

# Experimentální chirurgie a klinicky relevantní výzkum

Václav Liška

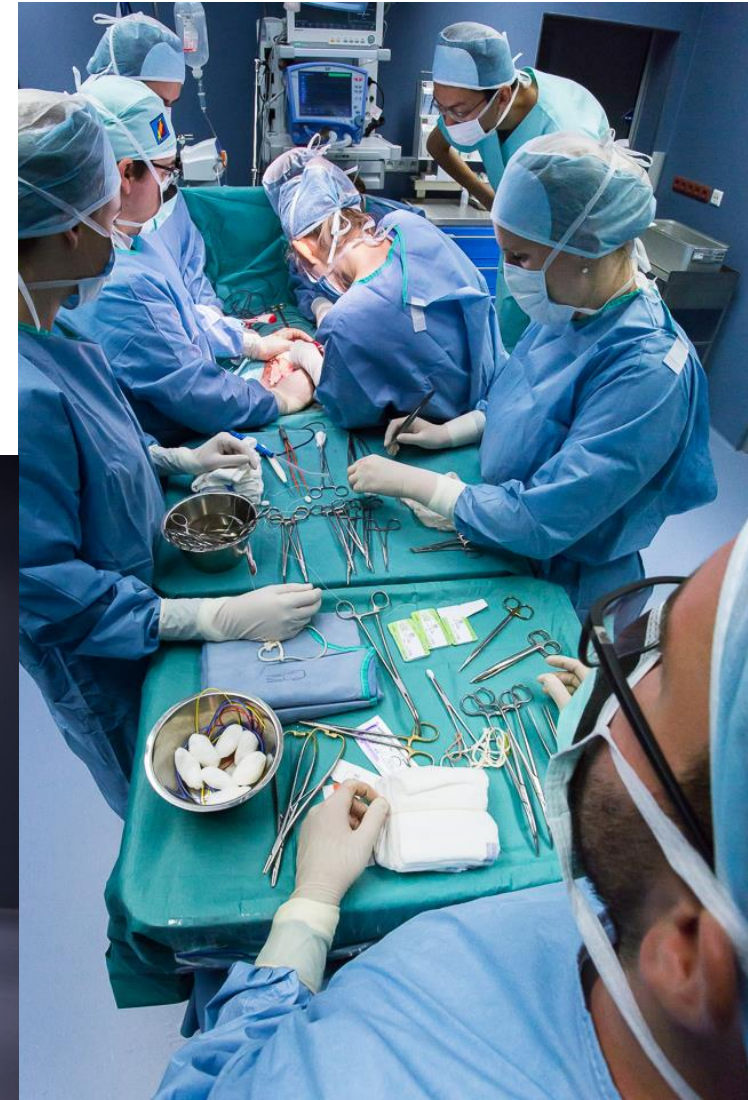
Biomedicínské centrum a Chirurgická klinika

Lékařská fakulta University Karlovy Plzeň

# Basics of education and professional growth

- Knowledge
- Experience
- Skills

# Large animal experimental facilities



# Allogeneic venous grafts used for portal vein reconstruction after pancreaticoduodenectomy in pig



LÉKAŘSKÁ FAKULTA  
V PLZNI  
Univerzita Karlova



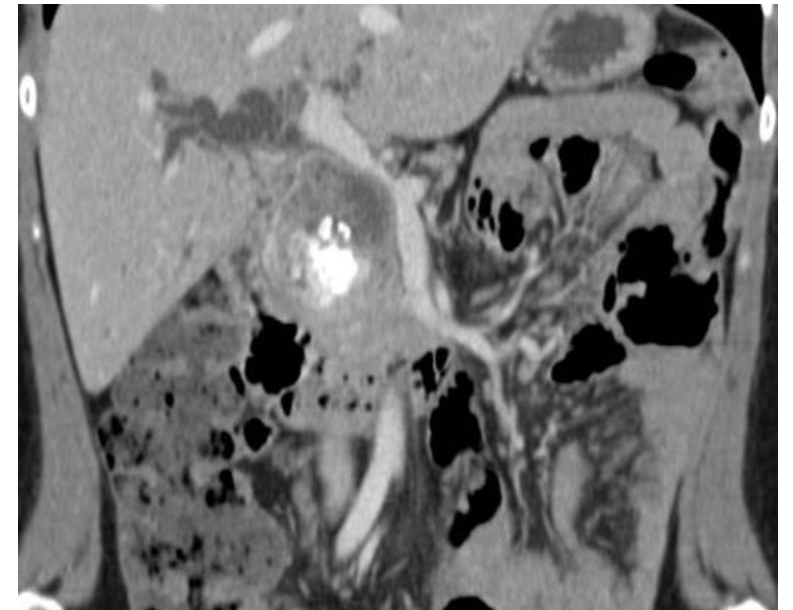
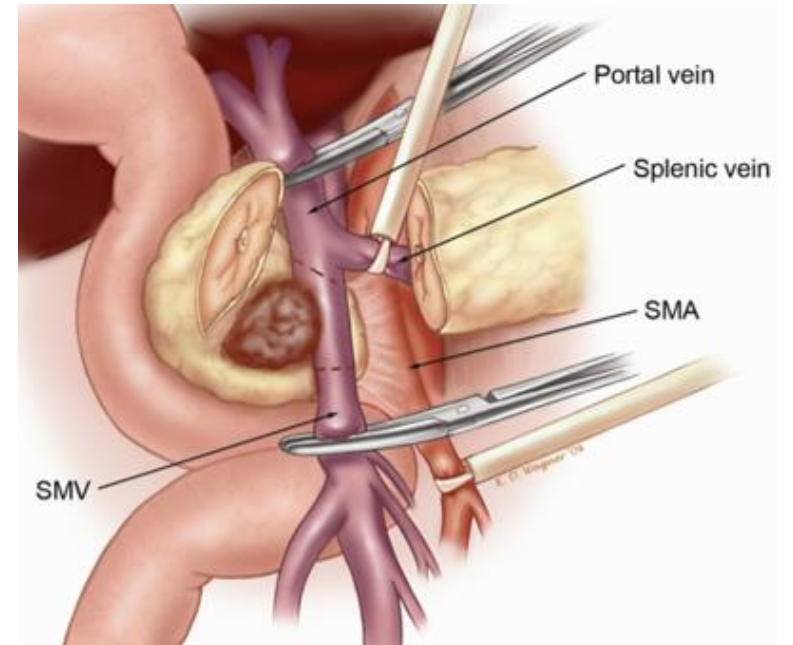


# Pancreatic cancer

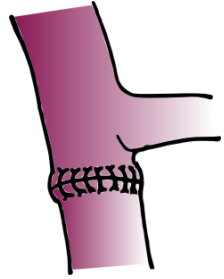
- Surgical treatment – the only potentially curative therapy
  - Late diagnosis
- ↓
- Venous infiltration  
(portal vein – PV, superior mesenteric vein – SMV)



- **Resection of infiltrated vein together with the tumour**

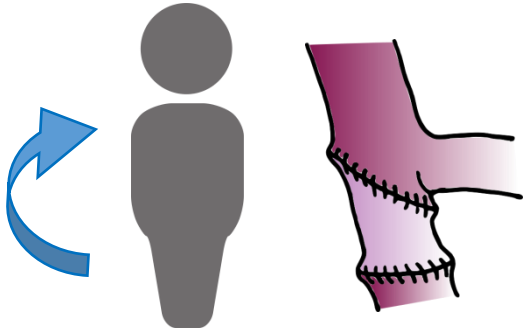


# Portal vein reconstruction



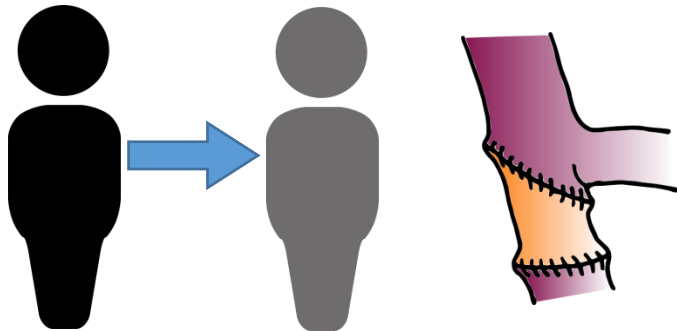
## Primary anastomosis

- short segment resections



## Autologous venous graft

- not always available, complications after harvesting

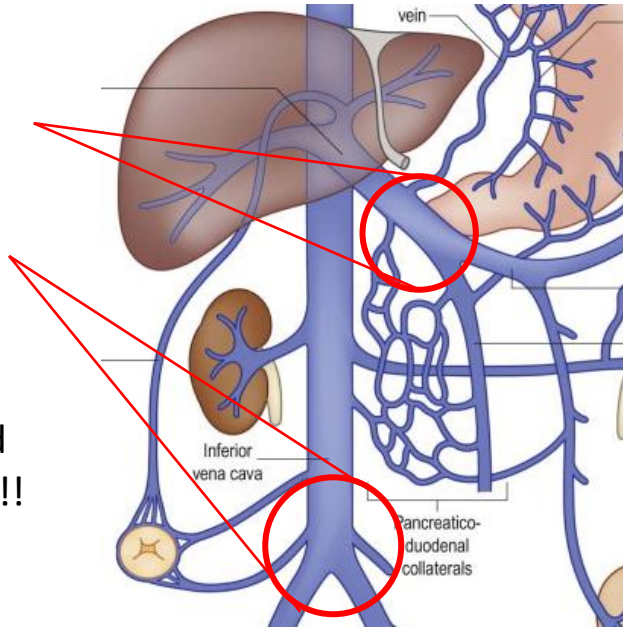


## Allogeneic venous graft?

- minimal clinical experience

## Possible origin of allogeneic grafts:

- **portal venous system**  
(portal vein)
- **caval venous system**  
(vena cava, iliac veins)
- different pressure and circulation physiology!!

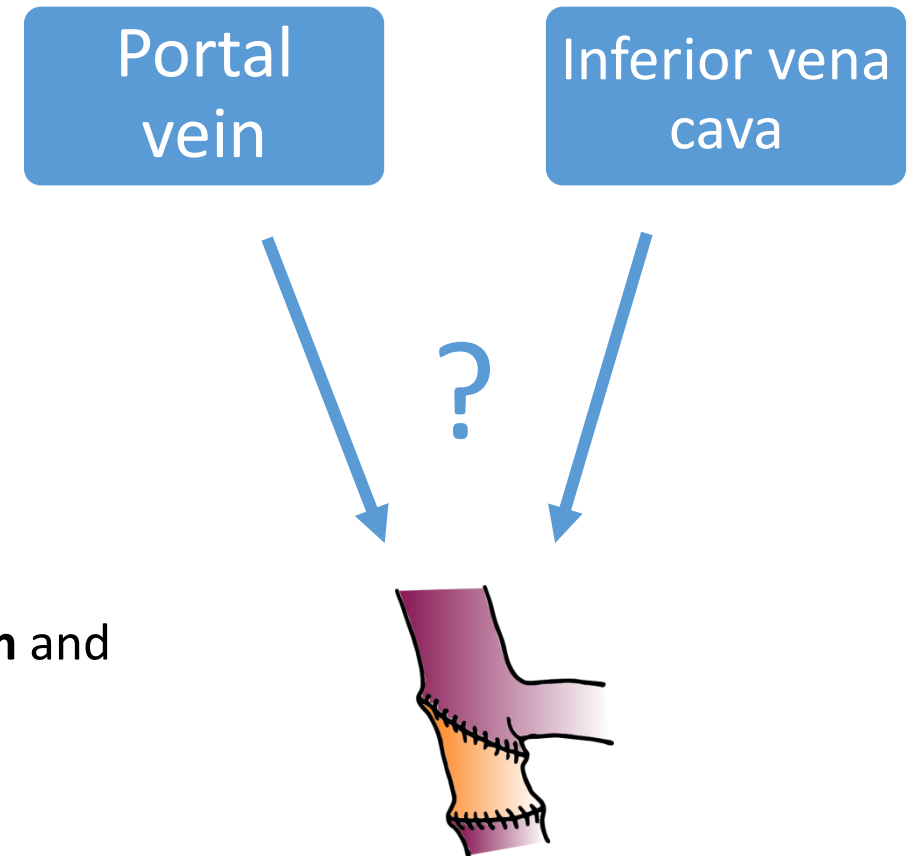


## Different characteristics of PV and ICV wall?

- Has not been studied in human / pig
- Type of the graft could influence the behaviour of the portal system?

