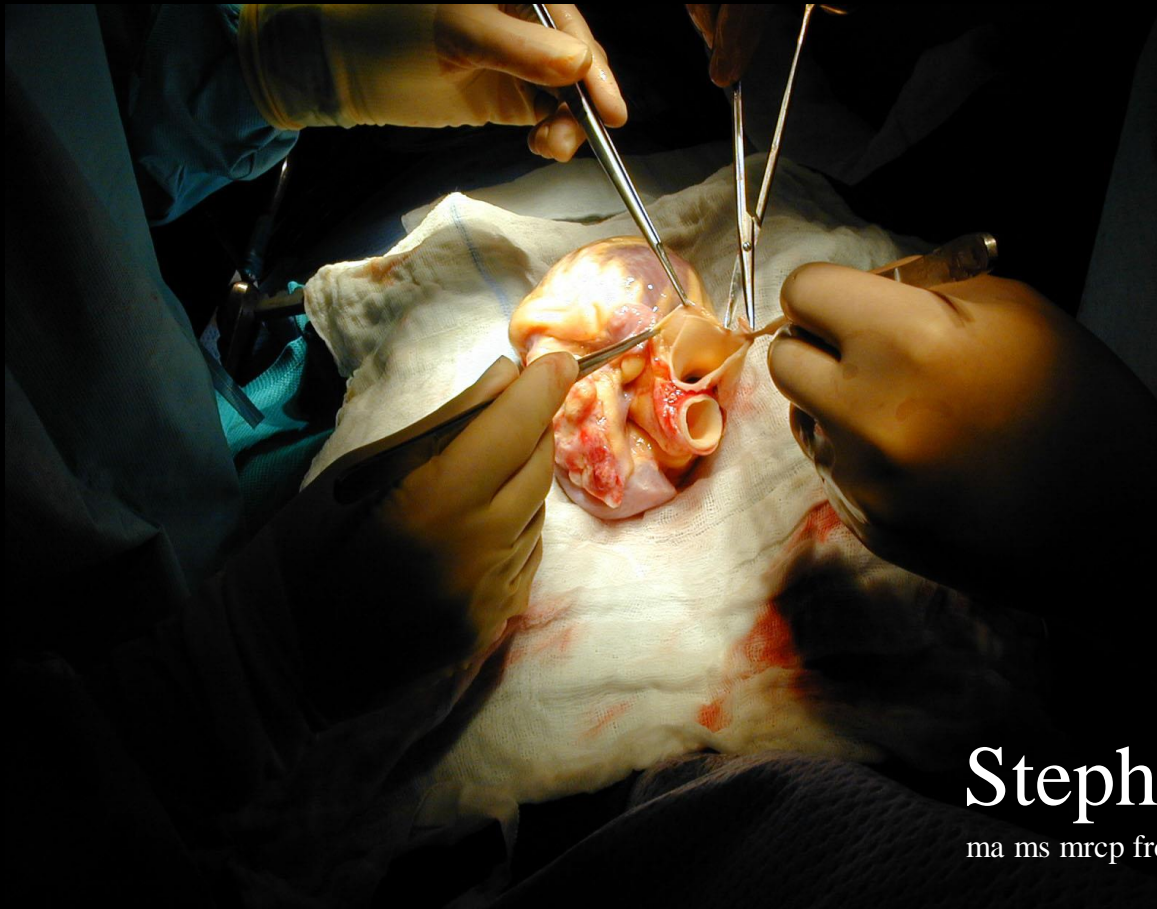


# BANFF-SCT

Will Normothermic Perfusion become the new standard for the maintenance of DCD donors?



31<sup>st</sup> March 2017

Stephen Large

ma ms mrep frcs(cth) frcs mba pae(rcp)

# conflicts of interest

*TransMedics halved cost of disposables in one of our experiments*

## Aims:

1. describe NP and TA-NRP
2. demonstrate the good results of TA-NRP, NP and DCD heart tx
3. consider the value of NRP and benefit to abdominal organ tx

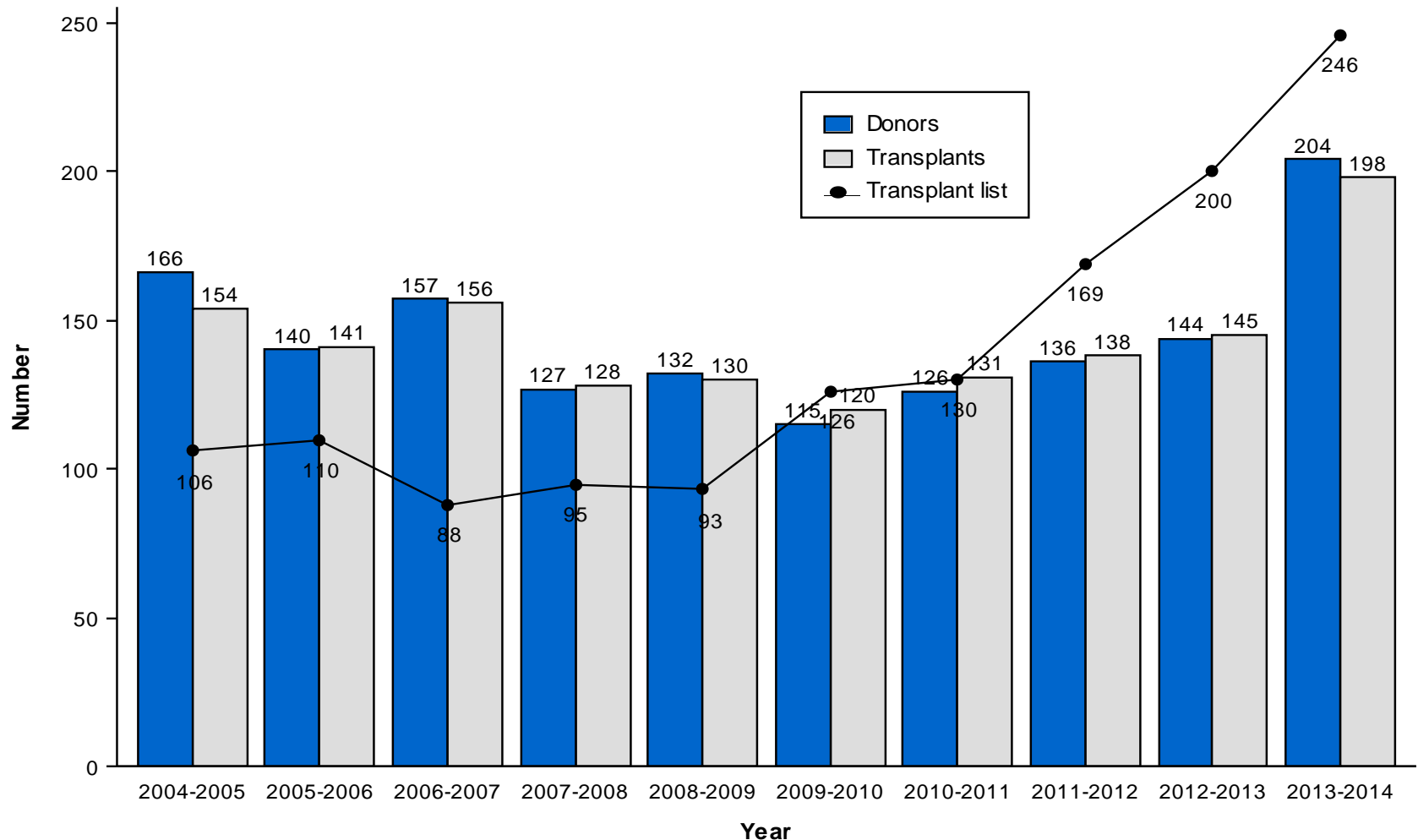
## Objectives:

1. to present our DCD heart transplant experience to date February 2017
2. to offer a Q&A session to present identified problems
3. to present our vision for future DCD activity

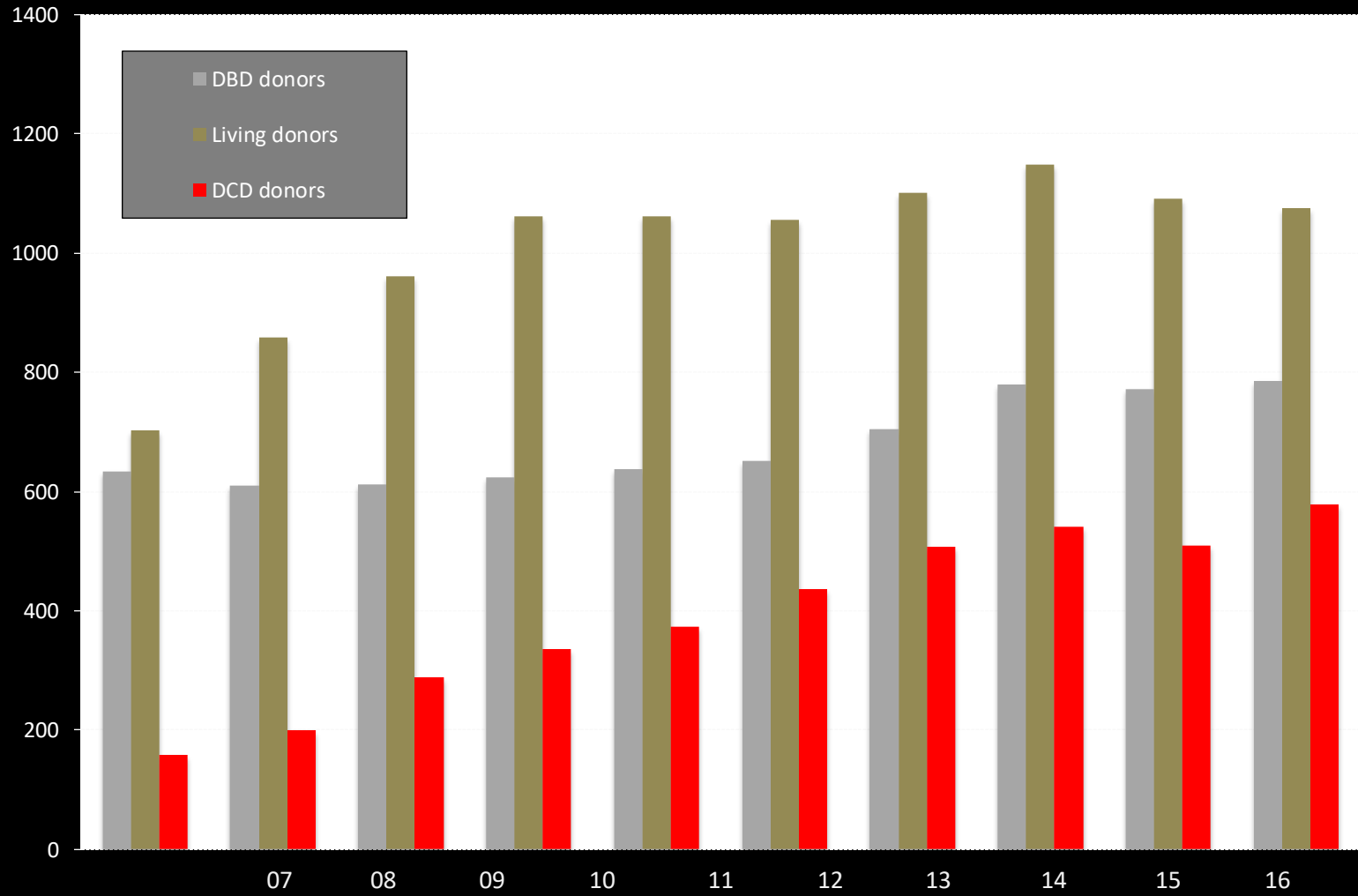


# UK Heart Transplant Activity

**Figure 7.1** Deceased donor heart programme in the UK, 1 April 2004 - 31 March 2014, Number of donors, transplants and patients on the active transplant list at 31 March



# NHSBT 2016 report



*NHSBT Annual Report on Cardiothoracic Transplantation 2013/2014. Available at [http://www.odt.nhs.uk/pdf/organ\\_specific\\_report\\_cardiothoracic\\_2014.pdf](http://www.odt.nhs.uk/pdf/organ_specific_report_cardiothoracic_2014.pdf)*

