MHIF FEATURED STUDY:  
OCS DCD Heart CAP

DESCRIPTION: The Portable Organ Care System (OCS™) Heart for Resuscitation, Preservation and Assessment of Hearts from Donors After Circulatory Death Continued Access Protocol (OCS DCD Heart CAP)

To enable continued clinical access to DCD heart transplantation in the U.S. and to continue to collect additional data on the performance of the OCS Heart System to resuscitate, preserve and assess hearts donated after circulatory death for transplantation to increase the pool of donor hearts available for transplantation.

A prospective, single arm, continues access protocol.

CRITERIA LIST/ QUALIFICATIONS:

Donor Heart Inclusion

- Maastricht Category III DCD donor, defined as expected death after the withdrawal of life-supportive therapy (WLST)
- Donor age 18-49 years old inclusive
- Warm ischemic time (WIT) ≤ 30 mins, with warm ischemic time defined as: Time from when mean systolic blood pressure (SBP) is < 50 mmHg or peripheral saturation < 70% to aortic crossclamp
- and administration of cold cardioplegia in the donor.

To date, MHIF has had eight successful uses of the TransMedics Organ Care System (OCS™), aka “Heart in the Box”
FRANKENSTEIN COMES TO ABBOTT:
A heart failure talk.

Bassam Shukrallah, MD and Karol Mudy, MD

Disclosures

• No COI
Objectives

- Organ care system (OCS) technology in greater details
- Donation after brain death (DBD) and donation after circulatory death (DCD)
- MHI OCS Data for DCD/DBD

Where it all began

- Waleed Hassanein, MD
  - Inventor and founder of TransMedics
  - Georgetown medical school, MD and residency
  - BWH/Roxbury VA, CT surgery research fellowship
  - OCS 2014
CONTINUOUS PERFUSION OF DONOR HEARTS IN THE BEATING STATE EXTENDS PRESERVATION TIME AND IMPROVES RECOVERY OF FUNCTION

Waleed H. Hassanein, MD
Lambros Zellos, MD
Tracey A. Tyrrell, BA
Nancy A. Healey, BS
Michael D. Crittenden, MD
Vladimir Birjanuk, MD
Shukri F. Khuri, MD

Fig 2. Schema of perfusion apparatus. Panel A shows the monitoring equipment and chamber for the heart. Panel B is a detailed enlargement of the heart chamber depicting the instrumentation. LA, Left atrium; RA, right atrium; PA, pulmonary artery.
Conclusion ➔ TIME Extended!

55% Δbaseline, P = 0.01. **Conclusion:** This new method extends the current preservation limit and avoids time-dependent ischemic injury, thereby allowing for distant procurement of donor organs. (J Thorac Cardiovasc Surg 1998;116:821-30)

Organ Care System

- **Wireless Monitor**: Controls and displays heart parameters.
- **Heart Perfusion Module**: Provides sterile blood circuit and protected environment for the donor heart.
- **Heart Solution Set**: Infused into blood circulation; provides nutrients and substrates.
- **Organ Care System**: Portable, integrated perfusion & assessment system, fits in all standard modes of transportation for donor organs.
Array of non-invasive, ultrasound sensors monitor critical parameters, such as blood pressure, blood flow and blood cell counts, to sustain the organ’s health while in transit.

A "solution set" infuses the organ with essential nutrients and substrates.

Wireless control monitor allows to manipulation of above after the organ has been attached to the OCS.

### Three main components

- Array of non-invasive, ultrasound sensors monitor critical parameters, such as blood pressure, blood flow and blood cell counts, to sustain the organ’s health while in transit.
- A "solution set" infuses the organ with essential nutrients and substrates.
- Wireless control monitor allows to manipulation of above after the organ has been attached to the OCS.

### DBD vs. DCD

<table>
<thead>
<tr>
<th>DBD (Donation After Brain Death)</th>
<th>DCD (Donation After Cardiac Death)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injury</td>
<td>Severe brain injury from trauma, cerebral vascular accident, anoxic event, other (INTERNAL TO OPO)</td>
</tr>
<tr>
<td>モニタリング</td>
<td>Severe brain injury from trauma, cerebral vascular accident, anoxic event, other (INTERNAL TO OPO)</td>
</tr>
<tr>
<td>Monitor</td>
<td>Classical brain death (including电气 test) is consistent with brain death. It usually complete any post cardiac death testing (in the case) is required (i.e., mearn plane).</td>
</tr>
<tr>
<td>Monitor</td>
<td>No. Some neurological reflexes is still present</td>
</tr>
<tr>
<td>Prolonge</td>
<td>Brain death: This is the legal time of death.</td>
</tr>
</tbody>
</table>
| Action | Brain death declaration is made for hospital physician (not OPO).  
  Signed brain death notes and consent form are signed and are signed.  
  spine and Regional coordination, all heart and brain death decisions made.  
  Anesthesiology is present for intraoperative heart and brain death management.  
  Four hours reconstituting organ in-situ.  
  Family/Nurse/Physician consultation with the donor family.  
  Consent. Signed fully, void and consent form obtained.  
  OPO and hospital work cooperatively on medical management of the donor patient.  
  Referral of support can take place in OR in ICU.  
  1. OR with a portable vent is used for ICU  
  2. OPO nurses institute nursing care for heart and brain death:  
  | Heart death |  
  | No blood pressure, pulse or cardiac sounds |  
  | No spontaneous respiration |  
  | Mri to ensure no autolysis |  
  | After five minutes of cardiac arrest, organ donor physician issues death declaration.  
  | Donor team immediately begins organ recovery, takes one to two hours to recover organs in-situ.  |

