Optimal Intraoperative support  
(Pump vs No Pump, CPB vs ECMO)

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The presenter has nothing to disclose.
### Published Incidence Rates of PGD grade 3

<table>
<thead>
<tr>
<th>Institution</th>
<th>Year</th>
<th># pts</th>
<th>T0</th>
<th>T12</th>
<th>T24</th>
<th>T48</th>
<th>T72</th>
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<tr>
<td>University of Minnesota</td>
<td>2006</td>
<td>402</td>
<td>25%</td>
<td>21%</td>
<td>17%</td>
<td>15%</td>
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<tr>
<td>Washington University</td>
<td>2010</td>
<td>1000</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>(any PGD grade)</td>
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<tr>
<td>Multi-institutional North America</td>
<td>2013</td>
<td>1255</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>31%</td>
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<tr>
<td>Sao Paolo</td>
<td>2012</td>
<td>118</td>
<td></td>
<td></td>
<td></td>
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<td>20%</td>
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<tr>
<td>Total</td>
<td></td>
<td></td>
<td>~30%</td>
<td></td>
<td></td>
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<td>15-20%</td>
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Snell et al.

*J Heart Lung Transplant. 2017 Oct;36(10):1097-1103*
Q1: What is the best method for intraoperative support?

CPB VS ECMO
Vienna Experience:

ECMO for intraop support during LUTX since 2002

Institutional experience with extracorporeal membrane oxygenation in lung transplantation

Clemens Aigner, Wilfried Wisser, Shahrokh Taghavi, György Lang, Peter Jaksch, Damian Czyzewski, Walter Klepetko


Overview of ECMO and CPB use

<table>
<thead>
<tr>
<th></th>
<th>Bridge to TX</th>
<th>Intraoperative</th>
<th>Prolonged</th>
<th>Postoperative</th>
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<tbody>
<tr>
<td>ECMO</td>
<td>2</td>
<td>130</td>
<td>51</td>
<td>5</td>
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<tr>
<td>CPB+ECMO</td>
<td>27</td>
<td>0</td>
<td>11</td>
<td></td>
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<tr>
<td>No support</td>
<td>149</td>
<td>0</td>
<td>6</td>
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**ECMO instead of CPB for intra-operative support during LuTX**

<table>
<thead>
<tr>
<th>Center</th>
<th>Year</th>
<th>Publication</th>
</tr>
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</table>
CPB: higher need for Intraop RBCs (p=0.01), Platelets (p<.01), Postop HD (p<.01), Postop ECMO support (p<.01)

In-hosp mortality (p=.004)

Multivariate analysis:
CPB support (OR=4.9; 95% CI=1.2-20; p=.026)


Lung transplantation on cardiopulmonary support: Venoarterial extracorporeal membrane oxygenation outperformed cardiopulmonary bypass

Fabio Ius, MD, Christian Kuehn, MD, Igor Tudorache, MD, Wibke Sommer, MD, Murat Avsar, MD, Dietmar Boetig, MD, Thomas Faehner, MD, Jens Gottlieb, MD, Marius Hoepfer, MD, Axel Haverich, MD, and Gregor Warnecke, MD

CPB n = 37 vs ECMO n = 44  2008 to 2011

survival CPB vs ECMO

p=0.004
CPB: longer mechanical ventilation, ICU stay, hosp stay


Outcomes of intraoperative extracorporeal membrane oxygenation versus cardiopulmonary bypass for lung transplantation

Tiago N. Machuca, MD, Stephane Collaud, MD, MSc, Olaf Mercier, MD, PhD, Maureen Cheung, MD, Valerie Cunningham, CCF, S. Joseph Kim, MD, PhD, Sassan Azad, CRA, Lianne Singer, MD, MSc, Kazuhiro Yasufuku, MD, PhD, Marc de Perrot, MD, MSc; Andrew Pierre, MD, MSc; Karen McRae, MD; Thomas K. Waddell, MD, PhD, Shaf Keshavjee, MD, MSc, and Marcelo Cypel, MD, MSc

**ECMO vs CPB**  2007 to 2013

- mechanical ventilation requirement 3 vs 7.5 d,  \( p = .005 \)
- length of ICU stay 5 vs 9.5 d,  \( p = .026 \)
- length of hospital stay 19 vs 27 d,  \( p = .029 \)

\[ P = 0.29 \]
CPB: more blood products, postOP bleeding, ReOP, PGD


Comparison of extracorporeal membrane oxygenation versus cardiopulmonary bypass for lung transplantation

Mauer Biscotti, MD, Jonathan Yang, MD, MPH, Joshua Sonett, MD, FACS, and Matthew Bacchetta, MD, MBA, MA, FACS

