

# Should Australia Undertake Normothermic Regional Perfusion?

A/Prof Andrew McGee PhD

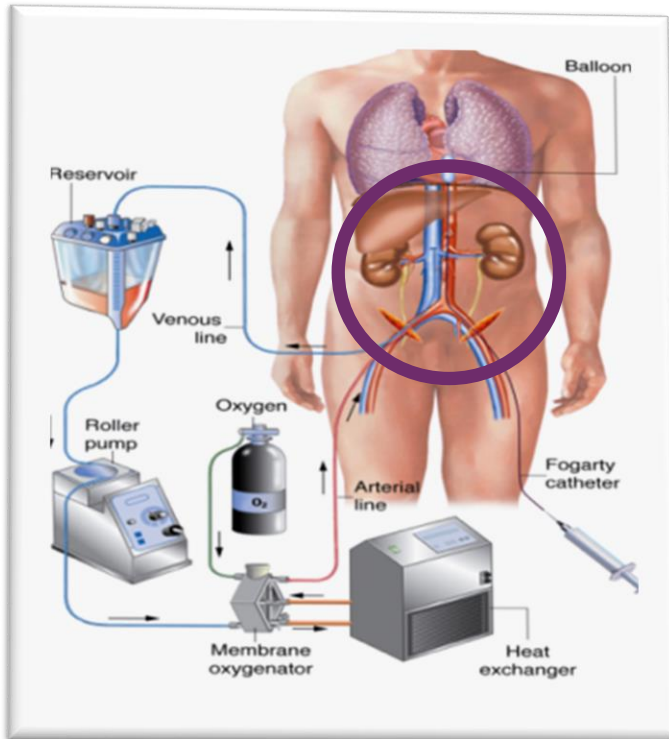
Dr Dale Gardiner MBBS, MBioeth, FRCA, FFICM

# NRP reperfuses and reoxygenates organs inside the donor in DCDD.

## A-NRP

Abdominal

Normothermic Regional Perfusion



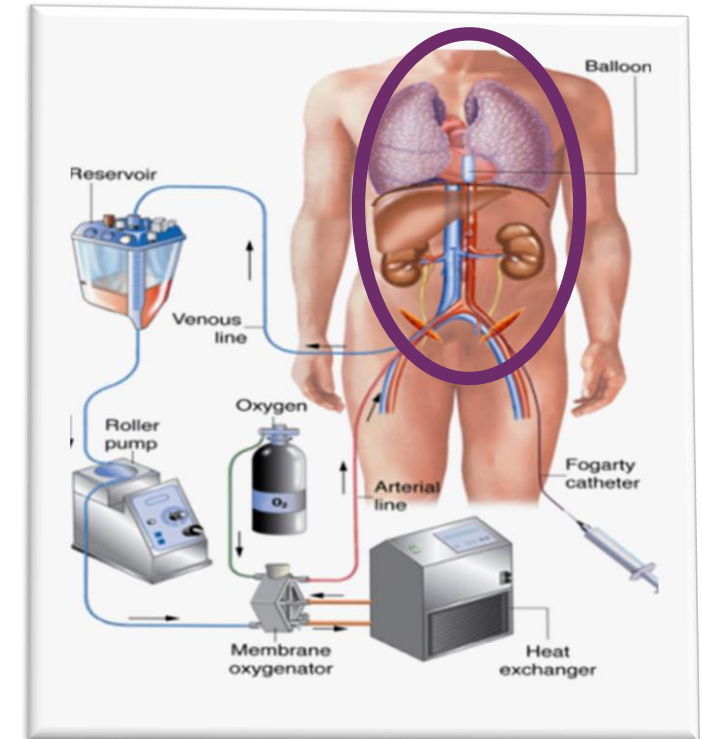
*The heart is prevented from restarting by surgical occlusion ('cross-clamping') of the major blood vessels.*

- NRP is a machine perfusion technology that reperfuses and reoxygenates organs *in situ* (inside the donor) in controlled donation after circulatory determination of death (cDCD).
- Two types of NRP.
  - A-NRP
  - TA-NRP
- In standard cDCD, unlike in donation after brain death (DBD), circulation has stopped and organ retrieval begins 5 minutes after mechanical asystole.
- NRP reduces damage to the organs meaning more organs become transplantable.

