

MARINELLA ZANIERATO

Perfusione Normotermica Regionale: come si valuta il potenziale donatore DCD?

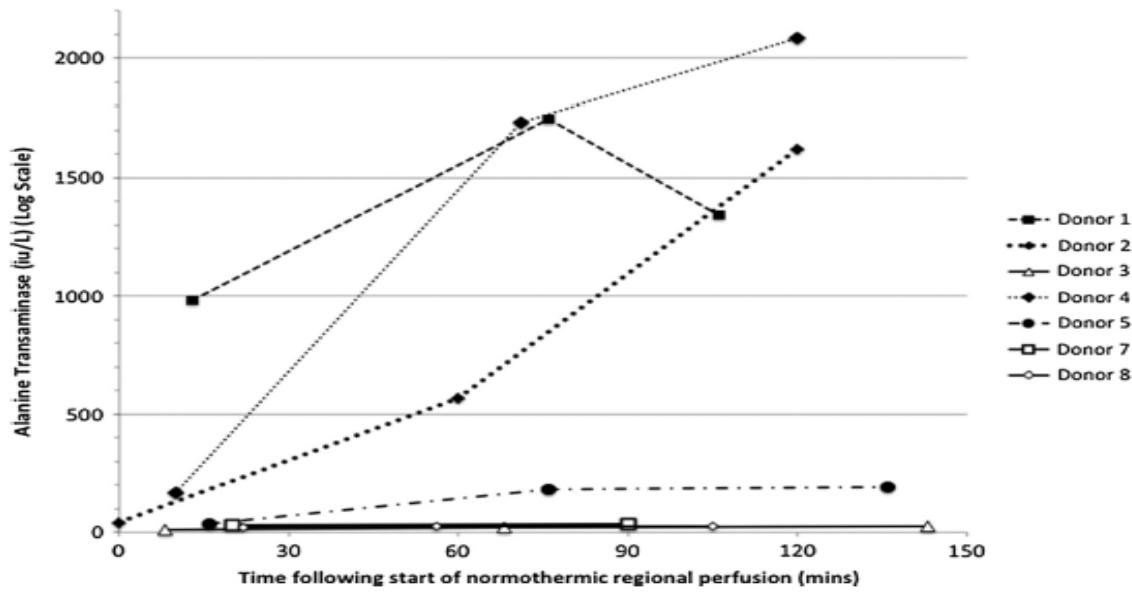
STATI GENERALI



RETE NAZIONALE
TRAPIANTI

6.7.8 NOVEMBRE

ROMA



(*Transplantation* 2014;97: 1272–1278)

Dynamic in-situ organ assessment: Ideal *criteria* for DCD graft selection during nRP

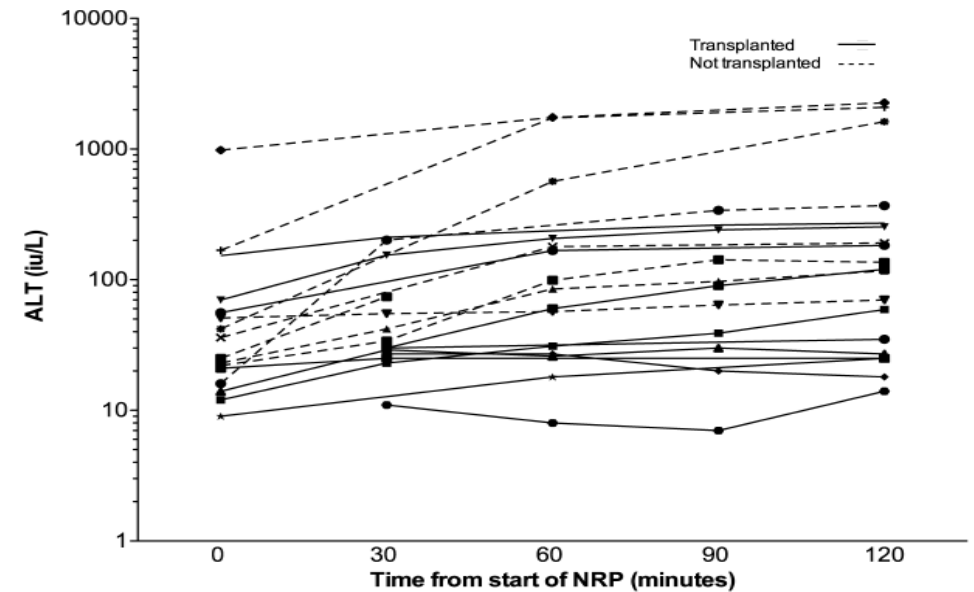
Liver donor after cardiac death acceptance criteria

Phase III: NECMO

Time	<4 h
Donor	Initial AST, ALT < 3 × ULN Final AST, ALT < 4 × ULN
Method	Pump flow >1.7 L/min, with fogarty in supraceliac aorta pH maintained 7.0–7.4

