

REMOVAL OF NEUTROPHIL EXTRACELLULAR TRAPS DURING EX VIVO LUNG PERFUSION SHOWS IMPROVEMENT OF LUNG FUNCTION IN A PORCINE LUNG INJURY MODEL

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Conflict of Interest

I have nothing to declare.

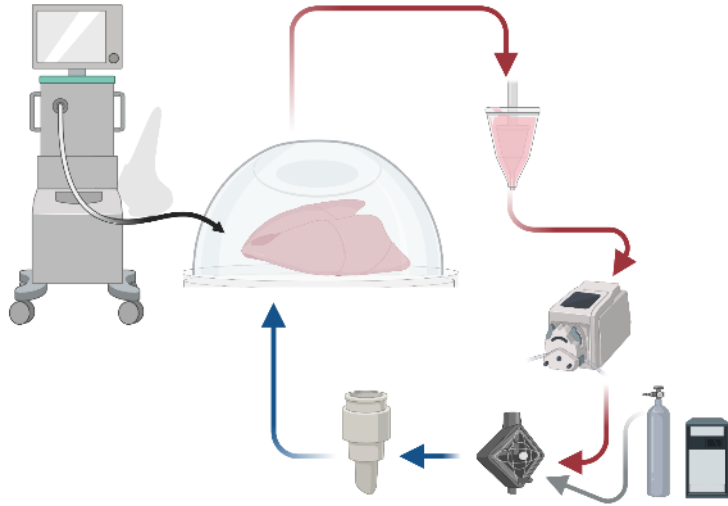
Andrew Aswani, Dmitry D. Genkin, Kirill Surkov who are co-authors on the paper are shareholders in *SanterSus AG*. The rest of the co-authors have nothing to declare.

Lung transplantation (LTx) outcome is lagging behind other solid organ transplants

- Low 5- year survival rate after lung transplantation (LTx)
- Low utilization rate of donor lungs due to eg.:
 - Donor age, infection, size mismatch, gastric aspiration

Options to increase the donor pool are urgently needed

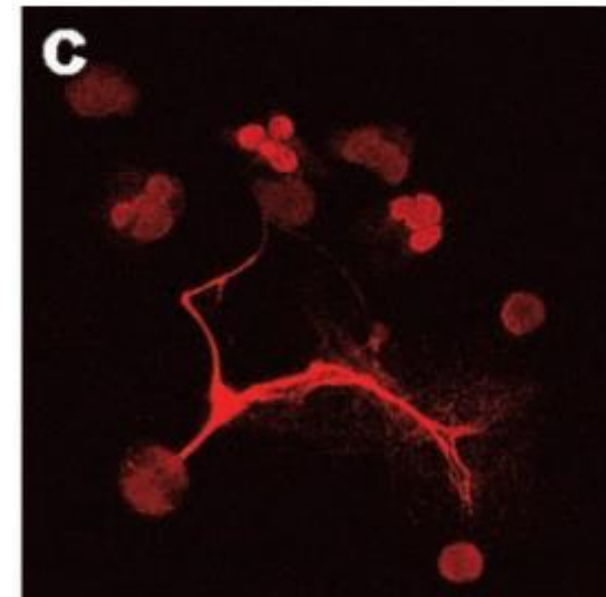
Ex-vivo lung perfusion (EVLP)



- Prolongation of transport and evaluation time of donor lungs
- Reconditioning of marginal lungs

Neutrophil extracellular traps (NETs) are indicated in transplant outcome

- NETs are web-like structures released by activated neutrophils
 - Trap and kill pathogens
 - Pathogenic if dysregulated



