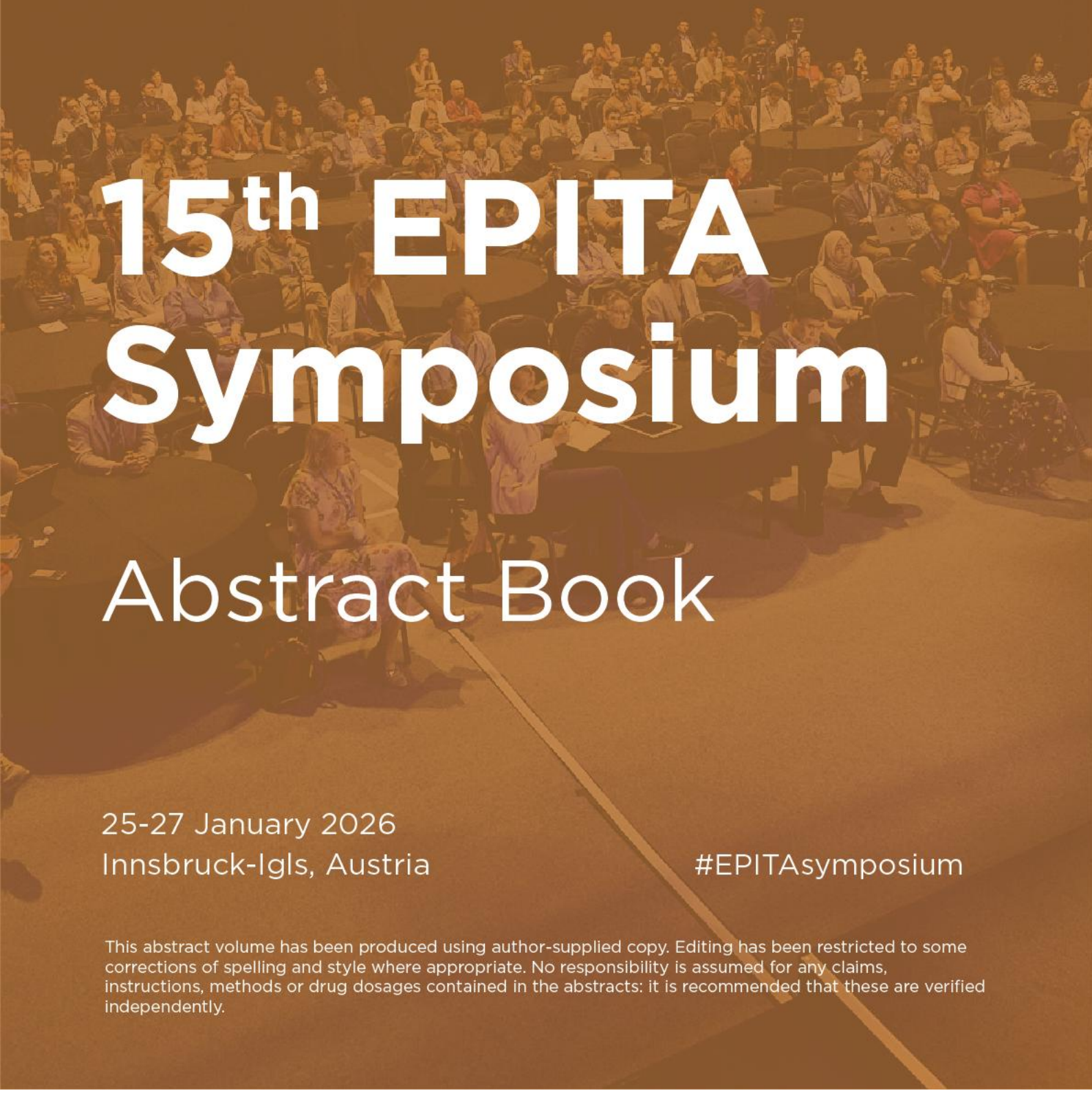
EPITA
ESOT

The European
Pancreas and Islet
Transplant Association



15th EPITA Symposium

Abstract Book

25-27 January 2026
Innsbruck-Igls, Austria

#EPITAsymposium

Table of Contents

Oral Presentations

……

Case Presentations

……

Poster Presentations

.....

Pitch Presentations

.....

OP01 - SIMULTANEOUS PANCREAS–KIDNEY VERSUS KIDNEY TRANSPLANT ALONE: REAL-WORLD OUTCOMES IN A PROPENSITY-MATCHED GLOBAL COHORT

Davide Catarinella[1], Rossana Caldara[1], Lorenzo Piemonti[1]

[11]*IRCCS Ospedale San Raffaele, Milan, Italy*

Background
The comparative effectiveness of simultaneous pancreas–kidney transplantation (SPKT) versus kidney transplantation alone (KTA) in patients with diabetes and end-stage renal disease remains uncertain in recent practice.

Methods
We analyzed the TriNetX Global Collaborative Network (2010–2024). Adults aged 18–59 years who underwent SPKT or KTA were included. Outcomes were all-cause mortality, kidney graft failure, death-censored graft failure, major adverse kidney events (MAKE), cardiovascular and transplant-related complications, rejection, infections, metabolic and microvascular complications, mental health, and malignancies. Laboratory outcomes included most recent HbA1c and eGFR. Absolute risks at 1, 5, and 10 years were calculated, with risk ratios, Kaplan–Meier curves, and Cox models. Propensity score matching (1:1, caliper 0.1) balanced demographics, diabetes type, and comorbidities.

Results
A total of 3,679 SPKT and 27,062 KTA recipients were identified. In unmatched analyses, SPKT recipients had lower mortality, graft loss, MAKE, and cardiovascular events, but higher rates of acute rejection, early infection, and metabolic decompensation. They also achieved better glycemic control (mean HbA1c 6.2% vs. 7.1%; $p<0.0001$). After matching, cohorts were well balanced. Long-term outcomes converged: survival (HR 1.00, 95% CI 0.90–1.10), kidney graft failure (HR 0.99, 95% CI 0.94–1.04), and cardiovascular events (HR 0.99, 95% CI 0.94–1.05) were neutral at 10 years. The only residual benefit was a modest reduction in MAKE during the first year (risk difference –2.4%, 95% CI –4.6 to –0.2). HbA1c remained significantly lower after SPKT, although the difference was attenuated post-matching (6.2% vs. 6.6%; $p<0.0001$). Sensitivity analyses restricted to type 1 diabetes and non-obese recipients confirmed comparable findings.