American Journal of Transplantation 2007; 7: 1849–1855

Oniscu et al



American Journal of Transplantation 2014; 14: 2846–2854

Parameters during NRP

Author Journal Year			SELECTION CRITERIA				OUTCOME						
	N	Donor type	Transaminase IU/L	Lactate	Flow L/min	pH	Liver biopsy	PNF %	EAD %	ITBL %	Patient surv. %	Graft surv. %	FU mo.
Fondevila AJT 2012 ¹	34	uDCD	Initial < 3 x ULN Final < 4 X ULN	N/A	> 1.7	7-7.4	N/A	N/A	N/A	8	82	70	12
Oniscu AJT 2014	11	cDCD	Initial < 3 x ULN Final < 4 X ULN	N/A	1.7 - 4*	7.35 - 7.45	N/A	9.1	36.4	0	81.8	81.8	10
Savier Liver Transpl 2015	13	uDCD	ALT _{2h} < 200	N/A	> 1.7*	7 - 7.4*	Ms < 20%	23	31	10	85	69	12
Caralt Transplant Proc 2016	3	cDCD	Initial < 3 x ULN Final < 4 X ULN	normal values	> 1.7	7.35 - 7.45	N/A	0	0	0	100	100	14
Minambres AJT 2016	11	cDCD	< 4 X ULN (at 30 and 60 min)	N/A	2 - 2.4*	7 - 7.4*	N/A	9.1	N/A	0	N/A	90.1	12
De Carlis Liver Transpl 2018 ²	20	uDCD cDCD	ALT ≤ 1000	downward trend	N/A	N/A	Ms ≤ 30% Ishak ≤ 1	10	24	10	95	85	12
Watson AJT 2018	43	cDCD	ALT < 200 ALT < 500	fall	2.5 - 3*	N/A	N/A	0	12	0	100	97.7	3
Ruiz Transplantation 2019	46	cDCD	Initial < 3 x ULN Final < 4 X ULN	decrease	> 1.7	7.35 - 7.45	N/A	0	23		100	100	19
Hagness Transplant Proc 2019	8	cDCD	N/A	drop	N/A	N/A	N/A	0	0	0	100	100	12 (6)
Hessheimer J Hepatol 2019	95	cDCD	Initial < 3 x ULN Final < 4 X ULN	N/A	> 1.7	N/A	N/A	2	21	2	93	88	20

cDCD = controlled donation after circulatory death, EAD = early allograft dysfunction, FU = follow-up, ITBL = ischemic-type biliary lesions, Ms = macrosteatosis PNF = primary nonfunction, uDCD = uncontrolled donation after circulatory death, ULN = upper limit of normal.

Perfusion parameters and graft evaluation

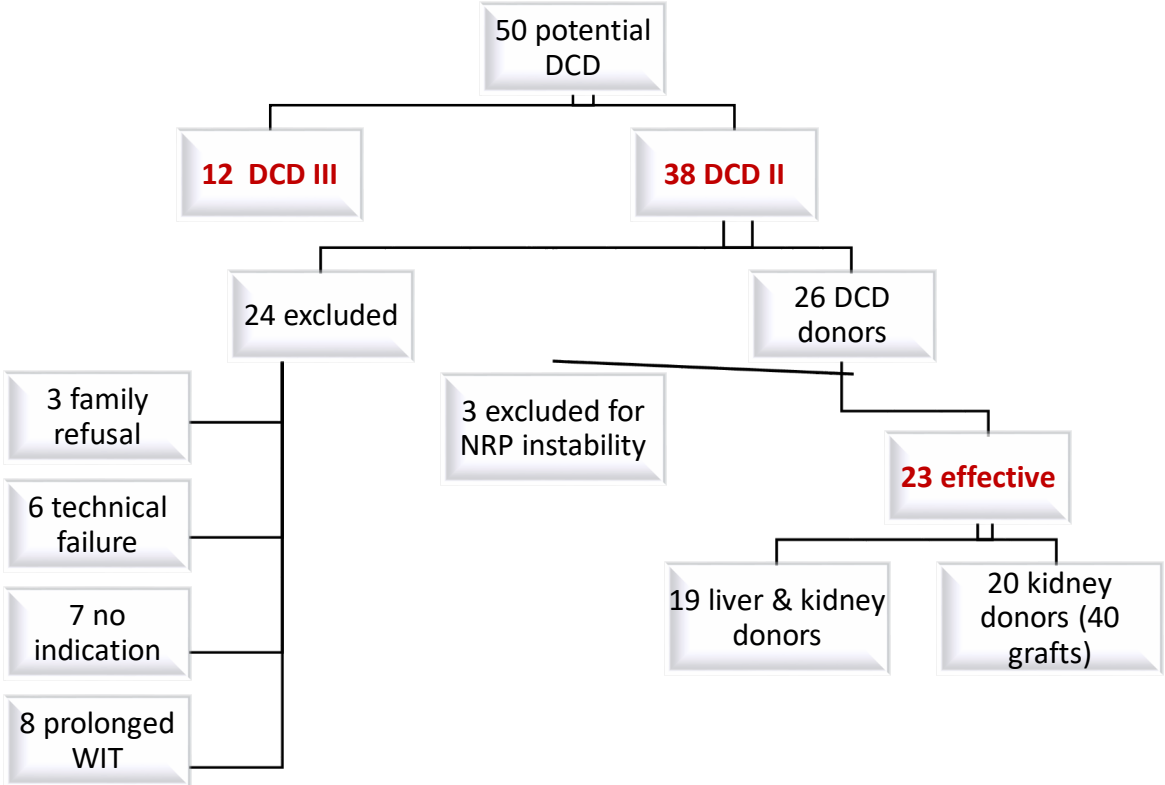
Author	BF	Lactates	Mean pressure	svO2	pH
Oniscu 2014	> 1.7 l/min/m2	NS	NA	NA	NA
Minambres 2017			<p>NRP setting (pump flow, fresh gas clearing, FiO2) are poor and there are no comparative studies</p>		
De Carlis 2018					
Watson 2018					
Peris 2018	2-2.4 lmin/m2	NS	60-65 mmmHg	NA	Increase during NRP
Hessheimer	> 1.7 l/min/m2	NA		NA	7.-7.4