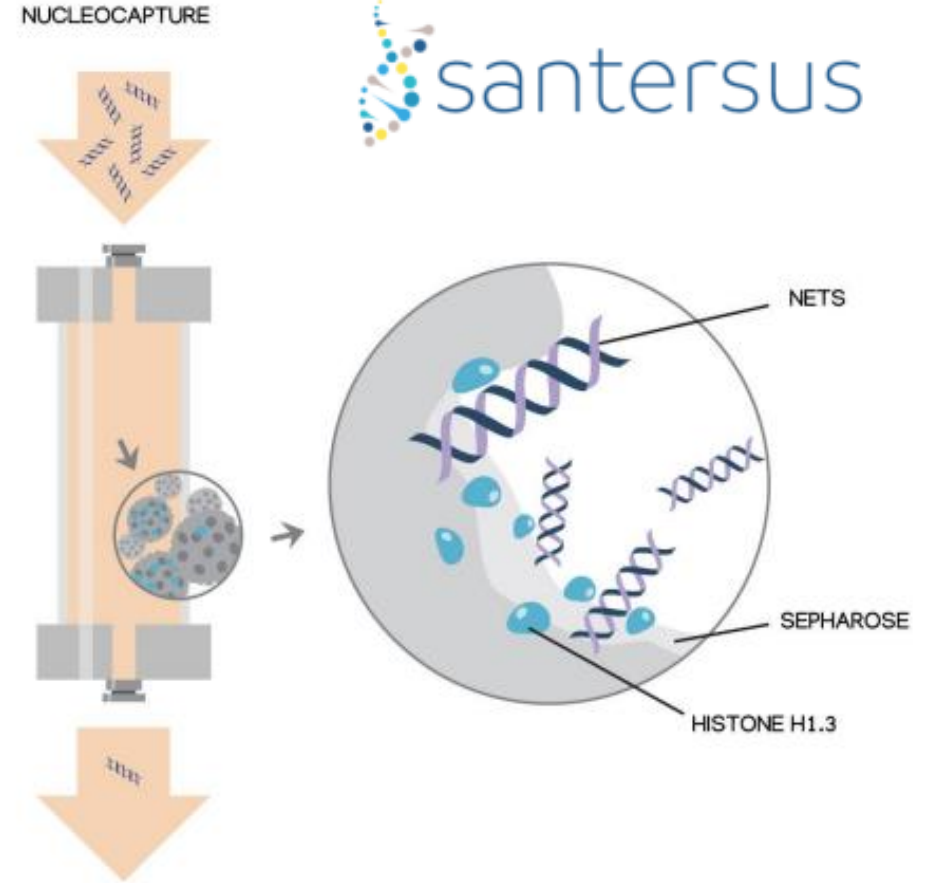
Brinkmann et al., 2004

NETs are indicated in lung transplant outcome

- Elevated levels of NETs shown in
 - EVLP perfusate connected to worse LTx recipient outcome
 - Primary graft dysfunction (PGD)
 - Acute lung injury (ALI)
 - Pre-clinical murine model of acid aspiration induced acute respiratory distress syndrome (ARDS)

NucleoCapture devices remove NETs from circulating blood

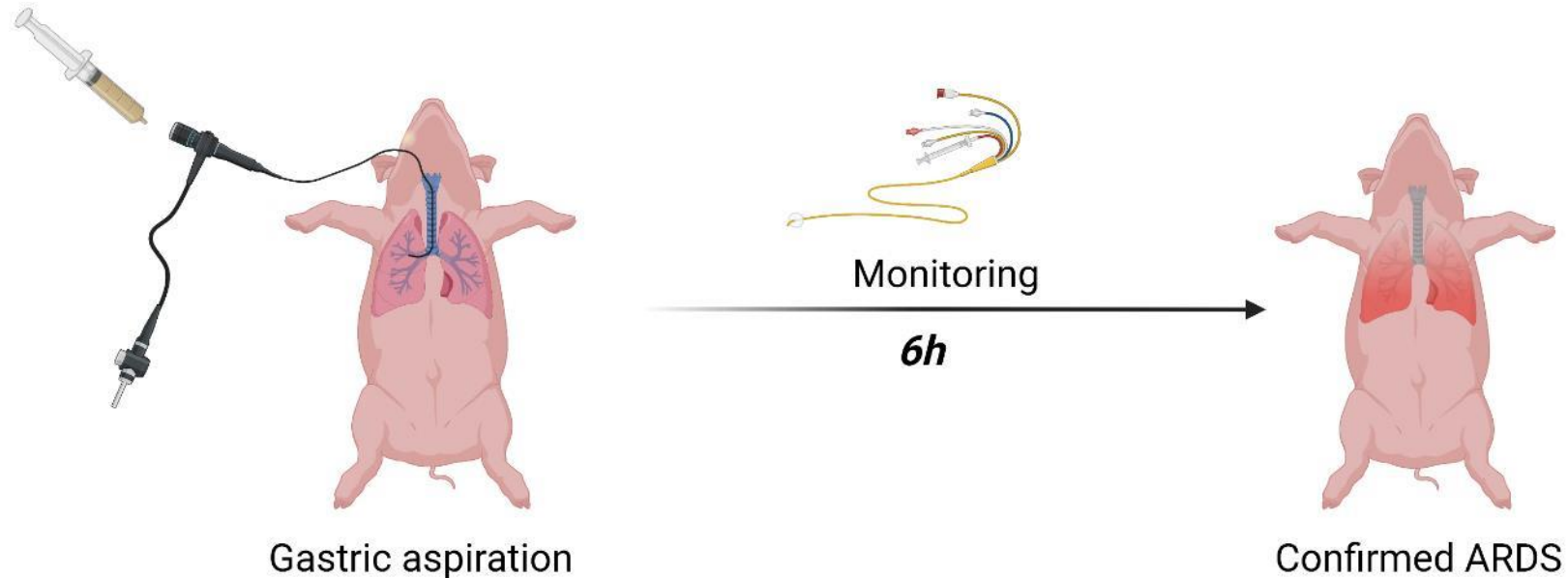
- Polymer beads conjugated with human recombinant histone H1.3 protein
- Histone H1.3 protein binds DNA