---

MHIF Cardiovascular Grand Rounds | March 22, 2021

Page 11 of 67
### DBD vs. DCD

**Donation After Brain Death (DBD)**

<table>
<thead>
<tr>
<th>Injury</th>
<th>Donor death: This is the legal time of death.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe brain injury from trauma, cardiac arrest, accident, anoxic event, or other - REFER TO OPO.</td>
<td>Severe brain injury from trauma, cardiac arrest, accident, anoxic event, or other - REFER TO OPO.</td>
</tr>
</tbody>
</table>

**Donation After Cardiac Death (DCD)**

<table>
<thead>
<tr>
<th>Injury</th>
<th>Donor death: This is the legal time of death.</th>
</tr>
</thead>
<tbody>
<tr>
<td>No neurological reflex is still present.</td>
<td>No neurological reflex is still present.</td>
</tr>
</tbody>
</table>

**Minutes Clocks for Brain Death**

- Yes: Clinical Death (including apnea test) is consistent with brain death. Once brain death is declared, OPO and hospital work cooperatively on medical management of the donor patient. Patient remains on ventilator throughout organ recovery. Anesthesiology is present for inotropic fluid and BP management. Transplant team can spend three to four hours recovering organs in situ.

**Action**

- Transplant team to withdraw support. Donation discussion with family. They consent. Signed kidney, lungs and consent forms are faxed to OPO. OPO and hospital work cooperatively on medical management of the donor patient. Withdrawal of support can take place in OR or ICU:
  - IT with a portable vent is used for DE and iodine injections administered for 60 minutes to ensure non-infectious.
  - After five minutes of cerebral circulation, hospital physician (not OPO) declares death.
  - Transplant team immediately begins organ recovery, takes one to two hours to recover organs on site.

---

### DBD vs. DCD

**Donation After Brain Death (DBD)**

<table>
<thead>
<tr>
<th>Injury</th>
<th>Donor death: This is the legal time of death.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe brain injury from trauma, cardiac arrest, accident, anoxic event, or other - REFER TO OPO.</td>
<td>Severe brain injury from trauma, cardiac arrest, accident, anoxic event, or other - REFER TO OPO.</td>
</tr>
</tbody>
</table>

**Donation After Cardiac Death (DCD)**

<table>
<thead>
<tr>
<th>Injury</th>
<th>Donor death: This is the legal time of death.</th>
</tr>
</thead>
<tbody>
<tr>
<td>No neurological reflex is still present.</td>
<td>No neurological reflex is still present.</td>
</tr>
</tbody>
</table>

**Minutes Clocks for Brain Death**

- Yes: Clinical Death (including apnea test) is consistent with brain death. Once brain death is declared, OPO and hospital work cooperatively on medical management of the donor patient. Patient remains on ventilator throughout organ recovery. Anesthesiology is present for inotropic fluid and BP management. Transplant team can spend three to four hours recovering organs in situ.

**Action**

- Transplant team to withdraw support. Donation discussion with family. They consent. Signed kidney, lungs and consent forms are faxed to OPO. OPO and hospital work cooperatively on medical management of the donor patient. Withdrawal of support can take place in OR or ICU:
  - IT with a portable vent is used for DE and iodine injections administered for 60 minutes to ensure non-infectious.
  - After five minutes of cerebral circulation, hospital physician (not OPO) declares death.
  - Transplant team immediately begins organ recovery, takes one to two hours to recover organs on site.
**Organ Donation after Circulatory Death**

- Widely accepted in Kidney, liver and lung
- Concerns in heart DCD donation:
  - Warm ischemia
  - Inability to assess the donor heart prior to transplantation
Outcomes of Donation After Circulatory Death Heart Transplantation in Australia

Hong Chee Chew, MS,1,2,*, Arjun Iyer, PhD,3 Mark Connellan, FC CAS SA,4 Sarah Scheuer, MD,5 Jeanette Villamoea, PhD,6 Ling Gao, PhD,7 Mark Hicks, PhD,8 Michelle Harkness, RN, MCN,9 Claudio Soto, MS,10 Andrew Dinale, BAvSc,11 Priya Nair, MD,12 Aladair Watson, PhD,13 Emily Granger, MBBS,13 Paul Jaraz, PhD,13 Kavitha Muthiah, PhD,13 Andrew Jabbour, PhD,13 Eugene Kotlyar, MD,13 Anne Keogh, MBBS,13 Chris Hayward, MD,13

RESULTS: Hearts were retrieved from 33 of 45 DCD donors. A total of 12 donors did not progress to circulatory arrest within the pre-specified timeframe. Eight hearts failed to meet viability criteria during normothermic machine perfusion, and 2 hearts were declined due to machine malfunction. A total of 23 hearts were transplanted between July 2014 and April 2018. All recipients had successful implantation, with mechanical circulatory support utilized in 9 cases. One case requiring extracorporeal membrane oxygenation subsequently died on the sixth post-operative day, representing a mortality of 4.4% over 4 years with a total follow-up period of 15,500 days for the entire cohort. All surviving recipients had normal cardiac function on echocardiogram and no evidence of acute rejection on discharge. All surviving patients remain in New York Heart Association functional class I with normal biventricular function.

