Modified In Vivo Lung Perfusion Allows for Prolonged Perfusion Without Acute Lung Injury

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Presenter Disclosure

Pedro Reck dos Santos

The following relationships exist related to this presentation:

- AATS Michael DeBakey Scholarship (M Cypel)
- Vitrolife (Provider of Steen solution)
Introduction

• Lung metastases are often the only site of disease in patients with cancer

• Intrathoracic recurrence of resected disease is common

• In Vivo Lung Perfusion (IVLP) allows for the localized delivery of higher doses of chemotherapy in lung tissue
Introduction

- IVLP is a promising treatment strategy to potentially increase disease-free interval and patient survival.  

- Perfusate drug concentration and the duration of perfusion are important factors in determining the final drug concentration in the lung.  

Clinical studies associating IVLP with resectable lung metastases

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Perfusion time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ratto</td>
<td>1996</td>
<td>60 minutes</td>
</tr>
<tr>
<td>Schroder</td>
<td>2002</td>
<td>20-40 minutes</td>
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<tr>
<td>Hendriks</td>
<td>2004</td>
<td>30 minutes</td>
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</table>
Introduction

- Specific perfusion and ventilatory strategies allow for 12h Ex Vivo Lung Perfusion without inducing lung injury. (Cypel et al. JHLT 2008; 27: 1319-1325).

<table>
<thead>
<tr>
<th>Ex Vivo Lung Perfusion</th>
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<tbody>
<tr>
<td>Acellular solution with an optimal colloid osmotic pressure</td>
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<tr>
<td>Protective flow to perfuse the lungs</td>
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<tr>
<td>Protective ventilatory strategy</td>
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<td>Positive left atrial pressure</td>
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<td>Pulmonary artery pressure within the normal range</td>
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<td>Normothermia</td>
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Objectives

• To demonstrate the feasibility and safety of 4h modified IVLP

• To demonstrate that the perfusion technique does not induce acute lung injury.
Material and Methods

Six Pigs → Four Hours of Left Lung IVLP → Single Pass Wash out → Four Hours of Reperfusion

**Ventilatory Parameters**
- Tidal Volume 8 ml/kg
- PEEP 5 cm H2O
- Respiratory Rate 16 / min
- FIO₂ 50%

**Perfusion Parameters**
- Flow Rate: 40% of calculated
  - Cardiac Output
- LA pressure 3-5 mmHg
- PA pressure 10-15 mmHg
- Normothermia 37°C
Material and Methods

Priming

1.2 liters of Steen solution
5000 UI of Heparin
500 mg of Solumedrol
1g of Cefazolin
End Points

• Gas exchange, Airway dynamics, and Pulmonary Vascular Resistance hourly

• Histology: Acute Lung Injury Score (range 0-12)  
  Pre IVLP, Post IVLP and Reperfusion

• Radiologic assessment of the perfused lung
Results

**PO2 / FiO2**

- Baseline: 400 mmHg
- 1h: 420 mmHg
- 2h: 410 mmHg
- 3h: 400 mmHg
- 4h: 390 mmHg

**PawpLL**

- Baseline: 20 cmH2O
- 1h: 21 cmH2O
- 2h: 22 cmH2O
- 3h: 21 cmH2O
- 4h: 20 cmH2O

**Pulm Vasc Resistance**

- Baseline: 2500 dynes/sec/cm
- 1h: 2400 dynes/sec/cm
- 2h: 2300 dynes/sec/cm
- 3h: 2200 dynes/sec/cm
- 4h: 2100 dynes/sec/cm

**Compl Dyn L L**

- Baseline: 15 cmH2O
- 1h: 16 cmH2O
- 2h: 17 cmH2O
- 3h: 16 cmH2O
- 4h: 15 cmH2O
Results - Histology

Pre IVLP

Reperfusion

After IVLP

Histological analysis  p=0.0784

Injury Score
Results – X Ray

Pre IVLP

Post 4 h IVLP + 4 h Reperfusion
Conclusions

- Four hours of IVLP is feasible.

- The modified technique does not induce acute lung injury.

- Prolonged and protective perfusion protocol may provide safer and more effective localized treatment to pulmonary metastases.
Thank you

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