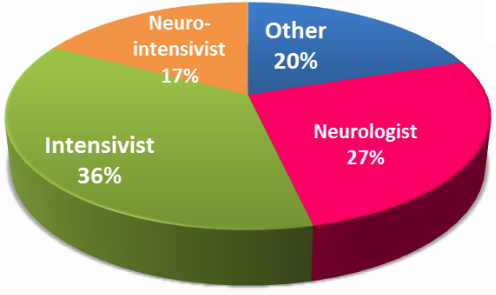
Decision of WLST

Intensivist

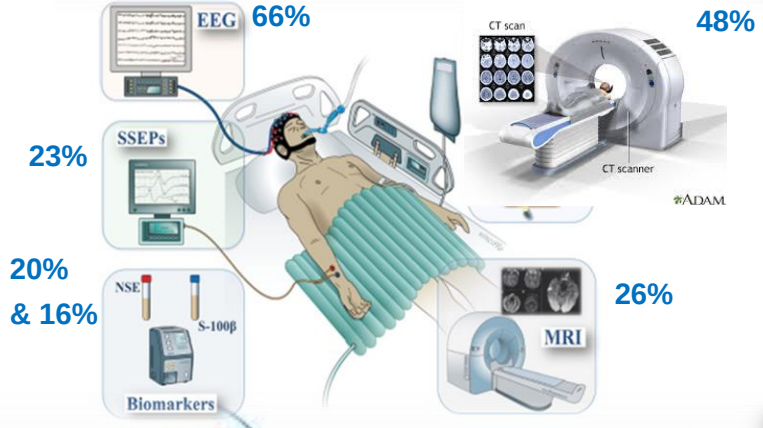
WLST decision : multimodal approach
317 potentials cDCDs

- ICU length of stay (admission to WLST decision)
  - **Mean : 10 days**, median 6,4 days (Q1 4d, Q3 12d, max 120d]
- Characteristics of potential donors
  - 71% were male, (76% of actual cDCDs)
  - **Mean age : 50 years** (median 53; 18-65, Q1 43, Q3 59)
- Devastating brain injury must be confirmed by neurological criteria

External second opinion: 100% **+** **Updated recommended investigations**



1 exam	36%
≥ 2 exams	61%
≥ 3 exams	28%



Decision of WLST
Intensivist

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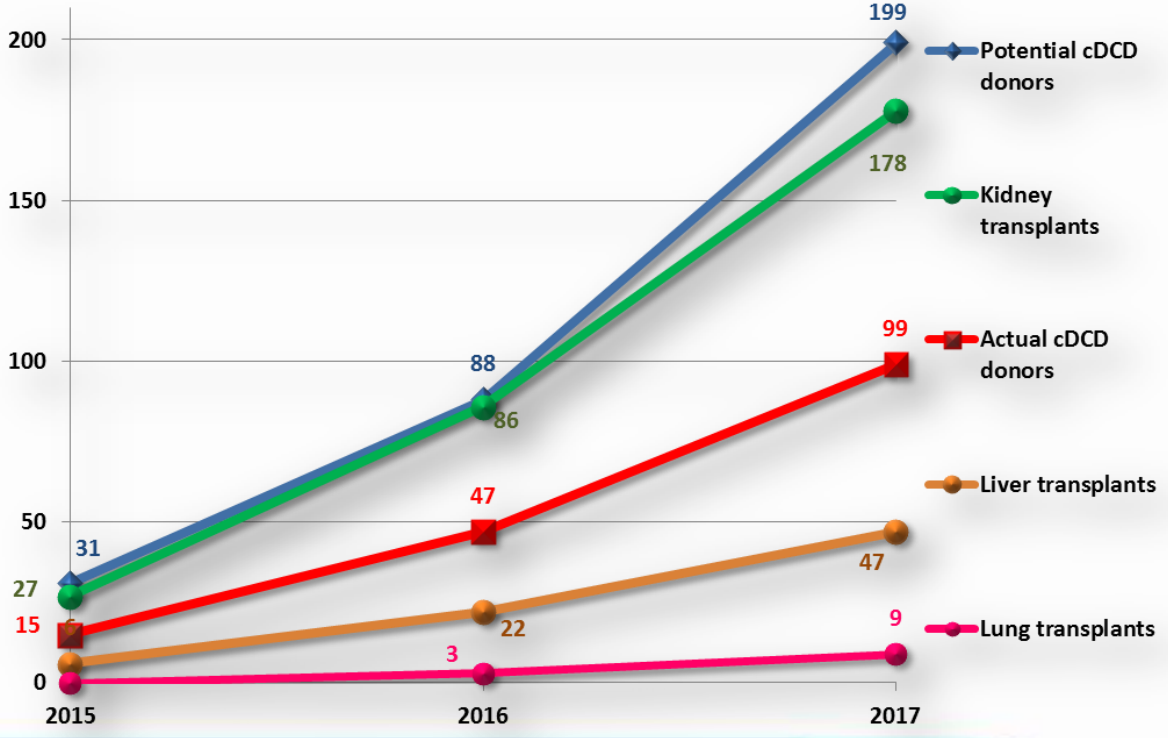
01/01/2015 to 31/12/2017 378 organ transplants