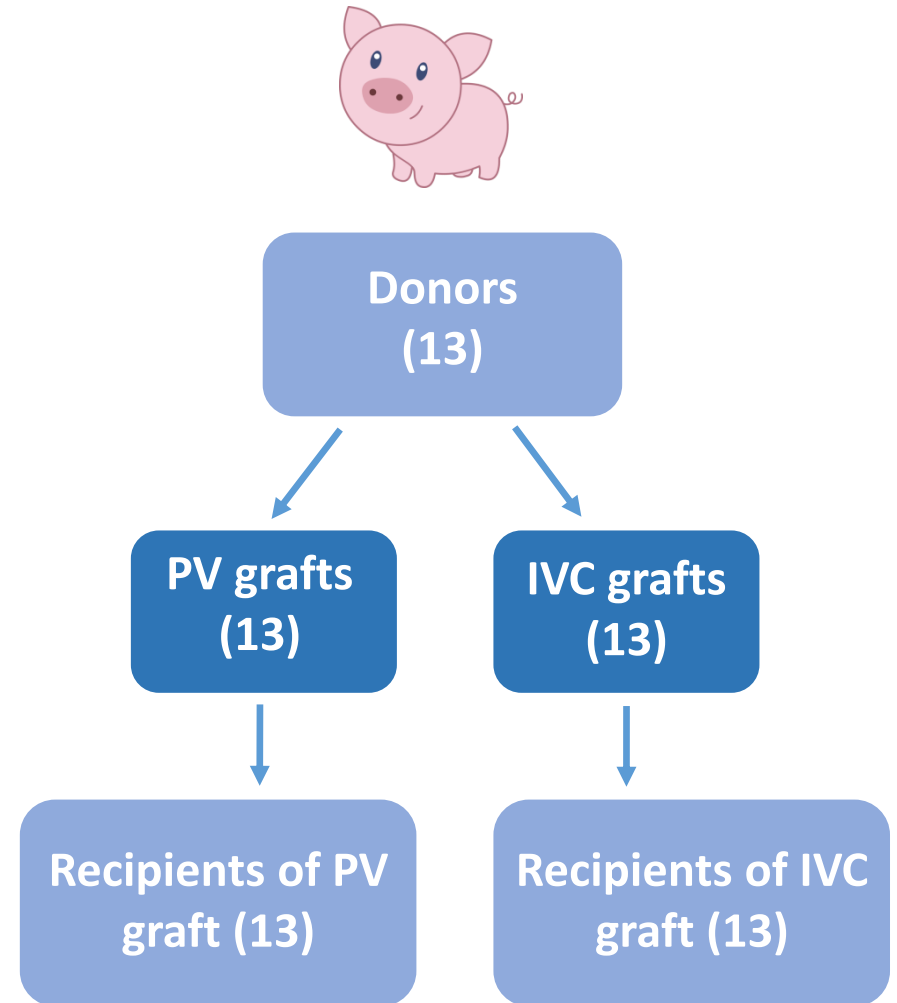
## Aim of the study:

- Compare the allogeneic grafts originating in **portal system** and **caval system** to verify their suitability for portal vein reconstruction after pancreaticoduodenectomy (PD)



# Structure of experiment

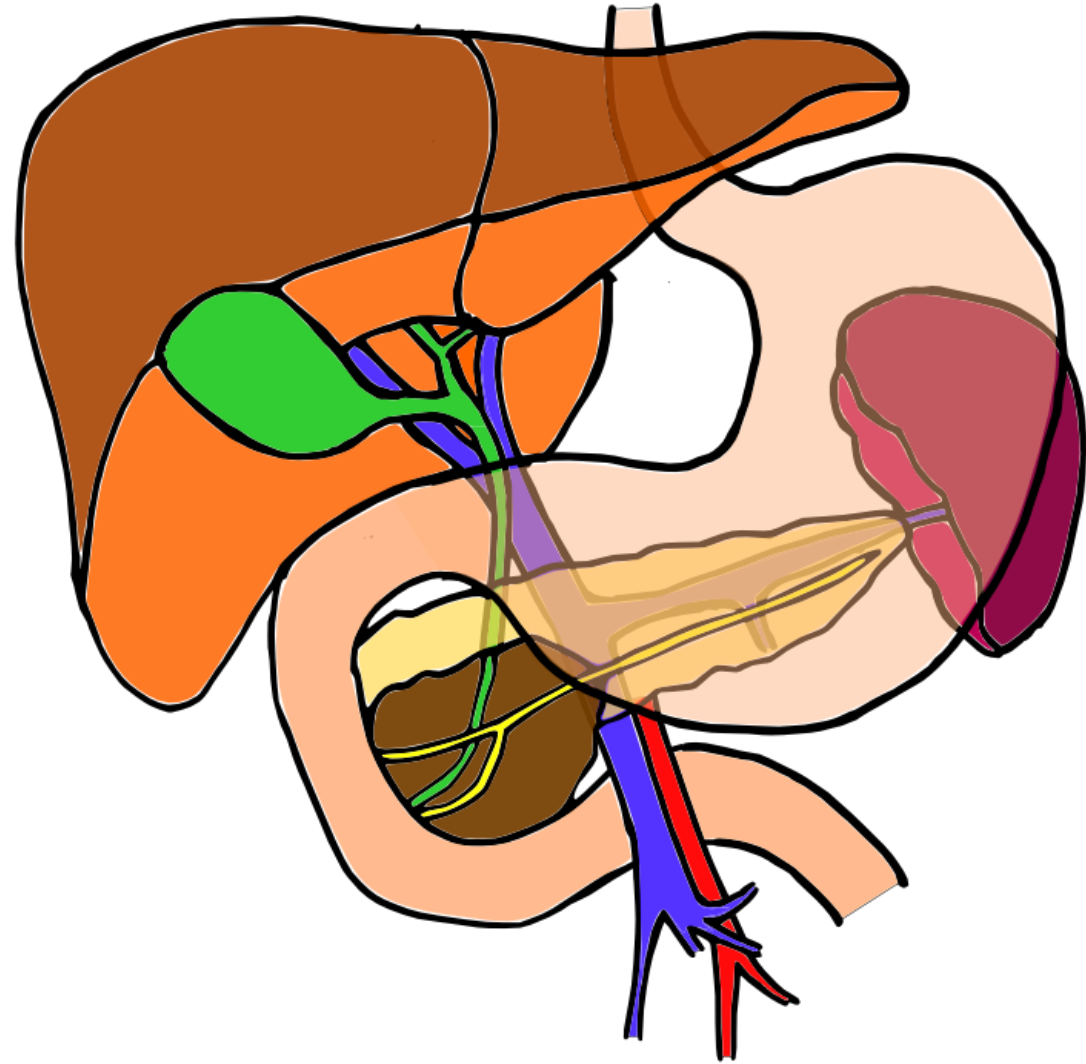
- Prestice black pied pig (25 – 35 kg)
  - 39 animals altogether (13 donors, 26 acceptors)
  - blood cross-matching test
1. Donor piglets (13) – harvesting of venous grafts
  2. Acceptor piglets (26) – pancreaticoduodenectomy with portal vein reconstruction





Methods II.

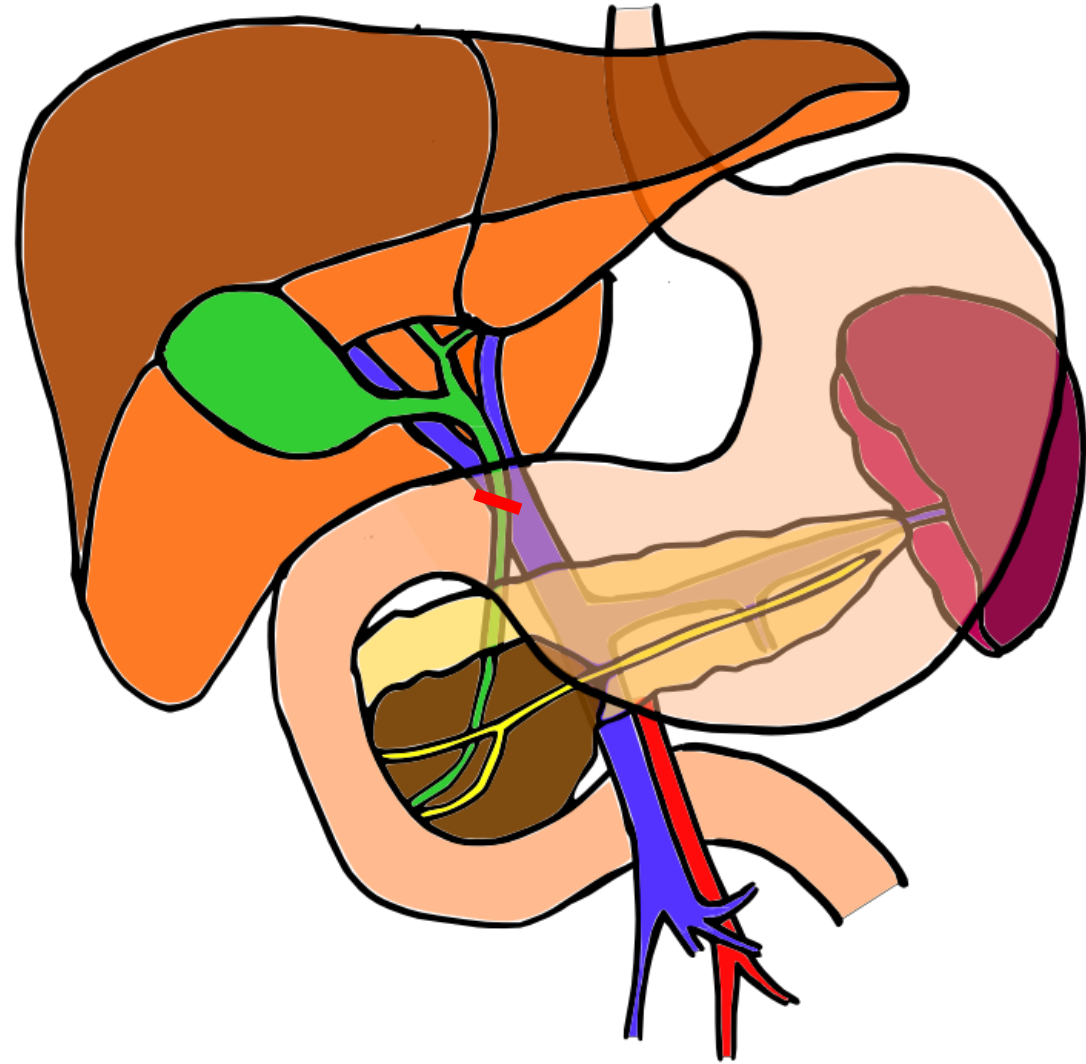
## Pancreaticoduodenectomy



Methods II.

## Pancreaticoduodenectomy

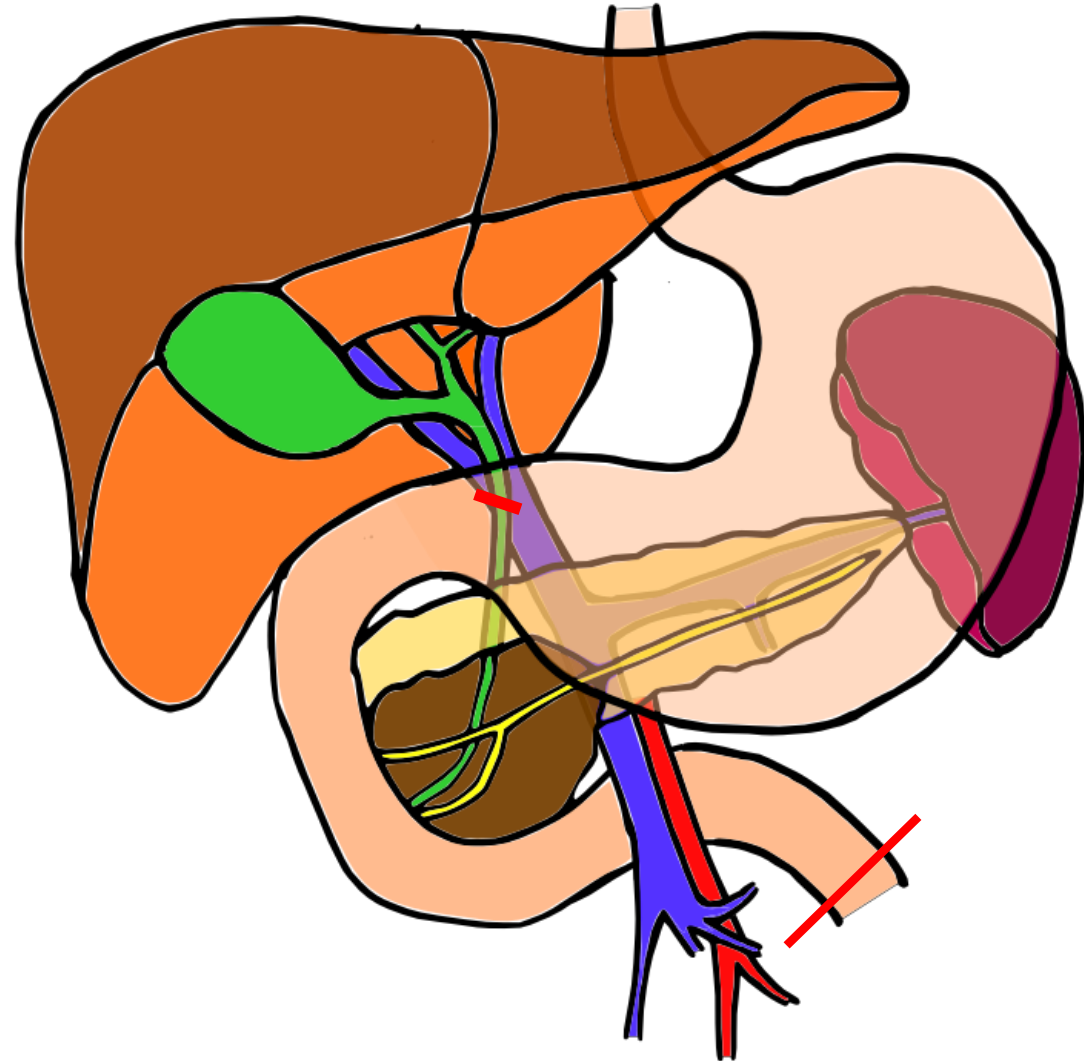
- Transection of common bile duct



Methods II.

