KEUHKOLÄÄKÄRIPÄIVÄT 17.—18.3.2022

KEUHKONSIIRTOKIRURGIA TÄNÄÄN JA HUOMENNA

Antti Nykänen, dosentti, sydän- ja rintaelinkirurgian erikoislääkäri

HUS Sydän- ja keuhkokeskus

HELSINKI VS TORONTO

HUS Sydän- ja keuhkokeskus

Toronto Lung Transplant Program

- 2017-2018 Lung Transplant Fellow
- 2018-2020 Postdoctoral Fellow (+CTEPH)
- 1983 onnistunut SLTX 1986 DLTX
- 200 keuhkonsiirtoa vuodessa

TÄNÄÄN VS HUOMENNA

Keuhkonsiirtokirurgia Suomessa tänään

Elinluovuttajat (NDD vs DCD)

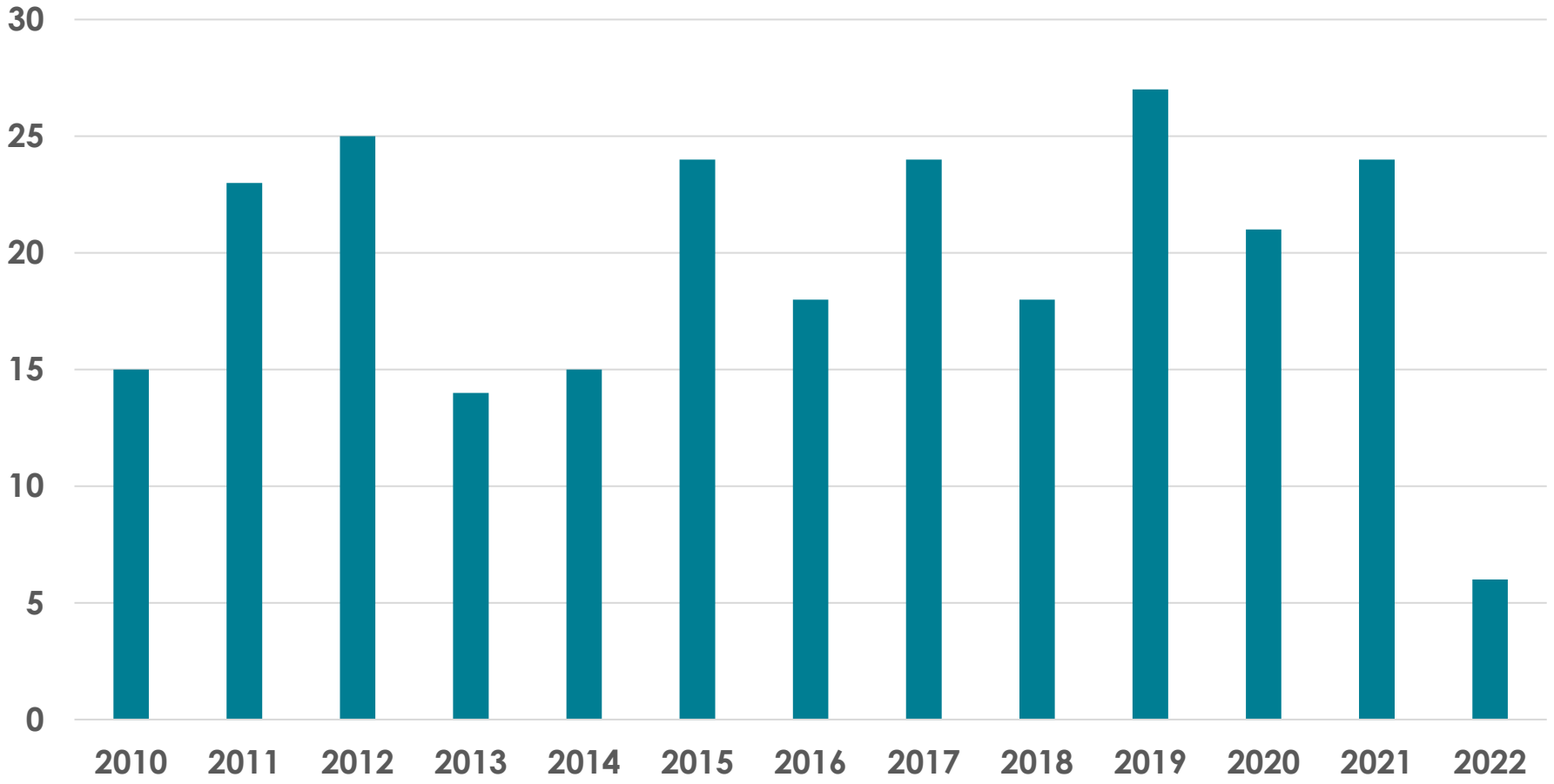
Ex Vivo Lung Perfusion (EVLP)

Miten keuhkonsiirtoja voisi lisätä?

Miten tuloksia voisi parantaa?

Keuhkonsiirtokirurgia ylihuomenna?

