

# Establishing a Normothermic Regional Perfusion (NRP) Programme for Donation after Circulatory Death (DCD) in Malaysia.

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## **Why should Malaysia be looking towards Donation after circulatory death and why NRP?**

In 2021, based on the data from the National Transplant Resource Centre presented on the Global Observatory on Donation and Transplantation database, a total of 7 liver and 15 kidneys were transplanted from donors after brain deaths. Table 1 provides the actual number of organs transplanted from various sources along with the number of donations per million population in our country in 2021. *As of May 2023, a total of 9097 patients are on the transplant waiting list with only a staggering 31 transplants in total performed.*

Worldwide, donation after circulatory death or DCD has undergone a resurgence and has mitigated many of the issues of shortage of viable organs as well as reducing the waitlist mortality. On the flip side of this, DCD grafts have their own inherent potential drawbacks, notably ischaemic type biliary strictures and higher rates of delayed graft function. Crucial and central to this is the role of Normothermic regional perfusion (NRP) as a means proven to mitigate some of these problems.

This article aims to provide some basic understanding of DCD organ donation and the use of NRP. The author also provides his opinion on how this can be established in Malaysia. At the time of writing, wheels are in motion to start a DCD programme in the country. Opinion may be divided as to whether NRP should be used for all DCD retrievals but one cannot argue against the proven benefits of NRP. (Table 2)

*Table 1*

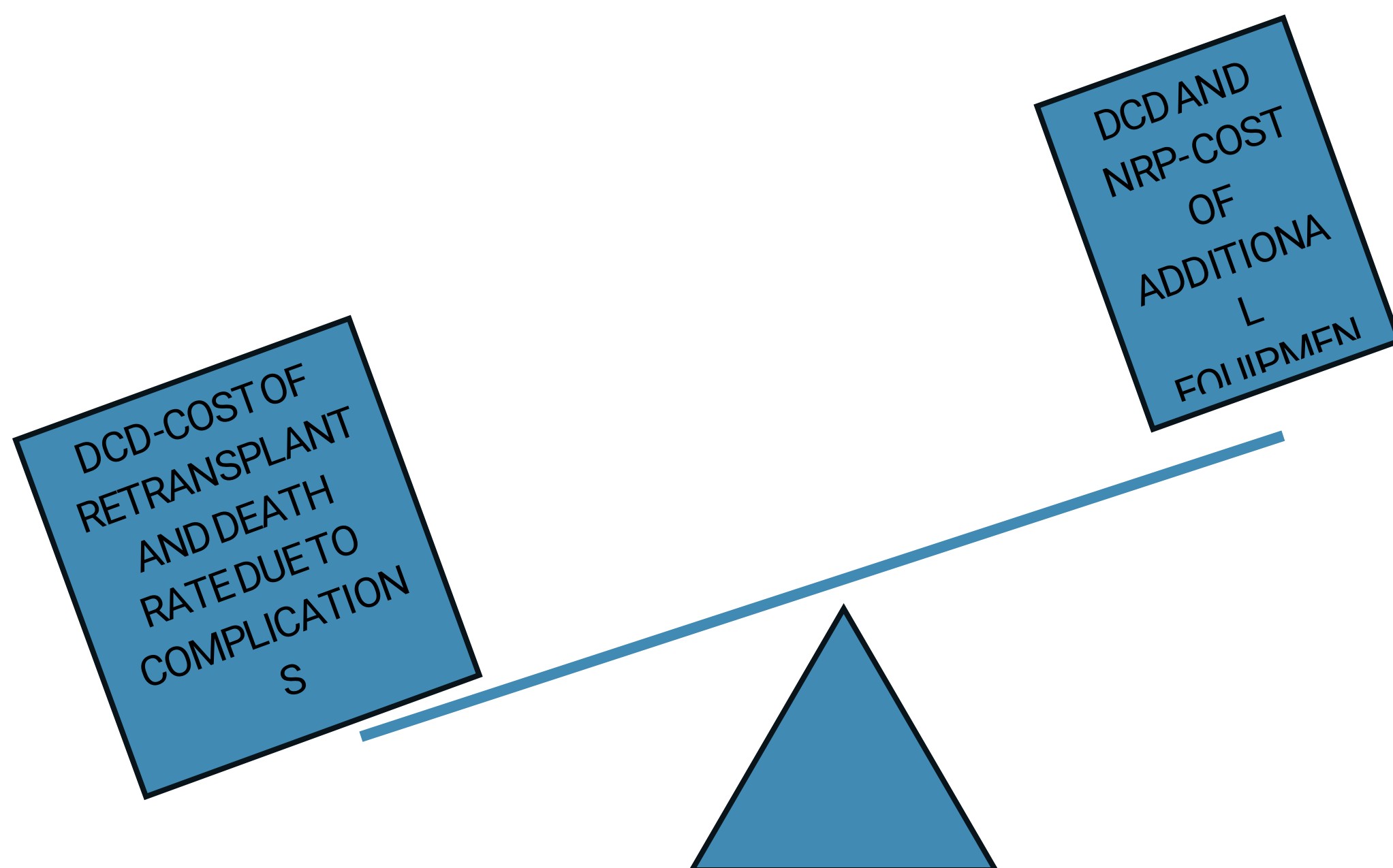
<i>Data presented in absolute number and rate per million inhabitants (pmp) (-): Data Not Available or Not Applicable</i>	Malaysia	Western Pacific	Global
ACTUAL DECEASED DONORS (DD)	7 (0.21)	6,311 (3.48)	38,156 (6.37)
ACTUAL DD AFTER BRAIN DEATH (DBD)	7 (0.21)	4,180 (2.3)	29,611 (4.94)
ACTUAL DD AFTER CIRCULATORY DEATH (DCD)	(-)	2,131(1.18)	8,545 (1.43)
TOTAL KIDNEY TRANSPLANTS	78 (2.38)	17,516 (9.66)	92,532 (15.44)
DECEASED KIDNEY TRANSPLANTS	15 (0.46)	11,260 (6.21)	57,365 (9.57)