CONCLUSIONS: DCD heart transplant outcomes are excellent. Despite a higher requirement for mechanical circulatory support for delayed graft function, primarily in recipients with ventricular assist device support, overall survival and rejection episodes are comparable to outcomes from contemporary brain-dead donors. (J Am Coll Cardiol 2019;73:1447-59) © 2019 Published by Elsevier on behalf of the American College of Cardiology Foundation.

A 5-year single-center early experience of heart transplantation from donation after circulatory-determined death donors

Simon Messer, PhD, Sendi Cemic, MD, Aravinda Page, MBChB, MBBChir,

RESULTS: During the 5-year study, DCD heart donation increased overall heart transplant activity by 48% (79 for DCD and 164 for DBD). There was no difference in survival at 30 days (97% for DCD vs 99% for DBD, p = 1.00) or 1 year (91% for DCD vs 89% for DBD, p = 0.72). There was no difference in the length of stay in the intensive care unit (7 for DCD vs 6 for DBD days, p = 0.24) or in the hospital (24 for DCD vs 25 for DBD days, p = 0.84).

CONCLUSIONS: DCD heart donation increased overall heart transplant activity at RPH by 48%, with no difference in 30-day or 1-year survival in comparison with conventional DBD heart transplantsations.

DBD vs. DCD procurement

• Warm ischemic time $\rightarrow$ SBP <50 mmHg or O2 sat <70%
• Cardiac death must occur with 30 minutes of WIT
DCD procurement

Lung/kidney/liver

DCD procurement

21

22
Cross-clamp/arrest/procurement

Instrumentation and attachment to the OCS
Organ Care System

- Continuously monitoring physiological measurements:
  - coronary flow - CF
  - aortic flow - AOF
  - Aortic pressure - AOP
  - mixed venous
  - Arterial saturation
  - hematocrit
  - blood temperature
  - pulmonary artery pressure
  - electrocardiogram

Assessing and monitoring parameters

- Hemodynamic parameters:
  - Aortic pressure (goal: 65-90 mm Hg)
  - Coronary blood flow (goal: 650-900 mL/min)

- Perfusate Lactate level
  - Arterio-venous difference
  - Absolute lactate level (goal: <5 mmol/L)

- Visual Inspection
OCS Update

Bassam Shukrallah, MD  Karol Mudy, MD
March 22, 2021

Disclosures

• Shukrallah’s original accent is not really southern
• Mudy’s accent is real
Successful Utilization of Extended Criteria Donor Hearts for Transplantation – Results of The OCS Heart EXPAND Trial


- Duke University Medical Center, Durham, NC, Massachusetts General Hospital, Boston, MA, Cedars-Sinai Medical Center, Los Angeles, CA, Spectrum Health, Grand Rapids, MI, University of Michigan, Ann Arbor, MI, University of Minnesota, Minneapolis, MN, Indiana University, Indianapolis, IN, Mount Sinai, New York, NY, Vanderbilt University, Nashville, TN, Minneapolis Heart Institute, Minneapolis, MN, Cleveland Clinic Foundation, Cleveland, OH, University of Washington, Seattle, WA,

*JHLT*, April, 2019; Volume 38, Issue 4

OCS Heart EXPAND Trial Design & Endpoints

- **Single Arm Study:**
  - These hearts are not routinely being utilized and could not be compared to standard criteria hearts

- **Donor Criteria** – Targeted donor hearts that may benefit from perfusion
  - Extended ischemia time ≥4 hours; or
  - Older donors >45 yo; or
  - Down time ≥20 mins; or
  - LVH hearts >12 ≤16 mm thickness; or
  - Non specific CAD

- **Effectiveness Endpoints:**
  - Primary: Composite of patient survival at day 30 and freedom from severe PGD in the first 24 hours
  - Secondary: Donor hearts utilization rate

- **Safety Endpoint:**
  - Rate of moderate and severe PGD up-to day 30 post transplant
OCS Heart EXPAND Donor Heart Utilization

81% Utilization Rate

OCS Heart Perfused Donor Hearts N=93

Did Not Meet Transplant Criteria on OCS Heart N=18

Met Transplant Criteria on OCS Heart N=75

OCS Reduced Ischemic Time on Donor Hearts

Total Out of Body Time
(mean ± SD) = 381 ± 93 min Range 173-682 min

DONOR

Time (min)

29.7 278.6 72.5

Pre-OCS Cold Ischemia (Harvest & OCS Instrumentation)
OCS Perfusion
Post-OCS Warm Ischemia (Reimplantation)
OCS Heart EXPAND – Total Out of Body Time vs. Ischemic Time

Mean Time (Minutes)

- Total Cross-Clamp (out of body) Time
- Total Ischemic Time

OCS Heart EXPAND – Incidence of PGD

Proportion (%)

- Moderate or Severe
- Severe
EXPAND Results

- The OCS™ Heart EXPAND Trial met its primary effectiveness and safety endpoints

- The use of OCS Heart System resulted in high utilization of ECD hearts with excellent short-term post-transplant outcomes, most notably a low rate of PGD

- These results provide clinical evidence supporting its use in ECD heart preservation and assessment, and may significantly increase donor utilization for transplantation
**Objectives**: To provide additional data evaluating the safety and effectiveness of the OCS Heart System to preserve and assess donor hearts that do not meet current standard donor heart acceptance criteria for transplantation to potentially improve donor heart utilization for transplantation at a range of transplant centers in the U.S. and to permit patients and physicians access to the OCS Heart System while a PMA application is under preparation and review.