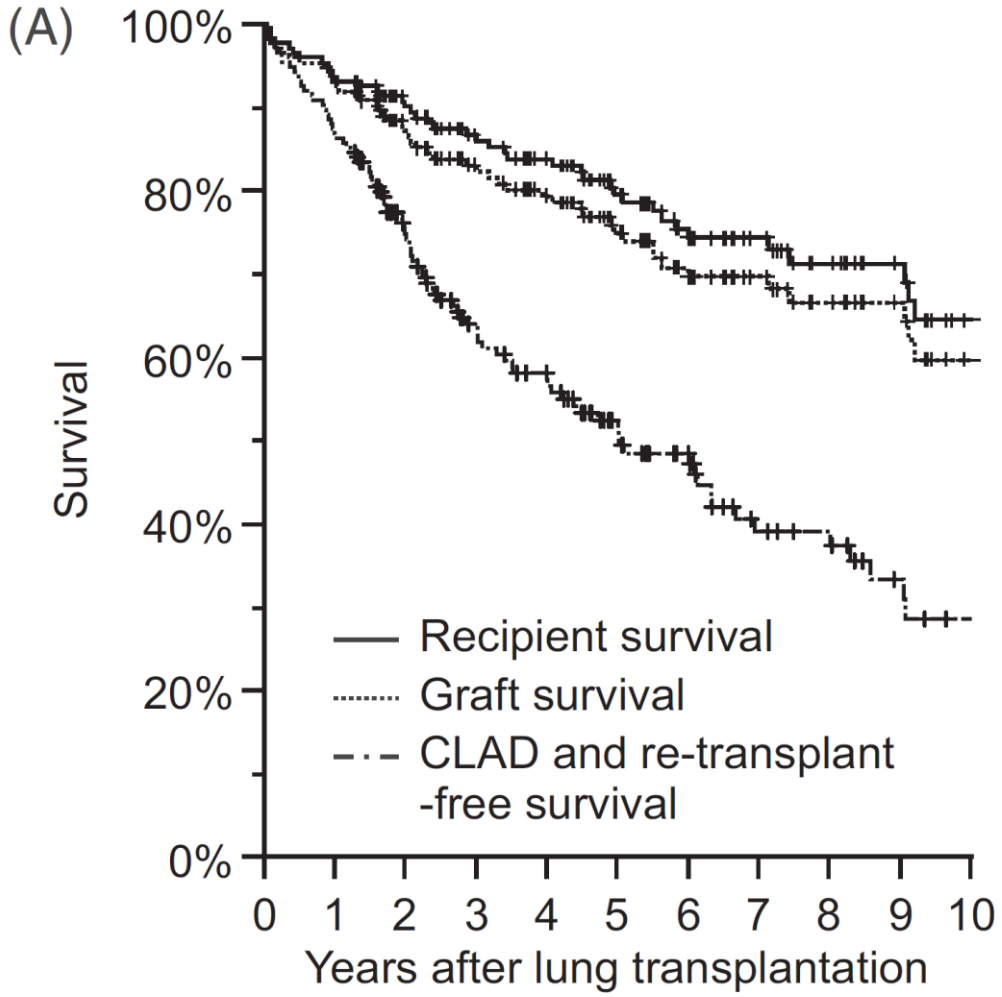
Keuhkonsiirrot Suomessa



Lista 13.3.2022

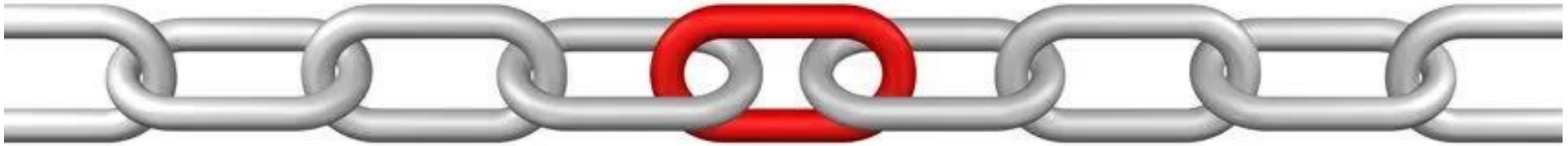
- 32 potilasta
- 2 kiireellistä
- Pisin dotusaika 2v 3kk

KEUHKONSIIRRON TULOKSET SUOMESSA 2003-2015 (N=175)



Nykänen et al. ScandCardvascJ 2020

- 1v 94%
- 5v 79%
- 10v 64%
- ISHLT 2009-6/2016 mediaani 6.5v
- CLAD-free
  - 1v 86%
  - 5v 52%
  - 10v 28%



