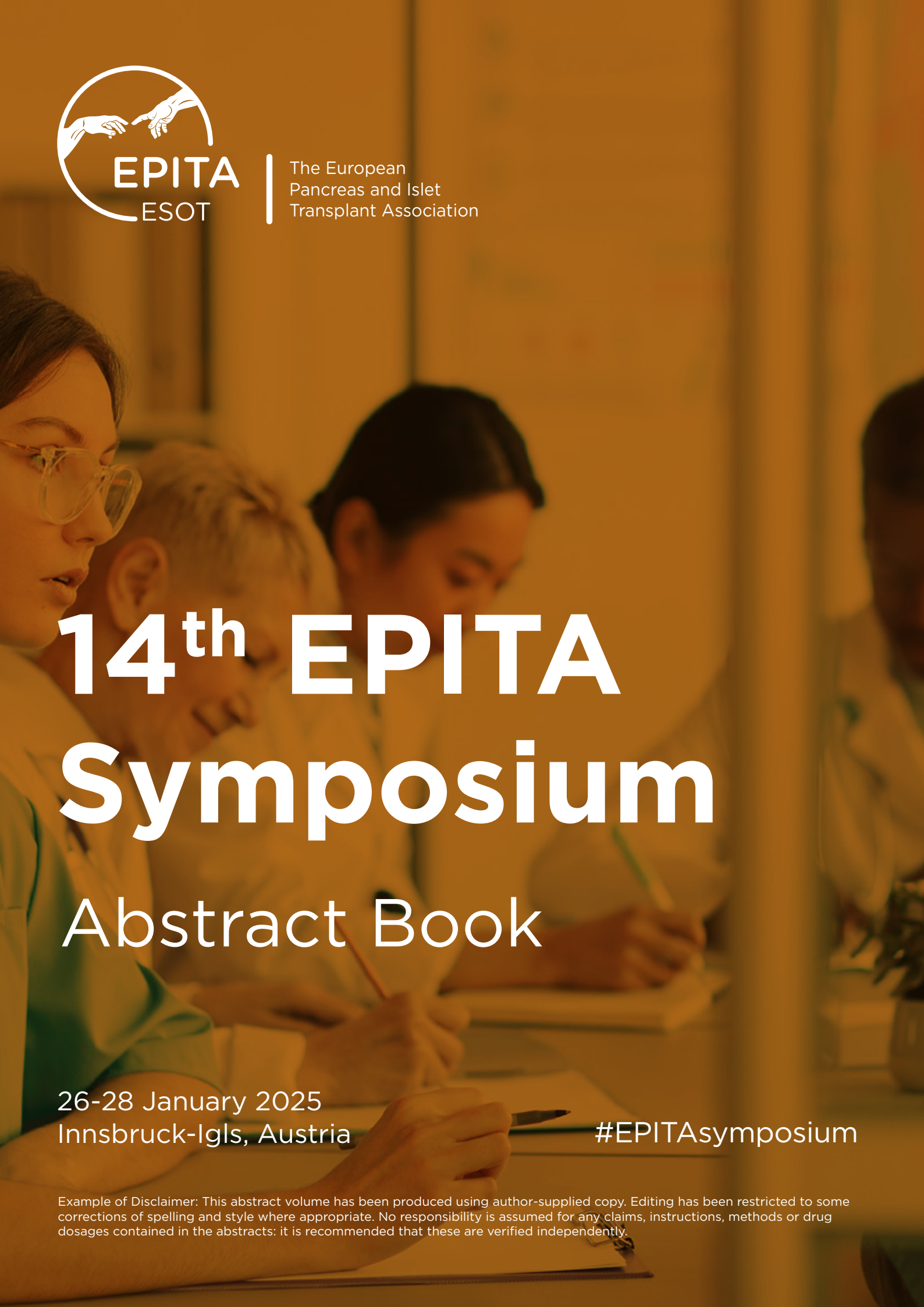
EPITA
ESOT

The European
Pancreas and Islet
Transplant Association



14th EPITA Symposium

Abstract Book

26-28 January 2025
Innsbruck-Igls, Austria

#EPITAsymposium

Table of Contents

OP01 - OPTN DATA REGISTRY NATIONAL COHORT STUDY – DONOR LIPASE AND AMYLASE DO NOT PREDICT PANCREAS TRANSPLANT OUTCOMES

Ning Xuan Ho[1], Samuel James Tingle[2], Georgios Kourounis[3], Abdullah Malik[4], Emily Thompson[5], Ali Abbasi[6], Peter Stock[7], Sanjay Pandanaboyana[8], Colin Wilson[9], Steve White[10]

[1]*Institute of Transplantation, Freeman Hospital; Hpb and Transplantation*
[2]*Institute of Transplantation; Hpb and Transplant Surgery*
[3]*Freeman Hospital; Institute of Transplantation*
[4]*Institute of Transplantation; Freeman Hospital*
[5]*The Newcastle Upon Tyne Hospitals NHS Foundation Trust; Institute of Transplantation*
[6]*University of California San Francisco; Department of Surgery*
[7]*University of California San Francisco; Surgery*
[8]*Institute of Transplantation, Freeman Hospital*
[9]*The Newcastle Upon Tyne Hospitals NHS Foundation Trust*
[10]*Newcastle Upon Tyne Hospitals NHS Foundation Trust; Dept of Surgery*

Background
Simultaneous pancreas-kidney (SPK) transplantation improves quality of life in people with diabetes and end-stage renal disease, and limits the progression of diabetes related complications. Many surgeons remain reluctant to accept the pancreas of a donor with raised serum lipase and amylase, due to concern of potentially inferior outcomes. We aim to establish whether donor serum lipase and amylase predict pancreas transplant outcome.

Methods
This retrospective cohort study utilised the Organ Procurement and Transplantation Network data registry on all adult SPK transplantation (2010-2023). Adjusted regressions models assessed the effect of donor serum lipase and amylase on pancreas transplant outcome at 1-year

Results
A total of 10,451 SPK recipients were included. Median peak donor lipase was 38 (Figure 1A; IQR 18-92, max 2985) and median amylase was 84 (Figure 1B; IQR 45-168, max 2831). Neither donor peak serum lipase, nor amylase, had a significant impact on pancreas graft survival when adjusting for multiple confounders (aHR=1.019; 0.980-1.059, and aHR=0.986; 0.943-1.031, respectively). Interaction terms were included to assess whether the impact of peak lipase/amylase on outcome differed based on trend; there was no evidence that lipase/amylase trend altered the impact on outcome (p=0.250 and p=0.492, respectively). Restricted cubic splines (Figure 2) were used to assess the relationship between these enzymes and pancreas graft survival without assuming linear relationships; these confirmed that neither lipase, nor amylase, had a significant impact on pancreas transplant outcome.

Conclusions
Donor lipase and amylase do not predict transplant outcomes. Therefore, raised donor serum lipase and amylase should not be considered a barrier to organ utilisation. The use of pancreas grafts from donors with raised lipase/amylase is a simple approach to prevent donor organ discard and expansion of donor pool.

Conflicts of interest
No conflicts of interest

OP02 - INTESTINAL COMPLICATIONS IN PANCREAS TRANSPLANTATION WITH DUODENODUODENOSTOMY FOR EXOCRINE DRAINAGE: A SINGLE-CENTER EXPERIENCE

Alba Torroella[1], Rongrong Hu Zhu[2], Ramón Rull[3], Rocío García[3], Clara Bassaganyas[4], Carlos Perez Serrano[5], Martí Manyalich[6], David Saavedra[7], Emma Folch Puy[8], Víctor Emilio Holguin[7], Pedro Ventura-Aguiar[9], Antonio J Amor[10], Fritz Diekmann[11], Mª Angeles Garcia-Criado[12], Josep Fuster[3], Joana Ferrer-Fàbrega[13]

[1]*Hospital Clínic, University of Barcelona, Barcelona, Spain.; Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (Icmdim),*

[2]*Clinic Institute of Digestive and Metabolic Diseases (Icmdim), Hospital Clínic; Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit*

[3]*Institute of Digestive and Metabolic Diseases (Icmdim). Hospital Clinic. University of Barcelona. Barcelona*

[4]*Hospital Clínic de Barcelona; Radiology*

[5]*Hospital Clínic de Barcelona*

[6]*1hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (Icmdim), Hospital Clínic, University of Barcelona, Barcelona, Spain.*

[7]*Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (Icmdim), Hospital Clínic, University of Barcelona, Barcelona, Spain.*

[8]*Iibb-Csic; Experimental Pathology; Experimental Pathology*

[9]*Hospital Clinic Barcelona; Hospital Clinic de Barcelona; Nephrology and Kidney Transplant Department*

[10]*Hospital Clinic de Barcelona; Endocrinology and Nutrition Department*

[11]*Hospital Clinic; Hospital Clinic de Barcelona; Nephrology and Kidney Transplant Department*

[12]*Radiology Department, Hospital Clinic; Hospital Clinic Barcelona; Radiology Department, Center for Biomedic Imaging*

[13]*Hospital Clínic Barcelona; Hepatobiliopancreatic Surgery and Transplantation Department*

Background

Duodenoduodenostomy as an exocrine drainage reproduce more accurately the physiology of the native pancreas and enables more conservative management of postoperative complications. We present our experience with duodenoduodenostomy (DD) for exocrine drainage, analyzing intestinal complications and their impact on patient and graft survival.

Methods

All pancreatic transplants performed between May 2016 and November 2024 were included. For exocrine secretion, enteric drainage was performed “side-to-side” with DD anastomosis.

Results

A total of 170 transplants were performed using DD. Recipient median age was 43 years [IQR 36 - 39], with 56.7% male. Median cold ischemia time was 8 hours [IQR 6.1-10.1]. According to the Clavien-Dindo classification, complications were: 7.6% Grade I, 17.1% Grade II, 2.4% Grade IIIa, and 21,8% Grade IIIB. The median hospital stay was 12 days [IQR 10 - 19.2]. Prevalence of intestinal complications was 10%, and were identified: intestinal occlusion (n=4); paralytic ileus (n=5); post-transplantectomy duodenal dehiscence (n=1); DD dehiscence (n=5); anastomotic bleeding (n=2). Eleven cases required surgical treatment due to intestinal complications: adhesiolysis (n=3); Hartmann’s procedure in an occlusive stercoraceous colitis (n=1), primary closure of the dehiscence (n=3); transplantectomy after

failed primary closures (n=2); redone of the enteric anastomosis (n=2). After a median followup of 39.79 months [IQR 18.1- 69], pancreas graft survival was 86.7% at 1 year, 3 years and 5

years, and patient survival was 100%, 99.2% and 99.2% at 1 year, 3 years and 5 years, respectively.

Conclusions
Duodenoduodenostomy for enteric drainage in pancreas transplantation is a feasible and safe technique, offering competitive outcomes in terms of graft and patient survival.

Conflicts of interest
No conflicts of interest

OP03 - THE ROLE OF PANCREAS GRAFT BIOPSIES IN THE MANAGEMENT OF PANCREAS TRANSPLANT RECIPIENTS

Alice Duret-Lamouroux[1], Maud Rabeyrin[2], Lionel Badet[3], Xavier Matillon[4], Xavier Charmetant[5], Thierry Berney[1], Olivier Thaunat[6], Emmanuel Morelon[7], Fanny Buron[8]
[1]*Hospices Civils de Lyon*
[2]*Hospices Civils de Lyon, Groupement Hospitalier Est; Hospices Civils de Lyon*
[3]*Pavillon V Urologie; Pavillon V Chirurgie-Urologie*
[4]*Urologue Département of Hospices Civils de Lyon*
[5]*Hospices de Lyon; Hospices Civils de Lyon; Dpt of Transplantation, Nephrology and Clinical Immunology*
[6]*Hôpital Edouard Herriot/Inserm; Hospices Civils de Lyon; Nephrology and Transplantation*
[7]*Hopital Edouard Herriot; Hospices Civils de Lyon; Service de Transplantation Nephrologie et Immunologie Clinique*
[8]*Hospices Civils de Lyon / Hôpital Edouard Herriot; Hospices Civils de Lyon; Transplantation Nephrologie et Immunologie Clinique*

Background
Follow-up of pancreas transplant recipients is commonly based on exocrine, endocrine, allo-immune and auto-immune markers. However, histology remains the gold standard to diagnose rejection or auto-immune recurrence. Our purpose was to evaluate the performance of pancreas biopsies in the management of pancreas transplant recipients.

Methods
We included all patients followed at the university hospital of Lyon who received a pancreas transplantation (with simultaneous kidney transplantation or alone) from January 2011 to December 2022 and who underwent at least one pancreas biopsy between transplantation and October 2023.

Results
We collected 121 biopsies (96 for cause, 25 protocol biopsies) in 85 recipients (81% SPK). 21 (17%) were non-contributive. There were 7 (5.8%) biopsy-related minor complications and 1 severe complication without graft loss. 83% of contributive biopsies performed for lipase increase showed rejection without any link between lipase value and presence or severity of rejection. 1 out of 6 biopsies performed for de novo DSA without any other abnormality showed cellular rejection. 2 out of 15 biopsies performed for abnormal OGTT showed rejection that is closed to subclinical rejection founded in 3 out of 21 (14%) contributive protocol biopsies. 36% of simultaneous pancreas and kidney biopsies (n=59) results were discordant. One-year pancreas graft survival after a normal or indeterminate for rejection biopsy is 100 % without any treatment. Overall one-year pancreas graft survival after rejection treated with steroids is 85 % (94% for grade I rejection and 78% for grade II rejection).

Conclusions
Pancreatic graft biopsy is a safe procedure, essential in cases of lipase increase to diagnose rejection, guide treatment according to severity, and for graft prognosis. Concordance with kidney graft biopsies is poor. Treatment is not necessary if the result is indeterminate for rejection. Systematic biopsies at 1 year show 14% of subclinical rejection.

Conflicts of interest
No conflicts of interest

OP04 - OUTCOMES AFTER PANCREAS RETRANSPLANTATION BASED ON THE PRIMARY CAUSE OF PANCREAS GRAFT FAILURE: A SINGLE CENTER ANALYSIS

Rongrong Hu Zhu[1], Alba Torroella[2], Ramón Rull[3], Rocío García[3], Clara Bassaganyas[4], Carlos Perez Serrano[5], Martí Manyalich[6], David Saavedra[7], Emma Folch Puy[8], Victor Holguín[9], Pedro Ventura-Aguiar[10], Antonio J Amor[11], Fritz Diekmann[12], Mª Angeles Garcia-Criado[13], Josep Fuster[3], Joana Ferrer-Fàbrega[14]

[1]*Clinic Institute of Digestive and Metabolic Diseases (Icmdim), Hospital Clínic; Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit*

[2]*Hospital Clínic, University of Barcelona, Barcelona, Spain.; Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (Icmdim),*

[3]*Institute of Digestive and Metabolic Diseases (Icmdim). Hospital Clinic. University of Barcelona. Barcelona*

[4]*Hospital Clínic de Barcelona; Radiology*

[5]*Hospital Clínic de Barcelona*

[6]*1hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (Icmdim), Hospital Clínic, University of Barcelona, Barcelona, Spain.*

[7]*Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (Icmdim), Hospital Clínic, University of Barcelona, Barcelona, Spain.*

[8]*Iibb-Csic; Experimental Pathology; Experimental Pathology*

[9]*Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (Icmdim), Hospital Clínic*

[10]*Hospital Clinic Barcelona; Hospital Clinic de Barcelona; Nephrology and Kidney Transplant Department*

[11]*Hospital Clinic de Barcelona; Endocrinology and Nutrition Department*

[12]*Hospital Clinic; Hospital Clinic de Barcelona; Nephrology and Kidney Transplant Department*

[13]*Radiology Department, Hospital Clinic; Hospital Clinic Barcelona; Radiology Department, Center for Biomedic Imaging*

[14]*Hospital Clínic Barcelona; Hepatobiliopancreatic Surgery and Transplantation Department*

Background

Recent improvements in the outcomes of pancreas transplantation have led to an increase in potential candidates for retrasplantation (PRT) following graft failure due to technical complications (TC) or chronic immunological rejection (IR).

The objective of this study is to assess the results of a 24-year study of pancreas retransplantations in terms of patient and graft survival, based on the cause of primary graft failure.

Methods

A retrospective study was implemented to analyze the PRT performed in a single center between January 2000 and November 2024. Pancreatic graft loss was defined by the return to insulin dependence.

Results

A total of 507 pancreas transplantations were performed in our institution, of which 47 were retransplantations. The retransplantation group had a median age of 43 (IQR 37-48) years, and 53.2% were male. The median time between the first and second transplant was 58.6 (IQR 25.3-101.6) months.

The primary graft failure was due to: immunological causes (n=27, 57.4%), technical complications (n=19, 40.4%) and a graft lymphoma requiring transplantectomy (n=1, 2.1%). A simultaneous pancreas-kidney (SPK) retransplantation was performed in 4 patients whereas pancreas alone retransplantation was carried out in 43 patients with a previously functioning kidney graft.

The most common surgically related complication following PRT was vascular thrombosis, with no significant variation related to the cause of primary graft failure.

After a median follow-up of 118 months (63.3 – 176.2), pancreas graft survival at 1,3, and 5 years was 82.1%, 72.7%, and 69.9% respectively, without differences between the two groups ($p<0.05$). No differences were found in terms of patient survival either at 1,3, and 5 years which were 100%, 95.5%, and 92.9%, respectively ($p<0.05$).

Conclusions
Pancreas retransplantation could be considered as a safe and effective second option in patients with previous graft failure, independently of the primary graft failure cause.

Conflicts of interest
No conflicts of interest

OP05 - WEIGHT LOSS AND SIDE EFFECTS IN WHOLE-PANCREAS TRANSPLANT RECIPIENTS TREATED WITH GLP-1 AGONISTS FOR OBESITY-ARE WE READY FOR PRIME TIME?

Ali Abbasi[1], Giulia Worner[2], Gerardo Gamino[3], Raphael Meier[4], Minnie Sarwal[5], Peter Stock[6]

[1]*University of California San Francisco; Department of Surgery*
[2]*University of California, San Francisco; Department of Surgery*
[3]*University of California, San Francisco*
[4]*University of Maryland; Surgery; Department of Surgery, University of Maryland School of Medicine, Baltimore, MD, United States*
[5]*Uc San Francisco*
[6]*University of California San Francisco; Surgery*

Background
Managing obesity in pancreas transplant patients is a critical challenge due to the increasing prevalence in this population, and the association between obesity and insulin resistance.[1,2] GLP-1 agonists (GLP-1A) have the potential to revolutionize obesity and diabetes therapy, but safety and efficacy in whole-pancreas transplant patients has not been established, especially in light of a black-box warning for a potential association with pancreatitis and pancreatic cancer.[3] Here we report the outcomes of whole-pancreas transplant recipients treated with a GLP-1A for obesity.

Methods
This is a retrospective cohort study of all pancreas transplant recipients followed at our institution treated with a GLP-1A for obesity. We extracted baseline characteristics of donors and recipients, as well as medications used for treatment of obesity, diabetes, and immunosuppression. We recorded patient weight and Hemoglobin A1c (HbA1c) at transplant, GLP-1A start, GLP-1A end (or current weight if still taking), and after GLP-1A cessation (if therapy was stopped permanently). We also recorded any complications and reasons for stopping GLP-1A. We compared weights and HbA1c values using paired t-tests.

Results
There were 19 pancreas transplant recipients treated with GLP-1A with a mean BMI at transplant of 28.5±3.5 kg/m^2 (Table 1). At the time of GLP-1A initiation, weight had increased 21kg from transplant and 8 patients (42%) were requiring either insulin or oral diabetes therapy. After a median 211 (IQR 127-436) days on GLP-1A therapy, patients lost nearly half this weight gain (9.8kg) ($p<0.001$, Figure 1) and HbA1c improved by 0.3 points ($p=0.01$). Ten patients (53%) stopped GLP-1A at least once, most commonly for insurance coverage (N=7) and GI side effects including nausea and abdominal discomfort (N=6). Eight patients (42%) stopped and did not restart and these patients regained 2.6kg ($p=0.04$) from cessation until the most recent weight check. Two patients experienced asymptomatic pancreatic enzyme elevations, one resolved without holding GLP-1A, the other resolved after holding GLP-1A. There were no cases of malignancy in this cohort.

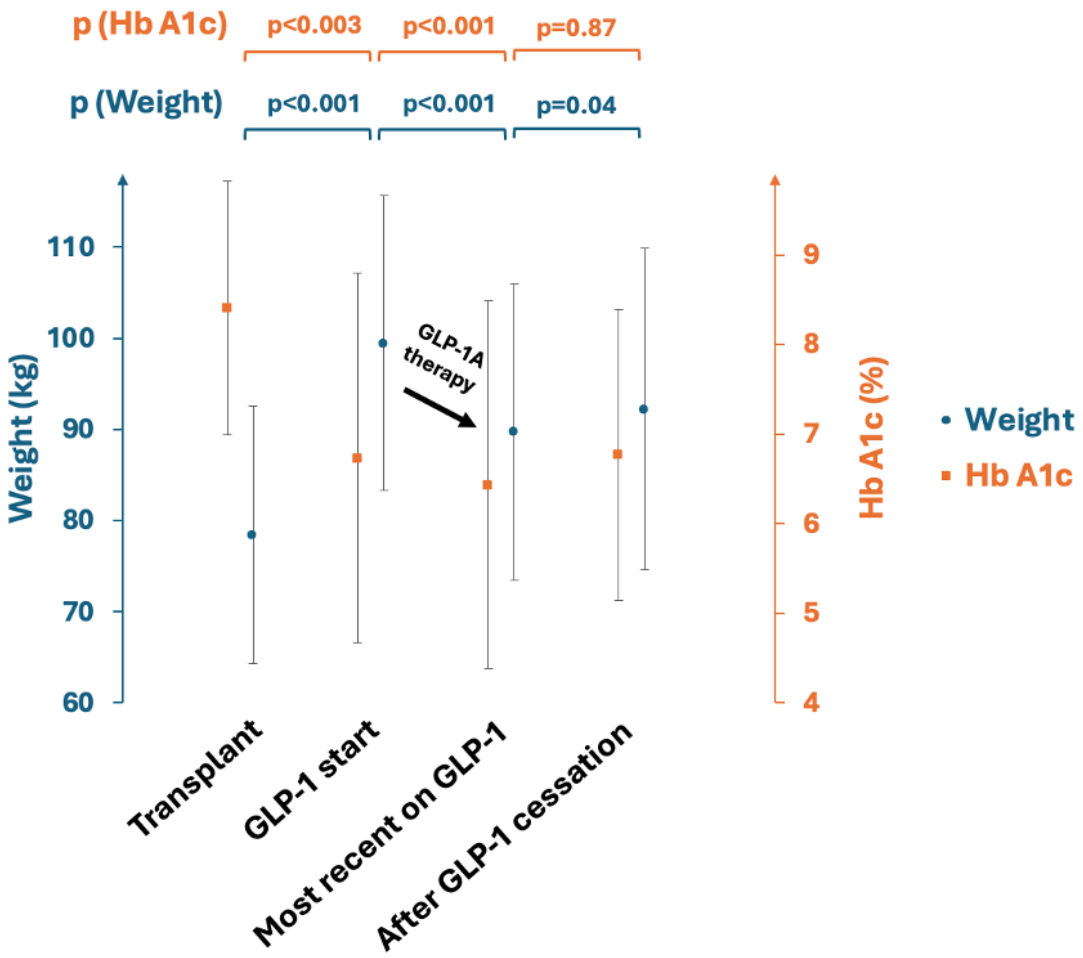
Conclusions
GLP-1A therapy result in substantial weight loss and improvement in Hb A1c in pancreas transplant recipients– including those with graft failure. The safety profile in this small cohort was acceptable, with no serious adverse events and no episodes of graft pancreatitis. However, GI side effects, high costs, and inconsistent insurance coverage are major barriers to widespread and consistent usage.

Table 1: Baseline characteristics of pancreas transplant recipients treated with GLP-1 agonists for obesity

Patients (N)	19
Age at transplant*	40.9 (9.4)
Race	
White[º]	10 (53)
Black[º]	2 (11)
Other[º]	7 (37)
Hispanic[º]	8 (42)
Sex Female[º]	6 (32)
Type 1 DM[º]	19 (100)
Transplant type	
SPK[º]	17 (89)
PAK[º]	2 (11)
GLP-1 agonist used	
Semaglutide	15 (79)
Tirzepatide	4 (21)
Duration of therapy (days)[a]	211 (127-436)
Recipient BMI at transplant (kg/m²)*	28.5 (3.5)
Recipient Weight (kg)	
Transplant	78.5 (14.1)
GLP-1 Start	99.5 (16.2)
GLP-1 End	89.7 (16.3)
After GLP-1 cessation	92.3 (17.6)
Hb A1c	
Transplant	8.4 (1.4)
GLP-1 Start	6.7 (2.1)
GLP-1 End	6.4 (2.1)
After GLP-1 cessation	6.8 (1.6)
Side Effects	
Nausea[º]	8 (42)
Asymptomatic Pancreatic enzyme elevation[º]	2 (11)
Therapy stopped at least once[º]	10 (53)
Currently on GLP-1A[º]	11 (58)
Reason for stopping (can be multiple)	
Coverage	7
GI side effects[º]	6
Pancreatic enzyme elevation	1
Second Pancreas Transplant	1
Elective surgery	1
Other Diabetes therapy	8 (42)
Oral[º]	6 (32)
Insulin [º]	5 (26)
Steroid maintenance	13 (86)

* Mean (SD) º N (%) [a]Median (IQR)

Figure 1: Weight and Hb A1c, at the time of GLP-1 therapy start, the most recent weight while on GLP-1 therapy (corresponding to the weight at GLP-1 stop for those that stopped therapy, and the most recent weight available for those that are still on therapy), and the most recent weight for those who stopped GLP-1 therapy. P-values calculated using paired t-tests.



Bibliography

1. Fridell JA, Mangus RS, Taber TE, et al. Growth of a nation part II: impact of recipient obesity on whole-organ pancreas transplantation. *Clinical Transplantation*. 2011;25(4):E366-E374. doi:10.1111/j.1399-0012.2011.01422.x

2. Parajuli S, Tamburrini R, Aziz F, et al. Risk Factors for Early Post-transplant Weight Changes Among Simultaneous Pancreas-kidney Recipients and Impact on Outcomes. *Transplant Direct*. 2024;10(11):e1720. doi:10.1097/TXD.0000000000001720

3. Drucker DJ. Efficacy and Safety of GLP-1 Medicines for Type 2 Diabetes and Obesity. *Diabetes Care*. 2024;47(11):1873-1888. doi:10.2337/dci24-0003

Conflicts of interest
No conflicts of interest

OP06 - ONE-YEAR HBA1C AS A PREDICTOR OF LONG-TERM GRAFT SURVIVAL IN SPK TRANSPLANTATION: A RETROSPECTIVE ANALYSIS OF UNOS REGISTRY DATA

Georgios Kourounis[1], Samuel James Tingle[2], Angeles Maillo Nieto[3], Caroline Wroe[4], James Shaw[5], Steve White[6], Colin Wilson[7]
[1]*Freeman Hospital; Institute of Transplantation*
[2]*Institute of Transplantation; Hpb and Transplant Surgery*
[3]*Freeman Hospital; Diabetes and Endocrinology*
[4]*Institute of Transplantation, The Freeman Hospital*
[5]*Newcastle University; Newcastle University; Translation and Clinical Research Institute*
[6]*Newcastle Upon Tyne Hospitals NHS Foundation Trust; Dept of Surgery*
[7]*The Newcastle Upon Tyne Hospitals NHS Foundation Trust*

Background
One-year graft survival is a key indicator of long-term function in pancreas transplantation. However, among patients with functional grafts at one-year, reliable predictors for long-term outcomes remain unclear. This study evaluates HbA1c at one year as a potential predictor of long-term graft function.

Methods
A retrospective cohort study using the UNOS registry on all simultaneous pancreas-kidney (SPK) transplants between 2017-2024. Regression models with multiple imputations for missing data were used to evaluate predictors of long-term function. Non-linear relationships were modelled with restricted cubic splines (RCS). Power calculations were conducted to compare the sample sizes between different outcome measures.

Results
There were 4,215 SPK transplants during the study period, of which 2,915 (69%) had a functioning graft at one year and >1 year of follow-up data. Median length of follow-up from time of transplantation was 44 (IQR 25-60) months. HbA1c at one-year post-transplant was the strongest predictor of subsequent graft survival (Fig 1A). The relationship was non-linear in RCS analysis ($p<0.01$,Fig 1B). A higher one-year HbA1C of 6.8% (95th percentile) compared to 4.4% (5th percentile) was associated with poorer subsequent graft survival (aHR=4.13, 3.56-4.88). Sample size calculations found that one-year HbA1C, being a continuous measure, required fewer patients per group to achieve adequate power compared to using the binary outcome for graft failure at one year (Fig 2).

Conclusions
At one year follow up, recipient HbA1c was the most important predictor of long-term pancreas graft function. This highlights its usefulness as a surrogate marker of outcome and supports its role in post-transplant monitoring. As a continuous outcome it could be an effective clinical trial endpoint, requiring far fewer participants than a trial powered for graft loss. Sensitivity analyses are being conducted to investigate differences in trends resulting from the recent change in the graft failure definition by UNOS.

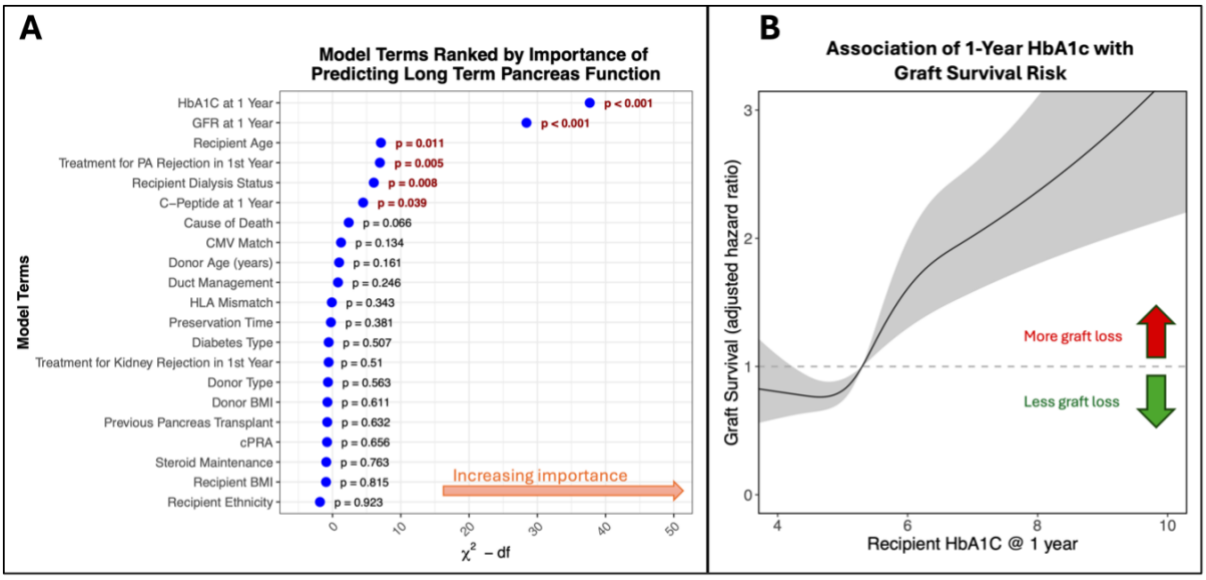


Figure 1. (A) Model terms ranked by significance in predicting long-term pancreas graft function. HbA1c at one year is the strongest predictor, followed by GFR and recipient age; (B) Adjusted hazard ratio for graft survival based on recipient HbA1c at one year. The non-linear relationship is shown with restricted cubic splines analysis, indicating higher HbA1c levels increase graft loss risk.

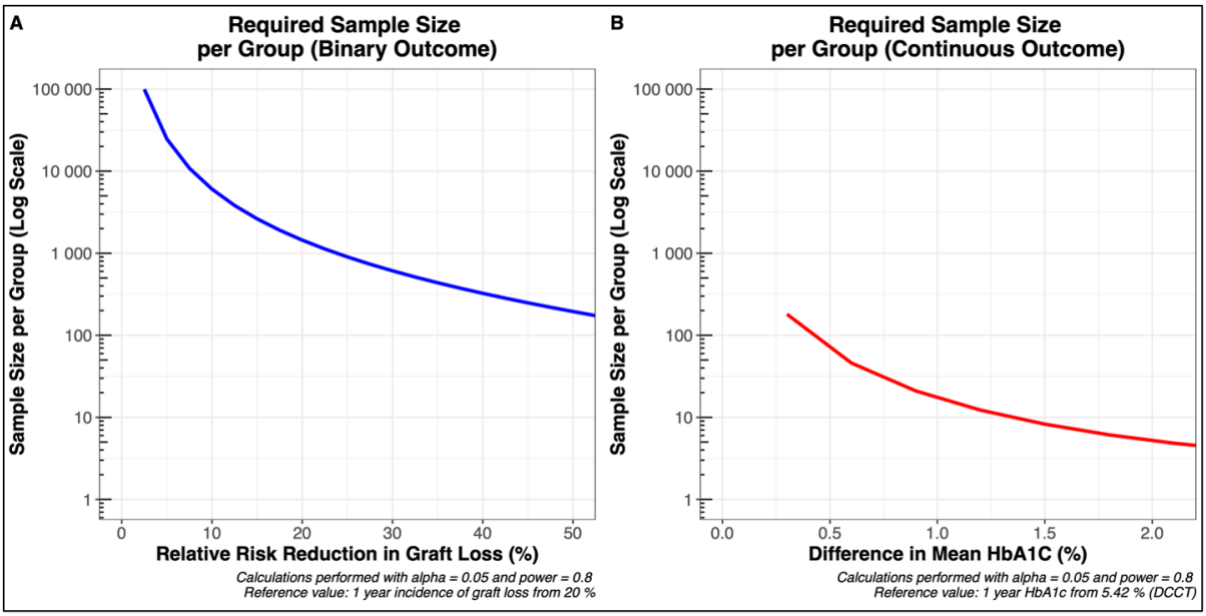


Figure 2. Sample sizes required to detect the desired minimum clinically important difference along the range shown on the x-axis: (A) relative risk reduction in graft loss from 20% at one year, and (B) change in one-year mean HbA1c from 5.42%.