**Trial Design**: A prospective single-arm trial

**Trial Size**: A maximum of 12 participating sites with 48 transplanted heart recipients

---

**Donor eligibility, at least one of the following**:

- Expected total cross-clamp time ≥ 4 hours
- Expected cross-clamp time ≥ 2 hours PLUS at least one of following risk factors:
  - Donor age > 55 yo.; or
  - Donor age 45 – 55 yo. without coronary catheterization data; or
  - LV septal or posterior wall thickness > 12 ≤ 16mm; or
  - Reported down time ≥ 20 min; or
  - Left heart Ejection Fraction ≥ 40% - ≤ 50%; or
  - Donor angiogram with luminal irregularities no significant CAD; or
  - History of carbon monoxide poisoning; or
  - Social history of alcoholism; or
  - History of diabetes with negative coronary angiogram for CAD
Heart EXPAND Clinical Trial Endpoints

**Primary Endpoint:** A composite endpoint of patient survival at Day-30 post-transplant and absence of severe primary heart graft dysfunction (PGD) (left or right ventricle) in the first 24 hours post-transplantation

**Secondary Endpoints:**
- Patient survival at day-30 post-transplantation
- Incidence of severe primary heart graft dysfunction (PGD) (left or right ventricle) in the first 24 hours post-transplantation
- Rate of donor hearts utilization that were successfully transplanted after preservation and assessment on the OCS™ Heart device

**Safety Endpoint:** Incidence of heart graft related Serious Adverse Events (SAEs) in the first 30 days post heart transplantation, defined as:
- Moderate or Severe primary heart graft dysfunction (PGD) (left or right ventricle), not including rejection or cardiac tamponade, according to 2014 ISHLT consensus manuscript
- Primary graft failure requiring re-transplantation

**EXPAND CAP**

- 66 Extended criteria hearts have been transplanted across 6 sites. There are 9 remaining enrollment spots
- There have been 4 hearts declined after OCS assessment resulting in an overall utilization of 94%
- >45% of the donors have had multiple inclusion criteria including longer expected cross clamp time, older age, left ventricular hypertrophy, low EF, etc.
EXPAND CAP

• >45% of the recipients have been on pre-transplant mechanical support (LVAD, RVAD, BiVAD, ECMO)
• Mean AOP has been in the range of 78 mmHg
• Mean CF has been in the range of 750 mL/min
• Mean perfusion time has been in the range of 4.5 hours with the longest in this study being 446 minutes
• 100% survival at 30 days and <10% incidence of severe PGD (L or R)

EXPAND CAP- MHI

• 6 patients enrolled- August 2019- January 2021
• 100% utilization rate- 6 runs-> 6 transplants
• 0% severe PGD- No need for MCS postoperatively
• All alive- 100% survival
• 66% preoperative MCS (LVAD)
Heart Transplantation from DCD heart donation provides comparable short-term outcomes to traditional DBD heart transplants (28 hearts).

**SPECIAL FEATURE**

**Outcome after heart transplantation from donation after circulatory-determined death donors**

Simon Messer, MBChB, Aravinda Page, MBChB, Richard Axell, PhD, Marius Berman, MD, Jules Hernández-Sánchez, PhD, Simon Colah, BSc, Barbara Parizkova, MD, Kamen Vatchanov, MD, John Dunning, MBChB, Evgeny Pavlushkov, MD, PhD, Sendhil K. Balasubramanian, MBBS, Jayan Parameshwar, MBBS, MD, MPhil, Yasir Abu Omar, MBChB, DPhil, Martin Goddard, MBChB, Stephen Pettitt, MBBS, PhD, Clive Lewis, MBChB, PhD, Anna Kydd, MBBS, MD, David Jenkins, MBBS, MS, Christopher J. Watson, MBChB, MD, Catherine Sudarshan, MBBS, MD, Pedro Catarino, MBChB, Marie Findlay, Ayyaz Ali, MBBS, PhD, Steven Tsui, MBChB, MD, and Stephen R. Large, MBBS, MS, MBA

From the Department of Transplantation, Papworth Hospital National Health Service Foundation Trust, Papworth Everard, Cambridgeshire, United Kingdom; Papworth Trials Unit Collaboration, Papworth Hospital National Health Service Foundation Trust, Papworth Everard, Cambridgeshire, United Kingdom; Medical Research Council Biostatistics Unit, University of Cambridge, School of Clinical Medicine, Cambridge Institute of Public Health, Cambridge, United Kingdom; and the Department of Surgery, Cambridge University Hospitals National Health Service Foundation Trust and the National Institute for Health Research, Cambridge Biomedical Center, University of Cambridge, Cambridge, United Kingdom.

