

**Protocol:  
Thoraco-Abdominal Normothermic Regional Perfusion (TANRP)**

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**1. Introduction:**

1.1 Organs from donation after circulatory death (DCD) have been used for liver, lung, kidney and pancreatic transplantation for over a decade.

1.2 The use of DCD organs has led to increased transplant activities.

1.3 Since 2015, DCD hearts have been retrieved and transplanted in the United Kingdom.

1.4 The results of DCD heart transplant compare well with transplantation of donor hearts following brainstem death.

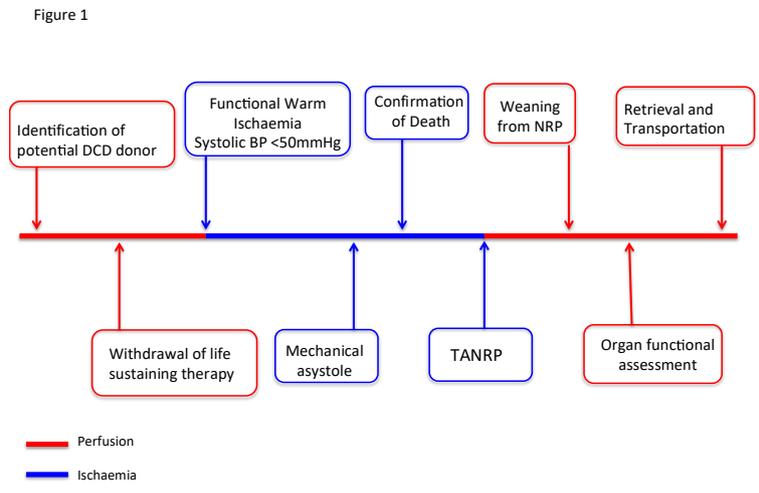
1.5 There are currently 2 approaches to DCD heart retrieval:

*Direct procurement and machine perfusion (DP-MP) - the asystolic DCD heart is removed from the donor and coronary perfusion is re-established ex-situ using a portable blood perfusion pump*

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

1.6 TANRP offers some advantages compared to DP-MP: the functional warm ischaemic time is reduced; there is the opportunity for direct functional assessment of the heart after re-animation; there is the possibility to avoid machine perfusion completely; abdominal organ perfusion is facilitated.

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



## **2. Constitution of retrieval teams for TANRP:**

### **2.1 Cardiothoracic Team (CT):**

*The cardio-thoracic team is made up of:*

- a lead surgeon (**LS<sup>CT</sup>**)
- an assistant surgeon (**AS<sup>CT</sup>**)
- the thoracic scrub nurse (**SN<sup>CT</sup>**)
- a donor care physiologist (**DCP<sup>CT</sup>**)
- a transplant practitioner (**TP<sup>CT</sup>**)
- a perfusionist (if no **TP<sup>Ab</sup>** present)

2.2 Either the **DCP<sup>CT</sup>** or the **TP<sup>CT</sup>** will be competent to perform machine perfusion of the donor heart if required.

2.3 If donor lung retrieval is also planned, the assistant surgeon (**AS<sup>CT</sup>**) will be required to be signed off to perform donor lung retrieval after the donor heart has been excised.

### **2.4 Abdominal Team (Ab):**

*The abdominal team is made up of:*

- a lead transplant surgeons (**LS<sup>Ab</sup>**)
- an assistant surgeon (**AS<sup>Ab</sup>**)
- the abdominal team scrub nurse (**SN<sup>Ab</sup>**)
- a transplant practitioner competent in organ perfusion techniques (**TP<sup>Ab</sup>**)

2.5 The teams should involve a transplant practitioner who can operate the NRP equipment (**PT<sup>NRP</sup>**) and can be the same as **TP<sup>Ab</sup>** or **TP<sup>CT</sup>**.

2.6 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.

2.7 In general, the abdominal team will provide the equipment and personnel, but there may be instances, including where there is no abdominal organ retrieval, where the CT team provide the equipment and personnel.

## **3. Co-ordination of teams:**

3.1 It is the responsibility of the SNOD to inform the recipient centres that organ retrieval will be by TANRP.

3.2 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.