Conflicts of interest

No conflicts of interest

OP07 - GLUCOSE VARIABILITY AND GLYCAEMIA RISK INDEX ARE INDICATORS OF GRAFT FUNCTION IN ISLET TRANSPLANT RECIPIENTS

Willemijn de Vos[1], Mandala Ajie[1], Cyril Landstra[2], Maarten Tol[3], Roxanna Hauck[2], Dirk Jan Cornelissen[4], Marten Engelse[5], Eelco de Koning[6]
[1]*Leiden University Medical Centre; Internal Medicine*
[2]*Leiden University Medical Centre (Lumc); Department of Internal Medicine*
[3]*Leiden Universitair Medisch Centrum: Leids Universitair Medisch Centrum; Nephrology*
[4]*Lumc; Nierziekten*
[5]*Leiden University Medical Center (Lumc); Leiden University; Nephrology*
[6]*Leiden University Medical Centre (Lumc); Dept of Nephrology*

Background
Allogeneic and autologous islet transplantation (ITx) is performed to stabilise glycaemic control by restoring endogenous insulin secretion. Continuous glucose monitoring (CGM) is used to monitor and improve glycaemic control post-ITx. We hypothesised that the CGM metrics of glucose variability and the glycaemia risk index (GRI; a composite metric representing glycaemic quality) are indicators of islet graft function during follow-up and could therefore serve as simple, fast and non-invasive methods to evaluate islet graft function.

Methods
Clinical outcome parameters related to glycaemic control from allogeneic and autologous islet transplantation recipients with at least three months of follow-up were analysed until one year post-ITx. As an indicator of islet graft function, we determined the area under the curve (AUC) of C-peptide during a mixed meal tolerance test (MMTT) at three months and one year post-ITx. Averaged CGM metrics of the fourteen days preceding the MMTT included time in range (TIR; 3.9-10.0 mmol/L), time in clinically relevant (level 2) hypoglycaemia (TBR Lv2; <3.0 mmol/L), glucose variability (%CV) and glycaemia risk index (GRI= (3.0 × Very Low) + (2.4 × Low) + (1.6 × Very High) + (0.8 × High)). Using Spearman-correlation analysis we determined the relation between glucose variability or GRI and islet graft function.

Results
We analysed a total of 24 (13 allogeneic/11 autologous) islet transplant recipients (41.7% female; BMI 24.1±2.8 kg/m^2; age 48.0±11.9 years). TIR was 85.0±15.3% at three months and 64.3±25.3% at one year post-ITx. In allogeneic transplant recipients TBR Lv2 decreased 16 fold from 0.48% [0.18 – 1.96] at baseline to 0.03% [0.00 – 0.46] at three months. This effect persisted up to one year (0.0% [0.00 – 0.17]). Autologous transplant recipients did not have notable hypoglycaemic events pre-ITx 0.00% [0.00 – 0.00], but showed a similar decline in TBR Lv2 post-ITx from 0.08% [0.00 - 0.45] at three months to 0.00% [0.00 – 0.00] at one year. At three months post-ITx, %CV was 25.7±8.3% with a C-peptide AUC of 127.8±85.2 nmol/L/120min. At one year, %CV increased to 30.5±7.6% and C-peptide AUC decreased to 96.5±73.2 nmol/L/120min. C-peptide AUC was negatively correlated with glucose variability %CV (R=-0.68, P<0.001) and GRI (R=-0.62, P=0.002) and positively correlated with TIR (R=0.63, P<0.01) at three months. Similar correlations with C-peptide AUC were found at one year for %CV (R=-0.73, P=0.015), GRI (R=-0.89, P<0.001) and TIR (R=0.84, P<0.01).

Conclusions
Glucose variability and glycaemia risk index may be used as indicators of graft function in islet transplant recipients during follow-up.

Conflicts of interest
No conflicts of interest

OP08 - SIMILAR ISLET GRAFT FUNCTION AND FEWER POST-TRANSPLANTATION INFECTIONS WITH BASILIXIMAB COMPARED TO ALEMTUZUMAB

Cyril Landstra[1], Roxanna Hauck[1], Willemijn de Vos[2], Rienke de Fijn[1], Sophie Jansen[1], Michiel Nijhoff[3], Eelco de Koning[4]
[1]*Leiden University Medical Centre (Lumc); Department of Internal Medicine*
[2]*Leiden University Medical Centre; Internal Medicine*
[3]*Leiden University Medical Center (Lumc); Internal Medicine*
[4]*Leiden University Medical Centre (Lumc); Dept of Nephrology*

Background
Before the coronavirus disease 19 (COVID-19) pandemic, in all first allogeneic pancreatic islet transplantations (ITx) in our centre, induction immunosuppression (iIS) consisted of T-cell depletion with alemtuzumab. Patients who had received a prior transplantation with alemtuzumab induction received the interleukin-2 receptor blocker basiliximab as iIS. During the pandemic, the standard iIS for all first ITx was switched to basiliximab, as it was considered to have a better safety profile in the context of the risk for infections.

Methods
This is a single-center, retrospective, pre-/post-implementation study comparing basiliximab to alemtuzumab as iIS for all first ITx recipients with at least 3 months of post-ITx data between 2007-2024 at the Leiden University Medical Centre. Islet graft function was assessed using the area-under-the-curve (AUC) of C-peptide during a mixed meal tolerance test (MMTT). Igls criteria 2.0 and beta score were used as clinical outcome parameters. Reported infections and side-effects were extracted from patients' electronic health records. Data were analysed at baseline (pre-ITx) and 3 months post-ITx.

Results
A total of 63 first ITx recipients were analysed, of which 28 (44.4%) received basiliximab and 35 (55.6%) alemtuzumab (77.8% islet-after-kidney, 19.0% islet-transplant-alone and 3.2% islet-after-lung; mean age 60.2 ± 10.0 years; 36.5% female). At 3 months post-ITx, patients receiving basiliximab showed similar islet graft function compared to recipients receiving alemtuzumab (AUC C-peptide 120.0 [76.6 – 235.1] *vs* 120.0 [83.7 – 193.2; p = 0.581]). There was no difference in treatment outcome between basiliximab and alemtuzumab (Igls 2.0 Treatment outcome was Optimal in 50.0% *vs* 67.6%, Good in 28.6% *vs* 11.8%, Marginal in 21.4% *vs* 14.7%, and Failure in 0.0% *vs* 5.9%; p = 0.166). CD3+ T-cells were lower in the alemtuzumab group (p < 0.001) and infections were less often reported in the basiliximab group (28.6% *vs* 55.9%; p = 0.031). Other side-effects were reported at a similar rate (basiliximab 46.4% *vs* alemtuzumab 52.9%; p = 0.320).

Conclusions
Basiliximab results in similar islet graft function as alemtuzumab, but with fewer reported infections and higher CD3+ T-cells at 3 months post-transplantation. Further outcomes at 1, 2 and 3 years post-ITx will follow at the time of the conference.

Conflicts of interest
No conflicts of interest

OP09 - ISLET TRANSPLANTATION OUTCOMES FROM DONORS OLDER THAN 55 YEARS

Esmay Hammink[1], Jason Doppenberg[2], Francoise Carlotti[3], Marten Engelse[4], Eelco de Koning[5]
[1]*Lumc*
[2]*Leiden University Medical Center*
[3]*Leiden University Medical Center; Internal Medicine*
[4]*Leiden University Medical Center (Lumc); Leiden University; Nephrology*
[5]*Leiden University Medical Centre (Lumc); Dept of Nephrology*

Background
Islets from older organ donors are often not accepted for clinical islet transplantation as they are suspected to result in inferior islet transplantation outcomes. Whether this exclusion of older donors is justified remains unclear. We compared islet function and clinical outcomes after transplantation of islet grafts from older and younger donors.

Methods
Islet isolation preparations from 2008-2023 that were transplanted were retrospectively analyzed, resulting in 81 preparations from donors <55 years and 34 preparations from donors ≥55 years. A cut-off age of fifty-five years was chosen to better reflect the older donor population, as previous studies have typically defined older donors using lower thresholds of 40 or 45 years, which may not accurately represent this group. As we also combine grafts for one infusion in our program to reach a suitable islet dose (>5,000 IEQ/kg recipient), recipients who received single or combined grafts from only younger donors (n=42) were compared to recipients receiving single or combined grafts from only older donors (n=10).

Results
The younger donor group had a mean age of 43 ± 7.5 years (range: 23-54 years) and the mean age in the older donor group was 61 ± 5.3 years (range: 55-69 years). The ratio of DBD/DCD donors was comparable, with 71% DBD in the younger donor group and 79% DBD in the older donor group (p=0.49) The islet yield did not differ significantly between the two donor groups (<55 vs ≥55 years, 761,836 ± 300,157 islet equivalents (IEQ) vs 656,809 ± 250,340 IEQ, p=0.09), as well as the transplanted islet mass (<55 vs ≥55, 12,974 ± 3,546 IEQ/kg recipient vs 11,637 ± 5,908 IEQ/kg recipient, p=0.38). In vitro insulin secretion following glucose stimulation revealed no significant difference in the AUC stimulation indexes (p=0.97). Three months post-transplantation, the mixed meal test C-peptide AUC corrected for transplanted islet mass showed similar graft function with 0.012 ± 0.006 (pmol/L)/(IEQ/kg) (<55 years) and 0.014 ± 0.007 (pmol/L)/(IEQ/kg) (≥55 years) (p=0.61). Random C-peptide/glucose ratios at 1 year post-transplantation also did not differ significantly (p=0.66). The IGLS 2.0 score at 1 year post-transplantation did not show significant differences in both graft function (p=0.81) and clinical outcome (p=0.81).

Conclusions
Islet grafts from older donors (≥55 years) are suitable for islet transplantation, as they demonstrate comparable graft function and clinical outcome when compared to younger donors (<55 years).

Conflicts of interest
No conflicts of interest

OP10 - EFFICACY OF INTRAMUSCULAR AUTOLOGOUS ISLET TRANSPLANTATION IM-IAT FOLLOWING EXTENDED PANCREATECTOMY

Mikael Chetboun[1], Frederique Defrance[2], Valery Gmyr[3], Violeta Raverdy[4], Mehdi Maanaoui[4], Delalleau Nathalie[5], Anais Codeville[6], Julien THEVENET[7], Gianni Pasquetti[8], Aurelie Lobez[9], Thomas Hubert[10], Robert Caiazzo[4], Jean-Marc Regimbeau[11], Michel Scotte[12], Alain Sauvanet[13], Jean-Robert Delpero[14], Julie Kerr-Conte[15], Marie-Christine Vantyghem[16], Francois Pattou[17]

[1]*Chu Lille; General and Endocrine Surgery*
[2]*Lille University Hospital; Claude Huriez Hospital; Department of Endocrinology, Diabetology, Medical Oncology and Metabolism*
[3]*Inserm U1190*
[4]*Chu Lille*
[5]*Univ Lille*
[6]*University of Lille*
[7]*"Translational Research for Diabetes" Lab; Faculté de Médecine*
[8]*Inserm U1190 - University of Lille / Chu Lille; Nord*
[9]*Chu de Lille*
[10]*University Hospital; Inserm U1190*
[11]*Chu Amiens*
[12]*Chu de Rouen*
[13]*Aphp*
[14]*Ipc*
[15]*Chu Lille; Faculty of Medicine*
[16]*Lille University Hospital; Endocrinology and Metabolism*
[17]*Univ Lille; U1190*

Background
Autologous islet transplantation can be proposed to preserve insulin secretion and reduce the risk of diabetes after extended pancreatectomy. Intramuscular transplantation may reduce the risk associated with standard intraportal route. The aim of this phase II multicentric prospective study was to evaluate the safety and efficacy of intramuscular autologous islet transplantation (IM-AIT) in preventing diabetes post-extended pancreatectomy.

Methods
Participants were nondiabetic patients undergoing extended pancreatectomy for non-malignant, non-genetic pancreatic diseases. Islets were isolated from resected non pathological pancreatic tissue. At day 1, islet preparation was injected into the brachioradialis muscle under local anesthesia. Islet graft function was evaluated at 3 months, by measuring the change of acute insulin response to iv arginine (AIRa) before and after vascular graft exclusion using arm-cuff inflation. Optimal islet graft function at 3 months was defined as an increase (≥30%) insulin secretion in the transplanted arm compared to the non-transplanted arm. Secondary outcomes included metabolic balance evaluations with continuous glucose monitoring metrics at one year.

Results
From 2013 to 2022, 14 patients were enrolled following left pancreatectomy (n=11), total pancreatectomy (n=2), pancreaticoduodenectomy (n=1), for the treatment of chronic pancreatitis (n=3), intraductal papillary mucinous neoplasms (n=4), neuroendocrine tumors (n=4), solid pseudopapillary epithelial neoplasms (n=1), mucinous cystic adenoma (n=1) and trauma (n=1), (Table 1). A total of 101,554 pancreatic islets ±79,775, with 45% ±21 purity and 92% ±4 viability, were transplanted into the brachioradialis muscle of the non-dominant forearm. 10 patients (71%) had a functioning transplant at 3 months demonstrated by a decrease in AIR to arginine when intramuscular transplant was excluded by arm-cuff inflation

(Fig. 1) (Wilcoxon matched-pairs signed rank test, p=0.018). Only, three patients demonstrated an optimal islet graft function 3 months following IM-IAT. At one-year post-transplantation, the mean HbA1c was 5.9 ±0.6% vs. 5.3 ±0.3% at baseline (p=0.008). The mean fasting glucose level was 111 ±20 mg/dL. The time spent in hyperglycemia (≥170 mg/dL) and hypoglycemia (<54 mg/dL) were 5.2 % ±9.8 and 1.3 % ±3.3, respectively. Notably, 7 patients (50%) required insulin therapy.

Conclusions

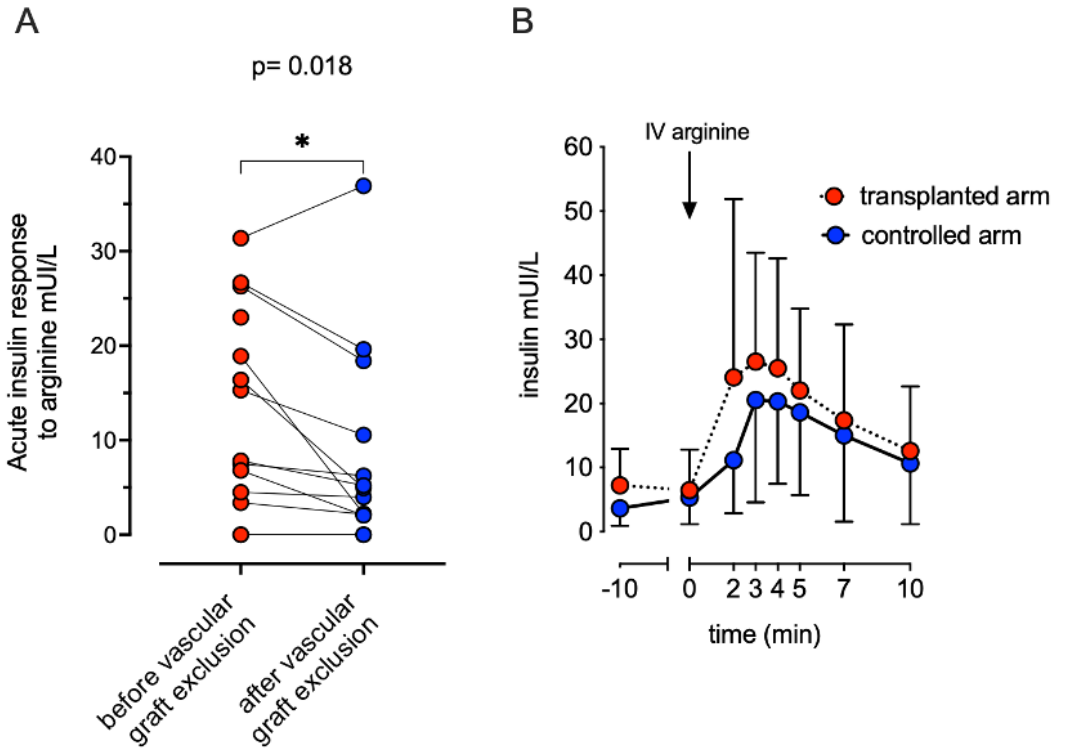
IM-AIT was associated with islet graft survival and function in 71%, of cases with no significant complications. This minimally invasive approach mitigated the metabolic impact of extended pancreatectomy, with the advantage of not being limited by tissue cell volume. However, the low rate of optimal islet graft function (21%), and insulin independence (50%) highlighted the need for further optimization of IM-AIT.

Table 1 : Transplantation characteristics of the fourteen patients included in the study.

patients	age at transplantation (years)	pancreatectomy procedure	histology	islet mass transplanted	islet mass transplanted (IEQ)	purity (%)	viability (%)
1	62	left pancreatectomy	IPMN	87,333	70,488	52.2	99
2	57	left pancreatectomy	CP	59,400	43,320	45	90
3	59	left pancreatectomy	IPMN	48,667	29,244	50	91.3
4	47	left pancreatectomy	SPEN	136,333	78,422	51.8	90
5	39	left pancreatectomy	mucinous cystic adenoma	38,667	56,444	70	93
6	71	left pancreatectomy	G1 NET insulinoma	206,000	128,067	38	91
7	30	left pancreatectomy	normal (trauma)	35,560	26,741	25	91
8	81	left pancreatectomy	G2 NET gastrinoma	192,667	94,356	70	96
9	35	TP	CP	73,800	39,180	5	99
10	26	TP	CP	45,000	26,640	30	97
11	74	left pancreatectomy	G1 NET insulinoma	302,000	115,778	75	88.8
12	74	left pancreatectomy	G1 NET insulinoma	93,333	76,511	62	88.2
13	63	pancreaticoduodenectomy	IPMN	51,000	49,422	38.3	86.3
14	55	left pancreatectomy	IPMN	52,000	25,532	12.5	89

TP: total pancreaticoduodenectomy; CP: chronic pancreatitis; IPMN: intraductal papillary mucinous neoplasms; SPEN: solid pseudopapillary epithelial neoplasm; G: grade; NET: neuroendocrine tumor

Figure 1: Insulin secretion at 3 months post-transplantation: acute insulin response to arginine before and after vascular graft exclusion (Fig. 1A), and comparison of insulin secretion in the transplanted and control arms (Fig. 1B).



The Wilcoxon matched-pairs signed-rank test was used to compare the acute insulin response (AIR) to arginine before and after vascular graft exclusion achieved through arm-cuff inflation in the transplanted forearm (Fig. 1A)

Conflicts of interest
No conflicts of interest

OP11 - ISLETNET SUPPORTS ACCURATE VOLUME ESTIMATION OF ISOLATED PANCREATIC ISLETS

David Habart[1], Jiří Janáček[2], Barbora Radochová[2], Sarah Suergiu[3], Klara Zacharovova[4], Zuzana Berková[5], Jan Kriz[6], Jakub Monhart[7], Jan Kubant[8], Adam Blazek[9], Filip Matzner[9], Petr Belohlavek[9], Frantisek Saudek[10]

[1]*Institute for Clinical and Experimental Medicine; Diabetes Center; Laboratory for Pancreatic Islets*
[2]*Institute of Physiology of the Czech Academy of Sciences*
[3]*Institute for Clinical and Experimental Medicine; Laboratory for the Islets of Langerhans (Lil)*
[4]*Institute for Clinical and Experimental Medicine; Centrum of Experimental Medicine, Laboratory of Pancreatic Islets*
[5]*Ikem; Laboratory of Pancreatic Islets*
[6]*Institute for Clinical and Experimental Medicine; Diabetes Center; Department of Diabetes*
[7]*Mild Blue L.T.D*
[8]*Mild Blue*
[9]*Iterait*
[10]*Institute for Clinical and Experimental Medicine*

Background
IsletNet.com is a web service designed to improve the accuracy of volume-based dosing of isolated pancreatic islets to improve reproducibility of transplantation outcome. Its accuracy depends on microscopic images, neural network-based segmentation of islets, and the model used to interpret these segmentations. The standard spherical model[1,2] implemented in IsletNet was validated against assessments by three experts and compared to the volumes estimated by alternative models derived from islet shapes.

Methods
Images of islets isolated by collagenase/ficoll-based method were acquired through standard and advanced (widefield, lightsheet) 2D and 3D microscopy were analyzed using Fiji and Ellipse. Islet shapes were characterized by ratios of axes from fitted Lagrange ellipsoids. Test samples were sequentially counted by three experts using stereo microscope with reticle-equipped eye piece, followed by imaging with conventional microscopy under various color settings to challenge the segmentation engine.

Results
Analysis of 1,732 digitized islets revealed shapes better represented as intermediate triaxial ellipsoids rather than spheres or prolate or oblate spheroids. Sphiracle model (spherical extrusion with statistical flatness factor), was developed and tested on 863 digitized islets with favorable relative bias and mean relative squared error compared to sphere (0.03 vs.0.37; 0.13 vs. 0.43). Accuracy of two alternative models (sphiracle and spinacle[3]) implemented in IsletNet was confirmed on 60 additional islets with measured volumes (**Fig. 1A**). Tested on 12 random samples of 549 dithizone-stained pure islets (**Fig. 1B**), IsletNet with sphere based conversion table was within the range of three experts (**Fig. 1C**). Both precise models revealed great overestimation on part of the experts using the table (**Fig. 1D**).

Conclusions
Islet shapes characterized here explain inherent limitation of the current model which was resolved by two alternative models. These are interim results from more extensive validation on rat and human islets.

Conflicts of interest
No conflicts of interest

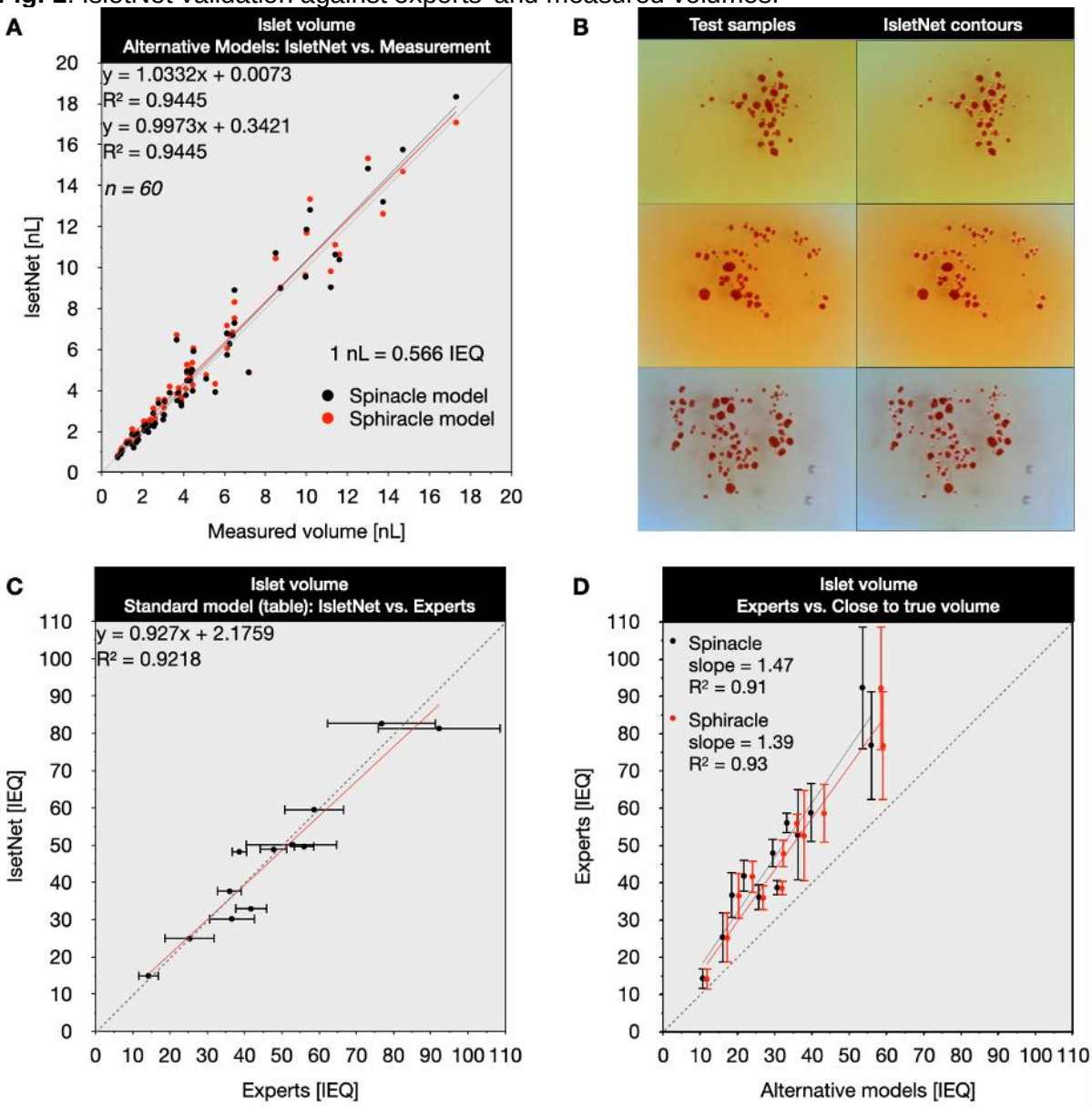
References

1. Ricordi C, et al: Acta Diabetol Lat. 27, 1990: 185–195; 2. Niclauss N, et al: Transplantation, 2008: 1603–9; 3. Habart, D. et al. 10th EPITA Symposium & 39th AIDPIT Workshop Abstract 3391 (2020).

Acknowledgements

Supported by the grants from Czech Ministery of Health (NU22-01-00141) and from EU program EXCELES (CarDia, LX22NPO5104). Thanks to Petr Raska, IT Dept. IKEM, for sustained support over the years.

Fig. 1: IsletNet validation against experts' and measured volumes.



OP12 - PHASE 1 AND 3 LICENSURE TRIALS IN ISLET CELL TRANSPLANTATION LEADING TO FDA APPROVAL

James McGarrigle[1], Giovanna La Monica[1], Jennifer Cook[2], Peter Rios[1], Yi Li[1], Sofia Ghani[1], Ira Joshi[1], David Cook[1], Daisy Lopez[1], Hafsa Nasir[1], Quetzalli Rodriguez[1], Yvette Calvillo[1], Yong Wang[1], Jose Oberholzer[1]

[1]*Celltrans Inc.*
[2]*Celltrans Inc.; Finance and Administration*

Background
Herein we present the results of pivotal clinical trials that led to the FDA approval of islet cell transplantation (Lantidra) in the U.S.

Methods
The safety and efficacy of Lantidra were assessed in two open-label, non-randomized, single-arm studies: UIH-001 (Phase 1/2; n=10) and UIH-002 (Phase 3; n=20). Eligible patients had T1D for >5 years with severe hypoglycemia episodes (SHEs) and reduced awareness. Median age was 46.5 years (range 21–67); 80% were female, 100% white, with a BMI of 23 kg/m² (range 20.2–27.3). Patients received 1–3 infusions to reach 10,000 EIN/kg body weight (11, 12, and 7 patients received 1, 2, or 3 infusions).

Results
Nineteen (63%) of the 30 participants achieved the composite endpoint (HbA1c ≤6.5% and no SHEs within a year after last transplant). Insulin independence was achieved by 67% (20/30) at 1 year. A dose-response relationship was observed with insulin independence at 1 year increasing progressively with higher EIN: 44% at 500,000 EIN, 57% at 500,000–750,000 EIN, 83% at 750,000–1,000,000 EIN, and 87% at >1,000,000 EIN.

Lantidra's safety profile aligned with the known risks of transplant procedures and long-term immunosuppressive therapy. Serious adverse events occurred in 90% of subjects, primarily due to immunosuppression, with two infusion-related complications but no procedure-related deaths. Renal function, monitored via eGFR, showed that at baseline (n=30), 69% of patients had mild or moderate impairment. One year after last transplant, 52% remained in the same category, 31% worsened, and 17% improved (mean follow-up: 2.3 ± 1.8 years), with no cases of severe impairment or renal failure.

Conclusions
In conclusion, Lantidra provides an FDA-approved treatment option for patients who present with T1D complicated by SHEs and metabolic instability despite intensive diabetes management. Benefits of Lantidra include elimination of SHEs, improved glycemic control, and often insulin independence leading to a significant improvement in quality of life.

Conflicts of interest
James McGarrigle, Giovanna La Monica, Jennifer Cook, Peter Rios: CellTrans Inc. Employee, Stock/Shareholder and Board Member
Yi Li: Consultant at CellTrans Inc. Employee: Cytel Inc.
Sophia Ghani, Ire Joshi, David Cook: CellTrans Inc. Employee and Stock/Shareholder
Daisy Lopez: CellTrans Inc. Employee
Hafsa Nasir, Quetzalli Rodriguez, Yvette Calvillo: Employed at CellTrans Inc.
Yong Wang: CellTrans Inc. Stock/Shareholder and Board Member, Employee: University of Zurich
Jose Oberholzer: CellTrans Inc. Stock/Shareholder and Board Member

OP13 - TRANSPLANTATION OF PANCREATIC ISLETS ISOLATED USING THE PANCREATIC ISLET SEPARATION METHOD (PRISM) MACHINE – A CASE REPORT

Rutger van Rooden[1], Jason Doppenberg[1], Mandala Ajie[2], Marten Engelse[3], Eelco de Koning[4]
[1]*Leiden University Medical Center; Transplantation Center*
[2]*Leiden University Medical Centre; Internal Medicine*
[3]*Leiden University Medical Center (Lumc); Leiden University; Nephrology*
[4]*Leiden University Medical Centre (Lumc); Dept of Nephrology*

Background
The most commonly used pancreatic islet isolation technique is an open method that requires 3-5 highly trained operators, utilizes several machines and varies strongly among centers.
To refine and standardize the islet isolation procedure, we recently developed a novel, automated, islet isolation technique (PancReatic Islet Separation Method, PRISM). Here we report on the first clinical islet transplantation with islets isolated using the PRISM machine.

Methods
A donation after brain death pancreas was procured from a 22-year-old female with a BMI of 32. The isolation was performed using the PRISM machine in our GMP facility.
After purification, density fractions were pooled based on purity and aspect, total IEQ was determined, a dynamic Glucose Stimulated Insulin Secretion (dGSIS) test performed, and islets were cultured for 2 days.
After our standard release criteria were met, the islets were transplanted in a 54-year-old female (BMI 21 kg/m^2) with T1D complicated by recurrent hypoglycemia and kidney failure for which she had received a kidney transplantation. Three months after transplantation, a mixed meal tolerance test (MMTT) was performed.

Results
The islet isolation using PRISM yielded a total IEQ of 1,018,913 (figure 1). On average, 77% of the islets were embedded by surrounding exocrine tissue. Functionality was confirmed via dGSIS with a peak stimulation index of 21.5. The patient received 945,652 IEQ in a pellet volume of 3625 µL and with 60% islet purity. At 3 months the patient used only 12 units of long-acting insulin. The glucose time in range had improved from 52% to 86% and time below range decreased from 1.4% to%. HbA1c improved from 7.7% to 5.4% and glucose variability from 31% to 29%. The MMTT showed a maximum C-peptide of 3.6 nmol/L.

Conclusions
Islet isolation using the PRISM machine is safe and can yield a high number of islets with good functional secretory capacity after transplantation.

Figures

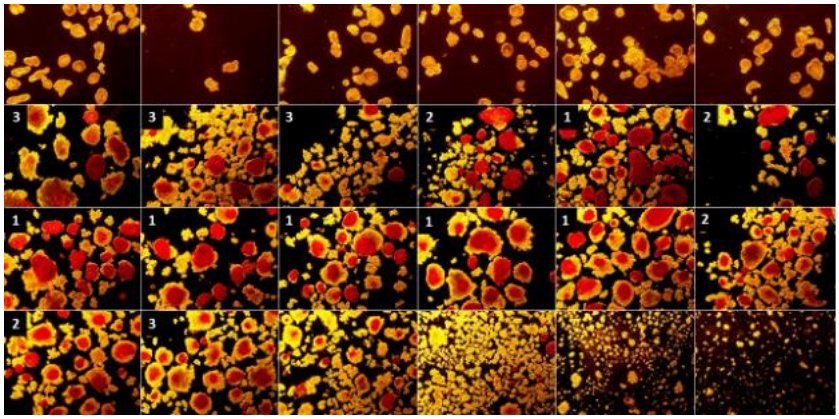


Figure 1. PRISM islet isolation. Microscopic images of dithizone-stained tissue fractions collected after density gradient separation. Islets are stained red. Magnification 40x. Fractions were made per 25 ml medium. From top left (density 1.045 g/ml) to right bottom (density 1.17 g/ml). Three pooled groups of fractions were created: pooled group 1: 1800 µL of 75% purity and 65% embeddedness, pooled group 2: 1225 µL of 50% purity and 47% embeddedness, and pooled group 3: 1270 µL of 30% purity and 52% embeddedness.