Conclusions
In this large real-world study, apparent survival and cardiovascular advantages of SPKT over KTA were explained by baseline imbalances. In the new era of transplantation, SPKT ensures superior long-term glycemic control, while major clinical outcomes are largely comparable, underscoring the importance of individualized candidate selection.

OP02 - IMPACT OF DONOR-RECIPIENT SEX MATCHING ON PANCREAS TRANSPLANTATION: A SINGLE-CENTER EXPERIENCE

Rongrong Hu Zhu[1], Maria Magdalena Llompart[1], Marco Pavesi[2], Ramón Rull[1], Rocío García[1], Carlos Perez Serrano[3], CLARA Bassaganyas Vancells[3], Alba Torroella[1], Emma Folch Puy[4], Víctor Emilio Holguin[1], Enrique Montagud-Marrahi[5], Pedro Ventura-Aguiar[5], Antonio J Amor[6], Fritz Diekmann[6], Angel Ruiz[7], Mª Angeles Garcia-Criado[8], Josep Fuster[9], Joana Ferrer-Fàbrega[9]

[1]*Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (ICMDiM), Hospital Clínic, University of Barcelona, Barcelona, Spain*
[2]*Barcelona Clinical Coordinating Center (BCCC) - Fundació Món Clínic Barcelona, Barcelona, Spain*
[3]*Department of Radiology, Hospital Clínic, University of Barcelona, Barcelona, Spain*
[4]*Experimental Pathology Department, Institut d'Investigacions Biomèdiques de Barcelona (IIBB). Consejo Superior de Investigaciones Científicas (CSIC), Barcelona, Spain*
[5]*Renal Transplant Unit, Nephrology and Kidney Transplant Department, Hospital Clínic, University of Barcelona, Barcelona, Spain*
[6]*Diabetes Unit, Department of Endocrinology and Nutrition, Hospital Clínic, University of Barcelona, Barcelona, Spain*
[7]*Donation and Transplantation Coordination Unit, Hospital Clinic,, Barcelona, Spain*
[8]*Department of Radiology, Hospital Clínic, University of Barcelona,, Barcelona, Spain*
[9]*Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (ICMDiM), Hospital Clínic, University of Barcelona, Network for Biomedical Research in Hepatic and Digestive Diseases (CIBERehd), August Pi i Sunyer Biomedical Research Institute (IDIBAPS), Barcelona, Spain*

Background
Donor-recipient sex mismatch has been identified as a potential risk factor in solid organ transplantation. However, its impact on pancreas graft survival remains underexplored. In this study we aim to evaluate the influence of donor and recipient sex on graft and patient survival outcomes following pancreas transplantation in a single-center cohort.

Methods
We retrospectively analyzed data from pancreas transplant recipients at our center between November 2000 and July 2025. Patients were stratified into four donor-recipient sex matching groups—male/male, female/female, male/female, and female/male—based on donor sex (male or female) and whether the donor and recipient were sex-concordant (male/male and female/female) or sex-discordant (male/female and female/male).

Results
A total of 525 pancreas transplants were carried out in a period of 25 years. Gender-matched transplants were performed in 52.6% (n = 276) of cases whereas gender-mismatched transplants were performed in 47.4% (n = 249) cases. Donor to recipient cases of male/male accounted for 37.5% (n = 197) of the cohort. Female/female represented 15% (n = 79), while male/female comprised 22.1% (n = 116) and female/male accounted for 25.3% (n = 133).

Ten-year graft survival was 74.1% (n = 389), with no statistically significant association observed between donor-recipient sex group and graft outcome (p value = 0.64). Similarly, no significant differences were found between gender-matched and gender-mismatched groups (p value = 0.96) nor between male and female donors (p value = 0.44).

Ten-year patient survival was 94.3% (n = 495), with no significant association between donor-recipient sex group and patient mortality (p = 0.83). Likewise, sex matching (p = 0.50) and donor sex (p = 0.67) showed no significant impact on long-term patient survival.

Conclusions
Gender matching and donor-recipient sex combinations do not significantly impact long-term graft or patient survival in pancreas transplantation.

These findings indicate that donor-recipient sex concordance does not constitute a significant determinant of long-term outcomes in pancreas transplantation.

OP03 - DONOR FACTORS INFLUENCING PANCREAS TRANSPLANT UTILISATION DECISIONS; USING US REGISTRY DATA TO MODEL EVOLUTION IN DECISION-MAKING OVER TIME

Chahana Patel[1 2 3], Georgios Kourounis[1 2 3], Leonie van Leeuwen[4], Matthew Holzner[4], Vikram Wadhera[4], Mohammed Zeeshan Akhtar[4], Sander Florman[4], Angeles Maillo-Nieto[2], James Shaw[1 2 3], Steven White[1 2], Samuel Tingle[1 2 3], Colin Wilson[1 2 3]

[1]*NIHR Blood and Transplant Research Unit, Newcastle Upon Tyne, United Kingdom*
[2]*Institute of Transplantation, Freeman Hospital, Newcastle Upon Tyne, United Kingdom*
[3]*Translational and Clinical Research Institute, Newcastle University, Newcastle Upon Tyne, United Kingdom*
[4]*Recanati Miller Transplant Institute, Mount Sinai Hospital, New York, United States*

