

Initial successful clinical transplantation using Negative Pressure Ventilation Ex-Situ Lung Perfusion with extended criteria donor lungs.

**Max T Buchko^{1,2}, Nasim Boroumand¹⁻², Jeffrey C Cheng¹⁻², Kieran Halloran^{3,5},
Alim Hirji^{3,5}, Darren H Freed¹⁻⁴, and Jayan Nagendran¹⁻⁴.**

¹Division of Cardiac Surgery, Department of Surgery, University of Alberta, Edmonton, AB, Canada

²Mazankowski Alberta Heart Institute, Edmonton, AB, Canada

³Alberta Transplant Institute, Edmonton, AB, Canada

⁴Canadian National Transplant Research Program, Edmonton, AB, Canada

⁵Division of Pulmonary Medicine, Department of Medicine, University of Alberta, Edmonton, AB, Canada



UNIVERSITY OF ALBERTA
FACULTY OF MEDICINE & DENTISTRY
Department of Surgery

Disclosures

- Dr. Freed and Dr. Nagendran are cofounders of TEVOSOL Inc.



Background

- Ex-Vivo Lung Perfusion (EVLP) has been shown to successfully increase the use of Extended Criteria Donor (ECD) Lungs in transplantation
- Negative Pressure Ventilation Ex-Vivo Lung Perfusion (NPV-EVLP) has been described pre-clinically to be associated with decreased ventilator-induced lung injury compared to positive pressure ventilation EVLP
- We report the first clinical experience utilizing NPV-EVLP for the assessment, preservation, and transplantation of ECD lungs (NCT03293043)



Donor Criteria

Inclusion:

- Best P:F Ratio < 300mHg
- DCD (Maastricht III or IV)
- Blood transfusion > 10 units
- Expected cold ischemic times > 6 hours
- Donor age >55 years old

Exclusion:

- Established pneumonia
- Severe mechanical lung injury
- Documented infectious disease in donor including HIV, Hepatitis, HTLV, and Syphilis



Recipient Criteria

Inclusion:

- Patients accepted on recipient waitlist for bilateral transplantation
- Age ≥ 18 years old
- Written informed consent

Exclusion:

- Multi-organ recipient or re-transplant
- HIV, Hepatitis, or other infection excluding patient from transplant
- Hemodialysis or severe chronic renal dysfunction
- Concurrent cardiac procedure
- Preoperative mechanical circulatory support or mechanical ventilation (excluding BiPAP or CPAP)



Donor Demographics

Donor	Age (yrs)	Height (m)	Weight (kg)	Cause of death	Donor Classification	Donor P:F Ratio	Eurotransplant ECD Donor Score
1	24	1.78	174	Overdose	NDD	253	12
2	45	1.70	76	Intracranial bleed	NDD	107	8
3	60	1.62	77	Hypoxic brain injury from aspiration	DCD	498	8
4	27	1.77	81	Overdose	NDD	151	10
5	39	1.63	110	Gunshot wound to head	NDD	172	12
6	54	1.57	65	Intracranial bleed	NDD	289	9
7	49	1.59	86	Intracranial bleed	NDD	110	9
8	40	1.6	118	Intracranial Bleed	NDD	172	11
9	45	1.81	94.1	CVA	DCD	338	8
10	36	1.71	79.1	Overdose	NDD	75	11
11	50	1.75	77	Intracranial Bleed	NDD	237	12
12	45	1.70	133	Bulbar ALS - MAID	DCD	410	6

Donor Eurotransplant ECD Characteristics

Recipient	Age (yrs)	Donor History	Smoking History	Chest Radiograph	Bronchoscopy	Donor P:F Ratio (mmHg)	Eurotransplant ECD Donor Score
1	24	Compromised	Yes	Clear	Clear	253	12
2	45	Uncompromised	No	Clear	Clear	107	8
3	60	Uncompromised	No	Clear	Clear	498	8
4	27	Uncompromised	Yes	Consolidation	Clear	151	10
5	39	Compromised	Yes	Clear	Clear	172	12
6	54	Uncompromised	Yes	Clear	Clear	289	9
7	49	Uncompromised	Yes	Clear	Clear	110	9
8	48	Uncompromised	No	Clear	Clear	172	10
9	70	Uncompromised	Yes	Consolidation	Purulent	338	8
10	60	Compromised	No	Clear	Clear	75	11
11	67	Compromised	Yes	Clear	Clear	237	12
12	38	Uncompromised	No	Clear	Clear	410	6

