Regional Ventilation-Perfusion Matching by Electrical Impedance Tomography After Single Lung Transplant

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Single lung transplantation (LUTX) can be the last therapeutic option for a growing cohort of patients suffering from end-stage respiratory failure. Postoperative ventilatory management of single LUTX recipients is challenged by the coexistence of the diseased native lung and a healthy—but fragile—graft. In this case report, in a single LUTX recipient with idiopathic pulmonary fibrosis, regional ventilation ($\dot{V}$), perfusion ($\dot{Q}$), and $\dot{V}/\dot{Q}$ matching and subsequent measurement of shunt fraction (Qs/Qt) and alveolar dead space (Vd/Vt) were obtained by integrating electrical impedance tomography (EIT) with volumetric capnography and pulmonary thermodilution technique. Although the preoperative pulmonary scintigraphy showed predominant right lung perfusion (79.8% *vs.* 20.2%), the EIT documented the postoperative re-establishment of $\dot{Q}$ between the lungs (demonstrating the adequate functioning of vascular anastomoses), the diversion of $\dot{V}$ to the graft and similar global Qs/Qt (17%) and Vd/Vt (29%) between native and graft lung. Electrical impedance tomography mapping allowed regional Qs/Qt and Vd/Vt assessment: the native right lung had a completely deranged distribution of $\dot{V}$ and $\dot{Q}$ (Qs/Qt 25%, Vd/Vt 46%), whereas the graft showed normal coupling of $\dot{V}$ and $\dot{Q}$ (Qs/Qt 8%, Vd/Vt 12%). Electrical impedance tomography may allow noninvasive, repeatable, bedside assessments of the lung $\dot{V}/\dot{Q}$ coupling after single LUTX. *ASAIO Journal* 2023; XX:XX–XX

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A 69 years old Caucasian man (weight: 75 kg, height: 170 cm) was enlisted for single left lung transplantation (LUTX) for end-stage respiratory failure caused by idiopathic pulmonary fibrosis (lung allocation score: 65.5225; forced expiratory volume in the first second of expiration [FEV1]: 39%, forded vital capacity [FVC]: 34%, diffusing capacity of the lungs for carbon monoxide [DLCO]: 9%) with moderate precapillary pulmonary hypertension. No other comorbidity affected the patient, except for therapy controlled arterial hypertension. Pulmonary perfusion analysis by Tc-99 marked human albumin pulmonary scintigraphy showed predominant right lung perfusion (79.8% *vs.* 20.2%) (Figure 1). The patient underwent an uncomplicated unilateral left LUTX, after 79 days on the waiting list. The donor was a woman aged 56 years, brain dead after cerebral hemorrhage, with no comorbidity. The graft showed optimal functioning, with no infiltrates, secretion, and a pre-explantation PaO_2/FiO_2 of 373 mm Hg. Surgery was carried out in lateral position, by means of single left thoracotomy. No major bleeding was observed and was transfused with just two fresh frozen plasma pools. No mechanical (*e.g.*, extracorporeal membrane oxygenation or cardiopulmonary bypass) was necessary. Standard immunosuppression by corticosteroids, aziatropin, and tacrolimus was provided.

On postoperative day 1, to assess whether the preoperative differential perfusion persisted after LUTX and evaluate the best clinical management, we assessed ventilation ($\dot{V}$) and perfusion ($\dot{Q}$) by electrical impedance tomography (EIT) (Pulmovista500; Drager, Lübeck, Germany). An EIT-dedicated belt with 16 electrodes was placed around the patient's chest at the fifth or sixth intercostal space and connected to an EIT monitor. Before belt application, surgical medications were removed, and the thorax was inspected for any sign of infection, erythema, or suppuration. Then, the skin was accurately cleansed, and the sterilized belt (chlorhexidine 2%) was applied. The surgical drainage was left unclamped. As per the manufacturer's instruction, the EIT ventilatory data were acquired at a frame rate of 50 Hz by injecting small electrical currents at adjacent electrode pairs around the patient's thorax.