**CPB vs ECMO**

**January 2008 - July 2013**

<table>
<thead>
<tr>
<th>Intraop</th>
<th>Cell saver V p=.043</th>
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<tr>
<td></td>
<td>FFP p=.014</td>
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<tr>
<td></td>
<td>Plt p=.001</td>
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<table>
<thead>
<tr>
<th>Postop</th>
<th>Plt p=.013</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Bleeding p=.006</td>
</tr>
<tr>
<td></td>
<td>Reop p=.009</td>
</tr>
<tr>
<td></td>
<td>PGD at 24 hrs p=.008</td>
</tr>
<tr>
<td></td>
<td>PGD at 72 hrs p=.034</td>
</tr>
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</table>

P=0.21
CPB: more reintub, tracheostomy, dialysis

July 2007 - April 2013

- Reintub p=0.04
- Tracheostomy p=0.05
- Dialysis p=0.028
- Need for Postop ECMO (p=0.83) and for periop RBC (p=0.64)
- No diff in 30-d or 6-m mortality

Outcomes of Intraoperative Venoarterial Extracorporeal Membrane Oxygenation Versus Cardiopulmonary Bypass During Lung Transplantation
Christian A. Bermudez, MD, Akira Shinose, MD, Stephen A. Esper, MD, Norihisa Shigemura, MD, PhD, Jonathan D'Cunha, MD, PhD, Jay K. Bhama, MD, Thomas J. Richards, PhD, Peter Arila, CP, Maria M. Crzapo, MD, and Joseph M. Pilewski, MD
CPB: More postOP ECMO, ICU-stay, intub., blood products

The Munich Lung Transplant Group:
Intraoperative Extracorporeal Circulation in Lung Transplantation
Dominik J. Hoechtle1, Vera von Dossow2, Hauke Winter3, Hans-Helge Müller4, Bruno Meiser4, Claus Neuhold5, Juergen Behr5, Sabina Guenther6, Christian Hagl6, René Schramm6

2011–2013
49 patients with intraoperative support of 188 total
22 CPB vs 27 ECMO

- ECMO prolongation (p=0.082)
- Ventilator support (p=0.013)
- ICU stay (p=0.03)
- No difference in 30-day and 1-year mortality
The alternative strategy for cardiopulmonary support during the recipient’s portion of LDLLT is to provide ECMO via the femoral artery and vein. ECMO allows less heparin use, which seems to reduce perioperative bleeding. This strategy is especially useful when extensive pleural adhesions are found. The activated clotting time is maintained at around 200 seconds. We have used ECMO instead of CPB in most LDLLT procedures since 2012.

STRATEGIES FOR DEALING WITH SIZE MISMATCH IN LDLLT

Oversized graft

For small children, an adult lower lobe might be too big. Use all the adult lungs you can
Conclusion

From existing literature: ECMO clearly outperforms CPB as intraoperative support during lung transplantation!
Q2: Pump vs No Pump

Should double lung transplantation

routinely

be performed with extracorporeal support?
Support: YES/NO?

- 47 y old male
- COPD,
- sPAP 43
- no other significant comorbidity

- Bilateral sequential LUTX
- Access via two separate thoracotomies
Support: YES/NO?

- 39 y old female
- IPF,
- sPAP 76
- Small chest

- High risk for: intraop instability and development of reperfusion edema
Arguments in favor of intraoperative support

- Provides complete cardiorespiratory stability
- Allows easier "mechanical" handling of heart during implantation
- Protects first lung from reperfusion injury

"controlled reperfusion" is the key to improved graft function
First lung syndrome

Parenchymal reperfusion damage

Full CO into the first implanted lung
First lung syndrome

POD 1  POD 2  POD 6  POD 18  POD 30
Rationale for the use of intra-Op v/a ECMO

> Protective ventilation

*Respiration with lower tidal volumes is lung-protective*

> Controlled reperfusion

*Controlled reperfusion protects lung grafts...*
(Bhabra et al., Ann Thorac Surg 1998)
Low-pressure reperfusion prevents edema.

Reperfusion pressure critical to subsequent graft integrity.

10 minutes of controlled reperfusion improves graft function – 5 minutes insufficient.
Controlled reperfusion prevents severe lung injury and edema formation. Excellent results with controlled reperfusion. Ischemia-reperfusion injury attenuated with 5 minutes of controlled reperfusion. 30 minutes superior to 15 or 5 minutes.
Controlled reperfusion decreases severity of reperfusion injury.