- 155 actual donors 51% of potential donor
- 291 kidney transplants
  - 92 % of retrieved kidney
- 75 liver transplants
  - 88% of retrieved liver
- 12 lung transplants

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Material and Methods – Preliminary outcome study

Study population : Data source: The CRISTAL French Transplant Registry

- Donor age < 66 years (cDCD and DBD)
- Adult recipients awaiting a 1st transplant

DCD

Inclusion 01/01/2015-31/12/2017

N=291 kidney transplants

DBD

Inclusion 01/01/2013-31/12/2017

N=7016 kidney transplants

Results - Preliminary outcomes study

- Renal transplant from cDCD donors :
  - Older donors
  - Higher incidence of diabetes among recipients
  - Less immunised recipients
  - Higher incidence of preemptive transplantation
  - Lower Cold ischemia time
  - Systematic perfusion machine (vs 20%)
  - % ECD : 10% (vs 31%)

		DBD (N=7016)		cDCD (N=291)		
		N	%	N	%	p-value
Donor Age		48,1		48,1		ns
Recipient Age		48,6		56,4		<0,05
Cause of ESRD	Diabetes	588	8,4%	39	13%	< 0,05
	PKD	1197	17%	47	16%	
	Nephroangio-sclerosis	585	8%	43	15%	
cPRA (%)	0%	4039	57%	172	59%	< 0,05
	1-84%	2361	34%	116	40%	
	85-100%	616	9%	3	1%	
Dialysis	Preemptive	753	11%	45	18%	< 0,05
Time spent on dialysis (months		41,8		35,2		ns
Waiting time (month), mean		27.6		24,3		ns
CIT (h), mean		16.3		10.2		<0.05

Results - Preliminary outcomes study

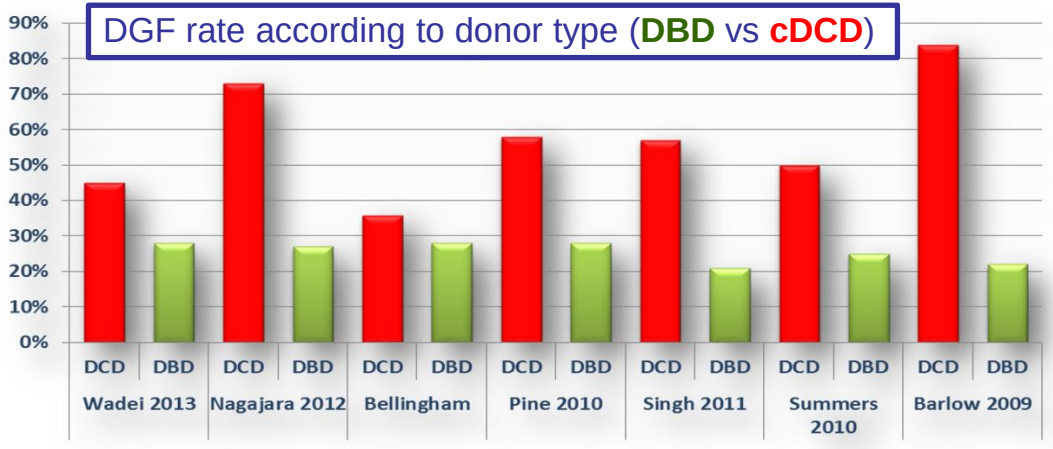
- **Similar PNF rate**
- **Lower DGF: rate 7%**
- **Lower eGFR at discharge**:

	DBD (N=7016)		cDCD (N=291)		
PNF	166/6201	2,7%	7/291	2,4%	NS
DGF	159/5961	19,4%	15/192	**7,8%**	**<0,05**
Initial hospitalization (day) , mean	14,5		13,4		NS
eGFR at discharge (MDRD, ml/min)	45,8		**49,3**		**<0,05**

Similar results after matching analysis

Criteria used for the matching

- Donor / Recipient Age +/- 10 years
- Time spent on dialysis : preemptive tx, < 36 months, ≥ 36 months
- Cause of ESRD : Diabetes vs other
- cPRA : 0%, 1-84%, 85-100%



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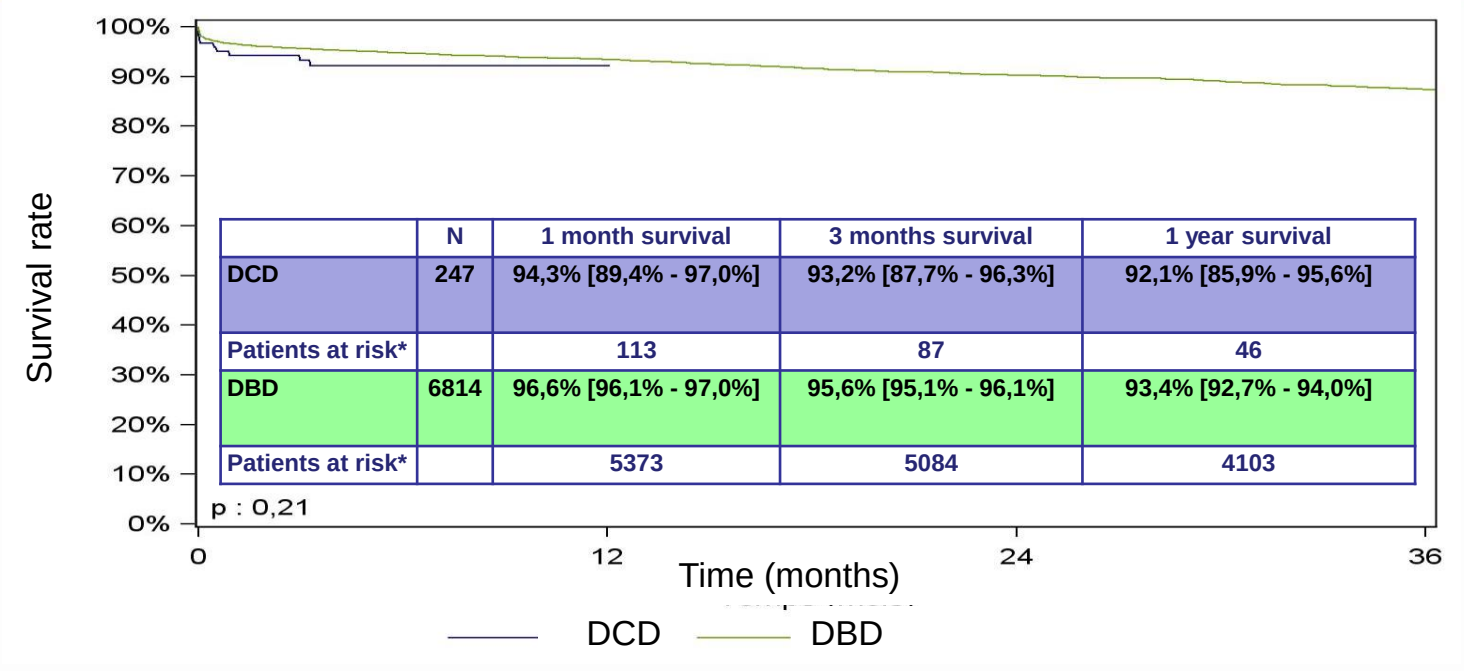
Short & medium term graft outcome similar to that of kidney recovered from DBD donors