Conflicts of interest

Marten Engelse, Jason Doppenberg, Rutger van Rooden: Receives royalty payments and consultancy costs from Biorep, Miami Lakes, FL, USA.

OP14 - HUMAN ISLETS OF LANGERHANS FROM PANCREATECTOMY REMNANTS: LESSONS LEARNED FROM 50 CONSECUTIVE ISLET ISOLATIONS.

Eriselda Keshi[1], Theresa Lohmann[1], Luna Haderer[2], Lene Änne Böhne[3], Alexander Arnold[3], Matthäus Felsenstein[1], Anja Reutzel-Selke[4], Thomas Malinka[5], Johann Pratschke[6], Igor Sauer[7], Karl Hillebrandt[8]

[1]*Charité Universitätsmedizin Berlin; Surgical Clinic; Experimental Surgery*
[2]*Charitè Universitätsmedizin Berlin*
[3]*Charité Universitätsmedizin Berlin; Department of Pathology,*
[4]*Dept. of Surgery, Charité, Campus Ccm|cvk, Universitaetsmedizin Berlin*
[5]*Charité Universitätsmedizin Berlin; Department of Surgery*
[6]*Charité Universitätsmedizin Berlin; Department of Surgery, Campus Charité Mitte and Campus Charité Virchow*
[7]*1dept. of Surgery, Charité, Campus Ccm|cvk, Universitaetsmedizin Berlin*
[8]*Charite Universitätsmedizin Berlin; Clinic for General, Visceral and Transplanation Surgery*

Background
Islet transplantation is a viable beta cell replacement therapy for patients suffering from type 1 diabetes mellitus. The success of this approach remains constrained by apoptosis and necrosis-mediated damage resulting from failed islet engraftment, necessitating multiple islet infusions. Tissue engineering-based approaches focus on enhancing engraftment prior to implantation. For superior translatability these methods need to be evaluated using human islets. Here we present a novel protocol for the isolation of human islets from pancreatectomy resectates retrieved from the operating room.

Methods
Between March and October 2024, 50 standardized consecutive islet isolations were performed. Following isolation, islets were maintained in culture for a period of 24h. On the next day, the islets were picked, counted, and subjected to viability staining. Finally, the functionality of the islets was assessed through the measurement of static insulin secretion upon glucose stimulation. A retrospective analysis was conducted to evaluate the impact of patient-, surgery-, and resectate-related factors on the number of isolated islets and the resulting islet functionality.

Results
The total number of isolated islets per gram of pancreatic tissue ranged from zero to 56,500, with an average of 6,690 IEQ/g pancreatic tissue (**Figure 1**). Male sex, advanced age, the presence of diabetes mellitus type 2, malignant disease, or fatty pancreatic tissue were associated with reduced islet yields. the functional analysis demonstrated that the islets not only reacted adequately to stimulation with high-molecular weight glucose, but the amount of secreted insulin increased over the five-day cultivation period (**Figure 2**). A significant negative correlation was identified between the duration of surgery and islet functionality.

Conclusions
To the best of our knowledge, this is the first study to closely investigate the impact of patient-, surgery-, and resectate-related factors on islet yield and islet functionality *in vitro* over extended cultivation periods. Our findings suggest that female patients with a benign disease and good pancreatic parenchyma appear may represent the optimal source for higher islet yields with superior functionality.

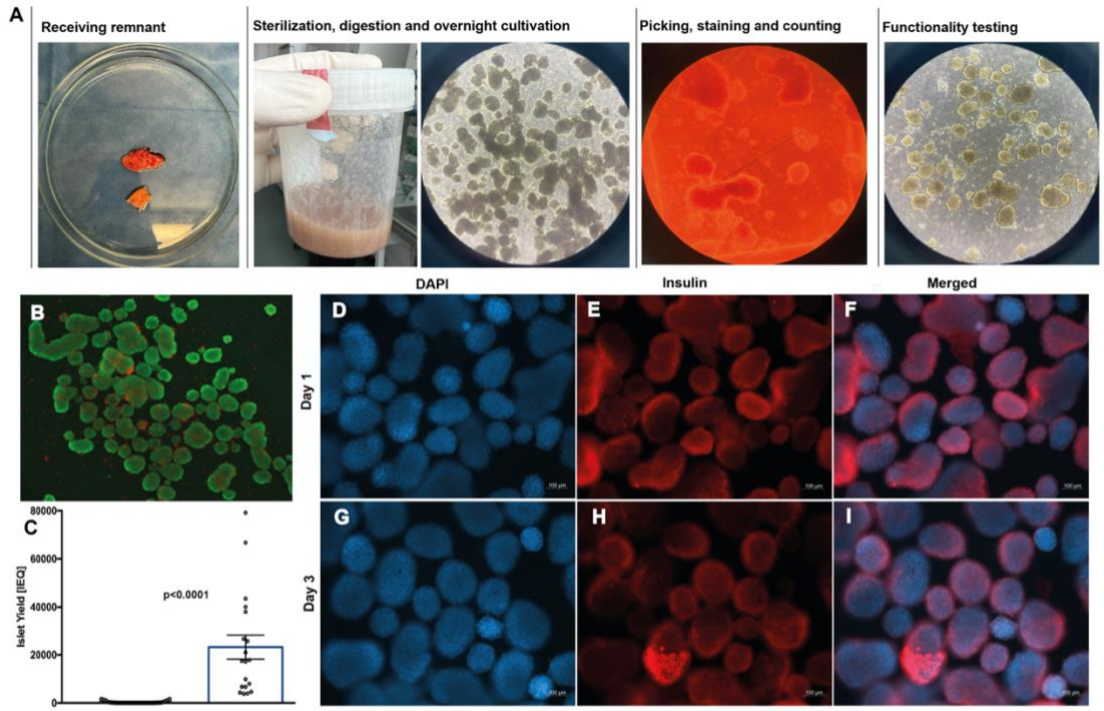


Figure 1: A) Isolation of human islets was performed according to a novel protocol established for pancreatectomy remnants. **B)** Islets were stained with FDA/PI for viability testing. **C)** The isolations were separated into low (<2000 IEQ) and high yield (>2000 IEQ) isolations, whereby there were n=31 low yield isolations, with the mean islet yield being 292,5 ± 477,08 IEQ and n=19 high yield isolations, with the mean islet yield being 23,209 ± 21113,8. The number of isolated islets was statistically different between the two groups (p<0.0001). **D-I)** After glucose stimulated insulin secretion on day 1 and day 3 of cultivation, insulin staining was performed

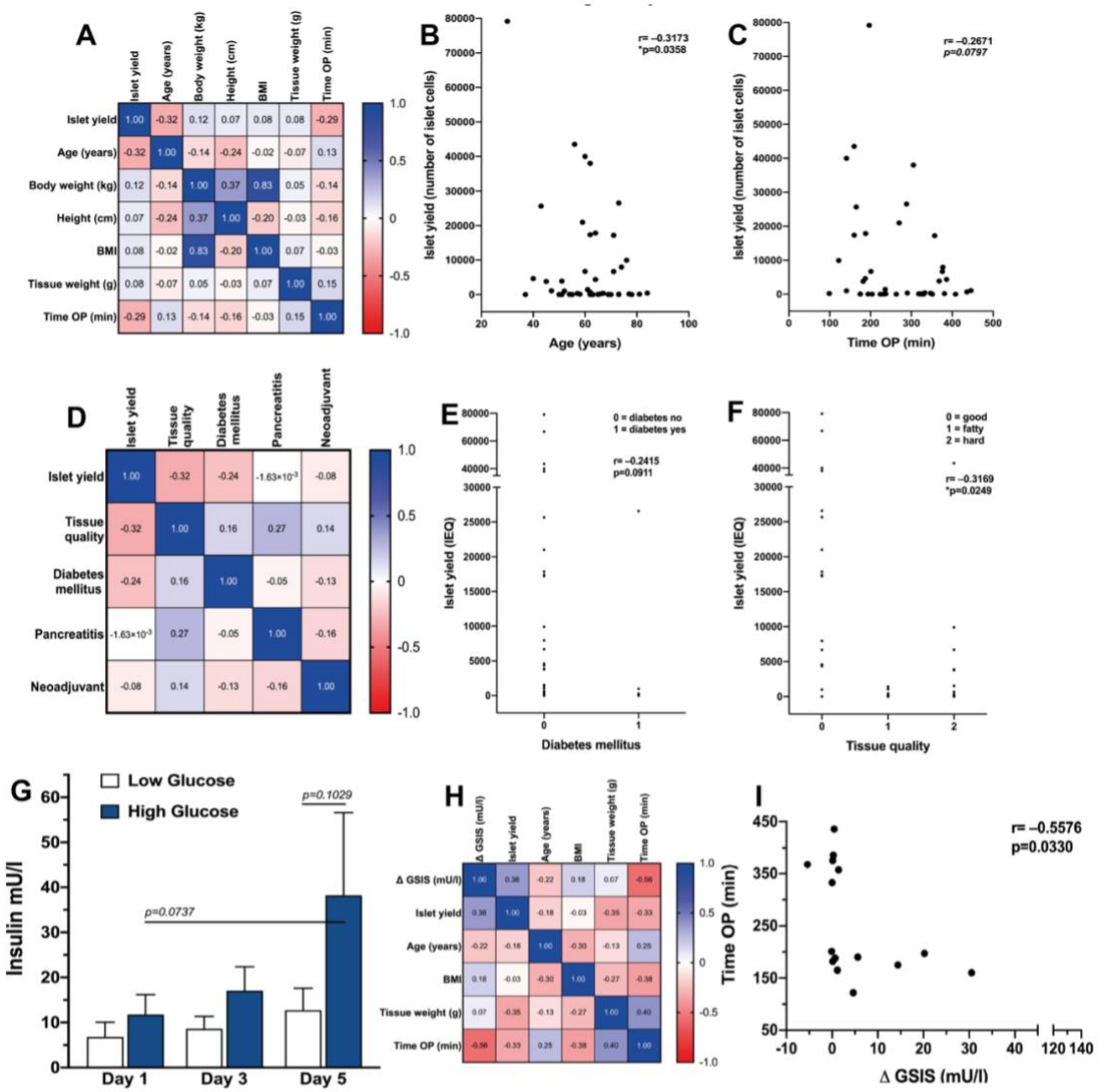


Figure 2: A-C) The correlation analysis revealed patient age (r=-0,31; p=0,03) and duration of surgery (r=-0,27; p=0,07) negatively correlated with islet yield. Body mass index (BMI) and tissue weight did not show any significant correlatio. **D-F)** Pancreatitis and neoadjuvant chemotherapy did not correlate with islet yield, but patients with diabetes mellitus type II and fatty or hard pancreas quality yielded less islets (r=-0,24; p=0,09, and r=0,31; p=0,02 respectively). **G)** Glucose stimulated insulin secretion test on day one, three and five of cultivation showed islet functionality not only remained intact, but insulin production increased with time. **H-I)** Our correlation analysis showed that while duration of surgery significantly correlated with islet functionality (r=-0,55; p=0,03), other parameters such as age, BMI, tissue weight, pancreatitis, diabetes mellitus, tissue quality and neoadjuvant chemotherapy did not correlate (p=0,05).

Conflicts of interest

No conflicts of interest

OP15 - OXYGENATED HYPOTHERMIC MACHINE PERFUSION IS A SUPERIOR METHOD OF PRESERVATION IN A PORCINE PANCREAS CIRCULATORY-DEATH MODEL.

Mohamed Elzawahry[1], John Fallon[2], Benoit Hastoy[3], Letizia Lo Faro[4], Sameena Nawaz[3], Julien Branchereau[5], Anne Clark[3], Rutger Ploeg[6], Peter Friend[7], James Hunter[8]

[1]*Oxford University; Nuffield Department of Surgical Sciences, University of Oxford, Oxford, United Kingdom; Nuffield Department of Surgical Sciences*
[2]*University of Oxford; Nuffield Department of Surgical Sciences*
[3]*University of Oxford; Oxford Centre for Diabetes, Endocrinology and Metabolism (Ocdem)*
[4]*University of Oxford; Nuffield Department of Surgical Sciences; Nhsbt Blood Donor Centre*
[5]*Nantes University Hospital; Centre de Recherche En Transplantation et Immunologie (Crti), Umr1064, Inserm, Université de Nantes*
[6]*Nuffield Department of Surgical Science*
[7]*Churchill Hospital; University of Oxford; Oxford Transplant Center*
[8]*Oxford University Hospitals; Nuffield Department of Surgical Sciences; Nuffield Department of Surgical Sciences*

Background
Beta cell replacement is an ongoing challenge. Pancreases are extremely vulnerable to ischaemia-reperfusion injury (IRI). During static cold storage (SCS) ATP is depleted, and by-products of anaerobic respiration, including succinate and lactate, accumulate. This injury affects quantity and viability of isolated islets, and in whole-organ transplantation, it is characterised by acinar necrosis, oedema, and endothelial disruption *'graft pancreatitis'*. The introduction of oxygenated hypothermic machine perfusion ($HMPO_2$) in liver and kidney preservation has resulted in a significant reduction in the consequences of IRI. Pancreas $HMPO_2$ was shown to be feasible in several pre-clinical studies. The aim of this study is to compare a 'continuous' to an 'end-ischaemic' approach in application of $HMPO_2$ in pancreas preservation using a porcine circulatory death model.

Methods
Porcine pancreases were retrieved from an abattoir after exsanguination. Pancreases were flushed with UW cold storage solution and prepared surgically, then either preserved on $HMPO_2$ for the totality of the cold storage time (n=6), preserved in SCS then with $HMPO_2$ for the last two hours of the cold storage time (n=6), or kept in SCS throughout (n=6). After a mean of 524 minutes of hypothermic preservation, the 3 groups then underwent normothermic reperfusion (NR) with autologous whole blood to mimic transplantation and instigate IRI. Perfusate and tissue were sampled at regular intervals for assessment of injury. Glucose Stimulated Insulin Secretion (GSIS) was measured during NR for functional assessment (n=3 in each group).

Results
The warm ischaemia and cold ischaemia times were comparable between the three groups. All groups had no significant difference in wet-to-dry ratio (oedema) between start and end of the experiment. Perfusion flows were higher throughout both $HMPO_2$ and NR in the Continuous group. Amylase, Lipase, LDH and cell-free DNA increased throughout the study for all pancreases and showed no statistically significant difference between the groups (Figure 1). The Continuous group had a significantly greater insulin secretion in response to glucose stimulation and followed a biphasic pattern (Figure 2). Histological assessment ongoing.

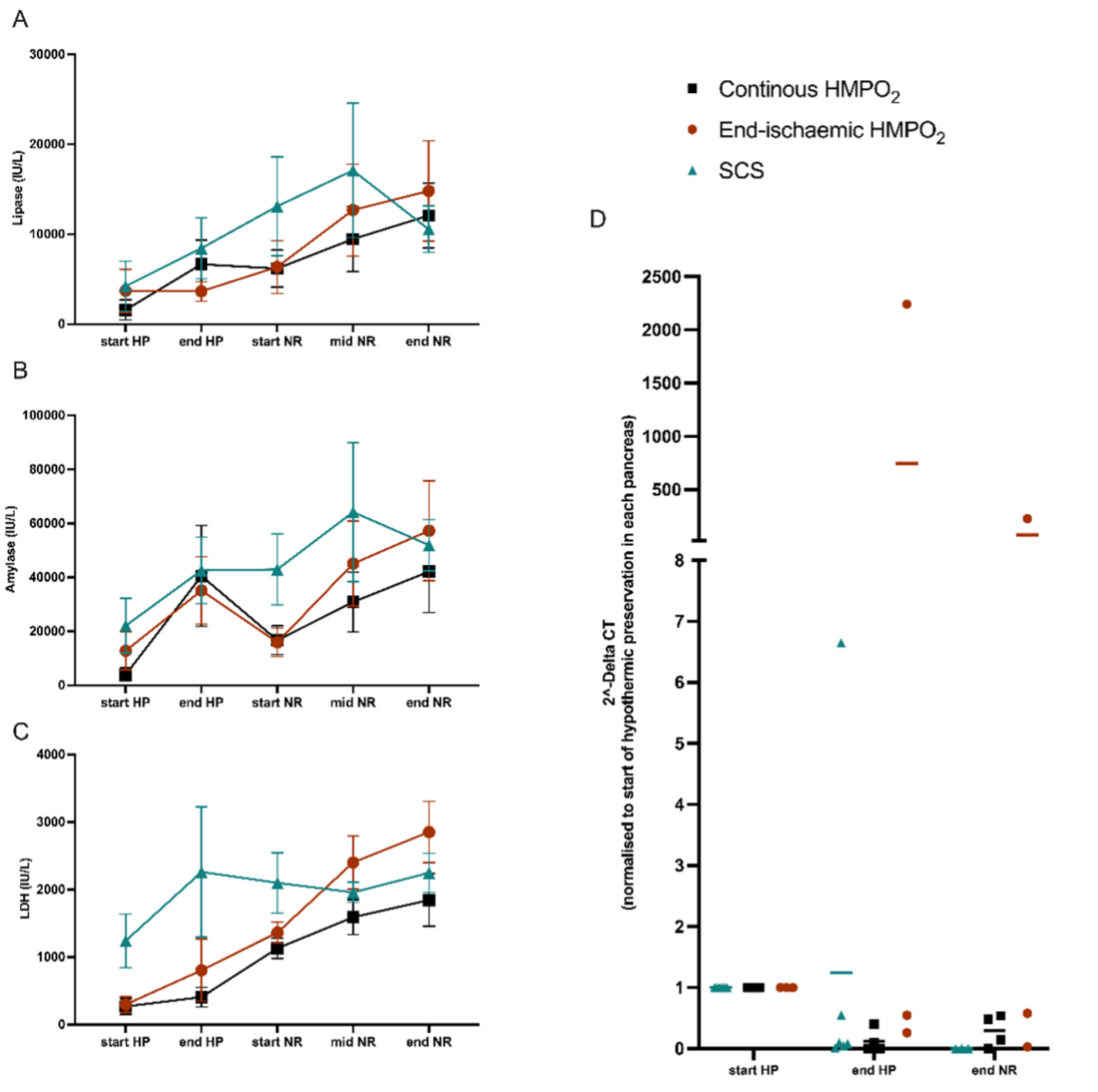


Figure 1: **Analysis of injury markers. A.** Amylase, **B.** Lipase and **C.** LDH. mean +/- SEM. **D.** Scatter plot of cell-free DNA levels. Lines represent group mean. HP is Hypothermic preservation. NR is Normothermic Reperfusion.

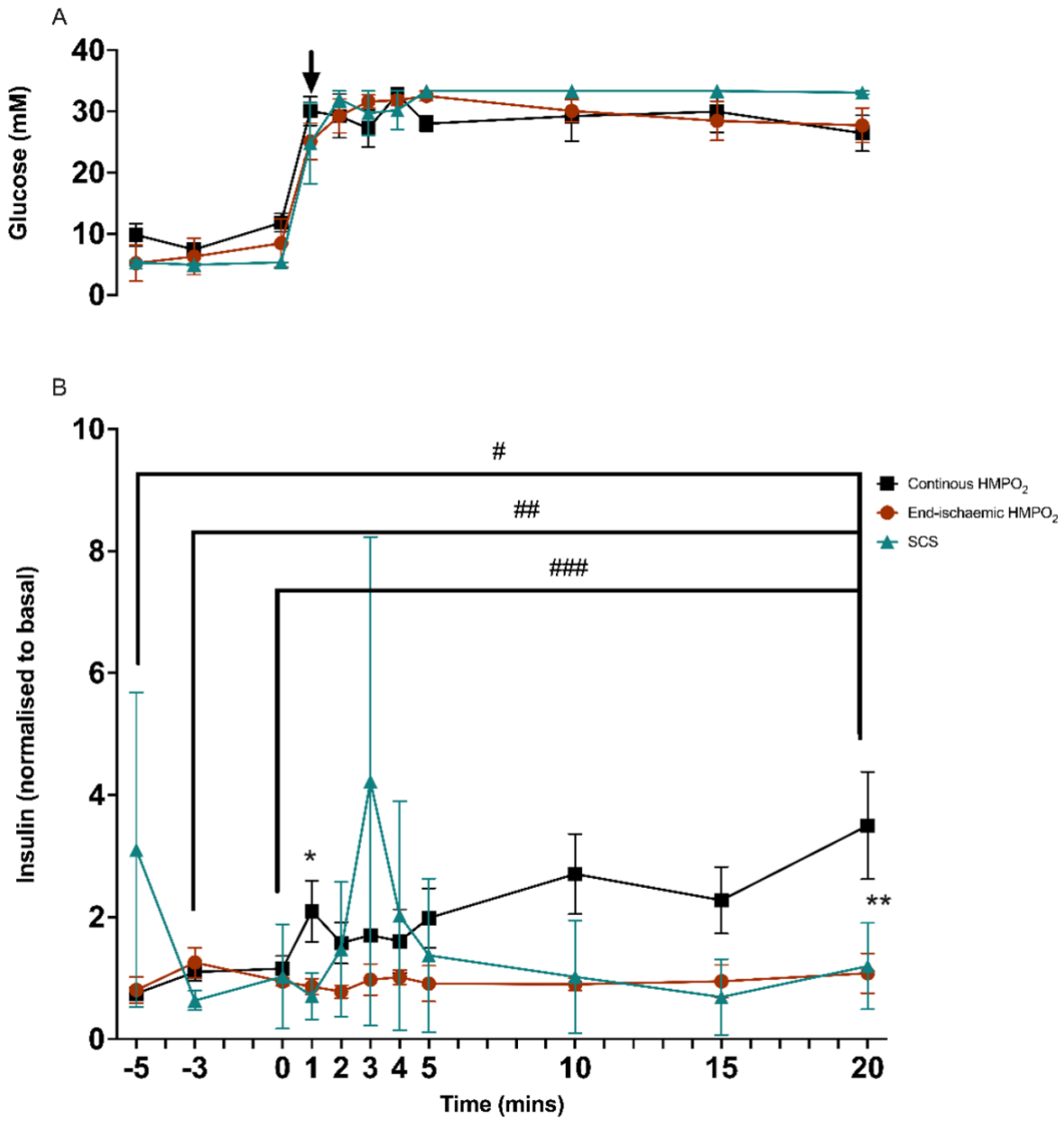


Figure 2: **Glucose measurements (A) and Glucose Stimulated Insulin Secretion (B)** during Normothermic Reperfusion after continuous $HMPO_2$ (n=3), end-ischaemic $HMPO_2$ (n=3) and SCS (n=3). The black arrow signifies the administration of glucose. # minute -5 to minute 20 P<0.000, ## minute -3 to minute 20 P=0.0007 and ### minute 0 to minute 20 P=0.0011.

Conclusions

We have shown in this circulatory death porcine pancreas model, that continuous $HMPO_2$ is associated with superior islet function and improved perfusion parameters, without evidence of any difference in parenchymal oedema or perfusate markers of tissue damage.

Conflicts of interest

Prof Peter Friend is co-founder and shareholder in OrganOx Ltd. (a University of Oxford spin out company), he is currently Chief Medical Officer (part-time), he receives payment as a non-executive director.
Prof Rutger Ploeg has previously received funding for advice to BridgeToLife on matters of organ preservation.
John Fallon has received consulting fees from OrganOx Ltd.
Mohamed Elzawahry has received consulting fees from OrganOx Ltd.

OP16 - UNVEILING THE CRITICAL ROLE OF NEUTROPHIL EXTRACELLULAR TRAPS IN ISLET TRANSPLANTATION

Mattia Albiero[1], Francesco Amendolagine[2], Gabriela Singureanu[3], Ludovica Migliozzi[4], Roberta Cappellari[5], Massimo Menegazzo[6], Verdiana Ravarotto[6], Erica Nuzzolese[7], Lucia Rizzato[6], Caterina Di Bella[8], Lucrezia Furian[9]

[1]*University of Padova; Department of Surgery, Oncology and Gastroenterology*
[2]*Università Degli Studi di Padova*
[3]*Veneto Institute of Molecular Medicine*
[4]*University of Padova*
[5]*Azienza Ospedale Università di Padova; Centro Regionale Per la Terapia Cellulare del Diabete*
[6]*University Hospital of Padova*
[7]*University Hospital of Padova; Uoc Chirirgia Trapianti Rene e Pancreas*
[8]*University of Padua; Kidney and Pancreas Transplant Unit*
[9]*University of Padua; Kidney and Pancreas Transplantation Unit, Department of Surgical, Oncological and Gastroenterological Sciences, University of Padova, Padova, Italy; Kidney and Pancreas Transplantation Unit*

Background

Inflammation during the early stages of islet transplantation has been identified as a key factor contributing to damage and the loss of a significant portion of transplanted islets. A primary compromise in graft function may arise from a group of innate immune responses referred to as the Instant Blood-Mediated Inflammatory Reaction (IBMIR). The coagulation cascade, complement system, innate immune cells, and platelets collectively act as drivers of IBMIR. This immunothrombotic environment creates an optimal setting for the activation of neutrophils, which could release decondensed chromatin to form neutrophil extracellular traps (NETs). These structures amplify the inflammatory response. While the harmful role of NETs has been established in atherothrombotic diseases and in the complications of diabetes, their role in the development of IBMIR remains largely uninvestigated. This study aims to explore the contribution of NETs to IBMIR and assess their impact on islet graft survival.

Methods

We generated NET-deficient mice by ablating Padi4, the key enzyme involved in chromatin decondensation, through a Cre-Lox strategy to target hematopoietic cells using a Vav1 promoter. Islets were isolated from wild-type C57Bl/6j mice. Diabetes was induced in Padi4KO mice and their control (Floxed) littermates by a 175 mg/kg intraperitoneal injection of streptozotocin. Animals with non-fasting blood glucose levels exceeding 300 mg/dl were considered diabetic. Bone marrow neutrophils were isolated via negative immunomagnetic selection. Liver cell suspensions were prepared by enzymatic digestion and analyzed by flow cytometry. Gene expression was quantified by qPCR. Syngeneic marginal islet transplantation was performed in diabetic Padi4KO and Floxed mice by intraportal injection of 250–300 islets.

Results

We observed that islet-conditioned medium, particularly from less pure fractions, induced IL-1β expression in neutrophils. Padi4KO neutrophils, transcriptionally similar to Floxed neutrophils, did not release NETs and exhibited significantly reduced IL-1β levels in response to islet-conditioned medium. Baseline metabolic characterization showed that Padi4 deletion did not affect islet size or glucose-stimulated insulin secretion. After diabetes induction, Padi4KO and Floxed mice exhibited comparable blood glucose levels (353 ± 33 vs 377 ± 17 mg/dl, $p = 0.51$). We confirmed that islet transplantation led to rapid neutrophil recruitment to the liver. Remarkably, islet transplantation in diabetic Padi4KO mice resulted in a sustained reduction in blood glucose compared to Floxed mice (average blood glucose: 185 ± 21 vs 235

± 21 mg/dl, $p < 0.05$). At the endpoint, insulin mRNA was significantly higher in the livers of Padi4KO mice compared to Floxed mice, suggesting a greater preservation of islet mass.

Conclusions

Our findings indicate that NETs may represent a novel contributor to islet loss after transplantation by exacerbating the inflammatory environment. Targeting NETs could provide a promising strategy to preserve islet function and improve long-term clinical outcomes.

Conflicts of interest

No conflicts of interest

OP17 - ADOSHELL®, A NON-FIBROTIC IMMUNOPROTECTIVE SCAFFOLD FOR ISLETS TRANSPLANTATION SHOWS EFFICIENT AND SUSTAINED IN VIVO FUNCTIONALITY.

Julie Brun[1], Xavier Gaume[1], Romain Besnard[1], Camille Gautier[1], Clément Cocita[1], Jonna Saarimäki-Vire[2], Diego Balboa[2], Ouardane Jouannot[3], Nicolas Laurent[1], Anne-Lise Gaffuri[1], Rosy Eloy[1], Karim Bouzakri[4], Francois Pattou[5], Olivier Soula[1]

[1]*Adocia*
[2]*Biomedicum Stem Cell Center, Faculty of Medicine, University of Helsinki*
[3]*Adocia; .*
[4]*Ceed*
[5]*Univ Lille; U1190*

Background
AdoShell® is an implantable and retrievable scaffold for islet transplantation to cure diabetes by cell therapy without immunosuppression. It is based on a permselective hydrogel film allowing insulin diffusion while preventing immune cell invasion and antibody contact. Allogeneic transplant of rat islets in immunocompetent diabetic rats has demonstrated insulin secretion and glycemic regulation. The aim of this study was to demonstrate the compatibility of AdoShell® with human islets and stem cell derived islets (SCDI).

Methods
In vitro encapsulation - Human islets were encapsulated and evaluated using perifusion after up to 4 months *in vitro*.

In vivo – In two independent studies, human islets were encapsulated and implanted in NXG mice (2 implants in the peritoneum, 2.2-3.1 kIEQ/mouse). *In vivo* functionality was evaluated by quantifying plasmatic Human C-peptide. After at least 2 months, AdoShell® implants were explanted and analyzed *in vitro* and by histology.

Domestic pig was implanted by laparoscopy with AdoShell® for proof of concept of surgery.

Results
In vitro, AdoShell® Human Islets has shown functionality at 4 months. It has also shown immunoprotection by preventing PBMC-mediated islet death.

In vivo, Human C-peptide secretion increased to reach an average of 700 pM and was maintained in 100% of mice until explantation (Fig 1). *In vitro* secretion indexes of the explants were also maintained at 105% compared to preimplantation values, with 65% insulin secretion levels (n=6 explants at 3 months post implantation). AdoShell® was well tolerated with no fibrosis.

The laparoscopy to deliver AdoShell® in pig with the capacity to deliver a therapeutic islet dose was successful.

Finally, a preliminary experiment showed that AdoShell® enabled SCDI maturation and maintained functionality for 2 months in immunodeficient mice (n=3 mice, Fig 2).

Conclusions
These results show the tolerance, the immunoprotection, the compatibility with human islets, and the feasibility of the surgery at human scale, opening the way towards clinical trials. The compatibility with SCDI is promising to circumvent human islet scarcity.

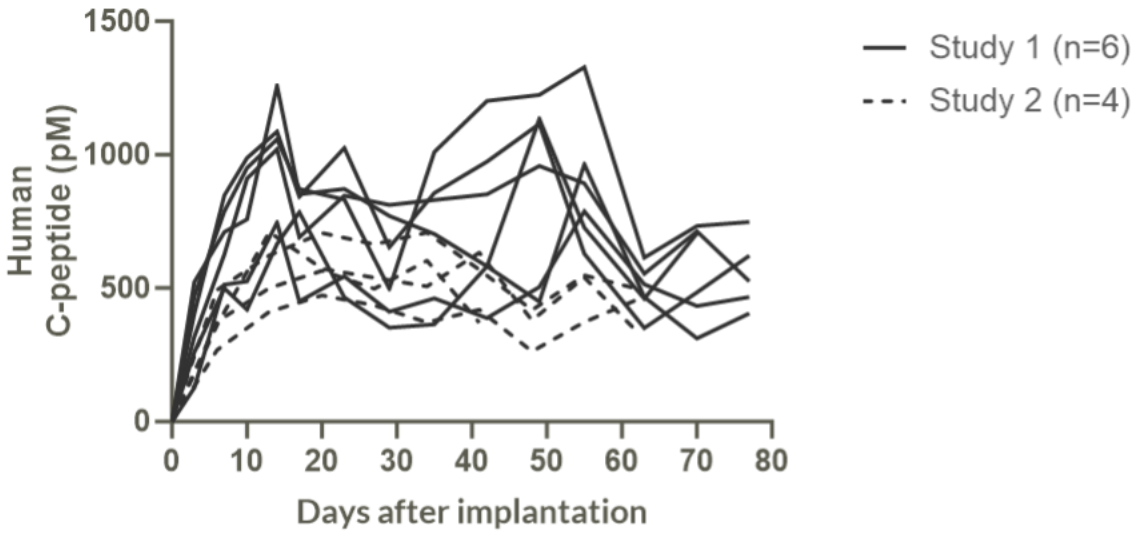


Figure 1: Evolution of Human C-peptide secretion over time in AdoShell® Islets implanted in NXG mice.

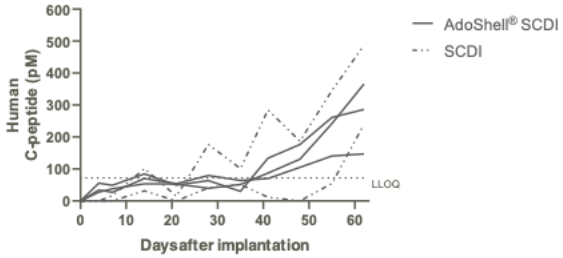


Figure 2: Evolution of Human C-peptide secretion over time from SCDI.

