Pre-clinical renal transplantation

3rd International Conference on Functional Renal Imaging 2019

Bente Jespersen, professor
Renal Medicine
Aarhus University Hospital
Denmark

Pigs in Denmark

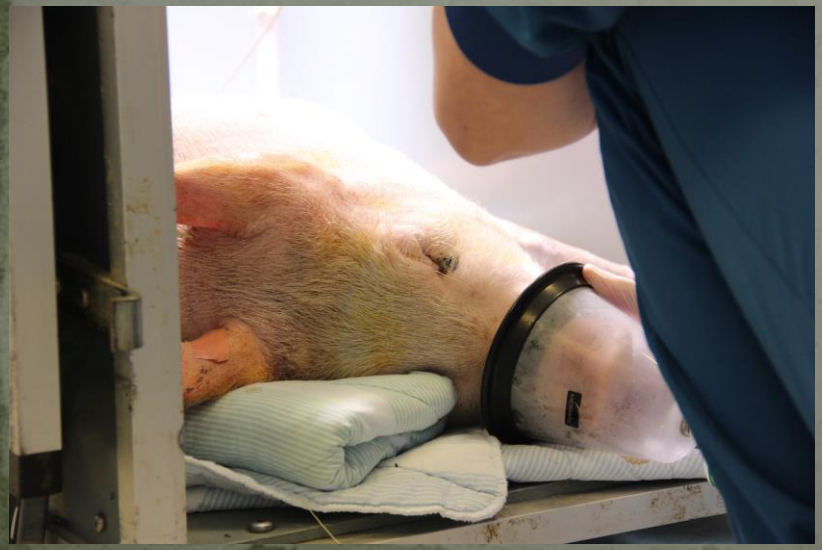
- Danish pig production: 32 mio. pigs/year[1].
- Worlds highest pig/people ratio.
- Mostly bacon.

- Research and surgical training : 5.669 pigs[2].

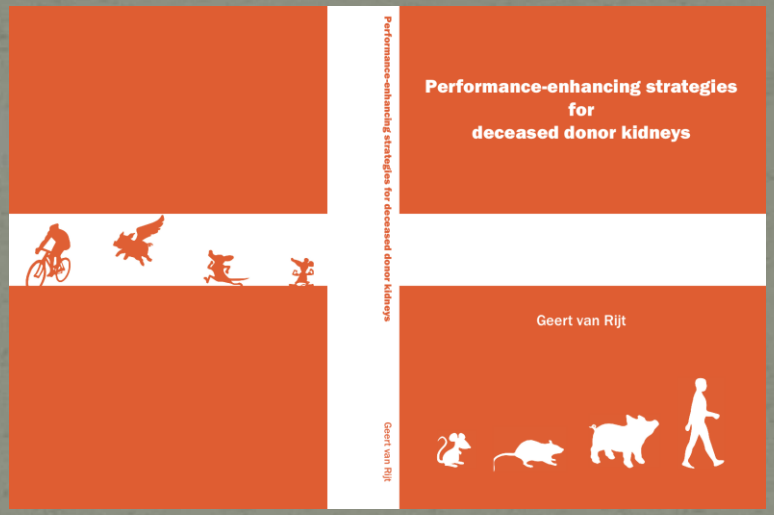
1. Statistics Denmark
2. The Animal Experiments Inspectorate, 2017

