

# Is “lung repair centre” a possible answer to organ shortage?—transplantation of left and right lung at two different centres after ex vivo lung perfusion evaluation and repair: case report

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**Abstract:** Ex vivo lung perfusion (EVLP) has become a reality as a technique to evaluate and recondition lungs from marginal donors. We report the first case on the use of EVLP followed by separate transplantation in two different centres. The local organ procurement organization proposed the lungs of a 53-year-old non-smoker donor who died for cerebral haemorrhage. P/F ratio was 294 after lung recruitment manoeuvres. Oto score was 10. Two centres accepted the grafts for two single transplantations under the condition of EVLP evaluation. After usual retrieval, the bi-pulmonary block was transferred to Centre 1 and EVLP was run as previously described. At the end of the procedure the two lungs were evaluated separately and both judged suitable for transplantation. After cooling and storage on ice, the block was separated on the back table. The left lung was transplanted in a patient with pulmonary fibrosis at Centre 1; surgery was complicated by cardiac arrhythmias that required several defibrillations. The right lung was transferred on ice to Centre 2, 250 km away from Centre 1, and transplanted in a patient with idiopathic pulmonary fibrosis. Thirty months after transplantations Patient 1 and Patient 2 are both alive, in good clinical conditions. This is the first report of the separate use of lungs after EVLP for non-urgent recipients in two different centres. This experience opens the door to a new allocation model with great potentials on organ shortage. Actually, we demonstrated that the perspective of a ‘lung repair centre’ is feasible and effective.

**Keywords:** Lung transplantation; ex vivo lung perfusion (EVLP); organ shortage

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## Introduction

Ex vivo lung perfusion (EVLP) has become a cornerstone in clinical practice of lung transplantation centers as a platform to assess the function of questionable organs, as well as a tool to recondition lungs from marginal donors (1).

Actually, EVLP opens the door to new organizational assets in the process of donation and transplantation. It is widely debated whether to promote the development of

EVLP programs in every transplant center, or to identify specialized centers that carry out the process on behalf and in favor of other transplant teams (2). The latter possibility would offer the opportunity of creating a working platform with a dedicated team dealing with a greater number of procedures, enabling cost containment and possibly more favorable outcomes.

The Toronto group previously proved the feasibility of such an ‘EVLP Center’ concept in a case of urgent



**Figure 1** The lungs during EVLP. EVLP, ex vivo lung perfusion.

transplantation (3) and the Perfusix trial is ongoing in order to extend this approach to the daily clinical practice (4). Hereafter we report of a successful transplantation of two recipients after lung procurement, EVLP reconditioning and subsequent lung offer to a distant lung transplantation center in an elective setting, with a long favorable follow-up.

### Case presentation

In May 2014 the local organ procurement organization (Nord Italian Transplant program, NITp) proposed the lungs of a 53-year-old male donor, non-smoker, who died from cerebral hemorrhage. The chest X-ray showed hilar reinforcement and basal dysventilation. The bronchoscopic examination revealed a moderate quantity of secretions;  $\text{PaO}_2$  ratio at the time of offer was 264. After recruitment maneuvers  $\text{PaO}_2/\text{FiO}_2$  ratio was 294. The donor was ventilated with protective setting: TV 7 mL/kg, PEEP 8 mmHg. The time of intubation was 36 hours. Bronchoscopy revealed moderate, central, non-purulent secretions. At visual inspection lungs were wet and moderate bilateral basal atelectasis were present at visual inspection, reopened after recruitment maneuvers. Selective blood gases were not performed. Oto score was 10.

The transplant team of Milan decided to accept the graft for a left single transplantation, under the condition of EVLP evaluation, while the Padua transplant center agreed to accept the right lung if suitable for transplantation.