**Conclusion:** Controlled reperfusion in human lung transplantation may impact favorably on outcomes and warrant further study.
Length of Controlled Reperfusion

- 5 min
- 10 min
- 30 min

During entire implantation procedure
Indications for use of intraoperative ECMO

- Marginal donor lungs
- Intraop haemodynamic or respiratory instability
- According to underlying indication

Indication: preTX bridging pronounced instability (PPH)
Better venous drainage
No additional incision in groin
Excellent central saturation

Anticoagulation:
Low dose heparin 50-70 IU/kg
Flow level adjusted to maintain **pulsatile** PA flow in first lung

- Monitoring with PAP and EtCO2
Intraoperative ECMO and the possibility of postoperative prolongation improve survival in bilateral lung transplantation
Retrospective analysis of 582 BLTX

Retrospective single-center study

582 standard lung transplantation Jan 2010- Jun 2016

Exclusion criteria: single-lung, heart/lung, retransplantations, bridging to LTx

- **group I**: transplantation w/o ECMO
  - n=116

- **group II**: intraOp ECMO
  - n=343

- **group III**: intraOp ECMO + prolongation
  - n=123
Patient demographics

<table>
<thead>
<tr>
<th>Diagnosis (n; %)</th>
<th>no ECMO (group I)</th>
<th>intraOp ECMO (group II)</th>
<th>prolonged postOp ECMO (group III)</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>COPD</td>
<td>66 (56%)</td>
<td>110 (32%)</td>
<td>17 (14%)</td>
<td>&lt;0.001</td>
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<tr>
<td>Fibrosis</td>
<td>20 (17%)</td>
<td>97 (28%)</td>
<td>32 (26%)</td>
<td></td>
</tr>
<tr>
<td>Cystic Fibrosis</td>
<td>13 (11%)</td>
<td>89 (26%)</td>
<td>15 (12%)</td>
<td></td>
</tr>
<tr>
<td>PPH</td>
<td>0 (0%)</td>
<td>6 (2%)</td>
<td>41 (33%)</td>
<td></td>
</tr>
<tr>
<td>AAD</td>
<td>6 (5%)</td>
<td>19 (6%)</td>
<td>2 (2%)</td>
<td></td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>1 (1%)</td>
<td>7 (2%)</td>
<td>4 (3%)</td>
<td></td>
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<tr>
<td>LAM</td>
<td>1 (1%)</td>
<td>8 (2%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>9 (8%)</td>
<td>7 (2%)</td>
<td>12 (10%)</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Type of transplant</th>
<th>no ECMO (group I)</th>
<th>intraOp ECMO (group II)</th>
<th>prolonged postOp ECMO (group III)</th>
<th>p-value</th>
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<tbody>
<tr>
<td>whole lungs</td>
<td>45%</td>
<td>46%</td>
<td>37%</td>
<td>0.006</td>
</tr>
<tr>
<td>Size reduction (n; %)</td>
<td>45%</td>
<td>40%</td>
<td>37%</td>
<td></td>
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<tr>
<td>Lobar Tx (n; %)</td>
<td>10%</td>
<td>14%</td>
<td>26%</td>
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</table>
Propensity score matching: 98 vs 98 pts

Matched cohorts: primary diagnosis/indication for transplant, listing priority, age, transplant type (no reduction, size-reduced, lobar transplantation)

PGD at 72h

Overall survival

Multivariate analysis: HR 0.56 (0.34-0.93), p=0.023
Prospective Analysis of PGD in 90 consecutive standard BLTX on intraop ECMO

Unpublished data, to be presented at ISHLT 2018

Excluded: SLTx, ReTx, Pediatric Tx, Multiorgan Tx, Bridging

No more prolonged ECMO at 72 hrs
Prospective Analysis of PGD in 90 consecutive standard BLTX on intraop ECMO

![Bar chart showing patients extubated at different time points]

- **0 hrs**: 50 patients
- **24 hrs**: 15 patients
- **48 hrs**: 10 patients
- **72 hrs**: 10 patients

72% extubated at t72
Prospective Analysis of PGD in 90 consecutive standard BLTX on intraop ECMO

- Median length of mechanical ventilation: 33 hours
- Median ICU stay: 6 days
- Median Total length of stay: 22 days
- In-hospital mortality: 0.00 %
The vicious circle of PGD .... how to interrupt it

- Non Optimal Donor Lung
- Ischemic Injury
- Reperfusion Damage
- Need for Aggressive Vent + Catecholamines
- Need for Unplanned ECMO
- Additional Damage
- Intraop ECMO
- Postop Prolonged ECMO
- EVLP
Vienna LuTx Team

Department of Thoracic Surgery, MUW

Programdirector
K Hoetzenecker

Surgeons
S Taghavi
G Lang
J Matilla
B Moser

Pulmonologists
P Jaksch
G Muraközy
C Lambers

eetc. etc. etc….