Aswani et al., Santerus AG

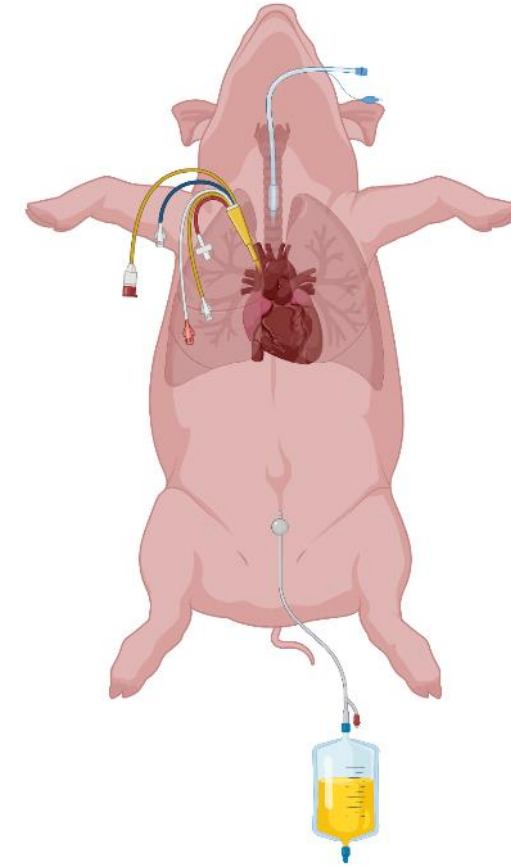
Porcine experimental model of gastric content aspiration induced acute lung injury

1. Induction of ALI



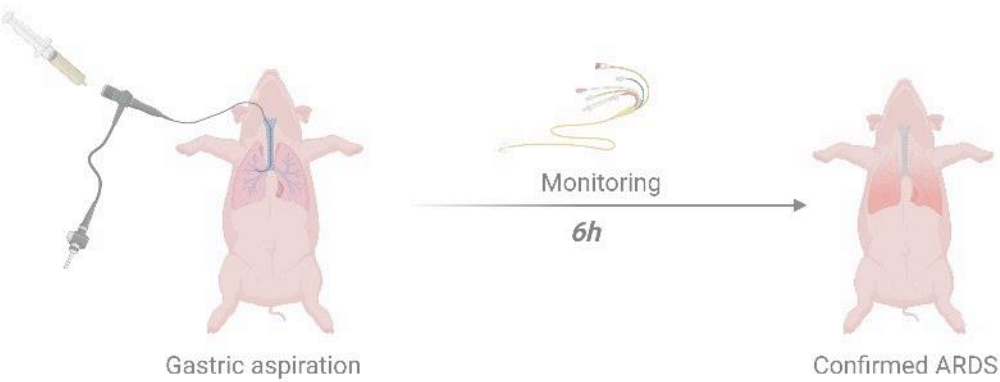
Porcine experimental model of gastric content aspiration induced acute lung injury or ARDS

- Extensive monitoring:
 - Vital parameters
 - Arterial blood gases
 - Hemodynamic measurements (Swan-Ganz catheter)
 - Ventilatory parameters
 - Diuresis

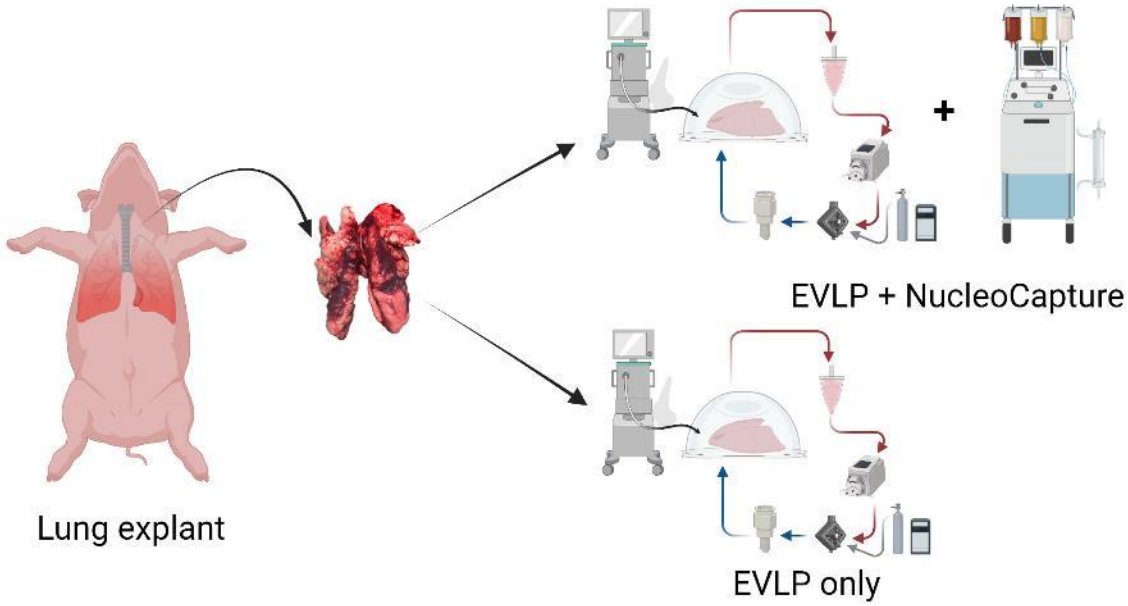


Porcine experimental model of gastric content aspiration induced acute lung injury or ARDS