Table 2

Benefits of DCD with NRP
Allows more time for a successful retrieval
Improves quality and function of retrieved organs
Less costly when compared to standard DCD in terms of number of

patients that survive / graft survival (Figure 1)

Figure 1



**Cost of significant morbidity from DCD grafts culminating in possible re-transplantation >>> Cost of NRP. It is very important to factor this especially for a country like Malaysia, where organs are scarce and there is almost negligible opportunity for a second graft**

**Donation after Circulatory death.**

The concept of organ donation from circulatory death is not new. DCD donors were the primary source of deceased donor organs prior to a universally accepted brain death criteria. Interestingly, the first 3 liver transplants performed by Thomas Starzl were from DCD donors and were on an ECMO!. Today, DCD donors provide a significant number of organ donors in many countries around the world (United Kingdom, Spain). This is in contrast to many Asian countries where living donation makes up for the low deceased donation rate.

Compared to DBD organ donors, DCD donors do not meet the criteria for brain death but have significant injury or impairment that makes them dependable on life sustaining treatment. This is where the ethical issues come into consideration. The table below provides the pre-requisites (Table 3) and ethical considerations (Table 4) in DCD organ donation.

*Table 3*

<b>PREREQUISITES</b>
<i>1. Does not meet criteria for DBD</i>
<i>2. Injury / illness is non-recoverable</i>
<i>3. Dependent on life sustaining interventions</i>
<i>4. Decision and consent to withdraw life sustaining therapy</i>

5. <i>Death is expected to be imminent following withdrawal of life sustaining therapy</i>
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Table 4

ETHICAL CONSIDERATIONS
1. Timing of withdrawal of treatment in patients who may be potential donors -deciding who is futile
2. Managing the potential donor prior to death to protect potential donor organs
3. Location of withdrawal of treatment (based on access to theatre)
4. Declaring death
5. Mandatory stand-off time period prior to retrieval
6. Choosing the right recipient -selection

**What is NRP ?**

NRP or Normothermic regional perfusion is a novel in-vivo perfusion technique that utilizes an extracorporeal device to re-establish circulation in circulatory death donors once death is certified and the retrieval process starts. What is the aim of NRP?

