UK Protocol for Normothermic Regional Perfusion (NRP) in controlled Donation after Circulatory determination of Death

NRP NATIONAL PROTOCOL

Version number: 1.4.2
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1 Preface

This protocol was produced by the NHSBT NRP implementation group (see section 11). The protocol reflects the combined experience of UK experts over many years developing NRP in the UK. It is acknowledged that it reflects practices that have evolved locally and which may be superseded as more evidence and experience accrues. It also reflects the equipment available to clinicians at the time of writing and is not meant to endorse any particular piece of equipment.

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3 Amendments

3.1 Version 1.0 Dated 18th March 2021

Final protocol agreed 18/3/21.

3.2 Version 1.1. Dated 19th March 2021

Removal of reference to previous antibiotic protocol and correction of typographical errors.

3.3 Version 1.2, dated 8th April 2021.

Introduction of clamping the SVC and IVC in the chest to prevent cardiac filling and reanimation.

3.4 Version 1.3, dated 10th April 2021

Additional note to make it clear that venting the ascending aorta is mandatory in all cases of A-NRP (including Maastricht 4) where no cardiothoracic team is attending.

3.5 Version 1.4, dated 26th June 2021

Change in requirement when an Endoclamp is used to require formal venting of the ascending aorta with a separate cannula.

Removal of requirement to clamp the IVC and SVC (amendment 3.3)

Revert to adding antimicrobials to the prime.

Recommendation to cannulate artery first.

Recommendation for someone to call out times at 10, 15, 20 minutes following knife to skin to guide surgeon on when to abandon and go cold.

Guidance on amount of red cells to be added to prime if donor is anaemic.

Suggestion to ligate the artery supplying the contralateral leg if femoral or iliac artery cannulation has taken place.

Alteration in requirement for liver function tests from every 30 minutes to every 30-60 minutes.

Further notes on Maastricht category 4 donors:

- Addition of 5 minute stand-off in 4 donors
- Possibility of delivery of UW down aortic root if heart fibrillates.
- No need to ligate neck vessels for TA-NRP

3.6 Version 1.4.2, dated 29th June

Addition of section 9 regarding documentation of NRP on organ passport.

4 Introduction

Abdominal in situ normothermic regional perfusion (A-NRP) is a technique to restore the circulation to the abdominal organs following circulatory arrest for the purpose of transplantation. This involves establishing a localised, abdominal perfusion Extracorporeal Membrane Oxygenation (ECMO) circuit, perfusing the organs with oxygenated blood at 37°C for a period of typically 2 hours.

This will allow:

1. Recovery from warm ischaemia and replenishment of ATP reserves
2. Assessment of organ function and quality
3. A less hasty retrieval.

NRP has been shown to increase the utilisation of all abdominal organs, and significantly improve the outcomes of liver and kidneys, with no adverse effects on the pancreas. For the liver it is associated with better transplant survival and a very low incidence of cholangiopathy when compared to conventional DCD donor livers; for the kidney it is associated with better renal function at 12 months.

This protocol details the technical aspects of the procedure. It is written with regard to the current legislation and observes the Academy of Royal Medical Colleges (AoRMC) code of practice for the diagnosis and confirmation of death that forms the basis of organ donation from deceased donors.

5 Composition of Organ Retrieval Team for A-NRP

With the addition of NRP to clinical practice, the core membership of the abdominal retrieval team should consist of:

- A theatre practitioner scrubbing for organ retrieval
- Organ preservation practitioner: A theatre practitioner competent in organ perfusion/preservation techniques:
- Advanced Perfusion and Organ Preservation Specialist (APOPS): A senior theatre practitioner competent in operating the NRP machine and monitoring the perfusion
- Two surgeons, at least one of whom has been accredited as competent to perform A-NRP

Thoracic and/or cardiac surgeons may attend for retrieval of thoracic organs; separate protocols exist for recovery of those organs and adaptations of this protocol in those circumstances are discussed at the end of this document.

6 Mobilisation

Mobilisation for A-NRP is the same as for any DCD retrieval, arriving 1 to 2 hours or more before the proposed withdrawal time. For combined procedures with cardiothoracic teams the scheduled arrival should be 2 hours ahead of proposed withdrawal time to enable full communication and rehearsal of the steps involved in retrieval to ensure a successful

outcome for both teams. It should be noted that the abdominal team will need at least 2 additional vascular clamps or equivalent when a combined retrieval is planned with the cardiothoracic team. These clamps, applied to large vessels to permit heart, and/or lung retrieval, will remain in place one the cardiac team have gone and must therefore be carried by the abdominal NRP team.