Potilas

Keuhkotauti

Lähettävät lääkärit

Ajoitus

Fysioterpia ja ravitsemus

Keuhkosiirre

Siirtoleikkaus

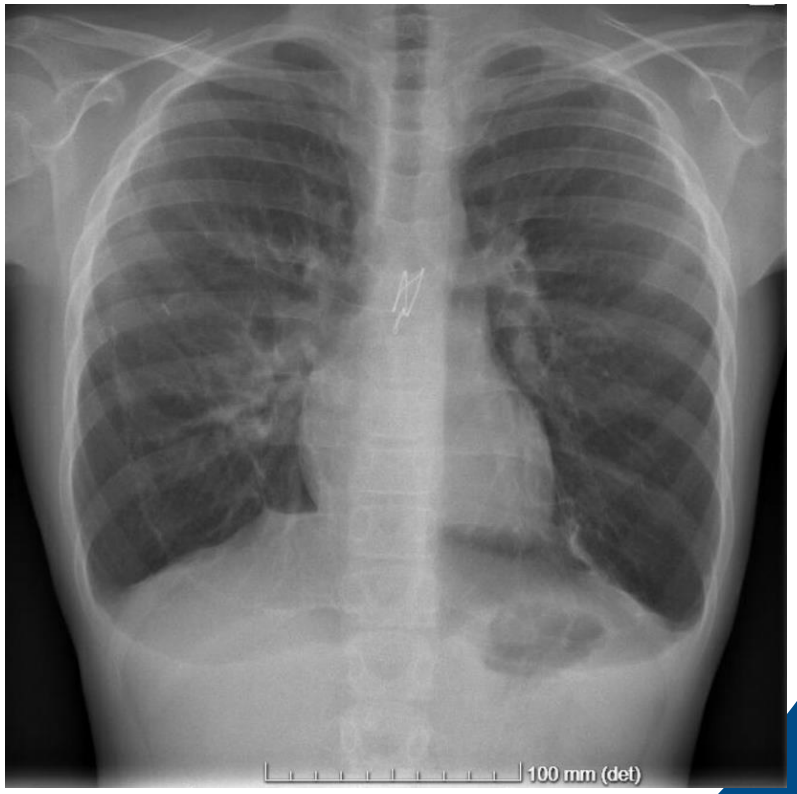
Immunologia

Perioperatiivinen hoito

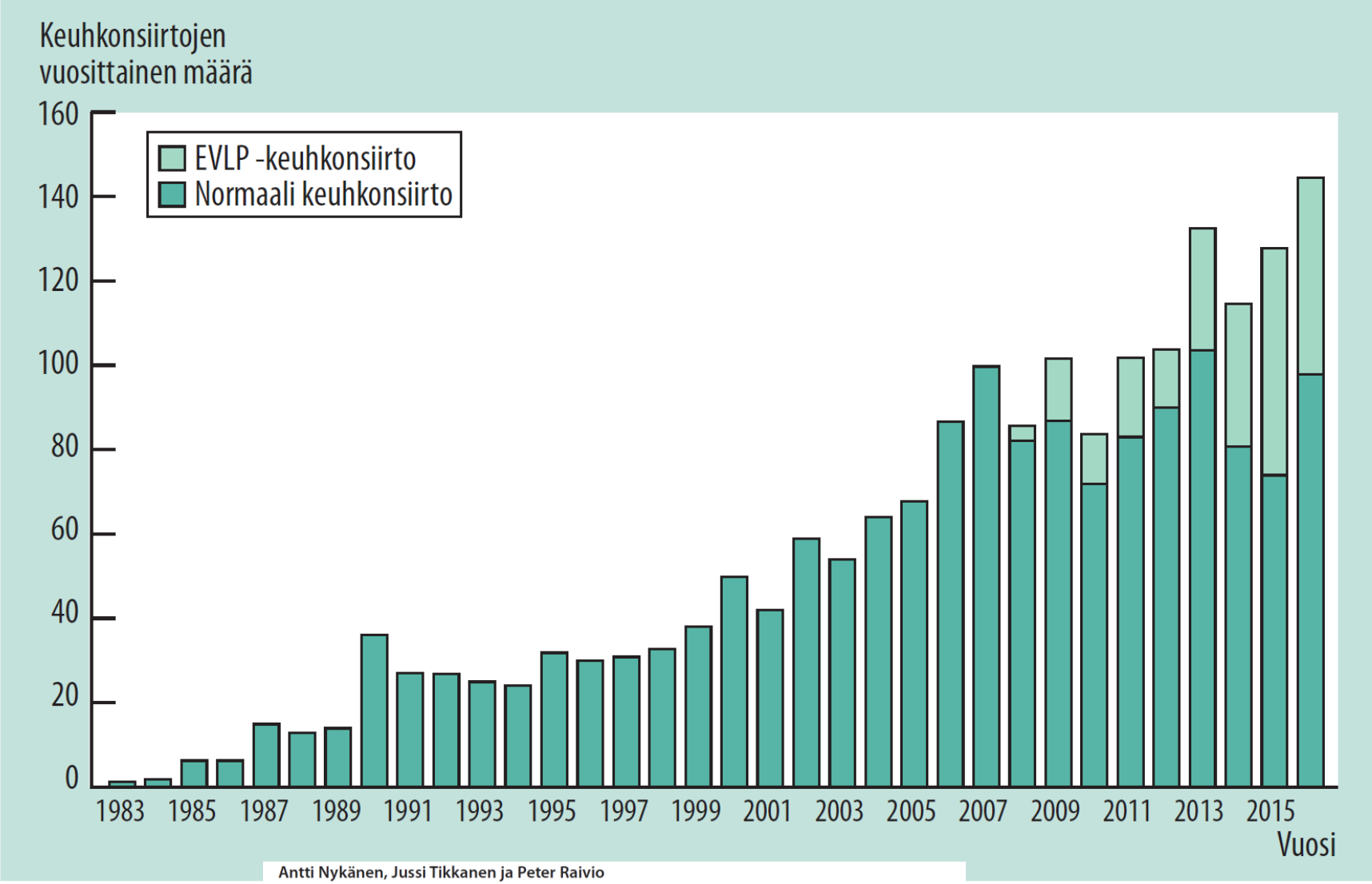
Seuranta

ESIMERKKI YHTEISTYÖSTÄ

- 12v aiemmin terve poika
- 1v hengenahdistusoireisto
- ULS tutkimuksissa vaikea PAH
- VA-ECMO, jonka aikana suolistovuoto ja hemikolektomia
- DLTX 2kk ECMO-hoidon jälkeen
- Siirtokeuhkojen resektio
- Kotiutui 73 päivää keuhkonsiirron jälkeen
- Vointi hyvä >1v siirrosta, käy normaalisti koulua
- ULS seuranta ja yhteistyö aikuispuolen kanssa jatkuu



KEUHKONSIIRROT TORONTOSSA



Antti Nykänen, Jussi Tikkanen ja Peter Raivio

Keuhkosiirteen kehonulkoinen perfuusio – lisää ja parempia siirteitä? Duodecim 2017;

200 siirtoa vuodessa

EVLP

Luovuttajat

LUOVUTTAJAT JA EVLP

TABLE I Currently accepted "ideal" donor

- Age <55 years
- ABO compatibility
- Clear chest radiograph
- PaO_2 >300 on FIO_2 = 1.0, PEEP 5 cm H_2O
- Tobacco history <20 pack-years
- Absence of chest trauma
- No evidence of aspiration/sepsis
- No prior cardiopulmonary surgery
- Sputum gram stain—absence of organisms
- Absence of purulent secretions at bronchoscopy