Aims of NRP
<i>Create warm perfusion to abdominal organs</i>
<i>Oxygenate blood</i>
<i>Maintain normothermia</i>
<i>Re-circulate blood back to the abdominal organs</i>

## The science behind NRP

Following circulatory death, the organs undergo warm ischaemia.

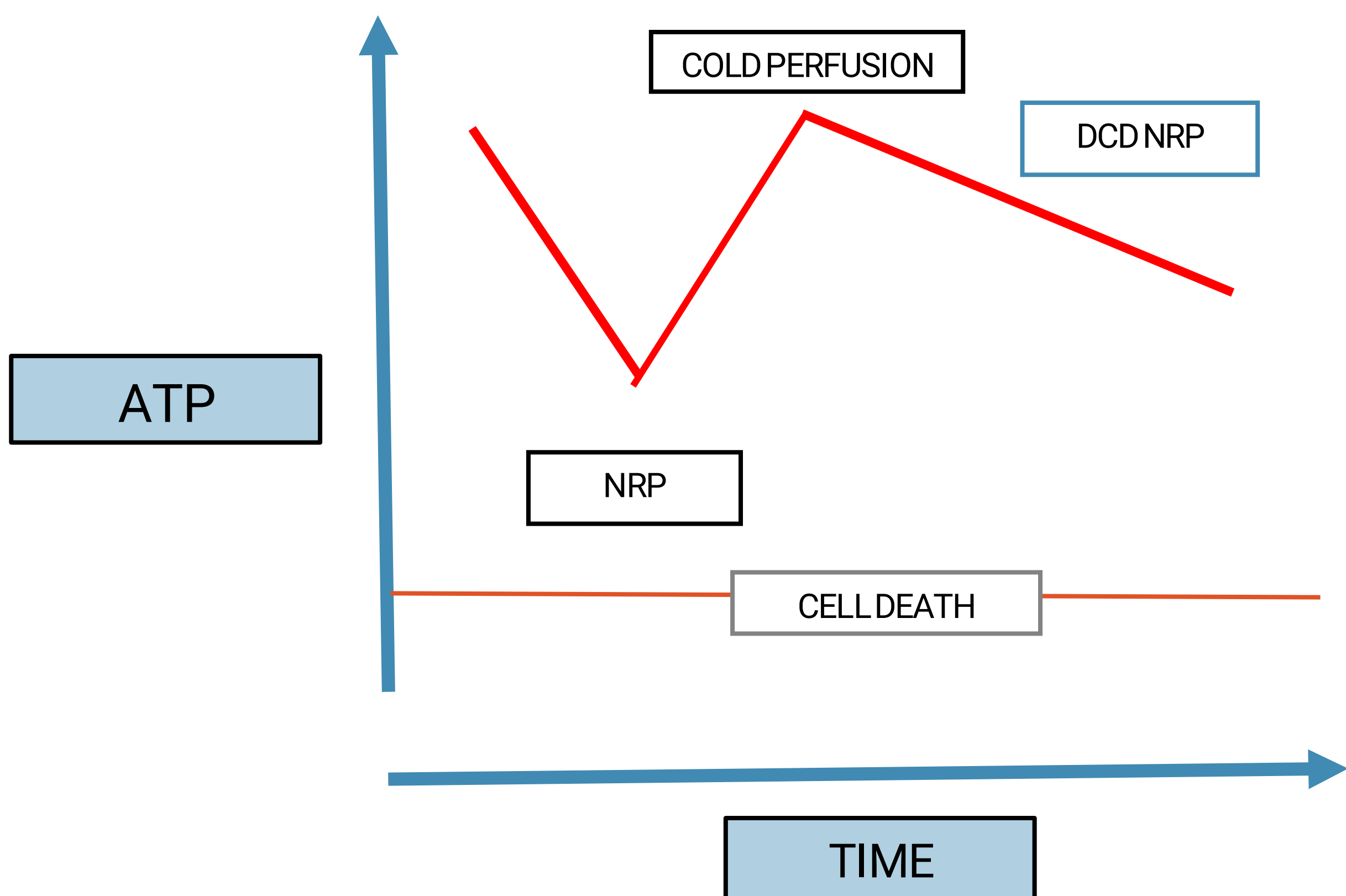
Warm ischaemia results in

Reduction of Adenine Nucleotides (ie ATP), and Nucleosides (ie Adenosine).

+ Increase of nucleotide breakdown products (ie xanthine)

