Donation after Circulatory Death in Canada Then & Now

Sam D. Shemie

Toronto Canadian Critical Care Forum
CCCF, TGLN, CBS Organ Donation Symposium Oct 26th 2015

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Medical Advisor, Deceased Donation
1. End stage organ failure and bridges to transplant are difficult burdens, life threatening to patients and expensive to the system

2. Transplantation is life saving, life preserving and cost effective but limited by insufficient transplantable organs

3. Donation/transplantation is widely supported by the Canadian public

4. Countries/regions have a responsibility to address their domestic supply of transplantable organs in ethically legitimate ways
Some History

Organ and tissue donation in the intensive care unit

Graeme M. Rocker,
for the Canadian Critical Care Society Working Group on Organ and Tissue Donation

When patients will not survive (e.g., after severe head injuries), intensive care unit (ICU) teams face the challenge of conducting empathetic, honest discussions about donation in all eligible circumstances. In consequence, alternative ways to achieve improved rates of consent to organ and tissue donation within ICUs have been proposed. In the United States, for example, these initiatives include mandating representatives of transplant procurement organizations rather than ICU or hospital-based teams to interact with families at the time of death in the ICU. In Canada, other initiatives have resulted in provincial legislation that requires ICU physicians to provide outside agents with details that they regard as potentially contentious for critical care specialists.

The irony is that ICU physicians are as committed as any to the concept of successful organ and tissue donation, but we act and must act in the interests of our patient — the potential donor in the ICU — and his or her family. Transplant surgeons and transplant organizations have

Called for a Moratorium on DCD
Non-heart-beating organ donation in Canada: Time to proceed?

Greg A. Knoll, John E. Mahoney

Despite the proven success of solid organ transplantation, relatively few Canadians benefit from this therapy because of a shortage of organ donors. Over the past decade, the number of Canadians waiting for a transplant has increased by 84%, to nearly 4000, while units (ICUs). The most successful education programs have been locally driven. In Spain, transplant coordinators from a successful NHBD program organized courses and workshops to educate hospital personnel, later expanding their educational initiative to include an annual
Established the medical, ethical & legal framework for the practice of DCD in Canada

The Canadian Council for Donation and Transplantation

Donation After Cardiocirculatory Death:
A Canadian Forum

February 17–20, 2005
Vancouver, British Columbia

Donation after cardiocirculatory death in Canada

Sam D. Shemie, Andrew J. Baker, Greg Knoll, William Wall, Graeme Rocker, Daniel Howes, Janet Davidson, Joe Pagliarello, Jane Chambers-Evans, Sandra Cockfield, Catherine Farrell, Walter Glannon, William Gourlay, David Grant, Stéphan Langevin, Brian Wheelock, Kimberly Young, John Dossetor*

There are 2 fundamental but not mutually exclusive perspectives on organ donation. As an important part of end-of-life care, patients who die should be provided the opportunity to donate organs and tissues. Potential transplant recipients, who would otherwise die or be substantially compromised, can benefit from initiatives that
Forum Committees

Steering:
Sam Shemie - pediatric critical care
Chip Doig - adult critical care
Andrew Baker - adult neurocritical care
Graeme Rocker - adult critical care, EOL care
Dan Howes - adult ER and ICU
Bill Wahl - adult/pediatric liver TP surgery
Greg Knoll - adult renal TP medicine
John Dossetor - bioethics, renal transplant
Janet Davidson - hospital administration
Kimberley Young - CCDT
Dorothy Strachan - Facilitation

Advisors:
Stephane Langevin, Cameron Guest, Clare Payne
Ron Moore, Peter Horton, Bill Barrable,
Penny Clarke-Richardson, Karen Hornby

Forum Recommendations Group

Andrew Baker - adult neurocritical care and anesthesia
Graeme Rocker - adult ICU, bioethics, EOL care
Dan Howes - adult ER and ICU
Joe Pagliarello - adult ICU and surgery
Catherine Farrell - pediatric ICU
Stephane Langevin - adult ICU and anesthesia
Brian Wheelock - neurosurgery
Bill Wahl - adult/pediatric liver TP surgery
Greg Knoll - adult renal TP medicine
John Dossetor - bioethics, renal transplant
Bill Gourlay - adult renal TP surgery
Sandra Cockfield - adult renal TP medicine
David Grant - adult/pediatric liver/bowel TP surgery
Janet Davidson - hospital administration
Jane Chamber-Evans - ICU nursing, bioethics
Walter Glannon - bioethics
Kathy O’Brien - health law
Kimberley Young - CCDT

Critical Care Participants
Len Baron (AB), Alan Baxter (ON), Stephen Beed (NS), Mary Bennett (BC), Vinay Dhingra (BC), Peter Dodek (BC), Peter Goldberg (Qc) Perry Gray (MB), Jim Kutsogiannis (AB), Anne Marie Guerguerian (ON), Mark Heule (AB), Draga Jichici (ON), Marcelo Lannes (Qc), Neil Lazar (ON), Pierre Marsolais (Qc), Vivek Mehta (AB), Sharon Peters (NFLD), Pramod Puligandla (Qc), Ian Scott (BC), Michael Sharpe (ON), Susan Shaw (SK), Chris Soder (NS), Dan Zuege (AB),
David Zygun (AB),
Canadian Critical Care Society Statement
Jan 2007

• Endorsement of the DCD recommendations was passed.