Similarly, as per manufacturer instructions, perfusion data were obtained by providing a bolus of 10 ml of 5% sodium
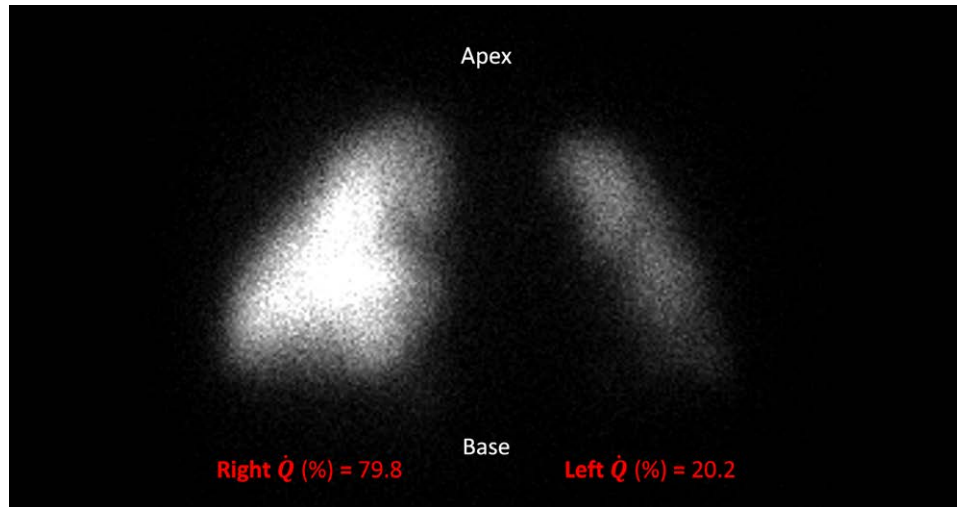
Figure 1. Preoperative lung perfusion scintigraphy. Pulmonary perfusion analysis by Tc-99 marked human albumin pulmonary scintigraphy shows predominant right lung perfusion (79.8% *vs*. 20.2%).
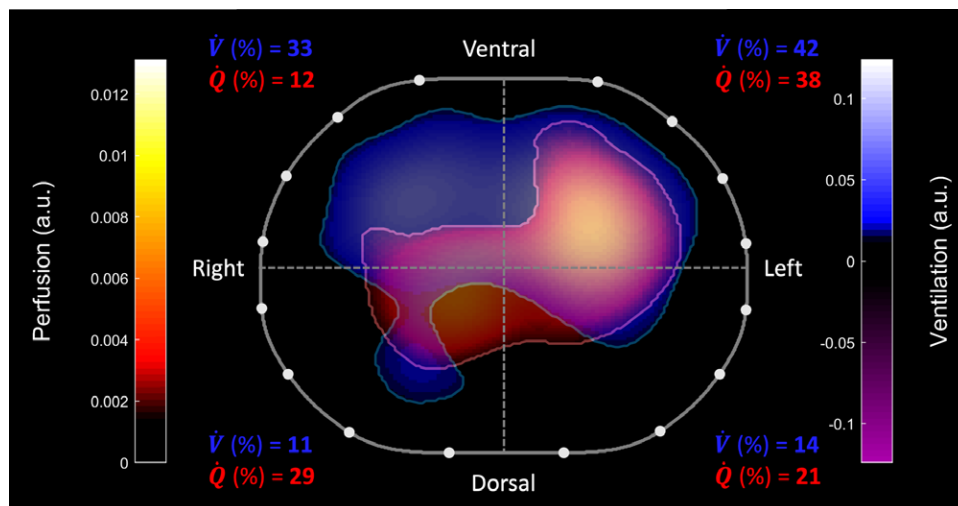

Figure 2. Postoperative day one regional ventilation ($\dot{V}$) and perfusion ($\dot{Q}$) analysis by EIT. Pulmonary $\dot{V}/\dot{Q}$ analysis by EIT was used to assess the distribution of $\dot{V}$ and $\dot{Q}$. The EIT perfusion was obtained by signal registration throughout a hypertonic saline injection during an end-inspiratory hold and analyzed offline (4). The distribution of $\dot{V}$ and $\dot{Q}$ is represented by blue-white and red-yellow gradients, respectively. Quadrant subanalysis of $\dot{V}$ and $\dot{Q}$ percentages are indicated respectively in blue and red. In addition, a representative map obtained by integrating $\dot{V}/\dot{Q}$ maps is represented. EIT, electrical impedance tomography.

chloride solution *via* the central venous catheter. The bolus of saline solution, injected in less than 2 s, passes through the pulmonary circulation producing an impedance dilution curve that follows typical first-pass kinetics. Data were collected for offline analyses. Then, we measured the shunt fraction (*Qs/Qt*) by mixed venous blood gas analysis obtained from a pulmonary artery catheter and alveolar dead space (*Vd/Vt*) by the modified Enghoff equation and pulmonary volumetric capnography. Of note, the pulmonary artery catheter was positioned preoperatively, per standard clinical practice, whereas EIT and volumetric capnography are noninvasive, radiation-free, bedside monitoring techniques frequently applied and approved for ventilatory monitoring in patients with respiratory failure.