**METHODS:** DCD hearts were retrieved using normothermic regional perfusion (NRP) or direct procurement and perfusion (DPP). During NRP, perfusion was restored to the arrested heart within the donor with the exclusion of the cerebral circulation, whereas DPP hearts were removed directly. All hearts were maintained on machine perfusion during transportation. A retrospective cohort of DBD heart transplants, matched for donor and recipient characteristics, was used as a comparison group. The primary outcome measure of this study (set by the United Kingdom regulatory body) was 90-day survival.
METHODS: DCD hearts were retrieved using normothermic regional perfusion (NRP) or direct procurement and perfusion (DPP). During NRP, perfusion was restored to the arrested heart within the donor with the exclusion of the cerebral circulation, whereas DPP hearts were removed directly. All hearts were maintained on machine perfusion during transportation. A retrospective cohort of DBD heart transplants, matched for donor and recipient characteristics, was used as a comparison group. The primary outcome measure of this study (set by the United Kingdom regulatory body) was 90-day survival.
Heart Transplantation from DCD heart donation provides comparable short-term outcomes to traditional DBD heart transplants (28 hearts)

DPP vs NRP

## Table 3 Heart Transplant Outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>DCD vs DBD</th>
<th>DCD procurement method</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Survival</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 days</td>
<td>26 (100)</td>
<td>26 (100)</td>
</tr>
<tr>
<td>90 days</td>
<td>24 (92)</td>
<td>25 (96)</td>
</tr>
<tr>
<td><strong>Cardiac performance</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac index, liters/min/m²</td>
<td>2.5 (2.2-2.7)</td>
<td>2.0 (1.8-2.4)</td>
</tr>
<tr>
<td>Cardiac output, liters/min</td>
<td>4.5 (4.0-5.2)</td>
<td>3.8 (2.8-4.4)</td>
</tr>
<tr>
<td>MAP, mm Hg</td>
<td>71 (64-76)</td>
<td>66 (60-70)</td>
</tr>
<tr>
<td>CPP, mm Hg</td>
<td>10 (8-11)</td>
<td>11 (9-12)</td>
</tr>
<tr>
<td><strong>Mechanical support</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IABP</td>
<td>7 (27)</td>
<td>4 (15)</td>
</tr>
<tr>
<td>ECMO</td>
<td>3 (12)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>^a</td>
<td>(9)</td>
<td>(0)</td>
</tr>
<tr>
<td>Pharmacologic support</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dopamine, µg/kg/min</td>
<td>4.8</td>
<td>5.0</td>
</tr>
<tr>
<td>Adrenaline, µg/kg/min</td>
<td>0.04</td>
<td>0.04</td>
</tr>
<tr>
<td>Norepinephrine, µg/kg/min</td>
<td>0.01</td>
<td>0.03</td>
</tr>
<tr>
<td>Posttransplant outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventilation duration, days</td>
<td>0.0 (0.5-3.3)</td>
<td>1.0 (0.5-2.5)</td>
</tr>
<tr>
<td>Length of stay, days</td>
<td>5 (3-8)</td>
<td>7 (4-9)</td>
</tr>
<tr>
<td>Hospital</td>
<td>20 (17-28)</td>
<td>21 (21-34)</td>
</tr>
<tr>
<td>Hemofiltration</td>
<td>3 (11)</td>
<td>7 (27)</td>
</tr>
<tr>
<td>Ejection Fraction, %</td>
<td>63 (58-65)</td>
<td>63 (62-69)</td>
</tr>
<tr>
<td>Hospital rejection</td>
<td>10 (8-11)</td>
<td>11 (9-12)</td>
</tr>
<tr>
<td>PAF rejection</td>
<td>14 (12-17)</td>
<td>15 (12-19)</td>
</tr>
</tbody>
</table>

*Continuous values are median (interquartile range) or as indicated, and continuous values are as number (%).

*Indicated values are displayed between groups.

* Determined by transthoracic echocardiogram, with the first echocardiogram performed in the outpatient clinic.
Table 3 Heart Transplant Outcomes

<table>
<thead>
<tr>
<th>Variable*</th>
<th>DCD vs DBD (n = 26)</th>
<th>DCD vs DBD (n = 26)</th>
<th>p-value</th>
<th>DCD vs DBD (n = 12)</th>
<th>DCD vs DBD (n = 14)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival</td>
<td>30 days</td>
<td>26 (100)</td>
<td>26 (100)</td>
<td>1.00</td>
<td>12 (100)</td>
<td>14 (100)</td>
</tr>
<tr>
<td>Cardiac performance</td>
<td>2.5 (2.2-2.7)</td>
<td>2.0 (1.8-2.4)</td>
<td>0.04</td>
<td>2.5 (2.4-2.7)</td>
<td>2.3 (1.7-2.8)</td>
<td>0.62</td>
</tr>
<tr>
<td>Cardiac output, L/min/m²</td>
<td>4.9 (4.6-5.2)</td>
<td>3.8 (3.2-4.4)</td>
<td>0.006</td>
<td>5.0 (4.3-5.1)</td>
<td>4.6 (3.4-5.5)</td>
<td>0.60</td>
</tr>
<tr>
<td>MAP, mm Hg</td>
<td>71 (64-87)</td>
<td>66 (60-70)</td>
<td>0.08</td>
<td>69 (64-78)</td>
<td>70 (69-78)</td>
<td>0.79</td>
</tr>
<tr>
<td>CPP, mm Hg</td>
<td>10 (8-11)</td>
<td>11 (9-12)</td>
<td>0.10</td>
<td>10 (8-11)</td>
<td>9 (8-11)</td>
<td>0.57</td>
</tr>
<tr>
<td>PVR, dyn/cm²</td>
<td>14 (12-16)</td>
<td>15 (12-16)</td>
<td>0.65</td>
<td>13 (12-17)</td>
<td>18 (13-18)</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Pharmacologic support:

<table>
<thead>
<tr>
<th>Drug</th>
<th>DBD (n = 26)</th>
<th>DCD (n = 26)</th>
<th>p-value</th>
<th>DBD (n = 12)</th>
<th>DCD (n = 14)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine, μg/kg/min</td>
<td>4.8</td>
<td>5.0</td>
<td>0.04</td>
<td>5.1</td>
<td>4.8</td>
<td>0.15</td>
</tr>
<tr>
<td>Adrenaline, μg/kg/min</td>
<td>0.04</td>
<td>0.04</td>
<td>0.03</td>
<td>0.04</td>
<td>0.03</td>
<td>0.03</td>
</tr>
<tr>
<td>Noradrenaline, μg/kg/min</td>
<td>0.01</td>
<td>0.03</td>
<td>0.09</td>
<td>0.00</td>
<td>0.00</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Pre-transplant outcomes:

<table>
<thead>
<tr>
<th>Variable</th>
<th>DBD (n = 26)</th>
<th>DCD (n = 26)</th>
<th>p-value</th>
<th>DBD (n = 12)</th>
<th>DCD (n = 14)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilation duration, days</td>
<td>0.9 (0.5-3.3)</td>
<td>1.8 (0.7-5.5)</td>
<td>0.84</td>
<td>0.6 (0.4-1.1)</td>
<td>2.5 (0.3-3.6)</td>
<td>0.06</td>
</tr>
<tr>
<td>Length of stay, days</td>
<td>5 (3-8)</td>
<td>7 (6-9)</td>
<td>0.49</td>
<td>5 (4-6)</td>
<td>6 (3-10)</td>
<td>0.67</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>20 (17-28)</td>
<td>27 (21-34)</td>
<td>0.09</td>
<td>19 (17-27)</td>
<td>20 (19-27)</td>
<td>0.58</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>8 (3-11)</td>
<td>7 (3-7)</td>
<td>0.51</td>
<td>2 (27)</td>
<td>5 (36)</td>
<td>0.38</td>
</tr>
<tr>
<td>Ejection Fraction, %</td>
<td>63 (58-65)</td>
<td>63 (61-69)</td>
<td>1.00</td>
<td>65 (64-68)</td>
<td>62 (60-65)</td>
<td>1.00</td>
</tr>
<tr>
<td>Treated rejection</td>
<td>9 (10)</td>
<td>1 (1)</td>
<td>0.12</td>
<td>6 (11)</td>
<td>5 (10)</td>
<td>0.92</td>
</tr>
</tbody>
</table>

CD, cardiac death; BDD, brain death donor; DCD, donation after circulatory death; DCD, donor after circulatory death; DBD, donor after brain death; MAP, mean arterial pressure; PVR, pulmonary vascular resistance; CPP, central cerebral pressure; DPP, direct procurement and perfusion.

*Continuous variables are median (interquartile range) or as indicated, and continuous values as number (%).

†Indicated values are displayed between groups.

‡Determined by transthoracic echocardiogram, with the first echocardiogram performed in the outpatient clinic.
Heart Transplantation from DCD heart donation provides comparable short-term outcomes to traditional DBD heart transplants (28 hearts)

A 5-year single-center early experience of heart transplantation from donation after circulatory-determined death donors

Simon Messer, PhD, Sendi Cernic, MD, Aravinda Page, MBChir, Marius Berman, MD, Pradeep Kaul, PhD, Simon Colah, BSc, Jason Ali, PhD, Evgeny Pavlushkov, PhD, Jen Baxter, RN, Richard Quigley, RN, Mohamed Osman, PhD, Eyal Nachum, MD, Jayan Parameshwar, FRCP, Yasir Abu-Omar, DPhil, John Dunning, MBChB, Martin Goddard, MBChB, Sai Bhagra, PhD, Stephen Pettitt, PhD, Caitlin Cheshire, MBBS, Clive Lewis, PhD, Anna Kydd, MD, Ayyaz Ali, PhD, Catherine Sudarshan, MD, David Jenkins, MBBS, Steven Tsui, MD, Roger Hall, MBChB, Pedro Catarino, MBChB, and Stephen R. Large, MBBS, MS, MBA

BACKGROUND: In an effort to address the increasing demand for heart transplantation within the United Kingdom (UK), we established a clinical program of heart transplantation from donation after circulatory-determined death (DCD) donors in 2015. After 5 years, we report the clinical early outcomes and impact of the program.

METHODS: This is a single-center, retrospective, matched, observational cohort study comparing outcomes of hearts transplanted from DCD donors from March 1, 2015 to February 29, 2020 with those from matched donation after brain death (DBD) donors at Royal Papworth Hospital (RPH) (Cambridge, UK). DCD hearts were either retrieved using thoracoabdominal normothermic regional perfusion or the direct procurement and perfusion technique. All DBD hearts were procured using standard cold static storage. The primary outcomes were recipient 30-day and 1-year survival.

RESULTS: During the 5-year study, DCD heart donation increased overall heart transplant activity by 48% (79 for DCD and 164 for DBD). There was no difference in survival at 30 days (97% for DCD vs 99% for DBD, p = 1.00) or 1 year (91% for DCD vs 89% for DBD, p = 0.72). There was no difference in the length of stay in the intensive care unit (7 for DCD vs 6 for DBD days, p = 0.24) or in the hospital (24 for DCD vs 25 for DBD days, p = 0.84).