• These recommendations represent the most comprehensive deliberation on DCD in any jurisdiction.

• Not recommending or advocating DCD:
  Obtaining consensus on DCD throughout the entire CCM community is not a realistic objective.

• Individual health centres or regions should be free to adopt the recommendations as a guide the development of DCD programs.
For Hospitals or Health Regions, the question was:

• **Whether** to do it
  1. Concerns about ICU EOL decision-making and practice
  2. Donation option and interventions may arise before death is established
  3. Diagnosis of death and immediacy of procurement
  4. Resource implications
DCD in Canada

For Hospitals or Health Regions, the question is

- **Why Not** do it
  1. Withdrawal of life sustaining technology is standard practice prior to death
  2. Response to donor individual/family requests & expectations
  3. Advance of DCD programs outside of Canada
  4. Societal needs re transplantation
  5. Public support
In a twist of fate, just a week before she became gravely ill, Sarah Beth watched a documentary on organ donation. The program moved her to tell us: "Just so you know, I've signed a card." Organ donation can be difficult to discuss for a young, vibrant and healthy person. But she made it very clear: "If I'm gone, I want someone else to live." Who could have known how important this conversation was to be.

The family very much wanted to honour Sarah Beth's wishes to become an organ donor after the brief, sudden illness that placed her on life support. We approached an ICU nurse at the Ottawa Hospital and were told that brain death was the only criterion for organ donation.

Before making the independent decision to withdraw life support, we approached the health-care team about Sarah Beth's wishes to become an organ donor. The compassionate health-care team at the Ottawa Hospital and Trillium Gift of Life Network were determined to do their best to fulfill Sarah Beth's wish: She was always one to make things happen and they wanted to do the same for her. In this situation, donation after cardiac death (DCD) was the only option to make Sarah Beth's wish possible.

The work done to meet Sarah Beth's wish helped change the protocol and make DCD acceptable. DCD marks a new era for organ donation in Canada with the potential to increase donations by 25 per cent across the country. Shortly after her death, two people received her organs. They are now on their way to full recovery.
DCD Programs in Canada 2006-2015

Established:
• Ontario (Province-wide)
• Quebec (Montreal, Quebec City)
• British Columbia
• Nova Scotia (Halifax)
• Alberta (Edmonton)
• Manitoba (initiated)
• Alberta (Calgary- pending)
Deceased organ donation
Canada 2005-2014

44% ↑ total in donors for 2005 – 2014
(15% ↑ NDD donors 2005 – 2014)
(86% ↑ DCD donors 2013 – 2014)

sources & limitations - refer to data notes page
DCD organ donation by province 2005 - 2014

n = 499 DCD donors
= 1136 transplants
People on transplant waitlist
Canada 2005 - 2014

Sources & limitations - refer to data notes page
Deceased organ donors in the UK 2007-14

58% more donors
49% increase in ppm

13.4 ppm to 19.9 ppm

DCD 155%

DBD 27%

Dale Gardiner, Alex Manara, with thanks
The rise and rise of UK DCD

The most common donor pathway in ICU

Consents by quarter

<table>
<thead>
<tr>
<th>Quarter</th>
<th>DBD</th>
<th>DCD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oct 09 - Mar 10</td>
<td>300</td>
<td>300</td>
</tr>
<tr>
<td>Apr 10 - Sep 10</td>
<td>300</td>
<td>300</td>
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<tr>
<td>Oct 10 - Mar 11</td>
<td>300</td>
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<td>Apr 11 - Sep 11</td>
<td>300</td>
<td>300</td>
</tr>
<tr>
<td>Oct 11 - Mar 12</td>
<td>300</td>
<td>300</td>
</tr>
<tr>
<td>Apr 12 - Sep 12</td>
<td>300</td>
<td>300</td>
</tr>
</tbody>
</table>

April 2014 to March 2015

- Family Approaches: 1,283 (DBD), 2,012 (DCD)
- Consents: 858 (DBD), 1,045 (DCD)

Dale Gardiner, Alex Manara, with thanks
Number of deceased donors and transplants in the UK, 1 April 2005 - 31 March 2015, and patients on the active transplant list at 31 March

<table>
<thead>
<tr>
<th>Year</th>
<th>Donors</th>
<th>Transplants</th>
<th>Transplant list</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005-2006</td>
<td>765</td>
<td>2197</td>
<td>3508</td>
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<tr>
<td>2006-2007</td>
<td>793</td>
<td>2386</td>
<td>3339</td>
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<tr>
<td>2007-2008</td>
<td>809</td>
<td>2384</td>
<td>3339</td>
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<tr>
<td>2008-2009</td>
<td>899</td>
<td>2559</td>
<td>3508</td>
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<tr>
<td>2009-2010</td>
<td>959</td>
<td>2655</td>
<td>3508</td>
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<tr>
<td>2010-2011</td>
<td>1010</td>
<td>2706</td>
<td>3339</td>
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<tr>
<td>2011-2012</td>
<td>1088</td>
<td>2916</td>
<td>3339</td>
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<tr>
<td>2012-2013</td>
<td>1212</td>
<td>3118</td>
<td>3508</td>
</tr>
<tr>
<td>2013-2014</td>
<td>1282</td>
<td>3508</td>
<td>3508</td>
</tr>
<tr>
<td>2014-2015</td>
<td>1282</td>
<td>3339</td>
<td>3339</td>
</tr>
</tbody>
</table>
Controlled DCD