Donorit

NDD

Marginaaliset luovuttajat

DCD

NPOD

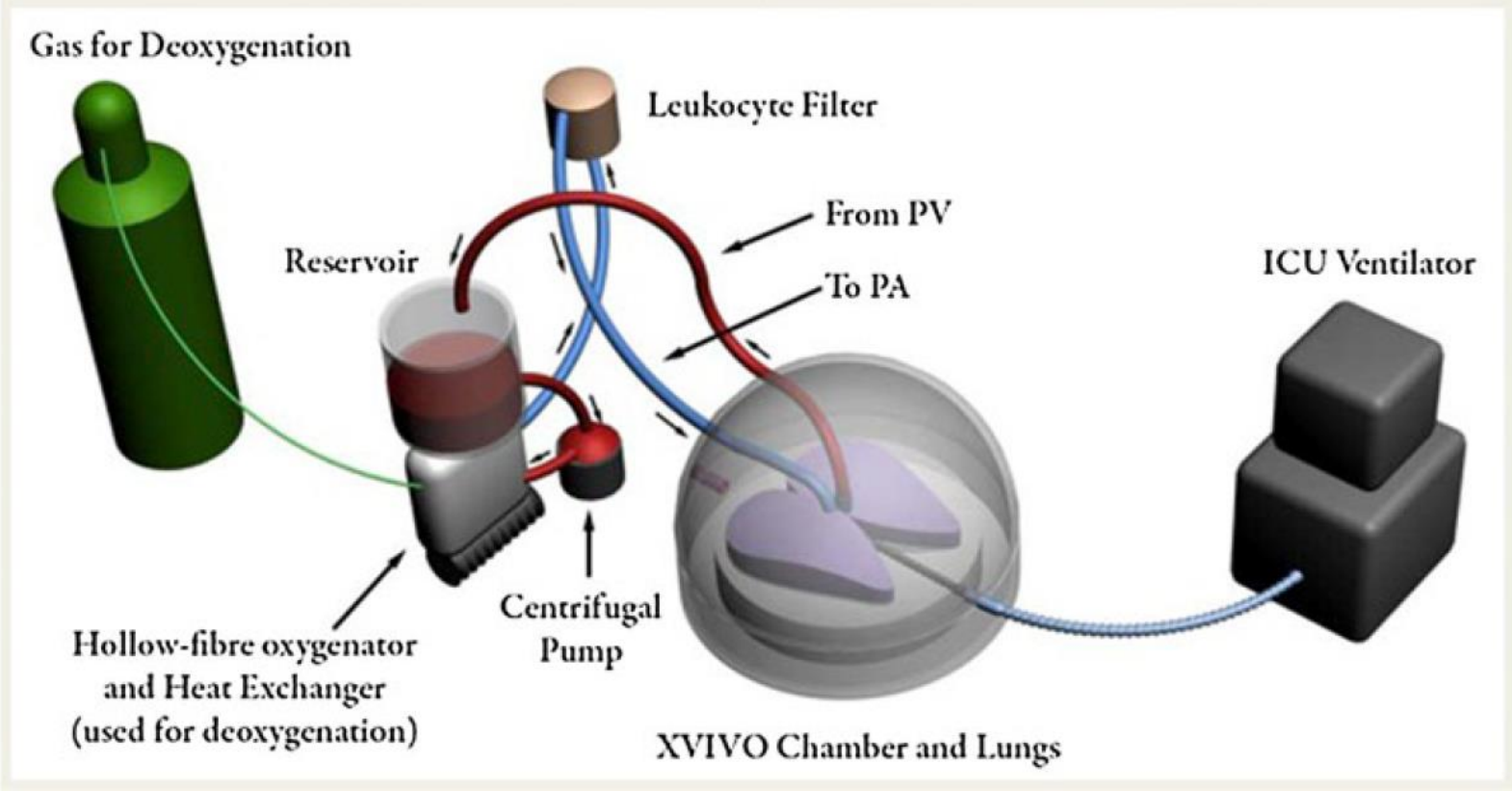
MAID

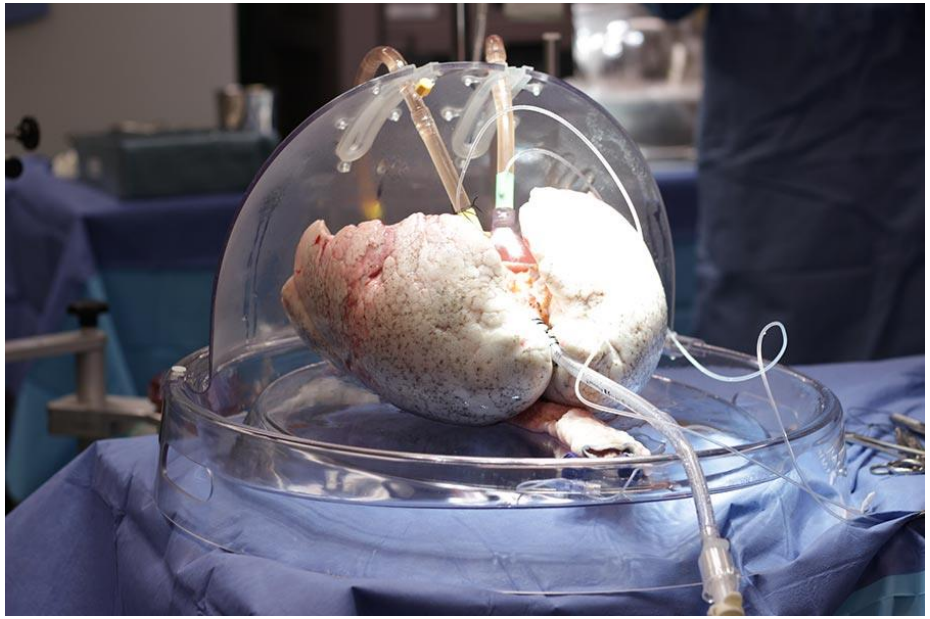
HVC+

EVLP

siirteen toiminnan varmistaminen

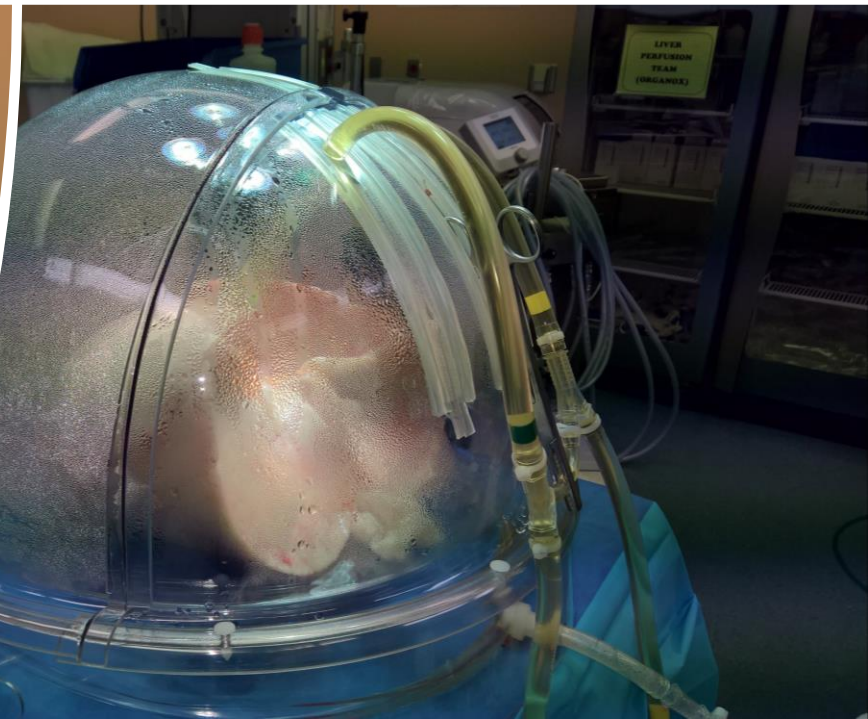
EX VIVO LUNG PERFUSION (EVLP)

