Protocol:

Thoraco-Abdominal Normothermic Regional Perfusion (TANRP) for DCD organ retrieval

Stephen Large[1], Christopher Watson[2], John Dark[4], Gabriel Oniscu[3], Steven Tsui[1], Claire Williment[4], Marion Ryan[4], Marius Berman[1], Aravinda Page[1], Simon Messer[1], Paul Murphy[4]

[1]Royal Papworth Hospital, [2]Addenbrookes Hospital, [3]Edinburgh Royal Infirmary, [4] NHSBT-ODT

1. Introduction:

- Organs from donation after circulatory death (DCD) have been used for liver, lung, kidney and pancreatic transplantation for over a decade
- The use of DCD organs has led to increased transplant activities
- Since 2015, DCD hearts have been retrieved and transplanted in the United Kingdom
- The results of DCD heart transplant compare well with transplantation of donor hearts following brain stem death

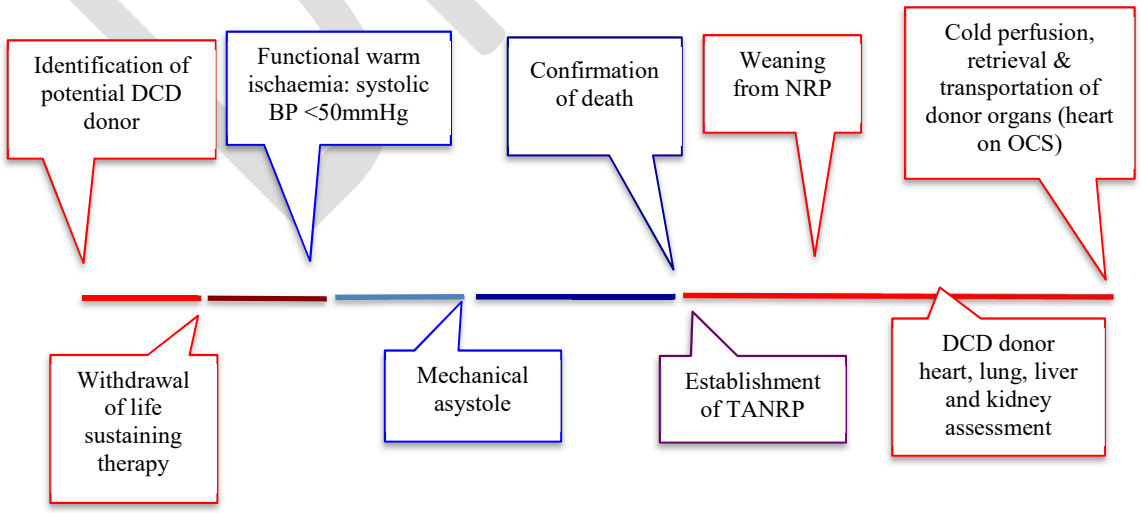
There are currently 2 approaches to DCD heart retrieval:

1.1. Direct procurement and machine perfusion (DP-MP) - the asystolic DCD heart is removed from the donor and coronary perfusion is re-established *ex-situ* in the Organ Care System (OCS, TransMedics Inc., Andover, MA)

1.2. Thoracoabdominal normothermic regional reperfusion (TANRP) – the thoracic and abdominal donor organs are reperfused *in situ* in the donor

This protocol describes the steps involved in TANRP for DCD organ retrieval. The sequence of events in DCD TANRP is outlined in Figure 1:

Figure 1: Time-line for DCD TANRP:



3. Constitution of retrieval teams for TANRP:

i. Cardiothoracic Team (CT):

The cardio-thoracic team is made up of:

a. a lead surgeon (**LS^{CT}**)
b. an assistant surgeon (**AS^{CT}**)
c. the thoracic scrub nurse (**SN^{CT}**)
d. a donor care physiologist (**DCP^{CT}**)
e. a transplant practitioner (**TP^{CT}**)

NB – either the DCP^{CT} or the TP^{CT} will be competent to perform machine perfusion of the donor heart if required

NB - if donor lung retrieval is also planned, a second lead surgeon (**2nd LS^{CT}**) will be required to perform donor lung retrieval after the donor heart has been excised

ii. Abdominal Team (Ab):

The abdominal procurement team is made up of:

a. a lead transplant surgeons (**LS^{Ab}**)
b. an assistant surgeon **(AS^{Ab}**)
c. the abdominal team scrub nurse (**SN^{Ab}**)
d. a transplant practitioner competent in organ perfusion techniques (**TP^{Ab}**)

iii. The teams should involve a transplant practitioner who can operate the NRP equipment (**PT^{NRP}**) and can be the same as **TP^{Ab}** or **TP^{CT}**.