## Pancreaticoduodenectomy

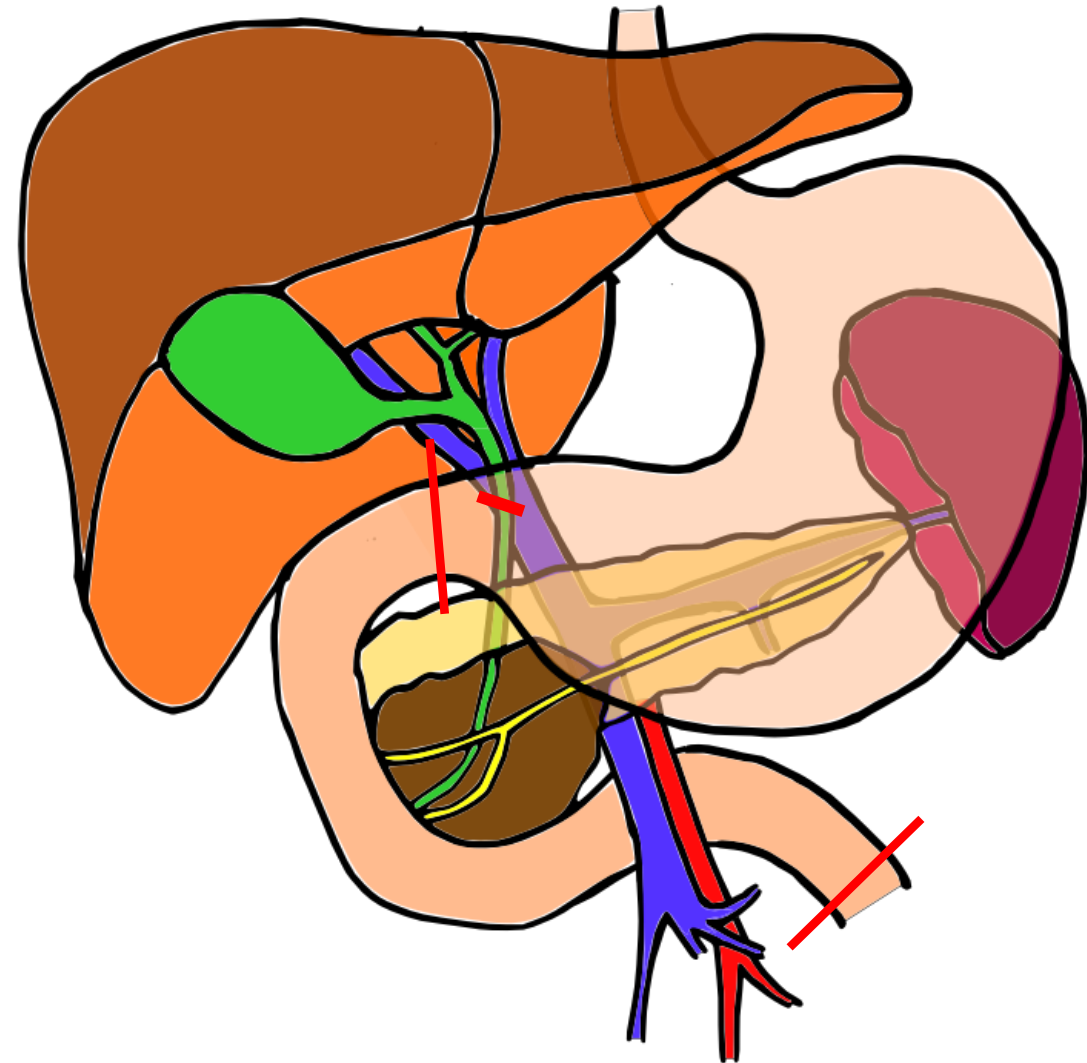
- Transection of common bile duct
- Transection of proximal jejunum



Methods II.

## Pancreaticoduodenectomy

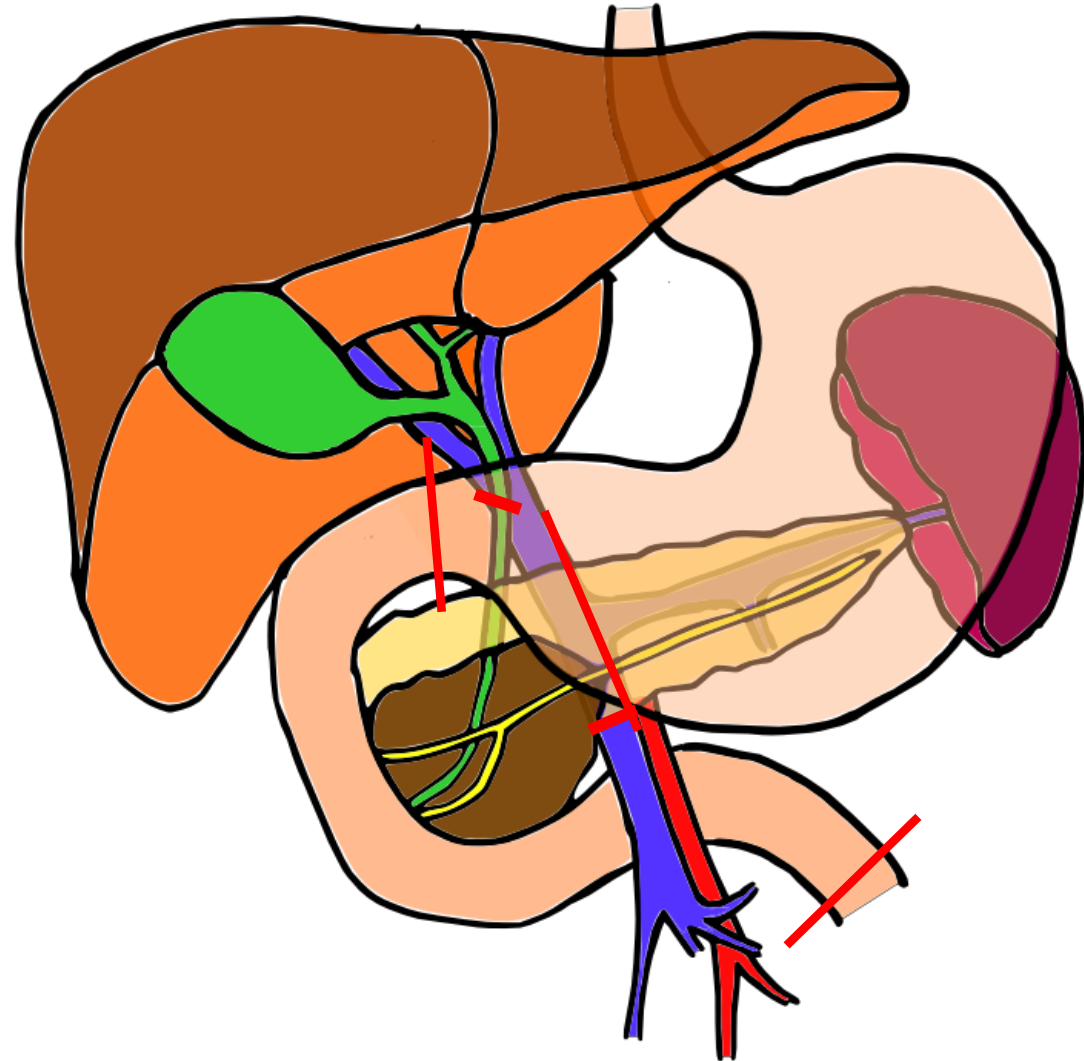
- Transection of common bile duct
- Transection of proximal jejunum
- Transection of duodenum right beyond the pylorus



Methods II.

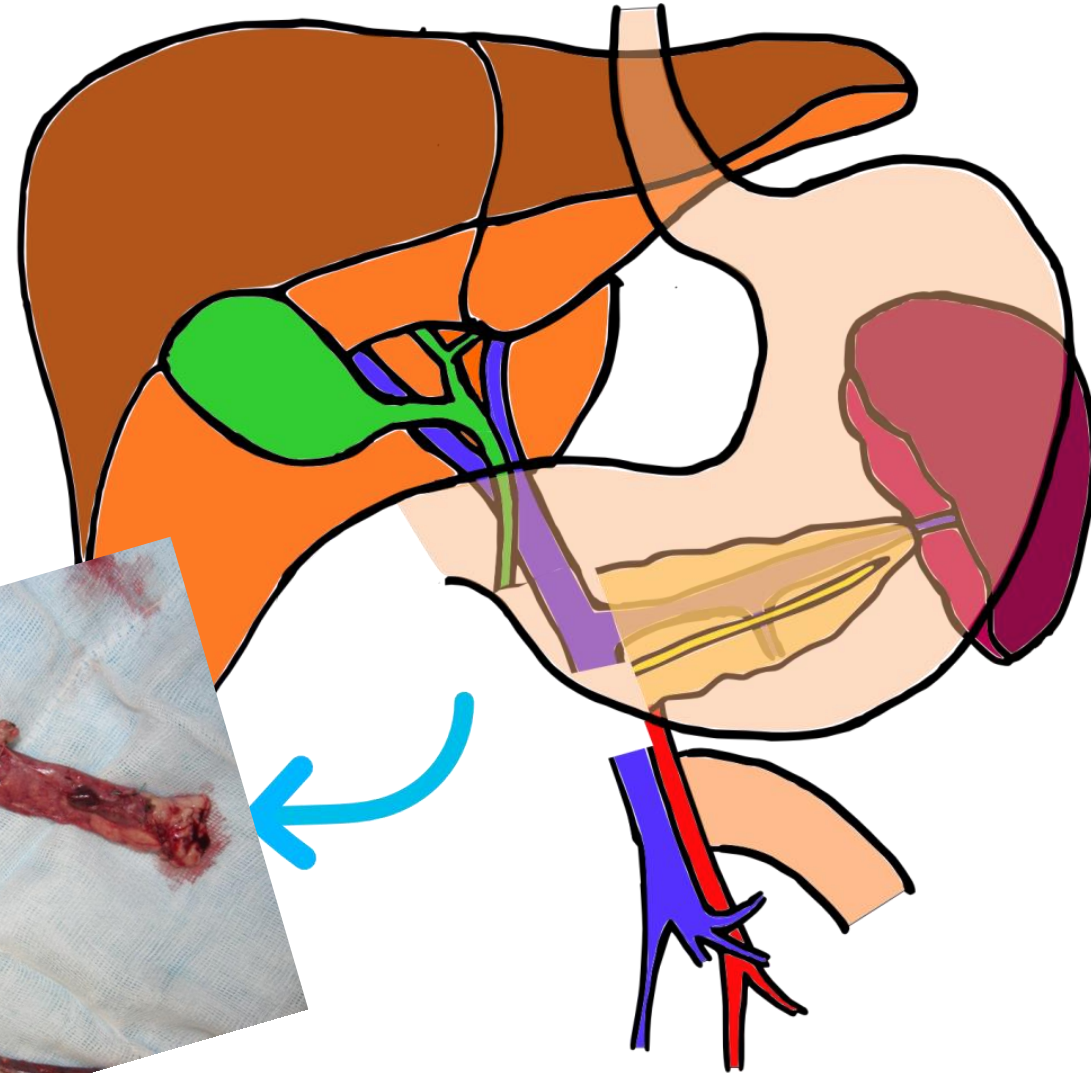
## Pancreaticoduodenectomy

- Transection of common bile duct
- Transection of proximal jejunum
- Transection of duodenum right beyond the pylorus
- Resection of pancreatic head with tumor, part of portal vein and duodenum



## Pancreaticoduodenectomy

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- Transection of proximal jejunum
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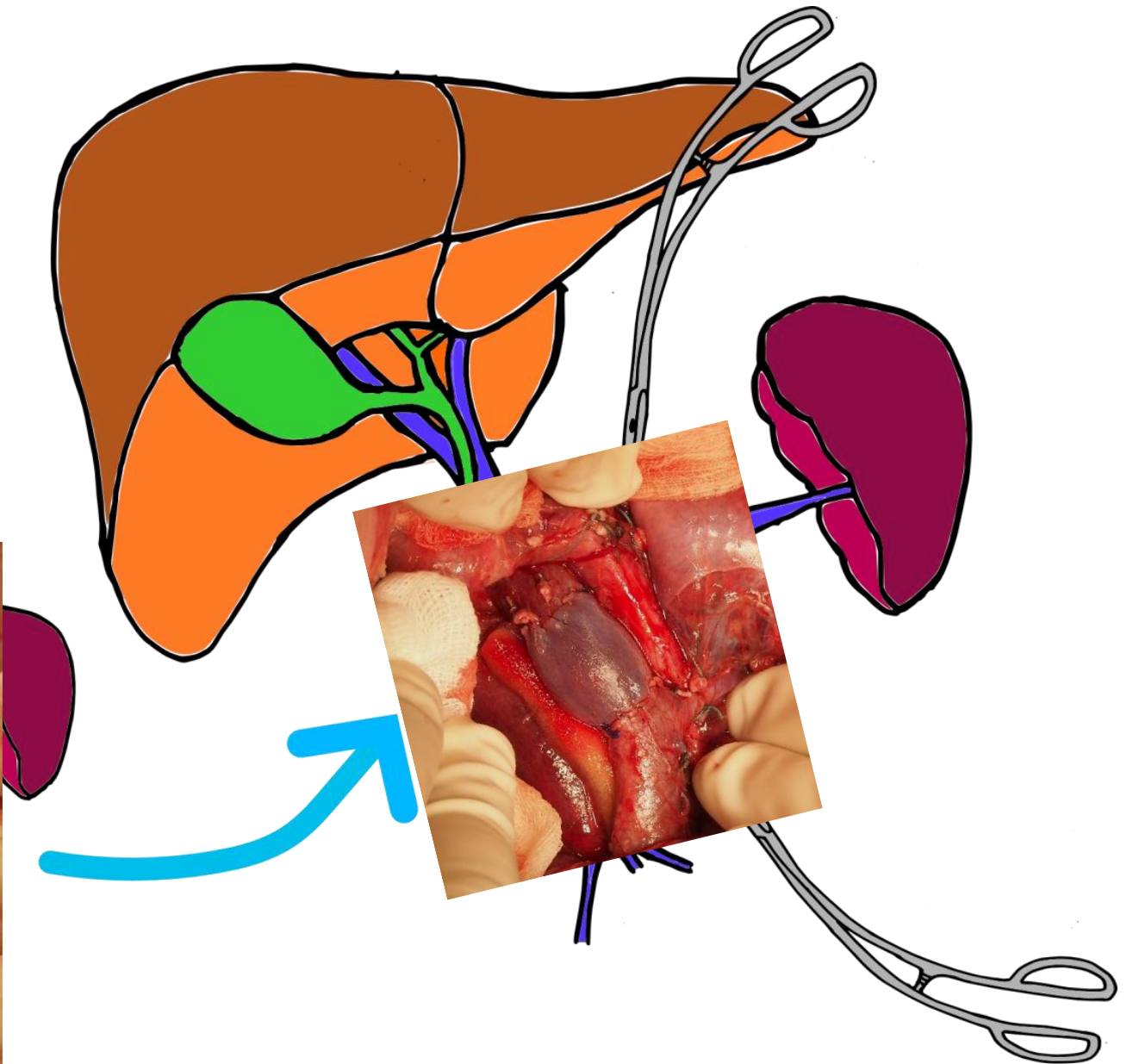
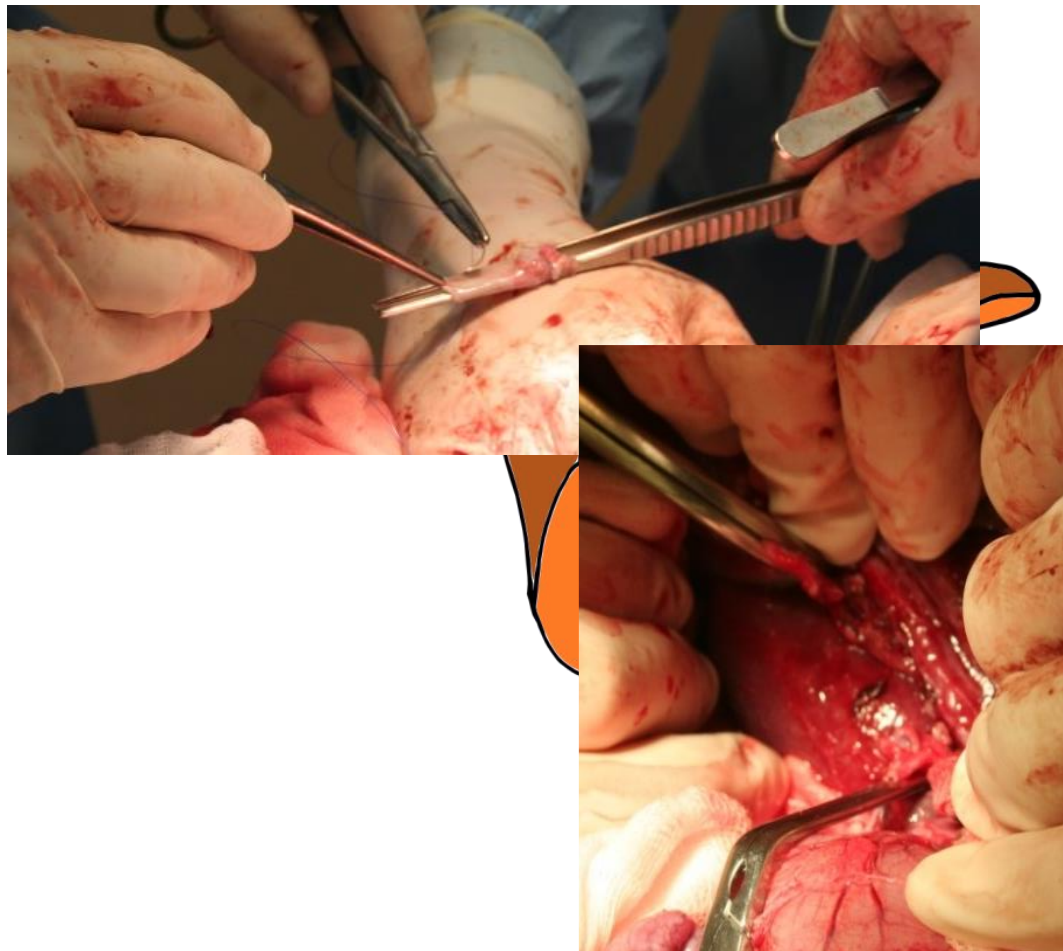