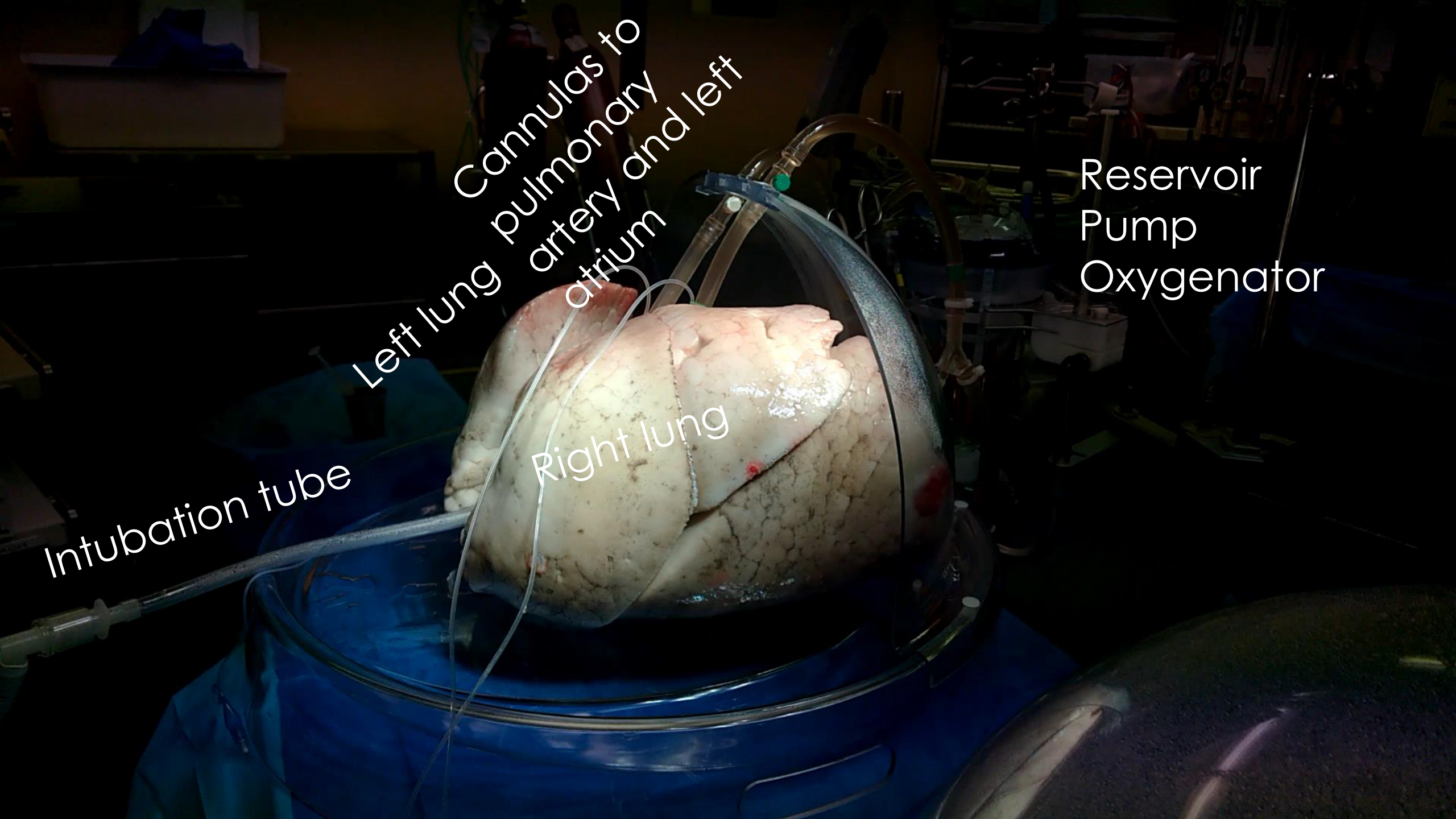




Keuhkosiirre
- Siirto vs EVLP vs hylkäys

EVLP
- Oma leikkaussali
- Organ perfusion specialist
- Keuhkon evaluaatio yleensä 3-6 tuntia
- Hapetus, komplianssi, ilmatiepaineet, laktaatti, pH, RTG, bronskoskopia, palpaatio




Cannulas to pulmonary artery and left atrium
Left lung
Reservoir
Pump
Oxygenator
Right lung
Intubation tube

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Normothermic Ex Vivo Lung Perfusion in Clinical Lung Transplantation

Marcelo Cypel, M.D., Jonathan C. Yeung, M.D., Mingyao Liu, M.D., Masaki Anraku, M.D., Fengshi Chen, M.D., Ph.D., Wojtek Karolak, M.D., Masaaki Sato, M.D., Ph.D., Jane Laratta, R.N., Sassan Azad, C.R.A., Mindy Madonik, C.C.P., Chung-Wai Chow, M.D., Cecilia Chaparro, M.D., Michael Hutcheon, M.D., Lianne G. Singer, M.D., Arthur S. Slutsky, M.D., Kazuhiro Yasufuku, M.D., Ph.D., Marc de Perrot, M.D., Andrew F. Pierre, M.D., Thomas K. Waddell, M.D., Ph.D., and Shaf Keshavjee, M.D.