<u>It should be agreed before NORS teams are dispatched whether the CT NORS or abdominal NORS will provide all the equipment and personnel required for NRP</u>

4. Co-ordination of teams:

- As per all donor organ retrievals, the specialist nurse in organ donation **(SNOD)** will meet with the NORS teams and theatre staff for a hand over and briefing
- Confirmation of donor consent, history, investigations and blood group are important before withdrawal of life supporting therapy (WLST).
- An overall lead for these groups will be appointed by mutual consent of all present, to ensure a co-ordinated, smooth running with effective communication between all involved
- The individual who will re-intubate and bronchoscope (if required) the donor is identified
- A recorder (**R^{Ab+CT}**) will be identified and ensures a complete record of events including patient details as well as all events, drugs and blood products administered to the patient. A copy of this record will be produced for submission to NHSBT with the approved DCD Supplementary Record registry. A copy will accompany each donor organ to their recipient hospitals.

5. Withdrawal of life supporting therapy (WLST):

- This will take place in the locally designated area within the donor hospital (ideally in the anaesthetic room)
- The abdominal and cardio-thoracic teams should be scrubbed and ready to proceed with surgery at the point of WLST
- The time of WLST and subsequent condition of the patient will be relayed to the NORS teams within the operating room at regular intervals by the **SNOD**

6. Confirmation of death:

- The confirmation of death is made in accordance with national professional guidance:
  - the Code of Practice for the Diagnosis and Confirmation of Death published by the Academy of Medical Royal Colleges in 2008
  - the Consensus Statement on Donation after Circulatory Death published by the British Transplantation Society and Intensive Care Society in 2011
- In accordance with such guidance, all measures will be taken to prevent restoration of cerebral blood flow after death has been confirmed

7. Preparation for withdrawal of life supporting therapy (WLST):

i. The **PT^{NRP}** will

a. check for donor drug allergies
b. prime the TANRP circuit ensuring sterile length of circuit for the operating table

Composition of NRP circuit priming solution:

- Heparin - 50,000IU
- Compound Sodium Lactate (Hartmann's) solution - 1L
- 20% Mannitol (to ensure a hypertonic perfusate) - 250mls
- Hartmann's solution- 500 mls
- 8.4% Sodium Bicarbonate - 1ml/kg (donor weight)
- Methylprednisolone - 1gm
- Meropenem (check for allergy in the donor)- 1 gm
- Vancomycin (check for allergy in the donor) - 1 gm
- Fluconazole (check for allergy in the donor) - 200mg

NB Packed red cells (PRC) - 4 Units of PRC should be available for TANRP

NB If donor haematocrit <100 g/L, it will be necessary to use PRC to prime the NRP circuit. If so, additional blood will need to be crossed matched to ensure that there are 4 units of PRC available during TANRP.

ii. The **DCP^{CT}** sets up:

- trolley for re-intubation - prepare intubation equipment + 2 suction lines (rough sucker and bronchoscopy)
- cardiac defibrillator
- event recording: ECG, pressure transducers for CVP/Swan Ganz and arterial pressure
- the operating table to receive the donor -ensure PATSLIDE on operating table
- the anaesthetic machine circuit: tidal volume set at 6-8 mls/kg donor weight
- TOE ready and switched on
- blood gas and ACT (point of care testing) monitoring available

- an ultrasound device to confirm absence of bilateral carotid artery blood flow during NRP

iii. The **SN^{CT}** sets up the sterile instruments required for TANRP and retrieval of heart and lungs:

- skin preparation
- scalpel with 22 blade
- battery sternotomy saw (and spare)
- rough sucker and tubing
- cardiotomy sucker and tubing
- pericardial stay stitches
- aortic cross clamp
- IVC cross clamp
- snugger for SVC
- cardioplegia cannula (DLP)
- aortic and atrial cannulae
- scissors for heart venting and excision
- 2x 28 Fr Foley catheters connected with a Y connector: pulmonary artery cannulation for donor lung perfusion
- 500ml N saline and 50ml syringe with Luer lock
- basin to receive donor heart and later lungs and sterile bags for the storage of the lungs for cold storage
- Two labelled 10 mL syringes, one containing 30,000IU heparin and the second 20,000IU (use concentrated heparin preparation i.e. 5,000 U/mL made up with normal saline to a final volume of 10 mL)

iv. The **TP^{CT}** to set up:

- cardioplegia,
- Perfadex Plus (if required)
- solutions for machine perfusion of the donor heart

v. The **TP^{Ab}** will set up:

- UW solution infusion as for standard DCD abdominal organ donation and be prepared to use them immediately should the NRP fail to be established
- The bags should be kept in the ice box, with the giving sets connected

vi. The **SN^{Ab}** will setup:

- the operating environment in a similar fashion to the current practice of DBD/DCD retrieval
- This includes setting up the diathermy machine (as available in the host theatre) and cannulae available should they be required
- A bulb syringe filled with N saline will be available for aortic cannula de-airing

vii. Surgeons:

- The **LS^{Ab}, AS^{Ab}**, **LS^{CT}** and **AS^{CT}** should be scrubbed and ready prior to WLST
- The CT and abdominal NORS team should start the sternotomy and laparotomy simultaneously
- Both teams should be present at the table throughout the procedure

8. **Surgical protocol:**

i. When the donor is brought into the operating room, the SNOD will show the patient name band to the NORS teams to confirm donor identity

ii. A donor hospital ODP should ensure the application of the diathermy plate and its connection

iii. If the lungs are to be assessed, the trachea **must** be re-intubated at this stage, and a bronchoscopy performed. It is essential that the airway is protected at the earliest opportunity and before the abdomen is opened if possible

iv. The thoracic and abdominal surgeons will prepare the skin with an alcohol-based skin preparation solution and apply the drapes as per standard retrieval practice.

v. A midline sternotomy incision is made and a Finochietto retractor is inserted with the cross bar towards the head to spread the sternal tables

vi. The abdominal surgeon should open the abdomen through a long midline incision at the same time as the chest is being opened

Cardiothoracic team:

vii. **LS^{CT}** opens the pericardium and injects 30,000 IU of heparin into the right atrium

viii. **AS^{CT}** injects 20,000 IU of heparin into the pulmonary trunk

ix. **AS^{CT}** applies caudal traction to ascending aorta, exposing the aortic arch

x. **LS^{CT}** cross-clamps the 3 aortic arch branches with Roberts clamp to prevent cerebral reperfusion

xi. **AS^{CT}** retracts the heart for atrial cannulation

xii. **LS^{CT}** inserts a 2-stage venous cannula into the right atrium and attaches it to the venous line of the perfusion circuit

Abdominal team:

viii. **LS^{Ab}** cannulates the abdominal aorta and

ix. **AS^{Ab}** de-airs cannula with a bulb syringe

x. **AS^{Ab}** steadies the aortic cannula in the aorta

xi. **LS^{Ab}** connects aortic cannula to the arterial tubing of the NRP circuit

xii. **LS^{Ab}** secure aortic cannula and ensures haemostasis (a nylon tape around the distal abdominal aorta and snugger works well)

xiii.