3.3 Confirmation of donor consent, history, investigations and blood group are important before withdrawal of life supporting therapy (WLST).

3.4 The SNOD is responsible for the consent process with the next of kin, including documentation of specific reference to reanimation of the heart in the donor.

3.5 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.

3.6 Prior to WLST the SNOD, Intensivist, CT and abdo teams, and theatre staff will meet, introduce themselves, rehearse the surgical protocol and complete the WHO check list.

3.7 Each team is responsible for ensuring a complete record of events during both TANRP and heart-sustained perfusion, including 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.

#### **4. Withdrawal of life supporting therapy (WLST):**

4.1 This will take place in the locally designated area within the donor hospital (ideally in the anaesthetic room).

4.2 The abdominal and cardio-thoracic teams should be scrubbed and ready to proceed with surgery at the point of WLST.

4.3 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.

#### **5. Confirmation of death:**

5.1 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*

5.2 In accordance with such guidance, all measures will be taken to prevent restoration of cerebral blood flow after death has been confirmed

#### **6 Preparation for withdrawal of life supporting therapy (WLST):**

6.1 The **PT<sup>NRP</sup>** will:

*-Check for donor drug allergies*

*-Prime the TANRP circuit ensuring sterile length of circuit for the operating table*

6.2 Composition of NRP circuit priming solution:

*-Heparin - 50,000IU*

*-Compound Sodium Lactate (Hartmann's) solution – 1.5L*

*-20% Mannitol (to ensure a hypertonic perfusate) - 250mls*

*-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*

6.3 Packed red cells (PRC) - 6 Units of PRC should be available for TANRP.

6.4 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.

6.5 The **DCP<sup>CT</sup>** 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

6.6 The **SN<sup>CT</sup>** sets up the sterile instruments required for TANRP and heart retrieval (if TANRP fails and DP-MP is to proceed):

- Skin preparation
- Scalpel with 22 blade
- Battery sternotomy saw (and spare)
- Rough sucker and tubing
- 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)
- 3/0 Prolene purse-string
- 2 stage atrial cannula
- Scissors and forcepsx2
- Aortic cross clamp
- Vascular stapler with 3 refills for ligation/division of supra-aortic vessels
- Pericardial stay sutures
- Green needle and manometer line for pressure recording
- IVC clamp, ties and snares
- DLP cardioplegia cannula, PA cannula
- Basins to receive organs

6.7 The **TP<sup>CT</sup>** to set up:

- Cardioplegia,
- Perfadex Plus (if required)
- Solutions for machine perfusion of the donor heart

6.8 The **TP<sup>Ab</sup>** 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

6.9 The **SN<sup>Ab</sup>** 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
- 24F aortic cannula for cannulation of the infrarenal aorta
- A bulb syringe filled with N saline will be available for aortic cannula de-airing

#### 6.10 Surgeons:

- The **LS<sup>Ab</sup>**, **AS<sup>Ab</sup>**, **LS<sup>CT</sup>** and **AS<sup>CT</sup>** 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

### 7. Surgical protocol

7.1 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.

7.2 A donor hospital ODP should ensure the application of two diathermy plates and their connection, one for each NORS team.

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

7.4 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.

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

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

#### **Cardiothoracic team:**

*Steps 7.7 – 7.12 are undertaken simultaneously*

**If the heart beats with manipulation, the CT team should be ready to clamp the ascending aorta to prevent perfusion of the brain at any point in the process.**

7.7 **LS<sup>CT</sup>** opens the pericardium and injects 30,000 IU of heparin into the right atrium  
**AS<sup>CT</sup>** injects 20,000 IU of heparin into the pulmonary trunk

7.8 **AS<sup>CT</sup>** retracts the heart for atrial cannulation allowing **LS<sup>CT</sup>** to place a 3/0 purse string  
**LS<sup>CT</sup>** inserts a 2-stage venous cannula into the right atrium and attaches it to the venous line of the perfusion circuit