7 Setting up the equipment for A-NRP

7.1 Ordering blood

The SNOD should order packed red cells cross-matched to the organ donor so they are available prior to the abdominal retrieval team arriving. The blood should be in the theatre suite *before* withdrawal of treatment. The amount ordered depends on circumstances:

- Standard abdominal NRP: 4 units
- Abdominal NRP with heart or lungs are being recovered by direct retrieval and cold perfusion: 8 units
- Thoraco-abdominal NRP: 6 units

7.2 Donor hospital handover

Once at the donor hospital the abdominal retrieval team should inform local theatre staff of the planned procedure. They should also discuss the relevant protocols for removal of heart or lungs with the respective retrieval team. Protocols are clearly defined for combined procedures and must be followed (see odt.nhs.uk microsite).

Someone should be identified who can perform blood gas analyses if a point of care device is not available in the donor theatre. Similarly, someone should be identified to run samples to the biochemistry laboratory if a point of care device is not available. However, each team should have the necessary equipment, fully maintained and quality assured, and be independent of laboratories for such assays.

The standard pre-retrieval handover should be undertaken, including verification of information in the core donor data form by reviewing the case notes, and checking the blood group and virology results.

7.3 Timing and Place of Withdrawal of Life Supportive Therapy (WOLST)

The normal practice at the donor hospital regarding the place of treatment withdrawal may be observed. The time of withdrawal, the time systolic BP falls under 50mmHg, and the time of circulatory arrest are recorded according to current practice. In addition, the time NRP is commenced and stopped will also need to be recorded.

As soon as death is verified, the patient is transferred to the operating theatre.

The acceptable duration between WOLST and death for retrieval of specific organs should be discussed with the implanting team, but these are likely to be longer than considered with DCD donors in whom NRP is not performed. As per NORS guidance the retrieval team is expected to stay for 3 hours. There should be no need for premature stand down since viability will be tested during NRP.

7.4 Pre-retrieval preparation

This involves several steps:

a) The scrub practitioner will setup the operating environment in a similar fashion to the current practice for DBD retrieval. This includes setting up the diathermy machine (as available in the host theatre) and the power saw for thoracotomy (where available).
b) Two 60 ml catheter tip syringes filled with heparinised saline should be prepared. They will be used to flush the aortic and IVC lines prior to connecting to the NRP circuit.
c) The aortic and IVC cannulas should be identified.
d) The connections between the proposed cannulae and the sash are checked to make sure they are compatible and no additional connectors are required.
e) Once the potential donor's systolic pressure has fallen below 50mHg or after circulatory arrest, the sterile part of the NRP circuit (the "sash") should be handed to the scrub practitioner.
f) Both limbs of the sash should be clamped approximately 10cm from the ends of the red and blue line tubes and divided.
g) The arterial and venous cannulae should be opened at this stage; opening them earlier may result in wastage if the donor does not die.
h) If a heart team is planning to recover the heart by direct recovery and perfusion in the cold, they will need 1.5L of donor blood to prime the OCS heart machine. This must be recovered before NRP commences. This is best facilitated by having a Y-connector on the blue venous return pipe above the reservoir that can be connected to their blood receptacle. This is best placed before priming if one is not already built into the circuit (figure 1).

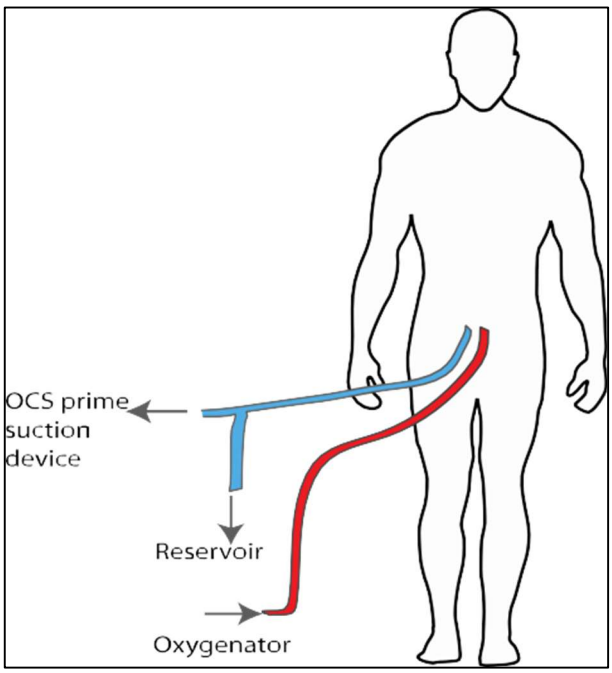


Figure 1 Y-connector to facilitate blood being removed to prime the OCS device.

7.5 NRP setup

The NRP setup depends on the machine used.

7.5.1 The heater

Maquet's Cardiohelp: The heater is separate and should be topped up with water and switched on with the temperature set at 37°C.

Organ Assist's Donor Assist: switching on the heater is part of the automated setup.