Methods II.

## Pancreaticoduodenectomy

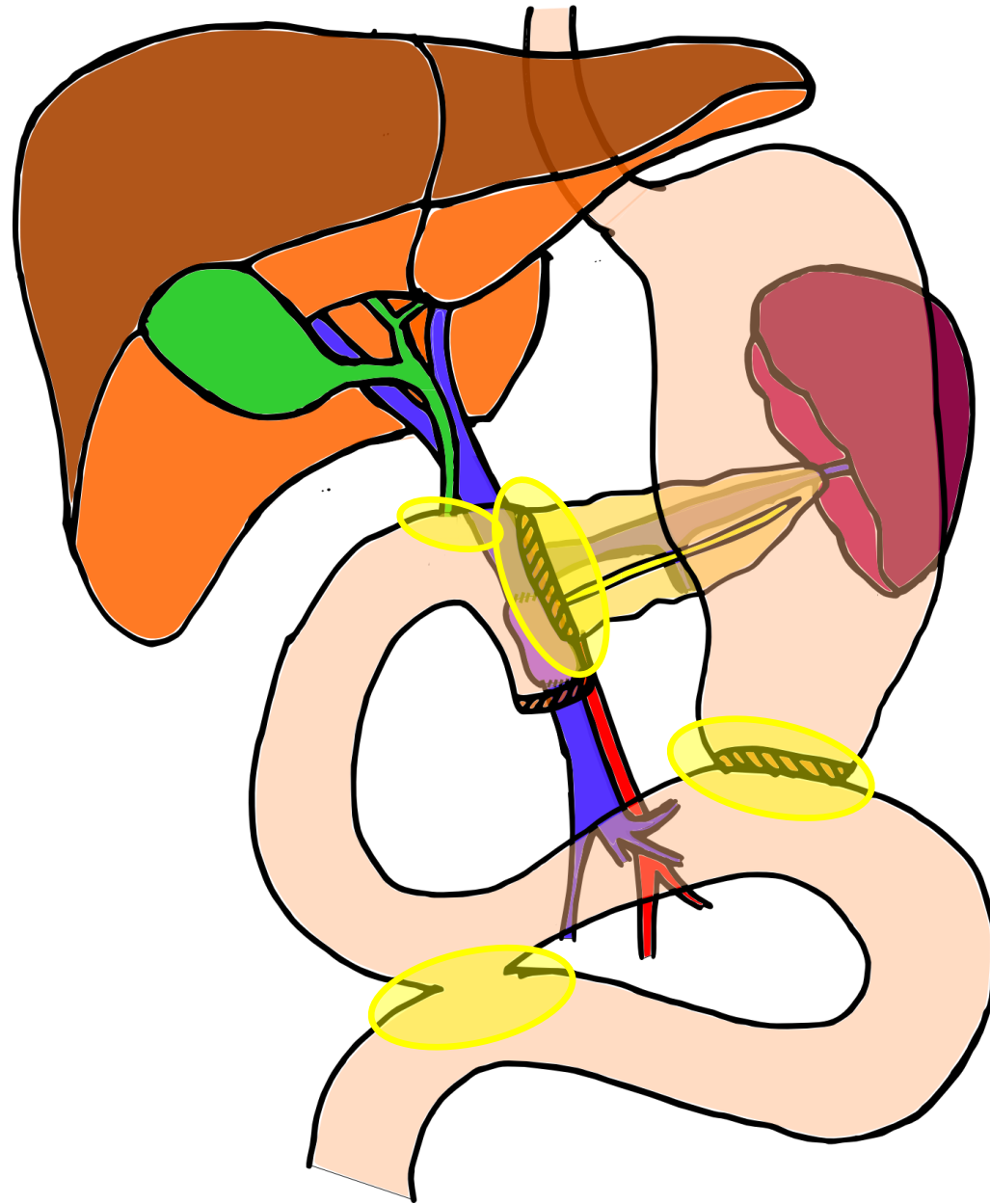
- reconstruction of portal vein



Methods II.

## Pancreaticoduodenectomy

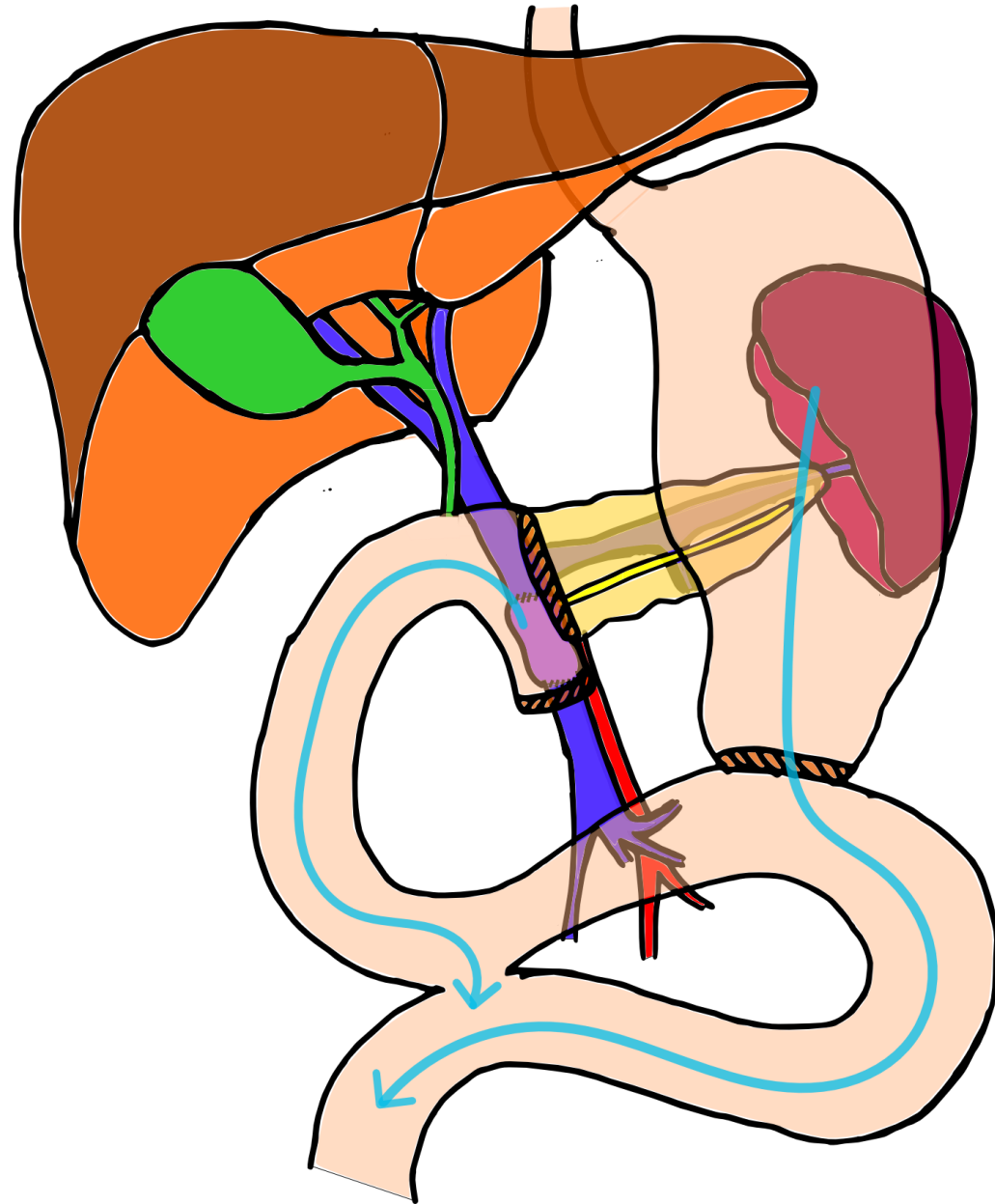
- Pancreicojejunostomy  
end-to-side
- Choledochojejunostomy  
end-to-side
- Pylorojejunostomy  
end-to-side
- Jejunojejunostomy  
side-to-side



Methods II.

## Pancreaticoduodenectomy

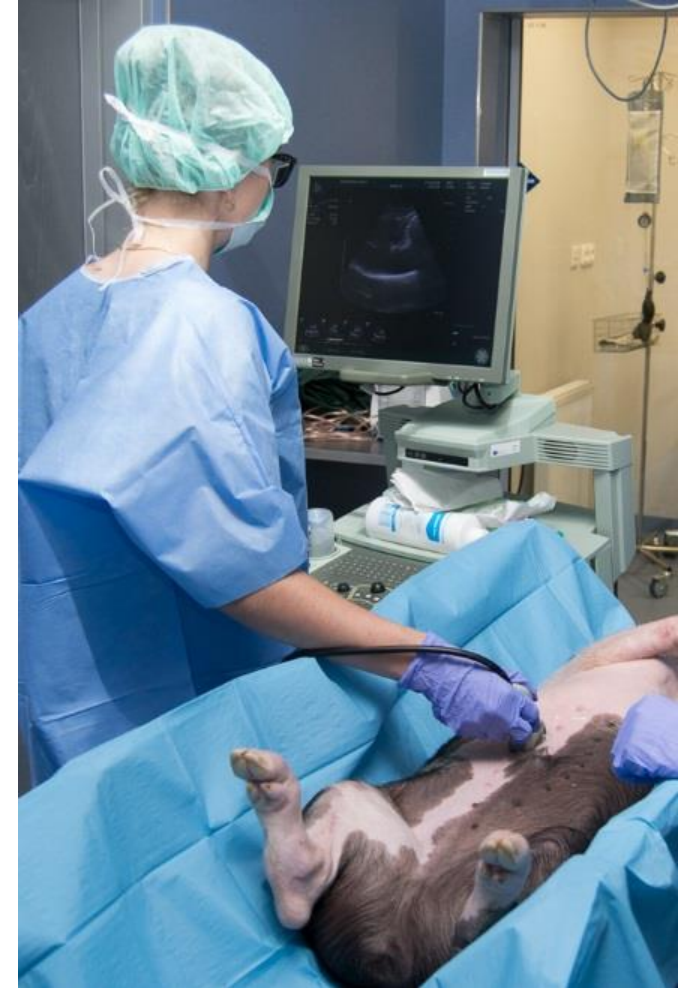
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side-to-side



Methods III.