Dependence upon Life-Sustaining Therapy and Consensual Decision to Withdraw Life-Sustaining Therapy

Option of Organ Donation and Consent

Withdrawal of Life-Sustaining Therapy

Determination of Death

Organ Procurement

From a medical, bioethical and legal perspective, the relevant phases of care:

a. before death

b. after death
Canadian Critical Care Society
Guidelines for the
Withdrawal of Life Sustaining Measures

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On behalf of the Canadian Critical Care Society’s Withdrawal of Life-Sustaining Treatment Working Group.
Death Prediction & Physiology After Removal of Treatment

DEPPART

autoresuscitation, predictors of death, family experiences

Sonny Dhanani  Amanda Van Beinum  Jennifer Chandler

Laura Hornby  Sam Shemie  Dale Gardiner  Jason Shahin

CNTRP, CIHR, CHEO RI, CCCTG

With thanks
Time to Loss of Brain Function after Circulatory Arrest

**Table 3. Types of measures of brain function or activity.**

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Spontaneous Cortical activity</th>
<th>Evoked</th>
<th>Spontaneous Brainstem activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of consciousness</td>
<td>EEG</td>
<td>SSEP</td>
<td>No known method</td>
</tr>
<tr>
<td>Brainstem Reflexes</td>
<td>BIS</td>
<td>MEP</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>BAEV</td>
<td></td>
</tr>
</tbody>
</table>
Monitored Asystole: Time to Loss of Consciousness & Isoelectric EEG

21 seconds asystole
@ 6s reaches for bedrail
@ 11s unconscious
@ 12s isolectric EEG

@ 21 seconds ROSC
@ 46s EEG normalizes followed by recovery of consciousness

Pacemaker implanted!

Pana et al, in submission, 2015
Loss of Neurological Function after abrupt Circulatory Arrest

1. Clinical loss of consciousness: 4-21 seconds

2. Isoelectric EEG: 10-30 seconds
   - May occur prior to circulatory arrest in progressive hypoxia-ischemia

Figure 2. Mechanisms of ischemia. This is for illustrative purposes only to demonstrate the various clinical contexts which were identified in the articles included in this review. It is understood that values for blood flow and time, as well as the slope, may vary significantly.
An Under-Recognized Benefit of Cardiopulmonary Resuscitation: Organ Transplantation

Alberto Orioles, MD\textsuperscript{1}; Wynne E. Morrison, MD, MBE\textsuperscript{1}; Joseph W. Rossano, MD, MS\textsuperscript{2}; Paul M. Shore, MD, MS\textsuperscript{3}; Richard D. Hasz, BS, MFS, CPTC\textsuperscript{4}; Amy C. Martiner, BA\textsuperscript{4}; Robert A. Berg, MD\textsuperscript{1}; Vinay M. Nadkarni, MD, MS\textsuperscript{1}

![Graph showing organ transplant percentages]

**Figure 3.** No difference in survival of overall organs, kidney, liver, and heart between cardiopulmonary resuscitation (CPR) organs and non-CPR organs.
### Four Leading Causes of Death by Donor Type

<table>
<thead>
<tr>
<th></th>
<th>Anoxia</th>
<th>CVA/Stroke</th>
<th>Head Trauma</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DCD</strong></td>
<td>86</td>
<td><strong>58</strong></td>
<td>61</td>
<td>13</td>
</tr>
<tr>
<td><strong>NDD</strong></td>
<td>188</td>
<td>292</td>
<td>119</td>
<td>40</td>
</tr>
<tr>
<td>% of DCD Donors</td>
<td>39</td>
<td>27</td>
<td>28</td>
<td>5</td>
</tr>
<tr>
<td>% of NDD Donors</td>
<td>29</td>
<td>46</td>
<td>19</td>
<td>6</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>274</strong></td>
<td><strong>350</strong></td>
<td><strong>180</strong></td>
<td><strong>53</strong></td>
</tr>
</tbody>
</table>

**Anoxic Brain Injury**
- 39% of DCD donors
- 32% of all donors

Total DCD Donors – 218
Total NDD Donors – 639
for the four leading causes of death.

*Apr 1, 2012 – Sep 30, 2015

TGLN, Sonny Dhanani, with thanks
Anoxic brain injury after resuscitated cardiac arrest is becoming the most common donor etiology.

Cardiac arrest & CPR after brain injury does not impact transplant outcomes including the heart.

DCD organs recover from $\geq 2$ distinct episodes of circulatory arrest—*the brain does not*. 
Oxygenated Circulation & Organ Resuscitation
intracorporeal, extracorporeal, *in situ*, *ex situ*
in vivo *ex vivo*

Madrid uDCD, Ivan Ortega with thanks

MCH, McGill ECMO
Adult heart transplantation with distant procurement and ex-vivo preservation of donor hearts after circulatory death: a case series

Kumud K Dhital, Arjun Iyer, Mark Connellan, Hong C Chew, Ling Gao, Aoife Doyle, Mark Hicks, Gayathri KumaraSinghe, Claude Soto, Andrew Dinale, Bruce Cartwright, Priya Nair, Emily Granger, Paul Jansz, Andrew Jabbour, Eugene Kotlyar, Anne Keogh, Christopher Hayward, Robert Graham, Phillip Spratt, Peter Macdonald

Summary
Background Orthotopic heart transplantation is the gold-standard long-term treatment for medically refractive end-stage heart failure. However, suitable cardiac donors are scarce. Although donation after circulatory death has been used for kidney, liver, and lung transplantation, it is not used for heart transplantation. We report a case series of heart transplantations from donors after circulatory death.

