

# Ethical Analysis of Normothermic Regional Perfusion (NRP)

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# White Papers and the OPTN Ethics Committee

- White papers are developed to analyze a complex issue
  - White papers often develop a stance on an issue or offer recommendations for future work
  - White papers do not change policy or dictate practice
- The OPTN Ethics Committee makes recommendations to Board of Directors for changing, creating, or eliminating policies if warranted by ethical concerns
  - Aims to guide the policies and practices of the OPTN related to organ donation, procurement, distribution, allocation, and transplantation so they are consistent with ethical principles
  - Does not develop policy or modify data collection

# Uniqueness of NRP as an approach to organ procurement

- Involves the restoration of circulation regionally in the donor body, before the organs are removed, and after circulatory death is declared
  - Standard donation after circulatory death (DCD) does not entail blood circulation within the body after death is declared owing to cessation of circulation
- Methods such as ligation of vessels are used to prevent circulation from reaching the brain
  - This is done to prevent cerebral blood flow
  - Thoraco-abdominal NRP (TA-NRP) also involves recirculation through the heart
- These unique elements of NRP raise questions whether the Dead Donor Rule is violated

# Need for Ethical Review

- NRP has become more prevalent, underscoring the importance of an ethical analysis
  - Reliance on local ethics committees while bringing questions to national organizations
  - Variation in NRP practices and disclosure
  - Lack of ethical consensus regarding use of NRP as a perfusion technique reflected in spectrum of willingness of programs and OPOs to participate
- Request to conduct an analysis given this context of increased adoption and ethical questions

# Deliberative Process

- We used a stakeholder engaged approach:
  - Diverse stakeholders engaged, transparent process, and agreeing to terms on the outset
- Workgroup reflected varying perspectives on NRP and included transplant surgeons, ethicists, lawyers, OPOs executives, coordinators, and a donor family member
- In 15 meetings over 9 months, Workgroup received presentations from diverse stakeholders and contributed to a literature library of 60+ relevant publications
  - Presentations included those from European and American practitioners of NRP, organizations opposed to NRP, intensivists and neurologists

# Uniform Declaration of Death Act (UDDA)

- The UDDA states that:
  - “An individual who has sustained either (1) irreversible cessation of circulatory and respiratory functions, or (2) irreversible cessation of all functions of the entire brain, including the brain stem, is dead. A determination of death must be made in accordance with accepted medical standards.”
- UDDA is not federal law, provides guidance and acts as a model for enacting state laws
  - 37 states have adopted the UDDA
- Analysis considers the UDDA as it is currently written
  - Uniform Law Commission is discussing potential revisions to the UDDA

# Purpose of White Paper

- Examine the ethical implications of NRP according to the ethical principles of
  - Nonmaleficence (do no harm)
  - Respect for persons (autonomy)
  - Utility
- Principles are established in the OPTN white paper *“Ethical Principles in the Allocation of Human Organs”*
  - Abiding by these ethical principles supports trust in the organ donation and transplantation system
  - Seeks to balance the ethical principles to which the Committee is bound

# Nonmaleficence and the Dead Donor Rule

- Nonmaleficence (do no harm) requires compliance with the Dead Donor Rule
- Dead Donor Rule states:
  - Donors must be dead at the time of organ procurement (i.e., meet criteria for brain or circulatory death) and
  - Organ donation must not cause death
- Definition used in this analysis is consistent with the OPTN Ethics Committee formulation of the Dead Donor Rule described in “*Ethical Considerations of Imminent Death Donation*”



# Implications of Nonmaleficence for NRP

- Unclear whether NRP violates the Dead Donor Rule
  - Circulation is restored after circulatory death has been declared, raising meaningful questions about whether the person continues to meet criteria required for determination of death
- More research is needed to confirm there is no blood flow to the brain or brainstem during NRP
  - Specifically, more robust evidence should address potential collateral flow through the spinal cord
  - Potential for harm if inadvertent cerebral blood flow occurs

# Implications of Respect for Persons for NRP

- Respect for persons requires transparency and informed decision-making
- May promote respect for persons by honoring first-person authorization for donation as a way of maximizing the gift
- Need to uphold informed decision-making for donor families, given that perspectives on NRP vary more than for other more established forms of organ transplant
- Informed decision-making indicates that the unique elements of NRP should be disclosed:
  - Circulation will be restored regionally (abdominal or A-NRP) and this may include the heart (TA-NRP), at a time the donor has not been assessed for brain death criteria
  - Potential for any cerebral perfusion for TA- and A-NRP

# Uncontrolled Scenarios

- Circulatory death occurs unexpectedly, not after withdrawal of lifesaving treatment (WLST)
  - The transition from living patient to organ donor is rapid and potentially confusing
  - Compressed timing and difficulty of informed decision-making raises concerns about nonmaleficence and respect for persons
- Concern regarding nonmaleficence and respect for persons do not justify performing uncontrolled scenarios for NRP

# Implications of Utility for NRP

- Great potential for increasing number and quality of solid organs procured from DCD donors
  - There may be an increase in average number of organs transplanted per donor with NRP and decreased rate of allograft failure post-transplant
- More data are needed to compare NRP to other machine perfusion techniques, which don't have same concerns with the Dead Donor Rule and may have similar utility gains.
- The Committee considers that utility and equity must be balanced
  - Justification for any one principle is necessary, but not sufficient, for arriving at a conclusion about NRP

# Conclusions

- Proceed, but cautiously, regarding the practice of NRP for organ procurement
- Ethical concerns requiring consideration and resolution include:
  - Assurance that NRP adheres to the Dead Donor Rule.
  - Nonmaleficence must not be violated in the pursuit of NRP, even if positive utility outcomes could result.
  - Standardized and transparent protocols, including adequate informed decision making with patients (pre-mortem) and of families approached about donation, are necessary pre-conditions for any ethical pursuit of NRP.
  - The Committee agreed that the uncontrolled scenarios for any form of NRP should not be performed at this time because of added concern regarding nonmaleficence and respect for persons.

# What do you think?

- What information should be disclosed to potential donors and next of kin regarding NRP, and how should one approach disclosure?
- Are there any ethical arguments or additional evidence that haven't been presented that should be taken into account in the analysis?