N ENGL J MED 364;15 NEJM.ORG APRIL 14, 2011

Functional outcomes and quality of life after normothermic ex vivo lung perfusion lung transplantation

Jussi M. Tikkanen, MD, PhD, Marcelo Cypel, MD, Tiago N. Machuca, MD, Sassan Azad, CRA, Matthew Binnie, MD, Chung-Wai Chow, MD, Cecilia Chaparro, MD, Michael Hutcheon, MD, Kazuhiro Yasufuku, MD, Marc de Perrot, MD, Andrew F. Pierre, MD, Thomas K. Waddell, MD, Shaf Keshavjee, MD, and Lianne G. Singer, MD

J Heart Lung Transplant 2015;34:547–556

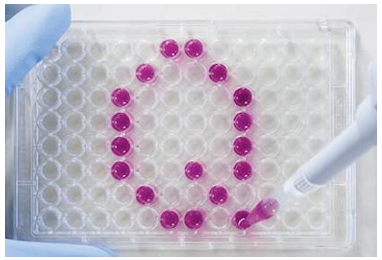
EVLP TÄNÄÄN JA HUOMENNA

Organ repair centers

Damaged lung → EVLP
- Assess
→ Safe TX
- More transplants

Damaged lung
Standard lung
→ EVLP
- Assess
- Repair
- Improve
→ Safe TX
- Improved results
- IRI/PGD
- CLAD