Conflicts of interest
Francois Pattou: ADOCIA consultant
Ouardane Jouannot: Employee and shareholder of ADOCIA
Julie Brun, Clément Cocita: ADOCIA emplolyee
Xavier Gaume: ADOCIA shareholder
Romain Besnard, Camille Gautier, Nicolas Laurent, Anne-Lise Gaffuri, Rosy Eloy, Olivier Soula: ADOCIA employee and shareholder

OP19 - DECIPHERING SENESCENCE DYNAMICS IN IPSC-DERIVED B CELLS AND THEIR FUNCTIONAL IMPLICATIONS

Laura Monaco[1], Chiara Ceriani[2], Valentina Zamarian[3], Manuela Marras[4], Federica Deambrogio[5], Kanako Iwasaki[6], Christopher Cahill[6], Cristina Aguayo-Mazzucato[6], Lorenzo Piemonti[7], Valeria Sordi[8]

[1]*Diabetes Research Institute, Irccs San Raffaele Hospital, Milano; Diabetes Research Institute*
[2]*Vita-Salute San Raffaele University Cf 97187560152*
[3]*Università Vita Salute San Raffaele; Diabetes Research Institute (Dri)*
[4]*Diabetes Research Institute, Irccs San Raffaele Hospital*
[5]*Diabetes Research Institute (Dri), San Raffaele Scientific Institute*
[6]*Joslin Diabetes Center, Harvard Medical School, Boston*
[7]*Irccs Ospedale San Raffaele/Università Vita-Salute; Diabetes Research Institute; Diabetes Research Institute*
[8]*Irccs San Raffaele Hospital; Irccs San Raffaele Hospital; Diabetes Research Institute*

Background
Human induced pluripotent stem cells (iPSCs) can differentiate in vitro into insulin-producing cells. The influence of senescence on β cell differentiation and the function of iPSC-derived β cell (iβ) remains unclear. Senescence is known to occur throughout life and plays a beneficial role during embryonic development. However, recent studies indicate that aging increases the number of senescent β cells, which impairs glucose sensing and insulin secretion. This study aims to elucidate the role of senescence at key stages of β cell differentiation and its impact on their function.

Methods
Six clones of the iPSC cell line DRI2 were differentiated into β cells. Aging markers were analyzed by measuring senescence-associated β-Galactosidase activity (SA-β-Gal), histone H2AX phosphorylation (γH2AX), and the superoxide production (mitoSOX) using flow cytometry. Immunofluorescence staining was performed to detect the presence of SA-β-Gal, γH2AX, mitoSOX, the cyclin-dependent kinases inhibitors p21 and p16, and the nuclear loss of HMGB1 at the iβ stage. Genes related to the senescence-associated secretory phenotype (SASP) and cellular senescence were quantified using TaqMan custom gene card. Somatic mutations were quantified with TwinStrand duplex sequencing. The senescence state of iβ was correlated to their function, which was assessed through dynamic glucose-stimulated insulin secretion (GSIS). Conditioned media was collected at the iβ stage and tested on EndoC-βH5 cell line to evaluate the effects of SASP. Released SASP in the conditioned media at the iβ stage is currently being quantified using the proteomic SOMAscan assay.

Results
Flow cytometry data revealed higher percentages of positive cells at the iβ stage compared to iPSCs for SA-β-Gal (iPSC: 9.6% ± 0.4%; iβ: 42.1% ± 1.4%), γH2AX (iPSC: 3.5 ± 0.5%; iβ: 18% ± 0.9%), and mitoSOX (iPSC: 5.6% ± 0.6%; iβ: 25.4% ± 4%). Immunofluorescence confirmed the presence of γH2AX, SA-β-Gal, superoxide, p21, p16 and the loss of nuclear HMGB1 at the iβ stage. Transcriptomic analysis indicated a significant increase in the expression of genes related to SASP, cell cycle arrest, DNA damage, and β cell senescence in the final stage of iβ. Sequencing data showed an increase in the SBS5 mutational signature during the differentiation process, which is known as a clock-like that correlates with aging. GSIS data indicated that cell senescence impacts on β cell function. When EndoC-βH5 were cultured with iβ conditioned media, they exhibited increased SA-β-Gal activity, p16 and β cell identity gene expression, and secretion index.

Conclusions

These results demonstrated a general increase in senescence and aging during the differentiation process. Further research is necessary to determine whether this senescence is detrimental, potentially affecting differentiation efficiency and β cell function, or beneficial for the full maturation of the cells. Therefore, it is essential to investigate both the negative and positive aspects of senescence to improve the effectiveness and safety of stem cell therapy for type 1 diabetes (T1D).

Conflicts of interest
No conflicts of interest

OP20 - OVEREXPRESSION OF CD155 IN HUMAN STEM CELL-DERIVED B-CELLS DIMINISHES AUTOREACTIVE T CELL RESPONSES

Holger Russ[1]
[1]*University of Florida; Diabetes Institute*

Background
Improved methods for generating human pluripotent stem cell (hPSC)-derived cells have rapidly expanded the field of regenerative medicine, holding extreme promise for treating diseases like type 1 diabetes, where stem cell-derived β-cells (sBC) represent a possible therapeutic intervention. However, sBC need to be protected, ideally in a localized manner, from an antagonistic host immune response.

Methods and Results
Here, we engineered hPSC to overexpress either a wildtype (WT) or high affinity mutant (rs1058402; G>A; Ala67Thr) (Mut) version of the checkpoint inhibitor CD155, which binds to TIGIT on T cells to suppress effector function. Engineered CD155 overexpressing hPSCs retain pluripotent stem cell markers and efficiently differentiate into functional stem cellderived beta cells (sBC), compared to the unmodified hPSC. Compared to CD155 WT cells, CD155 Mut sBC displayed increased TIGIT-Ig and CD226-Ig binding affinity and suppressed the proliferation of allogeneic CD8+ T cells. CD155 WT and Mut overexpression restrained the secretion of cytolytic effector molecules and autoreactive human CD8+ T cell avatarmediated sBC killing compared to control sBC, with further inhibition seen in the CD155 Mut sBC cultures. This protective effect was abrogated in the presence of TIGIT blockade.

Conclusions
Collectively, we provide evidence that high affinity CD155 expressed on sBC reduces autoreactive CD8+ T cell cytotoxicity and may confer localized immune protection to transplanted beta cells.

Conflicts of interest
No conflicts of interest

OP21 - OUTCOMES OF SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANTATION FROM OLDER DONORS-THE UK TRANSPLANT REGISTRY ANALYSIS

Jeevan Gopal[1], Titus Augustine[2], Raman Dhanda[3], David van Dellen[4], Zia Moinuddin[5]

[1]*Health Education England; Manchester Centre for Transplantation*
[2]*Manchester Royal Infirmary*
[3]*Manchester Royal Infirmary; Renal & Pancreas Transplant Unit*
[4]*Manchester Royal Infirmary; Dept of Renal & Pancreas Transplantation*
[5]*Manchester Royal Infirmary, Manchester University NHS Foundation Trust; Dept of Renal & Pancreas Transplantation*

Background
Donor age is one of the determinants of survival in simultaneous pancreas & kidney (SPK) transplantation. Advanced donor age is a barrier to organ acceptance due to perceived poor outcomes & hence, pancreas utilization rates from donors >45-years remain low. Studies reporting long-term outcomes using older donors are limited by relatively small number of transplants. Hence, we aimed to investigate the outcomes of SPK transplants from donors >45-years using the United Kingdom (UK) transplant registry data.

Methods
A retrospective analysis of the UK transplant registry data on 2523 SPK transplants performed from 2005 to 2020 was conducted. Outcome data was extracted in May 2023. The primary aim was to compare the pancreas graft loss (3-month & 1-year) from donors aged ≤45-years (D≤45) & >45-years (D>45). The secondary aim was to compare the long-term survival (patient & graft) between the two groups & define the impact of donor age on survival. Appropriate univariate & multivariate analyses were performed.

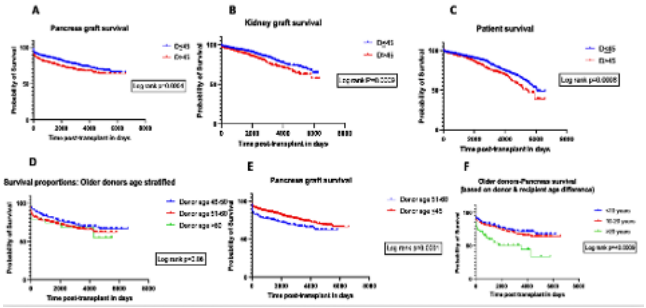
Results
After excluding 17 re-transplants, 2506 primary transplants were analysed (D≤45=1834 vs. D>45=672). The median donor age was 51-years (IQR 48-55) in D>45 & 28-years (IQR 20-38) in D≤45 group. The donors in D>45 group had higher median BMI (24.2kg/sq.m vs. 23 kg/sq.m, p<0.0001) & lower proportion of Donation after circulatory death (DCD) grafts (13.54% vs. 21.42%, p<0.0001). The rest of the baseline donor, recipient, & transplant characteristics are as shown in figure-1. The D>45 group had significantly higher proportion of pancreas graft loss at 3-months (11.6% vs. 7.4%, p=0.0009) & at 1-year post transplant (14.8% vs. 9.5%, p=0.0002). In univariate analysis, the overall survival was significantly inferior in D>45 group (Pancreas, log rank p=0.0004; Kidney, log rank p=0.0009; Patient, log rank p=0.0008), figure-2 A,B,C. Pancreas survival in subgroup analysis of D>45 cohort (46-50 vs. 51-60 vs. >60) was not significantly different (log rank p=0.08), figure-2 D. Compared to D≤45 cohort, pancreas survival from D>45 (51-60) cohort was significantly inferior (log rank p=0.0001), figure-2 E, whereas the difference was not noted with other 2 subgroups in D>45. Transplants using D>45 donors into younger recipients (donor-recipient age difference >10-years) resulted in inferior pancreas graft survival (log rank p<0.0009), figure-2 F. In cox proportional hazards regression model, donor age >45-years was an independent predictor for worse pancreas graft survival (HR 1.37, 95% CI 1.13 - 1.65, p=0.0011).

Conclusions
This is the biggest study so far reporting the long-term outcomes after SPK transplantation from older donors. Donor age >45-years is an independent risk factor for graft loss & adverse pancreas survival outcomes. Transplanting older donor organs to younger recipients (>10-years age difference) results in inferior pancreas survival outcomes. We are likely to be selective in accepting these donors as evidenced by less proportion of DCD grafts in this cohort. Avoidance of cumulative risk is essential to achieve optimal outcomes.

Figure-1:

Donor characteristics	Donor age above 45	Donor age 45 & below	p
Proportion of non-Caucasian donors (Number)	8.1% (55/672)	6.2% (115/1834)	0.09
Proportion of non-traumatic COD (Number)	95.3% (641/672)	83% (1523/1834)	<0.0001
Proportion of donors on insulin infusion (Number)	51.9% (349/672)	48.8% (895/1834)	0.16
Proportion of heavy alcohol drinking donors (Number)	70.3% (473/672)	70.5% (1294/1834)	0.92
Recipient characteristics			
Median recipient age in years (IQR)	44 (37-51)	41 (35-48)	<0.0001
Median recipient BMI in kg/sq.m (IQR)	24.9 (22.5-27.8)	24.4 (22-27.3)	0.0092
Median pre-Tx Insulin use in U/day (IQR)	42 (32-52)	40 (32-54)	0.79
Median duration of diabetes in years (IQR)	28 (22-35)	27 (21-33)	0.04
Proportion of highly sensitised recipients (Number)	3.8% (26/672)	3.3% (62/1834)	0.54
Median waiting time in days (IQR)	368 (159-602)	376.5 (156.3-593)	0.79
Proportion of non-Caucasian recipients (Number)	12.35% (88/672)	11.6% (213/1834)	0.60
Transplant characteristics			
Proportion of recipients with non-fav MM (Number)	96.2% (647/672)	96.1% (1764/1834)	0.90
Median CIT in mins (IQR)	666 (572-780)	672 (573-801)	0.36
Median WIT in mins (IQR)	36 (30-45)	35 (29-42)	0.0002

Figure-2:



Conflicts of interest
No conflicts of interest

OP22 - LONG TERM METABOLIC OUTCOMES FOLLOWING PANCREATECTOMY AND AUTOLOGOUS ISLET TRANSPLANTATION: SYSTEMATIC REVIEW AND META-ANALYSIS

Arianna Bertuol[1], Giovanni Marchegiani[2], Giulia Cirillo[2], Benedetta Quaratino[2], Lucia Rizzato[3], Mattia Albiero[4], Massimo Menegazzo[3], Roberta Cappellari[5], Erica Nuzzolese[6], Verdiana Ravarotto[3], Lucrezia Furian[7]

[1]*University of Padova; Kidney and Pancreas Transplantation Unit, University Hospital of Padova; Department of Surgery, Oncology and Gastroenterology, University of Padova*
[2]*University of Padova*
[3]*University Hospital of Padova*
[4]*University of Padova; Department of Surgery, Oncology and Gastroenterology*
[5]*Azienza Ospedale Università di Padova; Centro Regionale Per la Terapia Cellulare del Diabete*
[6]*University Hospital of Padova; Uoc Chirirgia Trapianti Rene e Pancreas*
[7]*University of Padua; Kidney and Pancreas Transplantation Unit, Department of Surgical, Oncological and Gastroenterological Sciences, University of Padova, Padova, Italy; Kidney and Pancreas Transplantation Unit*

Background
Total pancreatectomy with Islet Autotransplantation (TPIAT) is an established and effective therapeutic option for patients with Chronic Pancreatitis (CP) in order to mitigate the postoperative diabetes. A recent proposal has advocated that the criteria should now be expanded to include patients with a high risk pancreatic stump, extended parenchymal resections for benign disease and for the management of severe post operative complications. However, the metabolic outcomes for this patient cohort are unknown.

Methods
A systematic review and meta-analyses of the pre-existing literature was performed (PROSPERO ID 56603). The primary outcome measure was determining the long-term insulin independence rate following TPIAT and a secondary outcome was the number of severe hypoglycemia episodes. A meta-analysis of pooled outcomes was performed using a random-effects model incorporating the DerSimonian–Laird method.

Results
This review included 17 studies comprising a total of 1332 patients who underwent TPIAT. The median follow-up period was 1 year. Among the patients, the majority underwent TPIAT for CP (1101/1332, 83%). Upon meta-analysis, despite significant heterogeneity in considered endpoints, the overall pooled rate for insulin independence was 34% (29-40%). Notably, the cohort of non-CP indications for TPIAT demonstrated a significantly higher rate of insulin independence compared to CP TPIAT (68% vs. 33%). The overall pooled rate of severe hypoglycemic events was 11% (range: 9.2%-14%).

Conclusions
TPIAT represents an effective approach for reducing the post operative burden of iatrogenic diabetes following pancreatectomy, especially in cases not related to chronic pancreatitis, and should be available in centers of expertise. When Chronic Pancreatitis is the indication for TPIAT, early timing for surgery is key to ensure the best metabolic outcomes. However, further research is needed to more accurately define the long-term endocrine outcomes of TPIAT, as well as its impact on quality of life.

Conflicts of interest
No conflicts of interest

OP23 - 10-YEAR ANALYSIS OF THE IMPACT OF NORMOTHERMIC REGIONAL PERFUSION IN SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANT

Ruth Owen[1], Samuel Tingle[2], Georgios Kourounis[3], Emily Thompson[4], Claire Counter[5], Lewis Simmonds[5], Chris Callaghan[6], John Casey[7], Ian Currie[8], Martin Drage[9], Doruk Elker[10], Anand Muthusamy[11], Gavin Pettigrew[12], Neil Russel[13], Sanjay Sinha[14], Andrew Sutherland[15], David van Dellen[16], Derek Manas[17], Colin Wilson[18], Steve White[19]

[1]*Freeman Hospital; Hpb and Transplant*
[2]*Freeman Hospital; Newcastle University, Newcastle Upon Tyne, Uk; Institute of Transplantation*
[3]*Institute of Transplantation*
[4]*Institute of Transplantation, Freeman Hospital*
[5]*NHS Blood and Transplant; Statistics and Clinical Research*
[6]*Guys and St Thomas' NHS Foundation Trust*
[7]*University of Edinburgh*
[8]*NHS Blood and Transplant*
[9]*Great Ormond Street, Evelina Children's Hospital*
[10]*Cardiff Transplant Unit, Nephrology and Transplant Directorate, Cardiff and Vale University Health Board*
[11]*Imperial College Renal and Transplant Center, Hammersmith Hospital; Renal and Transplant Services*
[12]*Cambridge Hospital Trust*
[13]*Cambridge University*
[14]*Oxford University Hospitals NHS Trust; Churchill Hospital; Oxford Transplant Centre*
[15]*Royal Infirmary of Edinburgh*
[16]*Manchester Royal Infirmary*
[17]*NHS Blood and Transplant; Nhs Blood and Transplant*
[18]*The Newcastle Upon Tyne Hospitals NHS Foundation Trust*
[19]*Newcastle Upon Tyne Hospitals NHS Foundation Trust; Dept of Surgery*

Background
Deceased Cardiac Donors (DCD) organs are increasingly being used for simultaneous pancreas and kidney (SPK) transplant. The number recovered following in-situ normothermic regional perfusion (NRP) is also increasing. This study reviewed a 10-year UK experience of SPK transplantation following NRP in DCD.

Methods
Data were collected on all first DCD SPK transplants (n=426) performed during 2013-2023 from the UK Transplant Registry. NRP and non-NRP donors were compared using adjusted regression models. Multiple imputation was used to deal with missing data.

Results
Most grafts were from non-NRP donors n=379 (89%) with n=47 (11%) from NRP donors. Median warm ischaemic time (withdrawal to start of aortic cold or normothermic perfusion) was longer with NRP (17 vs 12 minutes; p=0.005). For all other parameters donors and recipients were well matched. Univariable analysis showed no statistically significant difference in one-year pancreas graft (NRP 93.6%, non-NRP 89.2%, p=0.206), Figure 1. A multivariable model adjusted for donor and recipient factors showed lower pancreas graft loss with NRP, but this did not reach statistical significance (aHR 0.56, 95%CI 0.17-1.80, p=0.327), Table 1. Sensitivity analyses adjusting for PDRI showed similar results. NRP was not associated with 3-month insulin independence (p=0.51) or pancreas graft rejection (p=0.48).

Conclusions

Concerns exist that NRP may be detrimental to the pancreas. This 10-year UK analysis is the largest reported. We found lower pancreas graft loss in the NRP group, though not statistically significant. This data, along with previous benefits demonstrated in liver and kidney, support continued expansion of the NRP programmes.

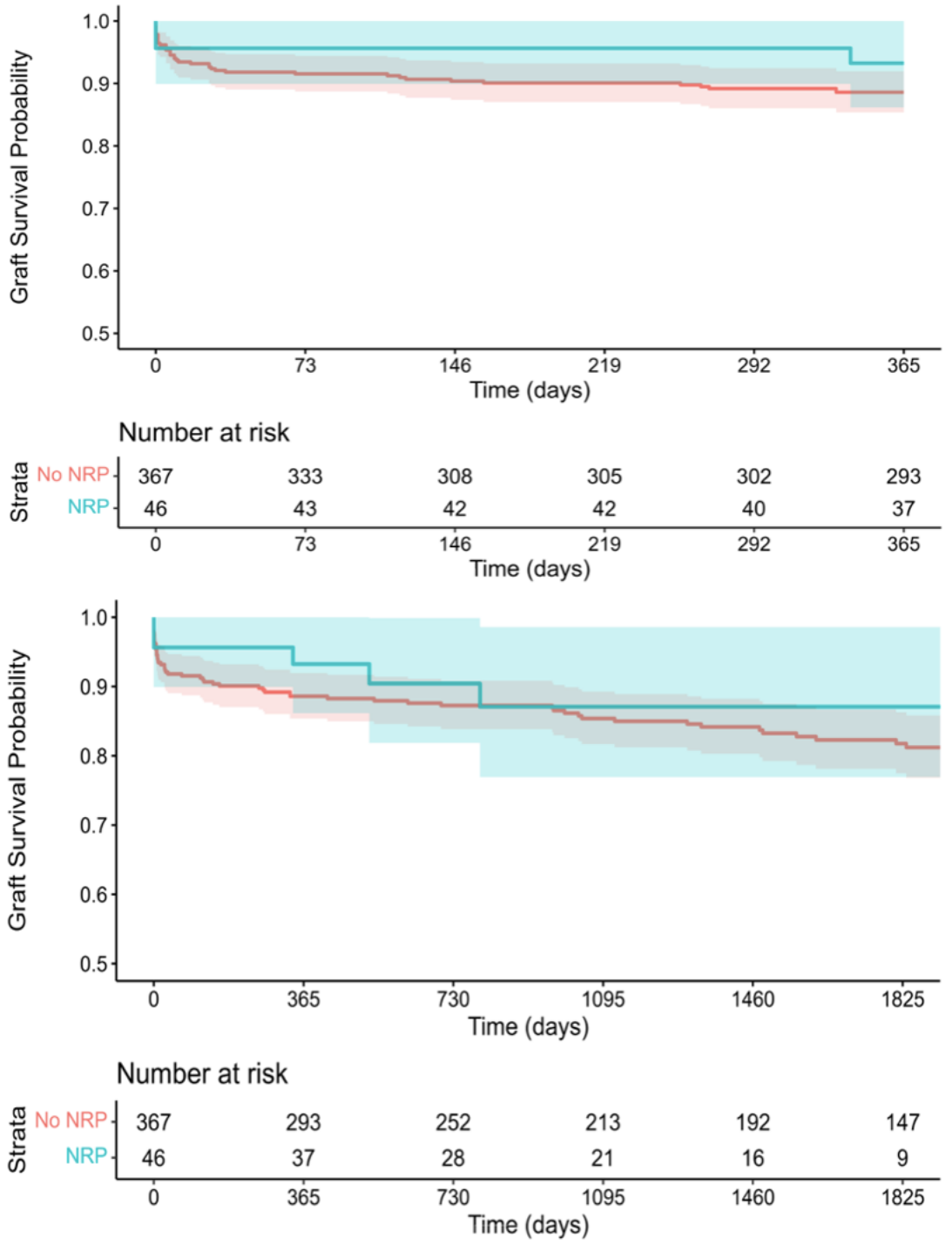


Figure 1. Kaplan Meier analysis of 1-year and 5-year pancreas graft survival. Recipients who received an SPK transplant from a donor who underwent NRP compared with those who received and SPK transplant from a non-NRP donor

Variable	Hazards Ratio	95% CI	p value
1 Year			
NRP	0.59	(0.18 - 1.86)	0.356
Recipient Age	**0.96**	**(0.93 – 0.99)**	**0.020**
Donor BMI	**1.14**	**(1.05 – 1.23)**	**0.001**
Cold Ischaemic Time (hours)	0.97	(0.84 – 1.13)	0.734
5 Years			
NRP	0.65	(0.26 – 1.62)	0.352
Recipient Age	**0.95**	**(0.92 – 0.98)**	**<0.001**
Donor BMI	**1.12**	**(1.05 – 1.19)**	**<0.001**
Cold Ischaemic Time (hours)	0.93	(0.82 – 1.05)	0.228

Table 1. Multivariable graft survival at 1 year and 5 years. *NRP- Normothermic Regional Perfusion BMI – Body Mass Index.*

Conflicts of interest
No conflicts of interest

OP24 - THE IMMUNOSURVEILLANCE OF HYPOIMMUNOGENIC IPSC-DERIVED ISLETS: IMPACT OF VIRAL INFECTIONS

Gabriel Siracusano[1], Raniero Chimienti[2], Carlotta Tacconi[3], Camilla Volpi[4], Matilde Certo[4], Federica Deambrogio[5], Valeria Sordi[6], Marco De Giovanni[4], Lorenzo Piemonti[7]

[1]*Università Vita Salute San Raffaele; Diabetes Research Institute*
[2]*University of Vita-Salute San Raffaele; Diabetes Research Institute*
[3]*Vita-Salute San Raffaele University; San Raffaele Scientific Institute, Division of Immunology, Transplantation, and Infectious Diseases, Dynamics of Immune Responses*
[4]*Vita-Salute San Raffaele University*
[5]*Diabetes Research Institute (Dri), San Raffaele Scientific Institute*
[6]*Irccs San Raffaele Hospital; Irccs San Raffaele Hospital; Diabetes Research Institute*
[7]*Irccs Ospedale San Raffaele/Università Vita-Salute; Diabetes Research Institute; Diabetes Research Institute*

Background

Immune evasive stem cell (SC)-islets are under preclinical and clinical development as emerging cell therapy for type 1 diabetes (T1D) [1]. The abrogation of MHC-I dampens CD8+ T cell killing but exposes cells to NK cell targeting, known as missing-self recognition. To address this issue, strategies were developed to express inhibitory ligands for NK cells, while the induction of an immune tolerant microenvironment was also explored. However, these approaches have shown variable results due to NK cell heterogeneity [2]. We developed an alternative approach targeting the NK activating axis by genetically abrogating the ligands B7-H3 and CD155 in MHC-I$^{-/-}$ induced pluripotent stem cells, to generate triple knockout (T-KO) derived islets. T-KO islets evaded both T and NK cell killing [3], persisted up to 8 months and restored glycemia in diabetic mice. However, the safety of hypoimmune SC-islets remains unaddressed. To explore the immunosurveillance of infections, we used Lymphocytic choriomeningitis virus, strain WE (LCMV-WE), to challenge T-KO islets as a proof of concept.

Methods

hIL-15 NOG mice were transplanted with 500 IEQ luciferase-expressing T-KO islets and after 10 days humanized with donor-derived NK cells. Mice were infected with 1x10^6 ffu/mouse of LCMV-WE 14 days later, according to the following experimental groups: non-humanized, uninfected (a) or LCMV-WE infected (b); NK-humanized, uninfected (c) or LCMV-WE infected (d). Platelets count was performed to assess acute LCMV-WE infection 7 days post infection (p.i). Immunophenotyping and quantification of viral titers were carried out at 3 and 10 (endpoint) days p.i.. Plasma levels of hC-peptide were measured at 3 and 7 days p.i.. At the endpoint, ex-vivo graft survival was analysed by in vivo imaging system (IVIS) and organs explanted for immunohistochemical analysis.

Results

A thrombocytopenic state indicated the occurrence of acute LCMV-WE infection. NK-humanized mice displayed higher viral titers than non-humanized mice at the endpoint, and the virus mainly accumulated in lungs independently of the presence of NK cells. Interestingly, at 7 days p.i., basal hC-peptide levels significantly decreased in NK-humanized mice compared to their non-humanized counterparts, correlating with an overall reduction in the bioluminescence signals of T-KO islets. Importantly, we found that NK cells were responsible for graft rejection, as CD56$^+$ cells were detected at the site of insulin-producing cells. Mechanistic evaluations confirmed that NK cell activation and recognition of islet cells were NKG2D-dependent, with LCMV-WE infection causing the upregulation of the NKG2D-activating ligands MICA/B and ULBP3 in T-KO islets.

Conclusions
This study highlights that the upregulation of activating ligands other than B7-H3 and CD155 enables NK cells to re-engage in missing-self recognition, targeting infected cells. As viruses might escape from NK immunosurveillance, these studies needs to be extended to viruses recognized for their tropism to pancreatic islets to address the safety concerns for clinical implementation of hypoimmune SC-islets.

Conflicts of interest
No conflicts of interest

OP25 - BIO-FABRICATION OF A HUMAN IPSC-BASED VASCULARIZED ENDOCRINE PANCREAS FOR THE TREATMENT OF TYPE 1 DIABETES

Francesco Campo[1], Alessia Neroni[2], Cataldo Pignatelli[1], Silvia Pellegrini[3], Ilaria Marzinotto[4], Fabio Manenti[5], Libera Valla[4], Vito Lampasona[4], Lorenzo Piemonti[6], Antonio Citro[1]

[1]*Irccs Ospedale San Raffaele; Diabetes Research Institute*
[2]*Irccs Ospedale San Raffaele/Università Vita-Salute*
[3]*Diabetes Research Institute; Irccs San Raffaele Hospital; Diabetes Research Institute*
[4]*Diabetes Research Institute*
[5]*Diabetes Research Institute; Irccs San Raffaele Hospital*
[6]*Irccs Ospedale San Raffaele/Università Vita-Salute; Diabetes Research Institute; Diabetes Research Institute*

Background
Intrahepatic islet transplantation in patients with type 1 diabetes is limited by donor availability and lack of engraftment. To address these issues, new sources of β cells as iPSCs and alternative transplantation sites are needed. Organ decellularization is an emerging strategy in organ regeneration. Based on our experience with decellularized rat lung as scaffold in generating a Vascularized Endocrine Pancreas (ECM scaffold repopulated by neonatal pig islet and BOEC cells), we bio-fabricated an iPSC-based version named iVEP (iPSC-derived Vascularized Endocrine Pancreas).

Methods
iPSC-derived β (iβ) and endothelial (iEC) cells were characterized by flow cytometry, then aggregated into functional vascularized iβ spheroids (SPH) for 7 days at a ratio of 90% iβ+10% iEC. Rat lung was decellularized by vascular perfusion with 1% SDS and 0.1% Triton and seeded with iECs and SPH from vascular and air accesses. The recellularized scaffold matured in vitro for 7 days in a customized perfusion bioreactor specifically designed to allow cell/compartment integration. iβ cell death was estimated during ex vivo organ maturation and compared to 7 days of iβ in vitro culture by evaluating miR-375 expression (droplet digital PCR). On day 7, fluoroangiography and dextran assays were performed to assess the vascular compartment structure and function while for the endocrine compartment, insulin production was measured by dynamic glucose perifusion and insulin quantification (ELISA/IF). Matured iVEPs were then transplanted subcutaneously into NSG diabetic mice followed for 13 weeks days and compared to the deviceless (DL) implantation site. Endocrine function was evaluated by glycemia levels, c-pep and OGTT metabolic test. Explanted iVEPs were used for IF evaluation.

Results
iEC/iβ maintained for 7 days in vitro their phenotype expressing endothelial (>95% CD31+/CD105+/CD73+/CD90- cells) and β-cell (>60% PDX1+/insulin+ cells) markers respectively. Matured iVEPs showed regenerated vascular network (CD31+) able to sustain the direct distribution of a perfusate with SPH (Chromogranin A/Insulin+) fully integrated in the engineered vasculature. Also matured iVEPs reduce β cell death: the amount of lost iβ was ≤18% during organ maturation, while >70% during in vitro culture. In iVEPs, vascularized ECM was able to significantly sustain iβ engraftment, survival and promote phenotypical maturation of iβ with physiologic insulin secretion. In vivo, iVEP engraft and restore normoglycemia in diabetic recipient mice compared to SPH alone implanted in the DL site preserving endocrine function up to 13 weeks after transplantation. iVEPs showed also higher c-pep levels starting from day 7 of transplantation and improved metabolic function.

Conclusions
In vitro, iVEP platform enables iPSC based SPH engraftment and survival in a pre-vascularized ECM promoting iβ in vitro endocrine function. In vivo, iVEPs showed immediate function restoring normoglycemia in diabetic NSG mice. To our knowledge, we assembled the first iPSC-derived VEP able to provide both controlled insulin secretion in vitro and in vivo function.

Conflicts of interest
No conflicts of interest

OP26 - CRAFTING CAR-TREG ANTIGEN-SPECIFIC IMMUNE PROTECTION OF STEM CELL-DERIVED BETA CELLS USING COMBINATORIAL GENOME ENGINEERING

Holger Russ[1]
[1]*University of Florida; Diabetes Institute*

Background
Generation of human pluripotent stem cell (hPSC)-derived beta cells (sBC) rapidly expanded cell replacement therapy for type 1 diabetes (T1D). Yet, sBC must be protected from antagonistic host immune responses, ideally in a localized manner. Chimeric antigen receptor (CAR) technology confers antigen specificities to effector or regulatory T cells (Tregs). However, identifying a CAR target molecule uniquely expressed by the cells of interest to prevent unwanted off-target effects is challenging.

Methods
We employed combinatorial genetic engineering to confer CAR-Treg-mediated immune protection specifically to transplanted sBC. We engineered hPSCs to express a truncated epidermal growth factor receptor (EGFRt) followed by differentiation into functional stem cell derived beta-like cells (sBC). We also generated EGFR CAR-Tregs that were activated by EGFRt-expressing sBCs without disrupting Treg identity.

Results
Activated CAR-Tregs suppressed innate and adaptive immune responses in vitro and prevented effector CAR-T-cell-mediated sBC graft destruction in vivo using a humanized T1D mouse model. FOXP3+ CAR-Tregs were readily detected surrounding sBCs marked by hormone expression.

Conclusions
Combinatorial genome engineering of hPSCs and Tregs can be harnessed to protect sBC from immune attack via localized immune tolerance and therefore could significantly enhance the efficacy of cell replacement therapies for patients with T1D. LAY OVERVIEW: We can now successfully generate unlimited numbers of insulin producing β-like cells from human stem cells to transplantation into patients, but once we transplant them, these beta cells are still threatened by the same autoimmune attack that caused the disease. Genetic engineering is at the forefront of scientific advances, allowing us to alter cells at will. My studies will provide critical insights on how engineering approaches can prevent immune rejection of transplanted beta cells, and will potentially open the door for improved transplantation survival without the secondary risks currently facing patients with T1D.

