

# Dual hypothermic machine perfusion mitigates early allograft injury regardless of prolonged cold ischemia times: A study with propensity score matching analysis

## Introduction

In consensus with worldwide shortage of suitable grafts for transplantation, centers need to extend the donor acceptance criteria.

To preserve the safety of the procedure, we have implemented a dual hypothermic machine perfusion program (DHOPE), which in some cases led to a significantly prolonged total cold preservation time (CPT) of liver grafts.

The aim of our study was to assess the extent and compare the difference in ischemia-reperfusion injury (IRI) between DHOPE- treated and conventionally stored liver grafts

## Financial support

This study was supported by an institutional grant of Center of Cardiovascular and Transplant Surgery, Brno, Czechia No.24001.



MUNI  
MED

Kolárik M, Oliverius M, Němec P

# Dual hypothermic machine perfusion mitigates early allograft injury regardless of prolonged cold ischemia times: A study with propensity score matching analysis

## Methods

### Prospective part

– 20 pairs (12 DHOPE, 9 SCS) of biopsies (post-procurement and post-reperfusion) were analyzed for signs of IRI

### Retrospective part

– a propensity score-matched control group (SCS) was created from historical cohort to analyze the postoperative outcomes

## Endpoints

- mortality/reLTx in first 30 days – primary
- EAD, CD  $\geq$  grade 3 complications, POD 7 laboratory values (ALT, AST, bilirubin) - secondary

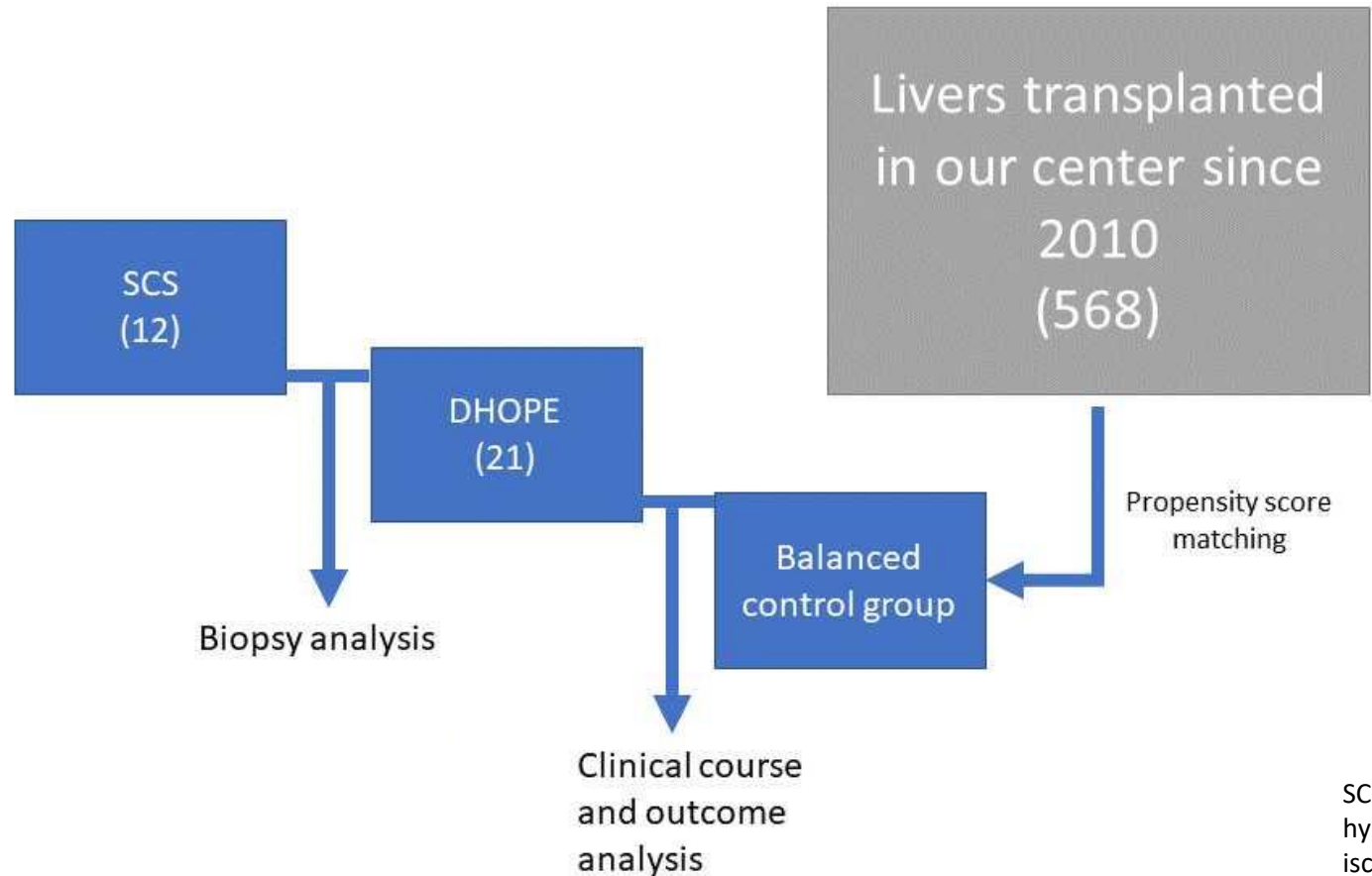
DHOPE – dual hypothermic oxygenated perfusion; SCS – static cold storage; reLTx – re-transplantation of the liver; EAD - early allograft dysfunction; CD – Clavien-Dindo classification; POD – postoperative day