	N	1 month survival	3 months survival	1 year survival
DCD	247	94,3% [89,4% - 97,0%]	93,2% [87,7% - 96,3%]	92,1% [85,9% - 95,6%]
Patients at risk*		113	87	46
DBD	6814	96,6% [96,1% - 97,0%]	95,6% [95,1% - 96,1%]	93,4% [92,7% - 94,0%]
Patients at risk*		5373	5084	4103

Mean and median creatinine at 1 year : 125 & 111 µmol/l (Q1 94, Q3 142)

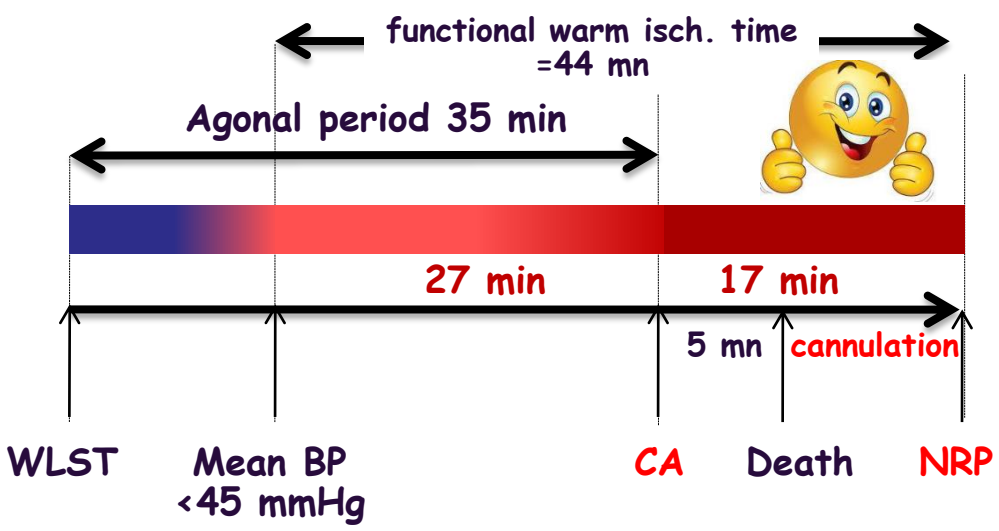
Case study of cDCD PNF

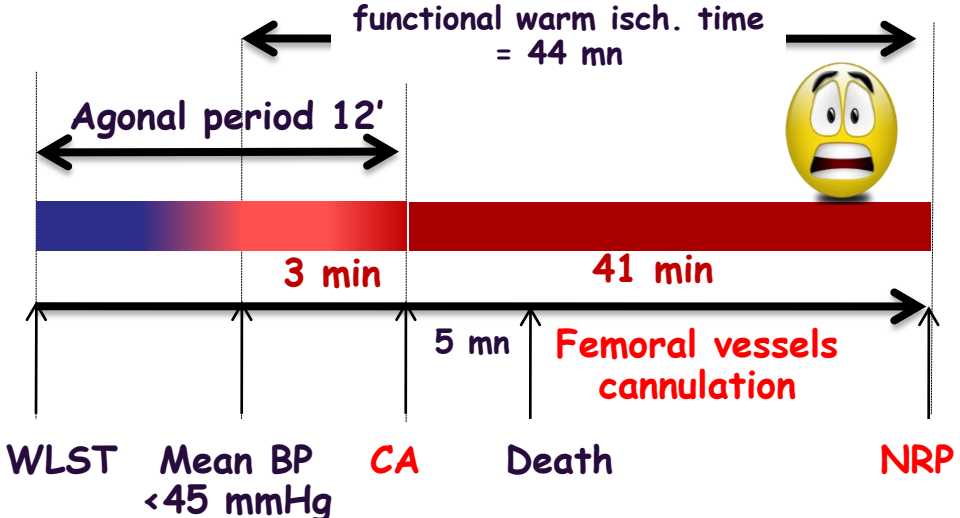
- Correlation between no flow period and renal function at discharge