4

ease
ng NRP
out
ection

Optimal in situ preservation

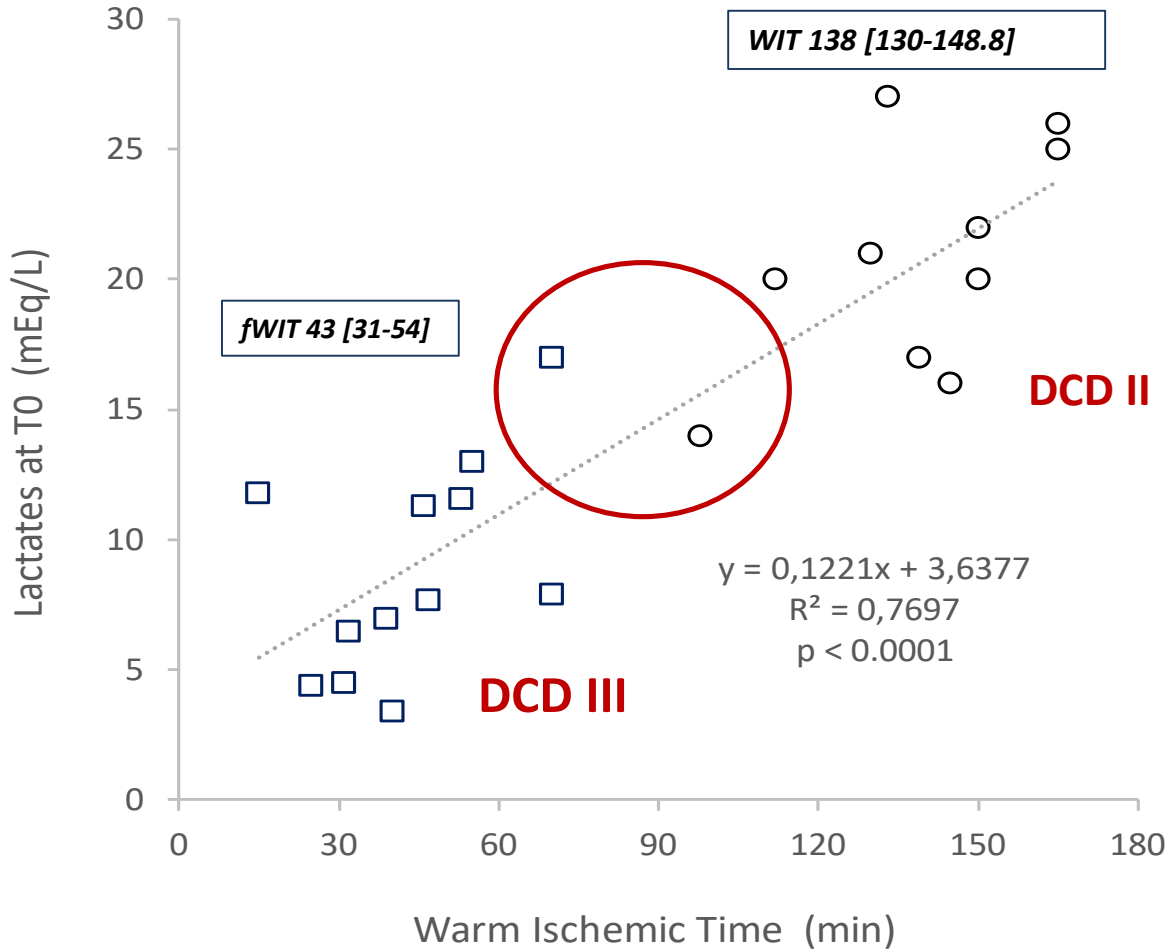
DCD (n.26)	
male,n (%)	24
Age, years	53
Ischemic times DCD II	
WIT	138.0 [130.0 to 148.8]
Ischemic time DCD III	
fwIT	43.0 [31.5 to 54.0]
Time ECLS pre-mortem (hrs)	30.11 (17.75-43.98)