Methods The recipients were patients at St Vincent’s Hospital, Sydney, Australia. They received Maastricht category III controlled hearts donated after circulatory death from people younger than 40 years and with a maximum warm ischaemic time of 30 min. We retrieved four hearts through initial myocardial protection with supplemented cardioplegia and transferred to an Organ Care System (Transmedics) for preservation, resuscitation, and transportation to the recipient hospital.

Findings Three recipients (two men, one woman; mean age 52 years) with low transpulmonary gradients (<8 mm Hg) demonstrated posttransplant survival of 1 year. One patient received an eighth thoracic donor heart from a brain dead donor and survived 4 years with a functioning heart.

Transmedic Organ Care System
DCD Sequence

Controlled

- Dependence Upon LST and Decision to WLST
- Option of Organ Donation and Consent
- Withdrawal of Life Sustaining Therapy

Determination of Death

- Organ Procurement

Uncontrolled

- Cardiocirculatory Arrest and Decision to Terminate or Not Initiate Resuscitation
- Option of Organ Donation and Consent

US, Canada, UK, Australia

Spain, France, others

Shemie et al, CMAJ 2006
Transplants (number & type of) done from uDCDD in Spain from 1995 to 2010
1. Viable option for increasing the OD pool with success in kidney, liver and lung transplantation

2. Wide practice variation and heterogeneity of outcomes

3. Significant medical and logistic complexity

4. Medical, ethical, legal and procedural challenges including:
   - Definitions of refractory cardiac arrest
   - Time limits for organ ischemia
   - Timing and type of consent required
   - Determination of death
   - Organ preserving interventions

Ortega-Deballon, L. Hornby, Shemie Crit Care 2015
CPR – to – ECMO vs. CPR – to – uDCD

Oxygenated Circulation & Organ Resuscitation

Same Interventions for Cardiac Arrest & uDCD

MCH, McGill ECMO
1. CPR techniques and outcomes are gradually improving
   Kovacs et al, Resuscitation, 2015

2. CPR-ECMO-coronary revascularization is evolving
   Siao et al, Resuscitation, 2015
1. age 16-75, refractory OOHCA, 20 studies
2. Failed CPR 10-30 min
3. Favorable prognostic factors:
   • initial *shockable* cardiac rhythms
   • witnessed events
   • reversible primary cause of cardiac arrest
4. Variable CPR duration, time to cannulation (49-140m), coronary revascularization, hemodynamic interventions & temperature management
5. n=833
   • 39% survival to hospital discharge
   • 12% good neurological recovery (CPC 1-2)
   • 17 actual (19%), 88 potential donors in 8/20 studies
Cardiopulmonary Resuscitation: Saving Life Then Saving Organs?

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organ injury, the provision of CPR does not necessarily preclude organ donation or impair transplant graft function.

Orioles et al (4) should be commended for pursing research that focuses on the evolving role of CPR as it intersects with organ donation. As clearly stated, before brain death has been established, all CPR attempts must be provided with the sole intention of patient resuscitation. After brain death has been established, this study should encourage clinicians to attempt CPR with the goal of preserving the opportunity for organ donation.

However, a number of important questions remain, related to the limitations of the United Network of Organ Sharing (UNOS) database used and the retrospective nature of the study. It is important to emphasize that this is not a study of patients sustaining traumatic brain injury who deteriorated...
Derivation of the Uncontrolled Donation after Circulatory Determination of Death Protocol for New York City


were collected and posted in a collaborative internet environment. Data were analyzed using an iterative coding scheme to discern themes, theoretical constructs and a summary narrative to guide protocol development. A clinically appropriate, ethically sound UDCDD protocol for out-of-hospital settings has been derived. This program is likely to be accepted by NYC residents since the protocol was derived through partnership with government officials, subject experts and community participants.
Uncontrolled DCD in Canada?

Personal opinion: Is not feasible nor justified because:

• Consent during refractory cardiac arrest
• Interventions that reinstitute oxygenated circulation to the brain invalidate determination of death
• Efforts to save patient’s organs before saving patient’s life

The system should invest in extracorporeal resuscitation & coronary revascularization for refractory cardiac arrest

Save life 1st, save organs 2nd
DCD in Canada: Summary

1. Controlled DCD has advanced in Canada
   • quantitatively, the most important contributor to increasing organ donation performance
   • actual kidney, lung, liver and heart (pending)
   • implemented in 6/10 provinces, lead by Ontario
   • 499 DCD donors and 1136 DCD transplants to date

2. Anoxic brain injury is the most common cause of DCD donation

3. International experience with uncontrolled DCD is favorable, but unlikely to work in the Canadian context

4. Research and clinical investment in advanced CPR-ECMO and coronary revascularization may benefit patients first, and organ donation secondarily
With appreciation and thanks

Collaborators
Dorothy Strachan, Damon Scales, Stephen Beed, Matthew Weiss, Nathan Scales, Sonny Dhanani, Jason Shahin, Amanda Van Beinum, Ivan Ortega, Raluca Pana, Kim Trickey, Jeanne Teitelbaum, Ali Rutman, Alexandra Fletcher