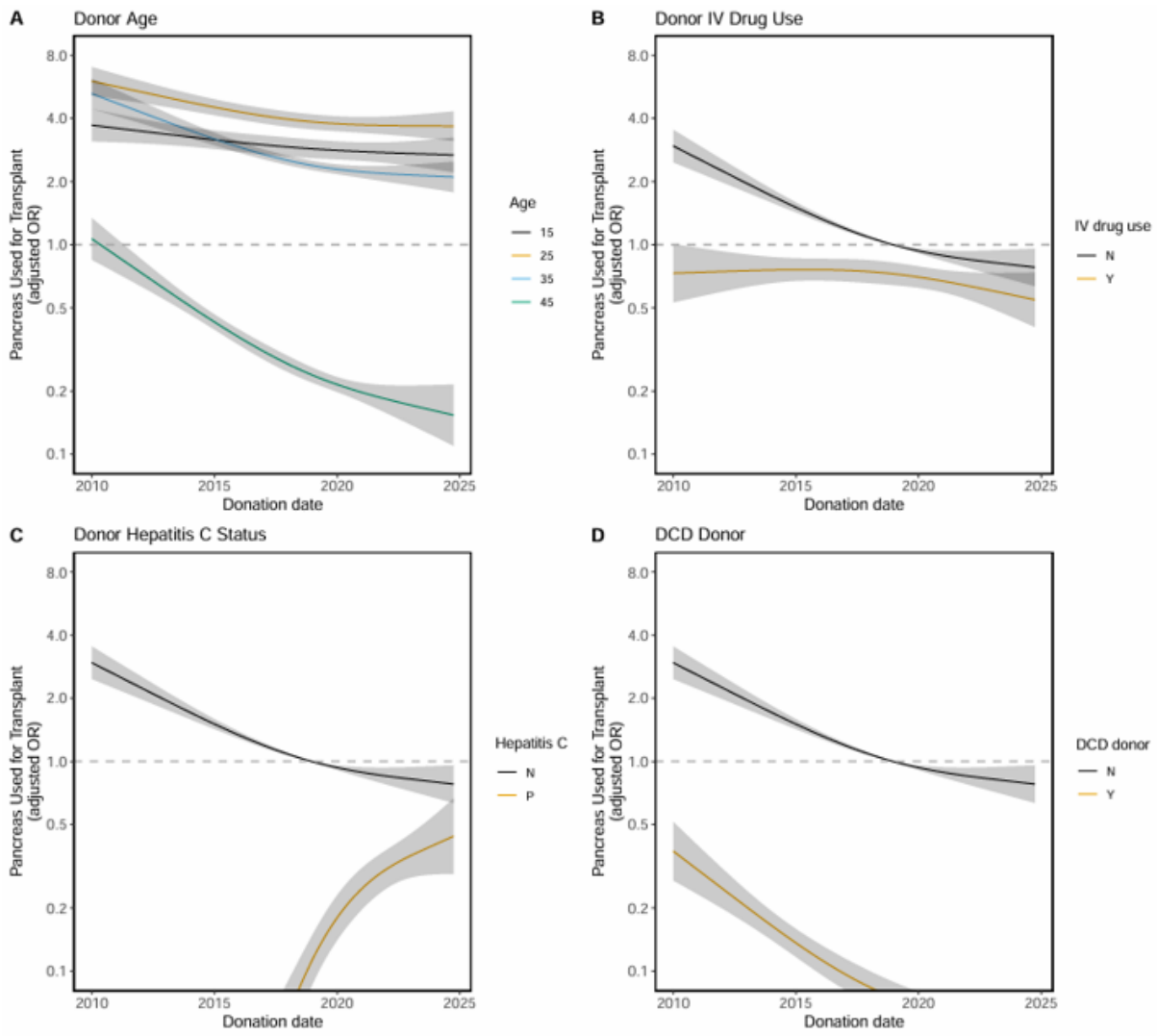
Background
Pancreas transplantation remains the only definitive treatment for diabetes mellitus. However, the global number of pancreas transplants and utilisation of pancreas grafts is declining. We aimed to identify significant donor factors associated with graft non-use.

Methods
We performed a retrospective population-cohort study using OPTN data (2010-2024). Multivariable regression models were constructed to assess interactions between donor characteristics associated with pancreas utilisation. Restricted cubic splines were used to preserve non-linear relationships and interaction terms with donation date were performed, to capture changing decision-making behaviours.

Results
Out of 133,986 donors, 14,612 (10.9%) pancreases were used for transplantation. We identified 23 donor factors significantly associated with utilisation. The most important continuous donor factors were age, BMI and peak creatinine; all showing highly significant non-linear relationships with utilisation (P<0.001). Donor type was the most important categorical variable, with donation after circulatory death (DCD) having 92% lower odds of utilisation (aOR=0.078, 95% CI=0.070 to 0.087, P=<0.001). Interaction analyses revealed increasing reluctance to use DCD donors or older donors over the study period (both interaction P<0.001, Figure 1A&D). Conversely, clinicians became more comfortable transplanting pancreases from Hepatitis C positive donors and IV drug use (IVDU) donors over time (both interaction P<0.001, Figure 1B&C).

Conclusions
Pancreas utilisation was strongly associated with donor age and DCD status, with interaction modelling revealing increasing avoidance of older donors and DCD donors over the study period. This is despite mounting evidence suggesting comparable post-transplant outcomes in DCD pancreases. Meanwhile, previously underused groups such as Hepatitis C positive and IVDU donors show growing acceptance, supporting the expansion of these donor populations globally.

Figure 1: Restricted cubic splines illustrating changing impact of key variables on pancreas utilisation over time. A) Donor age. B) Donor IV drug use. C) Donor hepatitis C antibody status. D) Donor DCD status.



OP04 - IMPACT OF HLA-DR MISMATCH ON OUTCOMES AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION

Moksh Sachdeva[1 2], Samuel Tingle[1 2], Colin Wilson[1 2], Georgios Kourounis[1 2], Abdullah Malik[1 2], Emily Thompson[1 2], Neil Sheerin[1 2], Steven White[1 2]