Conflicts of interest
No conflicts of interest

OP27 - THE USE EXTENDED CULTURE FOR COMBINED DONOR ISLET TRANSPLANTATIONS AND ITS EFFECTS ON ISOLATED ISLET QUALITY

Yun Suk Chae[1], Esmay Hammink[2], Ezra van der Wel[3], Francoise Carlotti[4], Eelco de Koning[5], Marten Engelse[6]

[1]*Leiden University Medical Center; Internal Medicine; Islet Lab*
[2]*Lumc*
[3]*Leiden University Medical Center ; Internal Medicine, Islet Group*
[4]*Leiden University Medical Center; Internal Medicine*
[5]*Leiden University Medical Centre (Lumc); Dept of Nephrology*
[6]*Leiden University Medical Center (Lumc); Leiden University; Nephrology*

Background
In pancreatic islet transplantation, isolated islets can be cultured prior to infusion. Islet culture provides logistical flexibility and the opportunity to combine multiple donor islet preparations for a single infusion. However, there is limited information on the characteristics and transplantation outcomes of combined donor islet transplantation (CDIT) compared to a conventional single donor islet transplantation (SDIT). There is also uncertainty on the effects of extended culture (beyond 3 days) on tissue quality. This study evaluated the use of CDIT as an alternative transplantation strategy to an SDIT and characterized the pancreatic tissue quality after extended culture.

Methods
Over a 16-year period, a cohort of first-time SDIT and CDIT recipients was examined. Donor pancreas, isolated islets, and islet transplantation characteristics of the two groups were compared. The graft function and clinical outcomes of the two groups were examined at 3-months and 1-year after transplantation. Tissue viability and islet cell composition were assessed on tissue that remained after medium change on culture day 3, 5 and 7. Tissue viability was determined by quantification of immunostaining for caspase-1 and TUNEL. Islet cell composition was evaluated by quantification of immunostaining for C-peptide and glucagon.

Results
Islets were isolated from 40 donor pancreases for transplantation into 40 SDIT recipients, while 31 donor pancreases were used in 15 CDIT recipients. The islet yield per donor pancreas was lower in CDIT preparations (SDIT vs CDIT, 845,625 islet equivalents (IEQ) vs 486,957 IEQ, $p < 0.0001$). Islet preparations for CDITs were cultured longer (SDIT vs CDIT, 2.2 days vs 2.65 days, $p = 0.0058$), and the longest culture duration for CDITs was 5 days. When combined for a single infusion, CDIT islet preparations had 1,062,935 IEQ, while SDIT had 897,783 IEQ ($p = 0.0693$). This resulted in 1.28 fold higher IEQ/kg per recipient for CDIT (14,619 IEQ/kg) compared to SDIT (11,415 IEQ/kg) ($p < 0.0195$). 3-months after transplantation, CDIT recipients showed similar graft function during mixed meal tolerance tests (C-peptide AUC, SDIT vs CDIT, 0.187 vs 0.113, $p = 0.151$). 1-year Igls 2.0 scores for graft function (Igls score 1-2, SDIT vs CDIT, 71% vs 78%, $p > 0.999$) and treatment outcome (Igls score 1-2, SDIT vs CDIT, 42% vs 78%, $p = 0.118$) were comparable between the two groups.

Assessment of tissue viability across the three culture days (day 3, 5 and 7) showed no difference in % caspase-1$^+$ area (day 3 vs day 5 vs day 7, 14.9% vs 11.6% vs 10.0%, $p = 0.604$) and % TUNEL$^+$ cells (day 3 vs day 5 vs day 7, 1.66% vs 2.03% vs 2.74%, $p = 0.415$). Islets on culture day 3 and 5 showed no differences in islet cell composition (glucagon$^+$ cells to C-peptide$^+$ cell ratio, day 3 vs day 5, 0.378 vs 0.542, $p = 0.209$).

Conclusions

CDITs can be used an alternative transplantation strategy to a conventional SDIT. Extended culture up to 5 days results in acceptable tissue quality and facilitates the use of CDITs.

Conflicts of interest
No conflicts of interest

OP28 - NKX6.1 EXPRESSION PREDICTS PRIMARY GRAFT FUNCTION (PGF) AFTER ISLET TRANSPLANTATION IN MAN AND IN MOUSE

Gianni Pasquetti[1], Julien THEVENET[2], Mikael Chetboun[3], Anais Coddeville[4], Nathalie Delalleau[5], Valentin Lericque[6], Natascha de Graaf[7], Francoise Carlotti[8], Eelco de Koning[9], Lorea Zubiaga[10], Isabel Gonzales Mariscal[11], Valery Gmyr[10], Caroline Bonner[12], Marie-Christine Vantyghem[1], Thomas Hubert[13], Francois Pattou[14], Julie Kerr-Conte[15]

[1]*Inserm U1190 - University of Lille / Chu Lille; Nord*
[2]*"Translational Research for Diabetes" Lab; Faculté de Médecine*
[3]*Chu Lille, Department of General and Endocrine Surgery; Univ.Lille, U1190 – Egid; Inserm, U1190*
[4]*Umr 1190 Recherche Translationnelle Sur Le Diabète*
[5]*Inserm U1190 - University of Lille; Nord*
[6]*Faculté Médecine Pole Recherche; U1190*
[7].
[8]*Leiden University Medical Center; Internal Medicine*
[9]*Leiden University Medical Center*
[10]*Inserm U1190*
[11]*Inserm Umr 1190*
[12]*Univ. Lille*
[13]*Inserm U1190 - University Hospital of Lille; Nord*
[14]*Univ Lille; U1190*
[15]*Chu Lille; Faculty of Medicine*

Background

Primary Graft Function (PGF), corresponding to the BETA score calculated 1 month after the last tx, predicts the long-term success (Lancet Diabetes Endoc, 2023). The absence of correlation between the number of islet equivalents (IEQ), the main current criterion for release of islets, and PGF, shows the functional heterogeneity of islet grafts. We assessed the relationship between NKX6.1 expression in islets, a major transcription factor to maintain beta cell identity and function, and PGF.

Methods

In this retrospective study, NKX6.1 mRNA copy number was measured by digital PCR in 114 clinical islet preparations, and correlated with islet function post tx in our nude mouse bioassay, followed for human c-peptide/glycemia over one month. Secondly, total NKX6.1 copy number per recipient, was compared between the patients with suboptimal PGF vs optimal PGF. A ROC curve defines the minimum threshold of NKX6.1 copies to achieve an optimal PGF in recipients. The effect of NKX6.1 specific inhibition in human islets with lentivirus-shRNA, on in vitro GSIS by perifusion (3 donors) and islet function in immunodeficient mice (2 donors, 12 mice) was studied.

Results

Contrary to the number of IEQ, NKX6.1 expression in islet preparations before tx, was significantly correlated with islet function in mice (r^2=0.21; p=0.0001****) and significantly better in patients with optimal PGF (p=0,0031**), independently of the number of islets grafted (**Fig. 1a, b**). For optimal PGF, the minimum threshold of NKX6.1 copy number per recipient, determined with a ROC curve, was estimated to 2.3M. We provide direct evidence that NKX6.1 knock-down, significantly reduced in vitro GSIS (p<0,0001****) and induced a progressive loss of graft function in mice (p=0,0008***) (**Fig. 1c**).

Conclusions

We suggest that NKX6.1 total copy number in islets before tx, could be a criterion to release islets for clinical tx, especially when the minimum number of IEQ required is not reached in young donors. Secondly, achieving >2.3M total copy numbers of NKX6.1 per recipient should increase the number of recipients with optimal graft function and thereby long-term function.

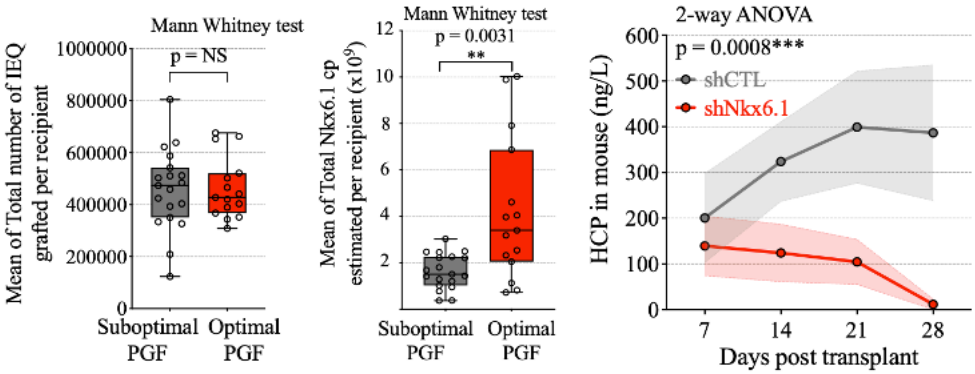


Figure 1. Mean of NKX6.1 total copy number received per recipient according to PGF (a) and effect of NKX6.1 permanent knock-down on islet graft in mouse (b).

Conflicts of interest

No conflicts of interest

CASE STUDY

CC01 - ACUTE NECROTIZING GRAFT PANCREATITIS: A CASE REPORT

Jaroslav Chlupac[1], Karol Sutoris[1], Tomas Marada[1], Peter Girman[2], Kvetoslav Lipar[1], Jiri Fronek[3]

[1]*Institute for Clinical and Experimental Medicine (Ikem); Transplantation Center; Transplantation Surgery Department*
[2]*Ikem; Diabetes Department*
[3]*Institute for Clinical and Experimental Medicine; Transplant Surgery Department*

Background
Simultaneous pancreas and kidney transplantation (SPK) is an effective treatment for individuals with type 1 diabetes mellitus (T1DM) and end-stage chronic kidney disease (CKD). We present the case of a patient who developed acute necrotizing graft pancreatitis following SPK.

Methods
Case description.

Results
A 51-year-old male with T1DM and CKD, who was on hemodialysis, underwent an SPK procedure with retroperitoneal placement of the grafts. The brain-dead donor was a 28-year-old male who had suffered brain hypoxia following a cardiac arrest. The pancreatic cold ischemia time was 12 hours and 17 minutes. Intraoperatively, the pancreas graft showed patchy areas, indicating reperfusion pancreatitis (Fig. 1A). The patient experienced hemodynamic instability. The renal transplantation proceeded without complications, and the estimated blood loss was 800 mL. Postoperatively, the pancreatic graft began functioning gradually, while the kidney experienced delayed graft function due to biopsy-proven acute tubular necrosis, requiring hemodialysis one month after surgery. The patient experienced a prolonged septic condition characterized by fever, fatigue, and bowel paralysis. There was no pathological discharge from the drains, and cultures remained negative. Repeated ultrasounds revealed enlargement of the pancreas graft and small adjacent fluid collections. On day 11 postoperatively, we performed revision surgery. Acute necrotizing graft pancreatitis was identified, along with necrosis in the retroperitoneal, omental, and subcutaneous fat tissues (Fig. 1B). The pancreas graft was still viable but had areas of superficial necrosis, which were black in color. The graft was left intact. Extensive debridement was carried out, and the retroperitoneum around the pancreas was lavaged with an antiseptic solution for 10 days. Negative pressure wound therapy was applied to the subcutis, followed by delayed wound closure. The bowel paralysis gradually resolved, and the kidney graft began functioning. The patient was discharged on day 34 with no need for insulin therapy and a serum creatinine level of 274 µmol/L. A pancreatic fistula developed and was managed conservatively with abdominal drains, persisting until day 48. At the current 4-month follow-up, the patient's serum creatinine is 123 µmol/L, and he continues to require no insulin.

Conclusions
Necrotizing pancreatitis is a severe complication that can lead to graft loss and significantly impact the patient's health. In this case, retroperitoneal debridement and lavage were sufficient to preserve the functioning graft.

Supported by the project National Institute for Research of Metabolic and Cardiovascular Diseases (Programme EXCELES, ID Project No. LX22NPO5104) - Funded by the European Union – Next Generation EU.

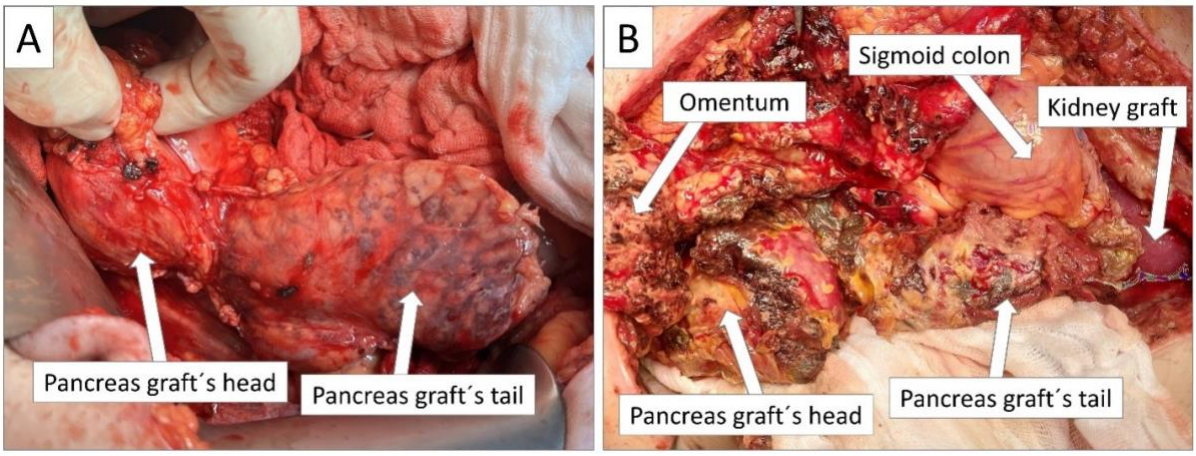


Fig. 1. A. Intraoperative view of reperfusion pancreatitis. **B.** Intraoperative view on day 11 post-transplantation showing acute necrotizing pancreatitis and necrosis of surrounding fat tissue.

Conflicts of interest

No conflicts of interest

CC02 - STEP-UP APPROACH FOR THE MANAGEMENT OF PERIPANCREATIC COLLECTION AFTER A SIMULTANEOUS PANCREAS AND KIDNEY (SPK) TRANSPLANTATION

Rongrong Hu Zhu[1], Alba Torroella[2], Ramón Rull[3], Rocío García[3], Clara Bassaganyas[4], Carlos Perez Serrano[5], Martí Manyalich[6], David Saavedra[7], Emma Folch Puy[8], Victor Holguín[9], Pedro Ventura-Aguiar[10], Antonio J Amor[11], Fritz Diekmann[12], Mª Angeles Garcia-Criado[13], Josep Fuster[3], Joana Ferrer-Fàbrega[14]

[1]*Clinic Institute of Digestive and Metabolic Diseases (Icmdim), Hospital Clínic; Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit*
[2]*Hospital Clínic, University of Barcelona, Barcelona, Spain.; Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (Icmdim),*
[3]*Institute of Digestive and Metabolic Diseases (Icmdim). Hospital Clinic. University of Barcelona. Barcelona*
[4]*Hospital Clínic de Barcelona; Radiology*
[5]*Hospital Clínic de Barcelona*
[6]*1hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (Icmdim), Hospital Clínic, University of Barcelona, Barcelona, Spain.*
[7]*Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (Icmdim), Hospital Clínic, University of Barcelona, Barcelona, Spain.*
[8]*Iibb-Csic; Experimental Pathology; Experimental Pathology*
[9]*Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (Icmdim), Hospital Clínic*
[10]*Hospital Clinic Barcelona; Hospital Clinic de Barcelona; Nephrology and Kidney Transplant Department*
[11]*Hospital Clinic de Barcelona; Endocrinology and Nutrition Department*
[12]*Hospital Clinic; Hospital Clinic de Barcelona; Nephrology and Kidney Transplant Department*
[13]*Radiology Department, Hospital Clinic; Hospital Clinic Barcelona; Radiology Department, Center for Biomedic Imaging*
[14]*Hospital Clínic Barcelona; Hepatobiliopancreatic Surgery and Transplantation Department*

Background

Simultaneous pancreas and kidney transplantation (SPK) is associated with great postoperative morbidity and graft pancreatitis is the second most common complication attributed to reperfusion injury. Generally, a conservative treatment is sufficient while in selected cases a surgical approach may be considered.

Case presentation

We present a 40 year-old male with a BMI of 27.8 kg/m^2 and a past medical history of hypertension, dyslipidemia and type 1 diabetes mellitus, presenting secondary diabetic complications including retinopathy and pre-dialysis nephropathy who received an SPK transplantation from a 47 year-old DBD donor, with a BMI of 28 kg/m^2, after a one day ICU stay with low dose requirements of vasoactive drugs and a cold ischemia time of 340 min, with no intraoperative adverse events.

The patient was promptly discharged from the ICU at 48h following surgery. However, at postoperative day 8, the patient presented with fever and abdominal pain, as well as an increased drain debit which, after analysis, was compatible with pancreatic fistula. A computed tomography (CT) scan evidenced a heterogenous enhanced pancreatic parenchyma with increased peripancreatic fluid.

Conservative treatment was carried out without much success as a peripancreatic collection was evidenced in control imaging tests. Thus, a CT-guided drainage of the pancreatic collection was indicated with yet again little improvement.

Given the persistence of the collection, an exploratory laparoscopy with drainage of the pancreatic collection was performed achieving optimal results as the patient was promptly discharged maintaining a correct functionality of both pancreas and kidney grafts after a follow up of 11 months.

Conclusions
Early graft pancreatitis is the most common cause of relaparotomy in up to 40% of SPK transplantations. However, a laparoscopic approach offers benefits by reducing the risk of complications, shortening hospital stay and allowing quicker recovery times.

Conflicts of interest
No conflicts of interest

CC03 - PITFALLS OF FIGHTING WITH MUCORMYCOSIS IN AN IMMUNOCOMPROMISED PATIENT ONE MONTH AFTER SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANTATION (SPK)

Barbora Hagerf (Voglová)[1], Michaela Kudlackova[1], Jiri Veleba[1], Jan Kriz[2], Frantisek Saudek[3], Peter Girman[4]

[1]*Institute for Clinical and Experimental Medicine; Department of Diabetes*
[2]*Institute for Clinical and Experimental Medicine; Diabetes Center; Department of Diabetes*
[3]*Institute for Clinical and Experimental Medicine*
[4]*Ikem; Diabetes Department*

Background
Fungal opportunistic infections are a rare, potentially fatal complication of post-transplant immunosuppression. We present a case of combined mucor and aspergillus infection after SPK.

Methods
51years old female, one month after SPK, presented with fever and anemia. Initial exams showed CRP of 155, moderate bacteriuria, stable hematoma next to kidney graft, CT raised suspicion of pancreas graft vein thrombosis, treated successfully with LMWH. Empiric antibiotic therapy initially brought satisfactory response. Few days later she complained about pressure in the maxillary sinus area and tooth pain. X-ray showed possible inflammation. The tooth was extracted, along with bone sequesters with unusual necrotic appearance, all sent to microbiology. Therapy was enhanced with metronidazole. After temporary improvement, fever relapsed, followed by inflammatory markers elevation. She was referred to ENT specialist, who confirmed sinusitis and performed lavage and sinus puncture.

Results
Preliminary tests showed growth of unspecified fungus, suspicious for mucor. We started i.v. amphotericine B therapy. Two days later she complained of pain and swelling around the right eye. Cultivations from the sinus puncture revealed massive fungal growth, highly suspicious for mucor and aspergillus. Therefore, the patient was acutely referred to endoscopic sinus surgery. Bone sequesters and mucus lining of maxillary and frontal sinuses were removed, bone appeared intact. Postoperative MRI ruled out residual infection. Mucor and aspergillus fumigatus were confirmed in the removed specimens. We continued antimycotic therapy with amphotericin B and isavuconazole and minimized

immunosuppression. The following period was further complicated with rejection, urinary tract infection, clostridium enterocolitis, electrolyte imbalances and malnutrition requiring parenteral nutrition. We repeatedly faced the challenge to treat rejection and life-threatening infection simultaneously. The patient was discharged after three months and readmitted four more times. Six months later, she is on maintenance isavuconazole therapy, with no detection of fungal growth so far and stable graft function.

Conclusions
This case of invasive fungal infection shows that timely diagnosis and treatment, including surgical removal of infectious foci can lead to remission. Nevertheless, immunosuppression withdrawal and long term antimycotics bring risk of subsequent complications and need for complex individual management.

Supported by the project National Institute for Research of Metabolic and Cardiovascular Diseases (Programme EXCELES, ID Project No. LX22NPO5104) - Funded by the European

Union – Next Generation EU and by MH CZ - DRO („Institute for Clinical and Experimental Medicine – IKEM, IN 00023001“)

Conflicts of interest
No conflicts of interest

POSTERS

PP01 – INSULIN-SECRETING SPHEROIDS ENGINEERED FROM ISLET AND EXTRAVILLOUS TROPHOBLAST CELLS TO TREAT TYPE 1 DIABETES

Hiba Msheik[1], Emilie Derisoud[2], Fanny Lebreton[3], Marie Cohen[2], Ekaterine Berishvili[4]

[1]*University of Geneva; Department of Surgery*
[2]*University of Geneva*
[3]*Université de Genève et Hopitaux Universitaires de Genève; University of Geneva; Department of Surgery*
[4]*University of Geneva; Diabetes Center, University of Geneva Medical Center, Geneva, Switzerland; Department of Surgery, Cell Isolation and Transplantation Center*

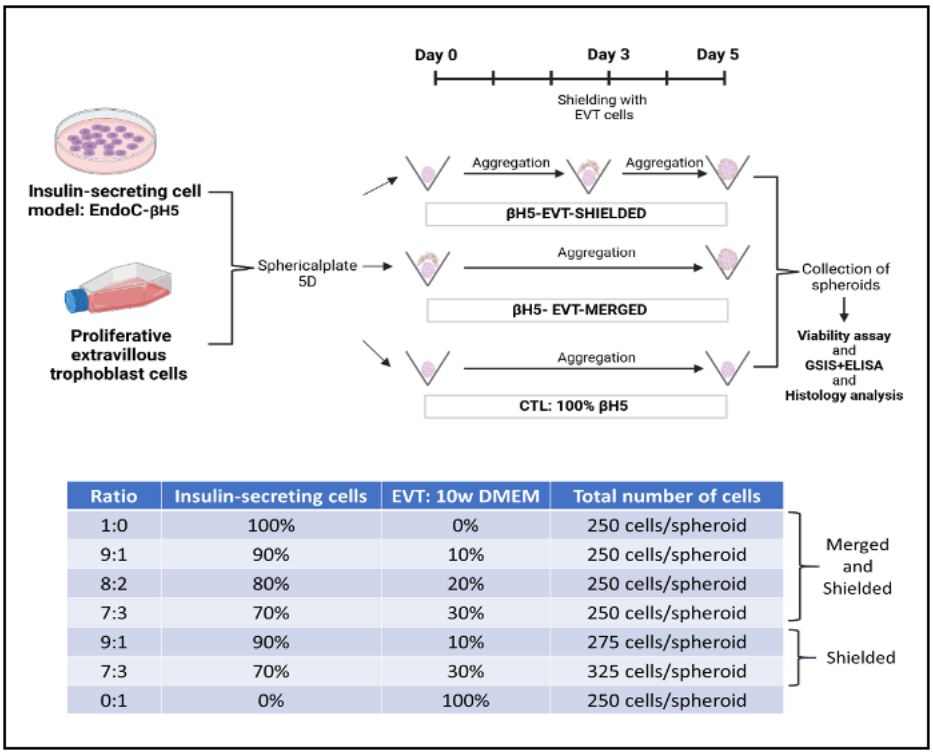
Background
Successful intraportal transplantation of pancreatic islets in type 1 diabetes (T1D) patients is impaired by poor vascularization, inflammation, and immunosuppressive drug toxicity. Novel therapeutic strategies are directed towards generating 3D aggregates of islet cells with other cell types, such as first trimester extravillous cytotrophoblast cells (EVT), which may aid in neovascularization and immune protection of the bioartificial pancreas. However, using EVT in clinical applications remains challenging due to the lack of suitable models.

Methods
To address this, we generated seven proliferative EVT populations from first-trimester trophoblast organoids using a novel protocol developed in our lab. We conducted qPCR, immunofluorescence, and flow cytometry assays to characterize these cells across different passages. We are currently using different generation strategies, spheroid sizes, and cell ratios to combine the EVT cells with the pancreatic beta cell model, EndoC-bH5, to create insulin-secreting spheroids (Figure 1). The function of these spheroids is evaluated through glucose-stimulated insulin secretion (GSIS) assay, and their viability is assessed by fluorescein diacetate/propidium iodide staining (FDA/PI).

Results
Our results revealed that the proliferative cell populations stably express markers of EVT cell identity and key immunomodulatory molecules, highlighting their EVT nature. Moreover, our preliminary results showed that both EndoC-bH5- and EndoC-bH5-EVT aggregates formed round spheroids within five days of culture with no apparent difference in cell viability. In addition, ELISA analysis revealed that incorporating 30% of EVT cells into the insulin-secreting spheroids enhanced insulin secretion of EndoC-bH5 cells twofold compared to the control. We are also investigating the use of other insulin-secreting cells, the human EndoC-bH1 cell line and pancreatic rat islet cells, to further assess the impact of EVT incorporation on the spheroids' functionality.

Future perspectives and conclusion
Subsequently, these spheroids will be assembled in a hydrogel scaffold to develop a bioartificial pancreas whose biocompatibility, immune protection ability, and functionality will be evaluated in vitro and in vivo. This innovative approach can potentially revolutionize T1D management and may also have applications in treating other diseases.

Figure 1. Strategies for engineering insulin-secreting spheroids with EndoC-βH5 and EVT cells



Ratio	Insulin-secreting cells	EVT: 10w DMEM	Total number of cells	
1:0	100%	0%	250 cells/spheroid	Merged and Shielded
9:1	90%	10%	250 cells/spheroid	
8:2	80%	20%	250 cells/spheroid	
7:3	70%	30%	250 cells/spheroid	
9:1	90%	10%	275 cells/spheroid	Shielded
7:3	70%	30%	325 cells/spheroid	
0:1	0%	100%	250 cells/spheroid	

Conflicts of interest
No conflicts of interest

PP02 - CHARACTERIZATION OF RAT BETA CELL'S CELL CYCLE

Katerina Bittenglova[1], Klara Zacharovova[2], Jan Kriz[3], Tomas Koblas[4]

[1]*Institute for Clinical and Experimental Medicine; Department of Diabetes; Diabetes Department*
[2]*Institute for Clinical and Experimental Medicine; Centrum of Experimental Medicine, Laboratory of Pancreatic Islets*
[3]*Institute for Clinical and Experimental Medicine; Diabetes Center; Department of Diabetes*
[4]*Institute for Clinical and Experimental Medicine*

Background
Activation of beta cell proliferation is a promising approach for beta cell replacement therapy. Given the fact that majority of beta cells are locked non-proliferative quiescent state, their cell cycle has not yet been investigated in detail. In this study, we aimed to clarify the cell cycle kinetics of replicating rat beta cells *in vitro* using flow cytometry (FC) assays. We analyzed the cell cycle kinetics in terms of lengths of individual cell cycle phases and typical markers for each phase.

Methods
Islet cell proliferation was induced by the ectopic overexpression of cell cycle activators. We analyzed islet cell samples at subsequent time points after the induction of proliferation. We performed cell cycle analysis using FC assays, with insulin staining and detection of specific cell cycle markers. We used Hoechst to detect DNA, 5-ethynyl-2′-deoxyuridine (EdU) to detect replicated DNA, phosphorylated form of retinoblastoma protein (pRB) as a marker of G1 phase, stem loop binding protein (SLBP), cyclin A2 and cyclin B1 as markers of S and G2 phases, and phosphorylated form of histone H3 (pHH3) to detect mitosis.

Results
After ectopic activation of cell cycle, the proliferation rate of beta cells reached up to 80-90% using cell cycle markers analyzed by FC. We revealed the whole cell cycle length of beta cells is 22-24 hours for most rapidly dividing beta cells. We found that G1 phase lasts 10-14 hours, the S phase 6-10 hours, and G2M phases 3-5 hours in case of the most rapidly dividing beta cells. However, the cell cycle length of most beta cells is significantly longer. Approximately half of proliferating beta cells divided within 32 hours while the other half of proliferating beta cells divided more slowly within 70 hours.

Conclusions
Using flow cytometry analysis of beta cells, we found that G1 phase occupies almost half of the entire cell cycle length of all beta cells. Additionally, we established a new combination of cell cycle markers that are convenient to analyze the individual phases of cell cycle in general. These findings can be used for stimulated proliferation of beta cells that can potentially impact diabetes treatment in the future.

Acknowledgement
Funded by the project National Institute for Research of Metabolic and Cardiovascular Diseases (Programme EXCELES, Project No. LX22NPO5104) - Funded by the European Union - Next Generation. Supported by MH CZ-DRO („Institute for Clinical and Experimental Medicine – IKEM, IN 00023001“) and by Charles University, project GA UK No. 299122.

Conflicts of interest
No conflicts of interest

PP03 - THE EFFECTS OF AMNIOTIC EPITHELIAL CELLS AND THEIR DERIVATIVES ON PANCREATIC ISLETS

Reine Hanna[1], Juliette Bignard[2], Domenico Bosco[3], Ekaterine Berishvili[4]

[1]*University of Geneva; University of Geneva; Surgery*
[2]*Laboratoire de Transplantation Cellulaire - Departement Chirurgie - Geneve*
[3]*Cell Isolation and Transplantation Center, Geneva University Hospitals and University of Geneva; Cell Isolation and Transplantation Center, Department of Surgery, Geneva University Hospitals and University of Geneva, Geneva, Switzerland; Diabetes Center, University of Geneva Medical Center, Geneva, Switzerland*
[4]*University of Geneva; Diabetes Center, University of Geneva Medical Center, Geneva, Switzerland; Department of Surgery, Cell Isolation and Transplantation Center*

Background
A considerable islet loss is observed following islet transplantation in type 1 diabetes patients due to hypoxia, inflammation and poor vascularization. Human amniotic epithelial cells (hAECs) have been shown to have cytoprotective effects on pancreatic islets under normal and stressful conditions, due to their anti-inflammatory, immunomodulatory and regenerative properties. The aim of this study is to investigate whether AEC- derivatives, such as conditioned media (CM) and extracellular vesicles (hAEC-EVs), would be able to exert similar properties.

Methods
The CM was collected from hAECs culture and the hAEC-EVs were subsequently isolated (by ultracentrifugation) and characterized (by nanoparticle tracking analysis, electron microscopy, western blotting and mass spectrometry). Islets (or β-cell spheroids) were cultured either with CM or hAEC-EVs. The islet function was assessed by glucose-stimulated insulin secretion assay.

Results
Characterization of hAEC-EVs showed the successful isolation of these vesicles. hAEC-EVs had a mean diameter of 160 nm and expressed EV markers such as CD9, CD63 and TSG101. Proteomics analysis showed the enrichment of EVs in proteins related to angiogenesis, apoptosis, inflammation, etc.

Islets exposed to the CM had an increased insulin secretion when compared to the control. On the other hand, less effects were observed with hAEC-EVs treated conditions under normal conditions. In contrast, hAECs-EVs had a positive effect on the insulin secretion of islets subjected to hypoxia (1% O2). In the future, we plan to better understand the mechanisms underlying the observed effects.

Conclusions
These results suggest that CM is beneficial to the islets and interestingly hAEC-EVs might be a potential tool to help against hypoxia-induced damages on islets function. These findings suggest a promising therapeutic avenue for improving outcomes in islet transplantation.

Conflicts of interest
No conflicts of interest

PP04 - USING A TRANSIENT COLD ROOM DURING COBE ISLET PURIFICATION REDUCES THE ENVIRONMENTAL MICROBIAL BURDEN AND ASSOCIATED ENERGY COSTS WHEN COMPARED TO THE USE OF A PERMANENT COLD ROOM

Lucy Crawford[1], Kalina Bednarek[2], Katarzyna Marszalek[3], Rebecca Spiers[2], Heide Brandhorst[4], Daniel Brandhorst[5], Paul Johnson[6]

[1]*Oxford University; Nuffield Department of Surgical Sciences*
[2]*University of Oxford; Nuffield Department of Surgical Sciences*
[3]*University of Oxford*
[4]*Radcliffe Hospital; Nuffield Department of Surgical Sciences*
[5]*Oxford Centre for Diabetes, Endocrinology and Metabolism (Ocdem); Nuffield Department of Surgical Science*
[6]*University of Oxford; University of Oxford; Nuffield Department of Surgical Sciences*

Background
Human islet isolation requires a balance between islet isolation optimisation and a strict regulatory framework. Most islet isolation labs cool the COBE machine during islet purification, but there is a clear risk of contamination within permanent cold rooms (CRP) due to a build-up of condensation within the space and higher overall energy usage for continuous temperature maintenance. Transient cold rooms (TCR) don't hold the same condensation risk and use less energy, but impact isolation times if they don't reach processing temperature within certain time frames. This retrospective study investigates the benefits of using a purpose-built TCR rather than a traditional CRP for islet isolation.

Methods
A TCR was installed in our purpose-built islet isolation facility from its outset. Environmental monitoring records spanning January 2016 to October 2024, 558 individual samples, were reviewed and microbial contamination instances recorded. These were compared to contamination levels identified in an equitable published study conducted in a CRP (*T. Sandle and K. Skinner, April 2013*). The TCR was maintained to GMP Grade B and the CRP to GMP Grade C. This difference was accounted for within the results. Energy consumption was calculated using with values extracted from the cooling mechanism specifications and then applying . These calculations were then applied to values from a CRP, of comparable size and specifications, provided by a collaborator (*J. Mock, October 2024*). The values were analysed and compared. Temperature within the cold room was tracked with readings taken continuously at 5-minute increments. Ambient and processing temperature were defined at 18ºC and 8ºC respectively. The average length of time from cooling initiation to processing temperature reached was calculated. This timeframe was applied to isolation procedure to determine whether processing temperature was reached prior to requirement for purification.

