“Lung in a Box”
Ex vivo Lung Perfusion (EVLP)
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Lung Transplant Facts

- As of February 8, 2013, 1658 patients waiting for lung transplant in 70 Lung transplant programs in the U.S
- California has the highest number on waitlist
- >50% wait more than 6 months on the list
- 12% to 15% die waiting for suitable organs

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Increasing waiting list has not been matched with donation rate

- Only 15-20% offered lungs accepted; 80% rejected due to:
  - poor quality
  - prolonged ischemia time

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No Disclosures
Supply : Demand

Optimizing Supply : Demand Ratio

- Recipient selection criteria
  - Age
  - Diagnosis
  - Single vs double lung transplant

LUNG TRANSPLANTATION
Kaplan-Meier Survival by Age Group (Transplants: January 1990 – June 2009)

Survival (%)
0% 20% 40% 60% 80% 100%

Year of Transplant

LUNG TRANSPLANTS:
Transplant Recipient Age by Year of Transplant
Transplants: January 1, 1987 – June 30, 2010

Survival (%)
0% 20% 40% 60% 80% 100%

Year of Transplant
2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010

HALF-LIFE
18-34: 6.4 Years; 35-49: 6.7 Years; 50-59: 5.3 Years; 60-65: 4.4 Years; >65: 3.5 Years

Median Age
Median recipient age (years)
% of transplants

LUNG TRANSPLANTATION
Kaplan-Meier Survival By Diagnosis (Transplants: January 1990 – June 2009)

Survival comparisons
All comparisons with Alpha-1 and CF are statistically significant at < 0.001

COPD vs. IPF: p < 0.0001

J Heart Lung Transplant. 2011 Oct; 30 (10): 1071

ADULT LUNG TRANSPLANTATION
Kaplan-Meier Survival (Transplants: January 1994 - June 2009)

Double Lungs: 1/2-life = 6.0 Years
Single Lungs: 1/2-life = 4.9 Years
All Lungs: 1/2-life = 5.5 Years

P < 0.0001

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Single vs Double Lung Transplant

Survival (%)

Years

Bilateral/Double Lung (N=16,628)
Single Lung (N=2,951)
All Lungs (N=19,579)

Optimizing Supply : Demand Ratio

• Recipient selection criteria:
  - Age
  - Diagnosis
  - Single vs double lung transplant

• Donor selection criteria:
  - Age
  - Single vs double lung transplant
Optimizing Supply: Demand Ratio

- Recipient selection criteria:
  - Age
  - Diagnosis
  - Single vs double lung transplant

- Donor selection criteria:
  - Age
  - Single vs double
  - Rehabilitation/reconditioning

Standard Lung Procurement
“Lungs in a Box”

- Bronchoscopy
- Antibiotic treatment
- Constant Monitoring
  - Dynamic compliance
  - Peak Inspiratory pressure
  - Pulmonary vascular resistance
  - P/F ratio

Ex Vivo Reconditioning Donor Lungs

*First Human Transplantation of a Nonacceptable Donor Lung After Reconditioning Ex Vivo*

Goal: This study describes the ex vivo method of reconditioning and transplantation of rejected donor lungs.

Methods: A 47-year-old man who was brain dead due to cardiac arrest underwent a stepwise reconditioning protocol. After maintaining normothermia, perfusion with cold Ringer’s lactate solution was performed to reduce the metabolic activity of the lung. The lungs were then reperfused with a warm oxygenated solution to activate the bronchodilators. The pulmonary vascular resistance was then measured, and if necessary, additional reconditioning was performed. Finally, the lungs were retransplanted into the recipient.

Results: The recipient’s native lung was retransplanted, and the donor lung was successfully transplanted. The patient recovered uneventfully with no complications.

Conclusion: Reconditioning of donor lungs can improve graft viability and survival in lung transplantation.

Normothermic Ex-vivo Perfusion in Lung Transplant

High Risk Donors:

- **Inclusion Criteria:**
  - PaO2/FiO2 < 300 mm Hg
  - Bilateral infiltrates w/o infection
  - Poor lung deflation or inflation intraoperatively
  - Blood transfusions exceeding 10 Units
  - Donation after cardiac death

- **Exclusion Criteria:**
  - Established pneumonia
  - Mechanical lung injury
  - Gross gastric aspiration