## Postoperative follow-up

- **Biochemical analysis**
- Before operation, right before PV resection, right after PV reconstruction, 2 hours after PV reconstruction, on postoperative days: 7, 14, 21, 28
- Parameters of liver and kidney functions: AST, ALT, GGT, ALP, bilirubin, urea, creatinine
  
- **Doppler ultrasonography**
- Before operation, right after operation, on postoperative days: 7, 14, 21, 28
- Diameter of: portal vein, graft, superior mesenteric vein, lienal vein
- Blood flow velocity in: portal vein, graft, superior mesenteric vein, lienal vein





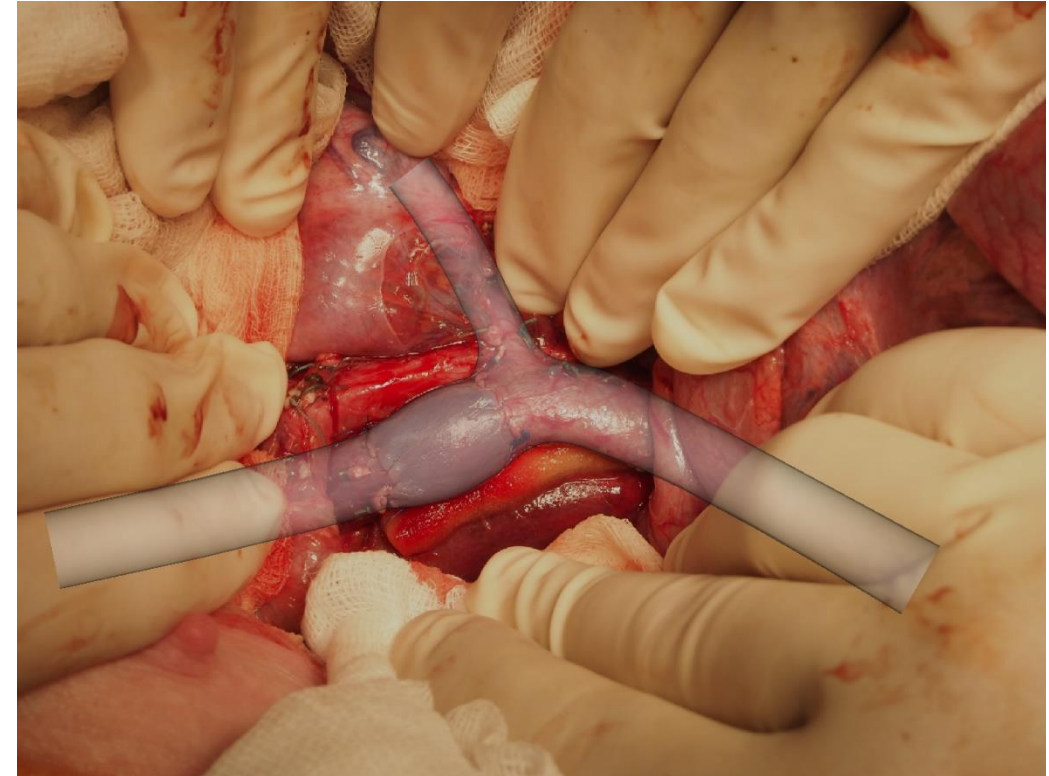
Methods IV.

## Histological examination

- PV specimens including the interposed graft – explanted on 28<sup>th</sup> postoperative day (or during the autopsy)
- Rests of grafts not used for PV reconstruction (native grafts)
- Qualitative and quantitative evaluation (area fraction of smooth muscle cells, collagen and elastin)

## Computer simulations

- Geometric models of PV
- The models used data from Doppler ultrasonography
- The impact on hemodynamic and risk of thrombosis
  - **velocity** (TAVM - velocity magnitude maps)
  - **wall shear stress** (TAWSS – time averaged wall shear stress)
  - **residence time** (RT<sub>c</sub>, virtual ink method to identify the zones with stagnation and recirculations)



Results I.

## Death during the experiment

	Graft	Day of death	Cause of death
1	ICV	1st postoperative	postoperative bleeding in retroperitoneum
2	ICV	1st postoperative	thrombosis of extrahepatic part of portal vein
3	PV	right after operation	thrombosis of extrahepatic part of portal vein
4	PV	1st postoperative	metabolic failure
5	PV	2nd postoperative	postoperative tachycardia and metabolic failure
6	PV	12th postoperative	pancreatic pseudocyst
7	PV	18th postoperative	gastrectasia

## Thrombosis of extrahepatic portal vein

	Graft	Diagnosis	Cause of death
1	ICV	autopsy	YES
2	PV	autopsy	YES
3	PV	ultrasound examination	NO
4	PV	autopsy	NO
5	PV	at the end of the experiment	NO



Results I.

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## Thrombosis of extrahepatic portal vein

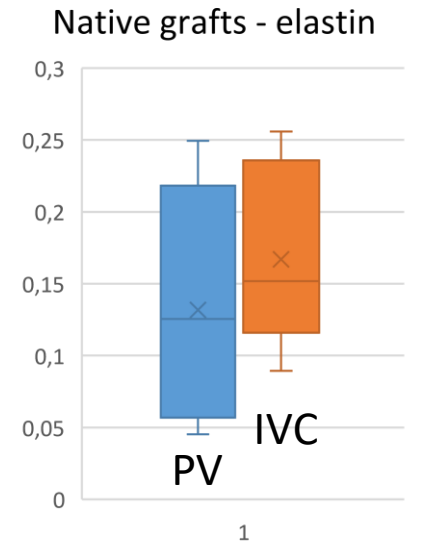
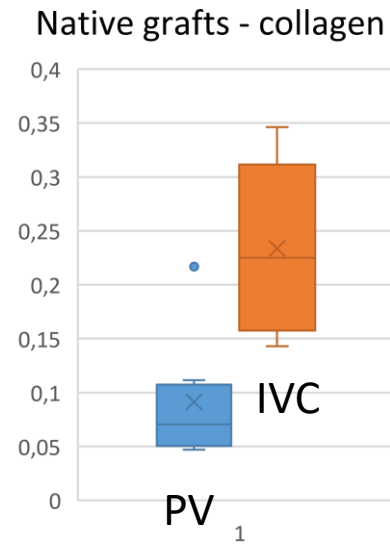
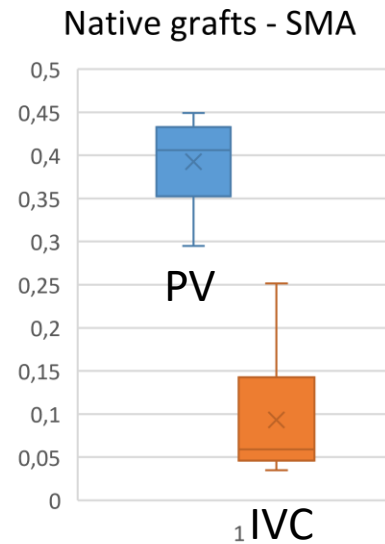
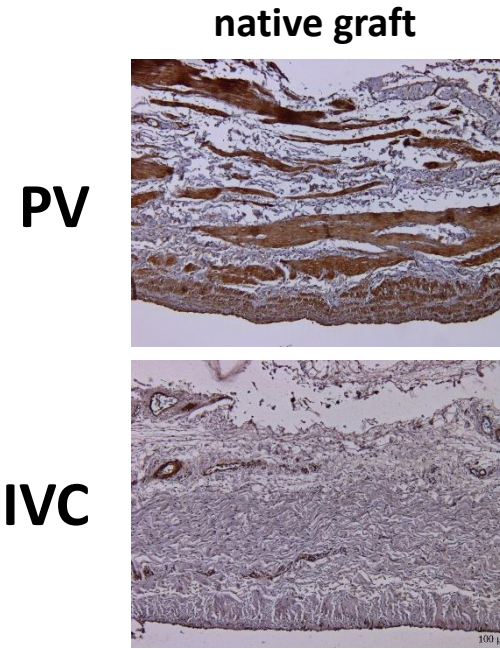
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Results IV.

## Histological examination

### Before implanation

- Higher amount of smooth muscle tissue in PV grafts
- Higher amount of collagen in IVC grafts



Results IV.

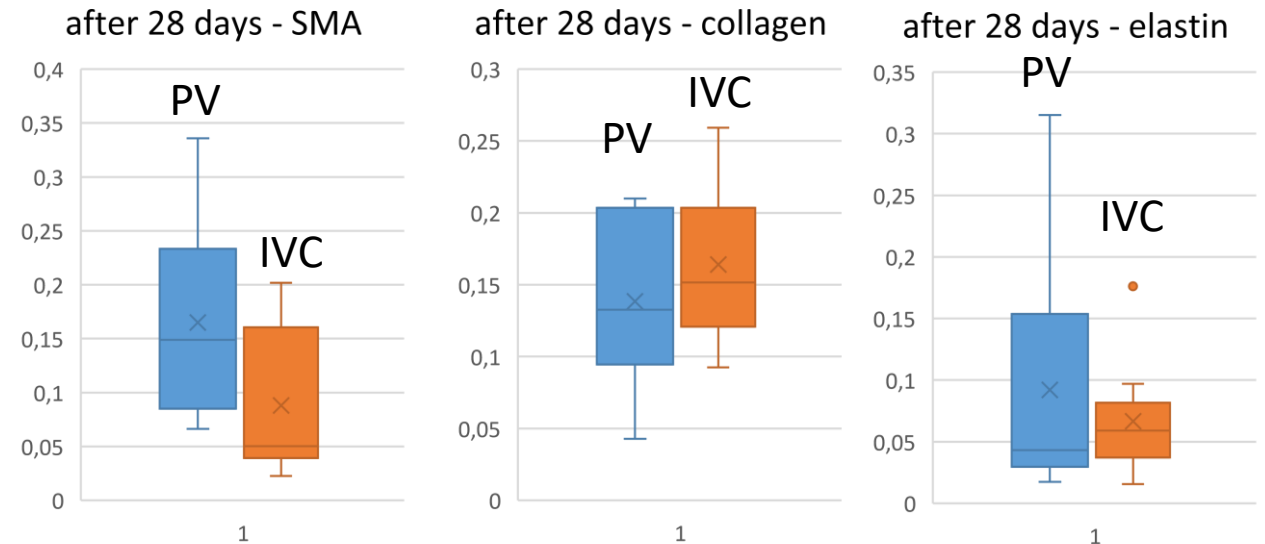
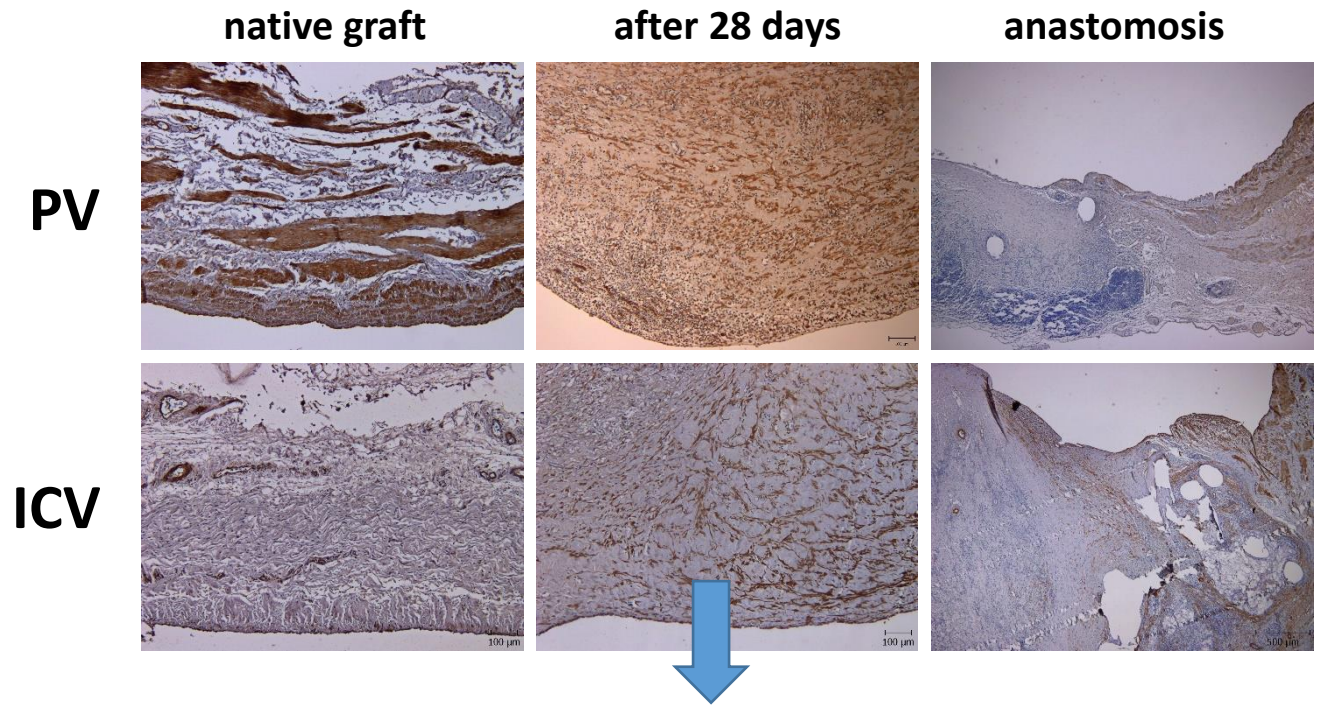
## Histological examination

### Before implanation

- Higher amount of smooth muscle tissue in PV grafts
- Higher amount of collagen in IVC grafts