The patient was still sedated and paralyzed from the operatory room, hemodynamically stable, and ventilated in pressure-controlled ventilation with FiO_2 of 40%, a positive end-expiratory pressure of 8 cm H_2O, a pressure control of +14 cm H_2O, and a respiratory rate of 14 bpm, leading to a tidal volume of 425 ml. With this setting, pH 7.39, partial pressure of carbon dioxide ($PaCO_2$) 50 mm Hg, partial pressure of oxygen (PaO_2) 134 mm Hg, ratio of partial pressure of oxygen and inspired fraction of oxygen (PaO_2/FiO_2) 335 mm Hg, and end-tidal CO_2 of 35 mm Hg were obtained. A global *Qs/Qt* of 12% and *Vd/Vt* of 30% were obtained, with EIT documenting similar global *Qs/Qt* (*i.e.*, 17%) and *Vd/Vt* (*i.e.*, 29%) (Figure 2).

Interpolating clinical data with EIT ventilation and perfusion mapping, we were able to evaluate regional $\dot{V}$ and $\dot{Q}$ in a 32×32 $\dot{V}/\dot{Q}$ matrix. In particular, minute ventilation of 5.95 L/min and cardiac output of 6.00 L/min (obtained by thermodilution technique) were integrated to evaluate subregional $\dot{V}$, $\dot{Q}$, and their ratio ($\dot{V}/\dot{Q}$) (Figure 3).

The EIT study was feasible (despite thoracic drainages and the impending surgical wound medications). Of note, in the
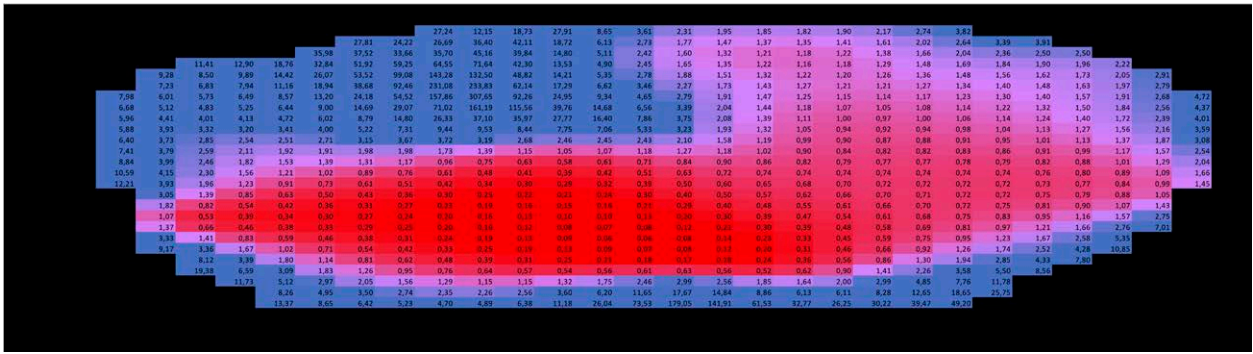
Figure 3. Ventilation ($\dot{V}$), perfusion ($\dot{Q}$), and ratio ($\dot{V}/\dot{Q}$) analysis by EIT. Pulmonary $\dot{V}/\dot{Q}$ mapping by EIT was achieved by integrating clinical data of ventilation (*i.e.*, minute ventilation) and perfusion (*i.e.*, cardiac output by thermodilution technique) in the $\dot{V}$ and $\dot{Q}$ EIT mapping. EIT, electrical impedance tomography.

context of the standard surgical incision for LUTX (*i.e.*, thoracotomy for single LUTX *versus* clamshell for double LUTX), utmost care must be taken in sterilizing the belt—chlorhexidine 2% is a feasible option, and applying the electrodes not immediately over the surgical incision, to limit the possibility of wound contamination. Moreover, no particular adaptation in data retrieval and analysis was necessary, and the EIT device provided an uncompromised output despite the surgical incision and the chest tube. Because this is just a case report of a single LUTX, we cannot extrapolate the feasibility of EIT for any LUTX case. Particularly, in double LUTX recipients or patients with consistent postsurgical pneumothorax, the EIT image quality may be impaired caused by interference with sternal metallic staples and air, respectively.

In our case, the EIT study was not associated with apparent complications. Nevertheless, two notes of caution are needed. Surgical wound infection is a dreadful complication after LUTX; any possible precaution should be taken to avoid it. In our opinion, careful cleansing of the surgical incision and sterilization by chlorhexidine of the probe belt may be a reasonable preventive measure, but further studies are necessary to confirm our approach. Moreover, pressure ulcers caused by skin compression should be avoided as well. In our case, the duration of the EIT was minimal (no more than 60 minutes). We suggest removing the belt for cases requiring long test duration as soon as data are acquired.