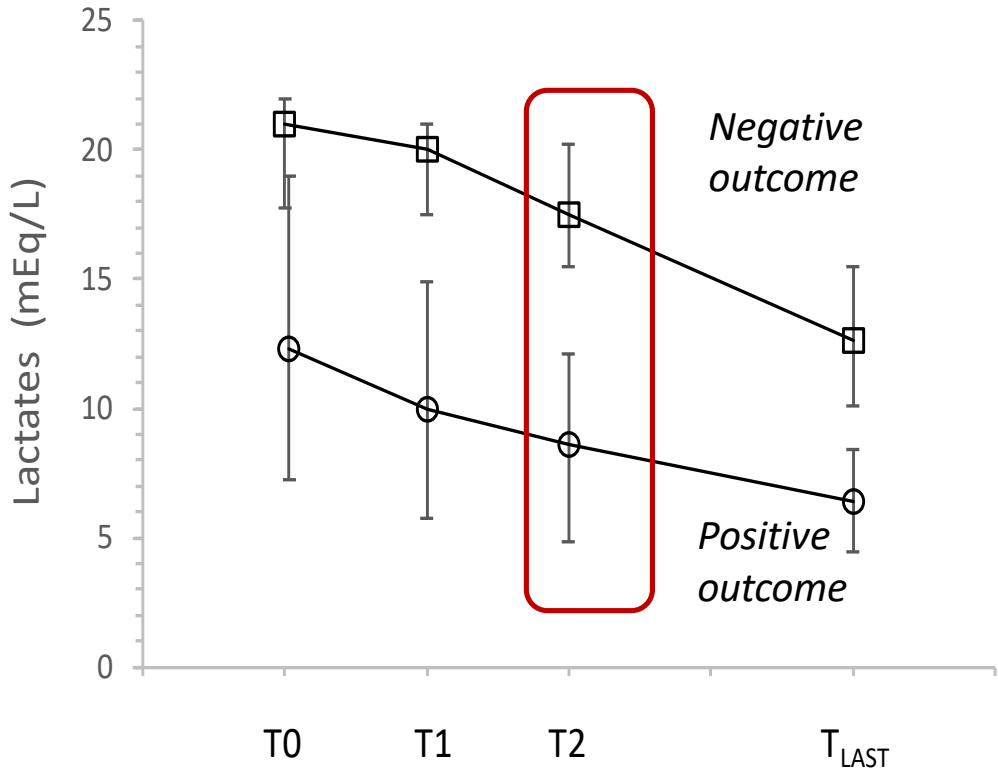
Positive short term graft recovery

Negative short term graft recovery

Optimal in situ preservation



lactates at T0 linearly increased with WIT
 Blood lactates decreased at a rate of -1.1 mEq/L/h [-2.1 to -0.5]