After usual procurement at the donor's hospital, the bi-pulmonary block was transferred to Milan and EVLP was run with a low-flow, open atrium and low haematocrit technique, as previously described (*Figure 1*) (5). The parameters and functional data during EVLP procedure

are shown in *Table 1*. At the end of the procedure the two lungs were evaluated separately and both judged suitable for transplantation: oxygenation assessed on perfusate output from left and right lungs was 553 and 496 mmHg, respectively, without signs of function deterioration over time, clear bronchoscopy and chest X-ray (*Figure 2*).

Throughout lung procurement and EVLP, donor's files and lung function data were shared between the two teams that both agreed about suitability for transplantation.

After cooling, the bi-pulmonary block was separated on the back-table, and the lungs were stored on ice. The left graft was transplanted in Milan to a 66-year-old male subject with pulmonary fibrosis (LAS: 35); the right lung was transferred on ice to Padua (250 km distant from Milan), and transplanted to a subject with idiopathic pulmonary fibrosis (LAS: 50). The ischemic times from cross-clamping to revascularization for left and right lung were 18 and 15 hours, respectively. Neither of the recipients suffered from primary graft dysfunction (PGD) in the first 72 hours.

The subject transplanted in Milan was extubated in the first post-operative day (POD). The subsequent course was complicated with a *Klebsiella pneumoniae* carbapenemase (KPC) respiratory infection and related multi-organ failure (MOF). After a slow recovery, he was discharged on POD 52 in good condition with a  $\text{FEV}_1$  of 55%. Six, nine and twelve-month surveillance trans-bronchial biopsy (TBB) showed a minimum degree of acute rejection, with no evidence of chronic rejection and with no neutrophilia. At one-year, the bronchoalveolar lavage was negative for KPC, but a stenosis in the main bronchus beyond the anastomosis was noted; such stenosis has been successfully treated with pneumatic dilations and a resorbable stent. Twenty-fourth months after surgery, pulmonary function tests (PFTs) showed  $\text{FEV}_1$ : 80% and FVC: 76%; the best  $\text{FEV}_1$  was 90%. The subject is alive thirty months after the transplantation without signs of chronic rejection.

The patient who was transplanted in Padua, had an uneventful post-operative period and was discharged 27 days after surgery. Also this patient is alive thirty months after the transplantation without signs of chronic rejection: his last PFTs showed  $\text{FEV}_1$ : 62% and FVC: 92%.

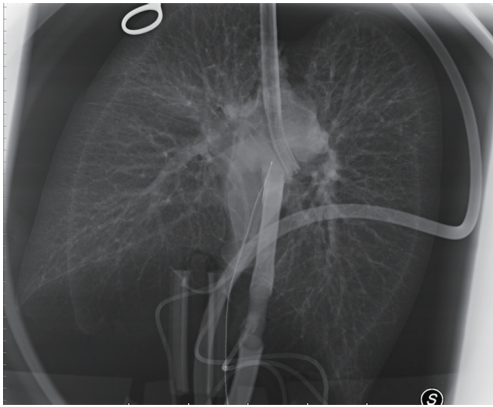
### Discussion

Wigfield previously reported a case of a marginal lung transferred from the donor's hospital to the 'organ repair center' in Toronto, and then back to the recipient's hospital