xiv. TANRP is commenced and lack of carotid blood flow confirmed by carotid Doppler

xv. **If it takes more than 10 minutes from knife to skin to restore circulation with NRP, this should be abandoned and procurement of organs made by immediate cold perfusion**

xvi. A DLP cannula is placed into ascending aorta for central arterial pressure monitoring

xvii. During TANRP, some dissection of the liver and mobilisation of the bowel can take place. However, pressure on the liver, or mobilisation of the liver, may result in loss of venous return, so any handling needs to be done with this in mind

xviii. The falciform ligament can be divided, the hilum exposed and common bile duct should be divided near the duodenum and allowed to drain freely. A distended gall bladder should not be squeezed, but preferably opened with a diathermy blade and its contents aspirated. The bile duct is flushed with UW solution to remove any bile that has been squeezed into the duct (UW has a physiological pH and is preferred to saline, which has an acidic pH)

xix. The external iliac arteries may be clamped at the inguinal ligament, as distal as possible, to increase arterial resistance and augment organ perfusion pressure if required (*note that head and arms represent 16% of total body weight and both legs a further 40.7% - de Leva 1996)*). This step would not be required if the distal abdominal aorta was encircled with a nylon tape and snugged down

9. Management during TANRP:

i. TANRP haemodynamic and biochemical goals:
- Flow index >2.4 $L.min^{-1}.m^{-2}$
- Temperature 36°C
- MAP 60-80 mmHg
- CVP 4-6 mmHg (cannulation with CVP and Swan)
- Hb >100 g/L – transfuse red cells if required
- Base excess 0 - 5 mEq/L
- Initial FiO2 at 0.21 (room air), aiming for PaO_2 > 12 kPa, S_vO_2 saturations > 60%
- Commence dopamine infusion at 2.5 $mcg.kg^{-1}.min^{-1}$ if MAP< 60 mmHg despite adequate NRP flow and clamping of external iliac arteries
- The ACT (activated clotting time) is measured by the **PT^{NRP}** promptly after starting TANRP and at intervals if required

ii. The first heart rhythm is recorded and DC Cardioversion used if required

iii. When NRP is commenced surgeons check that mean blood pressure is 60-80mmHg
- If MAP <60 mmHg, alert abdominal team and consider
  - Clamping external iliac arteries (not required if distal aorta ligated)
  - commencing Dopamine infusion at 2.5 $\mu g.kg^{-1}.min^{-1}$ – inform abdominal surgeons
  - if still a problem consider Vasopressin infusion – inform abdominal surgeons

iv. Lung ventilation can be commenced as soon as the aortic arch branches have been clamped:
- FiO_2 0.5 (to be reduced appropriately according to blood gases)
- Tidal volume 6-8 mL/kg
- PEEP 5-8 cmH_2O
- Perform fibre optic bronchoscopy, either with sealed system, or re-recruit lungs afterwards

v. Aim to wean TANRP when biochemical targets have been reached, usually after 30 – 45 mins, allowing the heart to generate blood flow through the lungs and the donor organs, aiming for the following parameters:
- MAP >60 mmHg
- CVP >6 mmHg
- FiO_2 0.5 (adjusted according to blood gases aiming for S_aO_2 >95%)
- Watch for clinical evidence of compromised organ perfusion (serum lactate and base deficit, cardiac output, arterial pressures and visual inspection, TOE).
- If poor perfusion, consider re-instituting TANRP or abandoning the heart

vi. Cardiac assessment after weaning from TANRP:

- Invasive haemodynamic monitoring with Swan Ganz catheter to assess RAP, PAP, PCWP and thermo-dilution cardiac output
- Perform trans-oesophageal echocardiogram (TOE)

vii. Lung assessment:
- fibre-optic bronchoscopy
- individual pulmonary venous blood gases after 5 minutes on FiO_2 of 1.0 and PEEP 8
- compare with systemic arterial blood gas
- record mean ventilator pressure and tidal volume for lung compliance

viii. If the MAP falls <60mmHg for a sustained period of time (>5 min) when the heart is being assessed, consider:
- Recommencing TANRP
- prepared for cold perfusion of the abdominal organs and retrieval

ix. The abdominal team should undertake dissection, assessment and cannulation of the IVC during this time (abdominal aorta already cannulated as part of TANRP circuit). A large pack is then placed on the cranial surface of the liver against the diaphragm to ensure sufficient IVC remains within the abdomen to allow later implantation of the liver.