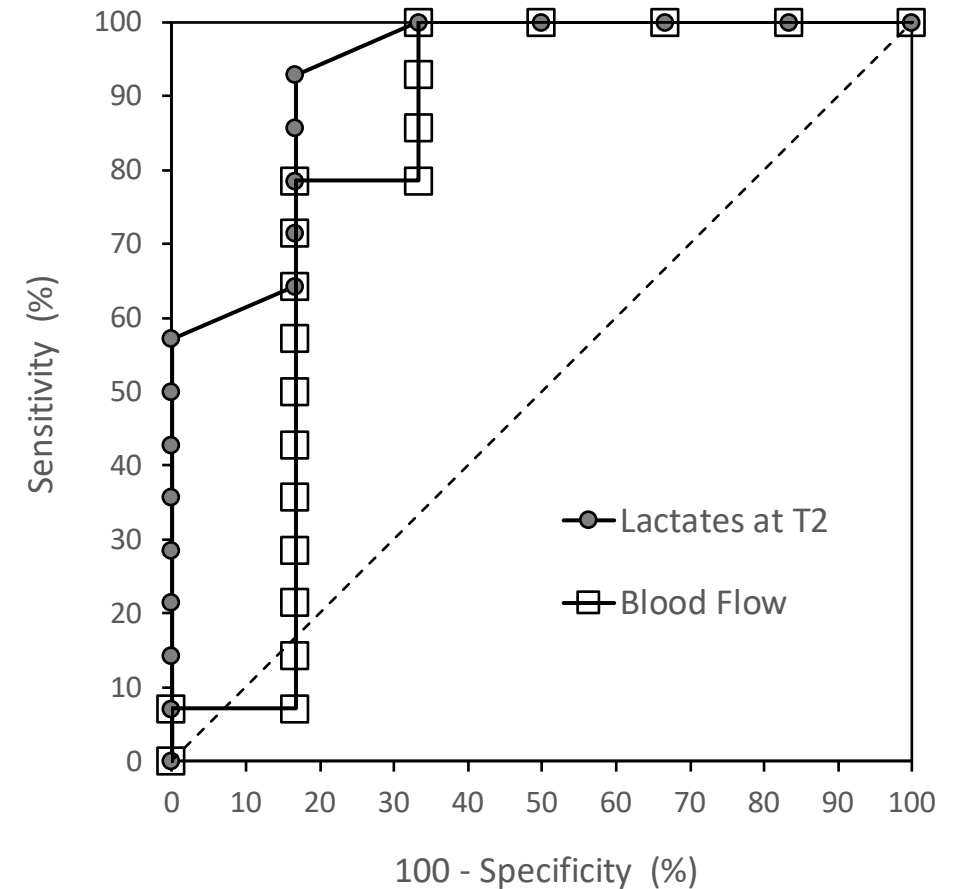
Kidneys in situ perfusion outcome

		Positive (donors n=14)	Negative (donors n=6)	P value
Age	(years)	53.5 [47.0, 57.0]	50.5 [49.0, 59.0]	0.8046
Male	(n [%])	13 [92.9]	6 [100.0]	1.0000
DCD 2 / 3	(n [%])	6 [42.9] / 8 [57.1]	5 [83.3] / 1 [16.7]	0.1571
Ischemic Time	(min)	62.5 [46.0, 130.0]	146.5 [138.0, 150.0]	0.0320
NRP length	(hours)	4.0 [3.0, 5.0]	4.0 [4.0, 5.0]	0.8322
Blood Flow	(L/min)	2.9 [2.8, 3.2]	2.0 [1.8, 2.8]	0.0320
Lactates T0	(mEq/L)	12.3 [7.1, 20.0]	21.0 [17.0, 22.0]	0.0391
Lactates T2	(mEq/L)	8.6 [4.3, 12.7]	17.5 [15.0, 21.0]	0.0030
Lactates T _{LAST}	(mEq/L)	6.4 [4.3, 8.6]	12.7 [9.7, 16.0]	0.0013
Δ Lactates	(mEq/L/h)	-1.6 [-2.2, -1.1]	-1.2 [-2.6, -0.4]	0.8046
Urea T0	(mg/dL)	44.0 [35.3, 56.0]	42.5 [35.0, 54.0]	0.9199
Urea T2	(mg/dL)	49.5 [47.0, 58.0]	59.0 [40.0, 64.0]	0.7042
Δ Urea	(mg/dL)	8.5 [3.0, 11.0]	7.0 [-5.0, 23.0]	0.9135
Creatinine T0	(mg/dL)	1.2 [1.1, 1.4]	1.3 [1.2, 1.5]	0.4537
Creatinine T2	(mg/dL)	1.3 [1.1, 1.6]	1.4 [1.3, 1.7]	0.3929
Δ Creatinine	(mg/dL)	0.1 [0.1, 0.3]	0.1 [0.0, 0.3]	0.8407

Independent factor associated with positive kidney recovery (p=0.003):

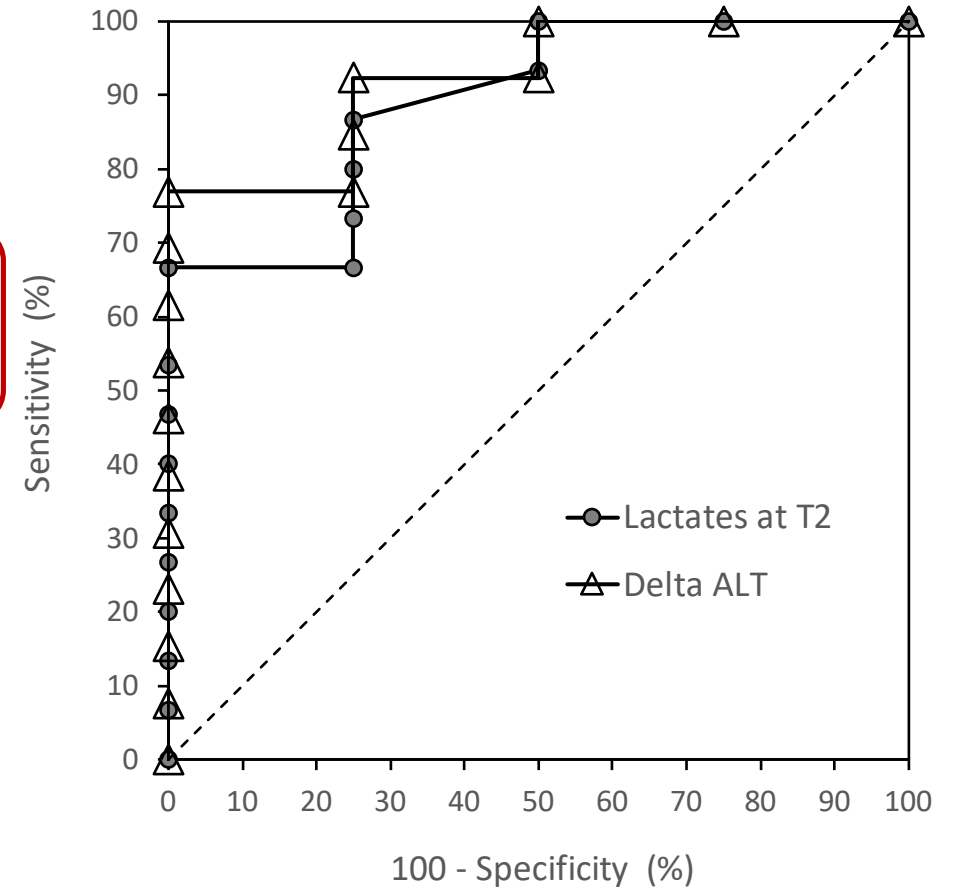
1. Blood lactates after 2 hours of NRP (T2)