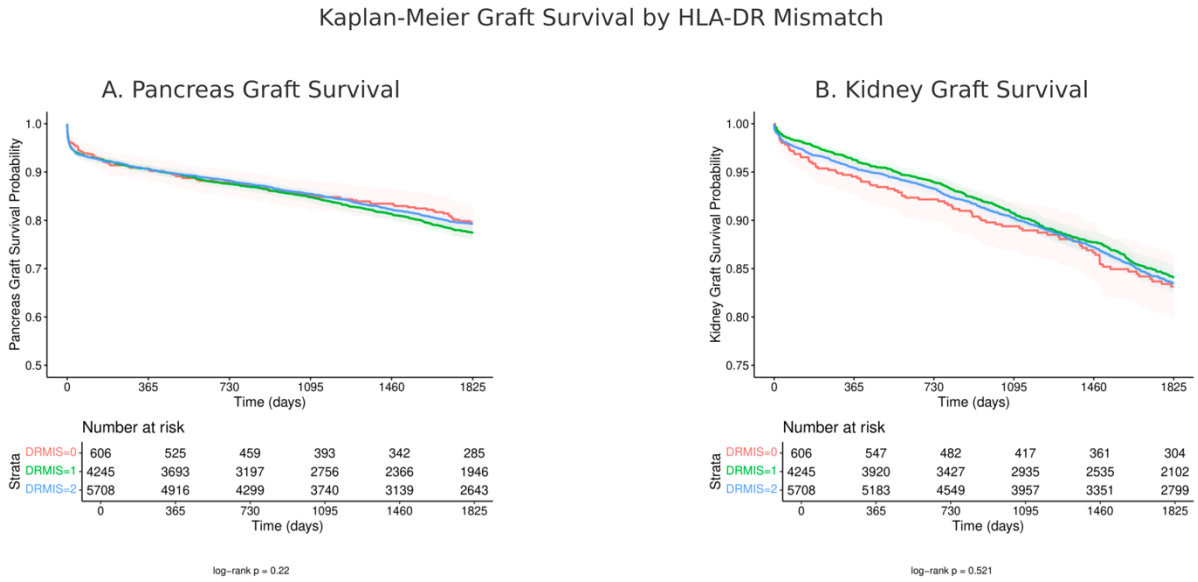
[1]*Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, United Kingdom*
[2]*Institute of Transplantation, Freeman Hospital, Newcastle upon Tyne, United Kingdom*

Background
HLA-DR mismatch has been linked to inferior outcomes following kidney-alone transplantation. However, the impact on kidney outcomes in the context of simultaneous pancreas-kidney (SPK) transplantation remains uncertain. This study aimed to assess the impact of HLA-DR mismatch on SPK outcomes.

Methods
A population-based cohort study was conducted using the United Network for Organ Sharing (UNOS) registry to identify adult SPK recipients transplanted between 2010 and 2023. Exclusion criteria included retransplants, multiorgan transplants other than SPK, donors with diabetes, and missing HLA-DR mismatch data. Multivariable Cox, logistic, and linear regression models with restricted cubic splines were used to assess associations between HLA mismatch and graft survival, acute rejection, and renal function, adjusting for a wide range of confounders. Sensitivity analyses included hierarchical frailty models to account for center-level effects and three-way interactions between HLA-A, -B, and -DR mismatches.

Results
In a cohort of 10,559 SPK recipients, 606 (6%) had zero HLA-DR mismatches, 4,245 (40%) had one mismatch, and 5,708 (54%) had two mismatches. Overall mismatch was frequent, with only 34 recipients (0.3%) having 0/0/0 mismatches across HLA-A, HLA-B, and HLA-DR. HLA-DR mismatch was not associated with pancreas or kidney graft survival at 5 years; two versus zero HLA-DR mismatches aHR=1.014 (95% CI 0.828–1.241) for pancreas and aHR=0.937 (0.747–1.176) for kidney graft survival. HLA-DR mismatch was also not associated with pancreas or kidney acute rejection or 12-month eGFR. Analyses with three-way interactions between HLA-A, B and DR revealed that DR mismatch was not associated with kidney or pancreas outcome, regardless of the level of A or B mismatch. HLA-A and HLA-B mismatches also showed no association with the outcome. These findings are further illustrated in the Kaplan-Meier survival curves (Figure 1), which show no significant difference in pancreas or kidney graft survival across HLA-DR mismatch groups.

Figure 1: Kaplan-Meier curves for pancreas and kidney graft survival stratified by the degree of HLA-DR mismatch



Conclusions

In the setting of SPK, HLA-DR mismatch was not associated with pancreas or kidney post-transplant outcome, in contrast to established findings in kidney-alone transplantation. These results suggest that prioritising HLA-DR matching is unlikely to improve outcomes, indicating that changes to allocation policy to prioritise HLA-DR matching are not warranted.

OP05 - UTILITY OF CONTRAST-ENHANCED ULTRASOUND IN THE DIAGNOSIS OF ACUTE VENOUS PANCREAS GRAFT THROMBOSIS

Carlos Perez Serrano[1], Rongrong Hu Zhu[2], Oriol Busquets Carrera[1], Alex Gil-Ordoñez[1], Lledó Cabedo[1], CLARA Bassaganyas Vancells[1], Gerard Rafart-Martínez[1], Sergio Jimenez-Serrano[1], Mario Matute-Gonzalez[1], Julian Moreno-Rojas[1], Enrique Montagud-Marrahi[3], Ramón Rull[2], Anna Darnell[1], Pedro Ventura-Aguiar[3], Joana Ferrer-Fàbrega[4], Mª Angeles Garcia-Criado[1]

[1]*Department of Radiology, Hospital Clínic, University of Barcelona, Barcelona, Spain*
[2]*Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (ICMDiM), Hospital Clínic, University of Barcelona, Barcelona, Spain*
[3]*Renal Transplant Unit, Nephrology and Kidney Transplant Department, Hospital Clínic, University of Barcelona, Barcelona, Spain*
[4]*Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (ICMDiM), Hospital Clínic, University of Barcelona, Network for Biomedical Research in Hepatic and Digestive Diseases (CIBERehd), August Pi i Sunyer Biomedical Research Institute (IDIBAPS), Barcelona, Spain*

Background
To determine the value of contrast-enhanced ultrasound (CEUS) in the diagnosis of acute venous pancreas graft thrombosis when colour Doppler ultrasound (CDUS) is inconclusive.

Methods
A retrospective, single-centre study was conducted, including all pancreas transplants performed between January 2008 and August 2025. Acute venous thromboses were defined as those occurring within the first 30 days post-transplantation, encompassing the full spectrum from minor events with no clinical repercussion to extensive thromboses requiring intervention. Our standard imaging protocol includes CDUS for all patients at 24–48 h post-transplant and at least once before discharge. In cases where grayscale ultrasound showed no thrombus but the Doppler study detected no flow signal, a CEUS was performed. The final diagnosis was confirmed with computed tomography (CT) or arteriography when clinically indicated.