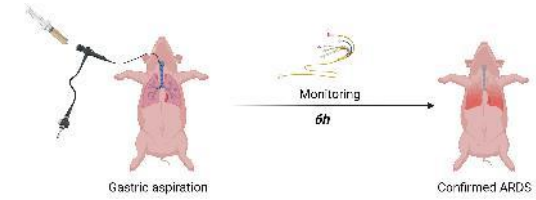
1. Induction of ALI



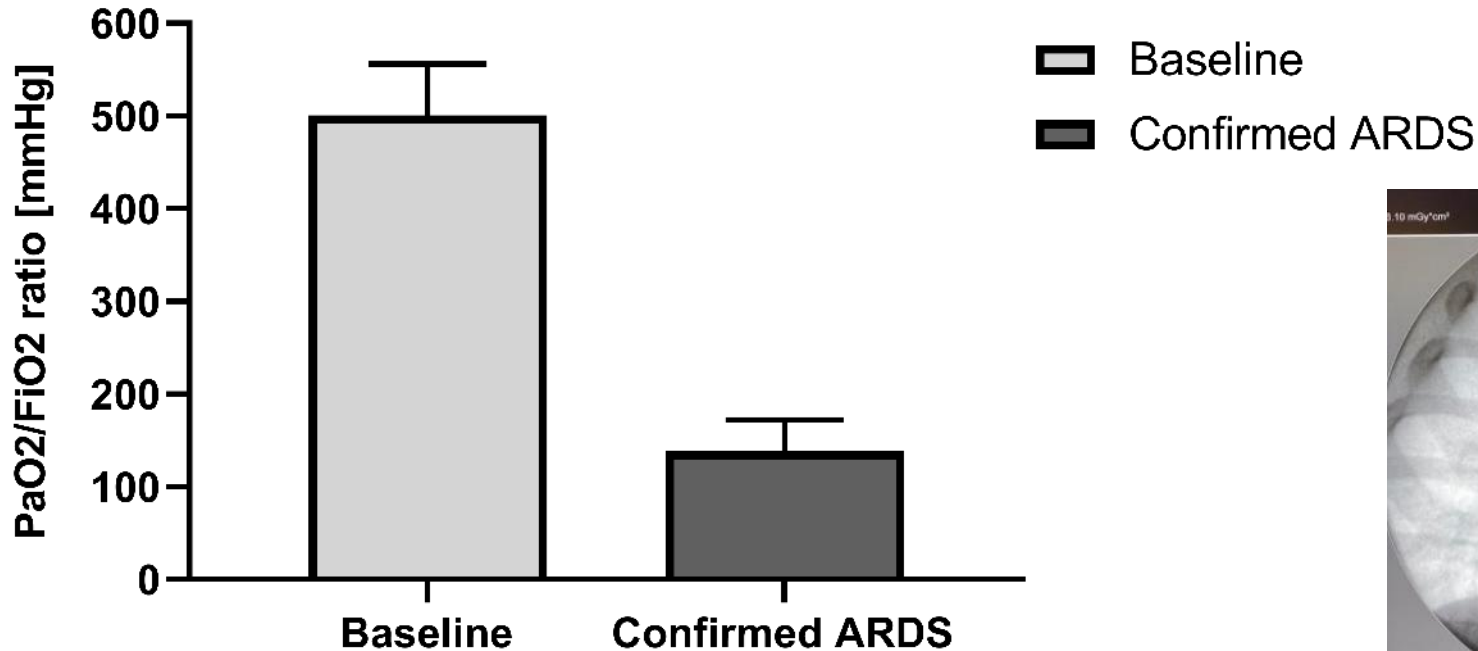
2. EVLP for 4 hours, with or without NucleoCapture



1. Establishment of acute lung injury was confirmed by PaO₂/FiO₂ ratio and X-ray

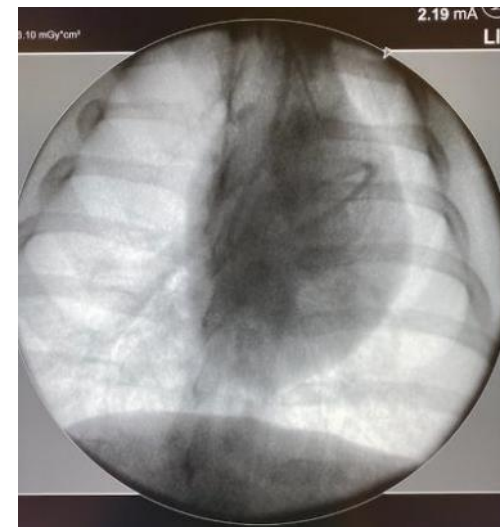


PaO₂/FiO₂ ratio ARDS

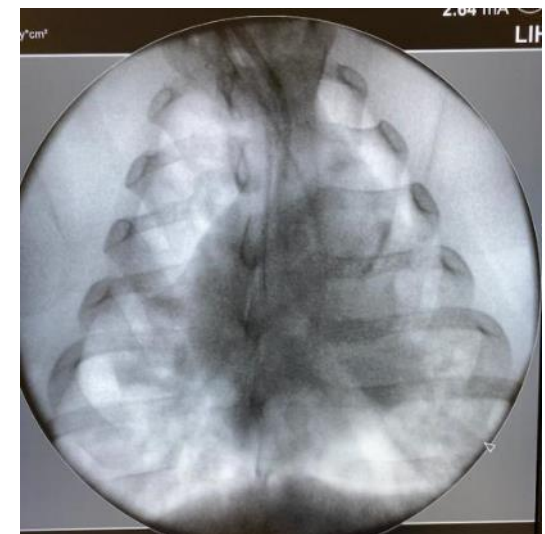


Berlin Criteria for PaO₂/FiO₂ Ratio:

- Mild ARDS: 201-300 mmHg
- Moderate: 101-200 mmHg
- Severe: ≤ 100 mmHg

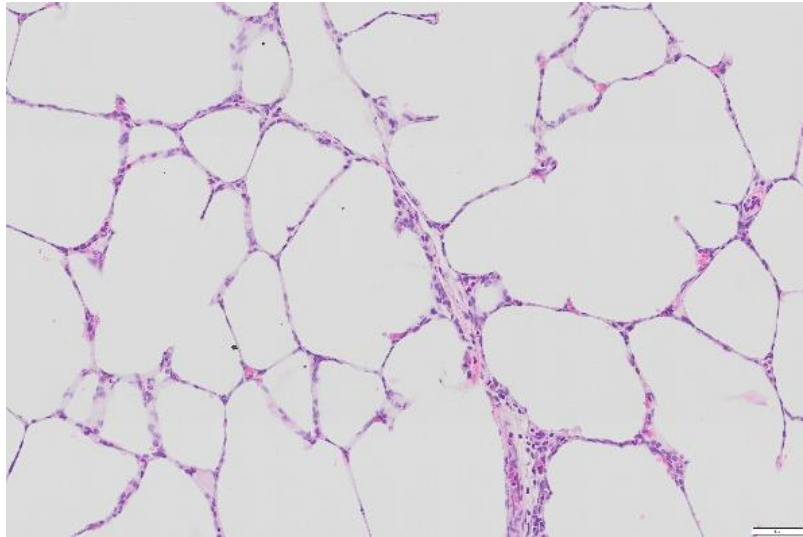
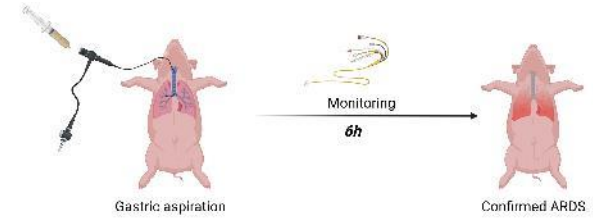