2. Mean blood flow of NRP: 2.9 L/min [2.6 to 3.1].



Liver in situ perfusion outcome

		Positive (n=15)	Negative (n=4)	P value
Age	(years)	53.0 [48.0, 56.8]	54.0 [49.0, 61.0]	0.6892
Male	(n [%])	15 [100.0]	3 [75.0]	0.2105
DCD 2 / 3	(n [%])	7 [46.7] / 8 [53.3]	3 [75.0] / 1 [25.0]	0.5820
Ischemic Time	(min)	70.0 [41.5, 130.0]	144.0 [96.5, 150.0]	0.0719
NRP length	(hours)	4.0 [2.3, 5.0]	4.5 [4.0, 5.0]	0.2197
Blood Flow	(L/min)	2.8 [2.6, 3.0]	2.4 [1.9, 4.4]	0.4839
Lactates T0	(mEq/L)	11.8 [7.3, 19.3]	21.0 [16.5, 22.0]	0.0717
Lactates T2	(mEq/L)	9.3 [4.8, 13.8]	18.0 [12.7, 23.5]	0.0188
Lactates T _{LAST}	(mEq/L)	7.0 [4.5, 9.3]	12.7 [10.2, 15.0]	0.0278
Δ Lactates	(mEq/L/h)	-1.6 [-2.1, -1.0]	-1.1 [-2.4, -0.3]	0.4839
ALT T0	(mg/dL)	302.0 [99.8, 397.5]	221.5 [187.0, 1616.5]	0.8415
ALT T2	(mg/dL)	289.0 [90.8, 519.8]	1284.0 [424.5, 2838.5]	0.0894
Δ ALT	(mg/dL)	12.0 [-112.8, 140.5]	513.0 [232.0, 1227.5]	0.0127
Bilirubin T0	(mg/dL)	0.4 [0.3, 0.8]	0.3 [0.3, 1.1]	0.6434
Bilirubin T2	(mg/dL)	0.3 [0.3, 0.5]	0.4 [0.3, 1.6]	0.8875
Δ Bilirubin	(mg/dL)	-0.1 [-0.1, 0.0]	0.1 [-0.1, 0.6]	0.5083

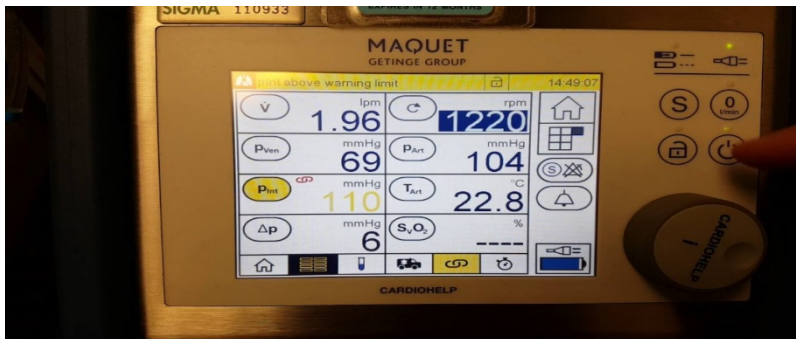


Donors with positive liver recovery had:

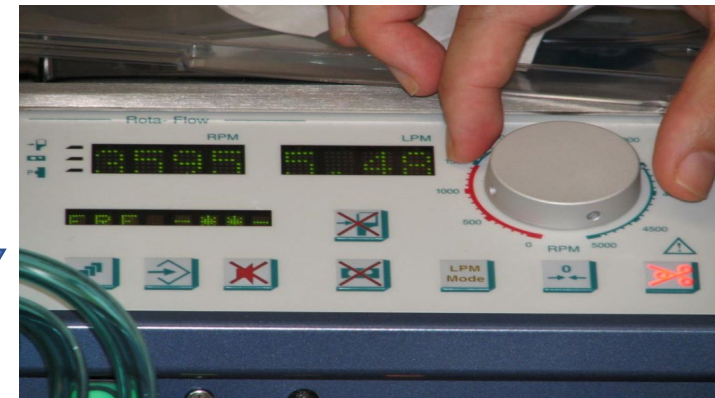
- 1. lower blood lactates at T2 and Tlast**
- 2. lower increase of ALT (Δ ALT during NRP)**

Donors with positive graft function outcome had:

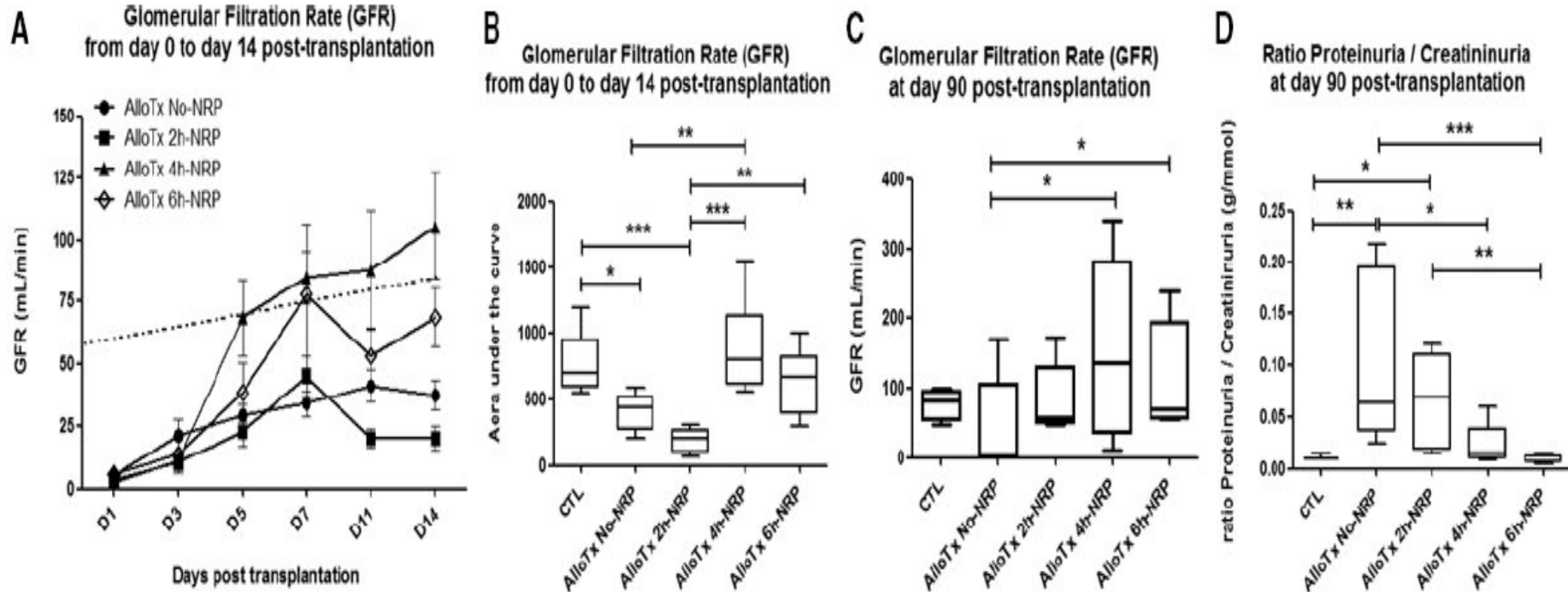
- shorter Warm Ischemic Time
- higher NRP blood flow
- lower blood lactates at T₀, T₂ and T_{LAST}



Blood flow and PAM



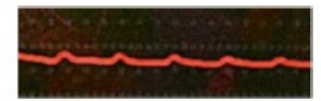
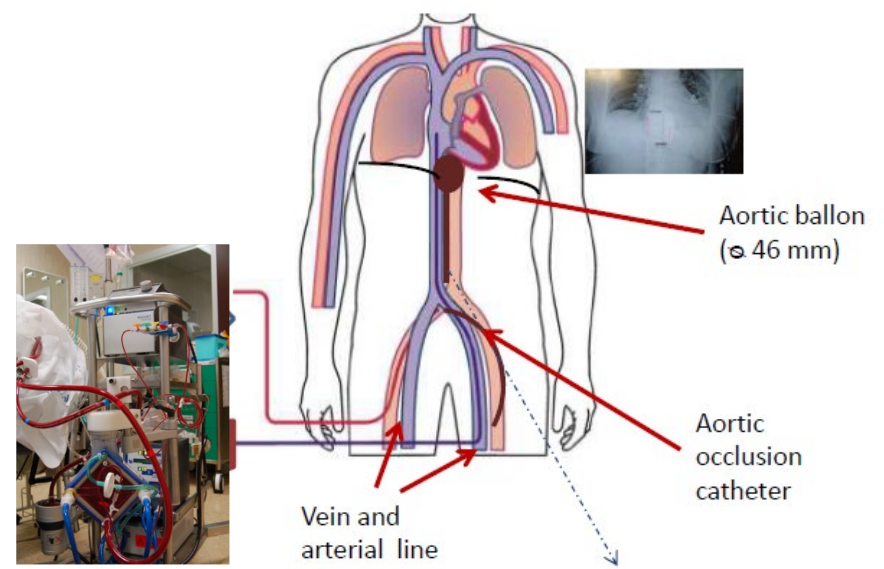
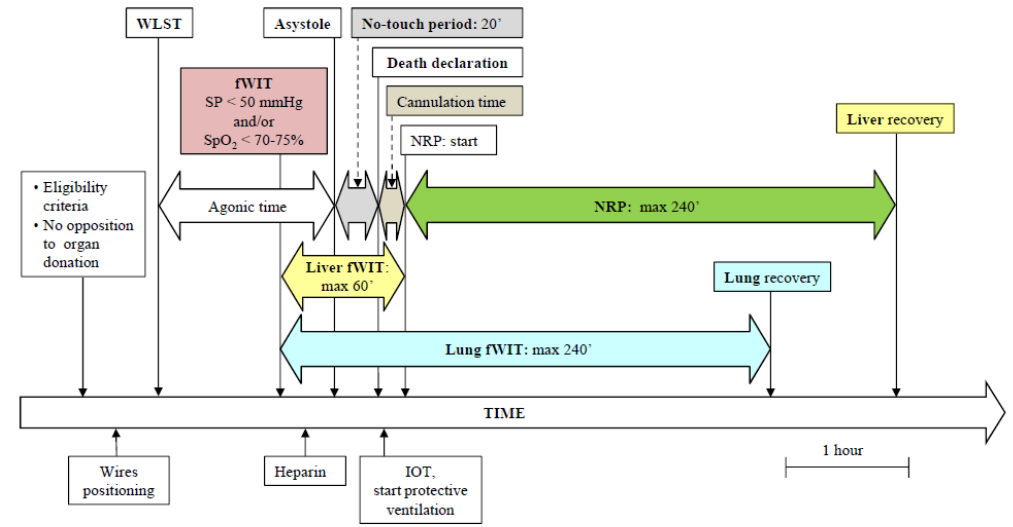
Defining the optimal duration for normothermic regional perfusion in the kidney donor: A porcine preclinical study