7.5.2 Heparin in the donor before circulatory arrest

Maastricht 3 donors: No pre-mortem interventions are currently allowed in the UK.

Maastricht 4 donors (donor is already certified dead by brain stem criteria): heparin can be given. A suggested dose is 300units/kg (around 25000 units for a 80kg person) given just prior to withdrawal of treatment

7.5.3 Preparation of cold perfusion fluids

Two one-litre bags of cold University of Wisconsin solution should be prepared with 300u/kg (around 25000 units for an 80kg man) of heparin added to *each*, as for a standard DCD, and run through a large bore 'Y' giving set so they can be used immediately should NRP fail to be established or problems are encountered during perfusion and rapid conversion to a standard technique is required. The giving set may be pre-connected to the NRP circuit and once primed the UW bags should be replaced in ice until needed. When cold perfusion starts it is imperative a clamp is placed on the arterial line proximally to prevent back flow into the pump/reservoir.

7.6 Composition of circuit priming fluid

7.6.1 Standard prime

- Bicarbonate 8.4%, 1ml/kg
- Hartmann's 2000 mls
- Heparin 50,000 u
- Methylprednisolone: 1 gram
- Phentolamine 5mg
- Pancuronium 12 mg – to prevent abrupt diaphragmatic contraction when phrenic nerve is divided which can cause distress to attending teams and host staff.
- Fluconazole: 400 mg
- Antibiotics to be added into the prime:
    - 200mg teicoplanin
    - 120mg gentamicin
    - 500mg metronidazole

7.6.2 Anaemic donor (Hb<70gm/L)

If the donor is anaemic a unit or more of packed red cells may be added to the reservoir in place of some of the Hartmann's solution. Typically if less then 6gm/L, add 2 units packed red cells; if between 6 and 8gm/L, add 1 unit packed red cells.

7.6.3 Small donor or paediatric donor

If the donor is small the dilution effect of the prime solution will be large. Therefore:

- *For donors >30kg but <50kg,* add 2 units of blood to the prime and only 1000ml of Hartmann's.
- *For donors ≤30kg*, use 3 units of blood in the prime with 500mls Hartmann's.

Flow rates will be proportionately lower in smaller donors.

7.6.4 Additional fluids during retrieval

During perfusion it is usually necessary to add more volume, in which case Gelofusine or blood are appropriate. *DO NOT ADD Hartmann's* once perfusion has started as it contains lactate and makes the lactate result impossible to interpret.

7.6.5 Additional heparin during retrieval

During perfusion an ACT *may* be checked or, in the absence of this, additional heparin *may* be given at 90 min using a dose of 150 u/kg.

Heparin should also be added if severe haemorrhage occurs, e.g. during cardiac retrieval, and is replaced by a lot of bank blood, since this will dilute out any existing heparin with the risk of clotting. This is not usually required in A-NRP only.

8 Surgical Protocol for DCD NRP

Before withdrawal of treatment the operating surgeon and pump operator should check how the chosen cannulae are connected to the circuit, and whether any additional connectors are necessary (see above).

8.1 Cannulation

Cannulation can either be in the groin using the femoral vessels, or in the abdomen with direct or indirect access to the aorta and IVC. Surgeons need to be familiar with all techniques. It is helpful to have the perfusion practitioner call out the time taken at 10, 15, and 20 minutes following knife to skin to inform the surgeon. Cannulation should not take longer than 20 minutes, and will typically take around 10 to 15 minutes.

8.1.1 Femoral cannulation

This is a simple and rapid technique, and is most appropriate in the following circumstances:

- for younger donors with little chance of occlusive ilio-femoral arterial disease
- when thoracic surgeons wish rapid access to the chest

- where access to the abdominal vessels may be delayed (e.g. previous surgery; ankylosing spondylitis where the patient may not be flat on the operating table)
- for known vascular anomalies seen on available cross-sectional imaging (e.g. known lower polar vessels coming off distal abdominal aorta/iliacs; retro-aortic left renal vein originating at confluence of iliac veins; left sided IVC, horseshoe or pelvic kidney).

A transverse or oblique incision is made immediately below the inguinal ligament. When the heart is being retrieved, the vein must be cannulated first to allow rapid blood drainage to prime the OCS machine; otherwise it may be easier to cannulate the artery first.

The femoral vein is isolated, the distal end either clamped or ligated. A venous cannula is passed up the femoral vein and secured either with a ligature or snugger. The cannula is then connected to the venous limb of the sash, and the sash's venous clamp removed to allow drainage into the reservoir.

The femoral artery is isolated, distal end ligated, and cannulated. The cannula is secured with a ligature or snugger, and connected to the arterial limb of the sash with care taken to exclude air.