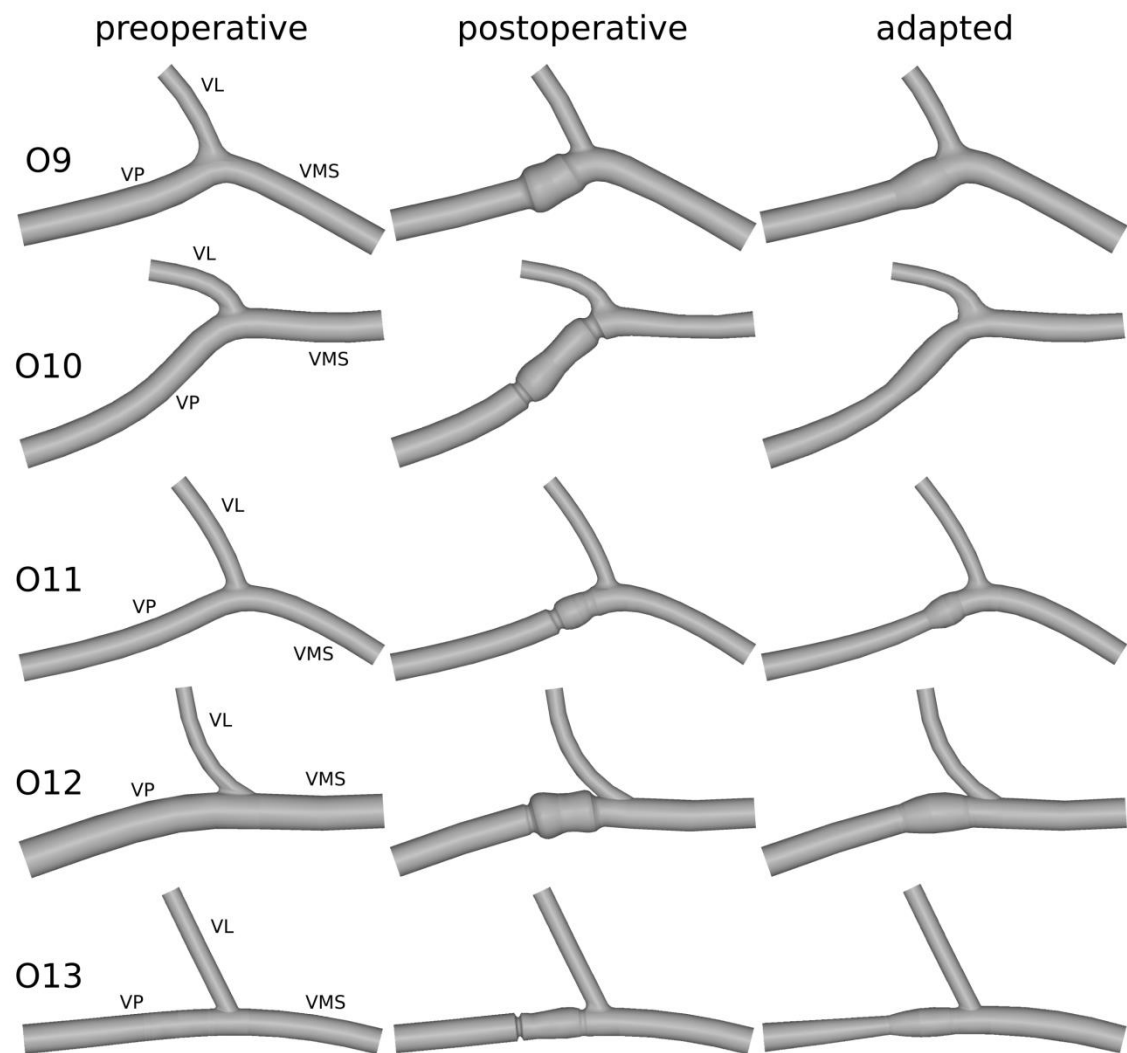
### After implanation

- No differences in amount of quantified parameters
- Both types of grafts developed wall thickening and were comparable at the end of experiment

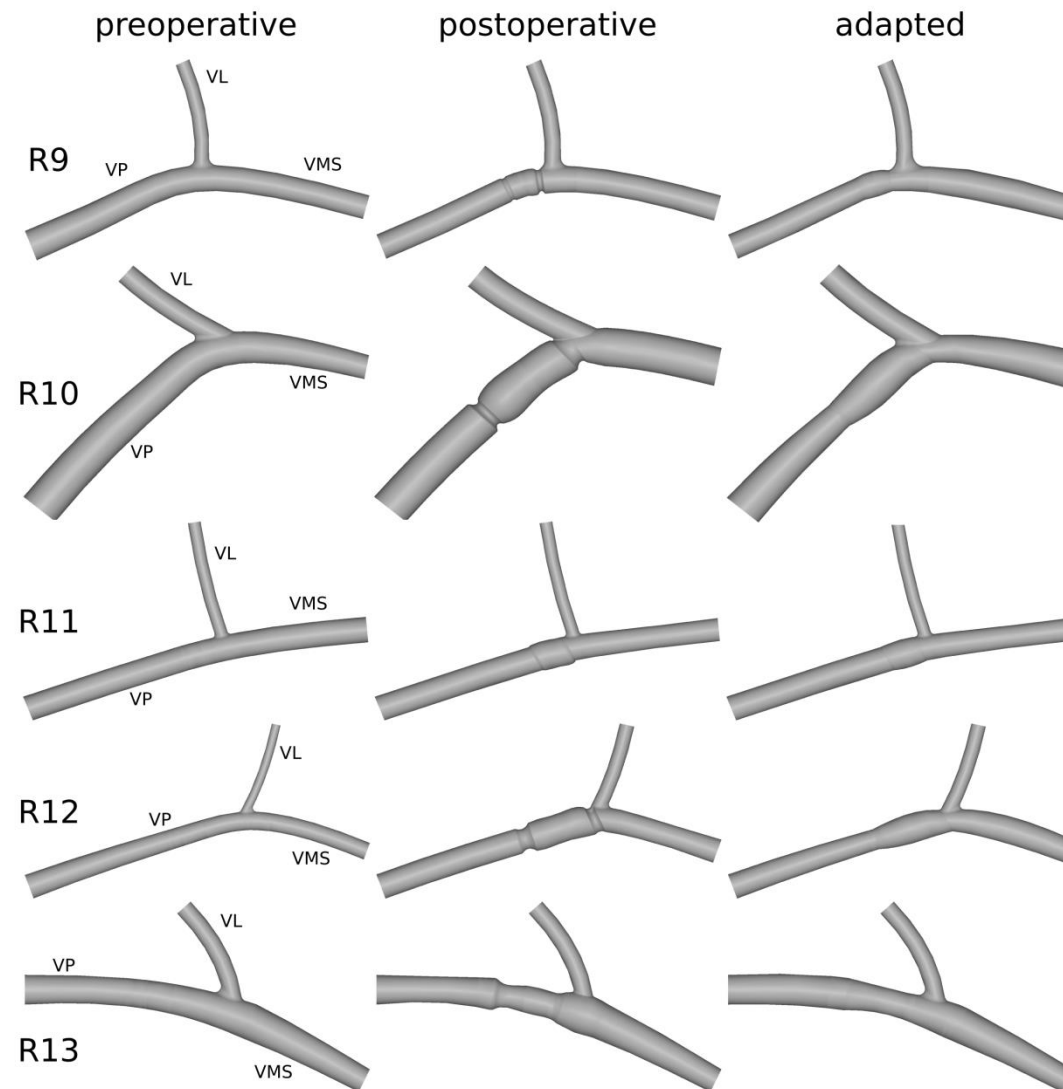


# Geometrical models

## PV graft

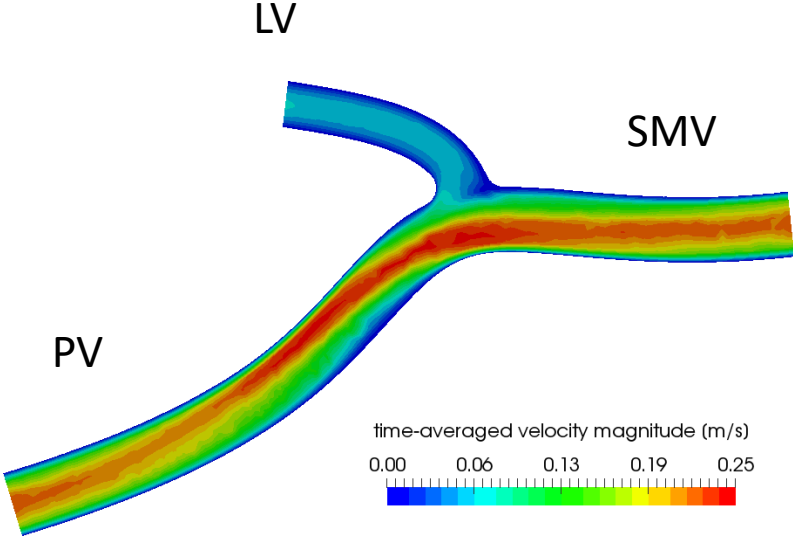


## ICV graft

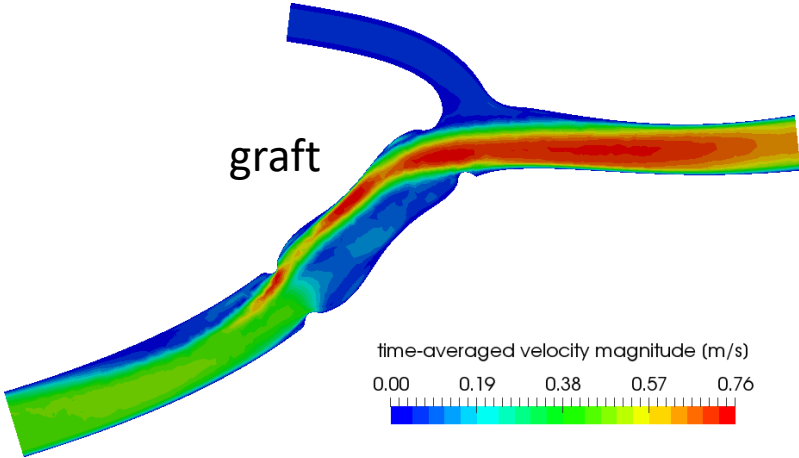


# Computer simulations

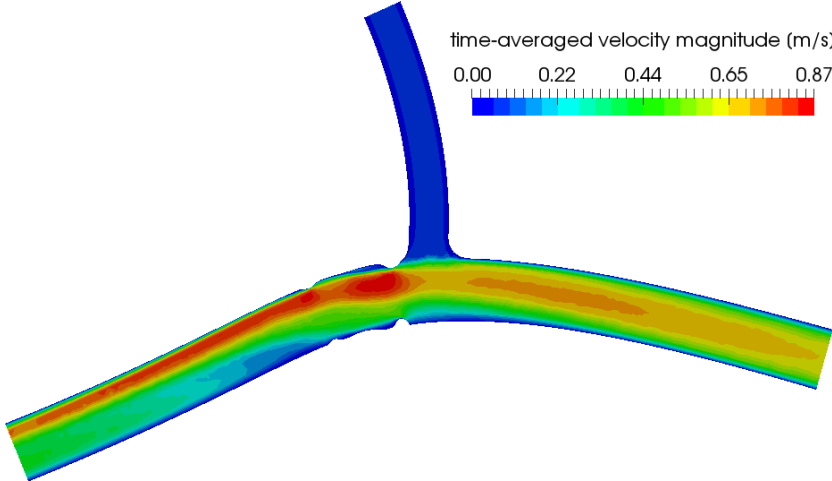
Time – averaged velocity magnitude (TAVM)



before reconstruction



after reconstruction

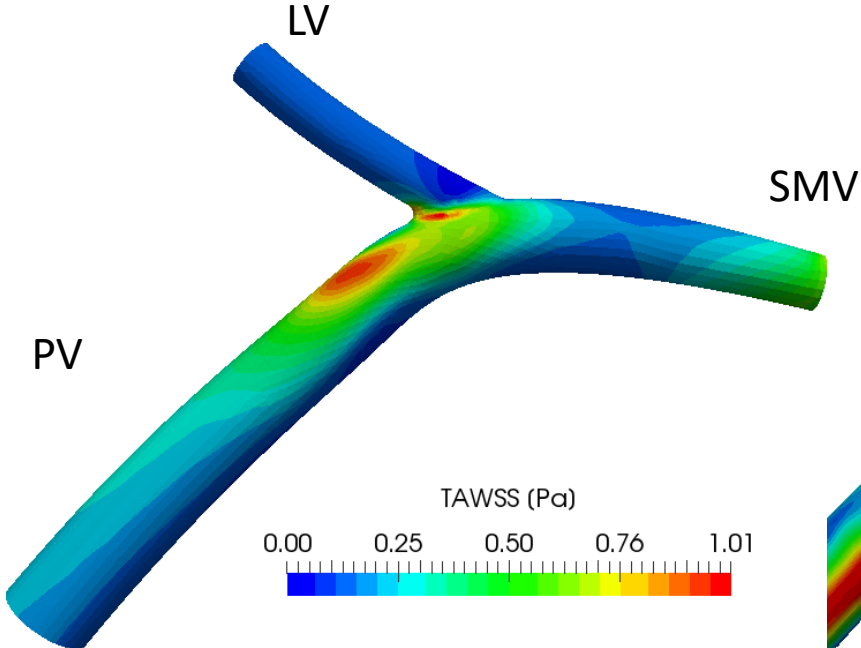


adapted

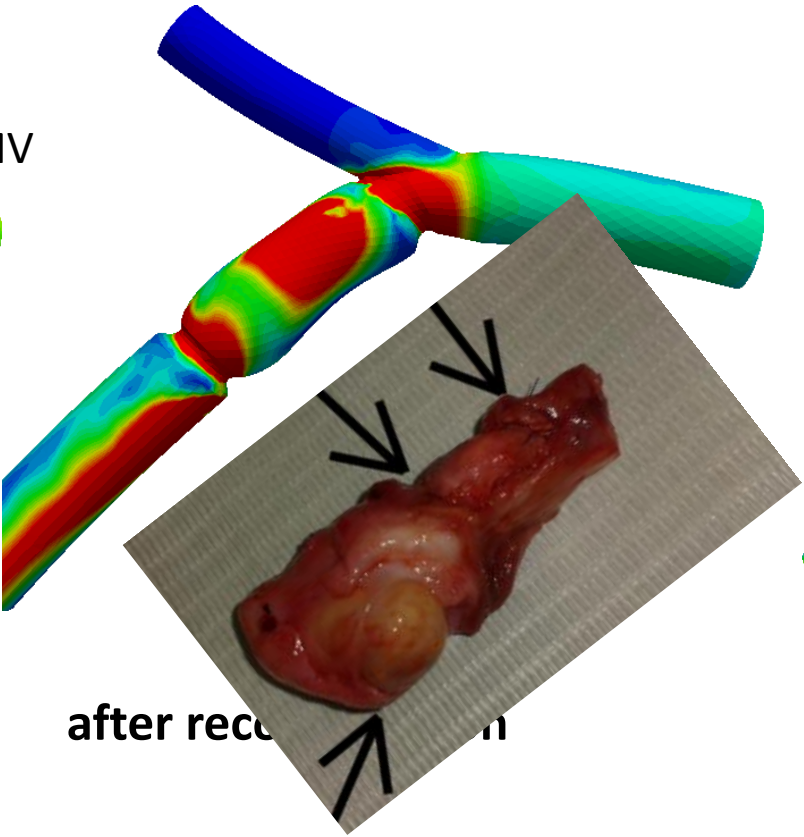


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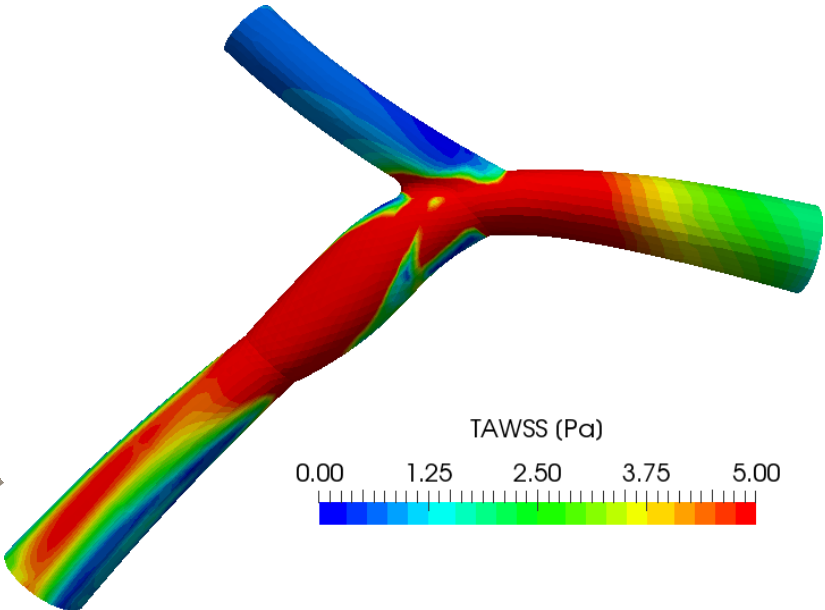
Time – averaged wall shear stress (TAWSS)