Circulatory arrest		Q1-2 < 20 min	Q3 :20-27 min	Q4 ≥ 27 min
eGFR	N	74	39	46
	Mean	52,8	51	36,5

7 cases of primary non function

- 3 related to recipient comorbidity ,
- 4 related to prolonged time of circulatory arrest and subsequent cortical necrosis



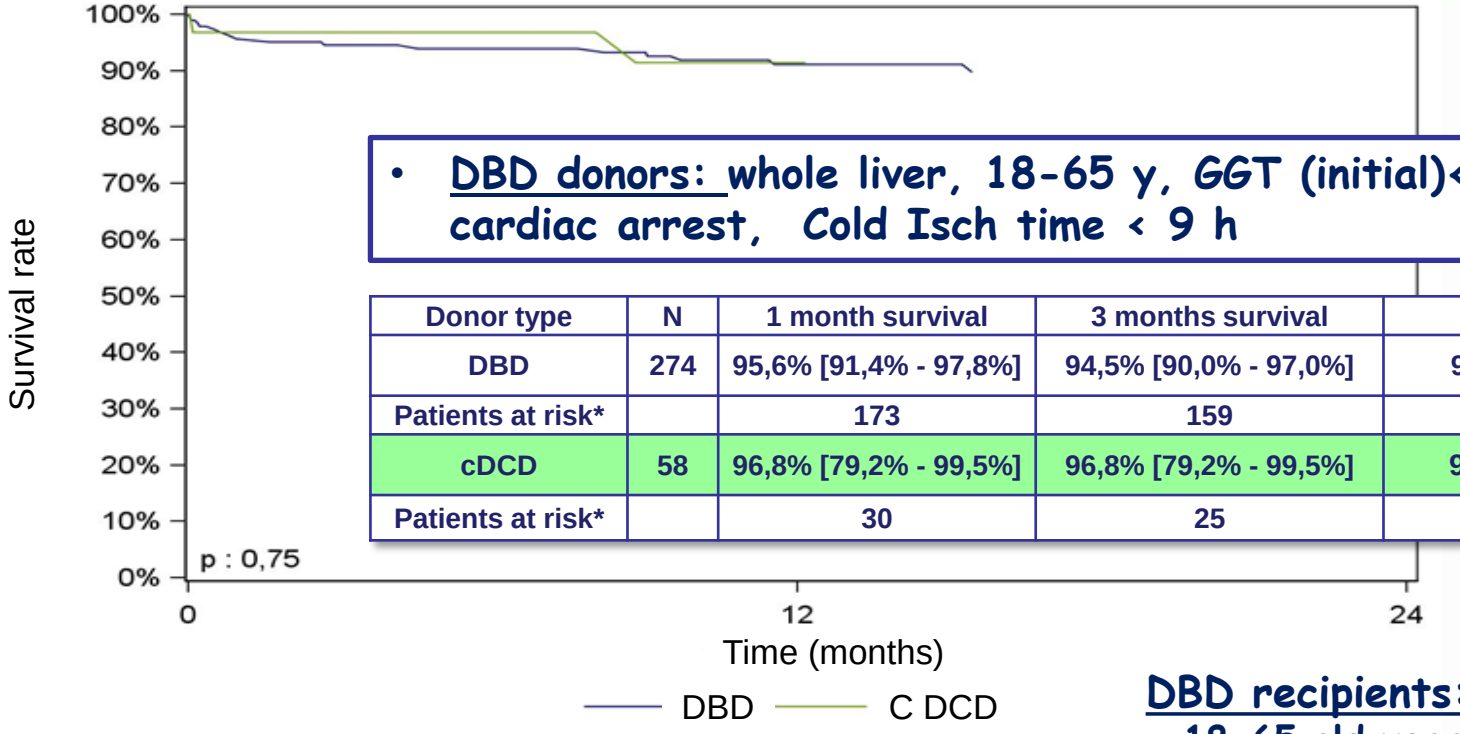


75 liver transplants NRP mandatory

National protocol

- **Recipient age** : mean 57 y , med: 59,3 y , +/- 8,1, max 66 ……..**< 66 y**
- Only **1srt transplant**.....……..**Retransplant excluded**
- Portal vein thrombosis 9 (14%) …….....**Not recommanded**
- History of hepatectomy (21%) ……**Major hepatectomy not recommanded**
- Liver disease : HCC (71%), cirrhosis (without HCC) 22%, other tumor 3%
- Waiting time : mean 6 months, median :4 months
- **MELD at transplant**: mean 13,1, median 12, +/- 3, 3 > 25 ……..…….. ……**< 25**
- **Functional warm ischemia time** mean 23 min, med 22 Q1 20 min, Q3 27 mn**…….. < 30 min**
- **Cold ischemia time** : mean 5,8 h, median 5,7 h……..…….....**≤ 8 h**
- **ALT kinetic**……... **< 4 x the upper normal value during NRP**
- **Frozen liver biopsy**…….. **Steatosis < 20%, Fibrosis < F2 (METAVIR)**

Short & medium term patient outcome similar to that of liver recovered from “ideal” DBD donors (2015-2017)