Canadian Blood Services
Sylvia Torrance, Kimberly Young, Laura Hornby, Karen Hornby, Nick Lahaie, Ken Lotherington, Jennifer Hancock, Amber Appleby, Sophie Gravel
Pro-Con Debate
Toronto Critical Care Medicine Symposium 1999

Sam Shemie, Canada
“ICU’s should take responsibility for organ donation”

Malcolm Fischer, Australia
“It’s not our fercucking problem”
1. CPR techniques and outcomes are gradually improving
   Kovacs et al, Resuscitation, 2015

2. CPR-ECMO-coronary revascularization is evolving
   Siao et al, Resuscitation, 2015
Cardiac Arrest and Ischemia Reperfusion II
Impact on life preservation and organ donation

When CPR doesn’t work to save the patient:

1. Cardiac arrest/CPR from catastrophic brain injury to brain death does not impact graft utilization & outcomes (incl. heart)
   Orioles et al, CCM, 2013

2. Anoxic brain injury after resuscitated cardiac arrest is becoming the most common etiology for donation
   CORR CIHI 2014

3. Organs removed after circulatory arrest in DCD can be reanimated and/or repaired and transplanted (incl. heart)
   Iyer, Am J Transplant, 2015
   Boucek et al, NEJM 2008
   Machuca et al, Am J Transplant, 2015
Intersections of CPR & Deceased Organ Donation

1. Resuscitated cardiac arrest & anoxic brain injury
   - Primary cardiac arrest
   - After catastrophic brain injury

2. CPR in potential organ donors during evaluation

1. Refractory cardiac arrest and uncontrolled DCD
Organ Resuscitation
intracorporeal, extracorporeal, in situ, ex situ
in vivo ex vivo

Stockholm to Berlin

Toronto ex vivo lung program
A cardioprotective preservation strategy employing *ex vivo* heart perfusion facilitates successful transplant of donor hearts after cardiocirculatory death

Christopher W. White, MD, Ayyaz Ali, MD, PhD, Devin Hasanally, BSc, Bo Xiang, DMD, Yun Li, MD, Paul Mundt, BSc, Matthew Lytwyn, BSc, Simon Colah, MSc, Julianne Klein, MD, Amir Ravandi, MD, PhD, Rakesh C. Arora, MD, PhD, Trevor W. Lee, MD, Larry Hryshko, PhD, Stephen Large, MD, Ganghong Tian, MD, PhD, Darren H. Freed, MD, PhD
Things You Can Do to Organs Outside the Body That You Cannot do Inside the Body

1. Targeting of organ-specific treatment to the specific organ

1. Supra-therapeutic dosing of drugs (eg. antimicrobials) without the toxicity

3. Modulate inflammation without infection risk

4. Cellular repair and/or repopulation?
Ex Vivo Heart Reanirmination

Transmedic Organ Care System
Aim: Extracorporeal resuscitation during cardiopulmonary resuscitation (ECPR) deploys rapid cardiopulmonary bypass to sustain oxygenated circulation until the return of spontaneous circulation (ROSC). The purpose of this systematic review is to address the defining elements and outcomes (quality survival and organ donation) of currently active protocols for ECPR in refractory out-of-hospital cardiac arrest (OHCA) of cardiac origin in adult patients. The results may inform policy and practices for ECPR and help clarify the corresponding intersection with deceased organ donation.

Methods: We searched Medline, Embase, Cochrane and seven other electronic databases from 2005 to 2015, with no language restrictions. Internal validity and the quality of the studies reporting outcomes and guidelines were assessed. The review was included in the international prospective register of systematic reviews (Prospero, CRD42014015259).

Results: One guideline and 20 outcome studies were analysed. Half of the studies were prospective observational studies assessed to be of fair to good methodological quality. The remainder were retrospective cohorts, case series, and case studies. Ages ranged from 16 to 75 years and initial shockable cardiac rhythms, witnessed events, and a reversible primary cause of cardiac arrest were considered favourable prognostic factors. CPR duration and time to hospital cannulation varied considerably. Coronary revascularization, hemodynamic interventions and targeted temperature management neuroprotection were variable. A total of 833 patients receiving this ECPR approach had an overall survival to hospital discharge rate of 39%, including 12% with good neurological recovery. Additionally, 88 potential and 17 actual deceased organ donors were identified among the non-survivor population in 8 out of 20 included studies. Study heterogeneity precluded a meta-analysis preventing any meaningful comparison between protocols, interventions and outcomes.

Conclusions: ECPR is feasible for refractory OHCA of cardiac origin in adult patients. It may enable neurologically good survival in selected patients, who practically have no other alternative in order to save their lives with quality of life, and contribute to organ donation in those who die. Prospective studies are required to clarify patient selection, modifiable outcome variables, risk-benefit and cost-effectiveness.
1. Death determination
   • When is dead dead??
2. Unified death based on cessation of brain function

Shemie et al, Int Care Med, 2014
1. Increased organ donor potential/pool
2. Increased transplants

Research/Policy Questions
• Predicting death after WLST
• Death after cardiac arrest?
• Implementation obstacles?
• Uncontrolled DCD?