before reconstruction



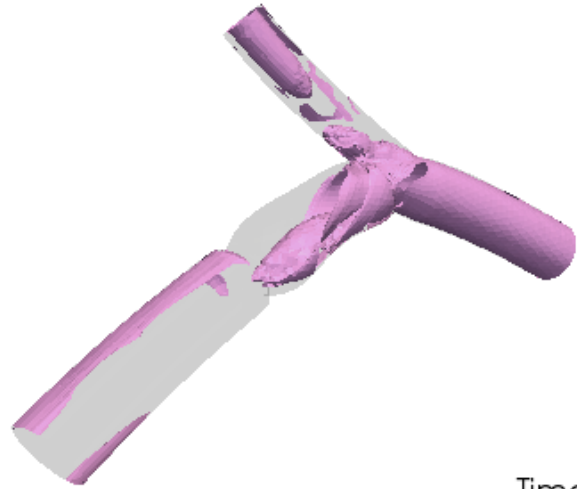
after reconstruction



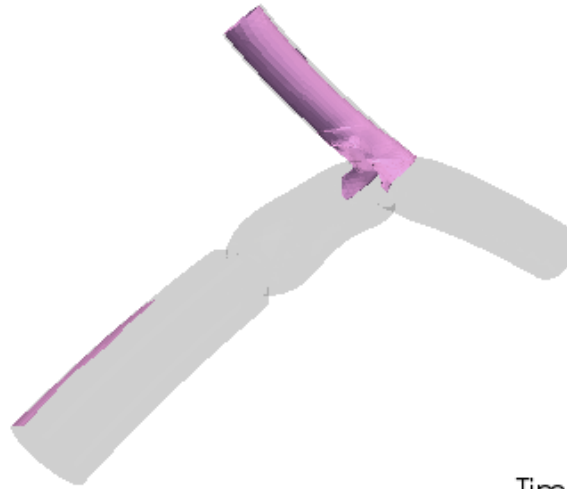
adapted

# Computer simulations

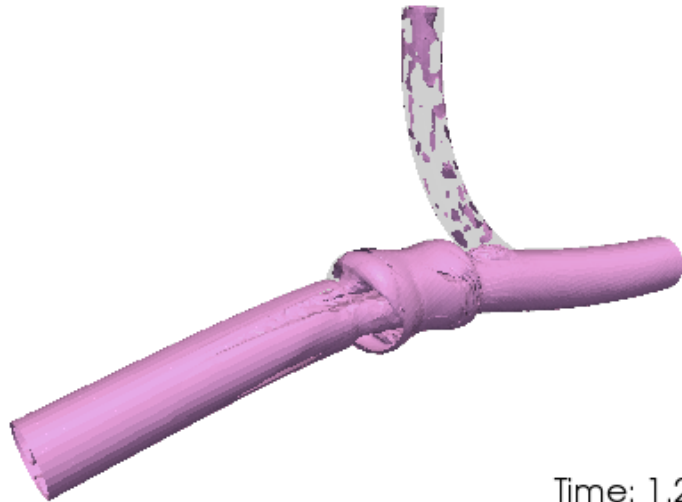
Residence time – virtual ink method (RTc)



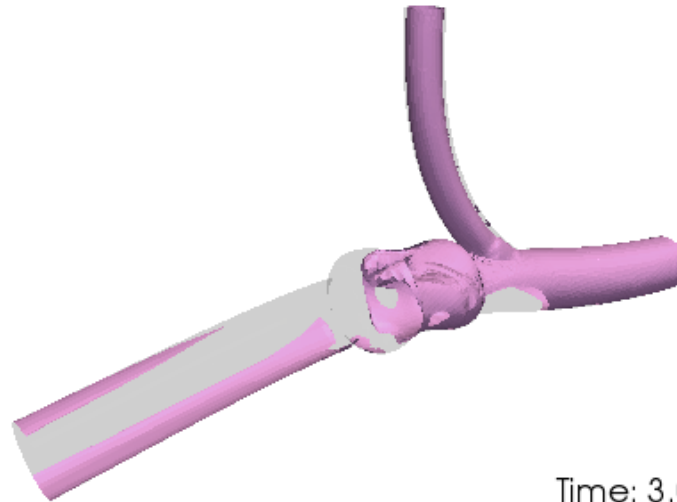
Time: 1.25 s



Time: 3.00 s



Time: 1.25 s



Time: 3.00 s

- Higher residence time values in case of grafts with larger diameter

# Conclusion

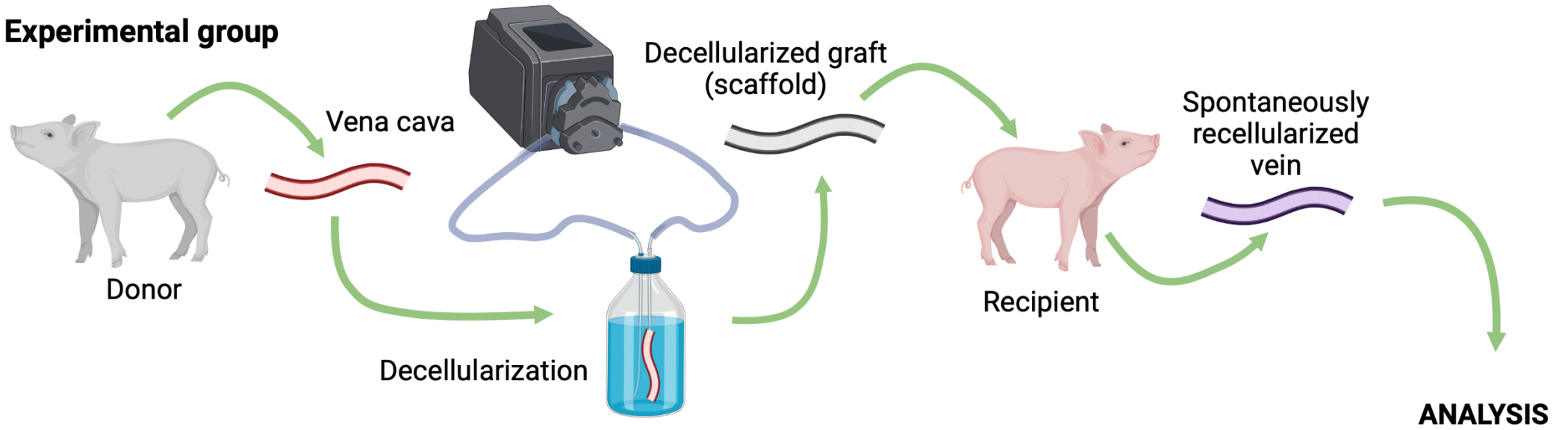
- Large animal model of pancreaticoduodenectomy with PV reconstruction using allogeneous venous grafts was established.
- The native grafts from portal system and from caval system vary in characteristics of their venous wall.
- These differences diminished during the healing process.
- However, they could affect PV hemodynamics and our results suggest that it might possess an increased risk of PV thrombosis in animals with implanted PV graft.
- We support the use of easily accessible allogeneic venous grafts from caval system in clinical medicine to increase the number of radical surgical resections for pancreatic cancer



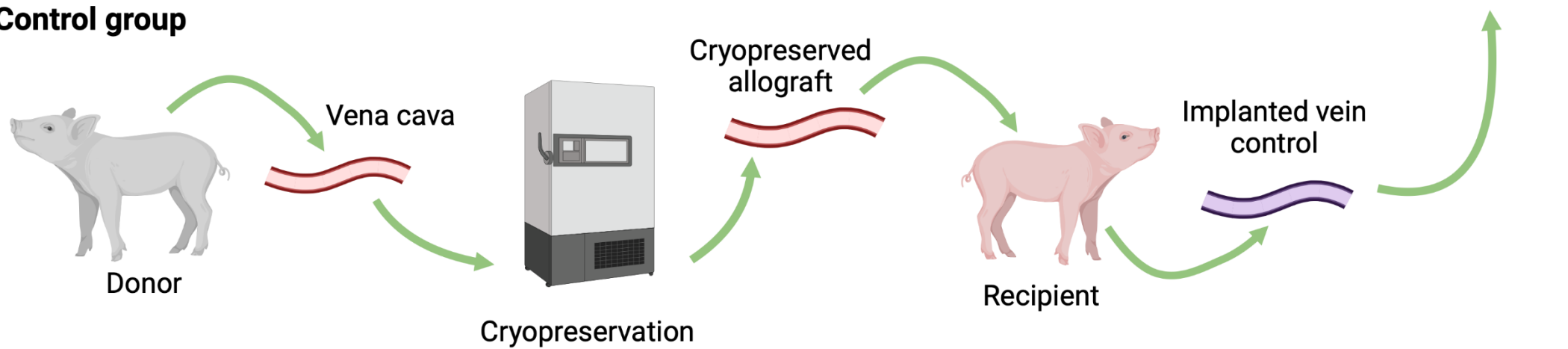
Each research could give  
answers but has to give new  
questions!

Characterization And  
Repopulation Of Decellularized  
Porcine Blood Vessels

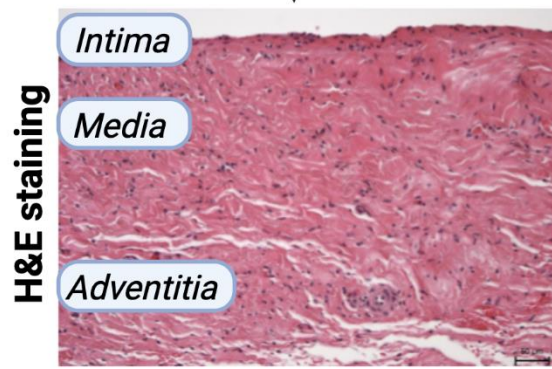
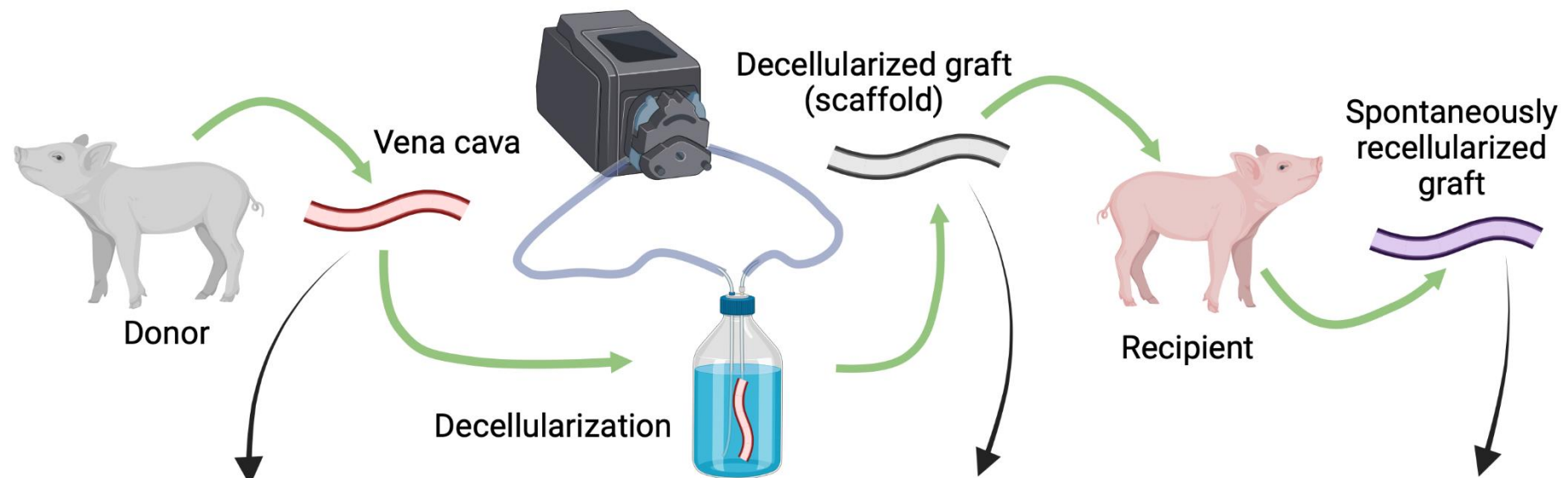
### Experimental group