- **DBD donors:** whole liver, 18-65 y, GGT (initial)<50, no initial cardiac arrest, Cold Isch time < 9 h

Donor type	N	1 month survival	3 months survival	1 year survival
DBD	274	95,6% [91,4% - 97,8%]	94,5% [90,0% - 97,0%]	91,1% [85,6% - 94,6%]
Patients at risk*		173	159	114
cDCD	58	96,8% [79,2% - 99,5%]	96,8% [79,2% - 99,5%]	91,4% [68,5% - 97,9%]
Patients at risk*		30	25	12

DBD recipients:

- 18-65 old years, MELD <25,
- 1st transplant, no Acute Liver Failure

75 liver transplants 8 centers

- 3 primary non function
  - 1 non eligible patient: UNOS status 2, MELD 29, complete portal thrombosis, history of major hepatectomy
  - 1 ABO incompatible transplant (blood group mistake)
  - 1 artery thrombosis (patient disability)
- 5 deaths
  - 2 non eligible patients with PNF
  - HCC recurrence
  - 2 post transplant malignancies
- 1 graft loss at D7 (initial graft function)
  - Thrombosis of sus-hepatic veins

- National survey
  - No ischemic cholangiopathy
- Hospital Pitié Salpétrière (Pr Scatton, Dr Savier)
  - No reperfusion syndrome
  - Rare and moderate EAD

EAD	DBD (control)	cDCD
Absent	21 (58%)	13 (87%)
Light	6 (17%)	0 (0%)
Moderate	6 (17%)	2 (20%)
Severe	2 (6%)	0 (0%)