Results
Five low-level non-actionable contamination events were detected within the TCR over the selected period. This equates to 0.89% of samples taken. In literature 28.70% of samples taken detected contamination. When normalised to GMP Grade B standard this equates to 5.74%. The levels of contamination detected were 6.5 times higher within the CRP. The TCR consumed 315.3 kWh/year and the comparable CRP consumed 9554.94 kWh/year. The TCR has 3.23% of the energy requirements of a CRP. The average time taken to reach processing temperature is 83 minutes and 40 seconds. In comparison, the transient room successfully reaches processing temperature prior to requirement for purification.

Conclusions
Our findings suggest that the TCR accrues lower levels of microbial contamination than a standard CRP set up. Our data also shows that TCRs are more energy efficient and can achieve processing temperature in a time efficient way so as to not impact islet processing times. Such data comes at a time of transition from.

Conflicts of interest
No conflicts of interest

PP05 - THE RATE OF PANCREATIC ISLET VOLUME REDUCTION IN CULTURE AFTER ISOLATION

Sarah Suergiu[1], David Habart[2], Klara Zacharovova[3], Zuzana Berková[4], Barbora Radochová[5], Jiří Janáček[5], Martin Čapek[6], Frantisek Saudek[7]

[1]*Institute for Clinical and Experimental Medicine; Laboratory for the Islets of Langerhans (Lil)*
[2]*Institute of Clinical and Experimental Medicine; Laboratory for the Islets of Langerhans (Lil)*
[3]*Institute for Clinical and Experimental Medicine; Centrum of Experimental Medicine, Laboratory of Pancreatic Islets*
[4]*Ikem; Laboratory of Pancreatic Islets*
[5]*Institute of Physiology of the Czech Academy of Sciences*
[6]*Institute of Molecular Genetics of the Czech Academy of Sciences*
[7]*Institute for Clinical and Experimental Medicine*

Background
The volume of isolated pancreatic islets is assessed immediately after isolation to estimate the graft dose (IEQ/kg). Islets in culture undergo morphological alterations[1], leading to volume changes that affect graft dosing, depending on the time lag between harvest and application. We studied the dynamics of individual islet volume reduction with respect to islet size.

Methods
Wistar rat islets were isolated[2] and transferred to the microscopy facility within 30 minutes. Two timepoint acquisition allowed for a high image quality, but a second technique was required due to the lack of timelapse options.

1. Two timepoints: Islets were seeded in HBSS/Albumin and imaged at t0 and after 21 hours using a Zeiss AxioZoom microscope with reflected light.

2. Time course: Islets were seeded in an Ibidi 3D µ-Slide with supplemented medium. Timelapse images were taken with a Leica DMi8 microscope (37°C, 5% CO_2) with transmitted light, every 10 minutes for 3 hours, then hourly up to 17 hours.
Images were segmented using the GraphCut plug-in in Fiji, islets size and area were calculated, and volumes were estimated applying the Spinacle[3] model.

Results

Two Timepoints: 8 islets from 2 donors were analyzed (160-350 µm). After 21 hours, the islets exhibited an average size reduction of 8% (range: 6% to 11%, STDEV: 0.02) and volume reduction of 21% (range: 16% to 28%, STDEV: 0.05).

Time Course: Out of 27 islets from 3 donors (110-320 µm), 9 were excluded due to poor quality segmentation. The remaining islets showed an average size reduction of 5% over 17 hours (range: 0% to 11%, STDEV: 0.02). The average volume reduction was 13% (range: 3% to 30%, STDEV: 0.07) (Fig. 1).

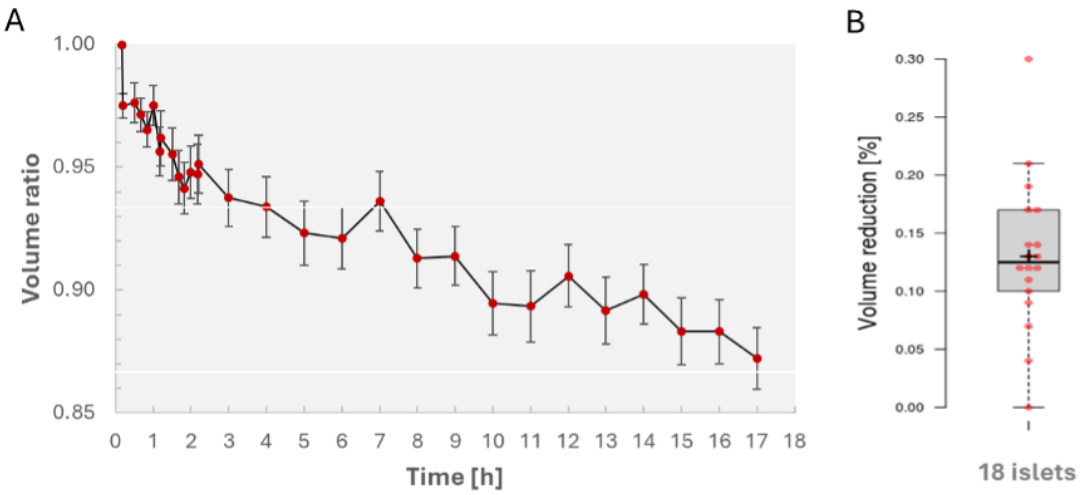


Fig.1 Average volume reduction time course (A) and for individual islet (B).

Conclusions

Islets showed a progressive volume reduction of 13% in the seventeen hours after the isolation. Notably, half of the size and volume reduction occurred within the first three hours. The segmentation plug-in had limitations, sometimes failing to exclude outgrowing cells. The reduction appears size-related, warranting further investigation. Additional islets are being collected, and the automatic segmentation will be improved.

Acknowledgments Supported by the grants from Czech Ministry of Health (NU22-01-00141) and from EU program EXCELES (CarDia, LX22NPO5104).

Conflicts of interest

No conflicts of interest

References

1.Pisania, A. *et al.* Quantitative analysis of cell composition and purity of human pancreatic islet preparations. *Lab. Investig. J. Tech. Methods Pathol.* 90, 1661–1675 (2010).
2.*Rat Experimental Transplantation Surgery: A Practical Guide*. (Springer International Publishing, Cham, 2015). doi:10.1007/978-3-319-14559-4.
3. Habart, D. et al. Spinacle: a novel method for islet volume estimation. 10th EPITA Symposium & 39th AIDPIT Workshop Abstract 3391 (2020).

PP06 - THE EFFECTS OF DIFFERENT ADENOSINE RECEPTORS ON INTEGRITY OF ISOLATED HUMAN ISLETS: INITIAL FINDINGS

Daniel Brandhorst[1], Heide Brandhorst[2], Rebecca Spiers[3], Lucy Crawford[4], Kalina Bednarek[3], Paul Johnson[5]

[1]*Oxford Centre for Diabetes, Endocrinology and Metabolism (Ocdem); Nuffield Department of Surgical Science*
[2]*Radcliffe Hospital; Nuffield Department of Surgical Sciences*
[3]*University of Oxford; Nuffield Department of Surgical Sciences*
[4]*Oxford University; Nuffield Department of Surgical Sciences*
[5]*University of Oxford; University of Oxford; Nuffield Department of Surgical Sciences*

Background
Previous studies have suggested that cold-storage of isolated human islets in UW-solution can preserve islet survival for a prolonged period of time. Addition of adenosine (ADO) further increased islet yield but decreased viability. The present study was performed to evaluate the effect of ADO on different ADO receptors expressed by human islets.

Methods
Prior to treatment with 5 mM of DMSO-dissolved ADO, isolated human islets (n = 5 DBD donors) were incubated for 90 min with 10 µM of the ADO receptor antagonists DPCPX, SCH58261, MRS1754 and VUF5574 specific for the receptors A1, A2a, A2b and A3, respectively. After CMRL culture for 4 – 5 days at 37ºC, islet assessment included yield of IEQ, viability (FDA-PI) and ROS production (DCFH-DA). Islet mortality was measured by apoptosis (Annexin V) and necrosis (PI). Data were related to IEQ and normalised to DMSO-treated controls (mean ± SEM).

Results
Results are shown in the table. After culture, significantly increased islet yield was observed after A1 unlocking whilst A3-unlocked islets had a reduced yield. ROS production was significantly enhanced in ADO-treated or A2a- and A3-unlocked islets while A1 unlocking decreased ROS. Compared with controls, all groups had a preserved viability except A3-unlocked and ADO-treated islets showing reduced viability. This corresponded with measured necrosis while ADO and unlocked A3 caused the largest extent of necrosis. A similar pattern was revealed for apoptosis being lowest after A1 and A2b unlocking and highest in A3-unlocked and ADO-treated islets. Thus, total islet mortality was low after A1 or A2b unlocking but significantly higher in ADO-treated and A3-unlocked islets.

Exp. Groups	Islet Yield (%)	ROS Production (%)	Viability (%)	Early Apoptosis (%)	Necrosis (%)
(A) Control	100 ± 0.0[c,e]	100 ± 0.0[i]	100 ± 0.0[i]	100 ± 0.0	100 ± 0.0[a]
(B) Adenosine	125 ± 6.5[a,h]	170 ± 8.1[b,j]	90.5 ± 2.1[a,g,j]	198 ± 18.4[c,f,j]	217 ± 38.1[b,f,j]
(C) A1	168 ± 1.3	86.1 ± 9.8	100 ± 1.0	59.5 ± 5.5	78.2 ± 3.9
(D) A2a	122 ± 5.8[a]	176 ± 33.1[b]	96.5 ± 1.5[e]	163 ± 17.6[b,e]	167 ± 37.6[a]
(E) A2b	130 ± 9.4	112 ± 20.6	104 ± 1.2	79.4 ± 13.4	90.4 ± 24.8
(F) A3	79.4 ± 6.0[c,d,f]	217 ± 23.0[c,f]	86.2 ± 4.8[a,g]	195 ± 33.9[b,e]	232 ± 32.9[c,d,g]

Data are normalised to DMSO-treated control islets.
[a]$P < 0.05$, [b]$P < 0.01$, [c]$P < 0.001$ vs **A1**; [d]$P < 0.05$ vs **A2a**; [e]$P < 0.05$, [f]$P < 0.01$, [g]$P < 0.001$ vs **A2b**;
[h]$P < 0.05$, [i]$P < 0.01$ vs **A3**; [i]$P < 0.05$ vs **control**.

Conclusions

This initial study is the first to assess the effect of different ADO receptors on survival and integrity of human islets indicating that A1 and A2b are related to protection while A3 has detrimental effecte. More studies are needed for to fully characterise of human ADO receptors.

Conflicts of interest

No conflicts of interest

PP07 - ENGINEERING BIOINKS FOR EXTRUSION BIOPRINTING OF ISLETS AND ENDOTHELIAL CELLS

Víctor Galván Chacón[1], Lorraine Couteau[1], Kevin Bellofatto[2], Philippe Compagnon[3], Ekaterine Berishvili[4]

[1]*University of Geneva; Centre Medical Universitaire; Tissue Engineering and Organ Regeneration*
[2]*Universite de Geneve and Hospitaux Universitaires de Geneve; University of Geneva; Surgery*
[3]*Geneva University Hospitals*
[4]*University of Geneva; Diabetes Center, University of Geneva Medical Center, Geneva, Switzerland; Department of Surgery, Cell Isolation and Transplantation Center*

Background
Type 1 diabetes (T1D), an autoimmune disorder, affects approximately 8.5 million individuals globally and imposes a significant strain on healthcare systems.. Islet transplantation is a viable treatment for restoring normoglycemia, despite being compromised by inflammation, poor vascularization and immune response. To address these challenges, researchers explored strategies such as islet encapsulation within biomaterials. In particular, bioprinting offers control over scaffold geometry, enabling the fabrication of complex porous structures conducive to vascularization.[1] Here, we aim to develop a bioink for extrusion bioprinting that enhances human islet functionality and supports endothelial cell growth.

Methods
In the past, our group has developed a decellularized extracellular matrix (dECM) hydrogel derived from the amniotic membrane, known as Amniogel. The composition of the Amniogel, assessed by mass spectrometry, confirms that the primary constituent of this matrix is collagen type I, and TEM imaging confirms that the collagen native structure is preserved.
Our in vivo study in a mouse model shows that islets encapsulated in Amniogel have shown superior performance in restoring normoglycemia and stimulating angiogenesis compared to commercial collagen type I. To assess the potential for printability of different inks, we used rotational and oscillatory rheological tests.[2] As Amniogel's rheological properties do not allow direct printing, we combined it with different natural polymers and selected those suitable for printing, and discarded the inks without adequate shear-thinning behavior. Next, we seeded GFP-modified blood outgrown endothelial cells (BOECs) in them for 5 days and discarded the materials that did not support BOECs growth or were fully degraded in culture medium. Last, we embedded human islets in the selected bioink and evaluated their functionality after 7 and 14 days by immunofluorescence staining and static glucose-stimulated insulin secretion.

Results
The analysis of the rotational and oscillatory rheology tests confirmed that the Amniogel is not suitable for extrusion printing alone (Fig. 1a). Thus, we tested the combination of Amniogel with four different natural polymers and evaluated their rheological properties (Fig. 1b), discarding those without adequate shear-thinning behavior.
The evaluation of the BOECs morphology in the candidate bioinks showed that in one of the candidates (Bioink 3) the cells adopted a spherical morphology and did not spread.
The islets in the bioink expressed insulin and glucagon (Fig. 2b) and were able to secrete insulin in response to theophylline (Fig. 2c), although the total insulin content remained lower than for the control and Amniogel (Fig. 2d).

Conclusions
The results showed that the bioink is suitable for extrusion bioprinting, supports BOECs growth, and preserves islets' capacity to produce insulin even after 14 days in culture.

However, the composition needs optimization to achieve a glucose stimulation index like that of Amniogel.

Conflicts of interest
No conflicts of interest

References
(1) Goswami, D.; Domingo-Lopez, D. A.; Ward, N. A.; Millman, J. R.; Duffy, G. P.; Dolan, E. B.; Roche, E. T. Design Considerations for Macroencapsulation Devices for Stem Cell Derived Islets for the Treatment of Type 1 Diabetes. *Adv Sci (Weinh)* **2021**, *8* (16), e2100820. DOI: 10.1002/advs.202100820 From NLM Medline.
(2) Paxton, N.; Smolan, W.; Bock, T.; Melchels, F.; Groll, J.; Jungst, T. Proposal to assess printability of bioinks for extrusion-based bioprinting and evaluation of rheological properties governing bioprintability. *Biofabrication* **2017**, *9* (4), 044107. DOI: 10.1088/1758-5090/aa8dd8 From NLM Medline.

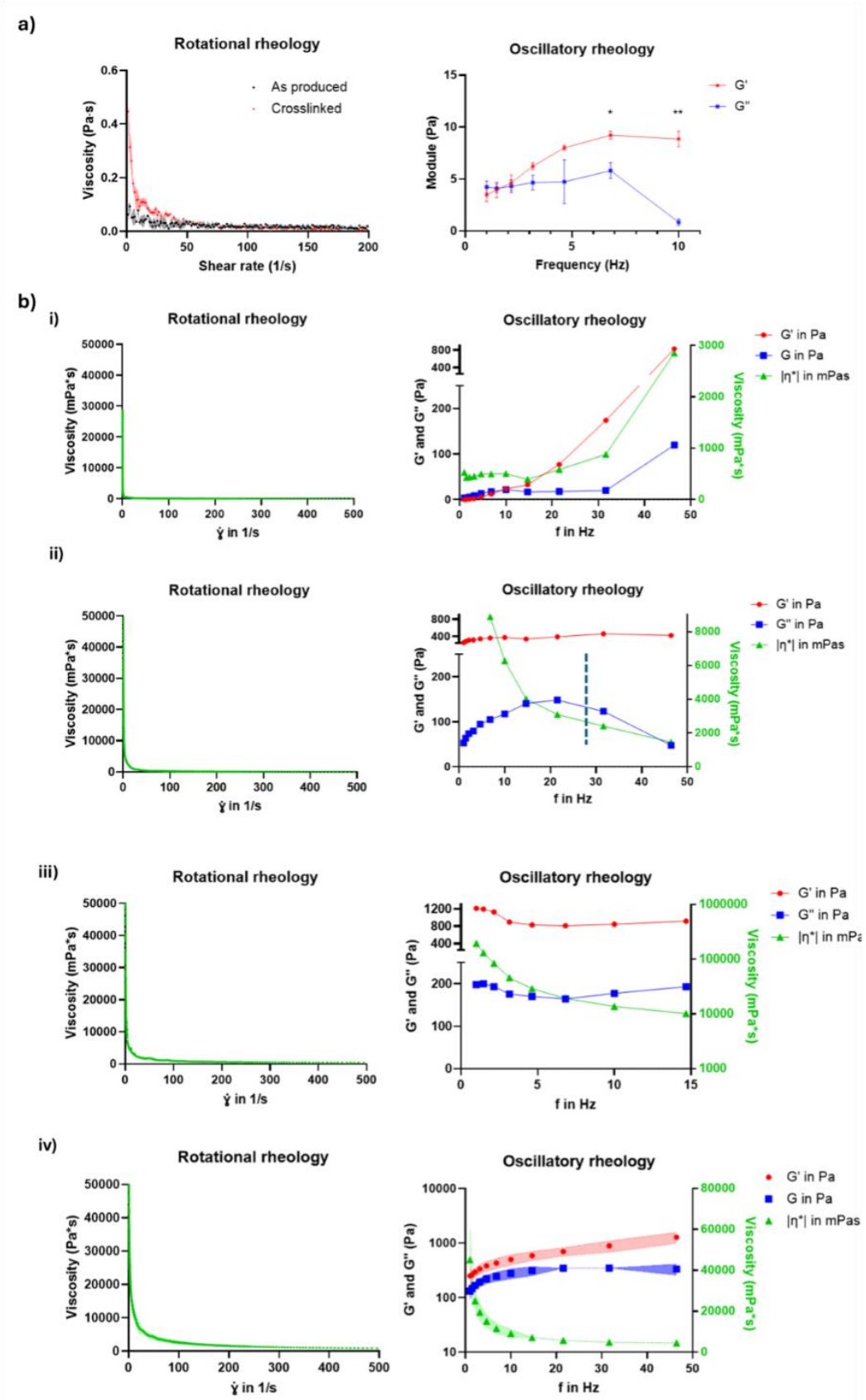


Figure 1. Rheological analysis of the different bioinks. a) Rotational and oscillatory rheology of pure Amniogel 8 wt%. b) Rotational and oscillatory rheology of the bioinks; i) Gellan gum and gelatine, ii) Gellan gum, gelatine and low concentration cellulose, iii) Gellan gum, gelatine and high concentration cellulose, iv) Alginate, gellan gum, gelatine, cellulose.

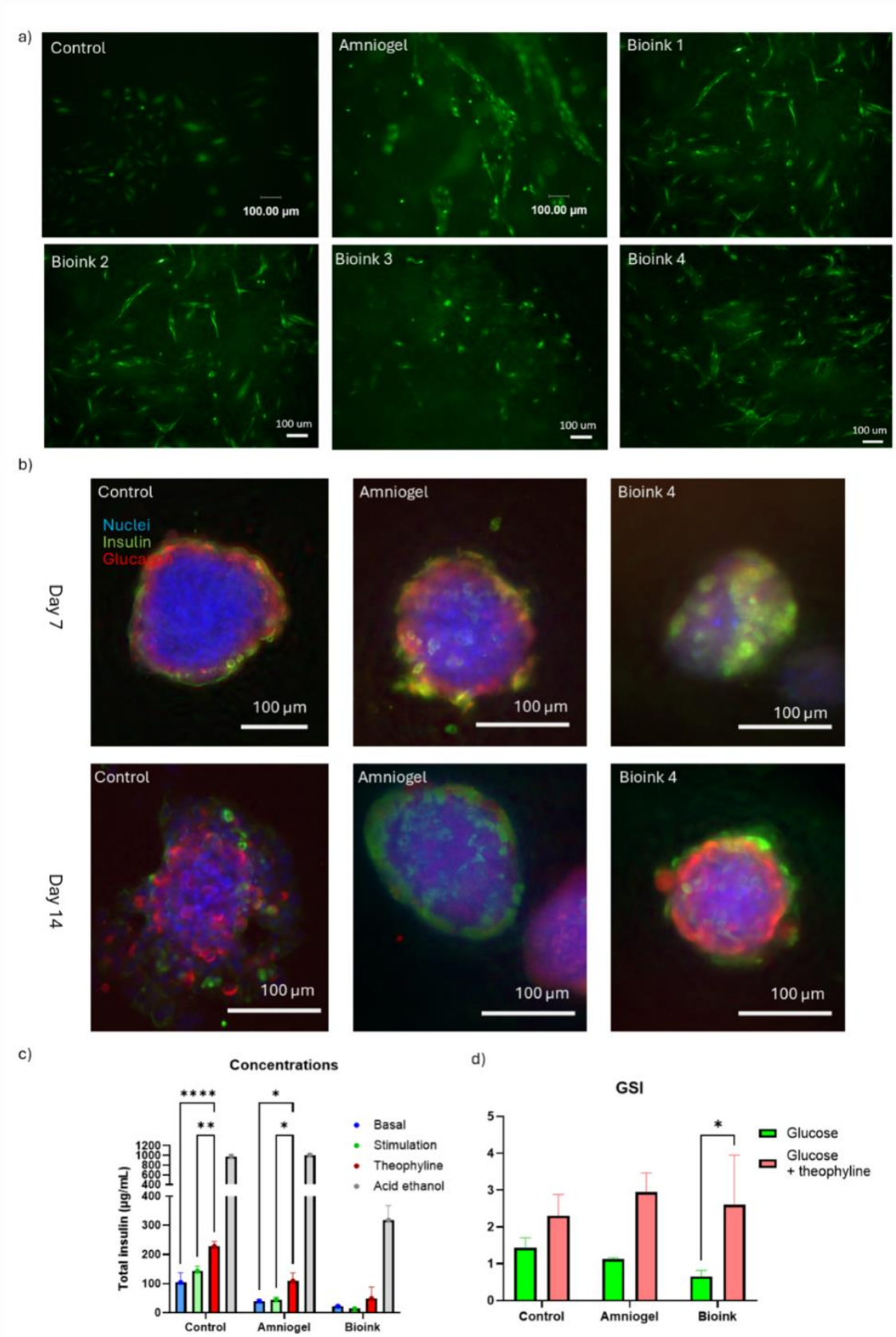


Figure 2. Fluorescence microscopy images of BOECs and human islets seeded in Bioink 4. a) Images of BOECs-GFP seeded inside on a well culture plate (control), in Amniogel and in Bioink 4, green color marking the cell cytoplasm. c) Results of the GSIS performed at day 14.

PP08 - IMPROVED METABOLIC ANALYSIS OF ISLETS OF LANGERHANS: DETECTION OF O2 CONSUMPTION DURING PHASES OF DYNAMIC INSULIN SECRETION

priyadarshini Gnanasekar[1], GMYR Valery[2], patrice Coddeville[3], Christophe Cappelaere[3], Thomas Fagniez[3], Vincent Martin[4], Anais Coddeville[5], Delalleau Nathalie[6], Julien THEVENET[7], Gianni Pasquetti[8], Isabel Gonzales Mariscal[9], Caroline Bonner[10], Caroline Bonner[11], Francois Pattou[12], Julie Kerr-Conte[1]

[1]*Umr1190*
[2]*Inserm Dr Nord Ouest; U1190*
[3]*Imt Nord Europe*
[4]*Centrale Lille Institut*
[5]*Umr 1190 Recherche Translationnelle Sur Le Diabète*
[6]*Univ Lille*
[7]*"Translational Research for Diabetes" Lab; Faculté de Médecine*
[8]*Inserm U1190 - University of Lille / Chu Lille; Nord*
[9]*Inserm Umr 1190*
[10]*Univ. Lille*
[11]*Institut Pasteur de Lille*
[12]*Univ Lille; U1190*

Background
Among different islet assessments, perifusion GSIS is a widely used technique in which islets are continuously perifused under different glucose concentrations to measure insulin secretion. Additional metabolic parameters such as OCR (oxygen consumption rate) appear to be relevant to analyze the relationship between energy metabolism and hormonal secretion. This could greatly improve islet assessment, making it possible to argue for the success or failure of islet transplantation. The study aims to develop a tool to enable real-time monitoring of the bioenergetic behaviour of human islets during perifusion to better understand their functional capacity in vitro.

Methods
In this study, we coupled an oxygen sensor to the post-chamber connectivity to measure the oxygen concentration in the perifused medium. Two types of sensors were tested: the non-invasive, single-use preSens sensor coupled to the PMS analysis software and the non-invasive, multi-use Pyroscience sensor based on Red Flash technology using the data inspector analysis tool. isolated human islets (300 IEq) (n=3) tested at different glucose concentrations (G3, G15) in the presence of oligomycin and FCCP.

Results
Real-time monitoring revealed in high glucose, in a carbogen-saturated environment (95%O2+5%CO2), a reduction in oxygen consumption when ATP synthase was targeted with a specific inhibitor (oligomycin) and increased metabolic activity when targeting a proton transporter with FCCP (n=3). This bioenergetic behaviour was correlated with changes in insulin secretion in response to glucose. The 2 sensors tested showed similar profiles. By using the inspector tool, the data showed alternative changes in the respiration rate at each stimulation phase (B1, S1 & S2). These results were observed independently of the carbogen concentrations in the perifusion media.

Conclusions
We describe the feasibility of developing a tool capable of measuring the respiratory behaviour of isolated islets of Langerhans during glucose stimulation phases. This tool could provide valuable insights into the evaluation process of islets for clinical or experimental use.

Conflicts of interest
No conflicts of interest

PP09 - POTENTIAL SIDE EFFECTS OF MICROPORATION ON PANCREATIC ISLETS (PI)

Veronika Tomsovska[1], Eva Fabryova[2], Ivan Leontovyč[3], Klara Zacharovova[4], Magdalena Špitálníková - Veřtátová[2], Peter Girman[5], Zuzana Berková[6], Jan Kriz[7]

[1]*Institute for Clinical and Experimental Medicine; Laboratory for the Islets of Langerhans*
[2]*Institute for Clinical and Experimental Medicine*
[3]*Ikem; Cem*
[4]*Institute for Clinical and Experimental Medicine; Centrum of Experimental Medicine, Laboratory of Pancreatic Islets*
[5]*Ikem; Diabetes Department*
[6]*Ikem; Laboratory of Pancreatic Islets*
[7]*Institute for Clinical and Experimental Medicine; Diabetes Center; Department of Diabetes*

Background
Microporation (Mi) as a type of electroporation technique using electric pulse which forms pores in the cell membrane allow siRNA enter into the cells. We tested the potential negative effects of Mi on the vitality and function of PI.

Methods
PI were isolated from BN rats and 5 experimental groups were compared: control without any treatment, exposition to siRNA without Mi, Mi alone, Mi with siRNA, and Mi with Poly (I:C), which was used as a positive control. Samples were subjected to the following tests: fluorescent test of membrane integrity, glucose stimulated insulin release (GSIR), fluorescent test of caspase activation, qRT-PCR of inflammatory markers, flow cytometry quantification of apoptotic and dead cells. Subsequently PI from control group and group Mi with siRNA were transplanted to diabetic BN rats. After one month IVGT tests were performed.

Results
Test of membrane integrity showed 90,4 % live cells in control sample while in Mi with siRNA (84,3%) and Mi with Poly (I:C) (75,4%) was seen significant decrease. Percentage of apoptotic cells was significantly increased in samples Mi alone (5,9%), Mi with siRNA (4,7 %), and Mi with Poly (I:C) (6,8%), in comparison with 2,7% in control samples. Inflammatory markers were significantly increased just for Poly(I:C). Our results didn't show significant differences in GSIR and IVGTT.

Conclusions
Only some of in vitro methods showed a significant difference among control and microporated PI samples. Microporation only slightly reduces in vitro vitality of PI while no differences were found in vivo after transplantation. Microporation represent the possible and effective method for transfection of PI.
Supported by the project National Institute for Research of Metabolic and Cardiovascular Diseases (Programme EXCELES, ID Project No. LX22NPO5104) - Funded by the European Union – Next Generation EU. Supported by MH CZ-DRO („Institute for Clinical and Experimental Medicine – IKEM, IN 00023001“)

Conflicts of interest
No conflicts of interest

PP10 - KYNURENINE MONOOXYGENASE (KMO) EXPRESSION IN HUMAN PANCREAS DURING ORGAN PRESERVATION - POSSIBLE IMPLICATIONS FOR ISLET TRANSPLANTATIONS

Valentina Giai[1], Andrew Sutherland[2]

[1]*Centre for Inflammation Research; Centre for Inflammation Research*
[2]*University of Edinburgh; Department of Transplantation*

Background

Ischaemia-reperfusion injury and the innate blood-mediated immune reaction (IBMIR) confound pancreatic islet transplantation at all stages from islet procurement to engraftment. Kynurenine-3-monooxygenase (KMO) is a key enzyme of tryptophan metabolism that contributes to the systemic inflammatory response, and KMO inhibition protects lung liver and kidney tissue during acute pancreatitis, and during ischaemia reperfusion injury. KMO is expressed in pancreatic islets and KMO inhibition improves glucose-stimulated insulin secretion in in vitro and in vivo models of type II diabetes. Here, we sought to define KMO expression (and other metabolites of the KMO pathway) in human pancreas and islets cells during static cold storage and perfused organ preservation, to further investigate the rationale for KMO inhibition as a potential therapeutic target in pancreas and islet cell transplant.

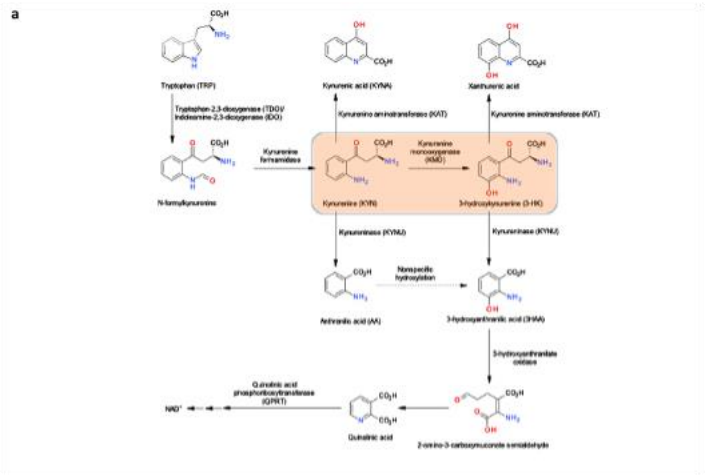


Figure 1: The kynurenine pathway of tryptophan catabolism. Taken from Mole DJ, et al. Kynurenine-3-monooxygenase inhibition prevents multiple organ failure in rodent models of acute pancreatitis. Nat Med. 2016 Feb;22(2):202-9. doi: 10.1038/nm.4020. Epub 2016 Jan 11. PMID: 26752518; PMCID: PMC4871268.

Methods

Human pancreases not suitable for transplantation were perfused with Belzer MPS UW solution or human blood products (RBCs and plasma). Experimental conditions explored oxygenated and non-oxygenated perfusate at 4°C (cold), or at 37°C (warm). Biopsies and perfusate samples at different timepoints were analysed by biochemistry, histology, immunohistochemistry (for glucagon, insulin and Kmo, quantified using QuPath), and mRNA expression of key kynurenine pathway genes and hypoxia inducible factors.

Results

Histological analyses reveal Kmo was present in islets and not within the exocrine acinar tissue. Kmo expression was present during cold and warm perfusion, and static cold storage. Serum analyses reveal out-of-range amylase levels following warm perfusion. RT-PCR shows Kmo to be expressed in human pancreas, Tdo2 to be increased following nonoxygenated perfusion, and kynunerinase to be increased following cold perfusion.

Conclusions
KMO was expressed within in islets cells at all time points during static cold storage, hypothermic perfusion and normothermic perfusion. The implications of such findings remain to be investigated. KMO inhibition remains a potential therapeutic target to preserve islet cell viability and function in pancreas and islet cell transplantation.

Conflicts of interest
No conflicts of interest

PP11 - CLICK-IT EDU AS A TOOL FOR RAT BETA CELL PROLIFERATION STUDY

Magdalena Špitálníková Veřtátová[1], Klara Zacharovova[2], Katerina Bittenglova[3], Tomas Koblas[4], Frantisek Saudek[4], Jan Kriz[5]

[1]*Institute for Clinical and Experimental Medicine; Experimental Medicine Centre, Laboratory for the Islets of Langerhans*
[2]*Institute for Clinical and Experimental Medicine; Centrum of Experimental Medicine, Laboratory of Pancreatic Islets*
[3]*Institute for Clinical and Experimental Medicine; Department of Diabetes; Diabetes Department*
[4]*Institute for Clinical and Experimental Medicine*
[5]*Institute for Clinical and Experimental Medicine; Diabetes Center; Department of Diabetes*

Background
The natural proliferation of pancreatic islet beta cells is very low. However, when working with the cell monolayer of islet cells, a small percentage of cells divide naturally. To identify proliferating beta cells, we introduced a method based on the principle of incorporation of the artificial nucleotide EdU and its subsequent detection by flow cytometry or fluorescence microscopy.