Translational approach



In vitro

- Cell culture
- Lung-on-a-chip

Small Animals

- Mouse TX
- Rat EVLP and Tx

Large Animals

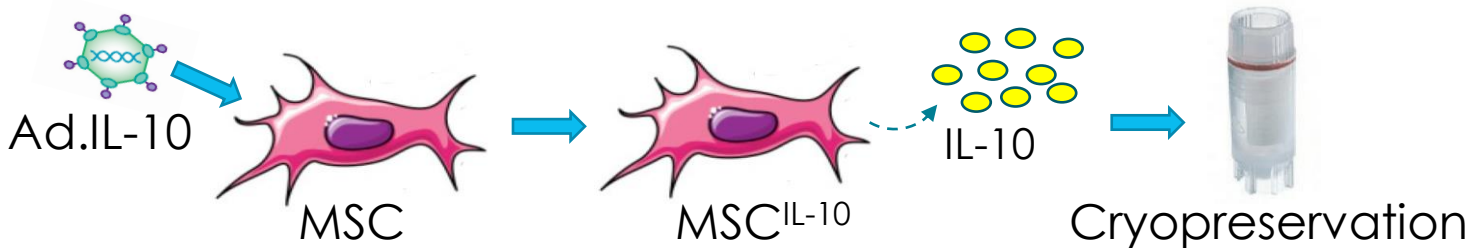
- Pig EVLP and Lung SLTX

Human EVLP

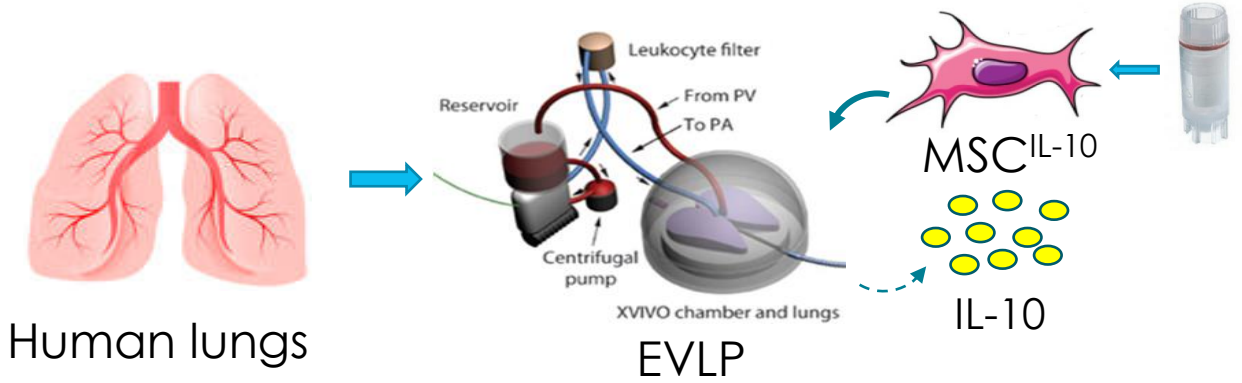
- Human Rejected Lungs

Clinical Trial

Mesenchymal Stromal Cells with augmented IL-10

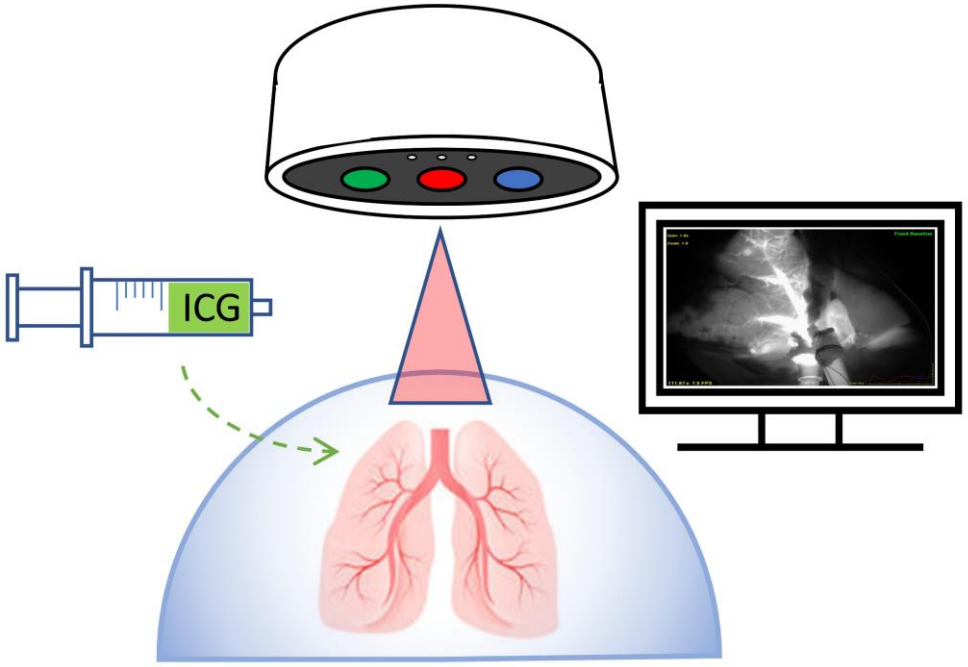


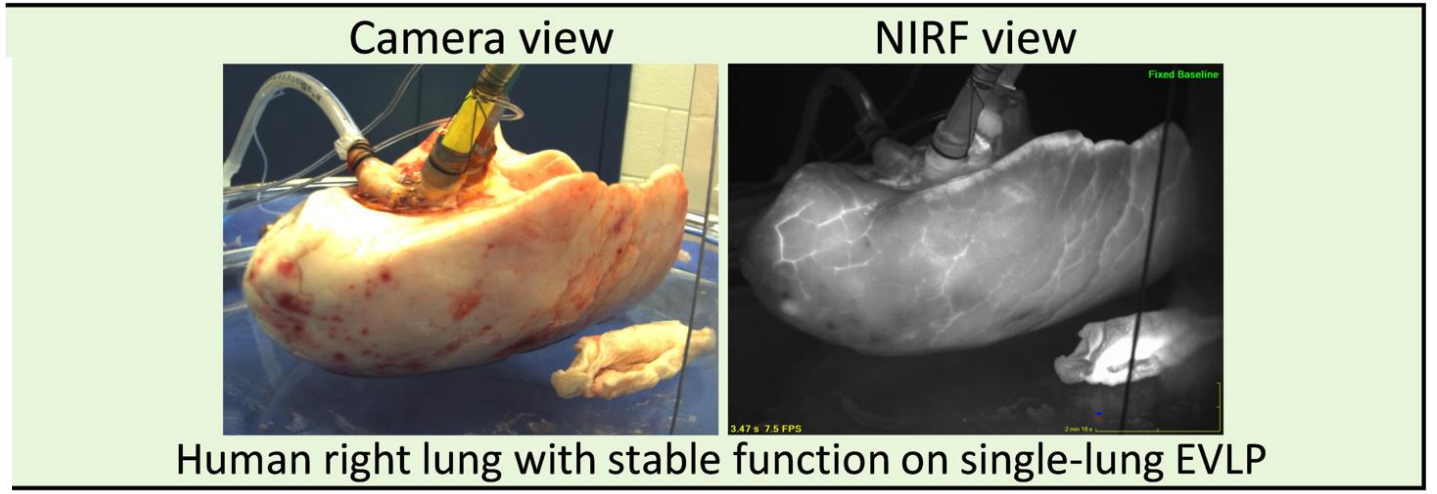
MSC^{IL-10} treatment during EVLP

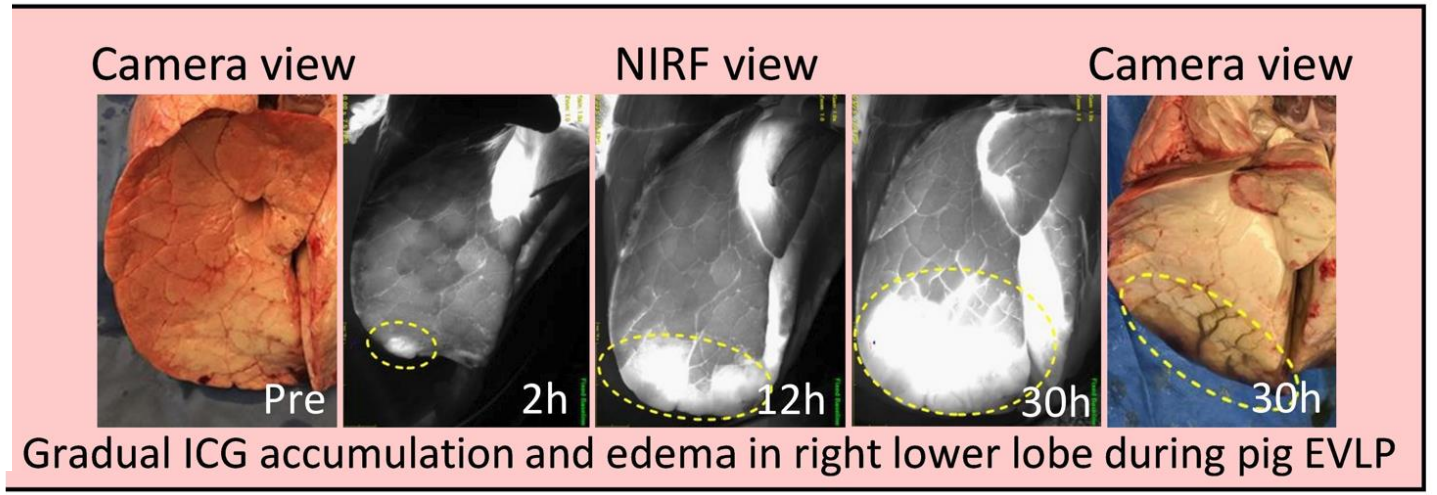


Nykänen et al. Mol Ther Methods Clin Dev 2021

Near-infrared fluorescence imaging during EVLP

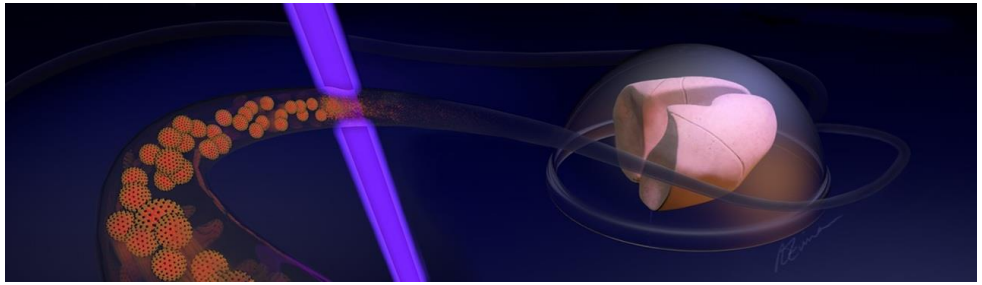






Nykänen et al. JTCV 2022

KEUHKONSIIRTOKIRURGIA YLIHUOMENNA?