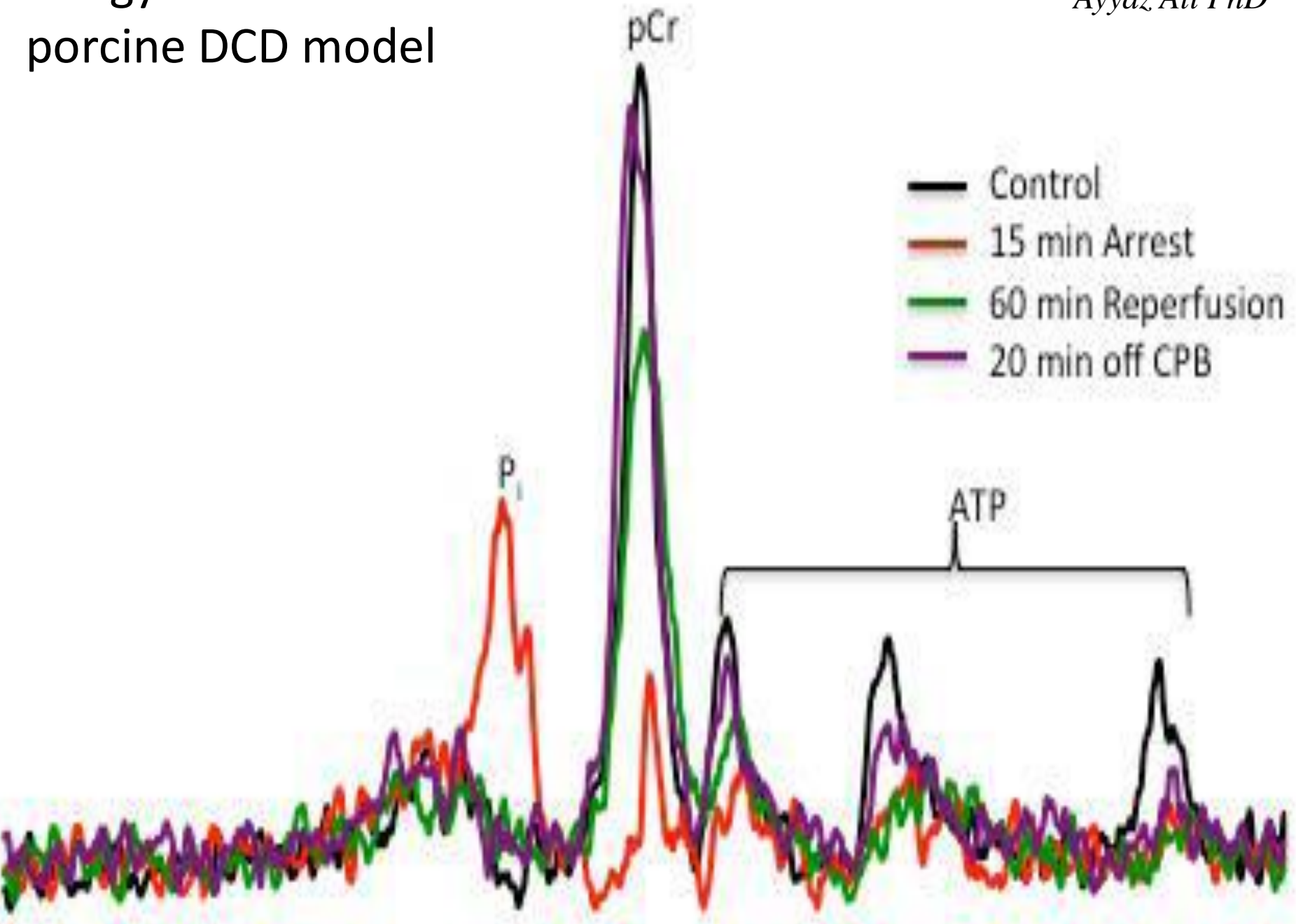
# What are we discussing today?

“Normothermic Perfusion as a standard for the maintenance of DCD donors”

- DCD results in profoundly ischaemic organs

# Energy stores in the porcine DCD model

Ayyaz Ali PhD



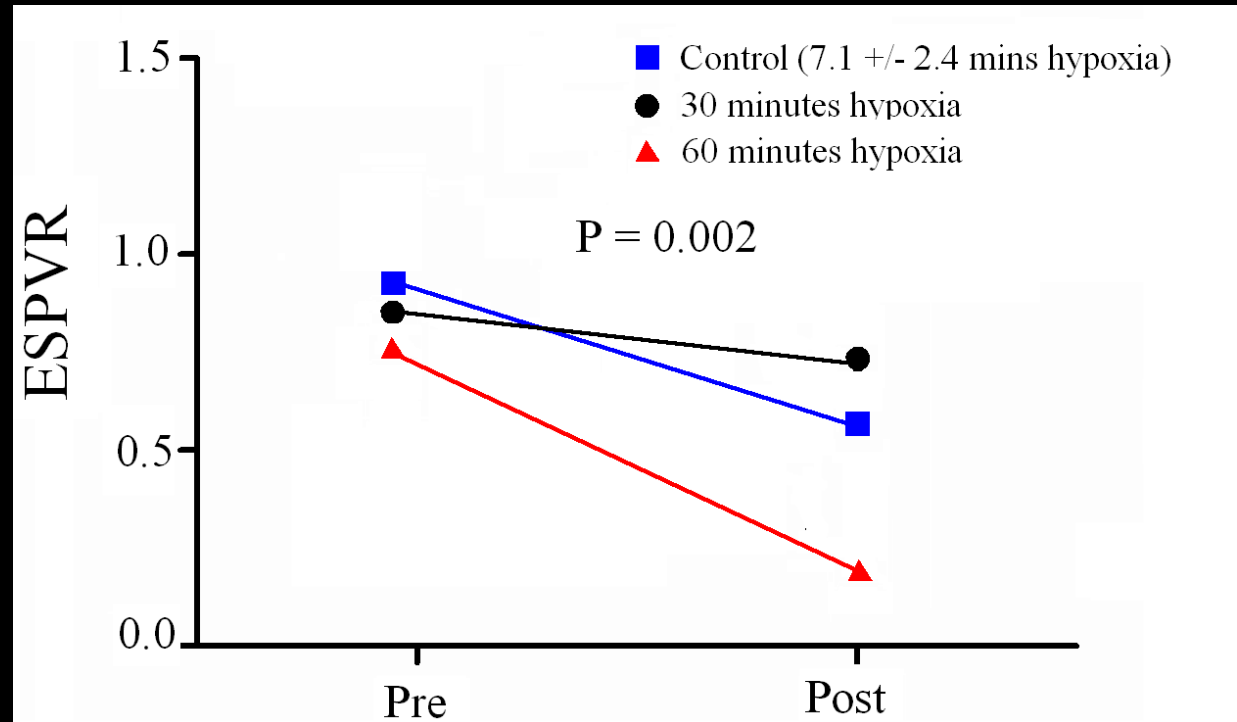
# What are we discussing today?

“Normothermic Perfusion as a standard for the maintenance of DCD donors”

- DCD results in profoundly ischaemic organs
  - There is a tolerance by the heart of ischaemia before irreversible organ damage.....

# DCD heart transplantation: How tolerant the heart to normothermic ischaemia?

1. Ayyaz Ali PhD



2. *Int Rev Cell Mol Biol.* 2012 ; 298: 229–317.

- and so for all organs

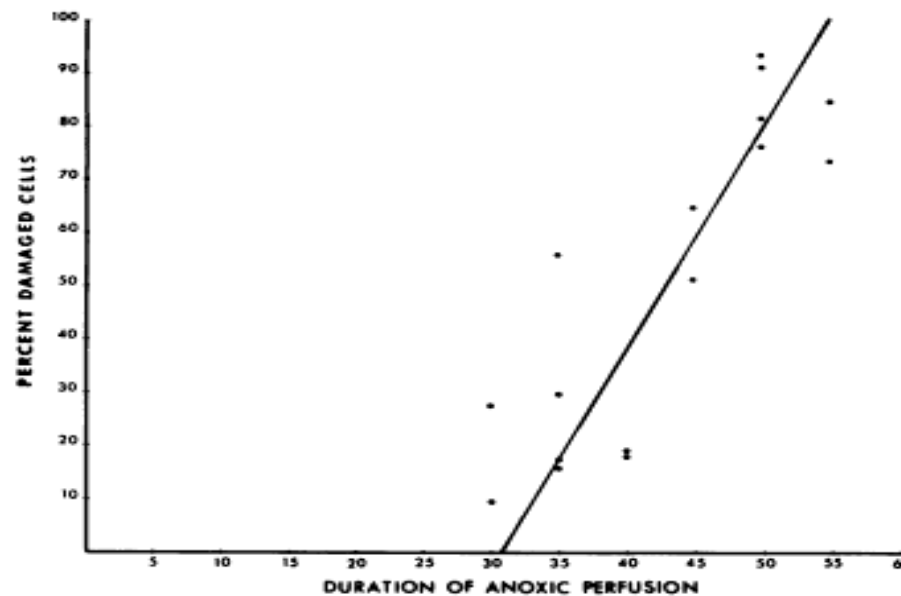


# Tolerance to duration of ischaemia (canine):

426

GANOTE ET AL

American Journal  
of Pathology



TEXT-FIGURE 4—The percent of severely damaged cells in hearts subjected to 30 to 55 minutes of anoxia and then reoxygenated for a total of 120 minutes perfusion was estimated by direct counts from four equally spaced light microscopic sections of each heart. The percent of damaged cells correlated linearly by regression analysis ( $r = 0.861$ ,  $P < 0.001$ ) with duration of anoxic perfusion between 30 and 55 minutes.

# What are we discussing today?

“Normothermic Perfusion as a standard for the maintenance of DCD donors”

- DCD results in profoundly ischaemic organs
- Must restore energy to the organ or lose the organ
  - In the donor (in-situ normothermic reperfusion or NRP)

# What are we discussing today?

“Normothermic Perfusion as a standard for the maintenance of DCD donors”

- DCD results in profoundly ischaemic organs
- Must restore energy to the organ or lose the organ
  - In the donor (in-situ normothermic reperfusion or NRP)
  - During transportation/storage (ex-situ normo-thermic organ perfusion or DPP)

# The Code Of Practice For The Diagnosis & Confirmation Of Death

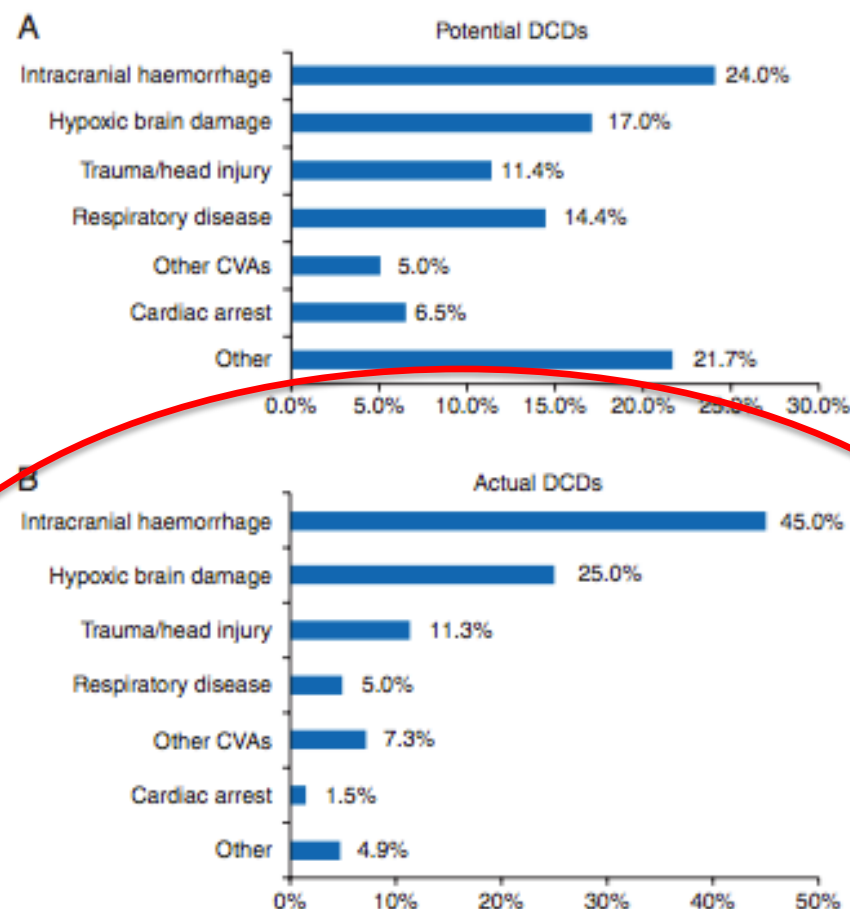
- After 5 minutes of continued cardiorespiratory arrest, the absence of pupillary responses to light, of corneal reflexes, and of motor response to supra-orbital pressure is confirmed
- Diagnosing death in this situation requires confirmation that there has been irreversible damage to the vital centres in the brain-stem due to the length of time in which the circulation to the brain has been absent.
- Cerebral perfusion should not be restored after death has been confirmed

ACADEMY OF  
MEDICAL ROYAL  
COLLEGES

A CODE OF PRACTICE FOR  
THE DIAGNOSIS AND  
CONFIRMATION OF DEATH

# Is DCD heart transplantation possible?

*Recent NHSBT update:  
probably 135 more donor /year*



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

*British Journal of Anaesthesia 108 (S1): i108–i121 (2012) Donation after circulatory death*  
*A. R. Manara 1\*, P. G. Murphy 2 and G. O’Callaghan 3*