The choice of cannulae for the femoral vessels varies according to the patient's size:

- *Femoral artery:* typically a 19F French cannula (e.g. Medtronic Biomedicus 19F), although alternative 15Fr, 16Fr or 18Fr cannulas may be required in small patients or for diseased arteries.
- *Femoral vein*: a 25 French (e.g. Medtronic Biomedicus 25F/38cm) cannula

It is possible that difficulties arise during femoral vein or arterial cannulation and the surgeon needs to be prepared to switch to abdominal cannulation in such eventualities. Typically the extra time taken is compensated by being able to restore a circulation to the abdominal organs before cold storage.

8.1.2 Aorto-iliac cannulation

A midline incision from xiphoid to pubis is made. The right colon and small bowel mesentery are mobilised and retracted to the left by the assistant. The aorta or right common iliac artery may be cannulated first in preference to the IVC, since any venous bleeding will make subsequent identification of the artery difficult.

The distal infrarenal aorta or right common iliac artery is identified and slung using a vascular snugger. The distal aorta is cross clamped or ligated. The aortic cannula is inserted, checking the proximal position of the tip is approximately 2 to 5cm above the cannulation point. The cannula is secured in place with the vascular snugger or ligature. The arterial limb of the circuit (the tube with the red line) is then connected to the cannula, with care taken to eliminate all air bubbles (alternatively, this can be pre-connected and the perfusion practitioner can forward flush slowly during cannulation).

The infrarenal IVC (or right common iliac vein) is dissected and encircled using a ligature or vascular snugger. The distal end is clamped or ligated. The venous cannula is inserted into the IVC. The cannula should be adjusted so its tip sits just below the diaphragm to allow the

clamping of the suprahepatic IVC without compromising the venous return in the circuit. The venous limb of the circuit (the tube with the blue line) is then connected to the cannula and the clamp released. Blood should flow back into the reservoir.

The choice of cannulae for the intra-abdominal vessels varies less with the patient's size than when cannulating in the groin. The same cannulas as used for a femoral approach may be used, or alternative larger cannulas may be used:

- *Aorta or common iliac artery:* a 20 or 24Fr cannula (e.g. DLP Medtronic cannula).
- *IVC or common iliac vein*: a multistage cannula of 25 French or more (e.g. 36/46 Fr 40 cm Edwards Lifesciences Q3 Trim-Flex two or three Stage).

8.1.3 The contralateral external iliac artery

If the cannulation has been into a femoral artery or common iliac artery, the contralateral common external iliac artery may be ligated or clamped to optimise abdominal organ perfusion. Care should be taken not to reduce the length available for subsequent vascular reconstructions.

8.2 Controlling the thoracic aorta

A rapid sternotomy is carried out using either a power saw or Gigli saw. If cannulation was in the groin the abdomen does not need to be opened first. The thoracic aorta is clamped below the level of the left subclavian artery close to the diaphragm. A stab incision is made in the ascending thoracic aorta with a number 11 blade and a 24G cannula (the hole left by an 11 blade inserted to its hilt is the same size as the 24G cannula) or a Medtronic DLP Aortic Root Cannula (avoiding the need for a prior stab) is inserted and left open to atmosphere to allow monitoring of pressure and flow in the aorta and intracranial arterial supply. Typically, there is a small column of dark deoxygenated blood 1 to 5cm. This aortic vent should have no flow within it; if there is flow the pump should be stopped and the thoracic aortic clamp repositioned. The aortic vent can be connected to the reservoir if the column of blood reaches the top of the cannula, so long as it does not represent oxygenated blood from the NRP circuit.

An alternative approach is to insert an aortic endo-clamp (e.g. Cook 32/37mm, 120cm Coda LP balloon catheter) in the descending thoracic aorta~~, venting the internal channel distal to the balloon, and commence the NRP before undertaking the sternotomy~~. It is critical to check the length prior to insertion to ensure that the balloon is positioned in the descending aorta, and not in the left subclavian or anomalous right subclavian artery. An ascending aortic vent cannula still needs to be inserted, after which the NRP circuit can be started. This approach would allow the cardiothoracic team to undertake the sternotomy and mobilise the lung and clamp the descending aorta (if simultaneous lung retrieval).

NOTE: The ascending thoracic aorta **MUST** always be vented before starting NRP including in Maastricht 4 donors, and the vent kept open for the duration of NRP.

8.3 Maastricht 4 controlled DCD donors

Maastricht 4 donors, which are brain stem dead donors going through the DCD pathway usually at the request of the next of kin, pose a number of issues worth noting.

i. The donor can be heparinised before ventilation is discontinued
ii. The National Organ Donation Committee have agreed that a no touch period of 5 minutes following circulatory arrest be respected before the donor is transferred to the operating room and surgery commenced.
iii. An aortic vent should always be placed in a category 4 donor
iv. Since the next of kin have concerns about the beating heart, the donor team should consider infusing UW solution (or cardioplegia) into the aortic root via the vent cannula, with a temporary clamp distal to this, to cause a cardioplegic arrest and suppress fibrillation if this occurs.
v. In cases of thoraco-abdominal NRP in category 4 donors, there is no need to ligate or separately vent the neck vessels.