Results
During the study period, 361 pancreas transplants were performed. After excluding 16 cases of immediate graft loss, 345 were assessed with an initial ultrasound. Of these, 19 grafts were considered unevaluable due to technical limitations. The remaining 326 evaluable grafts showed three distinct outcomes: 241 were classified as patent, 43 showed acute venous thrombosis on grayscale imaging, and 42 were inconclusive, with neither thrombus nor flow detected on Doppler. This final cohort of 42 cases became the primary focus. Of these, 35 underwent CEUS, which identified 15 thromboses and 20 patent vein grafts. The remaining 7 patients were studied directly by TC or arteriography, all confirming thrombosis. Of the 15 thromboses diagnosed by CEUS, two were minor, peripheral thromboses without clinical repercussions and therefore did not require further imaging. The remaining 13 were further evaluated by CT (x) or arteriography (x), confirming the diagnosis in 12 of them. The other case was a false positive of CEUS, with CT showing filiform but patent vessels.

Conclusions

CEUS is a valuable, and reliable tool for differentiating between low-flow states and true venous thrombosis when CDUS is inconclusive. Its incorporation into the diagnostic algorithm reduces unnecessary exposure to iodinated contrast and radiation from CT scans, enables rapid clarification, and supports timely therapeutic decisions that may improve graft survival.

OP06 - HEART FAILURE WITH PRESERVED EJECTION FRACTION AND CARDIAC AUTONOMIC NEUROPATHY IN TYPE 1 DIABETES PATIENTS AFTER SIMULTANEOUSE PANCREAS-KIDNEY TRANSPLANTATION

Eugene Zeltyn-Abramov[1], Svetlana Kondrashkina[1], Natalya Belavina[1], Nataliya Klochkova[1], Tatyana Markova[1], Alexandr Kondrashkin[2], Mariana Lysenko[1], Mogeli Khubutia[2]

[1]*MOSCOW CLINICAL SCIENCE AND RESEARCH CENTER 52, Moscow, Russian Federation*
[2]*N.V. Sklifosovsky Research Institute for Emergency Medicine, Moscow, Russian Federation*

Background
Cardiac autonomic neuropathy (CAN) and chronic heart failure with preserved ejection fraction (HFpEF) have a negative impact on long-term prognosis and patient`s quality of life after simultaneous pancreas-kidney transplantation (SPKT). The aim of the study is to evaluate the prevalence of CAN and HFpEF in patients with type 1 diabetes after SPKT and stable allograft function.

Methods
36 patients with LVEF ≥50% after SPKT were enrolled. The stability of both allografts function was confirmed by indicators of glycemia, HbA1C, C-peptide, immunoreactive insulin, continuous glucose monitoring (CGM), serum creatinine and proteinuria. 24-hour ECG monitoring and cardiovascular testing was conducted in all patients. The results of cardiovascular testing and the indicators of heart rate variability and QT duration were analysed. The diagnosis of CAN was confirmed in cases, were two or more indicators have been deviated from the normal range. The diagnostics of HFpEF was performed according to HFA-PEEF protocol after NT-pro-BNP, 6-minute walk test and echocardiographic parameters evaluation.

Results
Mediana values: age 42 [35; 49], female 64%, diabetes 1 type duration before SPKT 25 y [12; 36], duration of renal replacement therapy before SPKT – 12.5 mo [12; 36], transplants functioning duration – 106 mo [43; 143], the period of pancreas allograft conservation 9 h [8; 10], serum creatinine 100 μmol/L [80; 110], fasting blood glucose 4.73 mmol/L [4.31; 5.50], HbA1C 5.4% [5.1; 5.9], C-peptide 2.03 ng/ml [1.55; 3.21], immunoreactive insulin 17 mc/n/ml [10.9; 26.3], CGM – 5.6 mmol/L [5.5; 6.5], variability of glucose level 22.2% [17.7; 35.7], time-in-range 94% [69; 98], time above the range 0% [0; 1], time below the range 2.0% [1; 6]. The significant proteinuria was not detected. 24-hour ECG results: standard RR deviation 83 msec [57; 117] (N 143 ±32), root mean square RR deviation 12.5 msec [10; 14] (N 35 ±11), average weighted rhythmogram deviation 689 msec [551; 785] (N>1370), QTc 421 msec [402; 432]. Cardiovascular tests: K exhalation/inhalation 1.09 msec [1.05;1.19] (N>1.2), K Valsalva 1.20 msec [1.13; 1.37] (N>1.35), K 30:15 1,09 msec [1.02;1.15] (N>1.17). NT-proBNP 115 ng/L [82; 244] (N 0-125). Echocardiographic parameters: LVEF 64% [59; 65], global longitudinal stress -19.6% [-18.1; 21.1]. According to the data obtained in 33 pts (91.6%) CAN was diagnosed. In 11 pts (25%) HFpEf was detected after 6-minute walk test results evaluation. The direct correlation between the incidence of HFpEf and the duration of pancreas transplant conservation, (|r|=0.61), HbA1C (|r|=0.40) and diabetes 1 type duration (|r|=0.35) was confirmed.

Conclusions

The incidence of CAN and HFpEF among patients after SPKT is rather high despite of preserved function of both allografts. This phenomenon requires further study and observation.

OP07 - COMPARISON OF TOTAL PANCREATECTOMY AND ISLET AUTOTRANSPLANTATION (TPIAT) AND PARENCHYMA-PRESERVING SURGERY (PPS) AS TREATMENT FOR CHRONIC PANCREATITIS.

Noë Eggebeen[1], Yama Issa[1], Willemijn de Vos[1], Maarten Tol[1], Ian Alwayn[1], Marja Boermeester[2], Bert Bonsing[1], Marten Engelse[1], Jeanin van Hooft[1], Akin Inderson[1], Rens Kempeneers[2], Eelco de Koning[1], Marieke Niesters[1], Michiel Nijhoff[1], Sven Mieog[1], Volkert Huurman[1]

[1]*Leiden University Medical Center, Leiden, Netherlands*
[2]*Amsterdam University Medical Center, Amsterdam, Netherlands*

Background

Chronic pancreatitis (CP) is a progressive inflammatory disease characterized by persistent abdominal pain, which may result in opioid dependence and a reduced quality of life. Over time, the ongoing inflammation leads to impairment of both endocrine and exocrine pancreatic functions. Parenchyma-preserving surgery (PPS) is commonly performed as an initial surgical treatment, whereas total pancreatectomy with islet autotransplantation (TPIAT) is often reserved for patients in whom other treatments have failed. This retrospective observational study compares the clinical outcomes of TPIAT and PPS in the management of CP.