10. Following satisfactory donor cardiac assessment: The **DCP^{CT}** or **TP^{CT}** will prime the OCS as follows:
- TransMedics Priming solution
- 8.4% Sodium Bicarbonate - 20 mL
- Heparin - 10,000 IU
- Actrapid – 50 IU
- Transmedics Maintenance solution infusion
- Epinephrine infusion (5% Glucose 500ml + 0.25mg Epinephrine)

11. Blood sampling:

i. Blood for assay of ALT and AST to be taken at start of NRP, 30, 60, 90 and 120 minutes. An ALT rising over 500 implies significant hepatocellular damage and is a relative contraindication to using the liver

ii. Blood gases including lactate to be checked every 30 minutes

iii. QUOD NRP bloods to be taken at the start of NRP, and 60 minutes and at the end of NRP

12. Thoracic and abdominal organ retrieval:

i. When the abdominal retrieval team are ready, and have cannulated the distal abdominal aorta and IVC:
   a. The DLP cannula inserted into the distal ascending aorta is connected to a cardioplegia infusion line
   b. The donor is exsanguinated through the right atrial cannula (minimum of 1.2L of donor blood) with a raised table in Trendelenberg position, ensuring that no preservation solution is started until adequate donor blood has been collected. This should take no more than 90 seconds

ii. **LS^{CT}** clamps the descending thoracic aorta at the level of the diaphragm through the back of the pericardium

iii. Once adequate donor blood has been collected, the **LS^{CT}** removes the 2-stage venous cannula from the right atrium and clamps the intrapericardial IVC with a Roberts clamp

iv. **LS^{Ab}** commences abdominal cold perfusion with UW

v. **LS^{CT}** clamps the ascending aorta and commences cold crystalloid cardioplegia – 500ml of St. Thomas' solution supplemented with erythropoietin

vi. **TP^{CT}** or **DCP^{CT}** adds the donor blood to the pre-primed OCS circuit

vii. Abdominal organ retrieval is then undertaken as for standard DBD retrievals and heart procurement as for DBD

viii. Note if the lungs are to be retrieved, care must be taken to leave the posterior wall of PA carina when removing the heart. The **2nd LS^{CT}** places a Foley catheter into each of the opened right and left pulmonary arteries (with snares to secure their position) for antegrade donor lung perfusion followed by retrograde perfusion. Lungs are retrieved in standard fashion.

13. Preparation of the retrieved DCD heart:

- the excised heart is immediately placed into a basin of ice cold sterile saline solution
- the aorta is separated from the pulmonary artery
- an appropriately sized aortic tip cannula is inserted into the aorta and secured with a cable tie
- a PA cannula is inserted into the pulmonary trunk and secured with a black silk tie
- the heart is reperfused in the OCS
- 3 Teflon felt pledgeted stitches are used to further secure the aorta edge to reduce the risk of slippage during travel to the recipient hospital
- A vent is inserted into the LV via one of the pulmonary veins and secured

14. Notes for OCS perfusion during transportation: Preparation of Donor Heart for Machine Perfusion on OCS

- Commence OCS perfusion of donor heart aiming for:
  - i. AOP 60-70 mmHg
  - ii. aortic flow 800-1000 mL.min^{-1}
  - iii. Heart rate 70-80 BPM with V-pacing if required
- Acquire simultaneous AV blood samples half hourly as a minimum
- Perfusate targets
  - i. Hct >20 %
  - ii. Calcium 1.0-1.3 mmol.L^{-1}
  - iii. Bicarbonate 22-29 mmol.L^{-1}
  - iv. pH 7.3-7.45

15. Paperwork and DCD data logs

i. the **LS^{CT}** will complete an operation note and placed in the donor's hospital notes

ii. The **DCP^{CT}/TP^{Ab}** prepare tissue and blood samples as described in section 3 of Donor Run Perfusion Manual

iii. The **DCP^{CT}/TP^{Ab}** will ensure completion of HTA A form, plus DCD Heart Transplant Supplementary Record (NHSBT)

iv. The **SNOD** will arrange for copies of appropriate reports to accompany each organ

Supplement:

Table for infusion (Dopamine and Vasopressin)

Data management sheet (plan to replace all documentation)

For details of donor lung preservation, refer to NORS standard (updated April 2017)