8.4 Establishing NRP

- The pump must only be started once the circuit is completely connected, the thoracic aorta is cross-clamped/occluded and the aorta above the clamp is vented.
- The heater temperature should be 37°C.
- The air/O_2 mixer should be set to deliver gas flow at 2 litres/minute with a starting FiO_2 of 21% (air). High FiO_2 should be avoided. Changes to the oxygen/air mixture may be required subsequently depending on the blood gas analysis. High oxygen concentrations may generate reactive oxygen species and can exacerbate reperfusion injury to the organs.
- The preferred NRP duration is two hours.

8.5 Haemodynamic and biochemical goals

The following parameters are suggested:

- Pump flow 2-3 litres/minute
- Temperature 35.5°C - 37.5°C
- Air / O_2 to maintain a venous O_2 saturation (SvO_2) 60-80%
- Arterial pH 7.35-7.45
- Haematocrit > 20%
- Gas flow to maintain arterial pCO_2 4.5 to 6.0 kPa.

8.6 During NRP

8.6.1 Haemostasis

Once the NRP is established, meticulous haemostasis must be ensured from the abdominal wound edges, sternotomy and retroperitoneal tissues disrupted during aortic and IVC cannulation. Bleeding is not usually troublesome for the first 60 minutes or so.

As there is a potential for significant blood loss, volume replacement (blood or colloid) should be readily available. If volume is lost from the circuit, the two most common sites are in the chest where the thoracic aorta is clamped, and where an intercostal or vertebral branch may have been avulsed, and around the aortic and caval cannulae. Volume loss is also observed routinely with vasodilation consequent on loss of sympathetic tone, without overt blood loss, and volume replacement will be required during the NRP procedure.

8.6.2 Direct retrieval and perfusion of lung or heart

There is potential for significant bleeding when lungs / or heart are retrieved and therefore there is a separate protocol for combined A-NRP with cold thoracic retrieval (see odt.nhs.uk microsite). The supra-hepatic IVC is clamped at the cavo-atrial junction in the chest and therefore it is important to ensure that the tip of the venous cannula is below the level of the diaphragm to avoid compromising the venous return. The thoracic surgeon must ligate the azygous vein, the SVC, and leave a clamp across the descending thoracic aorta.

8.6.3 Additives to the perfusion fluid

- Heparin may be added every 90 minutes (150 u/kg). More frequent heparin boluses will be required if a large quantity of bank blood (or cell saved blood) are added as may happen in cardiac retrievals.
- Bicarbonate should be added according to the initial blood gas results: if the pH<7.0 after starting NRP give 25ml of 8.4% immediately. Correction is seldom necessary once NRP is established, since functioning liver and kidneys correct the acidosis quickly, and gas flow across the oxygenator can also be used to regulate pH.
- Subsequent volume replacement should either be red cells or gelofusine

8.7 Surgical dissection

Once NRP is established, the surgeon should perform a full laparotomy and a macroscopic evaluation of the abdominal organs, in particular the liver, pancreas and kidneys. At the start of NRP the liver will appear congested and feel stiff. As time passes the liver should feel less firm and a normal colour return. The bile duct should be divided early and the gallbladder incised, emptied and flushed with normal saline (0.9%), care being taken not to flush thick gallbladder bile into the common duct. A careful examination of small bowel, the blood supply to the cut end of the bile duct and the appearance of the gallbladder mucosa should be undertaken (indicative of ischaemia). If the lungs are not being retrieved the contents of the thoracic cavity should be inspected thoroughly looking for lung and oesophageal neoplasms and other pathology.

After these initial procedures it is often sensible to scrub out for 60 minutes to avoid unnecessary blood loss, leaving one person scrubbed in case of emergencies. In addition, dissection around the liver causes haemodynamic instability at a time when you are trying to allow the organs to recover from warm ischaemia.

In the face of excessive blood loss, it is preferable to stop NRP early, rather than to persist with transfusions for the full 2 hours.

8.8 Cold perfusion

The cold phase dissection is carried out as for DBD retrieval. The abdomen may be filled with ice slush just before cold perfusion commences. The cold inflow may be attached to a suitable port or Y-connector on the arterial side of the circuit distal to the oxygenator if not already attached – do not run the cold perfusate through the oxygenator as this will warm it up. Alternatively, the arterial line can be clamped and the cold UW giving set connected to tubing just proximal to the arterial cannula. The standard quantity of UW is infused into the aorta as for any normal retrieval.