MUNI  
MED

Kolárik M, Oliverius M, Němec P

# Dual hypothermic machine perfusion mitigates early allograft injury regardless of prolonged cold ischemia times: A study with propensity score matching analysis



# Dual hypothermic machine perfusion mitigates early allograft injury regardless of prolonged cold ischemia times: A study with propensity score matching analysis

## Demographic variables

variable	DHOPE (n=21)	SCS prospective (n=12)	SCS retrospective (n=84)
<b>ECD</b>	14 (66,66 %)	5 (41,66 %)	36 (42,85 %)
<b>Recipient MELD</b>	16 (9 – 29)	19,5 (7 - 27)	15,5 (7 – 32)
<b>Recipient age</b>	55 (32 – 68)	47 (44 – 65)	57 (20 – 69)

## Storage variables

	DHOPE (n=21)	SCS prospective (n=12)	SCS retrospective (n=84)	P value
<b>SCS (min)</b>	165 (30 - 400)	279,5 (194 – 478)	352 (150 - 834)	<b>&lt;0,0001</b>
<b>DHOPE</b>	385 (200 - 600)	-	-	-
<b>TCP</b>	618 (268 – 830)	279,5 (194 – 478)	352 (150 – 834)	<b>&lt;0,001</b>

All values presented as: absolute value (percentage) or: median (min – max)  
 SCS – static cold storage; ECD - extended criteria donor; MELD - model of end-stage liver disease;  
 DHOPE dual hypothermic oxygenated perfusion; TCP – total cold preservation time





# Dual hypothermic machine perfusion mitigates early allograft injury regardless of prolonged cold ischemia times: A study with propensity score matching analysis

## Biopsy analysis

- 20 biopsy pairs were evaluated
- no significant difference in IRI between two groups

N=29	DHOPE (n=17)	SCS (n=12)	P value
No. of valid	11 (64,7 %)	9 (75,0 %)	-
Suzuki score T <sub>0</sub> (0 - 12)	1 (0 - 5)	1 (0 - 2)	0,823
Suzuki score T <sub>1</sub> (0 - 12)	4 (0 - 7)	3 (1 - 4)	0,551
Suzuki score $\Delta$	2 (0 - 6)	2 (1 - 3)	0,655
IRI score T <sub>0</sub> (0 - 24)	3 (0 - 6)	3 (1 - 5)	0,710
IRI score T <sub>1</sub> (0 - 24)	5 (2 - 12)	7 (6 - 9)	0,260
IRI score $\Delta$	2 (0 - 8)	4 (3 - 6)	0,151