Porcine kidney similar to human –
anatomy
physiology

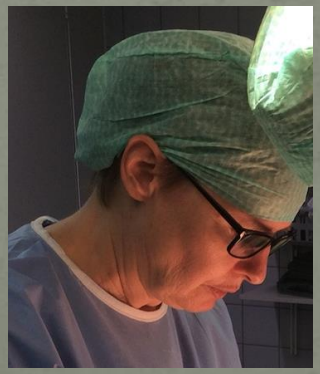
Ethics
Animal wellfare



Improving function of deceased donor kidneys



Henri Leuvenink



Ulla Møldrup

Danish/yorkshire landrace
Growing! 15 kg – 65 kg

Göttingen minipigs
Adult - 35 kg

Renal transplantation in the pig

Brain death models
Circulatory death model

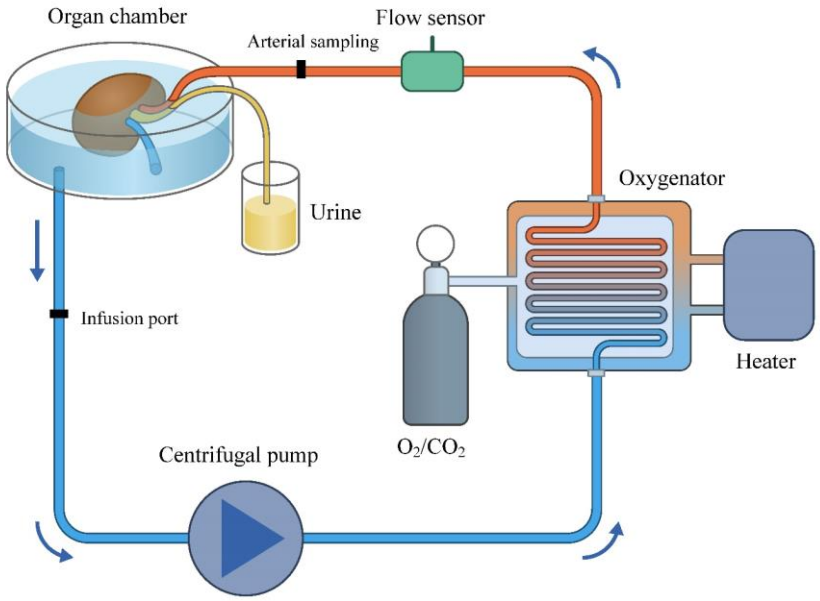
Acute models
Survival models

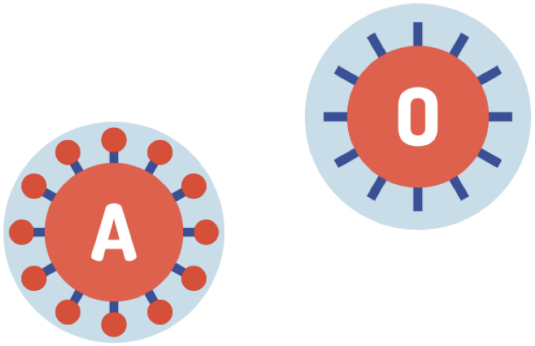
Allogeneic blood for NMP

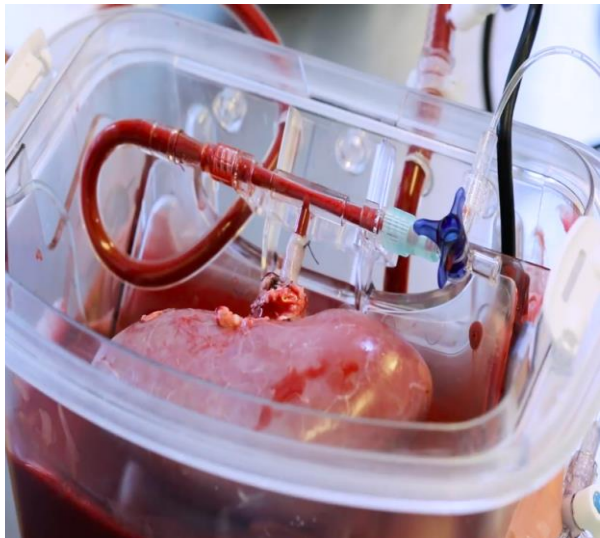
Several studies have previously shown that A-O -blood groups in pigs are **incompatible** in transfusion models. *Hunfeald et al. 354-359 **16** 1984, Sheil et al. 720-724 **104** 1972*

Human typing cards can be used for determining pig blood groups
*Martinez-Alarcon et al 2146-2148 **42** 2010*

Blood typing at the delivery farm

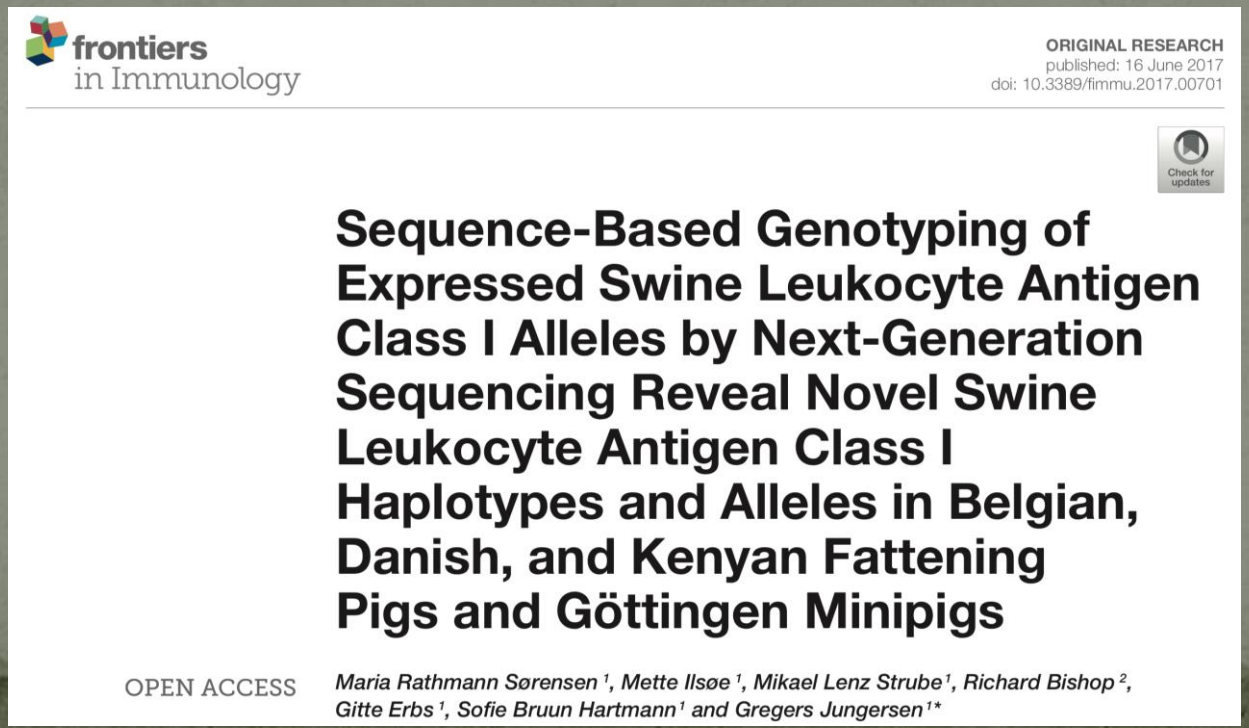






Need of immunosuppression?