The cannulation of the portal vein in the cold phase is at the discretion of the retrieving surgeon. The portal vein ***must*** be extensively flushed with UW on the back table if it is not cannulated and perfused *in situ*.

The venous cannula may be pulled back to aid drainage of the kidneys, as the cava will collapse on the cannula potentially impairing venous drainage. The venous effluent may be collected into the circuit's reservoir or separate drainage bag (depending on the NRP machine and circuit used), or it may be allowed to collect in the chest from where it can be sucked out.

8.1 Biochemical Evaluation

Serial samples (gases and ALT/AST every 30 to 60 minutes) are taken to assess the organs and to stay within the parameters described above; more frequent testing is appropriate where shortened periods of perfusion may occur, such as when cardiothoracic teams are involved. Blood cultures should be taken as soon as NRP starts and at the end of NRP (0 and 2 hours). Volume replacement to support flows, whether blood or colloid, will dilute the biochemical markers of damage and function; this should be borne in mind when interpreting them.

Biochemical assessment should be done on machines that are quality assured (Human Tissue Authority requirement). This may be by the retrieval centre's own biochemistry department.

8.1.1 Liver

The following biochemical parameters are important:

- *Transaminases as liver damage markers.* There is no international consensus on the degree of rise in ALT/AST which represents a usable liver. Current UK practice is to accept livers with a rise in ALT ≤ 500iu/L over 2 hours. Cases have been described in Italy where PNF occurred with the terminal ALT>1000iu/L.
- *Lactate as a function marker.* The lactate should fall over the course of two hours, but may not reach normal values due to venous return from the upper body and non-perfused limbs. Clamping the intrathoracic IVC may be associated with a greater fall in lactate measured in the circuit.

A routine **liver biopsy** before or after NRP (or both) is supported for quality assurance purposes where the NRP team feel it is appropriate. Biopsy sites in the liver should be sutured and noted on the A form

8.1.2 Pancreas

Amylase measured on the near patient analyser may indicate pancreatitis, but visual appearance is more useful.

8.1.3 Kidneys

Urine output falls off and may stop completely during NRP. There is no useful biochemical marker.

8.2 Post NRP

The appropriate paperwork should be filled in and a copy sent with each organ.

8.3 Failure to establish NRP

If NRP cannot be established, initial cold perfusion should follow the standard DCD protocol. If NRP is successful, cold perfusion should follow the DBD protocol. Back-table preparation should follow the current protocols.

9 Documentation

It is important that the perfusion characteristics during NRP, the blood gases, the fluids used and the timings, are all captured on the approved NHSBT NRP organ passport, and a copy sent with each organ for the recipient surgeons. A copy should also be retained by the NOORS team and a further copy sent to NHSBT.

10 Troubleshooting NRP

10.1 Communication

Many of the issues occurring during NRP can be avoided by a good team brief and handover before the procedure so that everyone knows what is expected of them. This is particularly important when a cardiothoracic team is present.

10.2 Volume loss

Volume losses occur for the following reasons:

- Relaxation of alpha-adrenergic vasoconstriction occurring prior to death and loss of sympathetic tone;
- Bleeding, typically in the chest near the thoracic aortic clamp, or in the pericardium if lung and/or heart have been removed. In the abdomen it is often around the venous/arterial cannulae;
- Occlusion of the venous cannula, usually due to pressure or manipulation on the liver or bowel;
- Increasing the flow rate may reduce the reservoir volume.

Sudden loss of venous return can rapidly exhaust the circuit reservoir resulting in failure of the circuit: a one litre volume in the reservoir will disappear in 20 seconds at a flow rate of 3L/min. The perfusion practitioner should keep careful watch on the reservoir level, caution the surgeon and replenish the reservoir as the volume falls.

If volume is lost suddenly it may be because the wall of the cava has been sucked onto the cannula and occludes the holes due to manipulation of the organs; temporarily stopping organ manipulation, and manoeuvres such as reducing the height difference between donor and pump, or partial occlusion of the venous return tubing may also be effective. Alternatively, this is remedied by stopping the pump, waiting a couple of seconds, then restarting at a lower flow rate.

10.3 Air in the circuit

Air in the arterial limb can embolise and impair perfusion of organs. It is important to de-air the cannula and circuit when establishing the circuit at the beginning to prevent air entry. Small amounts of air in the venous side will run off into the open reservoirs of currently used circuits and cause no harm. Large volumes of air, as may occur if the cannula becomes dislodged, will cause an airlock which will block blood returning to the reservoir. This airlock needs to be walked along the tube by holding the tube distal to the airlock upwards to allow the tube to fill from below, and displace the air.