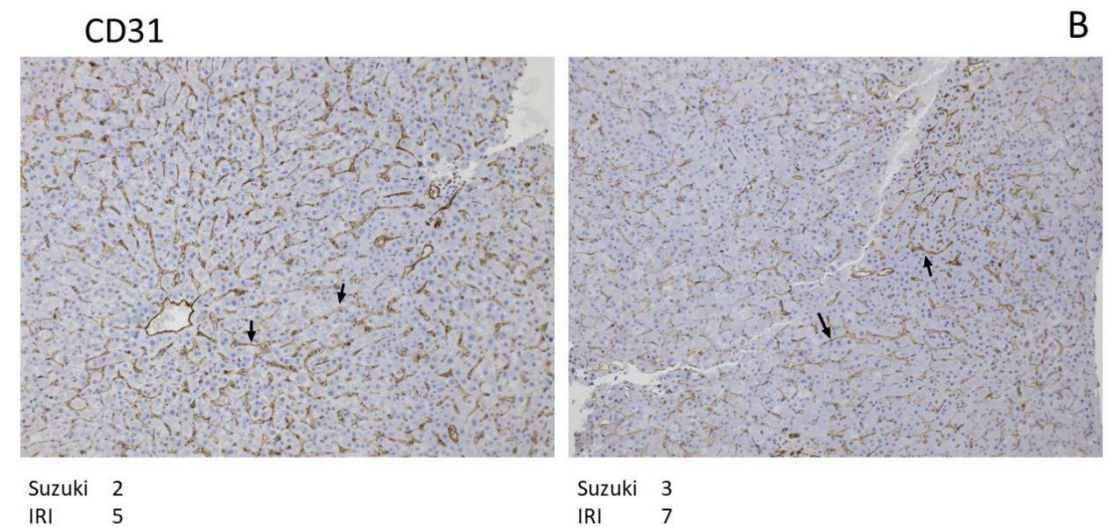
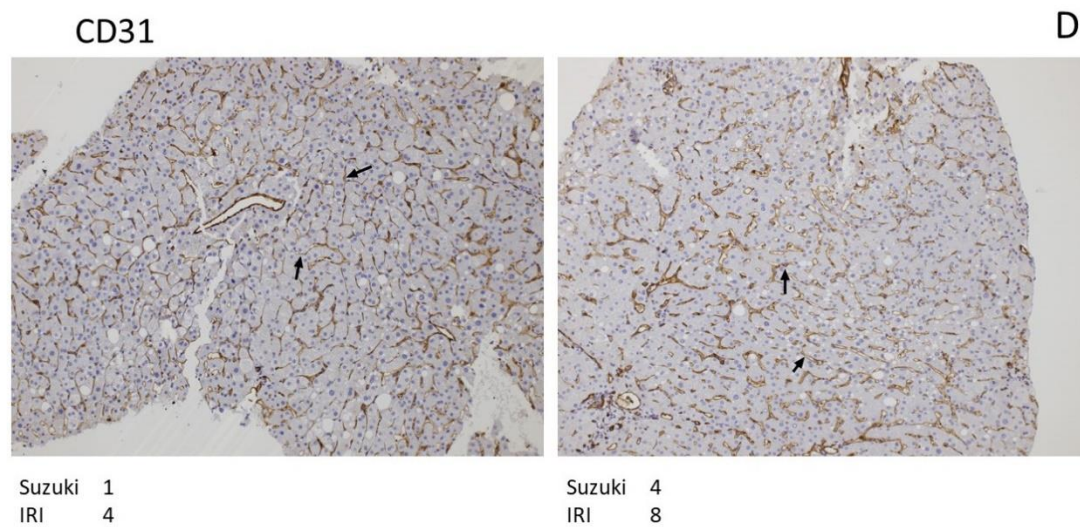
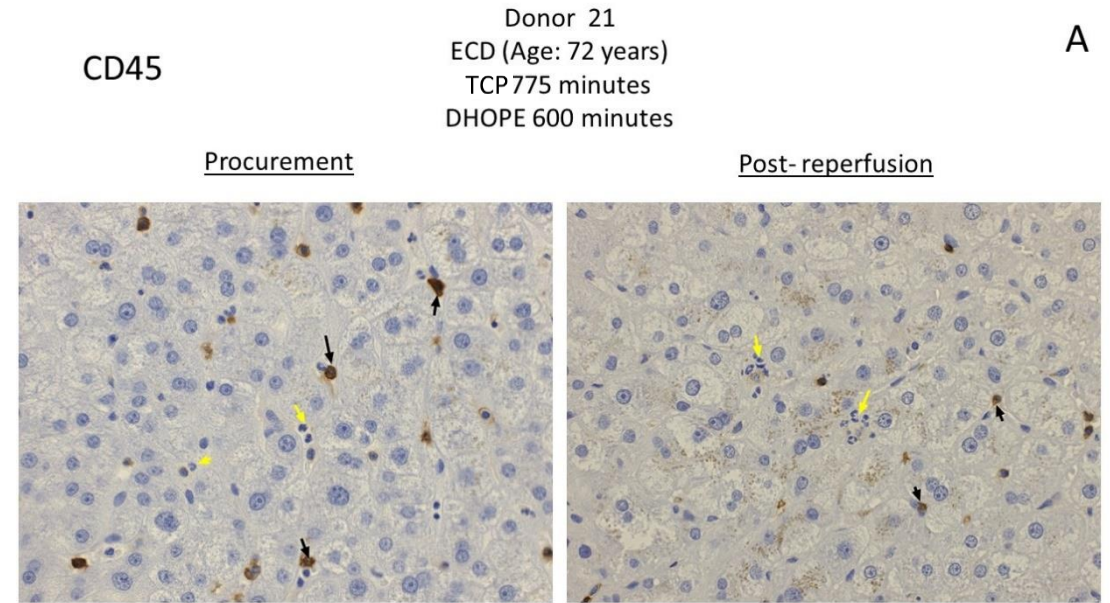
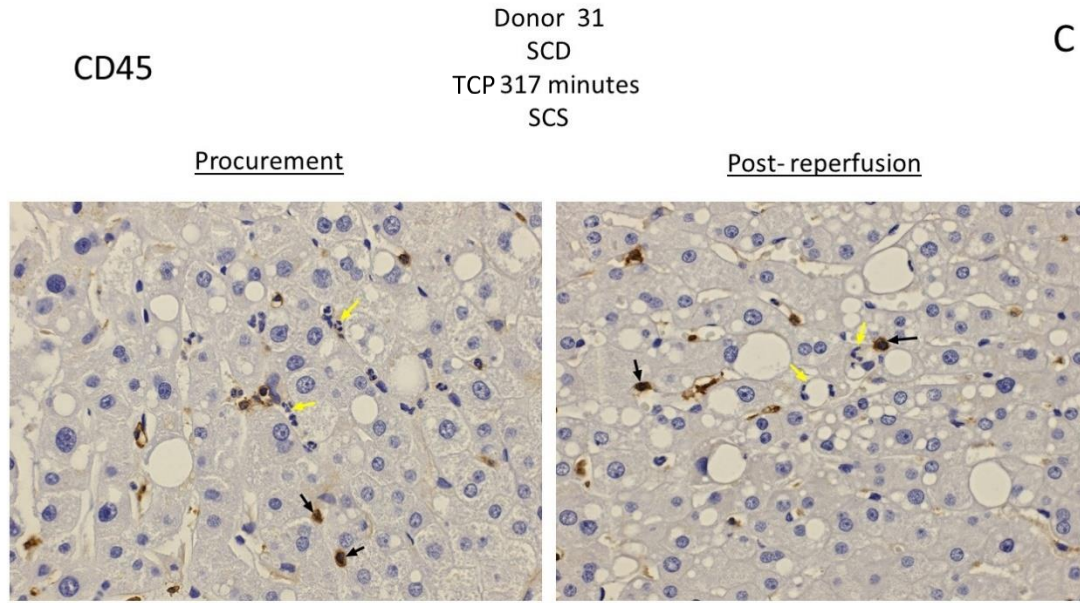
T<sub>0</sub> – biopsy taken immediately after procurement;  
T<sub>1</sub> – biopsy taken after complete graft reperfusion