Result: Increase oxygen free radicals during reperfusion

NRP ☐ Reverses this process as depicted in the ATP-Time graft below

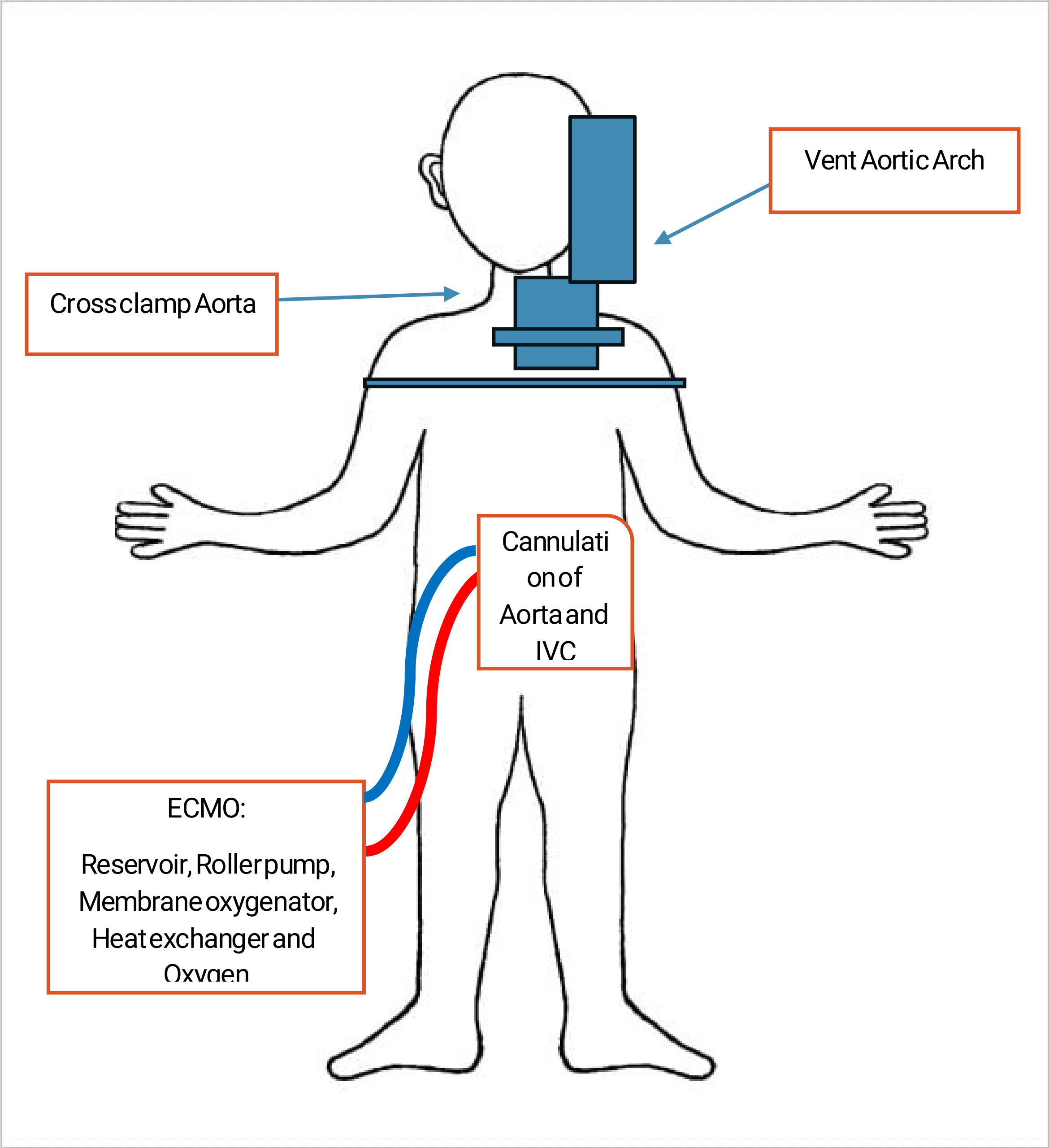




## **NRP – The team, The Procedure**

The NRP team comprises the following core members (see below). Essentially, the retrieval team includes members of a standard retrieval team plus an additional surgeon / surgical assistant along with another

member who will



- CORE TEAM**
- Surgeon
  - Scrub Nurse
  - Perfusionist
  - 2<sup>nd</sup> Nurse / Practitioner (analyzer, blood gas)
  - Organ retrieval coordinator (UPOH)
  - Donor hospital theatre staff, biochemistry lab
  - Transportation services

In addition to the standard retrieval equipment, the team will need to carry the cardiohelp (ecmo) pump, bring the aortic and vena cava cannula, ecmo circuit (sash) and if



available its own mini side lab analyzer (eg piccolo analyzer). In the early phases, the team can utilize the biochemistry laboratory services of the donor hospital. In essence, additional time will be required to set up the equipment, brief the team in the donor hospital prior to withdrawing life support.

Standard time to run the NRP would be around 2 hours during which time multiple blood test at different times during the NRP are performed. This aids in the assessment of organ perfusion and viability, allowing the team to change parameters in the pump, transfuse blood, etc. Such parameters include the SV02 levels, hematocrit, Hb level, glucose, pH, bicarbonate levels and liver function test parameters.

In the beginning, especially when starting a new programme, and establishing its cost effectiveness, it may seem logical to utilize the biochemistry lab as well as the ITU/theatre lab blood gas analyser. Decisions on organ utility are then based on these findings prior to the retrieval team going off NRP moving towards the cold phase. By this time, the implanting centres will have a good idea of accepting and matching the graft with potential recipients.