- Not with 10 h observation after tx
- Not in autotransplantations
- In allotx survival experiments tissue typing and immunosuppression is possible



frontiers in Immunology

ORIGINAL RESEARCH
published: 16 June 2017
doi: 10.3389/fimmu.2017.00701

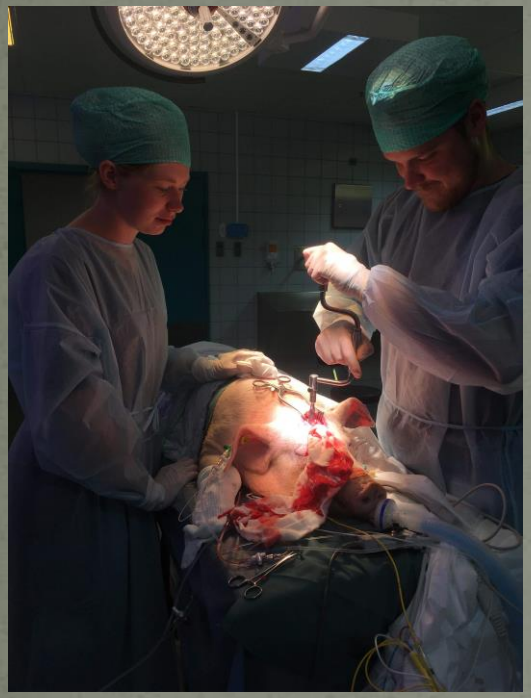
Check for updates

Sequence-Based Genotyping of Expressed Swine Leukocyte Antigen Class I Alleles by Next-Generation Sequencing Reveal Novel Swine Leukocyte Antigen Class I Haplotypes and Alleles in Belgian, Danish, and Kenyan Fattening Pigs and Göttingen Minipigs

OPEN ACCESS

*Maria Rathmann Sørensen [1], Mette Ilsøe [1], Mikael Lenz Strube [1], Richard Bishop [2], Gitte Erbs [1], Sofie Bruun Hartmann [1] and Gregers Jungersen [1]**

Brain death models in the pig



Acta Anaesthesiol Scand 2008; **52**: 621–627
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ACTA ANAESTHESIOLOGICA SCANDINAVICA
doi: 10.1111/j.1399-6576.2008.01607.x

Does brain death induce a pro-inflammatory response at the organ level in a porcine model?

A. Barklin[1,2], A. Larsson[2,3], C. Vestergaard[2,4], J. Koefoed-Nielsen[2,3], A. Bach[1,2], R. Nyboe[1,2], L. Wogensen[2,5] and E. Tønnesen[1,2]
[1]*Department of Anaesthesiology and Intensive Care, Aarhus University Hospital, Aarhus, Denmark,* [2]*Institute of Clinical Medicine, Aarhus University, Aarhus, Denmark,* [3]*Department of Anaesthesiology and Intensive Care, Aalborg Hospital, Aarhus University Hospital, Aarhus, Denmark,* [4]*Department of Dermatology and* [5]*Research Laboratory for Biochemical Pathology, Aarhus University Hospital, Aarhus, Denmark*

Acta Anaesthesiol Scand 2012; **56**: 995–1005
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ACTA ANAESTHESIOLOGICA SCANDINAVICA
doi: 10.1111/j.1399-6576.2012.02682.x

Brain death induced by cerebral haemorrhage – a new porcine model evaluated by CT angiography

C. L. Hvas[1,4], T. K. Nielsen[1], A. Barklin[1], J. C. H. Sørensen[2], M. Pedersen[3,4], G. Andersen[5] and E. Tønnesen[1]
[1]*Department of Anaesthesiology and Intensive Care Medicine, Aarhus University Hospital, Aarhus, Denmark,* [2]*Centre for Experimental Neuroscience (CENSE), Department of Neurosurgery, Aarhus University Hospital, Aarhus, Denmark,* [3]*MR Research Centre, Aarhus University Hospital, Aarhus, Denmark,* [4]*Institute of Clinical Medicine, Aarhus University Hospital, Aarhus, Denmark and* [5]*Department of Radiology, Aarhus University Hospital, Aarhus, Denmark*

TRANSPLANT INTERNATIONAL

Transplant International ISSN 0934-0874

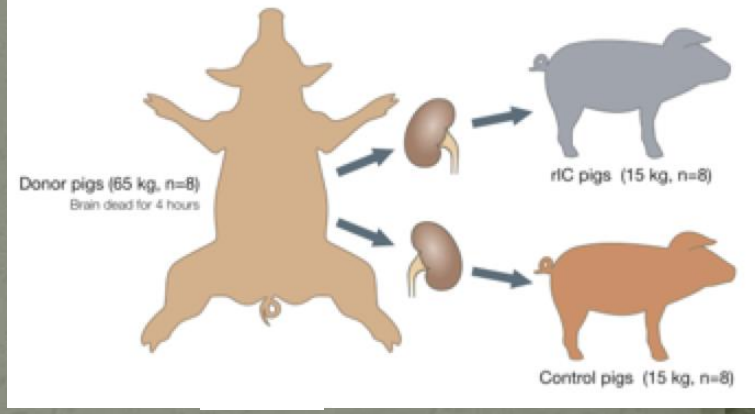
2012; 25: 1002-12

ORIGINAL ARTICLE

Improved GFR and renal plasma perfusion following remote ischaemic conditioning in a porcine kidney transplantation model