Injury markers were regulated by NRP
 At least 4 hours is necessary to obtain the highest benefits
 These levels increased significantly at 6 h-NRP

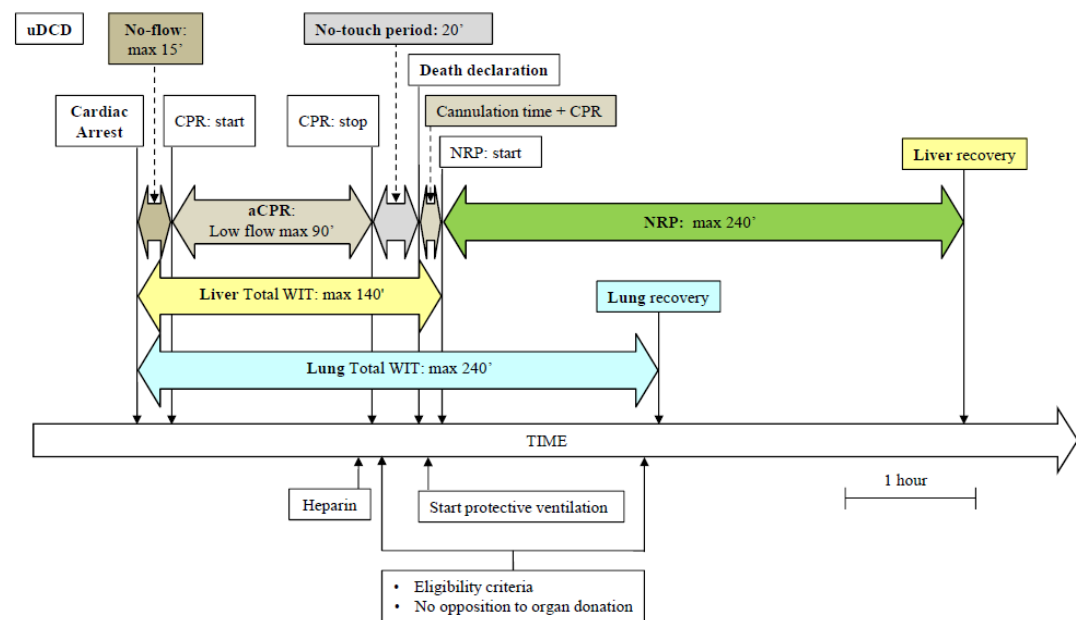
CPAP
PEEP 10 cmH₂O
FiO₂ 100%

cDCD



Non pulsatile perfusion pressure > 50 mmHg

Ventilatory Strategy:
 VT: 4-5 ml/kg
 RR 4
 PEEP 10
 FiO₂ 40%



NRP

What's next?

- REMOVAL OF INFLAMMATORY RESPONSE:
 - Cellular/molecular alterations in DCD
 - Pathways implicated in regeneration
- Safe extention of donor age due to minimization of other risk factors, such as prolonged ischemic time (in DCD III)

Conclusioni: quali parametri durante nrp?

- Lattati da 2 ore in poi
- Delta ALT
- BF > 2 l/min
- SvO2 > 60%
- PAM > 50 mmHg
- NRP durata: almeno 2 ore, meglio 4



STATI GENERALI
RETE NAZIONALE
TRAPIANTI

6·7·8 NOVEMBRE

ROMA