*Blood and Transplant*

Papworth Hospital

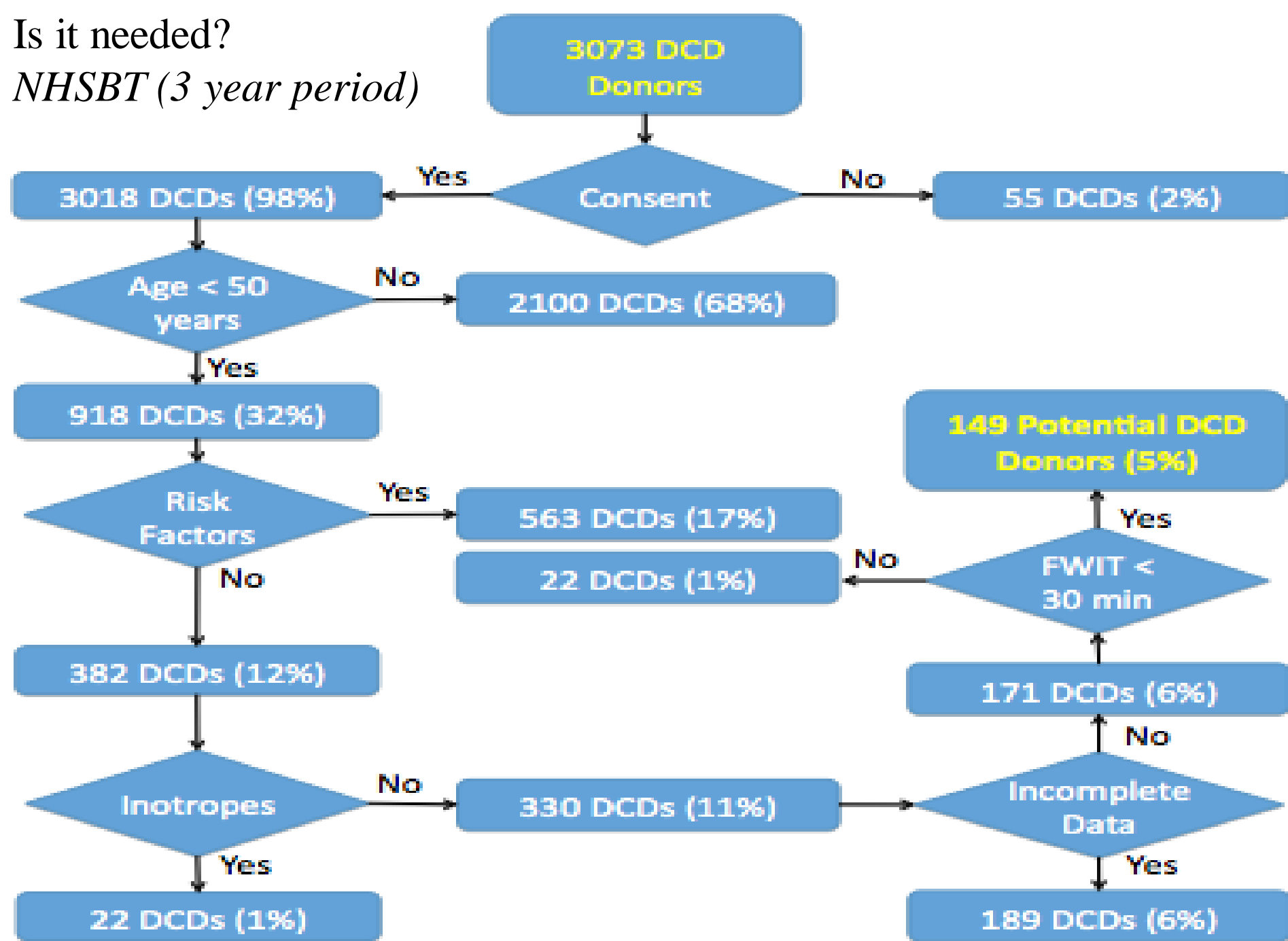


NHS Foundation Trust

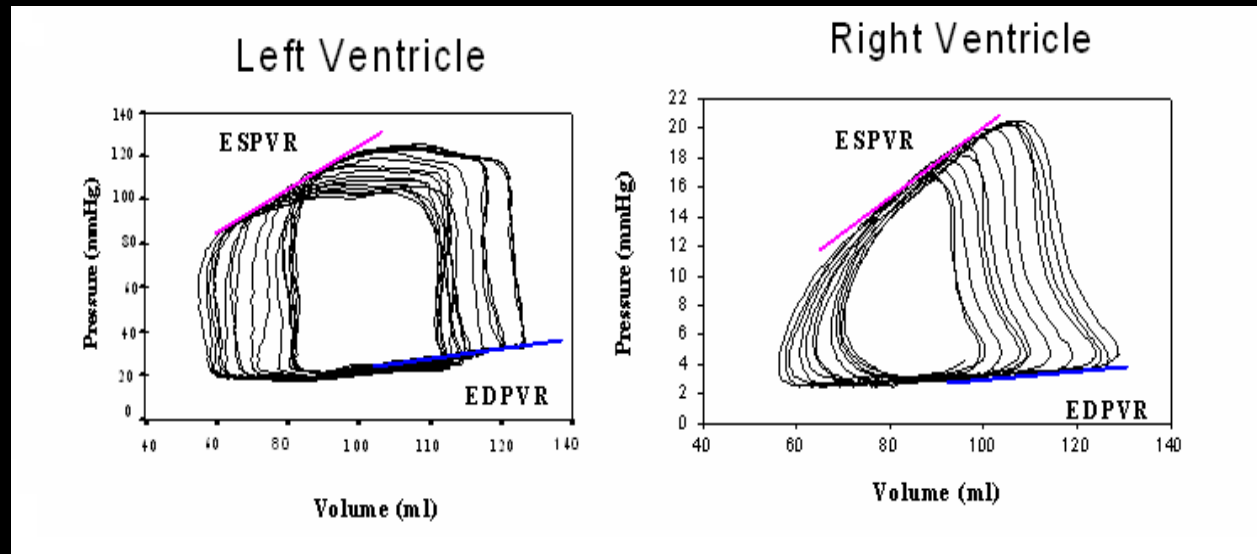
# **The Potential of Transplanting Hearts From Donation After Circulatory Determined Death (DCD) Donors Within the United Kingdom**

Messer S, Lannon J, R Axell, Wong E, Hopkinson C, Fielding  
S, Ali A, Tsui S, Large S

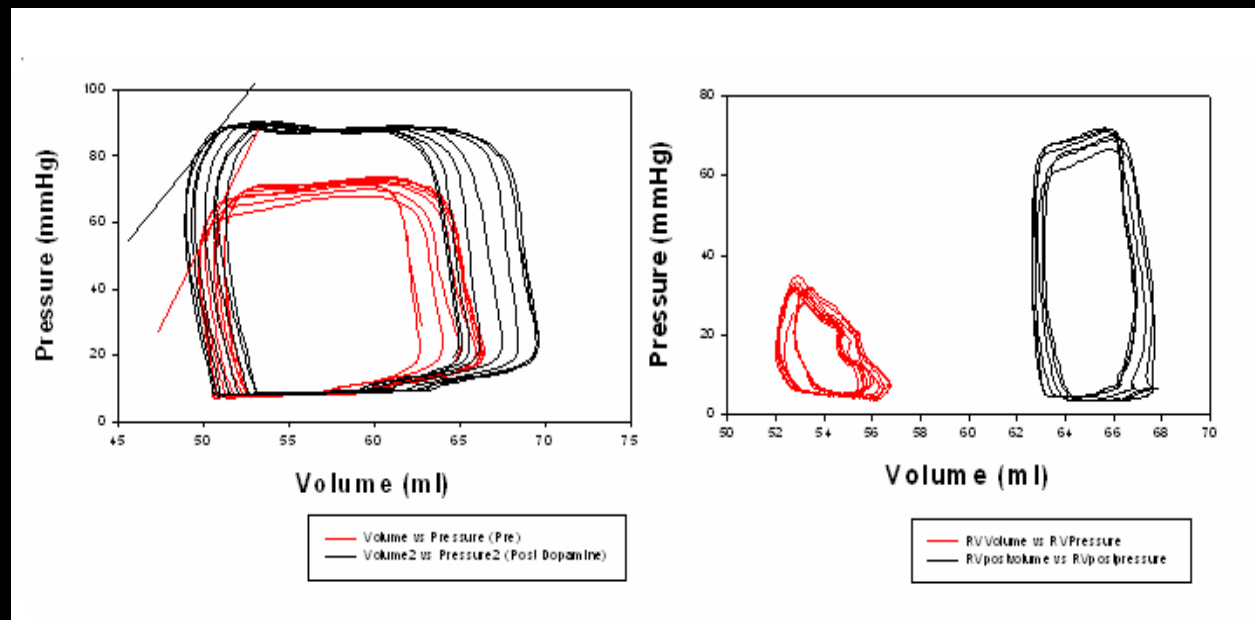
Is it needed?  
*NHSBT (3 year period)*



## Left and right ventricular pressure-volume loops from normal human heart.



## Left and right P/V loops after resuscitation following 23 min normothermic arrest in the human



*J Heart Lung Transplant.*  
2009 Mar;28(3):290-3.  
Ali A et al,

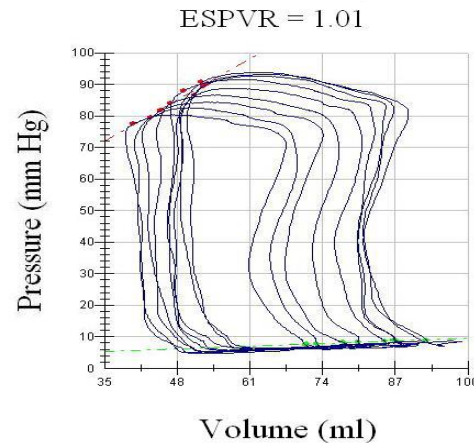
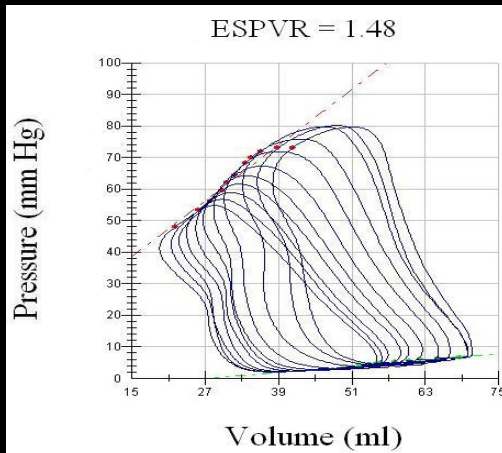


# Orthotopic porcine heart transplant model

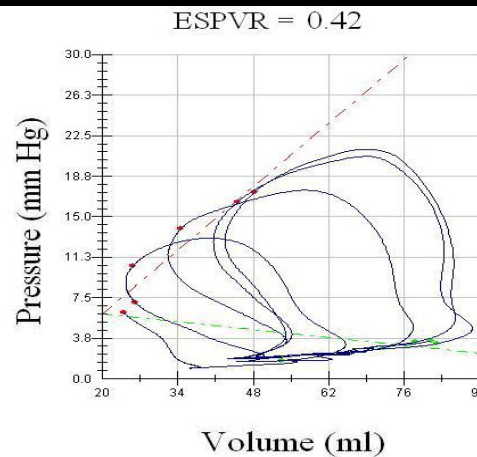
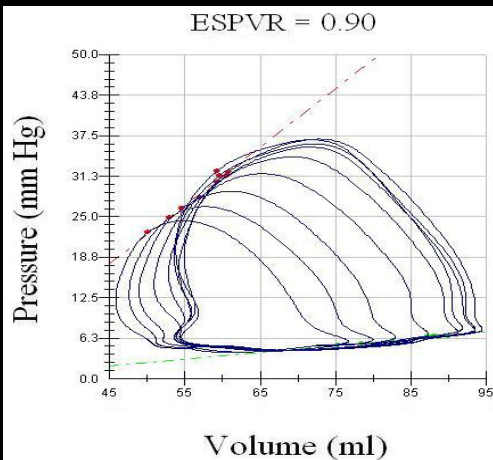
Hearts from DCD donors display acceptable biventricular function after heart transplantation. *Am J Transplant* 2011 11(8) 1621-32 Ali A et al.