Peter Soendergaard,[1]* Nicoline V. Krogstrup,[1]* Niels G. Secher,[4] Kristian Ravlo,[1] Anna K. Keller,[5] Else Toennesen,[4] Bo M. Bibby,[6] Ulla Moldrup,[2] Ernst O. Ostraat,[2] Michael Pedersen,[3,5] Troels M. Jorgensen,[2] Henri Leuvenink,[7] Rikke Norregaard,[5] Henrik Birn,[1] Niels Marcussen[8] and Bente Jespersen[1]

- Brain dead donor
- High risk of delayed graft function:
  - Long cold ischemia time (22h)
  - 65 kg donor to 15 kg recipients

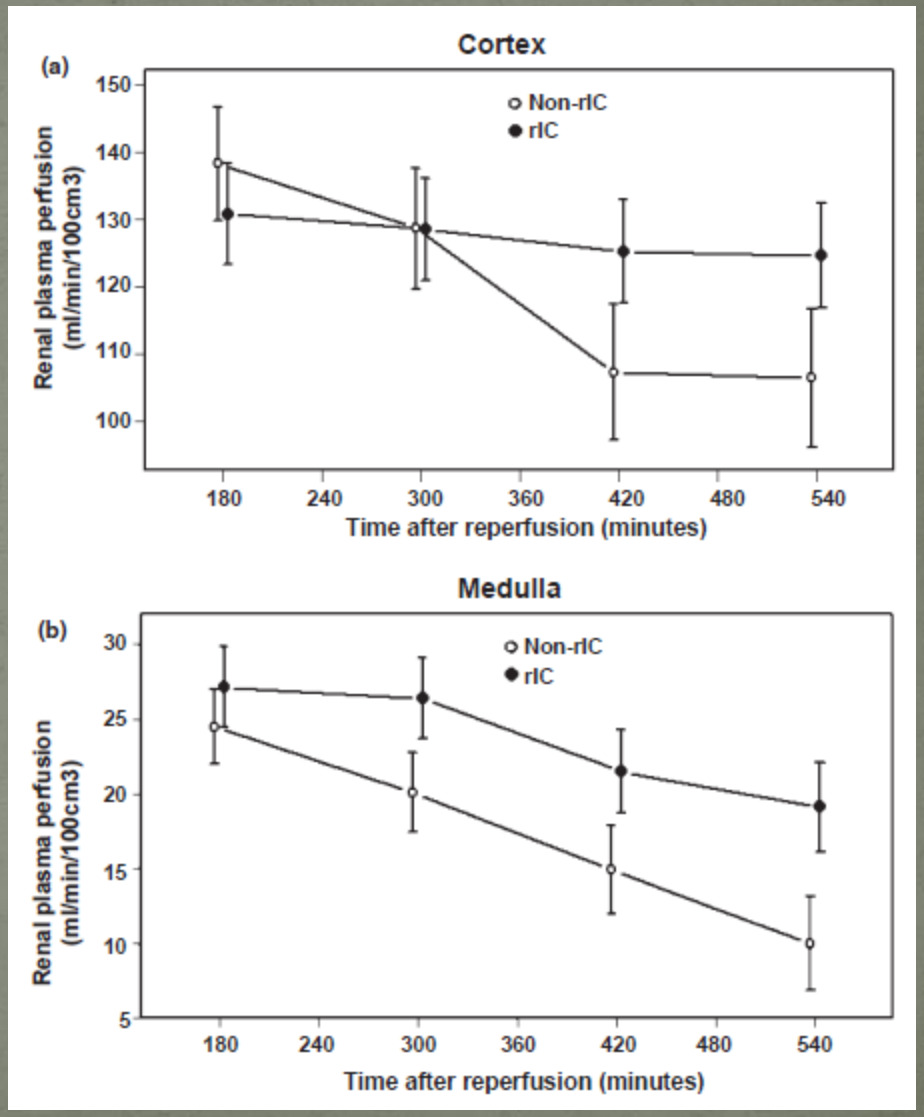


- RIC with clamping aorta

- 10 hour follow up after kidney reperfusion

RIC in a porcine DBD renal transplantation model

- Improved plasma perfusion in both cortex and medulla in RIC compared to sham
- The difference was time dependent and increased over time (p=0.001 and 0.024 respectively)