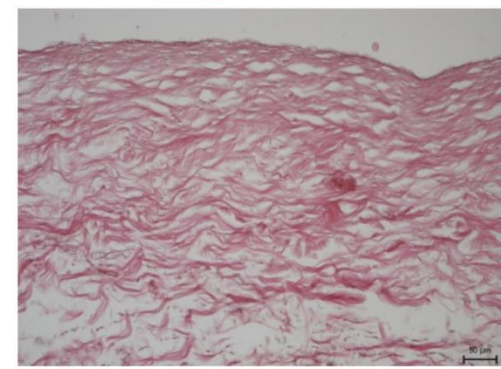
### Control group



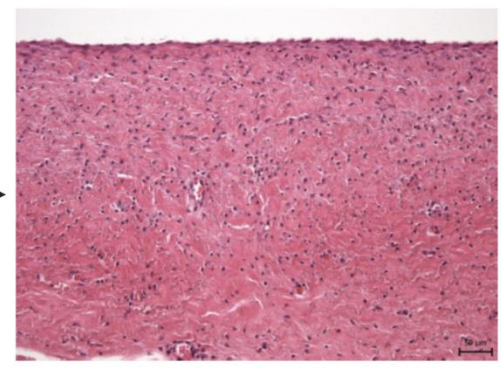




Vena cava



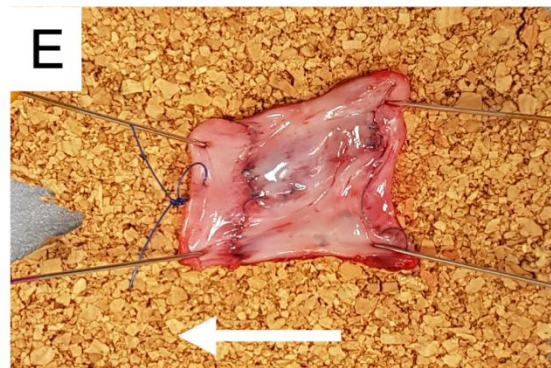
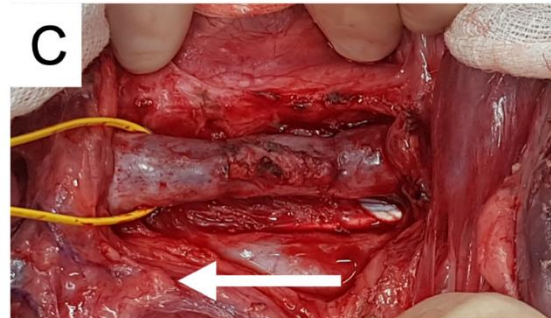
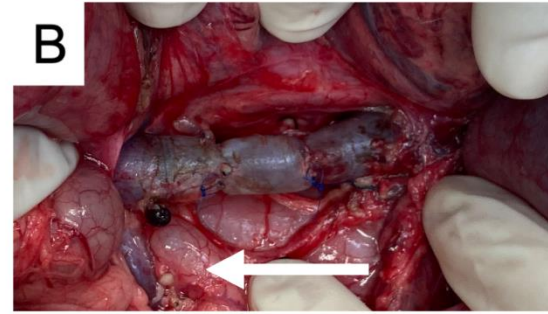
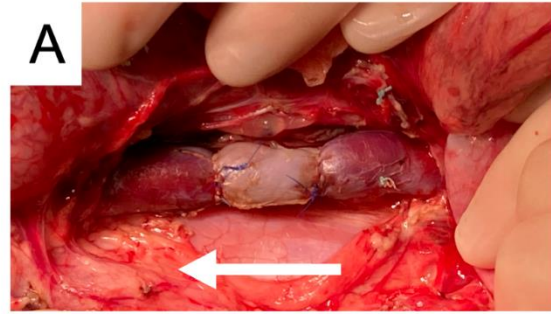
Decellularized graft (scaffold)

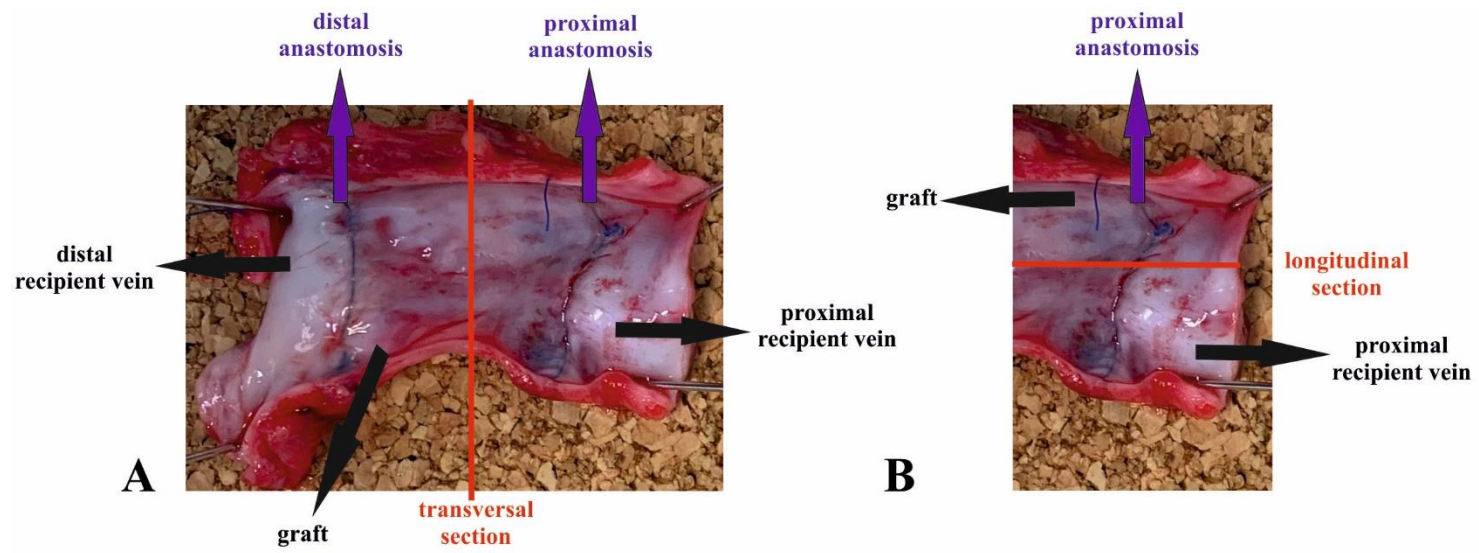


Recellularized graft

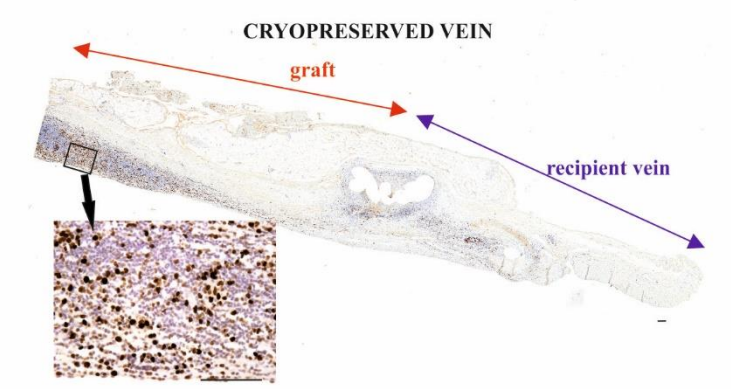
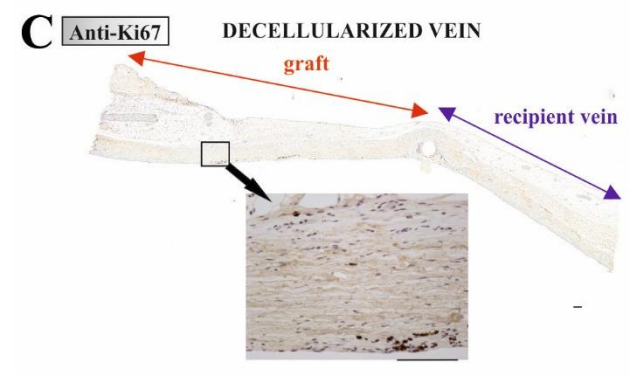
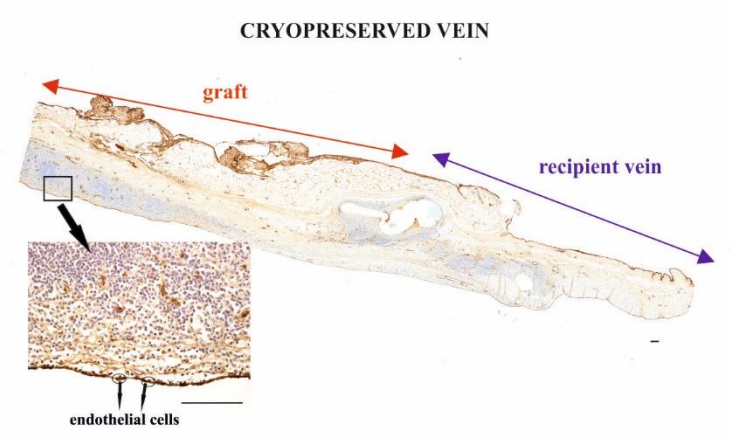
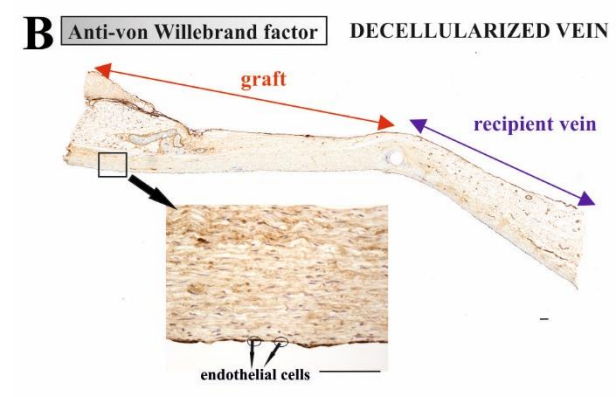
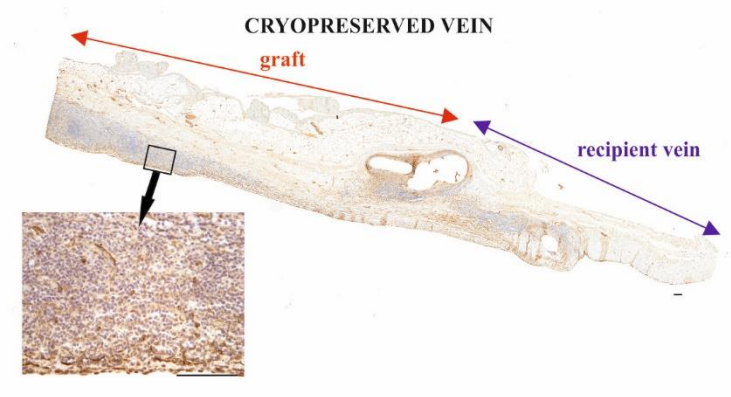
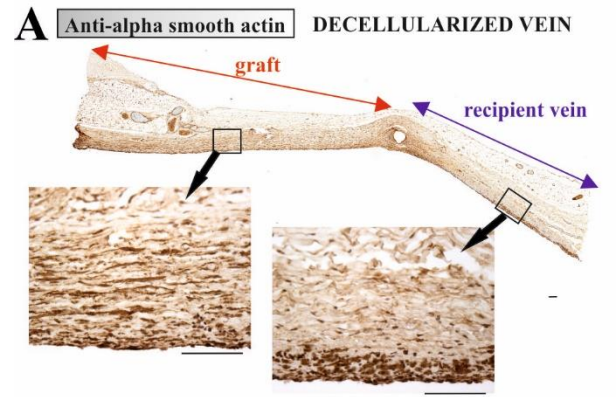
DECELLULARIZED

CRYOPRESERVED











## Summer School of Experimental Surgery Pilsen 2024



**1 July to 12 July 2024**  
in Pilsen, Czech Republic

**2000 EUR (1900 EUR early bird fee until 31 Dec 2023)**

the fee includes: tuition  
textbook (500+ pages)  
accommodation  
lunches  
scheduled excursions  
extracurricular activities

### **practical exercises & theoretical lectures**

(ca. 20 hrs at the operating theatre, performing surgeries from the 2<sup>nd</sup> day)

surgery, anesthesia, imaging, statistics, biomechanics,  
software models, stem cells, tissue cultures, transplantations,  
experimental methods **and more...**



**Charles University**  
**Faculty of Medicine in Pilsen**  
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phone: +420 608 792 488

[www.sses.eu](http://www.sses.eu)









Celebrating the 10<sup>th</sup> anniversary of the  
**Summer School of Experimental Surgery**  
 2014-2023



*Pretium laborum necopinatum*

Our operating theatre crew



Václav Liška  
on board since 2014



Jan Brůha  
on board since 2014



Petr Hošek  
on board since 2014



Richard Pálek  
on board since 2014



Jiřym Rosenzweig  
on board since 2014



Ondřej Vyčítal  
on board since 2014



Marek Brouil  
on board since 2017



Robert Polák  
on board since 2019



Jan Ševčík  
on board since 2019



Jitka Škrabalová  
on board since 2019



Lucie Kepková  
on board since 2020



Maria Stefania Massaro  
on board since 2020



Sima Sarčević  
on board since 2020



Zuzana Fibrová  
on board since 2021



Pavel Kryžl  
on board since 2021



Lenka Kuberková  
on board since 2021



Petra Havlíčková  
on board since 2022



Tomáš Polenda  
on board since 2022



Daniel Vydra  
on board since 2022



Lucie Bludovská  
on board since 2023



Martina Bošková  
on board since 2023



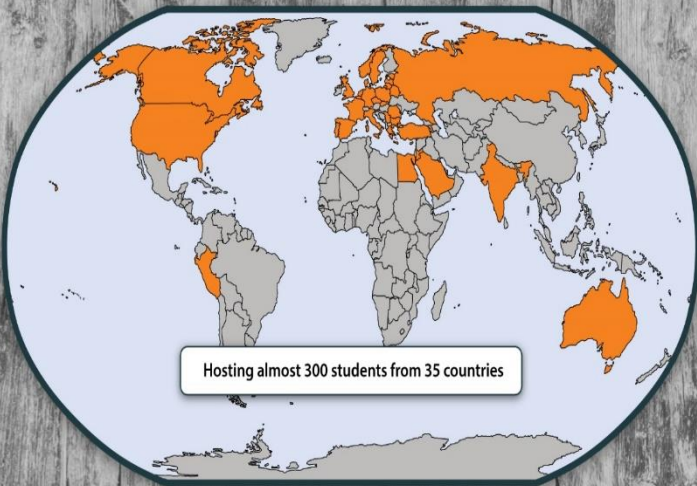
Oľekšandra Khmurtalova  
on board since 2023



Ilya Matsuyayonak  
on board since 2023



Yehor Pankratiev  
on board since 2023



Hosting almost 300 students from 35 countries



Martin Falco  
on board since 2023



Zdenka Hlavatá  
on board since 2023



Daniel Lehner  
on board since 2023



Martin Strouhal  
on board since 2023



David Volák  
on board since 2023