EAD : Salvalaggio, Einstein 2013

12 lung transplants

- Procurement in 4 sites : Bicêtre –Foch – Poitiers – Pitié Salpêtrière
- Transplant in 2 sites : Marie-Lannelongue – Foch
- Trachea is re-intubated and the lungs re-inflated after death.
- Transfer to theater without ventilator (tube clamped during transfer)
- Pneumoplegia and lung procurement with NRP in place and functional
- Ex vivo lung perfusion is mandatory
  - Rehabilitation and viability test
  - Extended criteria donors : circulatory arrest ≥ 60 min, ICU length of stay > 6 days, high frequency of Chest CT scan abnormalities
- Duration of post transplant mechanical ventilation : 1 to 13 days
- All patients were discharged with functioning graft

To conclude

- Importance of an optimal and standardized national guidance
  - To increase acceptance by medical community and civil society
  - To improve results and allow more powerful analysis
- Time between admission and WLST, and causes of brain injury : different from International literature
  - ICU stay > 8 days
  - 50% of post anoxic brain damaged
- Beware of asystolic time
  - Rapid cannulation of femoral vessels (limit the asystole period ?)

- Excellent transplant results
  - Major influence of systematic NRP use
  - warm and cold ischemia time compliance
  - Recipient selection criteria
- National study in progress
  - Ischemic cholangiopathy rate ? (systematic 1 year MRI)
- Impact of very low DGF rate in long term?
  - Wai et al conclude that recipients of DCD kidneys with DGF experienced a higher incidence of overall and death censured graft loss compared with those without DGF

Association Between Delayed Graft Function and Graft Loss in Donation After Cardiac Death Kidney Transplants—A Paired Kidney Registry Analysis

Wai H. Lim, MBBS, PhD, FRACP,[1,2] Stephen P. McDonald, PhD, FRACP,[2,3] Graeme R. Russ,[2,3] Jeremy R. Chapman, AC, MD, FRCP, FRACP,[4] Maggie KM. Ma,[5] Henry Pleass, MD,[4] Bryon Jaques,[6] and Germaine Wong, PhD[2,4,7,8]

Transplantation, 2017

Perspectives

- Program **expansion**
  - **Training** for professionals
  - Specific **financial sum** (multiplied by 2 / DBD sum)
- Develop **lung** procurement and transplant
- Initiate **pancreas** procurement and transplant
  - Procedures approved in Scientific & Medical committee
- Extend DCD program to **pediatric donors**
- Optimization of **normothermic perfusion period**
- Increase **donor age** according suitability criteria and restricted warm ischemia times
- Initiate discussion on **heart** procurement and transplant