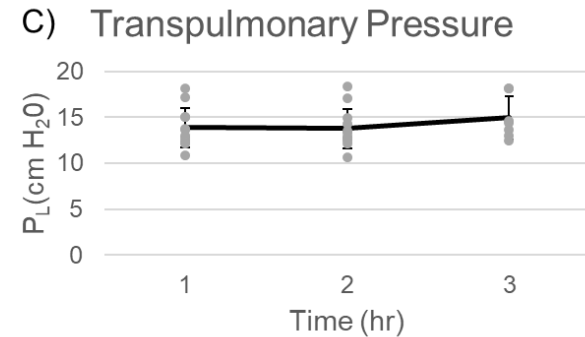
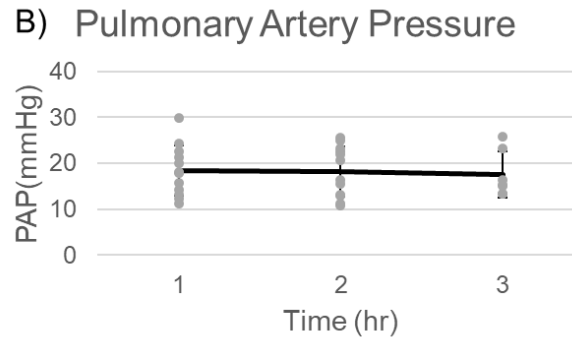
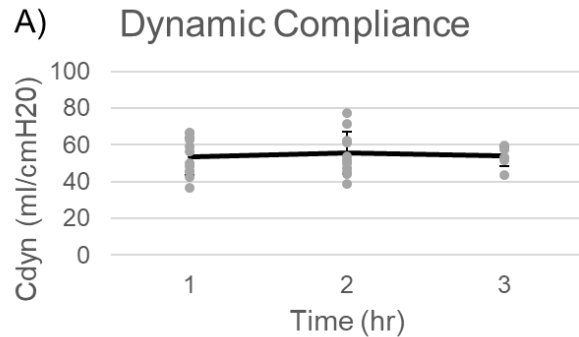
Graft ischemic and ESLP times

Donor	Cold ischemic time prior to ESLP	Warm ischemic time if DCD	Time on ESLP	Cold ischemic time following ESLP – Right Lung	Cold ischemic time following ESLP – Left Lung	Total time to implantation – Right Lung	Total time to implantation – Left Lung
1	278	N/A	174	184	87	636	539
2	252	N/A	229	65	151	546	632
3	218	23	217	163	69	621	527
4	124	N/A	185	154	73	463	382
5	193	N/A	143	180	180	516	516
6	235	N/A	143	179	91	557	469
7	84	N/A	159	122	69	365	312
8	120	N/A	135	114	43	369	298
9	268	14	179	76	185	537	646
10	238	N/A	162	207	100	607	500
11	225	N/A	201	178	81	604	507
12	251	15	261	208	84	735	611

Results

Recipient	Age (years)	Recipient Pathology	Mechanical Ventilation (hours)	ICU LOS (days)	Post-transplant ECMO	PGD Score at 24h	PGD Score at 72h
1	24	COPD	51	7	No	0	0
2	45	COPD	42	6	No	2	2
3	60	IPF	28	3	No	0	0
4	27	COPD	18	5	No	0	0
5	39	IPF	12	3	No	0	0
6	54	ILD	45	8	No	1	1
7	49	COPD	27	5	No	1	2
8	48	Talcosis	18.2	5	No	0	0
9	70	A1ATD	56.2	3	No	0	0
10	60	COPD	11.3	4	No	0	0
11	67	COPD	11.2	5	No	0	0
12	38	Cystic Fibrosis	12.9	3	No	0	0

NPV-ESLP demonstrated stable hemodynamic parameters over the course of perfusion.



- The average transpulmonary pressure within the chamber was 13.8 ± 0.6 cmH₂O amongst all lungs at T2
- This corresponds to driving pressures of 8.8 ± 0.6 cmH₂O in the setting of negative pressure ventilation

Results

- All grafts and patients recovered to discharge from hospital and are alive at 1 year post-op
- No patients with PGD 3 at 72 hours post-op
- Average pre-procurement donor P:F ratio:
 - Total cohort: 234 ± 38 mmHg
 - NDD: 174 ± 24 mmHg
- Average final P:F ratio on NPV-EVLP: 492 ± 30 mmHg
- Average recipient P:F ratio at 72 hours post-op: 407 ± 69 mmHg
- Average duration of mechanical ventilation: 24 ± 4 hours
- Average ICU length of stay: 4.4 ± 0.5 days

Conclusions

- Negative Pressure Ventilation Ex-Situ Lung Perfusion demonstrates safe preservation, evaluation, and successful clinical transplantation of Extended Criteria Donor lungs
- Further validation of this initial cohort is ongoing, including the development of a portable device for multi-centre international clinical trials



Acknowledgements