### **Team training for DCD and NRP**

At the time of writing, both DCD and NRP would be uncharted territory for the country. Team training will require commitment, dedication and potentially time spent out of core commitments. The following are some of the authors suggestions on how this can be best achieved

1. Trained surgeon establishes a team of existing retrieval surgeons and nurses (this can be the existing DBD team), in which the team “buys in” to both DCD and NRP
2. Team trains in DCD retrievals and achieve independence, competence and confidence

3. At the same time, team meetings are organized to understand the process from a theoretical point of view achieving “ familiarity” with the process
4. Team undergoes machine training (with the help of the trained surgeon and the cardiohelp representative)
5. Team practices in dry runs /simulations
6. Organize overseas “ visits” or training as and when required
7. Establish mentorship with overseas centres to discuss outcomes and share experience

### **Challenges to establish a DCD and NRP programme**

Following are some of the important aspects for implementation along with suggestions how to overcome this when developing both a DCD and NRP programme

***Identifying the need*** – With already low DBD donors, an established DCD programme should increase number of donors, transplants and reduce waitlist mortality. NRP would serve to complement this as well as provide further evidence as to the best choice of graft. The initial step could be to pilot this in major hospitals in the Klang Valley. This would allow the team to audit its outcome, assess feasibility and circumvent logistical issues. This would also put less pressure on the team as there is less travel time, better support, and shorter CIT.