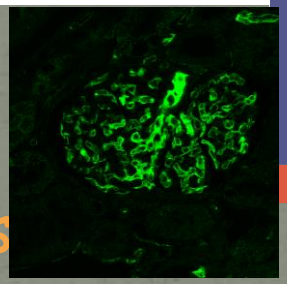


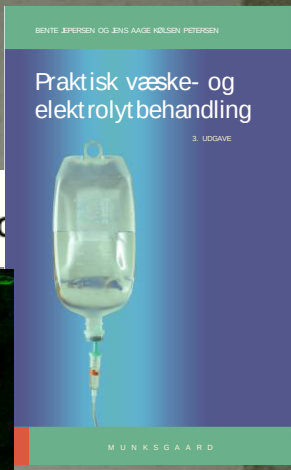
Transpl Int. 2012; 25: 1002-12

Porcine DBD renal transplantation model

- Testing drugs
- Testing fluid therapy regimens

Anesth Analg. 2019 Oct 9. d

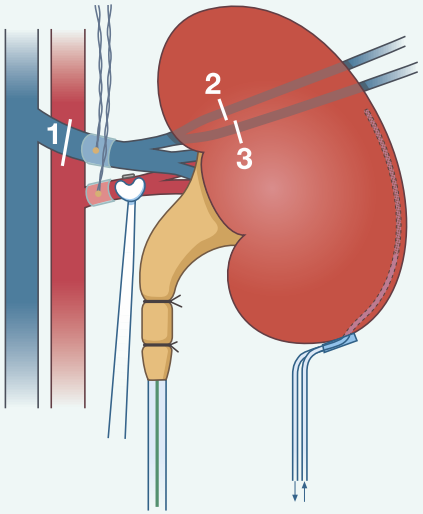




Porcine IRI and vascular occlusion models

- Testing drugs
- Testing device

Fig.1



PLOS ONE

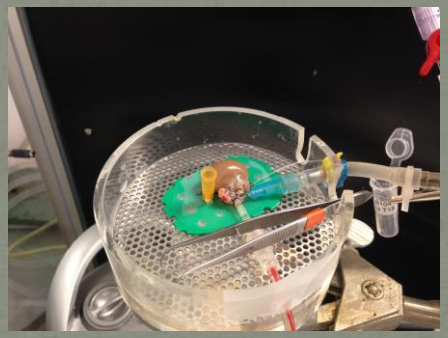
May 25, 2017

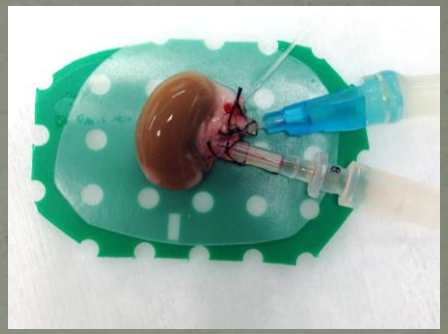
RESEARCH ARTICLE

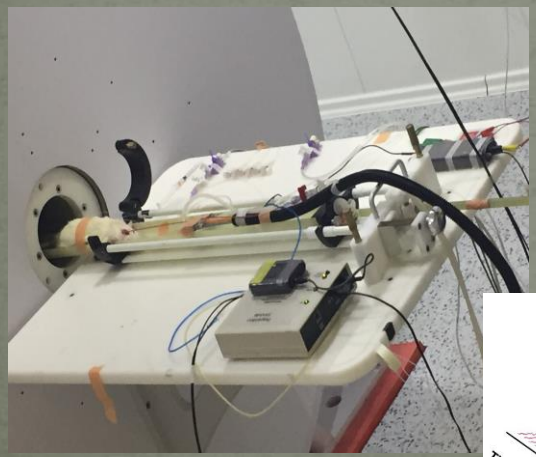
The unsuitability of implantable Doppler probes for the early detection of renal vascular complications – a porcine model for prevention of renal transplant loss

Chris Amdisen[1,2]*, Bente Jespersen[2], Ulla Møldrup[3], Anna K. Keller[3]

Organ perfusion and metabolism after experimental brain death

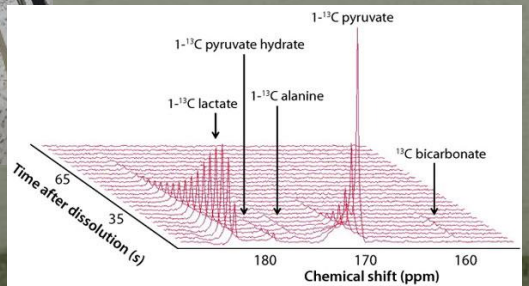






MRI:
Hyperpolarized pyruvate

Isolated perfused kidney model:
Tritiated glucose



MSC in kidney repair

- Better GFR in human renovascular hypertension

  Saad et al. J Am Soc Nephrol 2017; 28: 2777-85

STEM CELLS AND DEVELOPMENT
Volume 28, Number 18, 2019

DOI: 10.1089/scd.2019.0105

Mesenchymal Stromal Cells Are Retained in the Porcine Renal Cortex Independently of Their Metabolic State After Renal Intra-Arterial Infusion

Jesus M. Sierra-Parraga,[1,2] Anders Munk,[3] Christine Andersen,[3] Stine Lohmann,[2,3] Cyril Moers,[4] Carla C. Baan,[1] Rutger J. Ploeg,[5] Merel Pool,[4] Anna K. Keller,[2] Bjarne K. Møller,[6] Henri Leuvenink,[4] Martin J. Hoogduijn,[1] Bente Jespersen,[3] and Marco Eijken[3,6]