DCD heart Tx

BSD heart Tx



Left ventricle

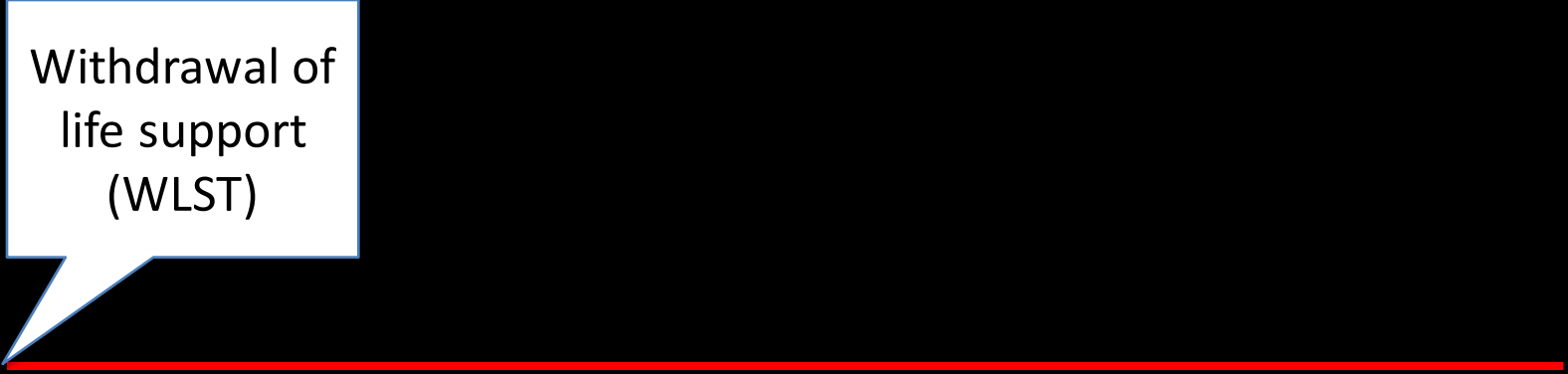


Right ventricle

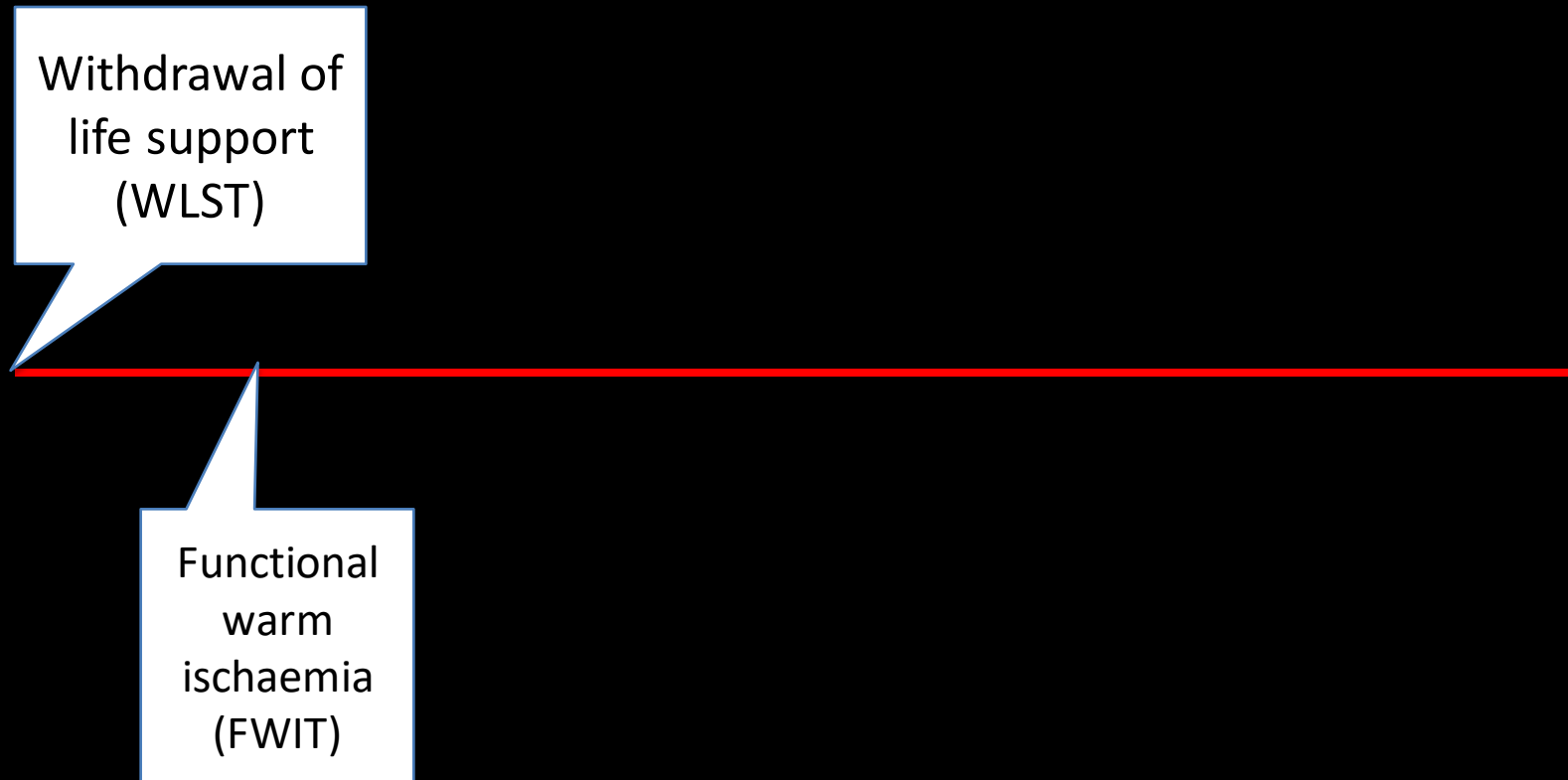
Ayyaz Ali PhD

# Timings following identification of futile treatment & consent for DCD organ donation:

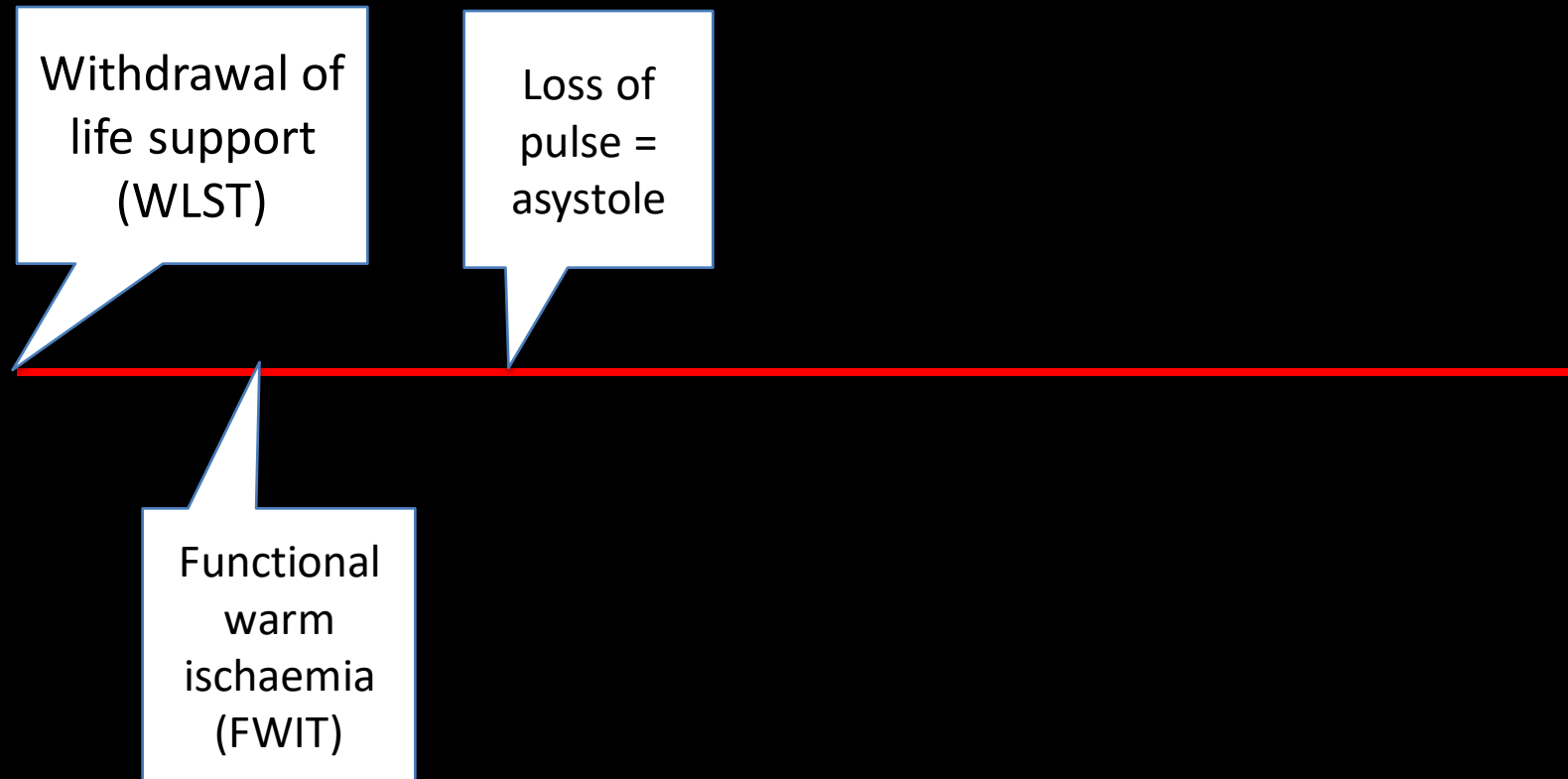
Withdrawal of  
life support  
(WLST)



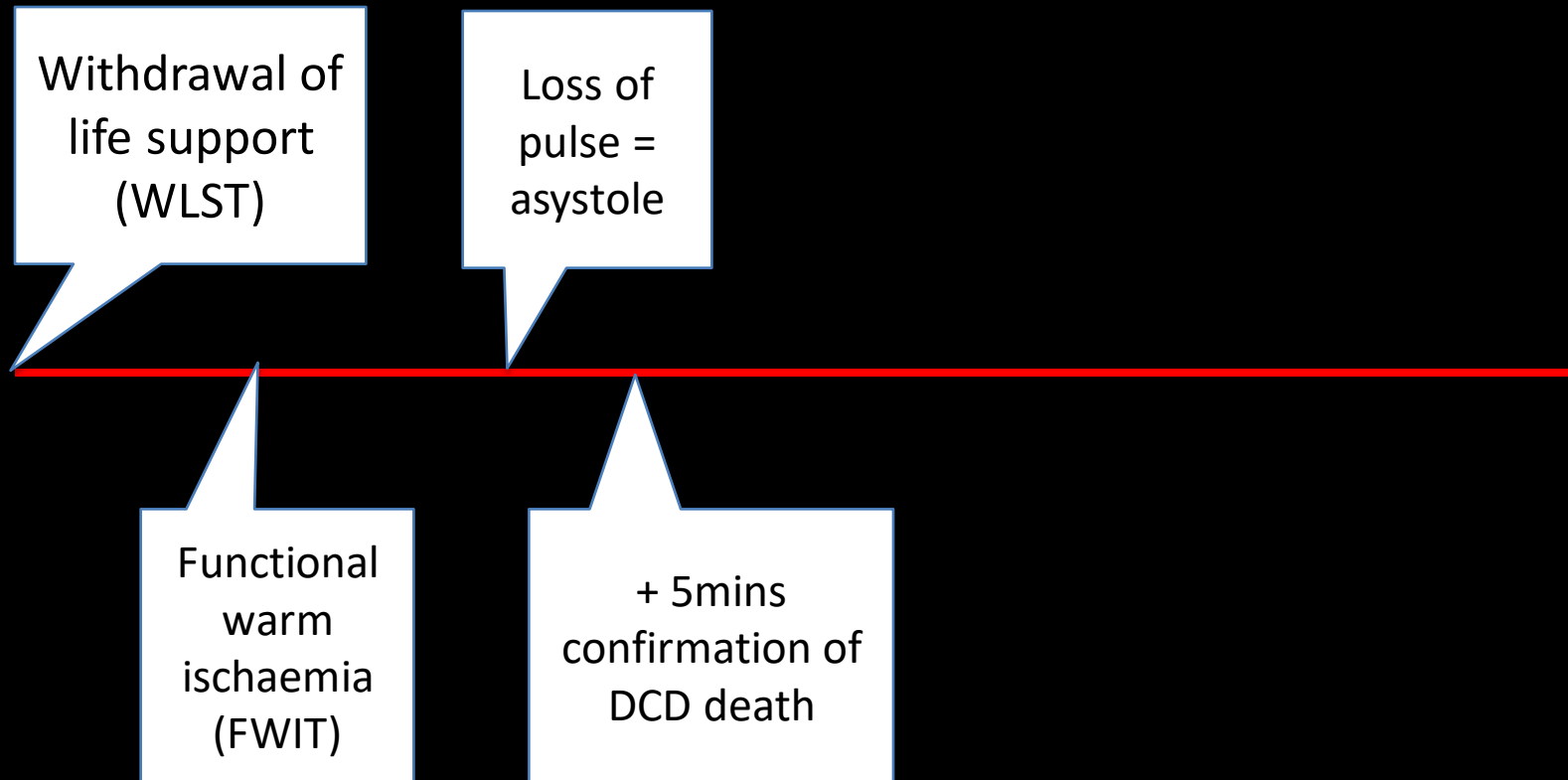
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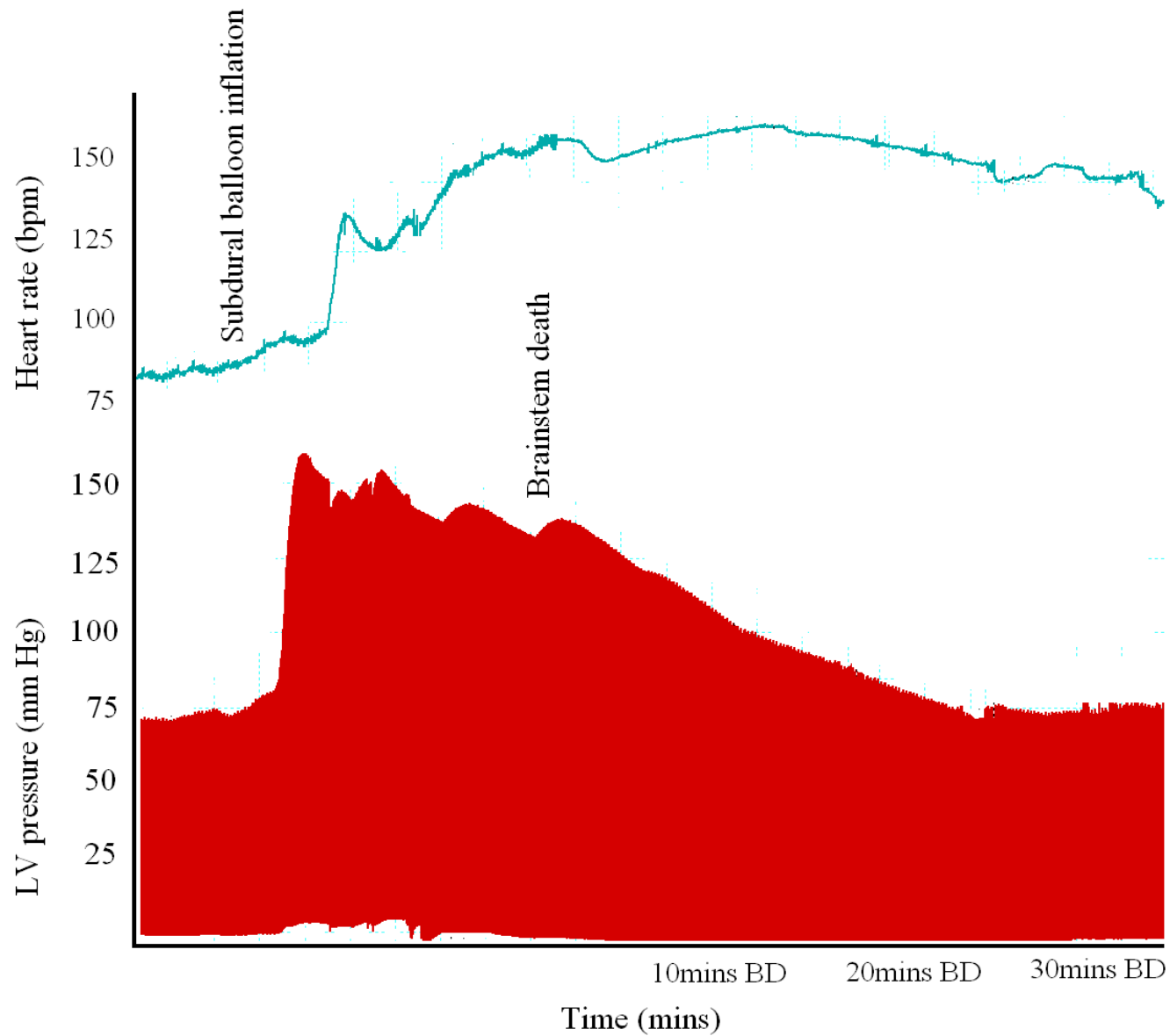
# Timings following identification of futile treatment & consent for DCD organ donation:



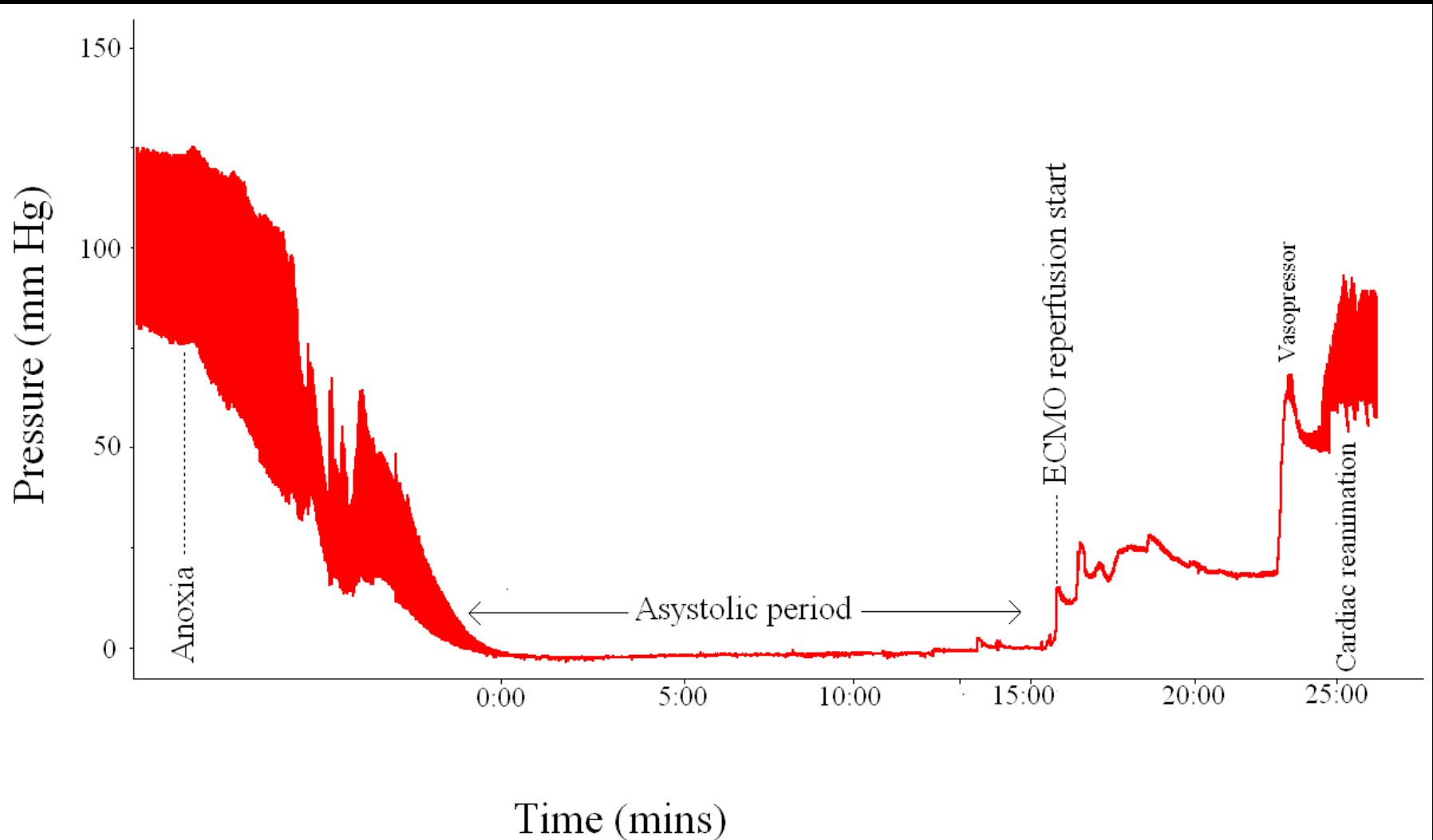
# DCD v DBD donation:

Problem:	DCD	DBD
Heart beating:	X	✓✓
Brain damage	✓	✓✓
Catecholamine storm	✓✓	✓

**Pig & rat model of brain death**

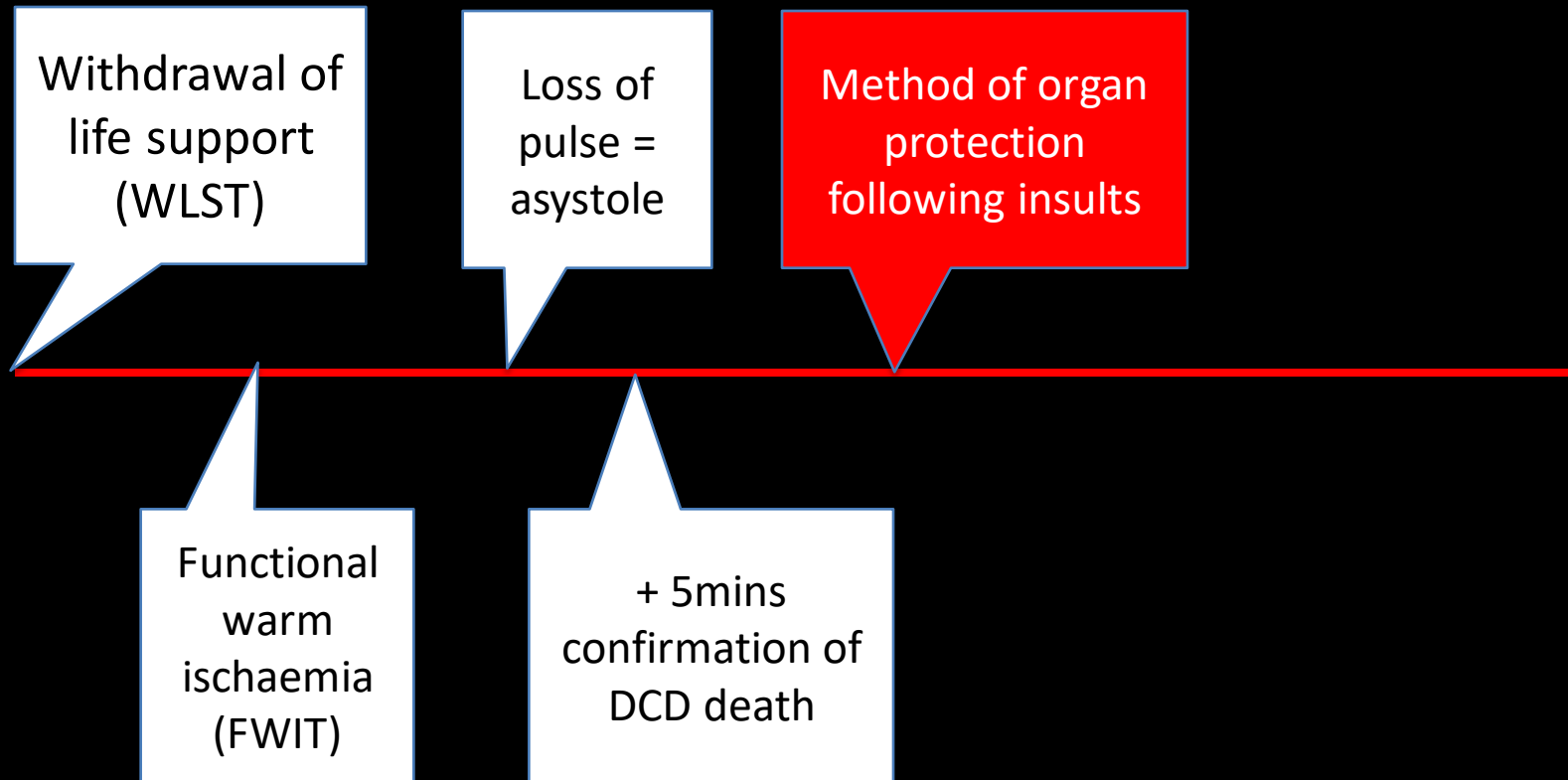


## Method for modelling DCD (rat and pig)

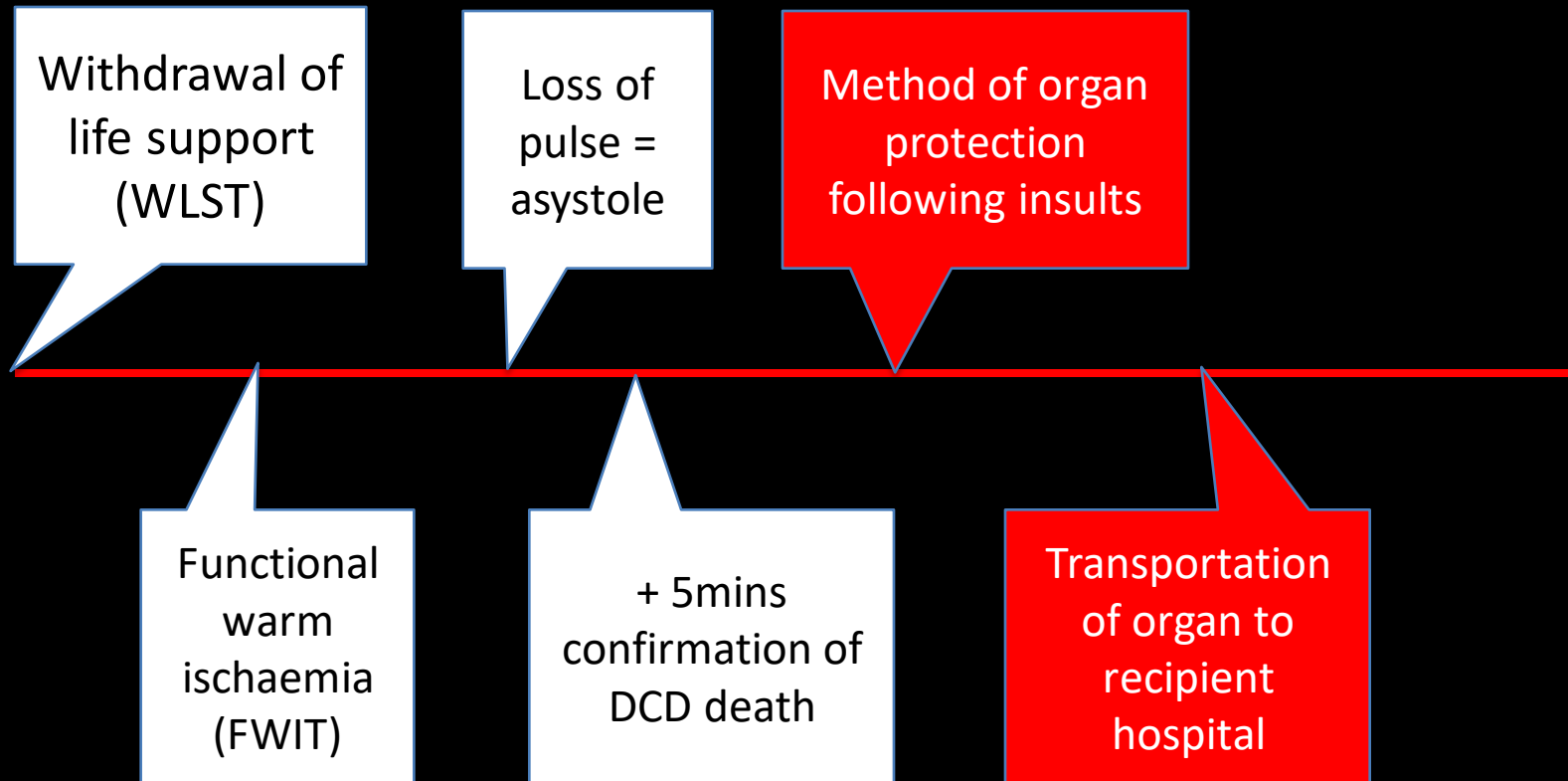




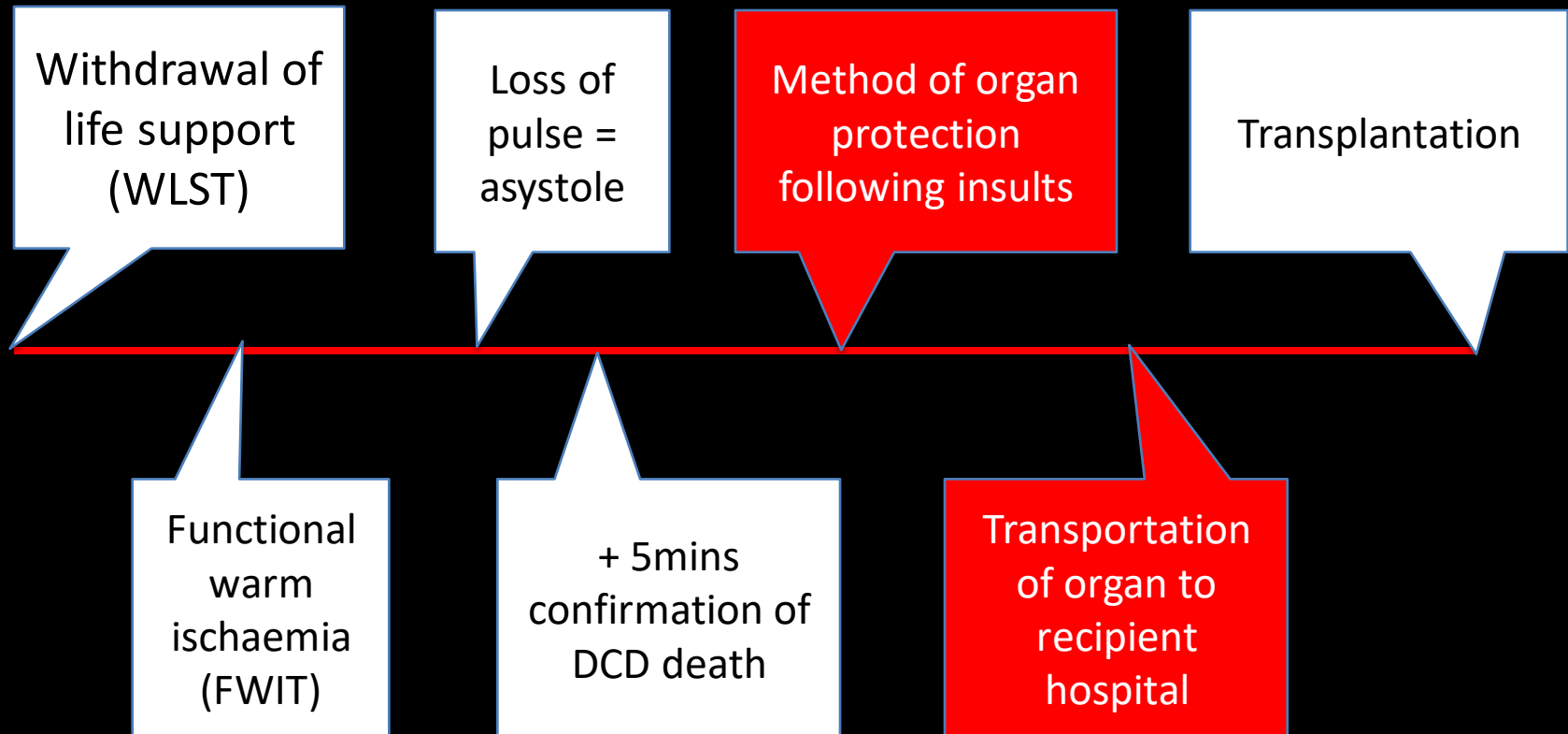
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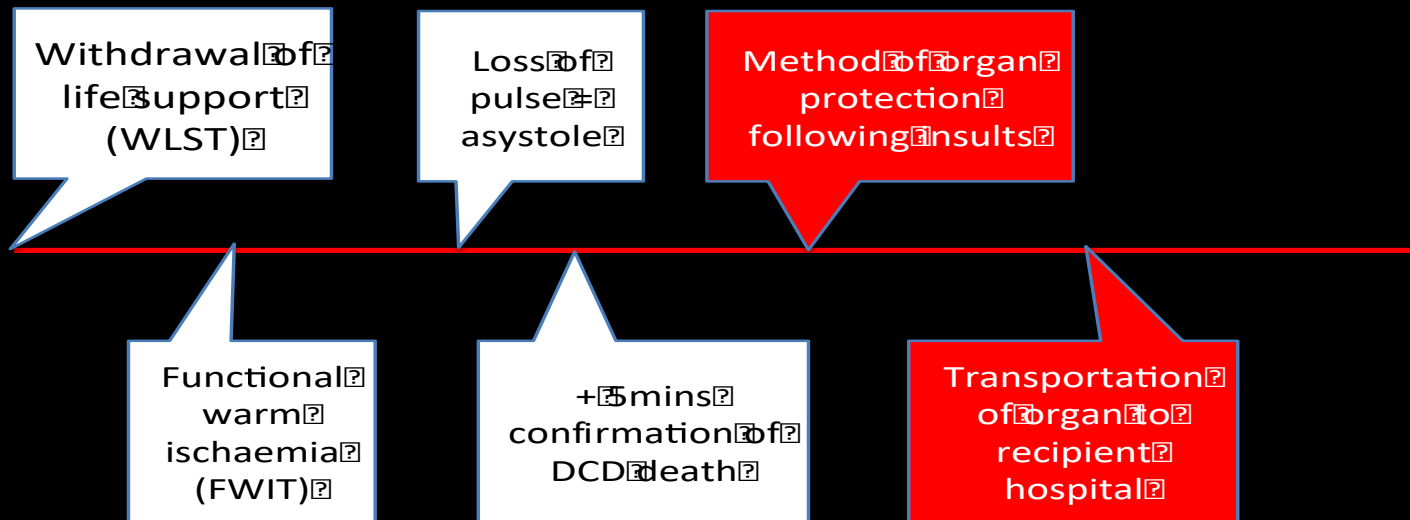


# Timings following identification of futile treatment & consent for DCD organ donation:

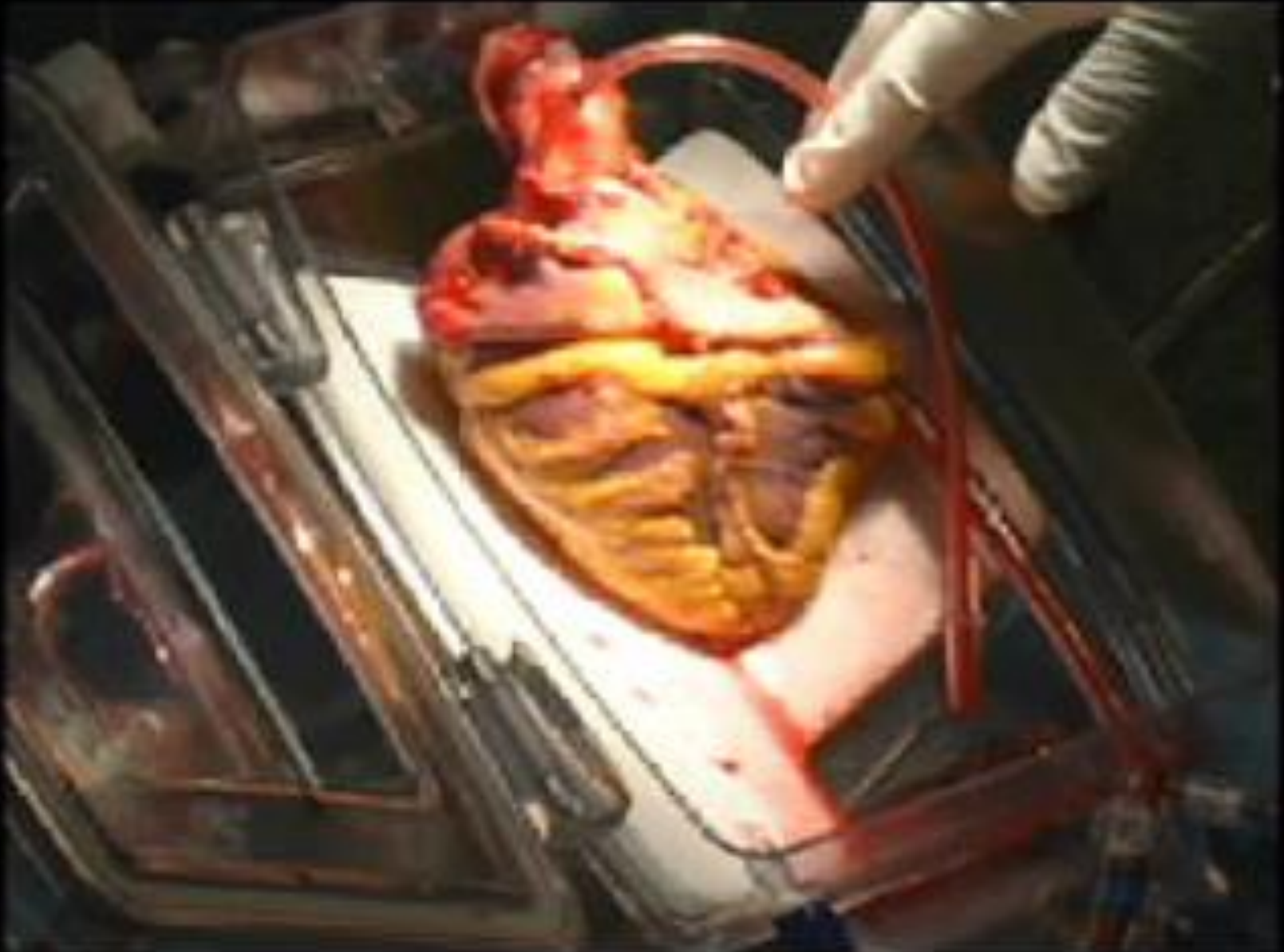


# Establishing blood supply for this ischaemic heart:

- DPP direct procurement to perfusion  
Langendorff blood perfusion



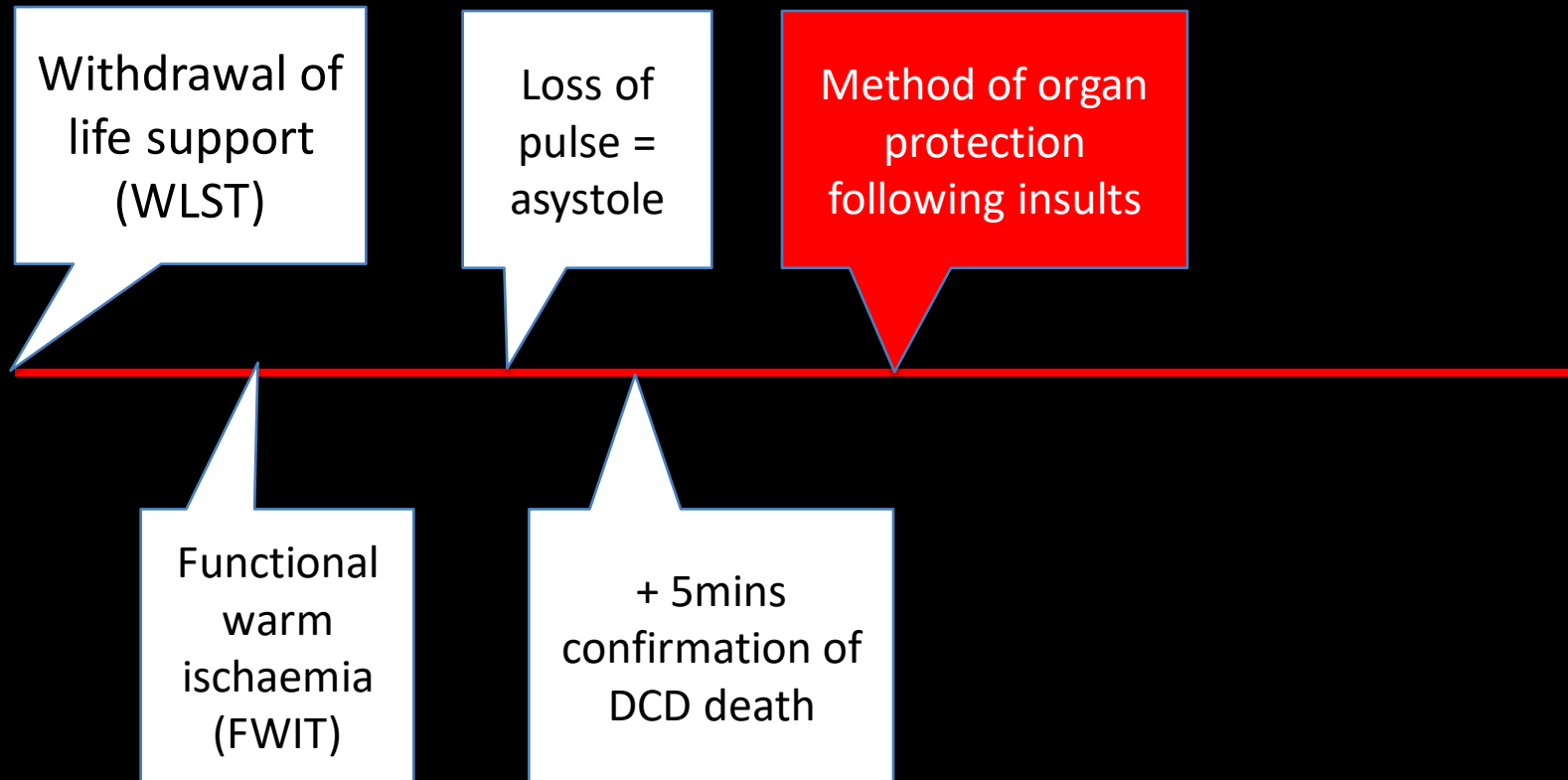
Establishing blood supply for this ischaemic heart:



## Establishing blood supply for this ischaemic heart:

- DPP direct procurement to perfusion  
Langendorff blood perfusion
- NRP Normo-thermic reperfusion  
neck vessels cross clamped to  
prevent brain perfusion  
- limited perfusion with ECMO

# Timings following identification of futile treatment & consent for DCD organ donation:







## Timings

**DPP** <sub>(14)</sub>

**NRP** <sub>(13)</sub>

---

Age

35

38

Male

86%

77%

## Timings

**DPP** <sub>(14)</sub>

**NRP** <sub>(13)</sub>

---

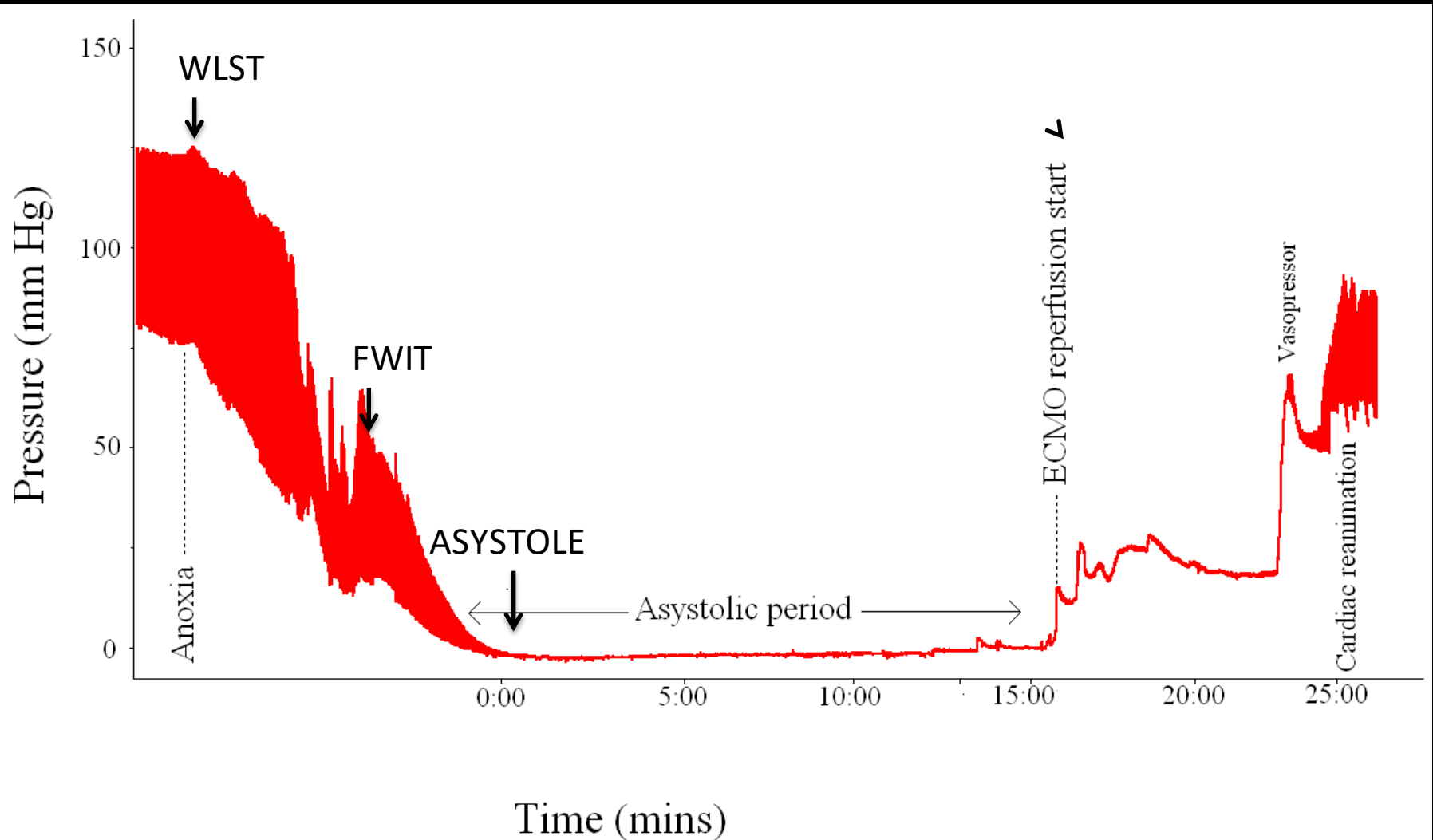
withdraw –

asystole

$33 \pm 53$

$25 \pm 39$

## Method for modelling DCD (rat and pig)



## Timings

**DPP** <sub>(14)</sub>

**NRP** <sub>(13)</sub>

---

withdraw –  
asystole

33±53

25±39

asystole –  
blood perf.  
(*ischaemia*)

21.6±2.2

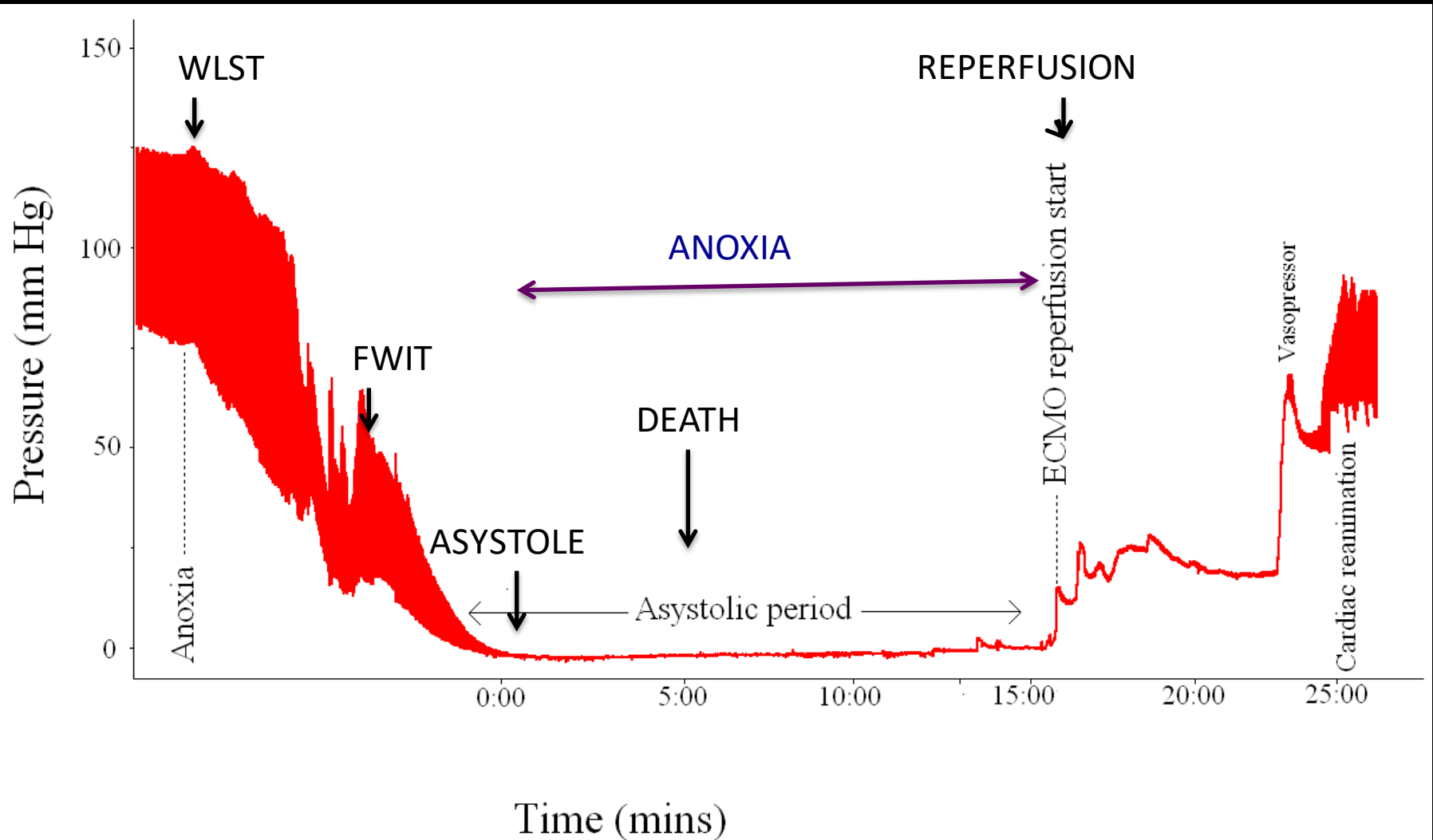
13.2±2.4

Death to  
Reperfusion

16

8

## Method for modelling DCD (rat and pig)



# Functional Assessment Donor

Technique	NRP 10 (DPP 13)
(Cardiac Index (L/min/m²)	3.4
CO (L/min)	6.7
Heart Rate (bpm)	114
CVP (mmHg)	5
PCWP (mmHg)	9
MAP (mmHg)	78
Ejection Fraction	65