***Leadership and Team*** – There is a clear need for staff who are trained and dedicated in both DCD retrieval and NRP. The retrieval team should be thought of as a single entity (whether it is retrieving the liver, kidneys or both) and are readily available when the need arises. Hence, a dedicated

selected team (surgeons, scrub nurse, perfusionist) which maintains its training regularly would be ideal till the team feels it has the capacity to train and further expand

***Designing organ procurement model*** – A protocol for both DCD retrieval and NRP is on the way and should form the ground work to start and implement this in the near future.

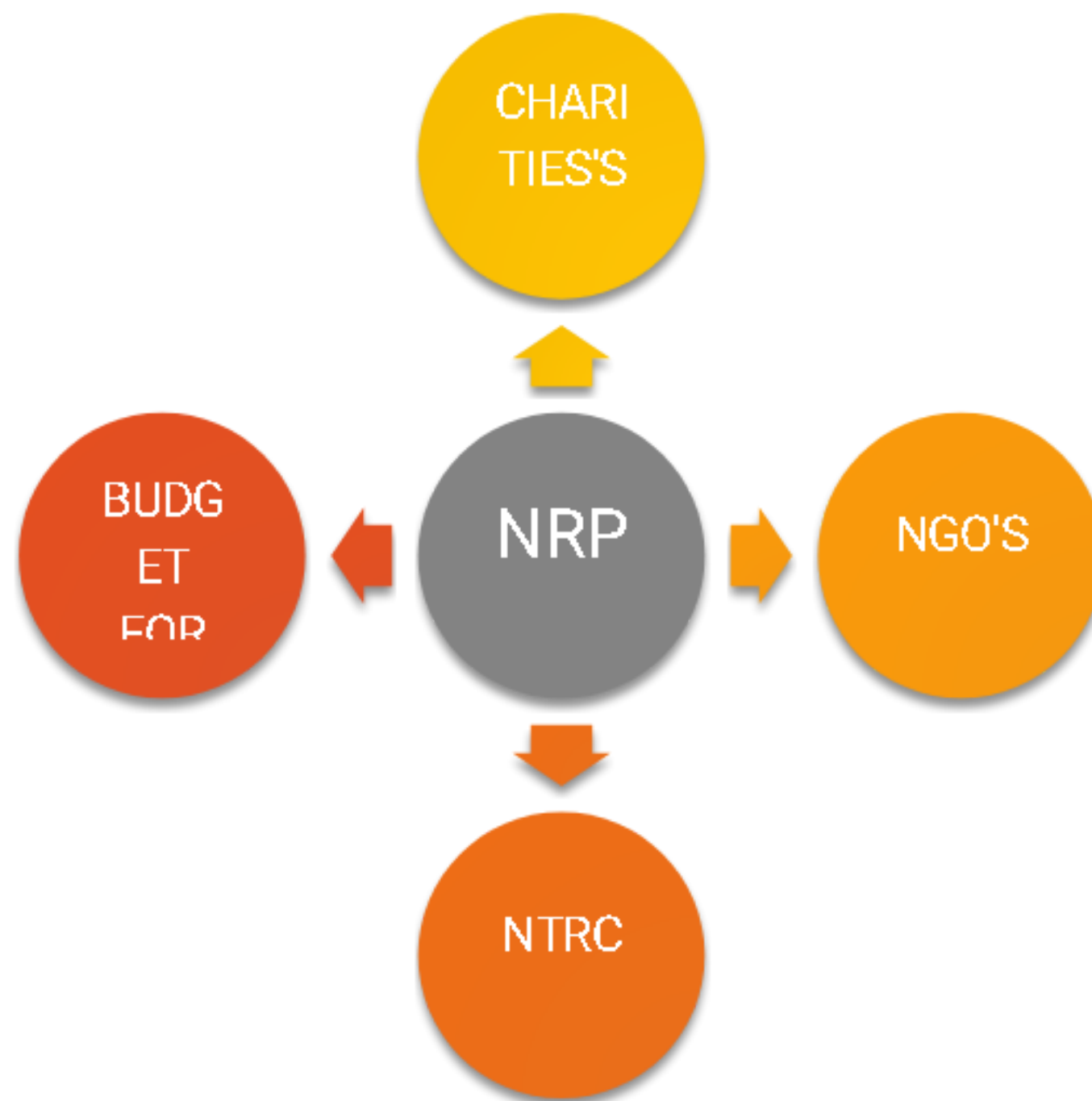
***Training and Implementation***– It is imperative that the initial phase is to familiarize with DCD retrievals and then move on to NRP. The team will then need to familiarize with the technical aspects of managing the DCD donor on the perfusion pump. This can involve dry runs / simulation followed by kidney only retrievals. At the same time, the team would still be able to analyse all the parameters as for a liver retrieval.