MSC in the renal artery

1) MSC MRI safety study

2) Fluorescent (Qtracker) MSC tracking

3) MSC survival - Y chromosome tracking

4) Effects of MSC given before transplantation

MSC safety study. Intrarenal delivery

Anders Munk

Gadolinium Perfusion MRI (DCE-MRI) after MSC infusion at T60

Controls

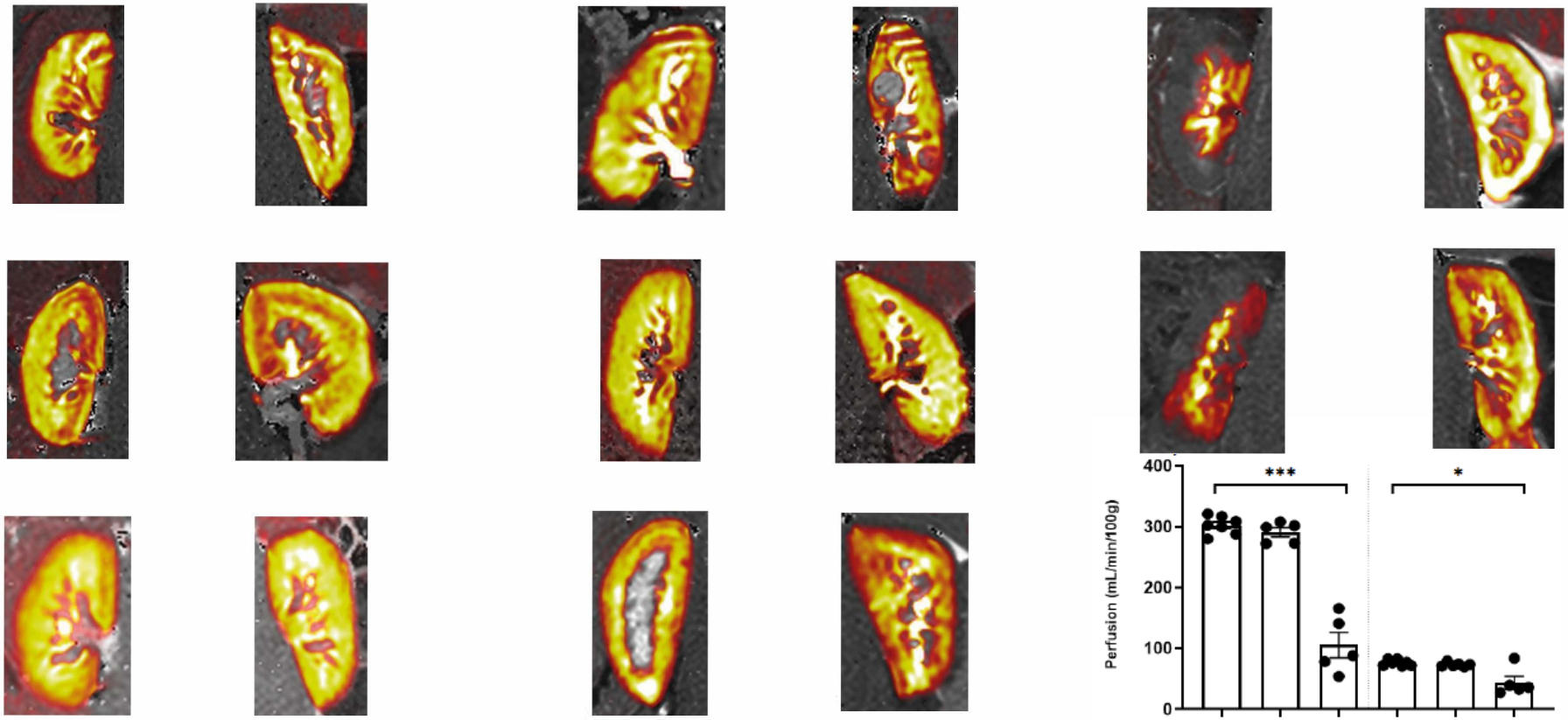
Right (treated) Left

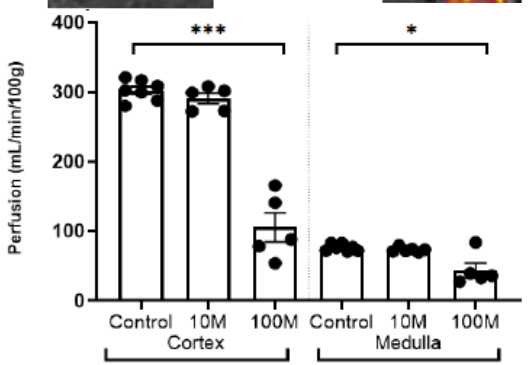
10 million MSC

Right(treated) Left

100 million MSC

Right(treated) Left





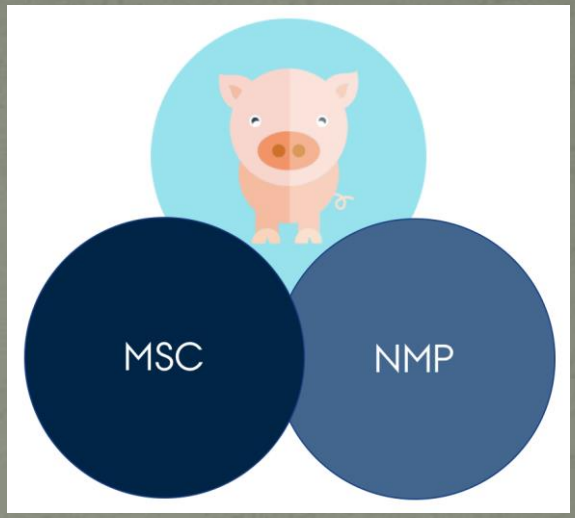
MePEP

LUNDBECKFONDEN

Kidney transplant regeneration with MEsenchymal stem cells in normothermic ex-situ PErfusion in Pigs