7.9 **LS<sup>CT</sup>** opens the posterior pericardium, bluntly dissects the descending thoracic aorta and cross-clamps this - **LS<sup>CT</sup>** informs **LS<sup>Ab</sup>** that perfusion may begin from here on

7.10 **LS<sup>CT</sup>** fully exposes the aortic arch, staple-ligates the innominate vein, and dissects each supra-aortic vessel in turn, ligating and dividing these (innominate, left carotid, left subclavian arteries) with the vascular stapler or other;

7.11 If the innominate artery is diminutive or CT chest suggests the presence of ARSA, then **LS<sup>CT</sup>** specifically visualises the posterior arch and excludes the presence of an aberrant right subclavian artery; if one is present then this too is dissected and ligated/divided

7.12 **LS<sup>CT</sup>** removes the descending thoracic aortic clamp allowing thoracic perfusion to proceed

#### **Abdominal team:**

7.13 **LS<sup>Ab</sup>** cannulates the abdominal aorta.

7.14 **AS<sup>Ab</sup>** de-airs cannula with a bulb syringe.

7.15 **AS<sup>Ab</sup>** steadies the aortic cannula in the aorta.

7.16 **LS<sup>Ab</sup>** connects aortic cannula to the arterial tubing of the NRP circuit.

7.17 **LS<sup>Ab</sup>** secure aortic cannula and ensures haemostasis (a nylon tape around the distal abdominal aorta and snugger works well).

7.18 Once the **LS<sup>Ab</sup>** has confirmed that the descending thoracic aorta is clamped, perfusion is started.

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

7.20 **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.**

7.21 A DLP cannula or green needle is placed into ascending aorta for central arterial pressure monitoring.

7.22 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.

7.23 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).

7.24 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.

#### **8. Management during TANRP:**

8.1 TANRP haemodynamic and biochemical goals:

- Flow index  $>2.4 \text{ L}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$
- Temperature  $36^{\circ}\text{C}$
- MAP  $60\text{-}80 \text{ mmHg}$
- CVP  $4\text{-}6 \text{ mmHg}$  (cannulation with CVP and Swan)
- Hb  $>100 \text{ g/L}$  – transfuse red cells if required
- Base excess  $0\text{-}5 \text{ mEq/L}$
- Initial  $\text{FiO}_2$  at  $0.21$  (room air), aiming for  $\text{PaO}_2 > 12 \text{ kPa}$ ,  $\text{S}_v\text{O}_2$  saturations  $> 60\%$
- Commence dopamine infusion at  $2.5 \text{ mcg}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  if  $\text{MAP} < 60 \text{ mmHg}$  despite adequate NRP flow and clamping of external iliac arteries
- The ACT (activated clotting time) is measured by the  $\text{PT}^{\text{NRP}}$  promptly after starting TANRP and at intervals if required

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

8.3 When NRP is commenced surgeons check that mean blood pressure is  $60\text{-}80\text{mmHg}$ .

8.4 If  $\text{MAP} < 60 \text{ mmHg}$ , alert abdominal team and consider:

- Clamping external iliac arteries (not required if distal aorta ligated)
- Commencing Dopamine infusion at  $2.5 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  – only after discussion with abdominal surgeons
- If still a problem consider Vasopressin infusion – only after discussion with abdominal surgeons

8.5 If  $\text{MAP} > 100 \text{ mmHg}$ , consider phentolamine  $5 \text{ gm}$ .

8.6 Lung ventilation can be commenced as soon as the aortic arch branches have been clamped:

- $\text{FiO}_2$   $0.5$  (to be reduced appropriately according to blood gases)
- Tidal volume  $6\text{-}8 \text{ mL/kg}$
- PEEP  $5\text{-}8 \text{ cmH}_2\text{O}$
- Perform fibre optic bronchoscopy, either with sealed system, or re-recruit lungs afterwards

8.7 Aim to wean TANRP when biochemical targets have been reached, usually after  $30\text{-}45$  mins, allowing the heart to generate blood flow through the lungs and the donor organs, aiming for the following parameters:

- MAP  $>60 \text{ mmHg}$
- CVP  $>6 \text{ mmHg}$
- $\text{FiO}_2$   $0.5$  (adjusted according to blood gases aiming for  $\text{S}_a\text{O}_2 > 95\%$ )
- 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

8.8 Cardiac assessment after weaning from TANRP:

- Invasive haemodynamic monitoring with Swan Ganz catheter to assess RAP, PAP and thermo-dilution cardiac output
- Perform trans-oesophageal echocardiogram (TOE)
- Haemodynamic and echo criteria for heart acceptance are the same as for DBD procurement

8.9 Lung assessment:

- Fibre-optic bronchoscopy*
- Individual pulmonary venous blood gases after 5 minutes on FiO<sub>2</sub> of 1.0 and PEEP 8*
- Compare with systemic arterial blood gas*
- Record mean ventilator pressure and tidal volume for lung compliance*

8.10 If the MAP falls <60mmHg for a sustained period of time (>5 min) when the heart is being assessed, consider:

- Recommencing TANRP*
- Preparing for cold perfusion of the abdominal organs and retrieval*

8.11 The abdominal team should undertake dissection, assessment and cannulation of the IVC during this time (abdominal aorta already cannulated as part of TANRP circuit). The IMV may be cannulated at this stage if the pancreas is not being retrieved, otherwise the portal vein will need to be cannulated, something that can be done during the exsanguination period. 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.

8.12 Following satisfactory donor cardiac assessment: The **DCP<sup>CT</sup>** or **TP<sup>CT</sup>** 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)*

## **9. Blood sampling**

9.1 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.

9.2 Blood gases including lactate to be checked every 30 minutes whilst on NRP and on heart-supported circulation.

9.3 QUOD NRP bloods to be taken at the start of NRP, and 60 minutes and at the end of NRP by the abdominal team.

## **10. Thoracic and abdominal organ retrieval:**

10.1 When the abdominal retrieval team are ready, and have cannulated the IVC:

10.2 The DLP cannula inserted into the distal ascending aorta is connected to a cardioplegia infusion line.

10.3 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 causes hyperkalaemia of the ex-situ perfusate). This should take no more than 90 seconds

- 10.4 **LS<sup>CT</sup>** clamps the descending thoracic aorta at the level of the diaphragm through the back of the pericardium.
- 10.5 Once adequate donor blood has been collected, the **LS<sup>CT</sup>** removes the 2-stage venous cannula from the right atrium and clamps the intrapericardial IVC.
- 10.6 **LS<sup>Ab</sup>** commences abdominal cold perfusion with UW.
- 10.7 **LS<sup>CT</sup>** clamps the ascending aorta and commences cold crystalloid cardioplegia.
- 10.8 **TP<sup>CT</sup>** or **DCP<sup>CT</sup>** adds the donor blood to the pre-primed OCS circuit.
- 10.9 Abdominal organ retrieval is then undertaken as for standard DBD retrievals and heart procurement as for DBD.
- 10.10 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 2<sup>nd</sup> **LS<sup>CT</sup>** 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.

## **11. Paperwork and DCD data logs**

- 11.1 The **LS<sup>CT</sup>** will complete an operation note and placed in the donor's hospital notes.
- 11.2 The **DCP<sup>CT</sup>/TP<sup>Ab</sup>** prepare tissue and blood samples as described in section 3 of Donor Run Perfusion Manual.
- 11.3 The **DCP<sup>CT</sup>/TP<sup>Ab</sup>** will ensure completion of HTA A form, plus DCD Heart Transplant Supplementary Record (NHSBT).
- 11.4 The **SNOD** will arrange for copies of appropriate reports to accompany each organ.
- 11.5 The outcomes of each organ transplanted following TANRP will be audited by NHSBT as will completed documentation.

## **12. Competency**

- 12.1 TA-NRP will only be carried out by an experienced cardiothoracic surgeon.
- 12.2 The retrieval team will need to be proctored for a minimum of three retrievals before being signed off as competent. This is in addition to proctored retrievals for Direct Procurement of a DCD heart.
- 12.3 Proctoring will be done by a surgeon competent in TA-NRP.