MUNI  
MED

Kolárik M, Oliverius M, Němec P





Immunohistological examination of acquired procurement and post-reperfusion biopsy with immunohistologic stain anti-CD45 (panels A and C) and anti-CD31 (panels B and D). CD45 stain visualizes monocytes (black arrows), intrasinusoidal neutrophil reaction (yellow arrows), more pronounced around regressive hepatocytes, including steatotic ones. CD31 visualizes the endothelia of vessels including hepatic sinuses and more accurately shows the presence/absence of sinusoidal dilation and congestion (black arrows).

SCD – standard criteria graft; ECD – extended criteria graft; TCP – total cold preservation time; SCS – static cold storage; DHOPE – dual hypothermic oxygenated perfusion; Suzuki – Suzuki score; IRI – ischemia-reperfusion score



# Dual hypothermic machine perfusion mitigates early allograft injury regardless of prolonged cold ischemia times: A study with propensity score matching analysis

## Propensity score matching analysis

- no significant difference in primary outcome measures

- no significant difference in EAD rate, CD  $\geq$  grade 3

- lower ALT and bilirubin on POD 7 in the DHOPE group

variable	DHOPE (n=21)	SCS retrospective (n=84)	P value
AST day 0 ( $\mu$ kat/l)	9,39 (2,04 - 25,34)	10,82 (0,91 - 233,5)	0,217
AST day 7 ( $\mu$ kat/l)	0,45 (0,15 - 2,12)	0,68 (0,13 - 128,25)	0,072
ALT day 0 ( $\mu$ kat/l)	6,27 (2,17 - 16,55)	7,08 (0,95 - 124,51)	0,217
ALT day 7 ( $\mu$ kat/l)	1,3 (0,44 - 5,85)	2,06 (0,23 - 50,83)	<b>0,048</b>
Bilirubin day 0 ( $\mu$ mol/l)	45,6 (12,7 - 296,6)	53,55 (11,1 - 240,5)	0,965
Bilirubin day 7 ( $\mu$ mol/l)	12,7 (1,61 - 77,8)	21,45 (5,8 - 157,1)	<b>0,048</b>
EAD	0	14 (16,66 %)	0,067
CD gr $\geq$ 3	6 (28,57 %)	23 (27,38 %)	1
30-day mortality	1 (4,47 %)	2 (2,38 %)	0,791
30-day ReLTx	1 (4,47 %)	0	0,933
Length of stay	19 (11 - 60)	19 (7 - 101)	0,870

DHOPE – dual hypothermic oxygenated perfusion; SCS – static cold storage; EAD - early allograft dysfunction; CD gr $\geq$ 3 - Clavien-Dindo grade 3 or higher; ReLTx – retransplantation of the liver; POD – postoperative day

# Dual hypothermic machine perfusion mitigates early allograft injury regardless of prolonged cold ischemia times: A study with propensity score matching analysis

## Conclusion

DHOPE is a vital method, facilitating the preservation of liver grafts in clinical settings. We have proved its use diminishes the adverse effect of prolonged cold ischemia time on early postoperative results. In scenarios where a long cold preservation time is needed the method helps to safely postpone the surgery without risk of severe injury to the graft.



There were no differences in histological signs of IRI between groups.



There were no differences in survival or postoperative complications. DHOPE had significantly lower ALT and bilirubin on postoperative day 7.



MUNI  
MED

Kolárik M, Oliverius M, Němec P