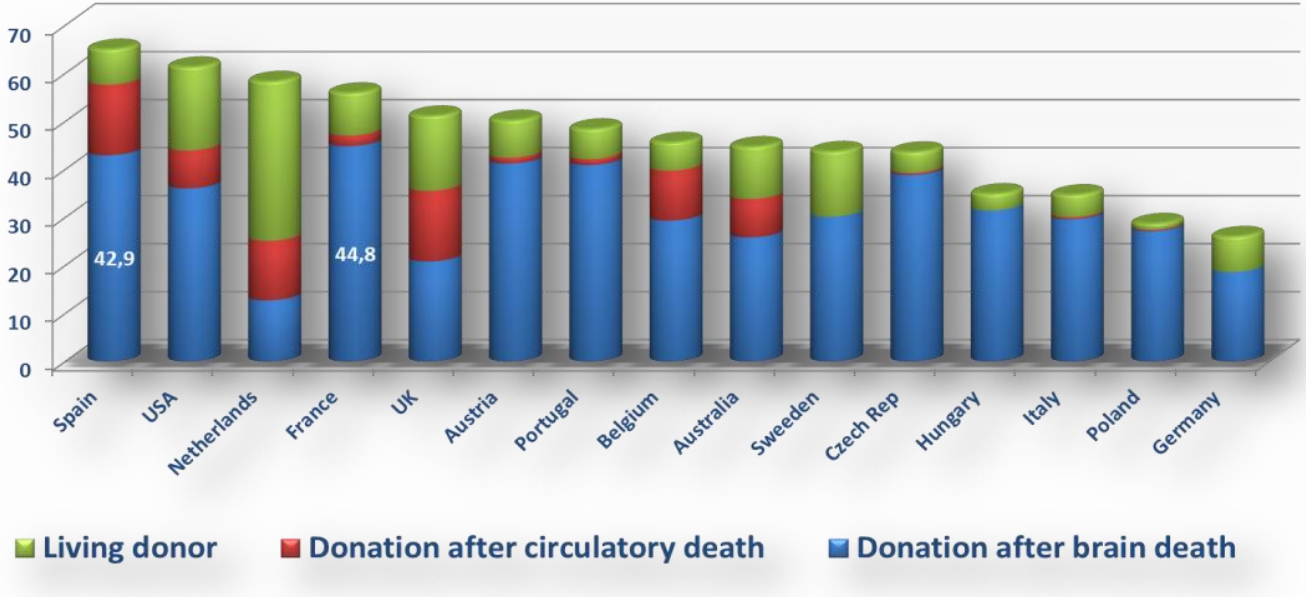
Appropriate training for professionals

Post-mortem interventions to preserve organs : how to place NRP lines in ICU, appropriate and well-functioning NRP,..

Program expansion

Potential & actual DBD donor rate increased in France during this period

- DCD should be considered only when donation after brain death will not possible;



Kidney transplant rate (pmp) according to the country in 2016

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Alone we go faster; Together, we go further !

Deep thanks to

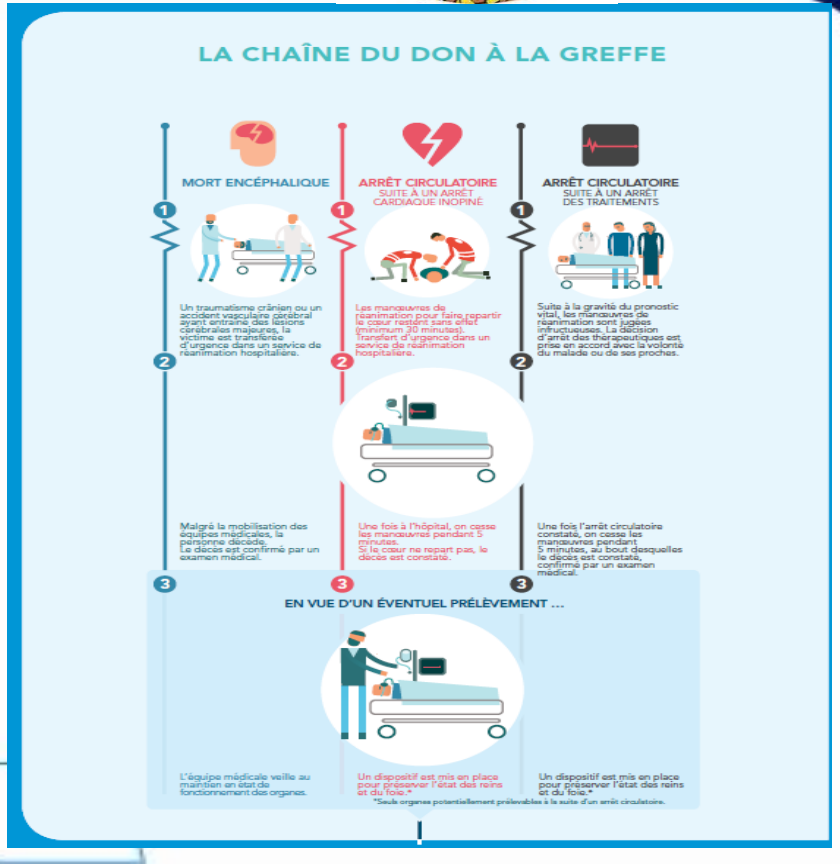
- The National Steering Committee of donors after circulatory death

And to

- Intensive care teams
- Coordination of organ donation
- Surgical and transplant teams

From all authorized centers

End-of-life care allows the opportunity to donate organs and tissues after death if this is the patient's will



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