The EIT analysis[1] allowed the calculation of regional Qs/Qt and Vd/Vt, documenting several pathophysiological outcomes of single lung transplants. 1) The re-establishment of $\dot{Q}$ between the left and right lung, with the left—transplanted—lung being perfused by 59% of cardiac output (*versus* the 20.2% preoperatively) and a reduction in $\dot{Q}$ of the right lung (from 79.8% to 41% of cardiac output). This data demonstrate the adequate functioning of vascular anastomoses. 2) The diversion of $\dot{V}$ to the graft, which receives the 56% of total ventilation. 3) Despite a quite similar distribution of $\dot{V}$ and $\dot{Q}$ among the two lungs, the native right lung shows a completely deranged distribution of $\dot{V}$ and $\dot{Q}$, with an upper quadrant that is ventilated but scarcely perfused and a lower quadrant being perfused but not ventilated, resulting in a Qs/Qt of 25% and Vd/Vt of 46%. 4) The left transplanted lung shows a normal coupling of $\dot{V}$ and $\dot{Q}$, resulting in a Qs/Qt of 8% and Vd/Vt of 12%. Of note, in healthy individuals, ventilation and perfusion are expected to be homogenously distributed in dorsal and ventral regions,

leading to a $\dot{V}/\dot{Q}$ ratio around 1. We refer the interested readers to seminal works on the topic.[2]

From these data, we inferred that a normal function of the implanted graft was associated with the permanence of the native lung dysfunction. Thus, the patient was rapidly weaned from mechanical ventilation, extubated, and had a favorable postoperative course. Consent for the publication of this case report was obtained thereafter.

To our knowledge, this is the first report of $\dot{V}/\dot{Q}$ mapping, shunt fraction, and dead space evaluation by EIT after a single LUTX. Previous cases documented the use of EIT to assess ventilation[3,4] in single LUTX, and a unique case documented the $\dot{V}/\dot{Q}$ EIT analysis in a patient receiving a double LUTX affected by pulmonary embolism,[5] whereas a recent case report used EIT to evidence bronchial anastomotic stenosis caused by necrosis.[6]

Given the scarcity of available grafts, the increasing age of recipients, and their burden of comorbidities, a growing larger cohort of patients may benefit from single LUTX rather than double. These patients have particularly challenging ventilatory management, given the coexistence of a diseased native lung and a healthy—but fragile—graft; as in this case, whence standard protective ventilation (with positive end expiratory pressure [PEEP] 8 cm H_2O) was optimal for the graft but overdistended the native lung. The gold standard to evaluate $\dot{V}/\dot{Q}$ mismatch is $\dot{V}/\dot{Q}$ scintigraphy, whereas computed tomography (combined with pulmonary angiography) is a viable option to assess the anatomical alterations leading to $\dot{V}/\dot{Q}$ mismatch (*i.e.*, anastomotic strictures). Nevertheless, their use in the LUTX scenario is limited by their availability, invasiveness, logistical burden, and radiation exposure. The implementation of EIT and the novel approach we are proposing of coupling EIT data with thermodilution-based cardiac output measurement and volumetric capnography, might have great potential after LUTX. Indeed, such an approach allows noninvasive, repeatable, bedside assessments of the lung $\dot{V}/\dot{Q}$ coupling, leading to the possibility of 1) personalizing mechanical ventilation by selecting the PEEP level providing a more homogenous $\dot{V}/\dot{Q}$ matching, 2) guiding weaning from mechanical ventilation by documenting $\dot{V}/\dot{Q}$ changes after diaphragm activation, 3) assessing the reperfusion of graft after implantation. Notwithstanding, some limitations apply to the technique and our study as well. Electrical impedance tomography has an intrinsically limited spatial definition until further technological developments become available. Thus, while it is useful in managing

mechanical ventilation and potentially capable of screening major anastomotic complications, it cannot be used to indicate surgical revision. In those cases, pulmonary angiography should be carried out. Moreover, since nonliquid media alter the thoracic impedance, the EIT accuracy might be compromised by pneumothorax and metallic staples. Further, more populated studies, including also double LUTX recipients, are necessary to assess EIT capability in this particular scenario. Finally, the interpolation of thermodilution-based cardiac output measurement, volumetric capnography, and EIT is still in a developmental phase, and further studies are necessary to evaluate this approach and eventually introduce $\dot{V}/\dot{Q}$ coupling into clinical practice. As an example, it is to be tested the possibility of integrating cardiac output measurements from transpulmonary thermodilution or beat-by-beat contour analyses.

In conclusion, EIT assessments of lung $\dot{V}/\dot{Q}$ coupling is a promising noninvasive, bedside, repeatable test for the postoperative management of LUTX recipients, but further studies are necessary to confirm its clinical impact.

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