10.4 Clots in the circuit

A clot in the circuit can embolise into the organs. Fresh clot is most likely to occur first on large surface areas such as the oxygenator and leucocyte filter, and will impede flow. Clots in the circuit occurs for the following reasons:

- Failure to add any or sufficient heparin to the prime solution
- Failure to circulate heparin around the circuit before starting perfusion
- A long delay between connecting the venous cannula and draining blood into the reservoir, and starting NRP. Non-heparinised blood in the venous line will clot; that in the reservoir should not as it mixes with heparinised prime solution.
- Excessive bleeding requiring replacement with large volumes of non-heparinised fluids
- Pre-existing venous clots associated with lines

10.5 Troubleshooting Cs for poor flows

The following Cs are worth remembering when trouble-shooting (courtesy of James Richards):

- **C**annulas: check position, check vein not collapsing on cannula (if so increase volume)
- **C**lamps: check cross-clamp on thoracic aorta is on aorta, and all clamps on circuit released? Check position of supra-hepatic caval clamp
- **C**ava: are you compressing on it in your dissection or is it collapsing?
- **C**ircuit: anyone or anything compressing the circuit

- **C**hest: a common site for bleeding
- **C**lots: venous or atrial clots preventing venous return; clots on leucocyte filter or oxygenator
- **C**OLD: if you can't resolve issue in timely fashion then go cold and salvage the organs

11 Appendix 1 Protocol for direct recovery and perfusion of the heart and A-NRP

Due to the complexity of the procedure and the risk to the abdominal organs this combined technique is only appropriate for use where the heart is being retrieved for transplant purposes.

11.1 Cardiac team requirements for successful cardiac recovery

The following are required:

- Senior surgeon who is experienced in DCD heart retrieval
- A cell saver, to enable blood to be washed plus disposables
- The *ex situ* normothermic heart perfusion machine.
- Technician to operate the *ex situ* perfusion machine and the cell saver
- The necessary sterile tubing and adapters to connect to the NRP circuit ($^{3}/_{8}$ and ½ inch tubing).
- An appropriately staffed and equipped lung retrieval team if the lungs are also being retrieved

11.2 Abdominal team requirement for successful cardiac recovery during A-NRP

- Senior surgeon who is experienced in NRP
- The NRP disposable circuit
- NRP heater/cooler and pump (e.g. Cardiohelp)
- Experienced NRP perfusion practitioner
- 2 x long vascular clamps for descending aorta and IVC clamping (e.g. long straight and curved DeBakey)
- 2 Roberts clamps, one for the SVC and one for the ascending aorta

11.3 SNOD requirements

8 units of bank blood, 4 to be added to prime

11.4 Circuit

11.4.1 Preparation

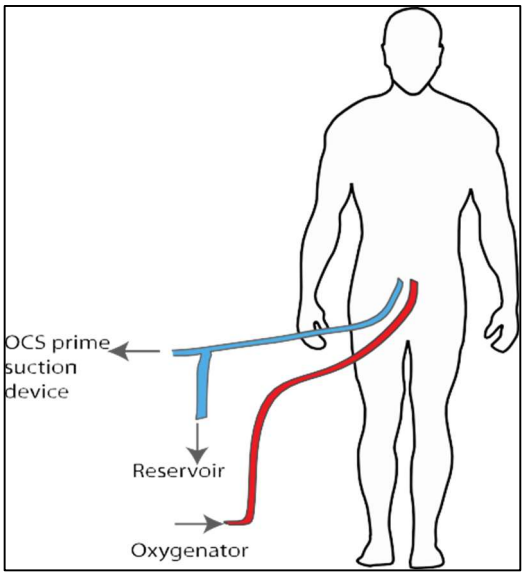
The NRP circuit needs to have a Y attachment on the venous return limb just above the reservoir, and needs to be fitted prior to arrest if it is not already present on the circuit. This needs to be connected to the cell saver to allow for donor blood drainage needed for *ex situ* heart perfusion, but clamped initially.

11.4.2 Prime solution

- 4 units packed red cells (approx. 1200mls)
- 1.5 litre Hartmann's solution
- 50000 units heparin
- Phentolamine 5mg
- Pancuronium 12 mg – to prevent abrupt diaphragmatic contraction when phrenic nerve is divided which can cause distress to attending teams and host hospital staff.
- 1ml/kg 8.4% sodium bicarbonate (=1mmol/kg)

- 1gm Methyl prednisolone
- Fluconazole: 400 mg
- Antibiotics to be added once perfusion begins:
    - 200mg teicoplanin
    - 120mg gentamicin
    - 500mg metronidazole

Figure 1. Drainage of blood for priming the OCS device



The NRP circuit is primed with 1.5 litres of Hartmann's, to which are added 4 units of red cells. The circuit needs to be set up before withdrawal of treatment, and warmed to 37°C by circulating through the oxygenator/heat exchanger.