Rotterdam, Groningen, Oxford and Aarhus

MePEP



Female pigs autotransplanted

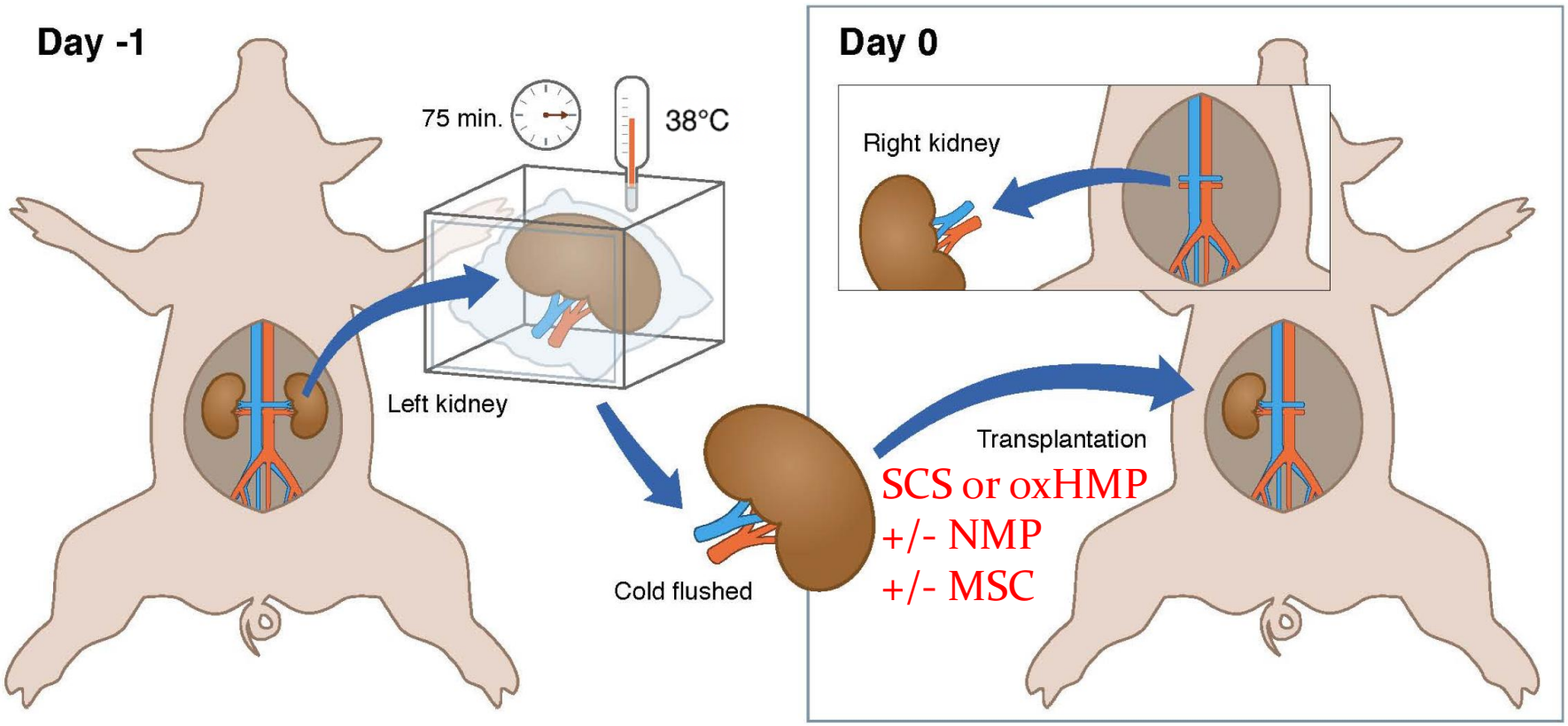
75 min WIT + 16 h CSS or oxygenated HMP +/- NMP

10 m male MSC

14 days survival model

Donation after circulatory death autotransplantation model

Surgical procedure



MePEP

Kidney transplant regeneration with MEsenchymal stem cells in normothermic ex-situ PErfusion in Pigs

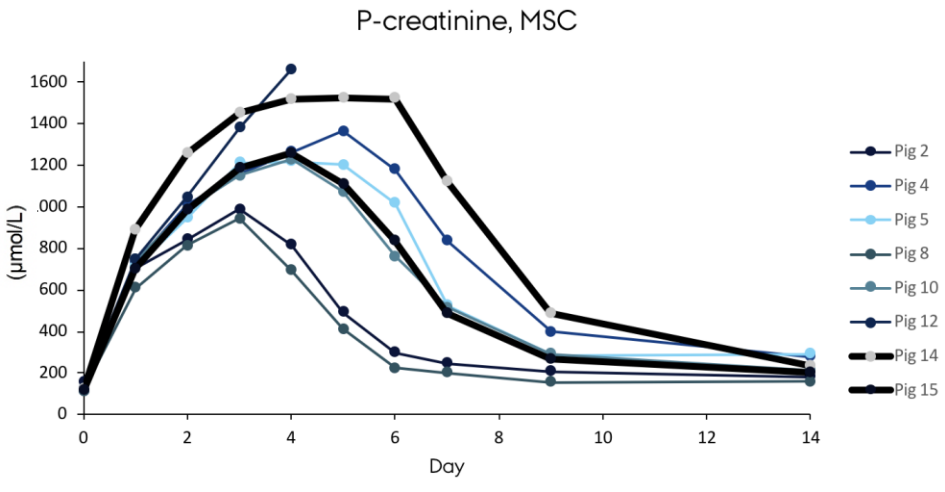
Autotransplantation with 14 days survival

