

## POINT: Does Normothermic Regional Perfusion Violate the Ethical Principles Underlying Organ Procurement? Yes

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Normothermic regional perfusion (NRP) uses extracorporeal technologies (such as cardiopulmonary bypass and extracorporeal membrane oxygenation) to preserve organs for transplantation, particularly hearts.<sup>1,2</sup> Notably, this is done by restarting circulation of the donor's own warm blood after irreversible circulatory death was declared. NRP is performed in a few countries and prohibited in others (eg, Australia). Sometimes called thoraco-abdominal NRP in controlled donation after circulatory determination of death (cDCD), NRP is used in much of the literature and therefore, used here.

Increasingly, ethical and legal concerns are being raised about NRP.<sup>3-8</sup> Use of the technology gets ahead of ethics and US law. In considering NRP, one must keep in mind

**ABBREVIATIONS:** ACP = American College of Physicians; cDCD = controlled donation after circulatory determination of death; DCD = donation after circulatory determination of death; DDR = dead donor rule; LST = life-sustaining therapies; NRP = normothermic regional perfusion; NRP-cDCD = normothermic regional perfusion with controlled donation after circulatory determination of death; UDDA = Uniform Determination of Death Act

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that a declaration of death does not mean an individual is dead if the declaration is invalidated by subsequent action. This is an issue only in the last of the following procurement circumstances:

- In cadaveric donation (eg, corneas, which may be procured hours after death), status of the donor is not ambiguous.
- In donation after brain death, cardiopulmonary support is continued to maintain solid organ viability because brain death is irreversible.
- In standard donation after circulatory death, life-sustaining therapies are withdrawn and not restarted; organs are procured once circulation has ceased irreversibly.
- In NRP, a patient is declared dead because circulation has ceased irreversibly, but then, in the interest of solid organ viability, circulation is restarted, which is a manifest contradiction.

Moreover, along with reinitiating donor circulation, NRP protocols call for the deliberate interruption of blood flow to the brain. NRP is thus distinct from other types of procurement and is distinctly ethically problematic.

### NRP Violates Ethical Principles Underlying Organ Procurement and the Dead Donor Rule and Alters the Criteria for Determining Death

The dead donor rule, a fundamental norm that governs organ procurement, states that organ procurement cannot cause death and that a patient's death cannot be caused in organ procurement.<sup>9</sup> Based in ethical principles of respect and nonmaleficence, it remains foundational to maintaining trust in voluntary organ donation. It assures patients and families of medicine's commitment to not harm patients and to not use one patient merely to serve the needs or goals of another.

NRP is used in cDCD when a patient does not meet criteria for brain death and is receiving cardiorespiratory support. Life-sustaining therapies are withdrawn consistent with patient and/or family wishes, resulting in the cessation of cardiorespiratory functions. But because the intention from the outset is to restart circulation, and recognizing the possibility of brain viability, active steps to prevent recirculation to



the brain (eg, ligation or balloon occlusion of the carotid arteries) are taken. **This violates the US definition of death.**



The Uniform Determination of Death Act (UDDA) **defines death** as the irreversible cessation of circulatory and respiratory functions or of all brain functions, including the brainstem. Restarting circulation reverses what was just declared to be the irreversible cessation of circulatory and respiratory function. It is no defense to suggest the patient was already dead when the action negates the conditions upon which that determination was made. Although there has been debate about whether permanence is a better description than irreversible, resuscitation was intentional, and circulation is restored; the loss of circulation was neither irreversible nor permanent.



### **NRP Proponents Respond to This Critique by Redefining Death: A Change Not Within Their Purview**

UDDA drafters defined the standard for determining death as either the irreversible cessation of circulatory and respiratory function or the irreversible cessation of the functions of the entire brain after apparently rejecting the idea of death defined only as the death of the brain, declared in either of these two ways.<sup>7</sup> Some proponents who support NRP, however, appear to adopt this rejected definition of death;<sup>2</sup> for example, defining death as the “cessation of circulation to the brain.”<sup>10</sup> Others seem to suggest circulatory/respiratory death is death only because it leads, eventually, to brain death.

However, linking the two types of death determination contravenes the intent of the UDDA. Moreover, given the timeline of NRP and organ procurement, whole brain death criteria could not have been evaluated or met. The transplantation community, limited expert panels, nor others have the authority or the requisite objectivity to change the **definition** of death, even for a noble cause.



### **Furthermore, Taking Active and Intentional Steps That Do Not Benefit and Actually Harm the Donor Violates the Fundamental Physician Ethical Obligation of Nonmaleficence**

Sometimes construed as a technical problem to be overcome in NRP,<sup>11</sup> the prevention of brain recirculation is anything but a technicality. Such actions

reflect recognition that brain death has not occurred. Restarting circulation while preventing blood flow to the brain cannot be justified by saying the actions are not intended to resuscitate or benefit the donor.<sup>12</sup> Intended or not, the actions do in fact resuscitate the patient. Similar concerns that were voiced years ago regarding NRP-like techniques<sup>7,8</sup> remain unaddressed.

### **Pro-NRP Language Is Often Misleading and Confusing**

Some say the disruption of brain circulation is to “maintain” brain death.<sup>4</sup> This makes no sense; if brain death had occurred, active steps would not be necessary; if it had not, those active steps caused it. Likewise, some say cutting off circulation to the brain ensures “natural” progression to brain death,<sup>12</sup> but this is not natural. Equally troubling is the argument that, if the patient were unintentionally resuscitated or experienced autoresuscitation, it would not result in “meaningful” recovery. This is not about death, but a value judgment about quality of life. Using this or similar language would be very confusing to family members approached for consent; however, it is unclear whether any meaningful attempt at all is made to explain NRP.

More importantly, even if completely and understandably explained to both the recipient and the donor’s family, consent alone cannot justify NRP nor override medicine’s obligations to help and not do harm. Also, respecting a person’s wish to be a donor does not itself justify NRP. It is possible to fulfill the laudable wish to donate under usual cDCD procedures.

### **Alternatives to NRP Exist**

Some proponents say NRP saves money, but it is an empiric question whether organs so procured result in lower overall costs. Moreover, avoiding cost is not a justification for pursuing an ethically problematic course of action. Use of ex vivo devices instead of in situ NRP shows promise. And after all, any cost is relative to the \$1.7 million dollar cost of a heart transplantation operation. More fundamentally, “Reperfusion devices can be applied after organs are procured via cDCD without restarting the donor’s circulation or intentionally occluding brain perfusion to render an individual brain dead. There is a large and ethically significant difference between perfusing an organ versus perfusing an individual.”<sup>6</sup>

## Conclusion

The burden of proof in this debate is with proponents of NRP. They have not met this burden. Their use of obfuscating language is unhelpful, as is their misapplication of both ethical principles and the law.

A declaration of death is voided when the grounds for that declaration are negated by subsequent action. In interrupting circulation to the brain, nature is not taking its course, but rather medicine is intervening to ensure death. We recognize the dire need to increase the supply of organs for transplantation and alleviate the suffering of those on wait lists. However, medicine's efforts, which include maintaining patient and public trust in voluntary donation, are better directed to increasing organ availability without violating ethical norms and US law.

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