Ideally, a pump sucker is connected to the reservoir for blood loss recovery during NRP, and the reservoir placed under negative suction. This is the preferred standard with teams working towards this, until then existing practice will prevail. This will only be used to recover blood from the pericardium if heart retrieval only, or to recover blood from pericardium and pleural space if combined heart-lung retrieval. Blood should not be recovered from the pleural space in the presence of chest sepsis. Additional care must be taken to avoid any perfusion fluid/saline being recovered using this sucker.

This additional sucker will not be used in cases of pericardial, mediastinal or systemic infection. Careful haemostasis should be performed in the chest even in the event of having a sucker available.

Two long DeBakey vascular clamps will be ready to use by the cardiothoracic team prior to WLST to clamp descending aorta and IVC. Two Roberts clamps will also be ready to clamp SVC and ascending aorta. It has been agreed that clamps will be provided by the abdominal team as they need to stay in place once the Thoracic team has left the operating theatre.

Due to the complexity of the technique, cardiothoracic organs will be retrieved only for transplantation purposes whilst the donor undergoes NRP. The heart for valves may be retrieved after NRP is concluded.

11.5 Operative procedure

Following verification of death 5 minutes after circulatory arrest, the patient is transferred to the operating table.

IT IS MANDATORY TO FOLLOW THIS STEP SEQUENCE

11.5.1 Abdominal team procedure

1. The circulating pump is stopped, and the sash is clamped and divided; the arterial cannula may be attached and primed at this point.
2. Once the donor is in theatre, the abdomen and right groin are prepared and draped.
3. The venous cannula is placed in the right common femoral vein common (or iliac vein or IVC) and connected to the venous limb of the sash, with care to exclude air. Care should be taken not to insert too much length of cannula to prevent it going into the right atrium.

   IF there is problem with achieving venous cannulation the thoracic team may choose to cannulate the let atrial appendage; this cannula should be removed and the appendage ligated before starting NRP or else air will be entrained in the circuit and NRP fail. For this reason atrial cannulation is a last resort.
4. Clamps are removed and 1.5L venous blood drained out and diverted into the collecting receptacle for the heart Organ Care System (OCS) (such as the cell saver system used by Harefield).
5. The Y-connector is then clamped and venous return blood now diverted to drain back into the reservoir (see figure 1)
6. The arterial cannula is placed in the right femoral artery, common iliac artery or aorta while the venous drainage occurs.
7. Once the cardiac team have clamped the descending thoracic aorta and stated that clearly for both teams to hear, and the 1.5L venous OCS prime has drained, the NRP pump is started aiming for flows over 2.5L/min. The time that the descending thoracic aorta is clamped will be recorded on the National DCD Heart Passport.

Abdominal NRP must not start until both teams have confirmed for all to hear that the descending aorta is clamped.

Once the heart is removed it is important to check the security of the supra-hepatic IVC clamp – this may need to be sutured in place to avoid inadvertent unclamping or slipping from the cut IVC. The cut ends of the pulmonary vessels and SVC may be oversewn with 3/0 Prolene at this stage also. While the cardiac surgeons should ensure haemostasis in the chest, in reality it is the abdominal surgeons who are usually free at this stage and can stop large vessel bleeding.

There should be no major bleeding.

11.5.2 Cardiac procedure

The chest is opened in the midline and sternum split while the abdomen or groin is opened for cannulation. The cardiothoracic team will apply a clamp across the descending thoracic aorta, and announce to theatre when this has been done. They will then place a DLP cannula, open to air, as vent in the ascending aorta to monitor for possible brain perfusion

Once the DLP cannula is in place and open to air, the cardiothoracic surgeon announces that the aortic arch is vented, at which point the NRP pump may begin. The time will be recorded on the National DCD Heart Passport. If there is copious arterial bleeding from the DLP cannula, the NRP pump must stop and the clamp on the descending aorta must be re-positioned to occlude the aorta. Only then can the NRP pump re-start.

Figure 2. DLP cannula

The details of heart and lung retrieval are in the separate cardiothoracic protocol for DCD donors "*Direct retrieval and perfusion (DPP) of DCD heart and lungs with or without A-NRP to ex situ normothermic perfusion*" at odt.nhs.uk microsite

11.5.3 Procedure for lung retrieval alone without heart while on A-NRP

See separate protocol for "*Direct retrieval and perfusion (DPP) of DCD heart and lungs with or without A-NRP to ex situ normothermic perfusion*" at odt.nhs.uk microsite.

The thoracic team will stand back for 30 minutes after cold in-situ perfusion of the lungs. Dissection of the lungs will then begin, which can be assisted by the abdominal surgeons as appropriate. This should be carried out with care and detail, to enable stability to be established on A-NRP, and to maintain stability during and after the lungs have been removed.

12 Appendix: UK NRP implementation group members involved in drafting the protocol

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