***Involvement of important stakeholders*** – The DCD NRP retrieval team is but one of the cogs in the multidisciplinary team dynamics. Trained ITU staff, anaesthetist, UPOH (Unit Perolehan Hospital) staff within the respected hospitals, blood bank, biochemistry laboratory staff and donor coordinators from NTRC are all equally important to ensure that NRP can be undertaken in an organized and safe fashion. As part of learning to establish that all members involved are working in unison, it is thus suggested that we should pilot this in certain hospitals.

***Establishing mentorship***- As NRP is a seemingly a new novel intervention, we can look forward to establishing mentors from abroad. For example centres in the UK that are established and are still learning from their own experiences.

***Evaluate, audit and appraise*** – Finally, like all services, we can only gain from evaluating and auditing. This should also include not only the outcomes of transplantation but a cost analysis as well.

***Support*** One of the biggest hurdles in establishing a programme which is both technical as well as time and labour intensive is cost. Below are some of the potential sources we can look to



NTRC= National Transplant Resource Centre  
NGO' s= Non-Governmental Organizations

### **Suggested blueprint for implementation**

These are some of the suggestions from the author on how this can be implemented

1. Stakeholders to agree and “ Buy-in”
2. Establish protocol and guideline (in the process)
3. Pilot a DCD programme in Klang Valley
4. Evaluate the process and decide if team is ready for NRP -consider separate rota?
5. NRP team undergoes inhouse training and dry runs (simulation) – ECMO setup and run through
6. Start DCD-NRP kidney only retrievals before full Liver Kidney retrieval-
7. Start “ slowly” with Ideal liver allografts

8. Identify suitable candidates who would benefit from DCD grafts and not to overwhelm the programme with extended DCD criteria (see ideal donor below)
9. Evaluate, assess if the programme is feasible, cost effective and proceed to a larger scale