## TA-NRP

Thoraco-abdominal

Normothermic Regional Perfusion



*The heart will restart in the donor's body, but cross-clamping across the major blood vessels supplying the brain prevents circulation reaching the brain.*



# NRP Ethical Criticism

2021



**Ethics, Determination of Death, and Organ Transplantation in Normothermic Regional Perfusion (NRP) with Controlled Donation after Circulatory Determination of Death (cDCD): American College of Physicians Statement of Concern**

Approved by the Board of Regents on April 17, 2021

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2022

## ETHICS IN CARDIOTHORACIC SURGERY

### Normothermic Regional Perfusion: Ethical Issues in Thoracic Organ Donation

John W. Entwistle, MD, Daniel H. Drake, MD, Kathleen N. Fenton, MD, Michael A. Smith, MD, and Robert M. Sade, MD, for the Cardiothoracic Ethics Forum\*

Division of Cardiothoracic Surgery, Department of Surgery, Thomas Jefferson University, Philadelphia, Pennsylvania; Department of Cardiac Surgery, University of Michigan Medical School, Ann Arbor, Michigan; William Novick Global Cardiac Alliance, Memphis, Tennessee; Norton Thoracic Institute, St Joseph's Hospital and Medical Center, Phoenix, Arizona; and Division of Cardiothoracic Surgery, Department of Surgery, Medical University of South Carolina, Charleston, South Carolina

“NRP-cDCD raises profound ethical questions regarding the dead donor rule... [We] recommend the use of NRP-cDCD be paused.”

“NRP should be limited to adult patients with severe neurological injury that has not progressed to brain death, and should not be used in children at this time.... DPP is less ethically complex than NRP, so its use is encouraged as the primary method for heart [retrieval] in cDCD.”

2022



**WHY ARCH VESSEL LIGATION IS UNETHICAL FOR THORACOABDOMINAL NORMOTHERMIC REGIONAL PERFUSION**

To the Editor:

**POINT:**  
Does Normothermic Regional Perfusion Violate the Ethical Principles Underlying Organ Procurement? Yes

Matthew DeCamp, MD, PhD  
Aurora, CO  
Lois Snyder Sulmasy  
Philadelphia, PA  
Joseph J. Fins, MD  
New York, NY

2022

“...develop methods of ex vivo support for organs, thereby obviating the need for in situ circulation that negates the legal basis for declaring death.”

American Journal of Transplantation  
Volume 22, Issue 5, May 2022, Pages 1289-1290

EDITORIAL  
Normothermic regional perfusion and US legal standards for determining death are not aligned

Alexandra K. Glazier<sup>1</sup>, Alexander M. Coarón<sup>2</sup>

2022

**OPTN**

Public Comment Proposal

**Ethical Analysis of Normothermic Regional Perfusion (NRP)**

2023

OPTN Ethics Committee

“NRP raises concerns about compliance with the Dead Donor Rule... additional evidence is needed to demonstrate that cerebral flow to brain is minimal.”



# The Law

- In 1977, the Australian Law Reform Commission recommended that death be defined as:
  - irreversible cessation of all function of the brain of the person; or
  - irreversible cessation of circulation of blood in the body of the person.
- Current Australian state and territory laws vary but all closely based on the ALRC recommendation
  - *Transplantation and Anatomy Act 1979 (Qld)*, s 45
  - *Criminal Code Act 1995 (Cth)* s 4(1) (Dictionary attached to Sch 1)

See also, Neera Bhatia, James Tibbals. Heart transplantation after circulatory death: it's time to redefine death... UNSWLJ 2022.

# The Law Interpreted



## Uniform Determination of Death Act 1981

An individual who has sustained either:

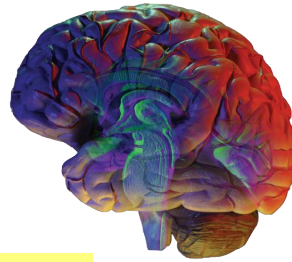
- (1) irreversible cessation of circulatory and respiratory functions, or
- (2) irreversible cessation of all functions of the entire brain, including the brain stem, is dead.