Established the medical, ethical and legal framework for the practice of DCD in Canada

Shemie et al, CMAJ, 2006
Decreasing NDD after TBI
Trend toward decreasing NDD after all forms of BI
NO CHANGE IN HOSPITAL MORTALITY

Table 2: Outcomes of critically ill patients with traumatic brain injury, anoxic brain injury, subarachnoid hemorrhage or intracerebral hemorrhage admitted to an intensive care unit in Calgary, Alberta, from Jan. 1, 2002, to June 30, 2012

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>% (no. of patients)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total: n = 2788</td>
</tr>
<tr>
<td>Traumatic brain injury, n = 1501</td>
<td>42.0 (388/924)</td>
</tr>
<tr>
<td>Anoxic brain injury, n = 516</td>
<td>27.5 (140/509)</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage, n = 408</td>
<td>73.8 (110/149)</td>
</tr>
<tr>
<td>Intracerebral hemorrhage, n = 363</td>
<td>54.4 (68/125)</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td></td>
</tr>
<tr>
<td>Total, n = 2788</td>
<td>42.0 (388/924)</td>
</tr>
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<td>Traumatic brain injury, n = 1501</td>
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<td>Anoxic brain injury, n = 516</td>
<td>73.8 (110/149)</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage, n = 408</td>
<td>54.4 (68/125)</td>
</tr>
<tr>
<td>Intracerebral hemorrhage, n = 363</td>
<td>54.4 (68/125)</td>
</tr>
<tr>
<td>Length of stay in intensive care unit</td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>3.0 (1.4–7.8)</td>
</tr>
<tr>
<td>Patients who died in an intensive</td>
<td>2.1 (0.7–4.6)</td>
</tr>
<tr>
<td>care unit</td>
<td>2.0 (0.9–5.5)</td>
</tr>
</tbody>
</table>

Note: IQR = interquartile range.
*Unless otherwise stated.
†Nonparametric testing (Kruskal–Wallis test) was used for continuous variables and χ² testing was used for discrete variables.

Kramer et al CMAJ 2013
In the UK, 50% of donors are DCD = most common donor pathway in ICU’s

Source: Transplant activity in the UK, 2011-2012, NHS Blood and Transplant
Logistics of DCD

Prior to Death:
1. Patients and etiologies
2. Decisions for WLST
3. Predictions of death after WLST
4. Consent discussions
5. Procedures to WLST
   1. Palliative and comfort care
   2. Mechanics and Responsibility
   3. Location
6. Death determinations
7. Separation of duties between ICU, OPO, TP team
Patient Conditions in Controlled DCD

1. Dependence on life sustaining therapy
   = airway, ventilatory and/or hemodynamic support

2. Consensual decision to withdraw LST

3. Anticipation of death

4. May include:
   i. Severe brain injury- irretrievably poor outcome
      i. Anoxia, trauma, CVA/ICH
   ii. End stage neuromuscular diseases
   iii. High spinal cord injuries
   iv. End stage single organ failure
WLST Requirements and Safeguards

1. The medical and ethical framework for WLST in the ICU falls within the domain of critical care practice and should not be influenced by donation potential.

2. The management of the dying process, including procedures for WLST, sedation/analgesia/ comfort care should proceed according to existing ICU practice in the best interests of the dying patient.

3. It is the responsibility of the critical care and neurocritical care communities to ensure optimal and safe practice in this field.
Donor-based Interventions Relative to Phases of Care

1. Variable international practice
   UK, Netherlands: - no interventions prior to death
   Canada: pre-mortem heparin
   USA: pre-mortem heparin +/- phentolamine +/- cannulation

2. Unclear relationship to allograft outcomes
Consent Rates and the ODR

Graph showing the consent/authorisation rate (%) over the years from 2003/04 to 2012/13. The rates are represented for ODR, DBD, and DCD. The highest rate is 67.7% in 2012/13 for ODR. The registrants (millions) are also shown on the graph, with the peak in 2012/13 at around 20 million.
Objective: Brain function during the dying process and around the time of cardiac arrest is poorly understood. In order to better inform clinical physiology and organ donation practices, we performed a scoping review of the literature to assess time to loss of brain function and activity after circulatory arrest.

Data Sources: Medline and Embase databases were searched from inception to June 2014 for articles reporting the time interval to loss of brain function or activity after loss of systemic circulation.

Study Selection: Original articles reporting time intervals to loss of brain function and/or brain activity during circulatory arrest were included.

Data Extraction: 39 studies met selection criteria. In humans, the data was extracted mostly from case reports and case series. Animal data was extracted from animal models of systemic circulatory arrest or global cerebral hypoperfusion.

Data Synthesis: Seven human studies and 10 animal studies reported that EEG activity is lost less than 30 seconds after abrupt circulatory arrest. In the setting of existing brain injury, with progressive loss of oxygenated circulation, loss of EEG may occur prior to circulatory arrest. Cortical evoked potentials may persist for several minutes after loss of circulation.

Conclusion: The time required to lose brain function varied according to clinical context and method by which this function is measured. Most studies show that clinical loss of consciousness and loss of EEG activity occur within 30 seconds after abrupt circulatory arrest, and may occur prior to circulatory arrest after progressive hypoxia-ischemia. Prospective clinical studies are required to confirm these observations.

Submitted, CCM, 2015
After a cardiac arrest, how long does it take before you are dead?
Definition of a Donor

1. NDD (brain death) only?

= deceased donor rates will not improve.