Methods
Isolated rat pancreatic islets were dissociated into cell suspension by Accutase (20 min, RT). Dissociated cells were seeded into 96 well plate coated with extracellular matrix produced by bladder cancer cells (HTB-9). After 3-day cultivation the islet cell medium was supplemented with EdU (5-ethynyl-2'-deoxyuridine, 20uM). The cells were analyzed in 12 and 24 hours. For immunofluorescence, cells were fixed and labeled on the surface of the culture plate. For flow cytometry, cells were detached from the culture plate by TrypLE™ and fixed and labeled in suspension. For both methods, cells were permeabilized and EdU was labeled by small molecule-based Click-iT™ EdU detection fluorescent reagent (part of the Click-iT™ EdU Cell Proliferation Kit for Imaging, Invitrogen). Insulin was detected by rabbit-anti-insulin antibody (Abcam) followed by fluorescent secondary anti-rabbit antibody (Invitrogen). Adhered cells were finally counterstained with DAPI and imaged by EVOS M7000 microscope (Thermo Fisher Scientific Inc). Image analysis was performed by Celleste software (Thermo Fisher Scientific Inc) to obtain percentage of proliferating beta cells. Cell suspension was analyzed by BD LSR II flow cytometer.

Results
Microscopic analysis of dissociated rat beta cells showed that they spontaneously proliferated in 2 % and 3,7 % after 12 hours and 24 hours, respectively. Flow cytometric analysis is a more sensitive method that gave slightly higher results. After 12 hours, beta cells represented 67% and of these, 3.3 % were identified as EdU positive, that means proliferating. After 24 hours, 63 % of all cells were beta cells and 6,8 % were proliferating.

Conclusions
We were able to detect the proliferation of rat beta cells among the dissociated islet cells cultivated in the monolayer. These methods could be utilized mainly for experiments promoting beta cells proliferation.

Funded by the project National Institute for Research of Metabolic and Cardiovascular Diseases (Programme EXCELES, Project No. LX22NPO5104) – Funded by the European Union - Next Generation EU and by MH CZ - DRO („Institute for Clinical and Experimental Medicine – IKEM, IN 00023001“).

Conflicts of interest
No conflicts of interest

PP12 - LIVER SURGICAL MACROBIOPSIES OF ISLET TRANSPLANT RECIPIENTS: ABOUT THREE CASES

Mehdi Maanaoui[1], Mikael Chetboun[2], Isabel Gonzales Mariscal[3], Jean-Baptiste Gibier[4], Julie Kerr-Conte[5], Frederique Defrance[6], Delalleau Nathalie[7], Valery Gmyr[8], Viviane Gnemmi[9], Marie-Christine VANTYGHEM[6], Francois Pattou[10]

[1]*Chu Lille; Univ.Lille, U1190 – Egid; Nephrology*
[2]*Chu Lille; General and Endocrine Surgery*
[3]*Inserm Umr 1190*
[4]*Chu Lille; Pathology*
[5]*Chu Lille; Faculty of Medicine*
[6]*Lille University Hospital; Claude Huriez Hospital; Department of Endocrinology, Diabetology, Medical Oncology and Metabolism*
[7]*Univ Lille*
[8]*Inserm U1190*
[9]*Chu Lille*
[10]*Univ Lille; U1190*

Background
Mechanisms of rejection in islet transplantation have been suggested in animal models, yet determinants of islet graft rejection in humans remains elusive. We detail here liver biopsy findings from three islet transplant recipients that presented with islet graft dysfunction or de novo donor-specific antibodies.

Methods
Liver biopsies were performed surgically after consent in three islet transplant recipients. Mini-invasive surgery was performed using coelioscopy and involved macrobiopsies (approximately 1cm² tissue resection). Tissues were paraformaldehyde-fixed and frozen for histological analysis, including light microscopy and immunostaining for insulin, glucagon, somatostatin (metabolic markers); CD68, CD3, CD20, C4d (rejection markers).

Results
Among the three patients, liver macrobiopsies were successfully performed, without any postoperative complications. Using light microscopy, islets could be witnessed in all patients' samples. The first patient, receiving islets from three donors, achieved insulin independence post-third infusion. She exhibited preformed DSAs against all donors and developed new DSAs against the first donor. Two years later, while insulin-independent, she benefited from a liver biopsy during a cholecystectomy, which revealed islets in the macrobiopsy with a density of 0.4 islets/mm3, with a median diameter of 140 µm (range 108-196). These islets were positive for insulin, glucagon, and somatostatin, with no rejection markers detected. The second patient also attained insulin independence after receiving islets from three donors and showed no preformed DSAs. Post-Covid19 infection, six years post-transplantation, he experienced a C-peptide decrease and resumed insulin therapy after seven years. Eight de novo DSAs emerged, targeting HLA antigens from all donors. Surprisingly, these islets showed no signs of immune infiltration or rejection. The last patient presented with early graft dysfunction after two islet transplantations, without reaching insulin-independence. Liver macrobiopsies revealed however insulin-secreting islets, without any signs of immune infiltration, excluding the diagnosis of rejection.

Conclusions
Surgical liver macrobiopsy is a reliable tool to assess islet viability in islet transplant recipients. In three patients presenting with signs of allosensitization or graft dysfunction, no infiltration or rejection could be assessed.

Conflicts of interest
No conflicts of interest

PP13 - THE NEW PROGRAM OF ALLOGENIC PANCREATIC ISLET CELLS TRANSPLANTATION IN PATIENTS WITH TYPE 1 DIABETES MELLITUS AFTER KIDNEY TRANSPLANTATION IN THE REPUBLIC OF BELARUS

Sviatlana Pazdniak[1], Ekaterina Nazarova[2], Aliaksei Fedaruk[3], Kirill Komissarov[4], Natalyia Dedyulya[5], Evgeniya Primakova[2], Ala Symanovich[5], Ekaterina Petrovskaya[2], Oleg Kozak[4], Irina Romanova[5], Dzmitry Fedaruk[6], Svetlana Krivenko[2], Aleh Kalachyk[7]

[1]*Minsk Scientific and Practical Center for Surgery, Transplantation and Hematology, State Institution; Kidney Unit; Nephrology*
[2]*Minsk Medical Center for Surgery, Transplantology and Hematology*
[3]*Minsk Scientific and Practical Center for Surgery, Transplantology and Hematology*
[4]*Minsk Scientific and Practical Center for Surgery, Transplantation and Hematology*
[5]*State Institution "Minsk Scientific and Practical Center for Surgery, Transplantology and Hematology"*
[6]*Minsk Center for Surgery, Transplantology and Hematology; Transplant, Hpb Surgery*
[7]*Minsk Scientific and Practical Center for Surgery, Transplantation and Hematology; Transplantation Department*

Background
The aim of the study was to evaluate the efficiency of first implication of intraportal infusion of allogenic pancreatic islets in patients after kidney transplantation. From November 2023 to November 2024, 3 pancreatic islets transplantations were performed at our center.

Methods
Islets were isolated from pancreas fragments of cadaveric donors (n=7).The weight of pancreas fragments varied from 40.3 g to 67.0 g. Enzymatic cleavage of pancreas tissue was performed in a Ricordi chamber with a warm (37℃) solution of type IV collagenase. The number of islet equivalents was counted by microscopy on a universal inverted microscope using the phase contrast method and staining with dithizone. The operations were performed under ultrasound and radiological control. Patients with type 1 diabetes mellitus after kidney transplantation were selected according to the following criteria: presence of recurrent episodes of hypoglycemia, HbA1c level not higher than 12%, body weight not higher than 85 kg, GFR not lower than 30 ml/min, absence of any significant infection and signs of portal hypertension. ATG was used as induction immunosuppression prior to islet transplantation. Followed by Adalimumab administration for anti-inflammatory purposes and Tacrolimus and MMF for graft rejection prophylaxis.

Results
In the static glucose stimulation test (16.7 mM/L), insulin production per 1000 islet equivalents was determined. The median was 5.0 [0.7; 15.3] uU/ml (n=7). The median viability was 90% [60; 98] (n=7) when taken into account on the lifetime imaging device Incucyte 'Sartorius' (USA) with vital dye Cytotox Green. **Case 1:** 1,248,528 islet equivalents were transplanted (24,010 IEQ/kg of the recipient's body weight). After 1 month, we achieved a reduction in short-acting insulin requirement from 18 U/day to 8 U/day (including days without short-acting insulin), a reduction in long-acting insulin requirement from 20 U/day to 16 U/day. **Case 2:** 844,782 islet equivalents were transplanted (10,559 IEQ/kg of the recipient's body weight). After 1 month, we achieved a reduction in short-acting insulin requirement from 32 U/day to 18 U/day, reduction in long-acting insulin requirement: from 28 U/day to 20 U/day. In both cases, patients reported better tolerance to hypoglycemia. **Case 3:** 1,090,000 islet equivalents were transplanted (14,155 IEQ/kg of body weight). The reduction in insulin requirement could not be achieved due to severe hyperglycemia caused by the patient's conversion from Cyclosporine to Tacrolimus. But the C-peptide level elevation till 0,11 ng/ml was achieved. A complication was noted in one case: a moderate increase in ALT and AST levels (completely normalized after 1 week).

Conclusions
Intraportal infusion of allogenic pancreatic islets is partially effective and a much less invasive procedure, unlike pancreas transplantation, and causes fewer complications. Islets transplantation holds great promise in the treatment of type 1 diabetes mellitus, as it offers the opportunity to reduce insulin dosage and improve tolerance to hypoglycemia.

Conflicts of interest
No conflicts of interest

PP14 - PIONEERING PANCREAS ISLET TRANSPLANTATION: THE FIRST SUCCESSFUL CASE IN LITHUANIA

Monika Vitkauskaite[1], Loreta Vareikiene[1], Marius Miglinas[2]

[1]*Vilnius University Hospital Santaros Klinikos; Nephrology Center*
[2]*Lithuanian Kidney Foundation; Nephrology and Kidney Transplantation Department*

Background
Pancreatic islet transplantation has become an established approach for *β*-cell replacement therapy in insulin-deficient diabetes worldwide. In kidney transplant recipients, pancreatic islet transplantation has proven highly effective in improving and maintaining metabolic control, without the need for additional immunosuppressive therapy. Furthermore, kidney function remains stable during long-term follow-up, with estimated glomerular filtration rate (eGFR) even showing signs of improvement over time. While challenges remain, the continued evolution of this multidisciplinary treatment strategy holds great promise in enhancing patient outcomes and overall survival in this complex patient population.

Methods
Herein, we report a case report of the first successful pancreatic islet transplantation after cadaveric kidney transplantation.

Results
A 59-year-old male patient presented as a potential recipient for pancreatic islet transplantation. He was diagnosed with type 1 diabetes 45 years ago, had poor glycemic control and frequent hypoglycemic episodes, occurring approximately five times per week. At the age of 34 years, he started hemodialysis, and nine years later, he underwent a cadaveric kidney transplant. For immunosuppression, he was taking mycophenolate mofetil 500 mg once daily and cyclosporine 50 mg twice daily. Methylprednisolone was discontinued due to hyperglycemia. His insulin regimen included 17–20 units of insulin glargine at bedtime and 8 units of short acting insulin (insulin lispro) before meals. The recipient was ABO blood group A and Rh positive. The HLA mismatch for the A, B, and DR loci was 2-1-1 (in total, four HLA mismatches). Prior to pancreatic islet transplantation, he received anti-thymocyte globulin (ATG) as part of the conditioning regimen. Afterwards 4,000 pancreatic islets were infused into the hepatic portal system. He was discharged 10 days after transplantation with immunosuppression consisting of tacrolimus 2.25mg daily and mycophenolate mofetil 1000 mg twice daily. His insulin regimen was adjusted, with insulin glargine reduced to 13 units at bedtime and insulin lispro titrated down to 2–6 units before meals.One month post-transplantation, good function of the pancreatic islet graft was noted, with a >50% reduction in insulin requirements. Glycated hemoglobin (HbA1c) decreased from 6.7% to 6.2%. Three years after transplantation, both the kidney and pancreatic islet grafts remained stable, with serum creatinine levels ranging from 73 to 86 µmol/L (normal range 64 – 104 µmol/L) and HbA1c at 5.8%. There was no increase in insulin requirements during this follow-up period. Moreover, the 90-day average blood glucose level was 7.1 mmol/L, with a TIR (time in range) of 71%.

Conclusions
Successful pancreatic islet transplantation following kidney transplantation represents a significant achievement in the management of patients with both end-stage renal disease and type 1 diabetes. This approach not only resolves insulin dependence but also improves glycemic control, quality of life, and long-term outcomes for patients.

Conflicts of interest
No conflicts of interest

PP15 - SUCCESSFUL TREATMENT OF CHRONIC PANCREATITIS >25 YEARS FOLLOWING SPK IN TRANSPLANTED PANCREAS WITH RENDEZVOUS TECHNIQUE

Ali Abbasi[1], Michael Larsen[2], Pallav Kolli[3], Chris Freise[4], Peter Stock[4]

[1]*University of California San Francisco; Department of Surgery*
[2]*University of California San Francisco; Medicine*
[3]*University of California San Francisco; Radiology*
[4]*University of California San Francisco; Surgery*

Background
Here we present a case of retrograde (scope passage through the anus) endoscopic cholangiopancreatography (ERCP)-rendezvous technique in a transplanted pancreas (>25 years post SPK) for treatment of chronic pancreatitis in the pancreas allograft.
CASE REPORT: A 67-y/o woman S/P SPK transplant in 1994 with systemic endocrine drainage (venous drainage to right common iliac vein) and exocrine drainage to the bladder with subsequent enteric conversion due to chronic urethritis, presented with recurrent pancreatitis of her transplanted pancreas. She also has a history of small bowel obstruction with small bowel resection with jejunal-ileal anastomosis distal to pancreas duodenal-ileal anastomosis. She was initially hospitalized with symptoms of right lower quadrant pain and found to have elevated amylase (920 U/L) and lipase (819 U/L). Ultrasound revealed dilation of the main pancreatic duct, most pronounced at the head measuring up to 9 mm with two stones in the ampulla. Magnetic resonance cholangiopancreatography (image 1) demonstrated markedly dilated main pancreatic duct and secondary uncinate duct both tapering smoothly to the ampulla, containing non-obstructing stones. Given improved labs, she was discharged.

Methods
We attempted an outpatient retrograde (scope passed through the anus) double -balloon enteroscopy (DBE) /ERCP. Retrograde DBE into the limb was a blind-ending pouch presumed to contain the transplanted duodenum and the major papilla. After exhaustive attempts, including utilizing contrast with fluoroscopy, administration of secretin, and discussion with the transplant team intraprocedurally, the ampulla could not be identified. The procedure was terminated with plan for rendezvous ERCP with IR.
The patient returned for the rendezvous procedure. With the patient in a supine position under general anesthesia, percutaneous access to the dilated main pancreatic duct in the head of the transplant pancreas was obtained using a 21-gauge needle under direct ultrasound visualization (Image 2). A 0.018-inch Cope wire was ultimately advanced into the Roux-en-Y limb of the donor duodenum and then into Roux-en-Y limb (recipient ileum). After repositioning, the DBE was then passed through the lower gastrointestinal tract with identification of the wire in the Roux-en-Y limb. Using a cannulatome, a 0.035-inch straight wire was passed into the main pancreatic duct . Dilation of the papilla was performed, and a 7 French by 5 cm double pigtail stent was placed into the pancreatic duct.

Results
Following the procedure, her abdominal pain improved and was rated 0/10 at discharge. At follow-up one-month post-procedure, the patient reported 90% improvement in abdominal pain since stent placement.

Conclusions:
Following stent replacement at 3 months, she has ongoing excellent pancreatic function (insulin independence) 28 years following SPK and resolution of pain and pancreatitis.

Image 1:

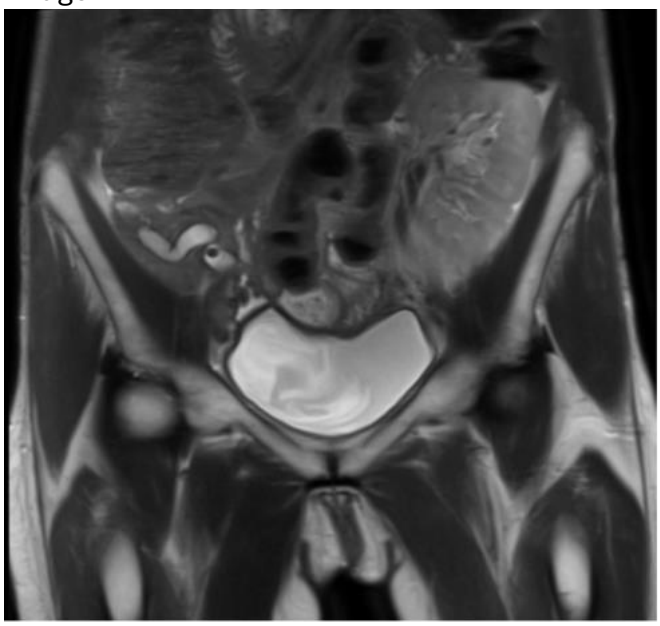
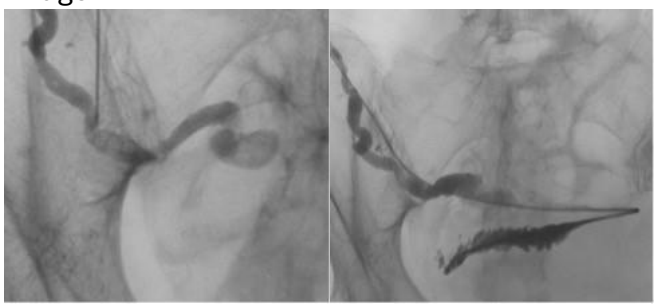


Image 2:



Contrast injection through dilated pancreatic duct with severe ampullary narrowing. Obstruction was crossed contrast injection confirmed location in small bowel.

Conflicts of interest

No conflicts of interest

PP16 - FEASIBILITY OF TYPE 3 DCD PANCREAS FOR ISLET TRANSPLANTATION IN ITALY: CHALLENGES AND PRELIMINARY FINDINGS

Gioia Sgrinzato[1], Mattia Albiero[2], Caterina Di Bella[3], Cristina Silvestre[4], Francesco Tuci[5], Marianna Di Bello[5], Massimo Menegazzo[6], Roberta Cappellari[7], Erica Nuzzolese[8], Verdiana Ravarotto[6], Lucia Rizzato[6], Federico Boscari[9], Adolfo Paolin[6], Lucrezia Furian[10]

[1]*University of Padova; Department of Surgery, Oncology and Gastroenterology, University of Padova*
[2]*University of Padova; Department of Surgery, Oncology and Gastroenterology*
[3]*University of Padua; Kidney and Pancreas Transplant Unit*
[4]*University of Padua; Kidney and Pancreas Transplantation Unit*
[5]*University of Padua*
[6]*University Hospital of Padova*
[7]*Azienza Ospedale Università di Padova; Centro Regionale Per la Terapia Cellulare del Diabete*
[8]*University Hospital of Padova; Uoc Chirirgia Trapianti Rene e Pancreas*
[9]*University of Padova*
[10]*University of Padua; Kidney and Pancreas Transplantation Unit, Department of Surgical, Oncological and Gastroenterological Sciences, University of Padova, Padova, Italy; Kidney and Pancreas Transplantation Unit*

Background
Allogeneic pancreatic islet transplantation is a therapeutic option for patients with type 1 diabetes who experience poor glycemic control and severe hypoglycemic events despite optimal insulin therapy. The literature suggests that islet transplantation from category 3 donors after circulatory death (DCD) could address the organ shortage. However, in Italy, the required 20-minute period of asystole for type 3 DCD donors is one of the longest among all countries, and pancreatic islets are highly sensitive to ischemia. This study aims to explore the feasibility of using category 3 DCD pancreases for pancreatic islet transplantation within the Italian legislative framework.

Methods
All isolations were performed using a modified automated Ricordi method at the Regional Center for Cellular Therapy of Diabetes, University Hospital of Padova. Pancreases were manually perfused with a Collagenase and Neutral Protease blend (Nordmark Biochemicals) tailored to pancreas weight. Islets were purified using a continuous gradient in a COBE 2991 cell processor. Islet yield and purity were assessed through dithizone staining. The glucose stimulation index (GSI) was calculated by measuring insulin using a commercially available human insulin ELISA kit (Mercodia).

Results
The isolation and purification procedure was conducted on 8 donation-after-brain-death (DBD) and 3 type 3 DCD donors over a one-year period. DCD donors had significantly higher GGT and ALT levels but showed no significant differences in other relevant parameters, such as age, sex, BMI, and last reported glucose concentration. The mean trimmed pancreas weight was similar between DCD and DBD groups (137 ± 19 g vs. 118 ± 9 g, p=0.41). However, the islet yield from DCD pancreases was significantly lower after digestion (585,470 ± 80,479 vs. 289,470 ± 107,080 IEQ, p<0.01) and remained lower after purification (p=0.0003).

When analyzed as IEQ per gram of pancreas, the islet yield from DCD pancreases was significantly worse than from DBD pancreases (2,320 ± 842 vs. 4,063 ± 738 IEQ/g, p=0.03). Additionally, DCD pancreases demonstrated poorer separation during density gradient purification, with the majority of islets segregating into fractions of lower purity. This resulted in a lower average islet purity for DCD pancreases (33% ± 2%) compared to DBD pancreases

(52% ± 2%, p=0.02). Despite these differences, in vitro functionality as assessed by static GSI showed no significant differences between DCD and DBD islets.

Conclusions
These preliminary results suggest that using pancreas from type 3 DCD donors within the Italian legislative framework poses challenges related especially to islet purification, likely due to the prolonged ischemia time the tissue is exposed to. While this does not necessarily exclude the possibility of using this donor type for islet transplantation, it may require significant optimizations in the isolation process.

Conflicts of interest
No conflicts of interest

PP17 - ISLET TRANSPLANTATION IN A PATIENT WITH CONGENITAL DIABETES RELATED TO GATA-6 MUTATION: ABOUT ONE CASE

Frederique Defrance[1], Francois Pattou[2], Julie Kerr-Conte[3], Mehdi Maanaoui[4], Mikael Chetboun[5], Marie-Christine VANTYGHEM[1]

[1]*Lille University Hospital; Claude Huriez Hospital; Department of Endocrinology, Diabetology, Medical Oncology and Metabolism*
[2]*Univ Lille; U1190*
[3]*Chu Lille; Faculty of Medicine*
[4]*Lille University Hospital; Claude Huriez Hospital; Nephrology Departement*
[5]*Chu Lille; General and Endocrine Surgery*

Background
A 32-year-old woman underwent islet allotransplantation for the treatment of her congenital diabetes caused by pancreatic agenesis.

She was born prematurely at 33 weeks of gestation due to cardiac rhythm abnormalities, and intrauterine growth retardation, and presented with neonatal insulinopenic diabetes linked to pancreatic agenesis.

A GATA6 mutation located on chromosome 11q18 was diagnosed. Associated manifestations included cholecyst agenesis, intra-abdominal ovarian malposition with bicornuate bicervical uterus, cardiac malformations (atrial septal defect, ostium secundum type - repaired at age 11, persistent ductus arteriosus - repaired at age 12, and ventricular septal defect).

Despite all these challenges, she was socially well-integrated, working full-time, and actively engaged in numerous sporting activities.

However, the diabetes remained difficult to control, with variability despite significant involvement from the patient and an external insulin pump.

Methods
She then received three islet preparations infusions in August, October, and December 2022.

The post-operative period was marked by complications, including a sub-occlusive syndrome and a bleeding caused by the rupture of a pseudoaneurysm in the left subclavian artery, secondary to the placement of a central venous device that needed endovascular embolization.

Results
Insulin therapy was discontinued after the third infusion, with favorable outcomes: 98% time-in-range (0.70–1.80 g/L), no hypoglycemia, and a mean blood glucose level of 1.25 g/L (6.8 mmol/L) on CGMS.

Glycemic control remained satisfactory for three months but deteriorated thereafter for unknown reasons. There were no infectious events, no discontinuation of immunosuppression, and no corticosteroid use.

Biological evaluation showed persistent insulin secretion, without any evidence of autoimmunity or alloimmunity (negative donor-specific antibodies, DSA).

Then, SGLT2 inhibitors were introduced, but led to acute functional renal failure. Metformin could not be used due to chronic diarrhea caused by pancreatic exocrine insufficiency. Diabetes remained well managed during one year with repaglinide and sitagliptin, but 13 months after transplantation, it was necessary to reintroduce insulin therapy.

Two years later, c-peptide is still detectable, but unsufficient to achieve adequate metabolic control and the patient is treated with multiple daily insulin injections.

Despite favorable initial prognostic factors—such as young age, low insulin requirements, absence of autoimmunity, and negative allo immunity—the results of the islet transplantation have been somewhat disappointing.

Conclusions
This is the first case of islet transplantation to treat a diabetes related to pancreatic agenesis linked to GATA 6 mutation. The evolution was good during about one year but then an islet dysfunction appeared and led to insulin therapy again.

The cause of this relative failure remains unclear, likely involving multiple factors, such as post-operative surgical complications and COVID-19 infection.

Conflicts of interest
No conflicts of interest

PP18 - ISLET AUTO TRANSPLANTATIONS FROM CALCIFIED PANCREAT

Yun Suk Chae[1], Dirk Jan Cornelissen[2], Eelco de Koning[3], Marten Engelse[4]

[1]*Leiden University Medical Center; Internal Medicine; Islet Lab*
[2]*Lumc; Nierziekten*
[3]*Leiden University Medical Centre (Lumc); Dept of Nephrology*
[4]*Leiden University Medical Center (Lumc); Leiden University; Nephrology*

Background
Total Pancreatectomy and Islet Auto Transplantation (TPIAT) offers patients with chronic pancreatitis a chance to improve their quality of life while reducing the risk for surgically induced diabetes. However, pancreata retrieved from these patients may contain calcifications. Calcified pancreata pose significant challenges in producing safe and transplantable islet products. As the islets are transplanted straight into the portal vein, failure to remove calcifications can put a patient at risk of haemolysis or liver damage. Our centre developed an islet isolation protocol with several calcium removal techniques, in order to produce safe islet products from a calcified pancreas.

Methods
A retrospective analysis was performed on data from 27 TPIAT procedures. After pancreatectomy all pancreata were digested according to our standard protocol. After digestion, 5 different methods of further tissue processing were performed to generate an islet product. .

1. No further purification : volume <10-12 mL, no calcification.
2. Standard density separation using a COBE2991: volume >12-15mL, no calcification.
3. Standard density separation using a COBE2991: volume >12-15mL, with calcification.
4. Repetitive washing, sedimentation and subsequent pipetting away of non-calcified tissue from the calcified tissue layer on the bottom of a conical tube.
5. Sedimentation of calcified digested tissue on top of a high density liquid layer [1,17 g/mL; mix of UW and Xenetix 350] in a conical tube. Non-calcified tissue remains on top of the liquid layer, calcified tissue is separated on the bottom of the tube.

Islet products from these 5 groups were transplanted in the portal vein. These TPIAT procedures were compared based on isolation yield (IEQ) and on transplantation outcome using a mixed meal tolerance test.

Results
From 27 pancreata, 14 were found to have calcifications during isolation. After digestion, 7 products were further processed using method 1, 6 were processed using method 2, 4 were processed using method 3, 4 were processed using method 4 and 6 were processed using method 5. When comparing non calcified pancreata (methods 1 and 2) to calcified pancreata (method 3, 4 and 5), no significant difference could be found in IEQ harvested (442k ± 289k vs 315k ± 236k IEQ, p=0.48). Furthermore, no significant difference could be found in the area under the curve for c-peptide values found during mixed meal tolerance test between patients receiving islets from non-calcified vs calcified pancreata after one year (0.224 ± 0.322 vs 0.302 ± 0.209 (pmol/L)/(IEQ/kg recipient), p=0.58).

Conclusions
We demonstrate that pancreatic islets can be isolated and transplanted from calcified pancreata using one of three calcification removal methods. Islet yield and transplantation

outcome are similar when comparing products from calcified and non-calcified pancreata. This allows for the treatment of patients that may otherwise not have been considered for TPIAT.

Conflicts of interest
No conflicts of interest

PP20 - CENTRAL EUROPEAN INTERNATIONAL ISLET TRANSPLANTATION PROGRAM

Jan Kriz[1], Štefan Hulik[2], Martin Varga[3], Juraj Miklušica[4], Tatiana Baltesova[5], Stefan Löb[3], Ivana Dedinska[6], Klaus Emmanuel[7], Peter Girman[8]

[1]*Institute for Clinical and Experimental Medicine; Diabetes Center; Department of Diabetes*
[2]*Univerzitná Nemocnica L. Pasteura*
[3]*Landeskrankenhaus Salzburg*
[4]*Jesseniova Lekárska Fakulta UK*
[5]*University Hospital ; Department of Nephrology*
[6]*University Hospital Martin; Transplant Center*
[7]*Landeskrankenhaus Salzburg; Universitätsklinik für Chirurgie*
[8]*Ikem; Diabetes Department*

Background
Pancreatic Islet (PI) transplantation (Tx) program needs a large experience and expensive equipment to be successful. Therefore, we have established a collaboration with several level 3 surgical departments (2 in Slovakia, 1 in Austria) in order to offer PI auto and allogeneic Tx to their patients as well. To fulfill all formal and administrative requirements the Tissue facility of IKEM was registered in Czech as well as European Authorities.

Methods
For allogeneic Tx, 2 pancreases in Košice, SK and 1 pancreas in Martin, SK were harvested from cadaveric donors as part of multi-organ procurement. For autologous transplantation 1 pancreas was excised in Martin, 1 in Košice, and 3 pancreases in Salzburg, AT. Organs were perfused, cooled down, and transported to IKEM as fast as possible (some by air some by land). PI were isolated using standard protocol (collagenase + Neutral Protease), followed by Ficoll gradient separation in case of allogeneic Tx. The PI grafts were quantified by IsletNet®, its function with GSIS test, and safety was confirmed by microbiology of transport and Tx media, and examination of spare tissue by experienced pathologist. Autologous grafts were transplanted into portal vein using its direct cannulation by surgeon, allogeneic grafts were transplanted by surgical catheterization of umbilical vein in Košice and by radiological transhepatic approach in Martin.

Results
All isolations were considered successful and safe enough to make Tx possible. Each Tx was performed without any serious side effects. There was confirmed a basic graft function by C-peptide detection in all patients and long-term function in most of them.

Conclusions
Within the region, the remote isolation of PI is possible, safe and effective for clinical practice. Great thanks for enthusiastic attitude of all participating teams.
Supported by the Programme EXCELES, ID Project No. LX22NPO5104 - by the Next Generation EU, and by MH CZ - DRO (IKEM, IN 00023001“).

Conflicts of interest
No conflicts of interest

PP21 - 20 YEARS OF PANCREAS TRANSPLANTATION PROGRAMME - SINGLE CENTRE EXPERIENCE

Katarzyna Baumgart-Gryn[1], Marek Durlik[2]

[1]*National Medical Institute of The Ministry of The Interior and Administration ; Clinical Dpt of Gastroenterological Surgery and Transplantation*
[2]*Csk Mswia; Gastroenterological Surgery and Transplantation*

Background
The pancreas transplantation programme in our Center started in 2004. From 2004 untill November 2024 overall 295 patients underwent pancreas transplantation in our Centre. Starting from February 2018 we changed our surgical technique. The main changes in the protocol include: exocrine drainage from duodenoduodenal to duodenojejunal anastomosis, venous anastomosis of graft's portal vein from recipient's iliac vein to recipient's vena cava, protocol with no anticoagulation intraoperatively. The qualification process of the recipient in our centre,optymalisation of CIT was also implemented.

Methods
We retrospectively analysed patients data.
The groups consisted of 196 patients with duodenoduodenal anastomosis and 99 with duodenojejunal anastomosis, 221 patients with anastomosis with iliac vein and 74 with vena cava inferior.

We divided the groups into 2 eras: 2004-2018 and 2018-2024.

Results
The results show better patient and graft survival after the implementation of the new protocol, however, the groups didn't reach statistical significance. Less vascular postsurgical complications like pancreas graft thrombosis were observed in the group with the new protocol with $p<0,05$

Conclusions
The continuous evolution of the pancreas transplantation programmer helped to achieve better results in our Centre.

Conflicts of interest
No conflicts of interest

PP22 - AUTOMATED DETECTION AND DEMARCATION OF PANCREAS FROM SURROUNDING TISSUE IN RETRIEVAL PHOTOGRAPHS

Georgios Kourounis[1], Rhys Pook[2], Aasha Duraisaminathan-Valli[3], Ali Elmahmudi[4], Brian Thomson[4], Samuel James Tingle[5], Balaji Mahendran[6], Emily Thompson[7], James Hunter[8], Hassan Ugail[9], Colin Wilson[10]

[1]*Freeman Hospital; Institute of Transplantation*
[2]*Nihr Blood and Transplant Research Unit in Organ Donation and Transplantation*
[3]*Newcastle University Medical School*
[4]*Bradford University*
[5]*Institute of Transplantation; Hpb and Transplant Surgery*
[6]*Freeman Hospital; Hpb & Transplant Surgery*
[7]*The Newcastle Upon Tyne Hospitals NHS Foundation Trust; Institute of Transplantation*
[8]*Oxford University Hospitals; Nuffield Department of Surgical Sciences; Nuffield Department of Surgical Sciences*
[9]*Bradford University; Centre for Visual Computing and Intelligent Systems, Faculty of Engineering and Informatics*
[10]*The Newcastle Upon Tyne Hospitals NHS Foundation Trust*

Background
Successful pancreas transplantation requires accurate assessment of donor pancreatic steatosis. Unlike other organs, the pancreas is not biopsied by any teams to assess quality prior to transplant. Subjective visual assessment of steatosis is current standard practice. Artificial intelligence (AI) methods offer an objective alternative, but only if computers can first identify the organ from surrounding tissue (image segmentation, Figure 1). We present the first automated segmentation model designed to identify the pancreas from adjacent tissue.