Methods

Patients who underwent TPIAT for CP at Leiden University Medical Center between December 2014 and February 2025 were included. Patients participating in the PPS arm of the ESCAPE trial were used as a comparison. Primary outcomes were pain measured with the Izbicki pain score, quality of life using the Short Form 36, and postoperative opioid use. Secondly, this study looked at adverse events (Clavien-Dindo ≥ grade III), length of hospital stay, endocrine insufficiency defined as the use of antidiabetics, graft function described as C-peptide levels ≥0,1 nmol/L and Igls 2.0 score, and exocrine insufficiency, for the TPIAT groups according to the M-ANNHEIM criteria, and in the PPS group defined as fecal elastase levels ≤ 200 microgram/ gram. The outcomes were analyzed one year postoperatively. This study hypothesizes that TPIAT would be as efficient in the reduction of pain and as safe as parenchymal-preserving surgery.

Results

In total, 26 patients underwent TPIAT and 41 PPS. The TPIAT group had a longer history of CP (60 months vs. 36 months) and higher mean Izbicki pain scores at baseline (85,0 vs 66,3 in the PPS group). Post-surgery, the mean Izbicki pain score decreased to 66,5 post-TPIAT and to 25,0 post-PPS, while mean VAS-scores decreased from 65,4 to 9,0, and from 63,8 to 2,0, respectively. There was no significant difference in the physical and mental component of the SF-36 for both treatment groups. The proportion of patients with opioid dependency improved from 76,9% to 31,8% after TPIAT versus 97,6% to 34,1% after PPS (P=1.0). As expected, TPIAT patients acquired statistically significantly more endocrine insufficiency (81,8% and 29,3%, P<0,001); however, all patients showed islet graft function, and 81,8% of the patients had an optimal or good Igls 2.0 score. Both treatments were comparable in exocrine insufficiency (TPIAT 100%, PSS 80%, P=1.0). The treatment options

were comparable in exocrine insufficiency, adverse events, and total hospital length of stay.

Conclusions
TPIAT and PPS are both safe procedures with a comparable effect on pain, quality of life, and opioid use. Though the TPIAT group had a larger proportion of endocrine insufficiency, all patients showed graft function post-TPIAT. Depending on individual circumstances, both treatments should be considered for patients needing primary surgical intervention for CP.

OP08 - DETERMINANTS OF PRIMARY GRAFT FUNCTION AFTER SINGLE ISLET ALLOTRANSPLANTATION: A RETROSPECTIVE, MULTICENTER, OBSERVATIONAL COHORT STUDY IN 869 PATIENTS FROM THE COLLABORATIVE ISLET TRANSPLANT REGISTRY

Mikael Chetboun[1], Chimène Amayene Amassogo[1], Francois Pattou[1]

[1]*University Hospital of Lille CHU Lille - INSERM, Lille University, Lille, France*

Background
Primary graft function (PGF), assessed 28 days after islet infusion, is a key early determinant of long-term success following islet allogeneic transplantation. Identifying donor, recipient, and procedural factors influencing PGF after islet transplantation could inform future in beta-cell replacement therapy.

Methods
Data were extracted from the Collaborative Islet Transplant Registry (CITR) and all adult recipients of a first allogeneic islet transplantation between 1999 and 2020 were enrolled. Variables with >35 % missing data were excluded, and cases with >50 % missing values were removed. Missing donor, recipient, and day-28 post-transplant data were imputed using Random Forest imputation. PGF, defined by the day-28 BETA-2 score, was dichotomized according to the cohort median. Classical univariable and multivariable logistic regression analyses (stepwise selection) identified independent factors associated with higher PGF (Table 1).

Results
Among 869 recipients (158 IAK; 18 %) with calculable PGF, univariate analysis identified younger donor age (p = 0.0269), higher donor BMI (p=0. 0087), lower pretransplant HbA1c (p< 0.0001), fasting plasma glucose (p =0. 0249), and daily insulin requirements (p=0.0007), longer diabetes duration (p=0.0086), absence of pretransplant GAD autoimmunity (p< 0.0001), islet after kidney recipients and T-Cell depletion induction immunosuppression as significantly associated with higher PGF. In multivariate analysis, **younger donor age** (adjusted OR 0.975, 95% CI 0.954–0.996; p = 0.019), **lower pretransplant HbA1c** (aOR 0.583, 95% CI 0.463–0.736; p < 0.0001), **lower daily insulin requirements** (aOR 0.121, 95% CI 0.025–0.578; p = 0.0081), and the **absence of pretransplant GAD autoimmunity** (aOR 0.586, 95% CI 0.346–0.993; p = 0.047) were the main variables associated with higher PGF (Table1).

Conclusion
Younger donor age, longer diabetes duration without pretransplant GAD autoimmunity and better pretransplant metabolic control before transplantation favor superior PGF.

Table 1: Determinants of Primary Graft Function after islet allogeneic transplantation: univariable and multivariable logistic regression analyses

