Is there Life After Death?
Using Lungs from Non-Heart-Beating Donors for Transplant

Thomas M. Egan, MD, MSc
Brent Myers, MD MPH

Division of Cardiothoracic Surgery
Department of Surgery

The University of North Carolina at Chapel Hill
HEAVEN IS REAL
A DOCTOR'S EXPERIENCE OF THE AFTERLIFE
Non-Heart Beating Donors for Lung Transplant

supply ≠ demand

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Non-Heart Beating Donors for Lung Transplant

Who is an Organ Donor?

- brain-dead individuals on ventilator
  - intubated before brain death
- living donors
  - usually related, not always
  - kidney, liver, bilateral lung lobes
- donation after cardiac death (DCD)
  - kidney, liver, a few lungs
## How many U.S. transplants?

<table>
<thead>
<tr>
<th>Organ</th>
<th>#/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>16,000 (6,000 living)</td>
</tr>
<tr>
<td>Liver</td>
<td>6,000 (300 living)</td>
</tr>
<tr>
<td>Heart</td>
<td>2,200</td>
</tr>
<tr>
<td>Lung</td>
<td>1,400</td>
</tr>
<tr>
<td>Corneas</td>
<td>50,000</td>
</tr>
</tbody>
</table>
Non-Heart Beating Donors for Lung Transplant

What is a Non-Heart-Beating Donor (NHBD)?

- someone who dies because circulation has stopped
- sometimes organs can be retrieved from NHBDs
- limitation for most organs is ischemic time
- the lung is different

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Rationale

- the lung parenchyma does not rely on blood flow for cellular respiration
- few metabolic functions means low energy requirements
- huge blood reserve after arrest
Hypothesis

*If* lung cells remain viable after circulatory arrest, then the lung may be suitable for transplant, *even if retrieved at substantial intervals after circulatory arrest and death.*
A Strategy to Increase the Donor Pool: Use of Cadaver Lungs for Transplantation

Thomas M. Egan, MD, C. Jake Lambert, Karl S. Ulicny, Jr, MD, Blair A. Keagy, Division of Cardiothoracic Surgery, University of North Carolina at Chapel Hill

A shortage of suitable donors is a serious obstacle to widespread application of isolated lung transplantation for end-stage lung disease. We hypothesized that tissue typing may be a feasible method for the identification of blood-typed lungs. Studies were conducted in a nonhuman model of canine lung allotransplantation. Donor animals were sacrificed, and subsequent lung harvest was performed as described. The lungs were then stored for 1 hour, 2 hours, or 4 hours. Pulmonary reperfusion was performed in a standard fashion, using flush solution. The lungs were then reperfused with blood and tested for graft function. Recipient animals were maintained anesthetized and followed up for 8 hours. By occlusion of the pulmonary arteries, arterial oxygen tension in the oxygen-ventilated, nitrogen-ventilated, and control groups was maintained at 81 mm Hg (n = 4), 88 mm Hg (n = 3), and 55 mm Hg (n = 2), respectively. Postmortem oxygen ventilation improved early recipient survival and gas exchange. Postmortem nitrogen ventilation improved early gas exchange and delayed recipient death compared with non-ventilated controls. The mechanics of ventilation appear to confer a functional advantage independent of a continued supply of oxygen. Transplantation of lungs harvested from cadavers after cessation of circulation might be feasible.

Cadaver Lung Donors: Effect of Preharvest Ventilation on Graft Function

Karl S. Ulicny, Jr, MD, Thomas M. Egan, MD, C. Jake Lambert, Jr, MD, Robert L. Reddick, MD, and Benson R. Wilcox, MD

Departments of Surgery and Pathology, The University of North Carolina School of Medicine, Chapel Hill, North Carolina

The pulmonary donor pool would increase substantially if lungs could be safely transplanted after cessation of circulation. To determine whether ventilation of cadaveric lungs could improve graft function, canine donors were sacrificed and then ventilated with 100% oxygen (n = 6) or 100% nitrogen (n = 6); 6 served as nonventilated controls. Four hours after death, the lungs were flushed with modified Euro-Collins solution and harvested. Controls were ventilated with 100% oxygen only during flush and harvest. Recipient animals were maintained anesthetized and followed up for 8 hours. By occlusion of the pulmonary arteries, arterial oxygen tensions were maintained at 81 mm Hg (n = 4), 88 mm Hg (n = 3), and 55 mm Hg (n = 2), respectively. Postmortem oxygen ventilation improved early recipient survival and gas exchange. Postmortem nitrogen ventilation improved early gas exchange and delayed recipient death compared with non-ventilated controls. The mechanics of ventilation appear to confer a functional advantage independent of a continued supply of oxygen. Transplantation of lungs harvested from cadavers after cessation of circulation might be feasible.
**Non-Heart Beating Donors for Lung Transplant**

*Ex-vivo human lung perfusion circuit*

- Perfusate is de-oxygenated by ventilating membrane with CO2 / N2
- Lungs slowly rewarmed to 37°C
- Flow slowly increased to 40% donor cardiac output
- PA pressure < 20 mm Hg ventilated with TV = 7cc/kg donor weight

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Ex-vivo evaluation of human lungs

- gas exchange
- bronchoscopy
- CT scan
What will this lung be like in three days?

- HRSA awarded a grant to CDS and UNC to investigate the NHBD donor pool
- *Ex-vivo* Evaluation of Human Lungs from Non-Heart Beating Donors for Transplant
Non-Heart Beating Donors for Lung Transplant

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Where are the challenges?

• Emergency Medical Services (EMS)
• County Medical Examiners (ME)
• Organ Procurement Organizations (OPO)
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How many recipients are there?

- Total COPD deaths = 13,000
- Total CF deaths = 400/year
- Total IPF deaths = 40,000/year
- Total deaths related to pulmonary hypertension = 15,000/year
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Could NHBD lungs be better?

cytokine soup

TGF-β, TNF-α, INF-γ, PDGF, IL-2, FDGF, β-FGF, IL-8, VEGF

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Where are we now?

• UNC awarded ARRA grant to perfect ex-vivo lung perfusion and plan a multi-center study of lung tx from NHBDs
  • we will use unsuitable lungs from conventional donors and DCDs

• the grant funds a study to learn about EMS attitudes about organ donation
  • develop a web-based teaching tool for EMS personnel that can be used nationally

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What Was the Plan?

• All cardiac arrests that were terminated in the field and:
  • Not suspicious (by law enforcement)
  • Between 18 and 65 years of age
  • Drivers License with affirmed donation status
What Was the Plan?

• Then, APP or DC:
  • Obtain family member phone numbers
  • Call Carolina Donor Services (CDS)

• CDS:
  • Calls family to obtain consent and history
  • Communicates with surgeon to accept or deny
What Was the Plan?

- If accepted, then:
  - Second EMS unit dispatched to move the patient
  - Crew will ventilate patient en route
  - Crew may remain for harvest
- Estimated 2 patients to be screened per week
Trainwreckology...
The study of impending failure and the “I told you so”'s that follow.
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Went for 3 Months

• 4 patients screened

• 2 accepted and had viable lungs
  • Size problems prohibited transplant
    (single hospital IRB)
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if you feel like a guinea pig…

you are… and we thank you!

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Next Steps

• Memo to law enforcement completed

• NIH funding application is scored

• We await funding to restart the project
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