**Transplant**

**DPP *14***

**NRP *13***

OCS time

$275_{\pm 76}$

$197_{\pm 89}$

implant

$37.4_{\pm 10.7}$

$35.2_{\pm 5.9}$

Recipient	DPP	TA-NRP
-----------	-----	--------

---

Age

55

58

Redo

50%

15%

TPPG

6.5

7

ITU stay

5.0

5.5

Hospital stay

19

20

Mortality

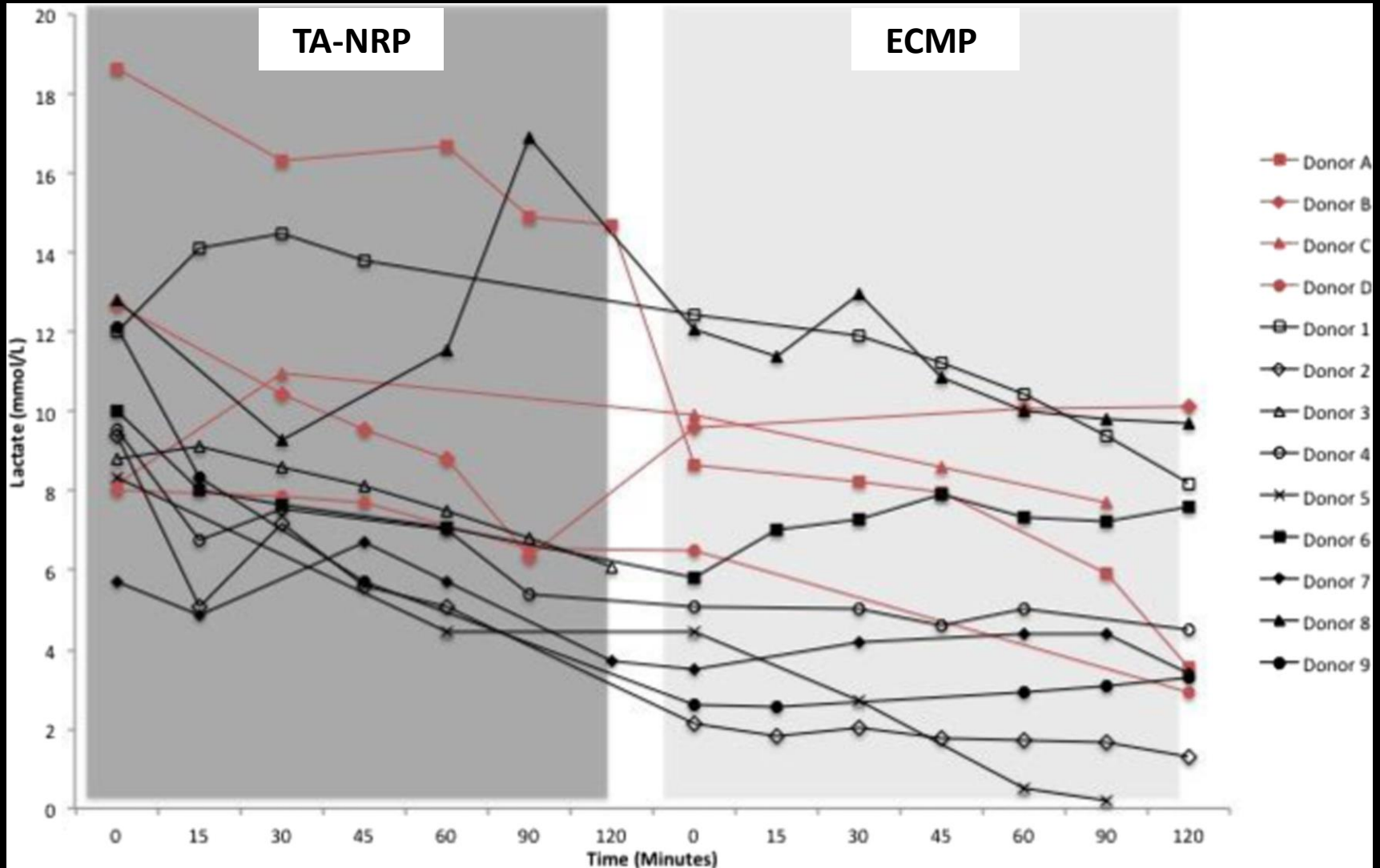
14%

0



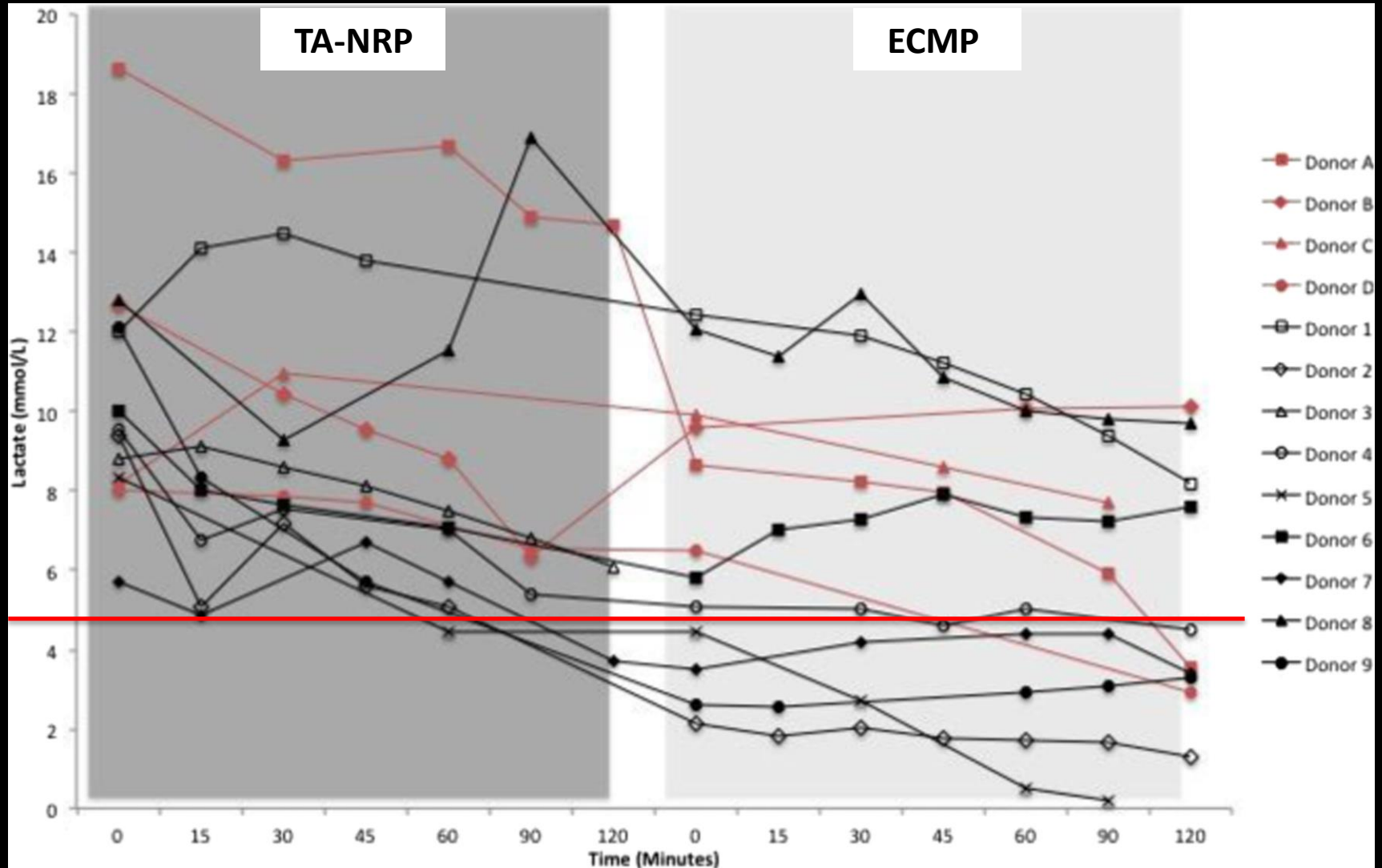
# Serum lactate levels in the blood based perfusate of the DCD donor heart on donor NRP and OCS or ECMS (extra corporeal machine perfusion)

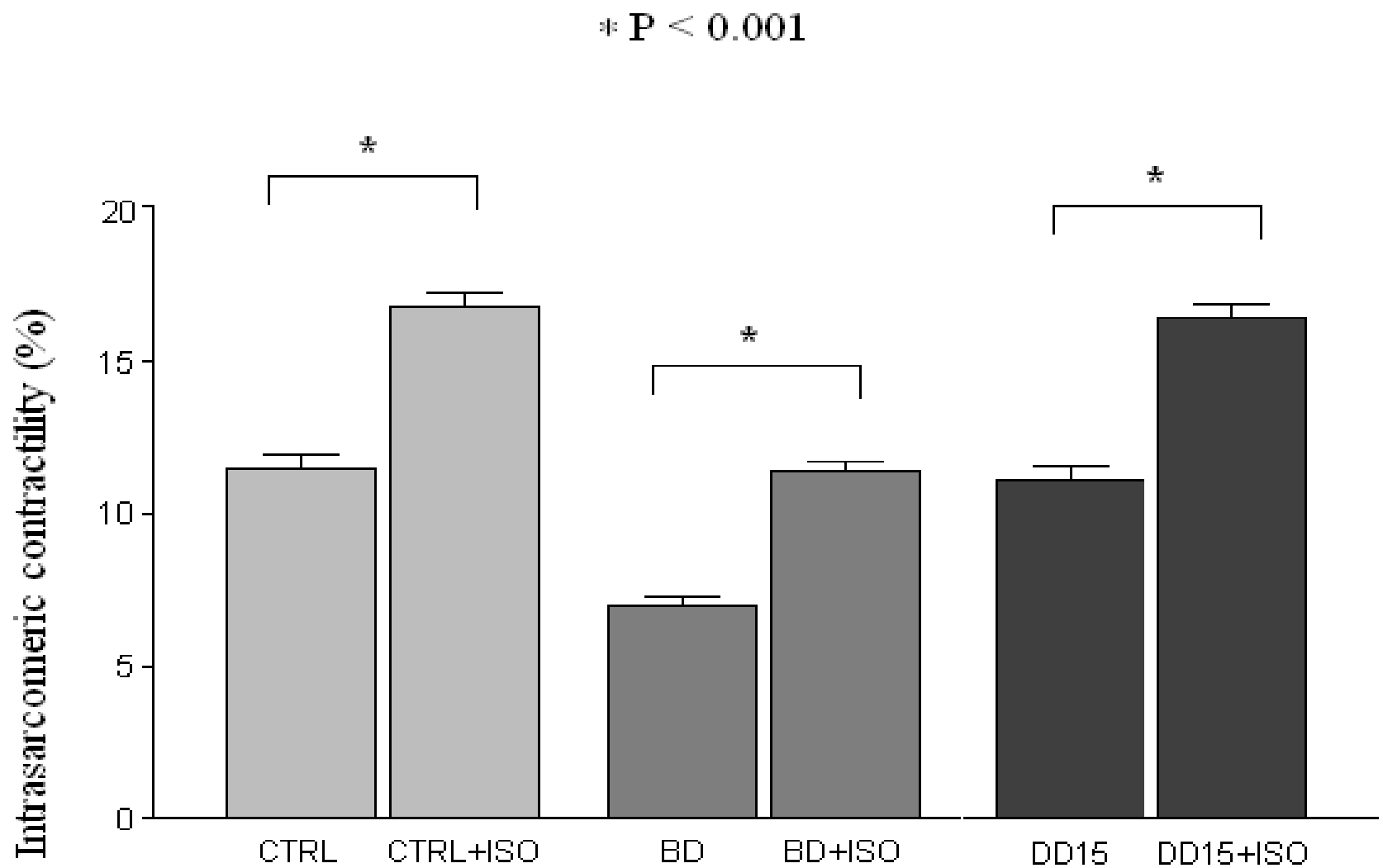
(Messer S 2016 by kind permission)



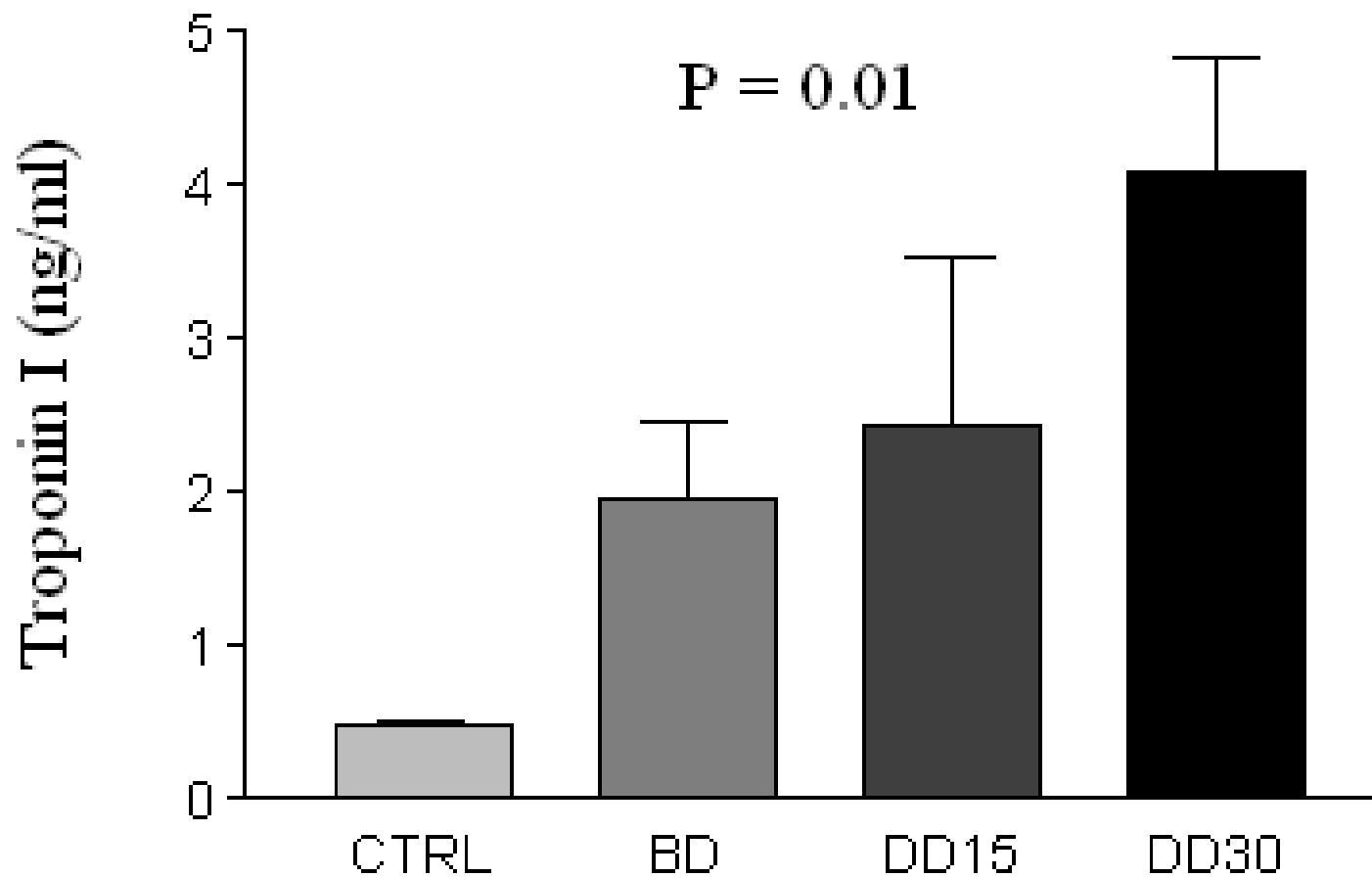
# Serum lactate levels in the blood based perfusate of the DCD donor heart on donor NRP and OCS or ECMS (extra corporeal machine perfusion)

(Messer S 2016 by kind permission)





**Contractile reserve in isolated cardio-myocytes after isoproterenol administration: BSD vs. 15 min NHBD heart**



## Follow up:

- 1 in 5 patients fail to arrest within 4 hours

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- 1 in 5 patients fail to arrest within 4 hours
- 13 NRP in the donor leading to 13 tx
  - Can assess the donor heart

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  - The DCD or non-heart beating donor is transformed in to a heart beating donor



## Follow up:

- 1 in 5 patients fail to arrest within 4 hours
- 11 NRP in the donor leading to 10 tx
  - Can assess the donor heart
  - Can assess the donor liver, kidneys, pancreas and bowel
  - The DCD or non-heart beating donor is transformed in to a heart beating donor
  - There is evidence to support better outcomes for NRP DCD liver & kidney

## Follow up:

- 1 in 5 patients fail to arrest within 4 hours
- 11 NRP in the donor leading to 10 tx
  - Can assess the donor heart
  - Can assess the donor liver, kidneys, pancreas and bowel
  - The DCD or non-heart beating donor is transformed in to a heart beating donor
  - There is evidence to support better outcomes for NRP DCD liver & kidney
  - DCD heart tx has at least as good an outcome early and mid-term as DBD.



2015 - TA

# Will TA-NRP become the new standard for (*the maintenance of*) DCD donors?

1. Yes!
2. ...as its associated with shorter normothermic ischaemia
3. ...as the donor becomes familiar as heart beating donor
4. ...as the donor heart can be assessed according to current practice
5. ...as its possible to assess the donor more thoroughly reducing mishaps

# Problems and future work:

1. Can the DCD heart become more tolerant of normo-thermic ischameia ?

2.

1.

# Problems and future work:

1. Can the DCD heart become more tolerant of normo-thermic ischameia ?
2. Can the I/R damage around death be reversed for DCD heart?

1.

## Problems and future work:

1. Can the DCD heart become more tolerant of normo-thermic ischameia ?
2. Can the I/R damage around death be reversed for DCD heart?
1. Can these be expanded to the abdominal organs?