	Univariate analysis		Multvariate analysis	
	OR (95% CI)	**p-value**	**OR (95% CI)**	**p-value**
Donor Characteristics				
Donor gender (female vs male)	1.030 (0.748–1.417)	0.8581		
Age (years)	0.986 (0.974–0.998)	**0.0269**	**0.975 (0.954 – 0.996)**	**0.0192**
BMI (kg/m²)	1.035 (1.009–1.062)	**0.0087**	-	
History of hypertension (yes vs no)	0.863 (0.620–1.201)	0.3826		
Cause of death (stroke = ref)		0.4541		
Anoxia or cardiac arrest	1.583 (0.826–3.034)	0.1664		
Head trauma	1.206 (0.850–1.711)	0.2932		
Other	1.027 (0.550–1.920)	0.9322		
ABO blood group (group O = ref)		0.2649		
Group A	0.847 (0.611–1.174)	0.3179		
Other groups	0.628 (0.337–1.170)	0.1427		
Use of Vasopressin/Desmopressin (yes vs no)	1.332 (0.759–2.338)	0.3182		
Recipient characteristics				
Gender (female vs male)	1.036 (0.787–1.362)	0.8018		
BMI (kg/m²)	0.994 (0.953–1.036)	0.7775		
Type of recipient (IAK vs ITA)	1.636 (1.152 – 2.324)	**0.0059**	-	
Pretransplant HbA1c (%)	0.712 (0.635–0.798)	**<0.0001**	**0.583 (0.463 – 0.736)**	**<0.0001**
Pretransplant fasting glucose (mg/dL)	0.998 (0.996–1.000)	**0.0249**	-	
Daily exogenous insulin (UI/kg/day)	0.335 (0.150–0.749)	**0.0077**	**0.121 (0.025 – 0.578)**	**0.0081**
Diabetes duration (years)	1.018 (1.004–1.031)	**0.0086**	-	
Pretransplant GAD Ab autoimmunity	0.475 (0.328–0.688)	**<0.0001**	**0.586 (0.346 – 0.993)**	**0.0470**
Islet infusion characteristics				
Islet tissue volume (mL)	1.022 (0.950–1.099)	0.5673		
Islet yield (IEQ ×100,000)	1.065 (0.992–1.144)	0.0821		
Pre transplant islet culture (yes vs no)	2.251 (1.642–3.086)	**<0.0001**	-	
Use of IL2R antagonist induction immunosuppression	1.092 (0.674–1.768)	0.7205		
Use of T Cell depletion induction immunosuppression	0.747 (0.563–0.991)	**0.0434**	-	
Use of TNFa induction immunosuppression	1.188 (0.890–1.586)	0.2435		
Use of m-TOR inhibitor maintenance immunosuppression	1.231 (0.927–1.635)	0.1503		
Use of Calcineurin inhibitor maintenance immunosuppression	0.949 (0.554–1.628)	0.8502		

OP09 - INDUCTION OF IMMUNE EDUCATION IN TYPE 1 DIABETES THROUGH CONTROLLED ALLOGENEIC ISLET REJECTION AT ONSET: A MONOCENTRIC OPEN-LABEL PILOT STUDY

Lorenzo Piemonti[1,2], Andrea Bolla[1], Amelia Caretto[1], Raffaella Melzi[1], Alessia Mercalli[1], Valeria Sordi[1], Paolo Monti[1], Paola Magistretti[1], Vito Lampasona[1], Ilaria Marzinotto[1], Rossana Caldara[1], Emanuele Bosi[1]

[1]*IRCCS Ospedale San Raffaele, Milan, Italy*
[2]*Università Vita Salute San Raffaele, Milan, Italy*

Background
Current immunotherapies for type 1 diabetes (T1D) have shown limited success in durably preserving β-cell function. We tested a novel strategy that repurposes allogeneic islet transplantation not for metabolic replacement, but as a platform for antigen-specific immune education.

Methods
In a monocentric, open-label pilot study, six patients with recent-onset T1D received a minimal islet mass (median: 3,452 IEQ/kg, range: 2,980–4,050 IEQ/kg) in combination with a short-term immunomodulatory regimen—including T cell depletion, transient mTOR inhibition, and G-CSF-mediated regulatory T cell (Treg) expansion. The transplanted islet mass was deliberately insufficient for metabolic replacement but aimed at providing controlled islet antigen exposure to promote immune regulation.

Results
The protocol was safe and well-tolerated. At 12 months, the median stimulated C-peptide AUC was preserved at 91–100% of baseline with all participants achieving a partial clinical remission (IDAA1c ≤9). At 5 years, median C-peptide AUC declined to 44–56% of baseline, with 2 patients maintaining stable secretion and 2 retaining ~50% of initial function. The intervention triggered a structured immune reset: early T cell depletion was followed by memory and Treg expansion, supported by transient IL-2, IL-10, and persistent sCD25 elevation. Cytokine profiling revealed biphasic immune modulation with early inflammation and delayed regulation. miR-375 peaks indicated transient β cell stress. No new autoantibodies emerged (no epitope spreading); only a transient increase of existing autoantibodies occurred, followed by return to baseline or disappearance. Class I anti-HLA donor specific alloantibodies (DSA) transiently appeared in 5 patients, whereas class II DSA emerged and persisted in 2 patients. No peripheral expansion of $CD3^+CD8^+$ T cells specific for GAD65 was detected.

Conclusions
This study introduces a paradigm shift in the use of islet transplantation—from a therapeutic endpoint to a tolerogenic stimulus. This approach may be further potentiated by emerging technologies, including stem cell–derived islets, enabling broader HLA matching, graft modification, and iterative antigen delivery.

OP10 - ASSESSMENT OF A 40% FALL OF C-PEPTIDE AS DIAGNOSTIC CRITERIA OF GRAFT DYSFUNCTION IN A MONOCENTRIC COHORT OF 45 ISLET-TRANSPLANTED ALONE PATIENTS.

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

[1]*Endocrinology and metabolism, Lille, France*
[2]*Inserm U 1190, Endocrinology and metabolism, Lille, France*
[3]*Nephrology, Lille, France*
[4]*Inserm U 1190, Endocrine Surgery, Lille, France*
[5]*Inserm U 1190, Lille, France*

Background
The success of islet transplantation can be compromised by graft dysfunction, potentially due to rejection. There is no histological classification of islet rejection as for pancreas transplantation. The clinico-biological criteria for islet rejection are poorly defined. An increase of blood glucose and decrease of C-peptide are usually considered but the time frame and the amplitude remain subjective. Two single cases of rejection, both treated with steroids, with rituximab and immunoglobulins in one case, have been reported (*Kessler et al*) while a case series with a historical control group has been published by *Landstra AJT 2023*. The **objective** of this study was to evaluate the criteria proposed by *Landstra* as diagnostic markers for dysfunction/suspected rejection, within a monocentric cohort.

Methods
Clinical and biological parameters of 45 consecutive patients who received islet transplantation alone (2 to 3 injections over 3 months) between 2003 and 2023, were collected every month the first year, every 6 months the second year, then yearly after the first islet injection until 2024. Two groups were defined according to the occurrence of a dysfunction defined by a 40% decrease of blood C-peptide level as compared to the level observed 1 month after the last islet injection, chosen as baseline. Values are expressed as median (IQR) or %.