Baseline

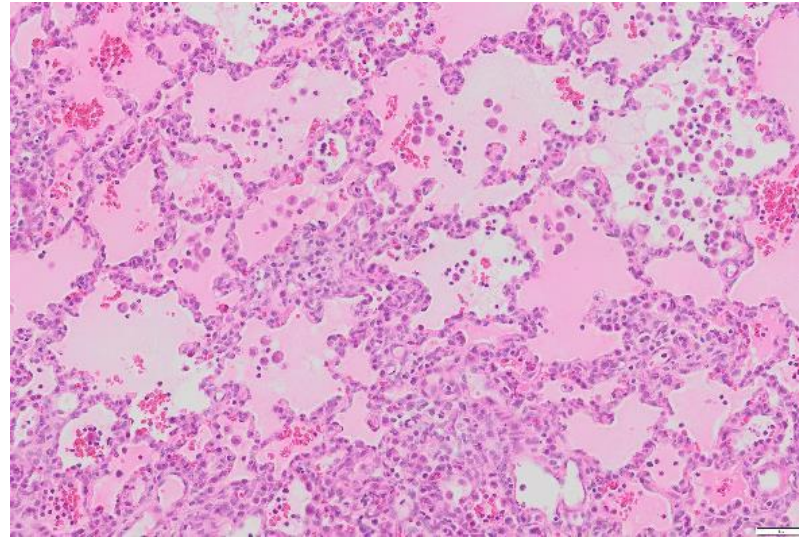


Confirmed ARDS

1. Establishment of acute lung injury was confirmed by micro- and macroscopic evaluation



Baseline

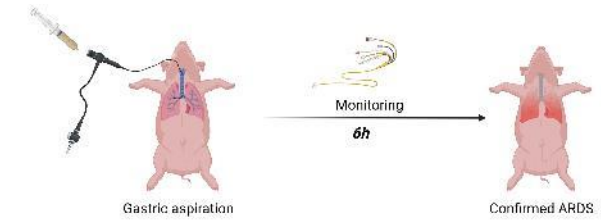


Confirmed ARDS

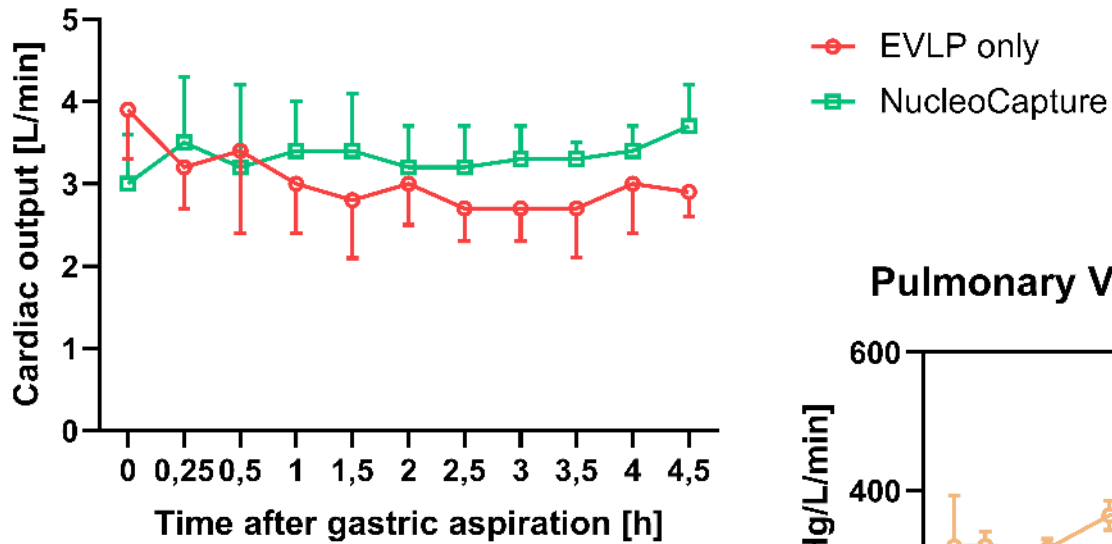


Confirmed ARDS

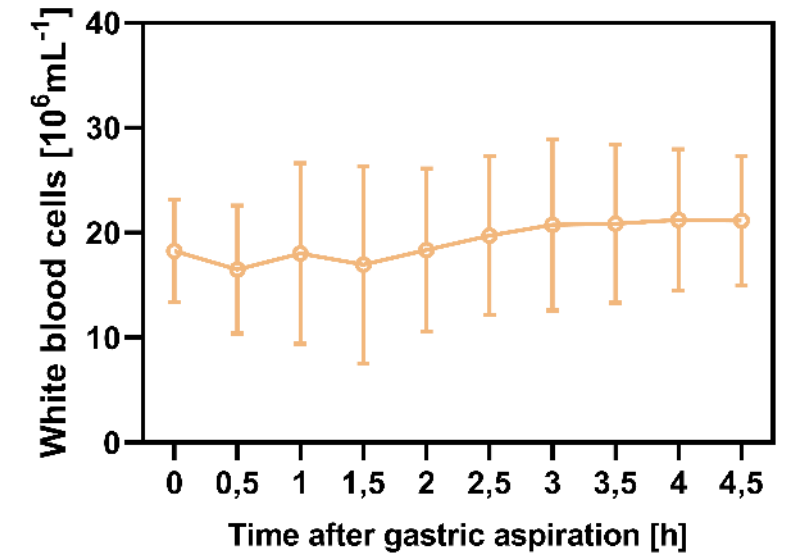
1. Clinically relevant parameters indicate a local lung injury



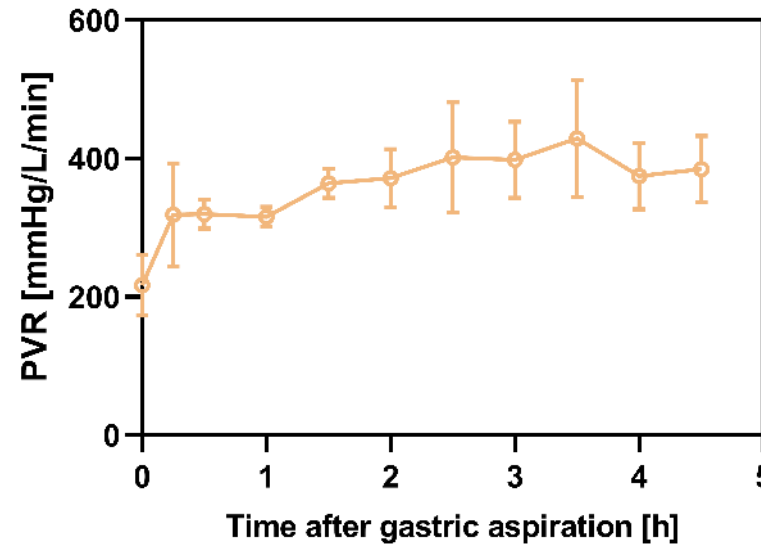
Cardiac Output (CO)