2. NDD & DCD = all patients with catastrophic brain injury who have withdrawal of mechanical ventilation?

= deceased donor rates (NDD & DCD) will likely improve
Wide international variability in criteria, diagnostic tests and wait periods for death determination after cardiac arrest
After Cardiac Arrest, How Long Does it Take for Your Brain to Stop Working?
Time from Circulatory Arrest to Isoelectric (Flat) EEG
Less than 20 seconds

1. Arrest of cerebral blood flow in mammals
   = 10-15 seconds (Hossmann and Kleihues, Arch Neurol 1973)

2. Arrest of cerebral blood flow in primates
   = 10-15 seconds (Steen et al, Anesthesiology, 1985)

3. Brief cardiac arrest in humans
   10 seconds (Clute and Levy, Anesthesiology, 1990)
   12 seconds (Lasasso et al, Anesth Analg 1992)
   12 seconds (Moss and Rockoff, JAMA 1980)
The circulatory–respiratory determination of death in organ donation*

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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 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 “inversible” 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: 963–970)

Key Words: organ donation; circulatory death; cardiac death; dead donor rule; auto-resuscitation; extracorporeal membrane oxygenation

The determination of human death continues to provoke public fascination and medical scrutiny. In its 1981 report Defining Death, the U.S. President’s Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research provided the most frequently cited comprehensive analysis (1). Defining Death had three principal goals: 1) to provide a conceptual basis for the new medical practice of death determination using neurological tests; 2) to explain the relationship between determining death on neurological and circulatory–respiratory grounds; and 3) to enhance the uniformity among jurisdictions by proposing and justifying a common standard of death.

“Death is the permanent cessation of circulation

The use of ECMO in DCD should be abandoned because by restoring brain circulation, it retroactively negates the previous death determination.
Autoresuscitation

Spontaneous, unassisted resumption of circulation

Anecdotal reports = lived experiences of clinicians

Unclear if related to misdiagnosis or spontaneous resumption after correct diagnosis

Often cited as an ethical and practical concern
Circulatory Death Determination in Uncontrolled Organ Donors: A Panel Viewpoint

James L. Bernat, MD; Thomas P. Bleck, MD; Sandralea A. Blosser, MD; Susan L. Bratton, MD, MPH; Alexander M. Capron, LLB; Danielle Cornell, BSN, CPTC; Michael A. DeVita, MD; Gerard J. Fulda, MD; Alexandra K. Glazier, JD, MPH; Cynthia J. Gries, MD; Mudit Mathur, MD; Thomas A. Nakagawa, MD; Sam D. Shemie, MD

One barrier for implementing programs of uncontrolled organ donation after the circulatory determination of death is the lack of consensus on the precise moment of death. Our panel was convened to study this question after we performed a similar analysis on the moment of death in controlled organ donation after the circulatory determination of death. We concluded that death could be determined by showing the permanent or irreversible cessation of circulation and respiration. Circulatory irreversibility may be presumed when optimal cardiopulmonary resuscitation efforts have failed to restore circulation and at least a 7-minute period has elapsed thereafter during which autoresuscitation to restored circulation could occur. We advise against the use of postmortem organ support technologies that reestablish circulation of warm oxygenated blood because of their risk of retroactively invalidating the required conditions on which death was declared. [Ann Emerg Med. 2013;xxxx.]

Programs of organ donation after the circulatory determination of death (DCDD) have increased in prevalence markedly during the past 2 decades.1 In the United States and Canada, DCDD programs are restricted to the “controlled” circumstance in which the surrogate decisionmaker of a hopelessly ill, ventilator-dependent patient in an ICU decides to withdraw life-sustaining therapy to allow the patient to die but additionally requests that the patient donate organs after death or honors the recorded wishes of the patient.2 A controlled donation after the circulatory determination of death (cDCDD) coordinates the process of withdrawing life-sustaining therapy with the readiness of the surgical team to remove the transplantable organs as quickly as possible after the patient’s death.3 Several European countries, particularly Spain and France, have implemented programs of “uncontrolled” donation after the circulatory determination of death (uDCDD) on the basis of a similar clinical approach.4,5

The one critical issue dogging all DCDD protocols is the validity of death determination in the donor patient. Since the earliest cDCDD protocol conducted at the University of Pittsburgh Medical Center more than 20 years ago, critics have questioned whether the donor is actually dead at the moment death is declared.9-11 The University of Pittsburgh protocol permitted donor death declaration once asystole and apnea had been present for 2 minutes.12 Criticism over the proper timing of donor death declaration has persisted because of the apparent arbitrariness of death determination: each cDCDD protocol stipulates its own criteria for determining death. For example, the Institute of Medicine recommended 5 minutes of asystole,13 some European countries require 10 minutes,14 and a DCDD heart transplantation protocol at Denver Children’s Hospital permitted death declaration in some neonates after only 75 seconds of asystole.15
DCD in Canada: Summary Messages

1. The medical, ethical and legal framework for practices in Canada have been established

2. Supported by the Critical Care community

3. Progressive implementation in Canada, lead by Ontario

4. Important contribution to donation and transplantation

5. Demanding process- requires leadership & planning

6. Challenges ICU and OR care processes and resourcing
Resource Implications

Timing of WLST dependent on readiness/orchestration of entire team process

OR suite and surgical procurement team on hold = an evening/night procedure

ICU access/ICU LOS
2\textsuperscript{nd} physician to declare death
ICU team (nurse, RT, MD) provides off service care

20-30\% of consented DCD do not proceed.....
A Donation After Circulatory Death Program Has the Potential to Increase the Number of Donors After Brain Death

Andrew R. Broderick, MSc\textsuperscript{1}; Alex Manara, FFICM, FRCA, FRCP\textsuperscript{2}; Simon Bramhall, MD, FRCS\textsuperscript{3}; Maria Cartmill, MB, ChB, FRCS (SN)\textsuperscript{4}; Dale Gardiner, MBBS, FFICM\textsuperscript{5}; James Neuberger, DM, FRCP\textsuperscript{6}

**Objectives:** Donation after circulatory death has been responsible for 75% of the increase in the numbers of deceased organ donors in the United Kingdom. There has been concern that the success of the donation after circulatory death program has been at the expense of donation after brain death. The objective of the study was to ascertain the impact of the donation after circulatory death program on donation after brain death in the United Kingdom.