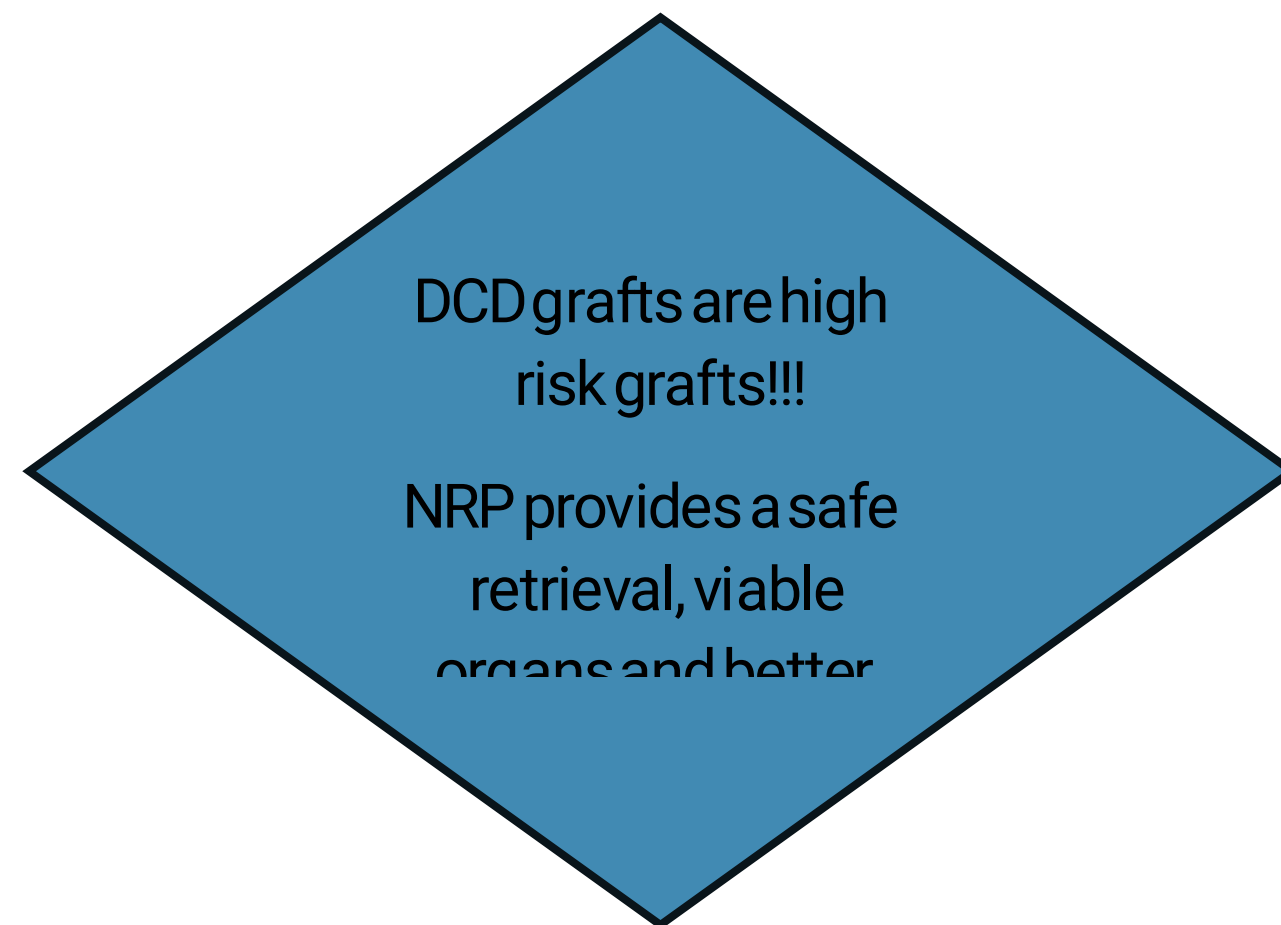
What is an ideal DONOR?
Age <60 (potentially <50 ?)
Donor BMI < 30 kg/m <sup>2</sup> (potentially < 25 ?)
ITU stay <5 days
Functional WIT <30 min (for liver), <120 min (for kidneys)
Cold ischaemia time 6-8 hours (no absolute cut off)

## Looking towards the future

The above article sheds light on both DCD and NRP retrieval. The need to establish a DCD programme in this country is long overdue to improve organ donation and transplantation. Committing to develop and sustaining a DCD-NRP transplant programme in many ways requires “reinvention” of the transplant programme. In the beginning, this may be an unknown territory to many and may draw scepticism. Nevertheless, with perseverance, believe and support, this would certainly be one way forward to establishing a new paradigm in the transplantation services in the country.

## Conclusion

Establishing a DCD and NRP programme is a challenging process but one that the country should look forward to. It is imperative that NRP should go hand in hand when performing all DCD retrievals.



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