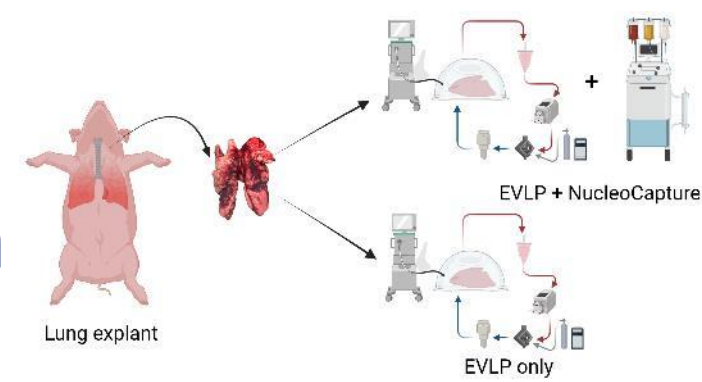
White Blood Cells



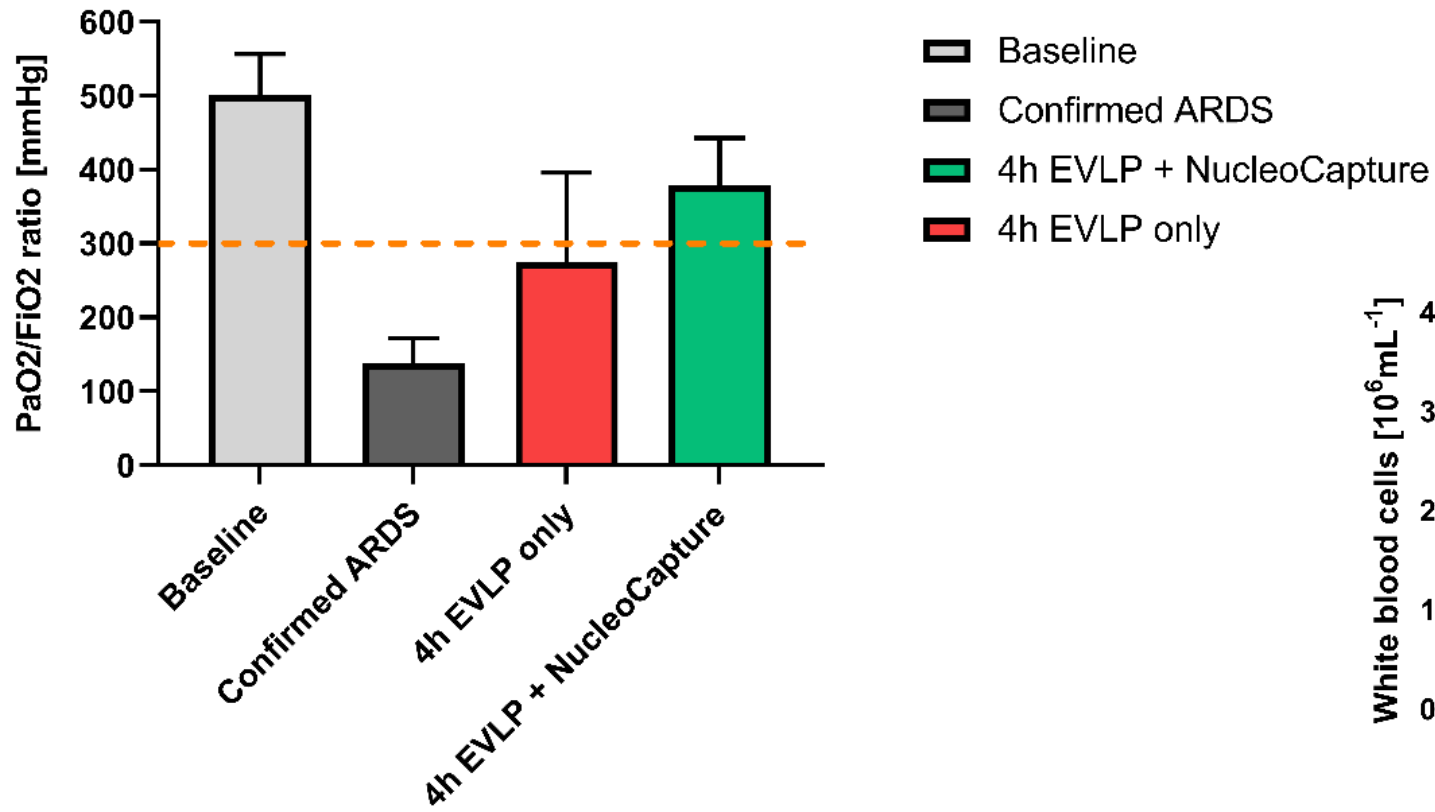
Pulmonary Vascular Resistance (PVR)



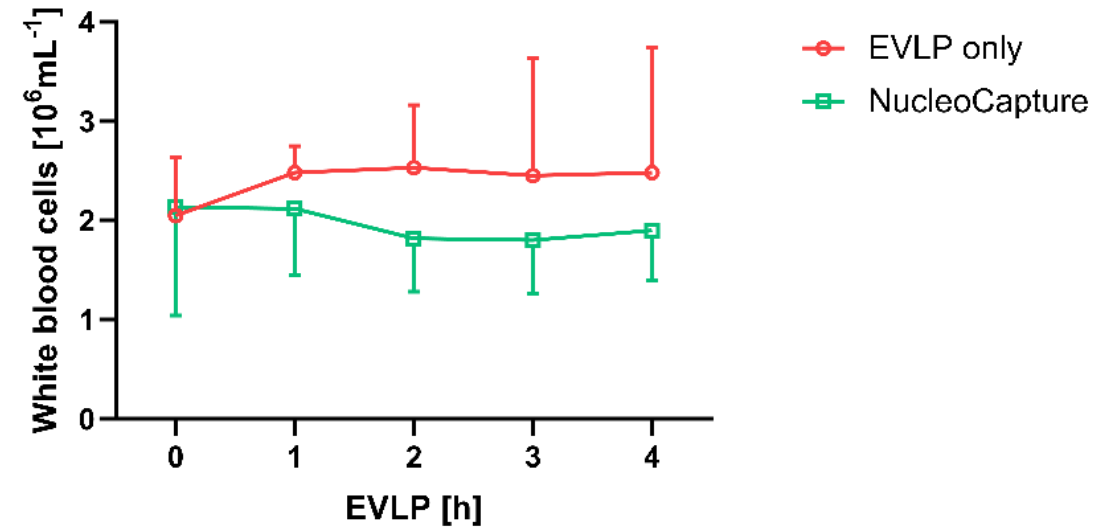
2. NucleoCapture connected to an EVLP circuit improves lung function