**Design:** Retrospective cohort study.

**Setting:** A national organ procurement organization.

**Patients:** Patients referred and assessed as donation after circulatory death donors in the United Kingdom between October and December 2013.

**Interventions:** None.

**Measurements and Main Results:** A total of 257 patients were assessed for donation after circulatory death. Of these, 193 were...
Hypothermia and Organ Resuscitation

1. Works for brain protection
   - Newborn asphyxia  
     
   - Cardiopulmonary bypass and circulatory arrest  
     
   - Out of hospital cardiac arrest  

   Bernard et al, NEJM 2002

2. Does not work for brain protection
   - Traumatic brain injury  
     
   - Out of hospital cardiac arrest  
     
   - Pediatric cardiac arrest  

   Hutchison et al, NEJM 2008

   Neilson et al, NEJM 2013

   Moler et al, NEJM 2015

3. Works for organ protection in situ/ex vivo/ex situ
   - Organ procurement and transplantation  
     
   - Organ function after brain death?

   Malinoski et al, NEJM in press 2015
Kidney transplant function using organs from non-heart-beating donors maintained by mechanical chest compressions

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Abstract

Objective: This study aims to determine the failure rate of transplanted kidney grafts in recipients of organs from non-heart-beating donors (NHBDs) who have had mechanical chest compressions to maintain a circulation before organ retrieval.

Methods: A retrospective observational study based on review of the emergency medical service database and case histories of NHBDs, and information periodically sent by transplant units about donors and organs. The following variables were studied: age, sex, transfer hospital, time to arrival on the scene of cardiopulmonary arrest, time to arrival in hospital, number and type of organs retrieved, use of mechanical chest compression devices, and kidney function in graft recipients. The study covered the period between January 2008 and November 2009. During 2008 standard manual chest compressions were used and during 2009 mechanical chest compression devices were used.

Results: In 39 transplanted kidneys from donors receiving mechanical chest compressions primary failure was documented in recipients on two occasions (5.1%). Kidneys transplanted from donors who had manual chest compressions resulted in three primary failures in recipients (9.1%). The difference between the two groups was not significant (p=0.5). Three patients achieved successful return of spontaneous circulation in the mechanical chest compression group after initiation of the NHBD donor protocol.

Conclusion: We have described our experience and protocol for non-heart beating donation using victims of out-of-hospital cardiac arrest in whom cardiopulmonary resuscitation has been unsuccessful as donors. Primary kidney graft failure rates in organs from non-heart-beating donors is similar when manual or mechanical chest compression devices are used during cardiopulmonary resuscitation.
Protocols for uncontrolled donation after circulatory death: a systematic review of international guidelines, practices and transplant outcomes

Iván Ortega-Deballon LL.B, CFRN, MSc (Ed)\textsuperscript{1,2,3,4,5} Laura Hornby MSc\textsuperscript{6,7}, Sam D Shemie MD\textsuperscript{8,9,10}

Uncontrolled DCD: Procedure Timelines

- **T 0** = Cardiac Arrest = NO-FLOW
- **T 1** = Start CPR = LOW-FLOW
- **T 2** = Termination of CPR
- **T 3** = Organ preservation during transport\textsuperscript{*}
- **T 4** = Arrival at the hospital
- **T 5** = Diagnosis of death and ‘No-touch period’\textsuperscript{**}
- **T 6** = Cannulation and preservation continues

Uncontrolled DCD: Clinical Pathway

- **T 0 – T 1** = Cardiac Arrest (NO-FLOW)
- **T 2 – T 1** = CPR total time (LOW-FLOW)
- Refractory Cardiac Arrest & decision to terminate CPR
- Rapid transport while organ preservation of potential donor begins\textsuperscript{*}
- Diagnosis of death\textsuperscript{**}
- Rapid cannulation and organ preservation continues at the hospital\textsuperscript{**}
- Possibility of organ donation & consent obtained\textsuperscript{***}
- Organ procurement

\textsuperscript{*} In Spain & France before declaring death. In NY City after declaring death.

\textsuperscript{**} In Spain & France, the diagnosis of death occurs upon arrival at the hospital but organ preservation begins during transport. In NY City, after the diagnosis of death on the field, organ preservation begins. The ‘no-touch period’ is not defined.

\textsuperscript{***} In NY City, consent is required for cannulation but in Spain & France consent is not required prior to cannulation.
Permanent Absence of Circulation and Cessation of Brain Function
DCD in Canada

For Hospitals or Health Regions, the question is

• **Why Not** do it
  1. Withdrawal of life sustaining technology is standard practice
  2. Response to donor individual/family requests & expectations
  3. Advance of DCD programs outside of Canada
  4. Advance of DCD in Canada
  5. Societal needs re transplantation
  6. Public support