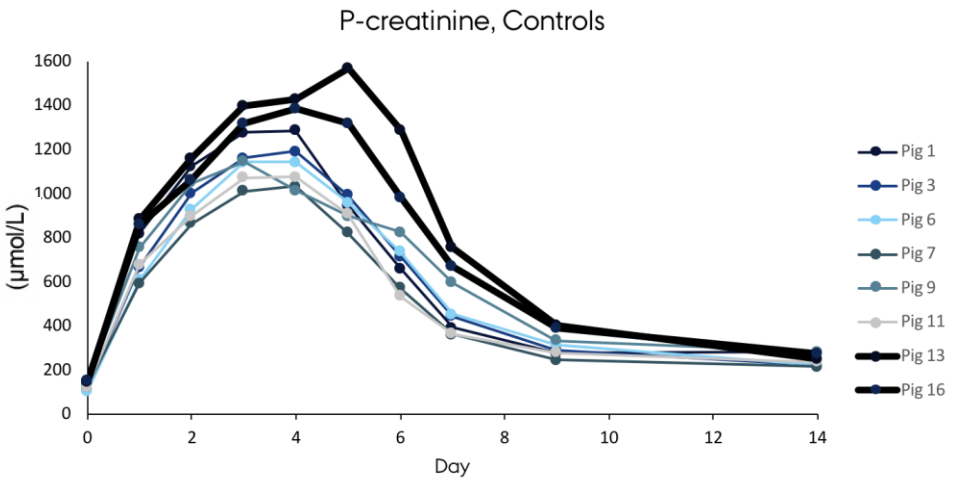
Stine Lohmann

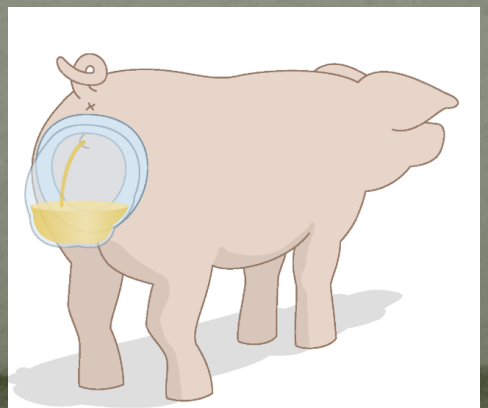
Anna Keller

Marco Eijken

Autotransplantation with 14 days survival

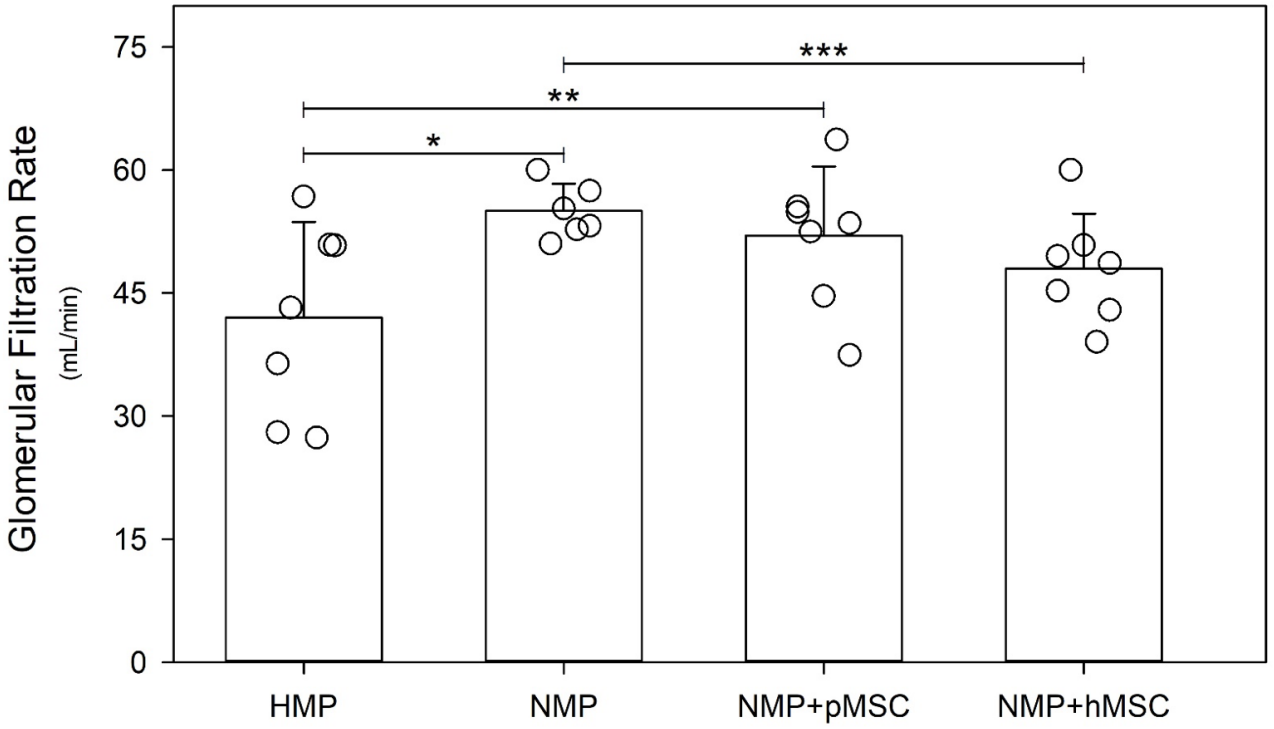






Autotransplantation model – at 14 days

MEASURED GFR



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