<table>
<thead>
<tr>
<th>Percentage of Deaths</th>
<th>0-30 Days (N=2,204)</th>
<th>31 Days – 1 Year (N=3,781)</th>
<th>&gt;1 Year – 3 Years (N=3,425)</th>
<th>&gt;3 Years – 5 Years (N=1,962)</th>
<th>&gt;5 Years – 10 Years (N=2,336)</th>
<th>&gt;10 Years (N=487)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graft Failure</td>
<td>40</td>
<td>45</td>
<td>37</td>
<td>35</td>
<td>30</td>
<td>30</td>
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<tr>
<td>Cardiovascular</td>
<td>30</td>
<td>34</td>
<td>31</td>
<td>32</td>
<td>35</td>
<td>25</td>
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<tr>
<td>Malignancy (non-Lymph/PTLD)</td>
<td>20</td>
<td>25</td>
<td>23</td>
<td>25</td>
<td>27</td>
<td>27</td>
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<tr>
<td>Infection (non-CMV)</td>
<td>5</td>
<td>5</td>
<td>7</td>
<td>7</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Bronchiolitis</td>
<td>0</td>
<td>0</td>
<td>0</td>
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</tbody>
</table>

CONCLUSIONS
Transplantation of high-risk donor lungs that were physiologically stable during 4 hours of ex vivo perfusion led to results similar to those obtained with conventionally selected lungs. (Funded by Vitrolife; ClinicalTrials.gov number, NCT01195099)

OCS INSPIRE Trial
International Randomized Trial

**Goals:** To compare the safety and effectiveness of the OCS Lung compared to cold storage for donor lung preservation

**Design:** A prospective, international, multi-center, randomized controlled trial comparing preservation of donor lungs using OCS-Lung perfusion device (Treatment Group) to cold flush and storage (Control Group)

**Size:** Up to 20 participating sites with up to 264 randomized male and female subjects who are primary lung transplant recipients.
OCS™ Lung Technology

The ONLY Portable, Integrated and Automated Perfusion & Ventilation System

INSPIRE Endpoints

Primary: A composite of patient and graft survival at day 30 post transplantation, and absence of ISHLT Primary Graft Dysfunction (PGD) Grade 3 at 72 hours post-transplantation.

Secondary:
- Incidence of ISHLT PGD Grade 3 at 72 hours post-transplantation
- Incidence of ISHLT PGD Grade 2 or 3 at 72 hours post-transplantation
- Patient survival at day 30
- Graft survival at day 30

INSPIRE Trial Centers To-Date

EU Sites
- Hannover
- Berlin
- Madrid
- Padua
- Leuven
- Strasbourg
- Bichat
- Harefield
- Leuven

US Sites
- Cleveland Clinic
- UCLA
- UPMC
- The Methodist
- UCSF

Australia
- Sydney

Canada
- Edmonton

Early Clinical Experience

- OCS Lung was released in the European market in Jan 2011
- Between February-July 2011, 13 double lung transplant procedures on the OCS™-Lung device
- Non-randomized and were consecutive case series at Hannover Medical School, Hannover, Germany and Puerta de Hierro Majadahonda Hospital, Madrid, Spain
The INSPIRE International Lung Trial
With The Organ Care System Technology (OCS™)

Early outcome

<table>
<thead>
<tr>
<th></th>
<th>OCS (N=9)</th>
<th>SOC (N=10)</th>
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<tbody>
<tr>
<td>ICU time (hours)</td>
<td></td>
<td></td>
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<tr>
<td>Mean +/- SD</td>
<td>170 +/- 350</td>
<td>97 +/- 91</td>
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<tr>
<td>Median</td>
<td>60</td>
<td>65</td>
</tr>
<tr>
<td>Range</td>
<td>15 - 1035</td>
<td>16 - 276</td>
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<tr>
<td>Mechanical ventilation time (hours)</td>
<td></td>
<td></td>
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<tr>
<td>Mean +/- SD</td>
<td>14.4 +/- 5.5</td>
<td>15.5 +/- 5.6</td>
</tr>
<tr>
<td>Median</td>
<td>14.5</td>
<td>15.0</td>
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<tr>
<td>Range</td>
<td>5 - 22</td>
<td>9 - 27</td>
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<tr>
<td>Survival at 30 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient [n(%)]</td>
<td>6 (100)</td>
<td>7 (100)</td>
</tr>
<tr>
<td>Graft [n(%)]</td>
<td>6 (100)</td>
<td>7 (100)</td>
</tr>
<tr>
<td>Primary Graft Dysfunction (PGD) Grade 3</td>
<td></td>
<td></td>
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<tr>
<td>T 0 [n(%)]</td>
<td>0 (0)</td>
<td>2 (20)</td>
</tr>
<tr>
<td>T 24 [n(%)]</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>T 48 [n(%)]</td>
<td>0 (0)</td>
<td>1 (11)</td>
</tr>
<tr>
<td>T 72 [n(%)]</td>
<td>0 (0)</td>
<td>1 (11)</td>
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"Lung in a Box" might be the ANSWER!
Improved Survival
Increased Supply

Thank You!