Methods
Two anonymized independent image datasets of pancreata on the backbench were used. The first dataset, comprising 264 images, was split 75:25 for training and testing. The second dataset contained 58 images for external validation. Ground truth photograph annotation labels were verified by a transplant surgeon. Two open-source pre-trained segmentation models were fine-tuned.

Results
Compared to human segmentation, internal validation with the two models achieved accuracies of 98%, Dice coefficients (DIC) of 57% and 49%, and Areas Under the Receiver Operating Characteristic Curves (AUC) of 88% and 79%, respectively (Figure 2A). In external validation, automatic segmentation achieved accuracies of 98%, DIC of 70% and 47%, and AUC of 89% and 77%, respectively (Figure 2B). Human annotation took a median of 33 (IQR:27-39) seconds per image. Detectron2 was 33 times faster at 0.99 (0.95-1.02) seconds, while YOLOv8 was 330 times faster at 0.09 (0.09-0.11) seconds.

Conclusions
The pancreas' resemblance to adjacent tissues presents a challenge for automatic segmentation. While these models demonstrate high accuracy and a strong true negative

rate, indicating effective rule-out performance, the true positive rate remains lower. Further work is required to optimise a photographic AI assessment tool.

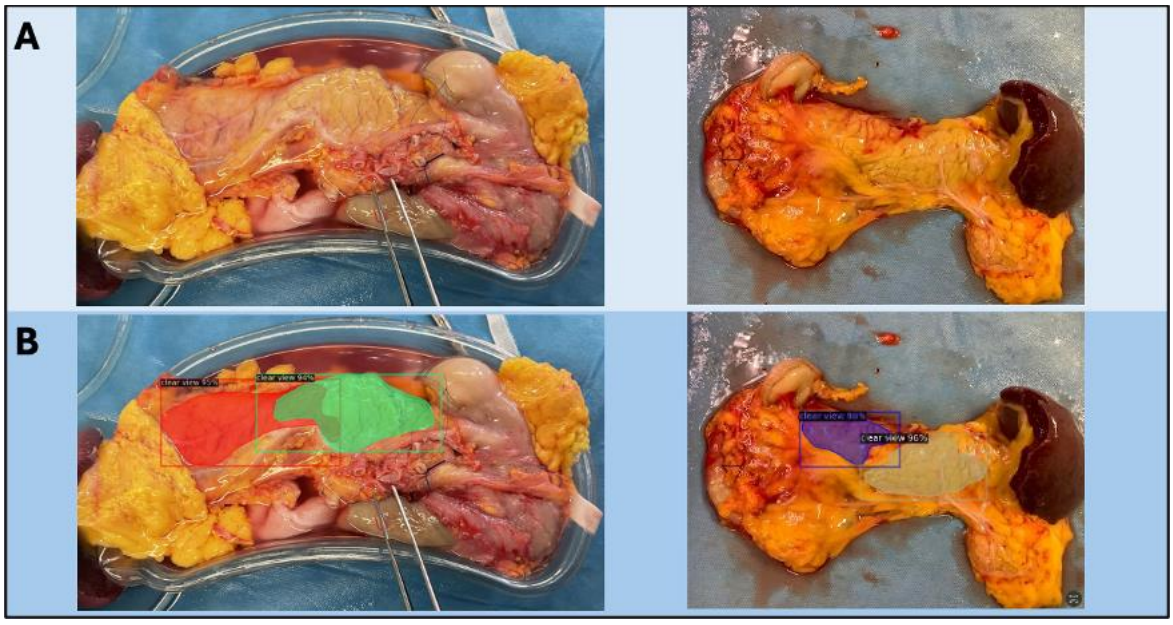


Figure 1. Example pancreas retrieval photographs (A) and the predicted segmentation regions generated by Detectron2, highlighting areas where the pancreatic parenchyma is clearly visualised (B).

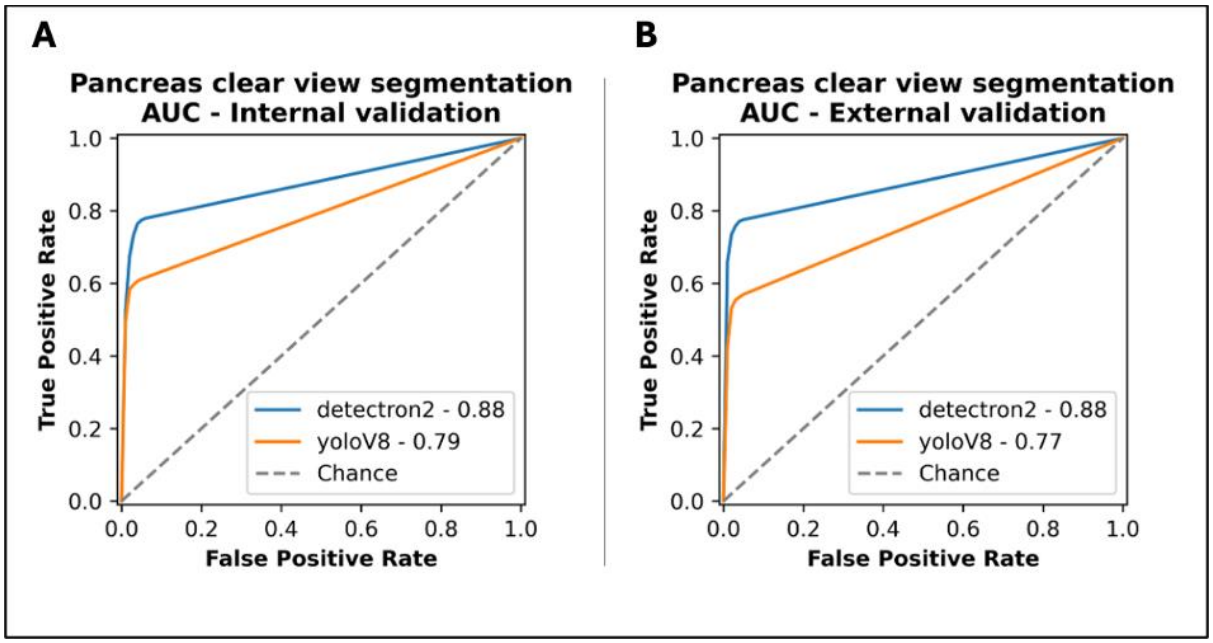


Figure 2. Validation performance across the segmentation models, shown for internal (A) and external (B) validations using Area Under the Curve.

PP23 - COMPARISON OF GLYCAEMIC CONTROL IN KIDNEY TRANSPLANT RECIPIENTS WITH TYPE 1 DIABETES WITH AND WITHOUT BETA-CELL REPLACEMENT

Nusrat Awan[1], Oluwatosin Kayode[2], Marcio Edbert[3], Recie Davern[2], Ayat Bashir[2], Angeles Maillo Nieto[4], James Shaw[5]

[1]*Royal Victoria Infirmary; Diabetes*
[2]*Newcastle Upon Tyne Hospitals NHS Foundation Trust*
[3]*Newcastle University*
[4]*Freeman Hospital; Diabetes and Endocrinology*
[5]*Newcastle University; Newcastle University; Translation and Clinical Research Institute*

Background
People with Type 1 diabetes mellitus (T1D) and end-stage renal disease (ESRD) should be evaluated for beta-cell replacement (BCR) therapy either at the time of or following kidney transplantation with the goal of restoring optimal glycaemic control. We set out to undertake a cross-sectional study to compare HbA1c and insulin independence rate in people with T1D pre- and post-kidney transplantation and to determine whether BCR was considered.

Methods
All individuals with T1D or type 2 diabetes who had received kidney transplant at a UK Institute of Transplantation between 2015 and 2023 were identified. Cross-sectional data analysed included HbA1c and insulin independence status with patient-reported outcome measures (PROMs) / qualitative interviews completed in a subgroup of participants.

Results
124 patients with diabetes and kidney transplantation were identified. 81 (65%) had T1D including 47 (58%) females. Mean age at transplantation was 45±10 (mean±SD) years. 37 (46%) had received kidney transplant alone (KTA); 40 (49%) simultaneous pancreas kidney (SPK); 2 (2.5%) pancreas after kidney (PAK), and 2 (2.5%) islet after kidney (IAK) transplant. At 5.6±2.8 (mean±SD) years post kidney transplant, HbA1c had improved significantly with BCR (from 71 mmol/mol pre- to 41 mmol/mol post-transplant; p<0.0001). In contrast, no significant improvement was noted with KTA (pre- 70, post KTA 68 mmol/mol; p0.53). 34 (77%) BCR recipients were insulin independent at time of assessment. 9 (24%) KTA recipients were using insulin pump therapy with or without hybrid-closed loop (HCL). BCR (pancreas and islet transplantation) had been discussed pre-transplant in 28 (76%) KTA recipients. Reasons for not proceeding described by participants included longer waiting list, an expectation from KTA to improve diabetes control in addition to renal function, and perceived risks versus benefits of BCR.

Conclusions
BCR in T1D successfully delivered sustained optimal HbA1c and insulin independence in the majority of recipients. In contrast, HbA1c remained high post KTA. Further interventions including HCL and BCR will be required to achieve optimal glycaemic goals in the latter cohort.

Conflicts of interest
No conflicts of interest

PP24 - PANCREAS TRANSPLANTATION IN POLAND: CURRENT CHALLENGES AND PROSPECTS IN EUROPE

Karolina Kedzierska-Kapuza[1], Marek Durlik[2], Edward Franek[3]

[1]*National Medical Institute of the Ministry of Interior Affairs and Administration in Warsaw; Department of Gastroenterological Surgery and Transplantology*
[2]*Csk Mswia; Gastroenterological Surgery and Transplantation*
[3]*National Medical Institute of the Ministry of Interior Affairs and Administration ; Clinical Department of Internal Medicine, Endocrinology and Diabetology*

Background
Pancreas transplantation (PT) in Poland is an effective but underutilized treatment for type 1 diabetes (T1D). In 2021–2022, the PT rate in Poland was only 0.5 per million (M), among the lowest in Europe. For comparison, Finland had 3.6 per M and Estonia 3.1 per M in 2022. This disparity arises from systemic and organizational barriers, such as the absence of patient qualification guidelines, limited collaboration between diabetologists and transplant surgeons, and low awareness of PT benefits among patients and doctors.

Methods
T1D affects around 200,000 people in Poland, including 20,000 children, leading to severe complications. Diabetic nephropathy affects 20–30% of T1D patients, with half progressing to end-stage renal disease (ESRD) within 10 years of overt proteinuria. Diabetic retinopathy impacts 80% of patients within 15 years of diagnosis, with 25% developing proliferative retinopathy. These complications reduce quality of life and may necessitate PT, which can improve outcomes and eliminate the need for insulin therapy.

Results
Poland performs few simultaneous pancreas and kidney (SPK) or pancreas-only (PTA) transplants. In 2023, only 24 procedures were completed despite 53 patients on the waiting list. This reflects a broader trend, with just four procedures conducted in 2020, despite 64 patients listed. However, 2024 shows improvement, with 39 SPK/PTA transplants performed and 34 patients on the waiting list as of December. This suggests better organization and qualification processes.
Key barriers to PT in Poland include inadequate collaboration between diabetologists and transplant surgeons. Many diabetologists view PT as experimental, discouraging patient referrals. The lack of standardized clinical pathways exacerbates this, leaving doctors unsure when to recommend PT. Most SPK referrals come from nephrologists, while PTA patients often seek information independently.
T1D patients considering PT report fears of complications, such as hypoglycemia and vision loss, and struggle with glycemic control. Few use modern technologies like insulin pumps or continuous glucose monitoring systems (CGMS), and access to diabetologists remains limited. Many patients skip regular care due to fear of judgment from healthcare providers.

Conclusions
Systemic reforms are crucial to increasing PT rates in Poland. This includes developing patient qualification guidelines and providing training for healthcare professionals. Promoting positive outcomes from successful PT can help improve public perception. Finland and Estonia serve as models, demonstrating that better healthcare organization, education, and positive narratives can significantly boost PT rates. Adopting similar strategies in Poland could yield measurable improvements.

Conflicts of interest
No conflicts of interest

PP25 - 3D-BIOPRINTED BIONIC PANCREAS-ATMP A REAL DISRUPTIVE INNOVATION IN THE FIELD OF TRANSPLANTOLOGY

Michal Wszola[1], Andrzej Berman[2], Marta Klak[3], Tomasz Dobrzański[4], Sylwester Domanski[4], Katarzyna Wozniak[4], Przemyslaw Wrochna[4], Dominika Ujazdowska[5], Jaroslaw Wejman[6], Dominika Szkopek[7], Katarzyna Roszkowicz-Ostrowska[7], Kacper Nowak[8], Urszula Paslawska[9], Robert Paslawski[9], Lukasz Kownacki[10], Dominika Piątek[11], Jarosław Woliński[7], Agnieszka Dobrzyń[12], Wojciech Swieszkowski[13], Artur Kaminski[14]

[1]*Foundation of Research and Science Development; Medical Department*
[2]*Polbionica Ltd; Laboratory*
[3]*Polbionica Ltd.*
[4]*Polbionica Sp. Z O.O.*
[5]*Foundation of Research and Science Development*
[6]*Center for Pathomorphological Diagnostics Ltd*
[7]*Institute of Animal Physiology and Nutrition Jan Kielanowski of Polish Academy of Sciences*
[8]*Wroclaw University of Environmental and Life Sciences*
[9]*Nicolaus Copernicus University*
[10]*European Health Center*
[11]*Medispace Medical Center*
[12]*Nencki Institute of Experimental Biology of Polish Academy of Sciences*
[13]*Faculty of Materials Science and Engineering, Warsaw University of Technology*
[14]*Department of Transplantology and Central Tissue Bank, Medical University of Warsaw*

Background

According to the WHO, the shortage of tissues and organs for transplantation is a serious problem, with it estimated that only 10% of global demand is currently met. Recently, 3D-bioprinting became an outstanding, potential method of customized treatment in reconstructive medicine and chronic disorders including chronic pancreatitis or type 1 diabetes. It holds promise for improving abovementioned statistics in the future. However, to use 3D-bioprinting in clinical application, several hurdles should be overcome. Scientific issues: (1) bioprinting of the vascular system - the challenge for scientists remains to create a dense vascular network throughout the organ. (2) proper mechanical strength of 3D-bioprinted organs, which should allow holding the pressure over 300 mmHg. (3) Development of the medical devices for the storage of the organ after bioprinting for flow culture which should allow to assess bioprinted organs functionality. The final point to consider is administrative and regulatory issues that will allow for the translation of preclinical research results into practical application in transplant medicine. **The aim of this study** is to show results of 10 years of preclinical study of 3D bioprinted bionic pancreas, which is currently entering the preparatory phase for clinical trials.

Methods

Materials and Method. Materials and Method. In vitro studies have been conducted over the last 10 years to assess the biological and physicochemical parameters of biomaterials and bioprinted models. After the analysis of the results, studies were conducted on small (mice) and large (pigs) animals. The observation of small animals lasted up to one year and aimed to assess the biocompatibility of biomaterials and the functionality of 3D constructs with pancreatic islets. Studies on the pig model, on the other hand, included observations up to one month and aimed to demonstrate stable flow in the bionic pancreas and its functionality in animals after pancreatectomy.

Results

Full biocompatibility in regards of biomateirals as medical device grade III has been achieved in preclinical in vitro and small animals studies according to ISO 10993. Study on large

animals showed stable graft function in terms of organ flow until the end of the observation period. In addition, the functionality of the implanted organ was demonstrated in daily glucose measurements and the required doses of insulin administered. Finally, it was shown that the insulin requirement decreased by 53% ($p<0.001$) with a still constant increase in the weight of the animals.

Conclusions

3D-bioprinted Bionic Pancreas-ATMP® is ready to start regulatory preparation for Clinical Trial in order to achieve Market Authorisation (EMA) and Biological License Authorisation (FDA).

Conflicts of interest

Andrzej Berman: Polbionica Ltd. – co-founders - MediSpace Medical Centre – Deputy Medical Director
Marta Klak: Polbionica Ltd. - co-founder
Michal Wszola: Foundation of Research and Science Development – Scientific Director

PP27 - A RETROSPECTIVE ANALYSIS OF PANCREAS GRAFT BIOPSIES

Mariia Bibik[1], Jan Kopecky[1], Terezia Havrdova[1], Ludek Voska[1], Barbora Hagerf[1], Jiri Veleba[2], Kvetoslav Lipar[3], Frantisek Saudek[4], Peter Girman[5]

[1]*Institute for Clinical and Experimental Medicine; Diabetes Centre*
[2]*Institute for Clinical and Experimental Medicine; Department of Diabetes*
[3]*Institute for Clinical and Experimental Medicine; Department of Transplant Surgery*
[4]*Institute for Clinical and Experimental Medicine*
[5]*Ikem; Diabetes Department*

Background
Allograft rejection represents significant reason for pancreas graft failure in the late period after transplantation and becoming a major clinical problem. In today's practice, a biopsy remains the gold-standard method to diagnose and treat pancreas graft rejection accurately. This study aims to retrospectively evaluate the safety of pancreatic biopsies and the impact of different types of rejection on one-year pancreas graft survival.

Methods
The data were collected from the hospital transplant registry, from 2017 to early 2024. During this time 194 pancreatic biopsies were indicated in 152 patients, with SPK (simultaneous pancreas-kidney) n=136, PTA (pancreas transplant alone) n=5, and PAK (pancreas after kidney) n=11. This study examines graft survival in all types of acute cellular rejection and borderline histopathology, classified according to the BANFF 2011 criteria, following on proving the safety of biopsies under ultrasound or CT scan guidance. Multivariate analysis was performed to identify the risk factors for rejection, where pancreas failure was defined as a return to intensified insulin regimen based on UNOS classification.

Results
Histologic examination confirmed rejection in 115 cases including indeterminate. There were 38 normal findings, 31 biopsies had a non-representative pattern and in 10 biopsies were other findings. The histopathological findings from the total number of rejections included subclasses of indeterminate n= 39, acute cellular rejection (ACR) grade one n= 52, ACR grade two n= 16, ACR grade three n= 3 and antibody-mediated rejection n= 4. The one-year graft survival in the subgroups of indeterminate ACR grade I, ACR grade II, and ACR grade III was 90%, 83%, 88%, and 0%, respectively. While the one-year survivals in the indeterminate, ACR grade I and ACR grade II subgroups were statistically insignificant, all pancreatic grafts failed with ACR grade III despite undergoing treatment. We detected 20 post-biopsy complications out of the 194, most of which were hematomas without surgical revision. In only 2% of cases, patients needed to undergo a surgical intervention, where 2 out of 194 terminated with a graft loss. After evaluating multiple parameters that could have a consequence on pancreas graft function, it was found that CIT (cold ischemic time) and DSA (donor specific antibodies) have a significant effect to graft failure ($p = 0.001$).

Conclusions
Pancreas graft rejection is a comprehensive process, where percutaneous graft biopsy plays a crucial role in identification of ongoing rejection. Our results demonstrate a safe performance of pancreas graft biopsy with a low possibility of major complications. This therefore supports clinical decision-making in tailoring anti-rejection therapy and helps undercover the impact on graft survival.

Supported from Czech Ministry of Education by grant LTAUSA19073. "Supported by MH CZ -DRO („Institute for Clinical and Experimental Medicine –IKEM, IN 00023001"). Supported by the project CarDia(Programme EXCELES, ID Project No. LX22NPO5104) - Funded by the European Union –Next Generation EU.

Conflicts of interest
No conflicts of interest

PP28 - DEVELOPING AN ENHANCED RECOVERY AFTER SURGERY (ERAS) PATHWAY FOR PATIENTS UNDERGOING SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANT (SPK)

Anna Stout[1], Helen Usher[2], Andrew Sutherland[2], Rachel Thomas[3]

[1]*Edinburgh Royal Infirmary*
[2]*Royal Infirmary of Edinburgh*
[3]*Edinburgh Royal Infirmary; Edinburgh Transplant Centre*

Background
Enhanced Recovery After Surgery (ERAS) pathways use evidence-based practices to optimize patient outcomes throughout their perioperative journey.
Simultaneous Pancreas-Kidney Transplant (SPK) is a treatment option for patients with insulin dependent diabetes and end stage renal disease, and confers improved quality of life, greater independence, and a reduction in diabetic complications[1].
Whilst ERAS for renal and liver transplant is well recognized, and efforts have been made to outline the necessary components for pancreas transplant[2], there is currently no pathway for SPK. We aimed to map the current SPK patient journey to identify points of good practice, inconsistencies, and areas to improve, to inform a novel SPK ERAS pathway development.

Methods
A retrospective audit of all patients undergoing SPK in a single UK centre from April 2023-February 2024 was undertaken. Acknowledging the recognized ERAS flowchart (figure 1), data was extracted included analgesia plan, timing of removal of central venous and urinary catheters, first mobilization, self-medication assessment, hospital discharge date and mode of transport home.

Results
Eight patients were identified. Analgesia was via thoracic epidural or patient-controlled analgesia. Median time to central venous and urinary catheter removal was post-operative day five (range 3-8), first mobilization day five (range 3-7) and self-medication was completed on day seven (range 5-10.) Median hospital length of stay was ten days (range 9-20) and all patients had access to their own transport home.

Conclusions
Areas of good practice included patient-centered analgesia plans and early pharmacy input. However, there were delays in time from documented decision to removal of invasive devices, and despite early pharmacy flagging, self-medication assessment was delayed leading to longer in-patient stay. This has downstream effects on patient discomfort and hospital costs.

These inconsistencies have been discussed with the multidisciplinary team to better understand their cause and identify solutions for the proposed SPK ERAS pathway. The SPK ERAS pathway will be implemented in our unit in 2025 to empower patients, improve their care and hospital management. Patient information is also being updated to reflect this with patient input.

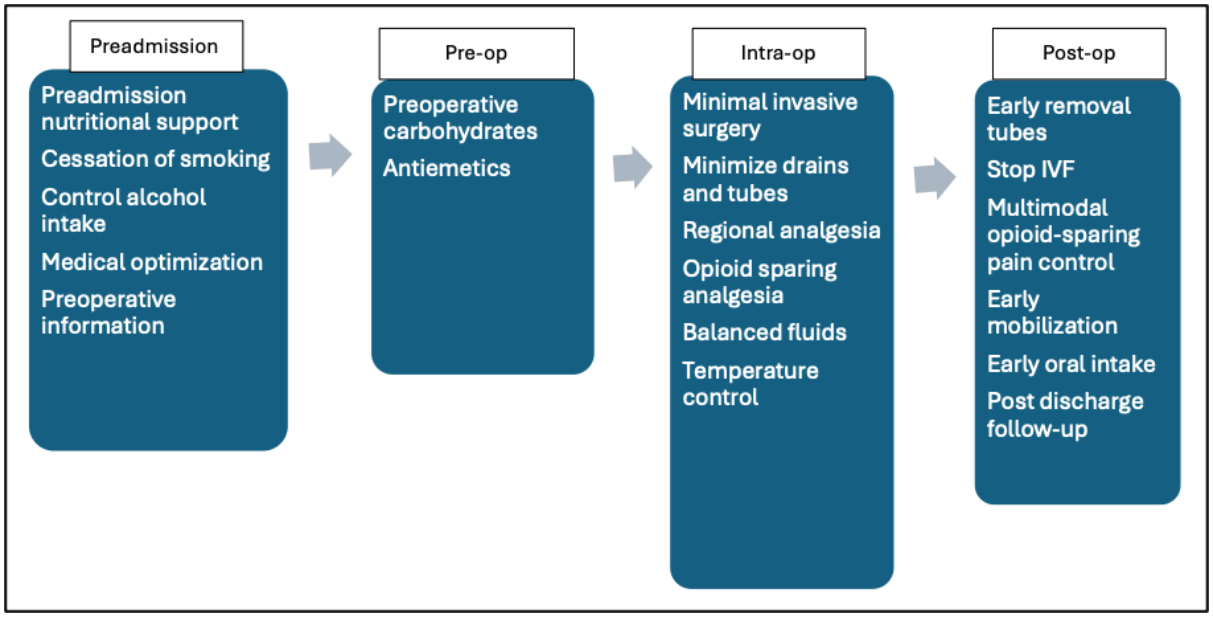


Figure 1 Exemplar pathway based on Ljungqvist O, Scott M, Fearon KC. Enhanced Recovery After Surgery: a review. Jama Surg 2017; 152: 292-298

Conflicts of interest
No conflicts of interest

References
1. Parajuli S, Arunachalam A, Swanson KJ, Aziz F, et al. Outcomes after simultaneous kidney-pancreas versus pancreas after kidney transplantation in the current era. Clinical Transplantation 2019; 33: e13732. DOI:10.1111/ctr.13732
2.Elango M, Paplois V. Working towards and ERAS Protocol for Pancreatic Transplantation: A Narrative Review. Journal of Clinical Medicine 2021; 10: 1418. Doi:10.3390/jcm10071418

PP29 - CRYOGEL-BASED, PREVASCULARIZED BIOLOGICAL PLATFORM FOR ISLET TRANSPLANTATION

Nicerine KRAUSE[1]
[1]*University of Geneva; Surgery*

Background
Intrahepatic islet transplantation restores insulin independence but is limited by donor scarcity, immunosuppression, and poor engraftment due to IBMIR and inadequate vascularization. Subcutaneous transplantation is safer but hindered by hypoxia and slow revascularization. Hydrogels provide structural support but restrict cell migration, while cryogels, with large, interconnected pores, show promise but struggle to replicate native ECM and support vascularization. Placenta-derived matrices closely mimic islet ECM, offering a promising alternative.

Methods
This study tested whether placenta-derived cryogels enhance islet transplantation outcomes by supporting islet survival and function. Hydrogels from human placenta were blended in varying ratios and crosslinked. Quality assessments included DNA quantification, structural integrity, and LC-MS/MS protein analysis. Pore interconnectivity, density, and water swelling capacity were measured. Rat (100 IEQ, n=4) or human islets (50 IEQ, n=3) were seeded on cryogels and assessed using static incubation.

Results
Cryogels showed DNA removal, successful decellularization, and intact structure. Composition analysis revealed collagen and glycoproteins comparable to Matrigel. Different hydrogel ratios showed no differences in interconnectivity, density, or swelling, though higher Collagen I content increased water uptake. By Day 14, islets on cryogels showed improved or stable stimulation index (SI) values (1.54±0.57 to 2.18 ±0.4), while conventional cultures declined (1.15 to 0.90) and Matrigel dropped sharply (2.12 to 0.60).

Conclusions
These results highlight placenta-derived cryogels as promising scaffolds for improving islet transplantation outcomes.

Conflicts of interest
No conflicts of interest

BOARD OF REVIEWERS

Shadab Abadpour, Oslo, Norway
John Casey, Edinburgh, United Kingdom
Joana Ferrer, Barcelona, Spain
Peter Girman, Prague, Czech Republic
Paul Johnson, Oxford, United Kingdom
Julie Kerr-Conte, Lille, France
Michiel Nijhoff, Leiden, The Netherlands
Steve White, Newcastle, United Kingdom

AUTHOR INDEX

*Bold – Presenting author

DISCLOSURE LIST

The following abstract authors have declared **POTENTIAL FINANCIAL AND/OR NONFINANCIAL CONFLICT OF INTEREST** regarding their presentation, or abstract:

J. McGarrigle
G. La Monica
J. Cook
P. Rios
Y. Li
S. Ghani
I. Joshi
D. Lopez
H. Nasir
Q. Rodriguez
Y. Calvillo
Y. Wang
J. Oberholzer
M. Engelse
J. Doppenberg
R. van Rooden
P. Friend
R. Ploeg
J. Fallon
M. Elzawahry
F. Pattou
O. Jouannot
J. Brun
X. Gaume
R. Besnard
C. Gautier
C. Cocita
N. Laurent
A. Gaffuri
R. Eloy
O. Soula
A. Berman
M. Klak
M. Wszola

The following abstract authors have declared **NO CONFLICT OF INTEREST** about their presentation, or abstract:

A. Coddeville
J. Janáček
A. Abbasi
C. Aguayo-Mazzucato
M. Ajie
M. Albiero
F. Amendolagine
A. Amor
V. Applegarth
A. Arnold
T. Augustine
N. Awan
L. Badet
D. Balboa
T. Baltesova
A. Bashir
C. Bassaganyas
K. Baumgart-Gryn
K. Bednarek
K. Bellofatto
P. Belohlavek
E. Berishvili
Z. Berková
T. Berney
A. Bertuol
M. Bibik
J. Bignard
K. Bittenglova
A. Blazek
L. Böhne
C. Bonner
F. Boscari
D. Bosco
K. Bouzakri
J. Branchereau
D. Brandhorst
F. Buron
C. Cahill
R. Caiazzo
C. Callaghan
D. Campbell
F. Campo
M. Čapek
C. Cappelaere
R. Cappellari
F. Carlotti
K. Carruthers
J. Casey
C. Ceriani
M. Certo
Y. Chae
X. Charmetant
M. Chetboun
B. Chikkala
R. Chimienti
J. Chlupac
G. Cirillo
A. Citro
A. Clark
P. Coddeville
A. Codeville
M. Cohen
P. Compagnon
D. Cook
D. Cornelissen
C. Counter
L. Couteau
L. Crawford
I. Currie
R. Davern
R. De Fijn
M. De Giovanni
N. De Graaf
E. De Koning
E. De Koning

The following abstract authors have declared **NO CONFLICT OF INTEREST** about their presentation, or abstract:

W. De Vos
F. Deambrogio
I. Dedinska
N. Dedyulya
F. Defrance
N. Delalleau
J. Delpero
E. Derisoud
R. Dhanda
C. Di Bella
M. Di Bello
F. Diekmann
T. Dobrzański
A. Dobrzyń
S. Domanski
M. Drage
A. Duraisaminathan-Valli
A. Duret-Lamouroux
M. Durlik
M. Edbert
D. Elker
A. Elmahmudi
K. Emmanuel
E. Fabryova
T. Fagniez
A. Fedaruk
D. Fedaruk
M. Felsenstein
J. Ferrer-Fàbrega
E. Folch Puy
E. Franek
C. Freise
J. Fronek
L. Furian
J. Fuster
V. Galván Chacón
G. Gamino
R. García
M. Garcia-Criado
V. Giai
J. Gibier
P. Girman
V. Gmyr
P. Gnanasekar
V. Gnemmi
J. Gopal
D. Habart
L. Haderer
B. Hagerf (Voglová)
E. Hammink
R. Hanna
B. Hastoy
R. Hauck
T. Havrdova
K. Hillebrandt
N. Ho
V. Holguín
R. Hu Zhu
T. Hubert
Š. Hulik
J. Hunter
K. Iwasaki
S. Jansen
P. Johnson
A. Kalachyk
O. Kayode
K. Kedzierska-Kapuza
J. Kerr-Conte
E. Keshi
T. Koblas
P. Kolli
K. Komissarov
J. Kopecky
G. Kourounis
L. Kownacki
O. Kozak
N. Krause
S. Krivenko
J. Kriz
J. Kubant
M. Kudlackova
V. Lampasona
C. Landstra
M. Larsen
F. Lebreton
I. Leontovyč
V. Lericque
K. Lipar
L. Lo Faro
S. Löb
A. Lobez
T. Lohmann
C. Longhorn
M. Maanaoui
B. Mahendran
A. Maillo Nieto
A. Malik
T. Malinka
D. Manas
F. Manenti
M. Manyalich
T. Marada
G. Marchegiani
I. Mariscal
M. Marras
K. Marszalek
V. Martin
I. Marzinotto
X. Matillon
F. Matzner
R. Meier
M. Menegazzo
M. Miglinas
L. Migliozzi
J. Miklušica
Z. Moinuddin
L. Monaco
J. Monhart
E. Morelon
H. Msheik
A. Muthusamy
D. Nathalie
S. Nawaz
E. Nazarova
A. Neroni
M. Nijhoff
K. Nowak
E. Nuzzolese
R. Owen
S. Pandanaboyana
A. Paolin
U. Paslawska
R. Paslawski
G. Pasquetti
S. Pazdniak
S. Pellegrini
C. Perez Serrano
E. Petrovskaya
G. Pettigrew
D. Piątek
L. Piemonti
C. Pignatelli
R. Pook
J. Pratschke
E. Primakova
B. Quaratino
M. Rabeyrin
B. Radochová
V. Ravarotto
V. Raverdy
J. Regimbeau
A. Reutzel-Selke
L. Rizzato
I. Romanova
K. Roszkowicz-Ostrowska
R. Rull
H. Russ
N. Russel
J. Saarimäki-Vire
D. Saavedra
M. Sarwal
F. Saudek
I. Sauer
A. Sauvanet
M. Scotte
G. Sgrinzato
J. Shaw
C. Silvestre
L. Simmonds
G. Singureanu
S. Sinha
G. Siracusano
V. Sordi
R. Spiers

The following abstract authors have declared **NO CONFLICT OF INTEREST** about their presentation, or abstract:

M. Špitálníková Veřtátová
P. Stock
A. Stout
S. Suergiu
A. Sutherland
K. Sutoris
W. Swieszkowski
A. Symanovich
D. Szkopek
C. Tacconi
O. Thaunat
J. Thevenet
R. Thomas
E. Thompson
B. Thomson
S. Tingle
M. Tol
V. Tomsovska