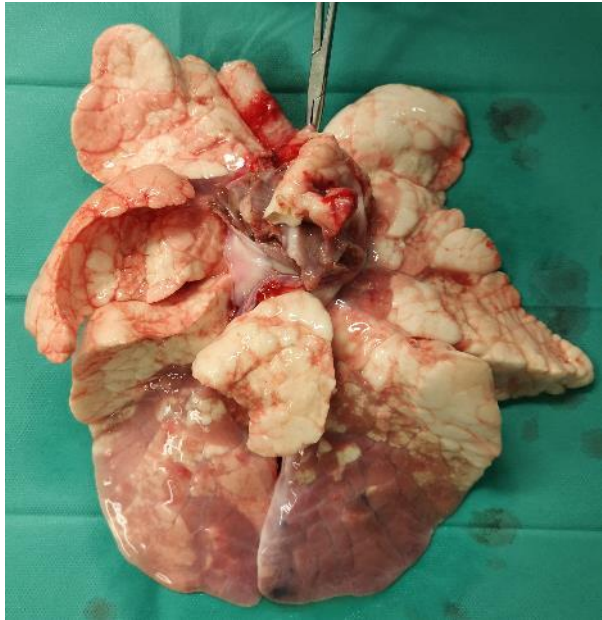
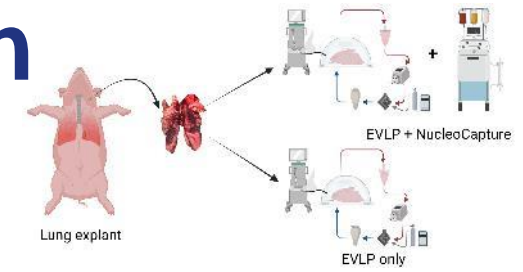
PaO₂/FiO₂ ratio summary



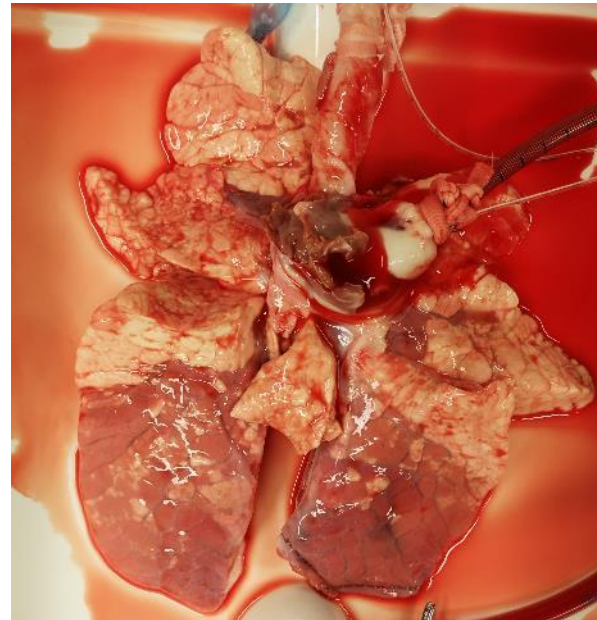
White blood cells



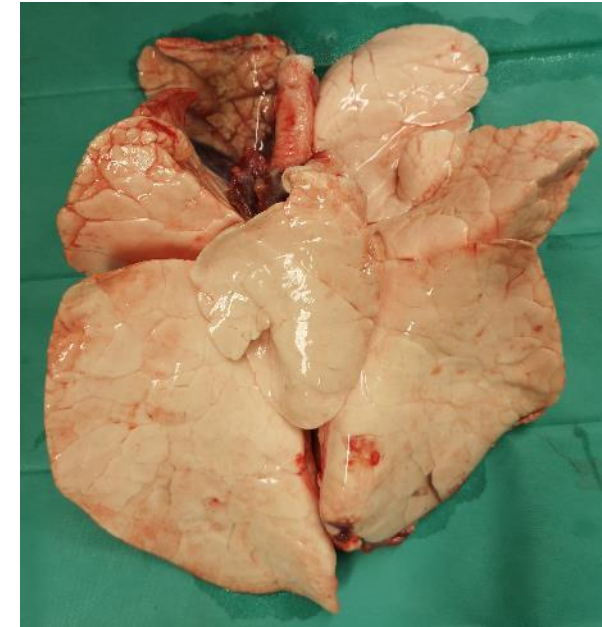
2. A NucleoCapture device connected to an EVLP circuit improves lung morphology



Confirmed ARDS



EVLP Base



4h EVLP + NucleoCapture

Conclusion

- A porcine model of gastric content aspiration induced ARDS was successfully established
- Treatment with a NucleoCapture device connected to an EVLP circuit for 4 hours improved lung function and morphology
- Isolated EVLP study, no prediction of their in vivo function
- Future directions: transplantation of treated lungs in pig models to investigate sustainability of LTx

Thank you for listening!

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