CONCLUSIONS: DCD heart donation increased overall heart transplant activity at RPH by 48%, with no difference in 30-day or 1-year survival in comparison with conventional DBD heart transplantations.
Figure 2  The annual proportion of DBD/DCD heart transplantations. DBD, donation after brain death; DCD, donation after circulatory-determined death.
Outcomes of Donation After Circulatory Death Heart Transplantation in Australia

Hong Chee Chew, MS, Arjun Iyer, PhD, Mark Connellan, FC CARDIO SA, Sarah Scheuer, MD, Jeanette Villanueva, PhD, Ling Gao, PhD, Mark Hicks, PhD, Michelle Harkness, RN, MCN, Claudio Soto, MSc, Andrew Dinale, BAppSc, Priya Nair, MD, Alasdair Watson, PhD, Emily Granger, MBBS, Paul Jansz, PhD, Kavitha Muthiah, PhD, Andrew Jabbour, PhD, Eugene Kotlyar, MD, Anne Keogh, MBBS, Chris Hayward, MD, Robert Graham, MD, Phillip Spratt, MD, Peter Macdonald, MD, Kumud Dhital, PhD

BACKGROUND Transplantation of hearts retrieved from donation after circulatory death (DCD) donors is an evolving clinical practice.

OBJECTIVES The purpose of this study is to provide an update on the authors' Australian clinical program and discuss lessons learned since performing the world's first series of distantly procured DCD heart transplants.

METHODS The authors report their experience of 23 DCD heart transplants from 45 DCD donor referrals since 2014. Donor details were collected using electronic donor records (Donate Life, Australia) and all recipient details were collected from clinical notes and electronic databases at St. Vincent's Hospital.

RESULTS Hearts were retrieved from 33 of 45 DCD donors. A total of 12 donors did not progress to circulatory arrest within the pre-specified timeframe. Eight hearts failed to meet viability criteria during normothermic machine perfusion, and 2 hearts were declined due to machine malfunction. A total of 23 hearts were transplanted between July 2014 and April 2018. All recipients had successful implantation, with mechanical circulatory support utilized in 9 cases. One case requiring extracorporeal membrane oxygenation subsequently died on the sixth post-operative day, representing a mortality of 4.4% over 4 years with a total follow-up period of 15,500 days for the entire cohort. All surviving recipients had normal cardiac function on echocardiogram and no evidence of acute rejection on discharge. All surviving patients remain in New York Heart Association functional class I with normal biventricular function.

CONCLUSIONS DCD heart transplant outcomes are excellent. Despite a higher requirement for mechanical circulatory support for delayed graft function, primarily in recipients with ventricular assist device support, overall survival and rejection episodes are comparable to outcomes from contemporary brain-dead donors. (J Am Coll Cardiol 2019;73:1447-59)
U.S. DCD Trial

• Study design
   A prospective, randomized and concurrent controlled, non-inferiority pivotal trial in which subjects who receive a DCD donor heart transplant will be compared to subjects who receive a standard criteria donor heart transplant (SOC1 and SOC2 - from both randomized and concurrent control groups), adjusting for differences in risk factors.
U.S. DCD Trial

Subject Meets Trial Eligibility: Randomize 3:1

DCD Heart Possible to SOC Heart Only

DCD Heart Possible
Depending on Match

SOC Heart Only
No possibility of DCD match

Matched with SOC Heart

Matched with DCD Heart
N = 53

Primary Endpoint: Non-inferiority study comparing 6-month survival for DCD Heart Recipients to 6-month survival for SOC Heart Recipients (SOC1 + SOC2) with risk factor adjustment

Other Endpoints: DCD Heart Recipients only
- Utilization rate
- Severe PGO within 24 hours
- Use of post-transplant mechanical circulatory support > 72 hours
- HGRSAEs and SAEs within 30 days

Trial Size and Subject Follow-up

A maximum of 15 participating sites with a minimum of 53 transplanted DCD heart recipients and at least 159 standard of care heart transplant recipients. Follow-up data for the SOC recipients will be obtained from UNOS/OPTN standard database for transplant recipients.
Donor Inclusion Criteria

• Maastricht Category III DCD donor, defined as expected death after the withdrawal of life-supportive therapy (WLST)
• Donor age 18-49 years old inclusive
• Warm ischemic time (WIT) ≤ 30 mins, with warm ischemic time defined as: Time from when mean systolic blood pressure (SBP) is < 50 mmHg or peripheral saturation < 70% to aortic cross-clamp and administration of cold cardioplegia in the donor.

U.S. DCD Trial

Primary Endpoint
A non-inferiority comparison of patient survival at 6 months post-transplant between recipients of DCD donor hearts preserved on the OCS Heart System (DCD Heart Transplanted Recipient Population) and recipients of standard criteria donor hearts preserved using cold storage (SOC1 + SOC2, SOC Heart Transplanted Recipient Population), adjusting for risk factors.
U.S. DCD Trial

Secondary Endpoint

Utilization Rate is defined as the number of eligible DCD donor hearts that met the warm ischemic time limit and were instrumented on the OCS Heart System that meet the acceptance criteria for transplantation after OCS Heart preservation divided by the total number of eligible DCD donor hearts that met the warm ischemic time limit above and were instrumented on the OCS Heart System.

