Analyze That: Ongoing Policy Efforts for Deceased Donor Intervention

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ASTS WINTER SYMPOSIUM
MIAMI BEACH, FL
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NO CONFLICTS TO DISCLOSE

NO DISCUSSION OF OFF-LABEL USE OF ANY MEDICATIONS
The Problem

• Demographics of the U.S. population project
  – Increased demand for transplantable organs
  – Decreased quality and low to modest increase of organs suitable for transplantation
• Brain death is physiologic, cellular, and molecular catastrophe that compromises organ viability and function
• The injury sustained in the donor is compounded by cold storage followed by ischemia / reperfusion injury in the recipient
• Organs procured from older, less healthy (diabetes, hypertension, obese) donors are especially vulnerable.
Conceptualizing Research to Improve Organ Quality

Brain death

Donor

Mitigate injury
Repair injury

Organ

Mitigate injury
Repair injury

Reperfusion

Recipient

Accelerate recovery from injury

Examples of randomized trials in kidney transplantation

- Dopamine
- Hypothermia
- Machine Perfusion
- Furosemide
- IGF-1
- α-ICAM-1
- Erythropoietin
- Pentoxyfilline
- YSPSL (rPSGL-Ig)
- Thymoglobulin
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Examples of randomized trials in kidney transplantation
Research in Deceased Donors: A Paradigm Shift

Donor

Heart
Liver
Bowel
Kidney
Bowel
Lung

Non-human subjects

Human subjects
• Waitlist candidates
• Transplant recipients

Intervention

Impact

Research subjects

Bystander patients

KEEP CALM
this requires a PARADIGM SHIFT
Ethical and oversight constructs

Deceased Donors
- Voluntariness and Transparency
- Dignity
- Maximizing the Gift

Authorization ??

Living Human Subjects
- Autonomy
- Beneficience
- Justice

Informed Consent
IRBs

Public Trust

Courtesy of A. Glazier
Authorization / Consent Issues, by Stage

**Intervention**
- Authorization for research
  - Scientific merit
  - Risk assessment
  - Ethical treatment of the donor

**Transplant**
- Informed consent to accept organ
  - Is this a consent for clinical care or for research?
  - Is the transplant itself research?

**Outcomes**
- Informed consent to participate in research
  - Data submission
  - Specimen collection
  - Other study procedures
Stakeholders

THE PUBLIC

JCAHO
CMS

Waitlisted Candidates

NIH
FDA

Donors
Donor Families
Donor Hospitals
OPOs

UNOS/
OPTN
CMS

Organ Recipients
Targeted / Bystander

Transplant Physicians and Centers

Prof Societies

UNOS/OPTN
CMS

HRSA
OHRP

THE PUBLIC

THE PUBLIC
Donor Intervention and Organ Preservation: Where Is the Science and What Are the Obstacles?

S. Feng

The organ shortage is widely acknowledged as the most critical factor hindering the full realization of success for solid organ transplantation. Innovation in the areas of donor management and organ preservation offers the most realistic hope to improve both the quality and size of the current organ supply. Although the basic science dissecting the complex processes of brain death and ischemia/reperfusion injury is replete with exciting discoveries, the clinical science investigating donor management and organ preservation is sparse in contrast. This review will survey the current landscape of trials to mitigate organ injury through interventions administered to donors in vivo or organs ex vivo. Consideration will then be given to the scientific, logistical and ethical obstacles that impede the transformation of laboratory breakthroughs into innovative treatments that simultaneously improve organ quality and supply.
Step 2: Find Reinforcements

HAPPINESS IS
...a partner
in crime.

ASTS
American Society of Transplant Surgeons
Engage Scientific Studies Committee
Form group to write paper with Ethics & Standards/Quality Committees

Share and Revise Working Document AST, AOPO, SCCM, ASBH

Discussions with Key Stakeholders

1st F2F Meeting
ATC 2011
ASTS, AOPO, ODRC

2nd F2F Meeting: ATC 2012
ASTS, AST, AOPO, SCCM, ODRC, and HRSA ODTA

ACOT 8/12
More Recent Timeline

HRSA / ODTA EFFORTS

DMRCC Meeting
Crystal City, VA
9/13

DIRREP Meeting
Crystal City, VA
11/14

DIRREP Meeting
Philadelphia, PA
5/15

SF/PA: Engaging the IOM

4/14 6/14
Initial Contact

Favorable Reception by Health Science Policy Board

9/14
DRAFT Statement of Task

3/15
Funding secured: Laura and John Arnold Foundation

IOM 7/15
Why the IOM?

• IOM reports are respected by the public and healthcare professionals as independent, objective, and evidence-based.
  ▪ Critically important, especially if issues involve ethics and controversy
• Prior IOM reports have had a proven transformative impact on organ transplantation.
  ▪ 1997: Non-Heart-Beating Organ Transplantation: Medical and Ethical Issues in Procurement
  ▪ 2000: Non-Heart-Beating Organ Transplantation: Practice and Protocols
  ▪ 2006: Organ Donation: Opportunities for Action
Upcoming Meetings for this Activity

Conference Call for the Committee on Issues in Organ Donor Intervention Research
January 31, 2017 (1:30 PM Eastern)
OPEN MEETING
AGENDA | REGISTER

Conference Call for the Committee on Issues in Organ Donor Intervention Research
February 13, 2017 (2:00 PM Eastern)
OPEN MEETING
AGENDA | REGISTER

Previous Meetings for this Activity

Committee on Issues in Organ Donor Intervention Research: Public Workshop
December 14, 2016 (8:30 AM Eastern)
VIEW AGENDA

First Meeting of the Committee on Issues in Organ Donor Intervention Research
September 29, 2016 (11:30 AM Eastern)
VIEW AGENDA
Summary

- Population demographics impose severe limits on both the quantity and quality of suitable organs for transplantation.
- Research is the **ONLY** approach that can mitigate the injury that results from brain death and reperfusion.
  - Improve the function organs that are utilized
  - Recruit additional organs for transplantation
- Heretofore, ethical, regulatory, and logistical challenges have stymied innovative research deceased donors.
- Substantial efforts to resolve these quandaries by partnering with multiple stakeholders and engaging the IOM may yield the necessary guidance to advance discovery.
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- ACOT
- AST
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- HRSA
- NIAID/NIDDK/NHLBI

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