***A determination of death must be made in accordance with accepted medical standards.***

Rationale for the Law – J L Bernat et al (2010):

They are not two criteria but two tests for a **single**, brain-based criterion

# Unified Brain Based Standard



2010

Special Article

## The circulatory–respiratory determination of death in organ donation\*

James L. Bernat, MD; Alexander M. Capron, LLB; Thomas P. Bleck, MD; Sandralee Blosser, MD; Susan L. Bratton, MD, MPH; James F. Childress, PhD; Michael A. DeVita, MD; Gerard J. Fulda, MD; Cynthia J. Gries, MD, MSc; Mudit Mathur, MD; Thomas A. Nakagawa, MD; Cynda Hylton Rushton, PhD, RN; Sam D. Shemie, MD; Douglas B. White, MD

**Objective:** Death statutes permit physicians to declare death on the basis of irreversible cessation of circulatory–respiratory or brain functions. The growing practice of organ donation after circulatory determination of death (DCDD) now requires physicians to exercise greater specificity in circulatory–respiratory death determination. We studied circulatory–respiratory death determination to clarify its concept, practice, and application to innovative circulatory determination of death protocols.

**Results:** It is ethically and legally appropriate to procure organs when permanent cessation (will not return) of circulation and respiration has occurred but before irreversible cessation (cannot return) has occurred because permanent cessation: (1) is an established medical practice standard for determining death; (2) is the meaning of “irreversible” in the Uniform Determination of Death Act; and (3) does not violate the “Dead Donor Rule.”

**Conclusions:** The use of unmodified extracorporeal membrane oxygenation in the circulatory determination of death donor after

death is declared should be abandoned because, by restoring brain circulation, it retroactively negates the previous death determination. Modifications of extracorporeal membrane oxygenation that avoid this problem by excluding brain circulation are contrived, invasive, and, if used, should require consent of surrogates. Heart donation in circulatory determination of death is acceptable if proper standards are followed to declare donor death after establishing the permanent cessation of circulation. Pending additional data on “auto-resuscitation,” we recommend that all circulatory determination of death programs should utilize the prevailing standard of 2 to 5 mins of demonstrated mechanical asystole before declaring death. (Crit Care Med 2010; 38: 972–979)

**KEY WORDS:** organ donation; circulatory death; cardiac death; dead donor rule; auto-resuscitation; extracorporeal membrane oxygenation

**The two standards for death determination – circulatory and neurological – “are essentially a single one based on brain functions.”**

Intensive Care Med (2014) 40:788–797  
DOI 10.1007/s00134-014-3242-7

CONFERENCE REPORTS AND EXPERT PANEL

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for Determination of Death  
phase 1 participants, in collaboration  
with the World Health Organization

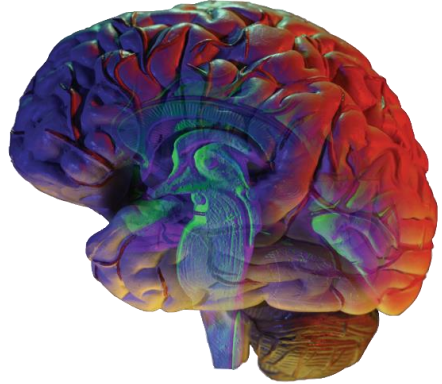
## International guideline development for the determination of death

... in collaboration with the WHO

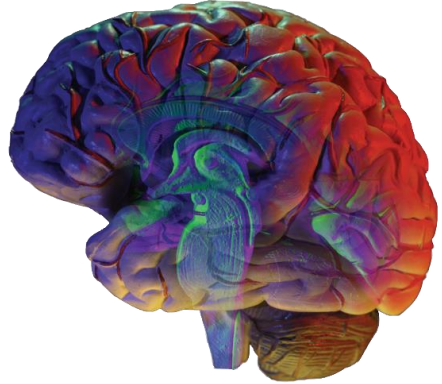
2014

**“Death occurs when there is permanent loss of capacity for consciousness and loss of all brainstem functions. This may result from permanent cessation of circulation or catastrophic brain injury.”**

# Brain Circulation which Counts



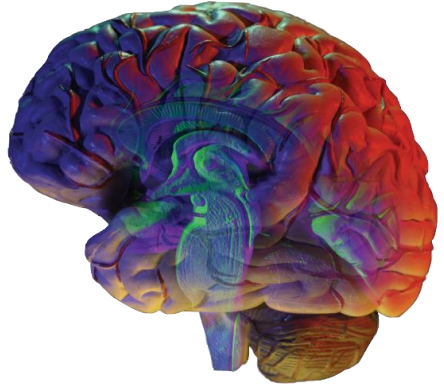
**Ultimately, the heart is just  
a pump for the brain and all  
human death is  
anatomically located to the  
BRAIN**



- All human death is brain-*based*.
- Two points in the alternative:
  1. This is the *only* way to make sense of existing legislation *medically*;

OR

2. We need to *revise* legislation so it captures the single-brain based criterion because current legislation *makes no sense medically*.