**Table 1** Parameters and functional data during EVLP procedure

Time (h:min)	FiO <sub>2</sub> (%)	TV (mL)	PEEP (cmH <sub>2</sub> O)	Peak (cmH <sub>2</sub> O)	Flow (L/min)	RPM	O <sub>2</sub> IN (mmHg)	CO <sub>2</sub> IN (mmHg)	O <sub>2</sub> OUT (mmHg)	CO <sub>2</sub> OUT (mmHg)	Glu in (mg/dL)	Glu OUT (mg/dL)	Lac IN (mmol/L)	Lac OUT (mmol/L)	pH IN	pH OUT	Cdyn (mL/cmH <sub>2</sub> O)
5:00	-	-	-	-	-	-	171	-	-	-	205	-	0.5	-	6.87	-	-
5:35	-	-	-	-	0.25	800	-	-	-	-	-	-	-	-	-	-	-
5:40	-	-	-	-	0.25	800	-	-	-	-	-	-	-	-	-	-	-
5:45	-	-	-	-	0.38	820	-	-	-	-	-	-	-	-	-	-	-
5:50	-	-	-	-	0.76	1,010	-	-	-	-	-	-	-	-	-	-	-
5:55	21	360	5	10	1.27	1,180	142	23	-	-	171	-	2.5	-	7.20	-	72.0
6:00	21	450	5	-	1.78	1,380	-	-	-	-	-	-	-	-	-	-	-
6:05	21	540	5	-	2.16	1,570	-	-	-	-	-	-	-	-	-	-	-
6:10	21	540	5	-	2.45	1,700	-	-	-	-	-	-	-	-	-	-	-
6:15	21	630	5	12	2.55	1,710	133	49	-	-	153	-	3.9	-	6.98	-	90.0
6:20	21	630	5	-	2.55	1,710	-	-	-	-	-	-	-	-	-	-	-
6:25	21	630	5	-	2.55	1,710	-	-	-	-	-	-	-	-	-	-	-
6:30	21	630	5	-	2.55	1,710	-	-	-	-	-	-	-	-	-	-	-
6:35	21	630	5	13	2.55	1,710	128	28	159	23	161	171	5.1	6.3	7.10	7.11	78.8
7:15	40	630	5	10	2.53	1,710	-	-	-	-	-	-	-	-	-	-	126.0
7:35	40	630	5	10	2.53	1,710	154	35	241	30	149	149	7.7	7.8	6.96	7.01	126.0
7:55	40	630	5	10	2.55	1,710	-	-	-	-	-	-	-	-	-	-	126.0
8:15	40	630	5	10	2.52	1,710	-	-	-	-	-	-	-	-	-	-	126.0
8:35	40	630	5	10	2.53	1,710	166	32	258	27	117	118	8.9	8.6	7.10	7.16	126.0
8:55	40	630	5	10	2.55	1,710	-	-	-	-	-	-	-	-	-	-	126.0
9:15	40	630	5	10	2.58	1,720	156	31	-	-	117	-	8.9	-	7.09	-	126.0
10:00	40	630	5	9	2.55	1,710	161	26	-	-	89	-	12.6	-	7.02	-	157.5
10:35	100	630	5	10	2.56	1,680	76	33	-	-	83	-	13.1	-	6.95	-	126.0

FiO<sub>2</sub>, fraction of inspired oxygen; TV, tidal volume; PEEP, positive end-expiratory pressure; RPM, revolutions per minute; IN, measured on inflow; OUT, measured on outflow; Glu, glucose; Lac, lactate; Cdyn, dynamic compliance.



**Figure 2** The lungs X-ray during EVLP. EVLP, ex vivo lung perfusion.

after EVLP reconditioning (3). The mentioned case was carried on in an urgent condition; on the contrary, we report a lung transplantation after assessment of the graft with EVLP and transplantation in a remote center in an elective setting.

The continuous sharing of information, timing of the procedure and functional data between the two centers have been the key of the success. Certainly, the expertise of the Padua center, which is confident with the Organ Care System (OCS) and *ex situ* lung perfusion techniques, played a role in their decision to accept an organ assessed from another center (6). However, the decision of both groups to closely collaborate for the benefit of their respective recipients was fundamental for the good outcome.

## Conclusions

In our view, this single experience opens the door to a new allocation model with great potential against organ shortage and with possible benefits on cost containment. In fact, our case is proof of the concept that a ‘lung repair center’ is feasible and effective, as shown by the long-term favorable outcome of both recipients. Such ‘hub and spoke model’, although promising, need to be fully explored before concluding on its validity.

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## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

*Ethical Statement:* The study was approved by Ethics committee of Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico Milano. Mortality risk factors in patients waiting and submitted to lung transplant. Ref. n° 181 (24/01/2017). Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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