Diagnostics

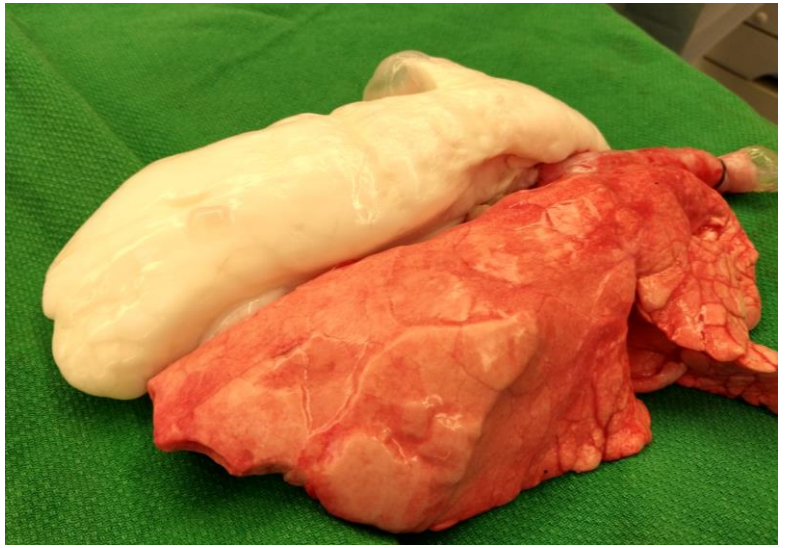
- Perfusate cytokines
- Toronto Lung Score
- Point-of-care

Therapeutics

- Pharmacological agents
  - Alpha-1-antitrypsin
- Cell therapies
  - Mesenchymal stem cells
  - Tregs
- Gene therapy
  - IL-10
  - Adenovirus, lentivirus, AAV
  - CRISPR-Cas

Other

- UV light/antimicrobial
- HVC, CMV
- Prolonged EVLP
- Dialysis, nutrition, +10C preservation
- Organ engineering



DRONE DELIVERS LUNGS FOR TRANSPLANT TO TORONTO HOSPITAL IN WORLD 1ST

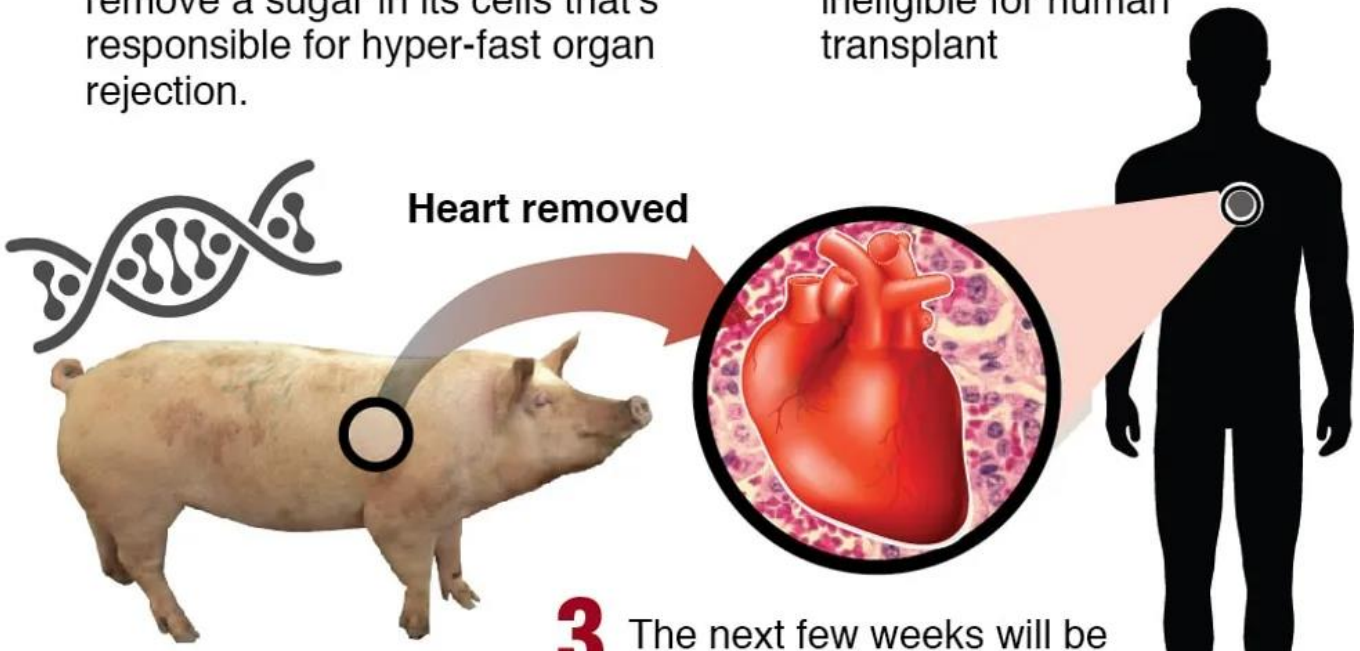
Oct 12, 2021

Pig-to-human heart transplant

In a medical first, doctors transplanted a pig heart into a patient in a last-ditch effort to save his life in a Maryland hospital. While it's too soon to know if the operation really will work, it marks a step in the decades-long quest to one day use animal organs for life-saving transplants.

1 The Maryland surgeons used a heart from a pig that had undergone gene-editing to remove a sugar in its cells that's responsible for hyper-fast organ rejection.

2 The patient, David Bennett, a 57-year-old Maryland handyman who was ineligible for human transplant



3 The next few weeks will be critical as Bennett recovers from the surgery and doctors carefully monitor how his heart is faring.

Source: Associated Press
Graphic: Staff, TNS

Kiitokset!