There aren't two types of death, just two ways of losing your neurological function:

- Brain death (brain swelling resulting in herniation)
- Circulatory-respiratory brain-based death (no herniation)

**Next issue: what does “irreversible” mean?**

- Crucial to both standard cDCDD and NRP.
- Sometimes been said to *mean* permanent.

# Permanence



## The Statement on Death and Organ Donation 2021

EDITION 4.1 | 2021



Published Ahead of Print on October 11, 2023 as 10.1212/WNL.000000000207740

SPECIAL ARTICLE

## Pediatric and Adult Brain Death/Death by Neurologic Criteria Consensus Guideline

Report of the AAN Guidelines Subcommittee, AAP, CNS, and SCCM

David M. Greer, MD, MA,\* Matthew P. Kirschen, MD, PhD,\* Ariane Lewis, MD,\* Gary S. Gronseth, MD, Alexander Rae-Grant, MD, Stephen Ashwal, MD, Maya A. Babu, MD, MBA, David F. Bauer, MD, MPH, Lori Billingham, MD, MSc, Amanda Corey, MD, Sonia Partap, MD, MS, Michael A. Rubin, MD, MA, Lori Shutter, MD, Courtney Takahashi, MD, Robert C. Tasker, MBBS, MD, Panayiotis Nicolaou Varelas, MD, PhD, Eelco Wijdicks, MD, PhD, Amy Bennett, JD, Scott R. Wessels, MPS, ELS, and John J. Halperin, MD

Neurology® 2023;101:1-21. doi:10.1212/WNL.000000000207740

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# 2023



Can J Anesth/Can Anesth  
<https://doi.org/10.1007/s12630-023-02431-4>

SPECIAL ARTICLE

## A brain-based definition of death and criteria for its determination after arrest of circulation or neurologic function in Canada: a 2023 clinical practice guideline

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## Permanent:

- (1) will not resume spontaneously, and
- (2) will not be restored through intervention.

Bernat explains relationship between ‘irreversible’ and ‘permanent’ as follows:

*‘Irreversible’ is an absolute and univocal statement that reflects the physical reality of immutability...*

*By contrast....‘permanent’...is an equivocal and contingent condition that admits of possibility. It may rely on our intent and action to be realized...*

*Bernat, “Are Organ Donors after Cardiac Death Really Dead?,” 125, our italics on “prognosis”.*

**Difficulty:**

Bernat also claims that “the concept of irreversibility is intrinsic to the concept of death” (Are Organ Donors...Dead, 124)



## UDDA

Crucial part of the case, legally, rests on the words “determination of death must be made in accordance with accepted medical standards”



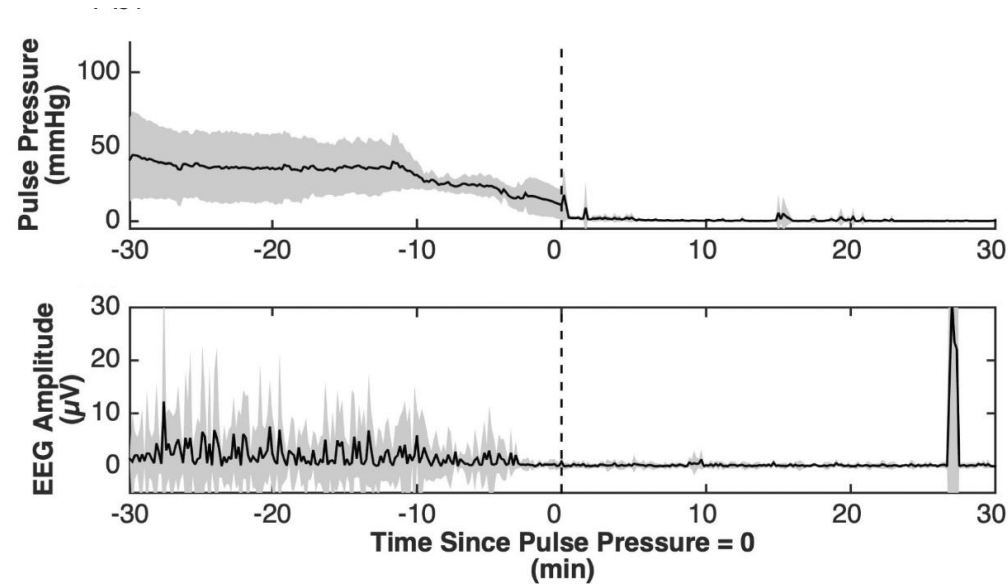
## No equivalent wording in the Australian statutes

- Sometimes requirements on doctors, but only for brain death declaration
- Guidelines have no legal authority, but can be persuasive, save for determining meaning in statutes.