90 (initially 53) DCD hearts were transplanted across 9 sites.

90 (initially 159) Cold static-preserved hearts were enrolled as well.

There were 11 hearts declined after OCS assessment resulting in an overall utilization of 89%.

Similar recipient MCS support as in EXPAND CAP.
U.S. DCD Trial

- Mean AOP has been in the range of 72 mmHg
- Mean CF has been in the range of 730 mL/min
- Mean perfusion time has been in the range of 4.5 hours with the longest in this study being 472 minutes
- PGD and survival cannot be reported at this time but are very favorable

U.S. DCD Trial - CAP

- 37 patients enrolled out of a possible (90)
- All results similar to the U.S. DCD Trial
U.S. DCD Trial- CAP- MHI

- 5 runs
- 3 patients enrolled
- 75% utilization rate - 4 runs with recovery of the organ/3 transplants (1 heart declined after arrival at ANW)
- 1 “dry run” - patient didn’t expire
- 2 of 3 required postoperative MCS (grade 3 PGD - 16-72 hours to full recovery)

Conclusions

- Organ shortage still a limiting factor
- Deaths on waitlists despite changes in allocation strategies
- Distance - major obstacle to allocate all organs
- Ex-vivo perfusion - future direction
- OPOs and centers working together
Special Thanks - MHIF!

- Ben Sun and Peter Eckman
- OPOs
- Transplant Coordinators
- Perfusionists
- Research Coordinators
- The whole Advanced Heart Failure Team
Surgeon waking up for a SCHEDULED morning transplant

Thank You
Content

• Demand- Supply mismatch
• Ex-vivo perfusion with DBD- Donation after brain death
• Ex- vivo perfusion with DCD- Donation after circulatory determined death

Organ Shortage
 Reason of removal from the list

<table>
<thead>
<tr>
<th>Removal reason</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deceased donor transplant</td>
<td>2331</td>
<td>2734</td>
<td>2811</td>
</tr>
<tr>
<td>Patient died</td>
<td>395</td>
<td>324</td>
<td>290</td>
</tr>
<tr>
<td>Patient refused transplant</td>
<td>24</td>
<td>25</td>
<td>27</td>
</tr>
<tr>
<td>Improved, transplant not needed</td>
<td>161</td>
<td>187</td>
<td>176</td>
</tr>
<tr>
<td>Too sick for transplant</td>
<td>297</td>
<td>261</td>
<td>290</td>
</tr>
<tr>
<td>Other</td>
<td>246</td>
<td>251</td>
<td>273</td>
</tr>
</tbody>
</table>

OPTN/SRTR 2017 Annual Data Report: Heart

1. Distance
2. Imperfect organ

...Hawaii
Ex-vivo perfusion
The TransMedics® Organ Care System (OCS) is a portable ex-vivo organ perfusion system, intended to preserve a donor heart in a near-normothermic and beating state from retrieval until the eventual transplantation.
Donor Characteristics

- 45 yr Female
- 162 cm, 54.4 kg
- Cause of brain death: Cerebrovascular hemorrhage
- Inclusion criteria:
  - Anticipated cross clamp time ≥4 hrs plus
- Additional risk factors:
  - Hypertension
Lactate Profile

AOP

CF

pH and Arterial pCO₂

MHIF Cardiovascular Grand Rounds | March 22, 2021
Critical Times

- Donor Cross-clamp to start of OCS perfusion: 29 minutes
- Warm Perfusion Time: 362 minutes
- Cooling Time: 6 minutes
- End of OCS perfusion/cooling to release of recipient cross-clamp: 59 minutes

Recipient Characteristics

- 67 yr Female
- 157 cm, 76.2 kg
- Diagnosis: Ischemic cardiomyopathy
Discussion

- Early perfusion characterized by rapid achievement of target mean AOP. Initial Use Model range for CF (700-800 mL/min) achieved within 10 minutes, however, TMDX recommends achieving 750 mL/min as early as possible.
- Lactate transitioned from secreting to absorbing between the first and second sample sets with mean AOP 82 mmHg and CF 790 mL/min. Parameters were maintained at these values prior to third lactate samples.
- There was a 1 hour interval between the second and third lactate samples. A 10-15 minute interval would have been appropriate as there had been an increase in lactate between the first and second sample sets despite transitioning from secreting to absorbing.

Discussion

- Based on the rapid decrease in lactate between the second and third sample sets, a decrease in pump flow would have been possible to avoid hyper-perfusion.
- There was a rapid trend of respiratory acidosis. An increase in gas flow rate from 150 mL/min to 200 mL/min at two hours of perfusion would have been appropriate.
- Mean AOP and CF for the case were 77.5 mmHg and 734 mL/min, respectively.
Conclusions

• Organ shortage still a limiting factor
• Deaths on waitlists despite changes in allocation strategies
• Distance- major obstacle to allocate all organs
• Ex-vivo perfusion- viable option to mitigate it
• Future- DCD!!!
• Future- OPOs and centers working together

Special Thanks

• OPOs
• Transplant Coordinators
• Perfusionists
• Research Coordinators
• The whole Advanced Heart Failure Team
Very Special Thanks

Dr. Bassam Shukrallah

Surgeon waking up for a morning transplant