## Significance?

Even if Bernat’s arguments persuasive, couldn’t be made in Australia

# Controversial Solution

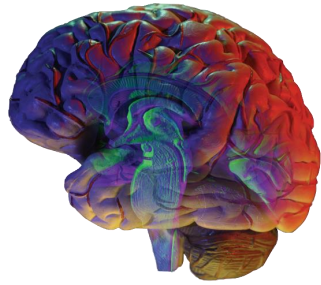


*Following WLST on ICU neurological function (EEG) ceases BEFORE circulatory function (pulse pressure). Circulatory recovery does not equal brain recovery.*

- Ontically, patient could have irreversible cessation of function.
- Epistemically, we don't know, but can judge on Balance of Probability.
- Permanence = rule allowing us to judge.
- The “could” in “someone could have function restored after five min asystole does not mean every single person could have function restored after five min asystole, but 3 or more out of 10 could.



VS



*Circulatory recovery does not equal brain recovery.*

- Ali et al – heart 23 mins after asystole with good function of heart. 2009. Cardiac recovery in human non-heart-beating donor after extracorporeal perfusion: Source for human heart donations? *Journal of Heart and Lung Transplant* 28(3):290–3.
- So: all donation after death = controversial
- Potentially requires: reading into statutes concepts that are absent.
- Single brain-based criterion means circulatory criterion has no intrinsic significance but is used only as way of knowing brain function has ceased.



## Common criticisms of NRP apply to all forms of deceased organ donation STAND or FALL together

1. Circulation has restarted in the body so death determination is invalid (Omelianchuk, Capron, Bernat, et al 2024)

Omelianchuk et al, Neither Ethical nor Prudent: Why Not to Choose Normothermic Regional Perfusion,” *Hastings Center Report* 54, no. 4 (2024): 14-23.

*Reply:* But if circulation only a test not an independent criterion, then a brain-dead person would also be alive, **since circulation is still occurring in brain-dead people** (authors support brain-death).



## Common criticisms of NRP apply to all forms of deceased organ donation STAND or FALL together

2. Clamping the arteries to stop blood getting to the brain causes death and makes a mockery of the determination of death after 5 min in NRP.

*Reply:* Exsanguination and clamping in standard cDCD has exactly the same effect

- *Soon after 5 minutes of asystole the donor is exsanguinated, the aorta clamped and the circulation to the respective organs flushed with cold, potassium rich preservation fluid. In real terms, this is therefore akin to the most effective clamping possible to prevent circulation from reaching the brain.*

*Another version of criticism 2: NRP causes brain death*

*Reply:* standard cDCD and normothermic machine perfusion (NMP) cause brain death! (Omelianchuk et al advocate for NMP)



## Common criticisms of NRP apply to all forms of deceased organ donation STAND or FALL together

3. Advocates of NRP read concepts into the statute that are not there.
  - eg, Advocates distinguish between restoring circulation and resuscitation. No mention of resuscitation in the legislation.
  - They also appeal to intent not to resuscitate. Not mention of intent in the legislation.
  - (Omelianchuk et al 2024)

*Reply: assume this is correct. It applies to standard cDCDD and DBD.*

- In brain dead people, circulation is not going to the brain but it continues in the torso.
  - If counter-reply that this is a different criterion – reject the single brain-based criterion, we can do so *but critics of NRP – Bernat, Capron advocate the single criterion (see above)*
- Appeal to *intent* also made by Bernat and Capron as a defence of *permanent*.
- More generally: reading the bifurcated criteria as two tests for a single criterion not even mentioned in the legislation = reading in concepts that aren't there!

**Point is not: NRP is OK then!**

**Point is: all forms of deceased donation stand or fall together.**

**Criticisms of NRP apply to standard DCD and some to DBD.**



We should stop all the hand-waving, and work out how to craft law to accommodate deceased organ donation.

*For NRP critics have revealed one thing at least: these laws are outdated and no longer fit for purpose.*