Results
The group "non-treated dysfunction" (NTD) defined by a 40% decrease in C-peptide (NTD: C-peptide: 0.9 *vs.* ND (no-dysfunction): 1.75 ng/ml), included 28 patients, showed a 50% decrease in the C-peptide/glucose ratio (NTD: 0.04(0.03) *vs.* ND: 0.1(0.04), p<0.0001) and a median 3-mark drop in the beta-score (delta betascore: NTD: 3(2) *vs.* ND: 1(3), p=0.04; absolute betascore: NTD: 3(1) *vs.* ND: 6(3), p=0.009) compared to the ND group (n=17). The mean time elapsed between the first islet injection and the occurrence of dysfunction or last news was 3.5(5.9) years in the NTD group *vs.* 6.0(7.0) in the ND group. Compared to the ND group, the NTD group tended to be younger at the occurrence of dysfunction (52(16) *vs.* 57(8) years; p=0.07) and to have a poorer primary graft function (Betascore one month after the last injection: NTD: 6(1) *vs.* ND: 7(2); p= 0.08). NTD group included more male patients (60% *vs.* ND: 23 %; p<0.001) and showed a higher percentage of patients treated with the Edmonton protocol (71% *vs.* 53%; p<0.001). Islet mass and anti-GAD antibodies did not differ between groups. One year after the suspected

rejection, the delta of betascore compared to one month after last injection was: NTD: 4(2) *vs.* ND: 1(3) (p=0.001), demonstrating the continued deterioration of beta cell function in the NTD group.

Conclusions

A 40% reduction in C-peptide or a 3-mark fall of betascore appear as significant threshold for islet graft dysfunction. The male sex is confirmed to be associated with a less favorable long-term prognosis. The unfavorable role of Edmonton protocol may be due to a longer follow-up. The mechanisms of this dysfunction (alloimmune? inflammatory? senescence?) and the benefit of a treatment remain to be determined, taking to account the time frame.

OP11 - IMMUNOMODULATORY AND VASCULOGENIC GRANULAR COMPOSITE GRAFT FOR STEM CELL–DERIVED BETA CELL TRANSPLANTATION

Rea Tresa[1], Benjamin Hansen[2], Luana A De Abreu Queiros Osorio[3], Jonathan Wojciechowski[1], Daniel Reumann[1], Luca Panariello[1 4], David Peeler[1 5], Ildem Akerman[6], Victoria Salem[2 3], Molly Stevens[1 2 5]

[1]*Department of Physiology, Anatomy and Genetics, University of Oxford, Kavli Institute for Nanoscience Discovery, University of Oxford, Oxford, United Kingdom*
[2]*Department of Bioengineering, Imperial College London, London, United Kingdom*
[3]*Department of Diabetes, School of Cardiovascular and Metabolic Medicine & Sciences, King's College London, London, United Kingdom*
[4]*Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, Sweden*
[5]*Department of Materials, Imperial College London, London, United Kingdom*
[6]*Institute of Biomedical Research, University of Birmingham, Birmingham, United Kingdom*

Background
Beta cell replacement represents a promising therapeutic avenue for type 1 diabetes, yet its widespread clinical translation remains constrained by donor scarcity, recurrent immune attacks, and rapid graft loss following transplantation. To overcome these challenges, we are developing an immunomodulatory and vasculogenic granular composite graft for the minimally invasive delivery of stem cell–derived beta cell (SCB) clusters into the subcutaneous space.

Methods
A custom microfluidic platform was engineered to enable encapsulation across the nano- to microscale, providing a physical barrier against immune components while preserving cell viability and functionality. The system employs poly(ethylene glycol) (PEG) based hydrogels which gelate under mild, cytocompatible conditions. Material characterisation of PEG variants with distinct architectures was conducted via rheology, immunofluorescence, and fluorescence recovery after photobleaching (FRAP), alongside in vitro evaluation of their biocompatibility using a custom vasculogenic assay. In parallel, extracellular matrix (ECM) inspired vasculogenic microgels were fabricated and assessed to evaluate endothelial organisation and vessel formation.

Results
The microfluidic platform enabled fabrication of highly uniform microgels (coefficient of variation < 1%) across multiple size regimes (150–600 µm), depending on chip geometry and flow parameters. PEG-based hydrogels demonstrated efficient and reproducible gelation with tunable mechanical properties, and both nano- and microencapsulation of cell clusters were successfully achieved. Vasculogenic microgels supported endothelial cell organisation as demonstrated by immunofluorescence, indicating potential for perivascularisation and improved nutrient exchange post-transplantation.

Conclusions
This platform integrates immune- and vascular engineering strategies to address the key challenges of immune protection, vascularisation, and long-term graft survival. Through modular click chemistry and an ECM-inspired design, we provide a versatile

material foundation for the next-generation of beta cell replacement therapies that are durable, scalable, and translatable to the clinic.

OP12 - IN VITRO INSULIN BIOSYNTHESIS PREDICTS PRIMARY GRAFT FUNCTION AFTER FIRST ALLOGENIC ISLET CELL TRANSPLANTATION

Diedert De Paep[1 2], Lisa Van den Berghe[1], Zhidong Ling[1 2], Pieter Gillard[1 3], Daniel Jacobs-Tulleneers-Thevissen[1 2], Robert Hilbrands[1 4]

[1]*Vrije Universiteit Brussel (VUB), Diabetes Research Center, Diabetes Pathology & Therapy, Brussels, Belgium*
[2]*Vrije Universiteit Brussel (VUB) / Universitair Ziekenhuis Brussel (UZ Brussel), Oncologische, Thorax- en Transplantatieheelkunde, Beta Cell Bank, Brussels, Belgium*
[3]*University Hospitals Leuven, Department of Endocrinology, Leuven, Belgium*
[4]*Vrije Universiteit Brussel (VUB) / Universitair Ziekenhuis Brussel (UZ Brussel), Diabetes Clinic, Brussels, Belgium*

Background
Quantitative measures of islet cell mass remain the primary release criteria for clinical islet cell grafts. Although several variables have been found to correlate with metabolic outcomes, significant heterogeneity in primary graft function (PGF) and graft survival persists. An in vitro functional biomarker that predicts graft performance could help reduce this variability. The present study investigates insulin biosynthesis as a potential qualitative marker for in vivo graft function.

Methods
Sixty C-peptide negative patients with type 1 diabetes who received an allogeneic intraportal islet cell graft containing at least 2×10^6 beta cells/kg and an ATG-induction/tacrolimus-MMF-maintenance immunosuppression were included for this study. The association between graft insulin biosynthesis and PGF after a first islet cell transplantation was evaluated together with other graft characteristics in uni- and multivariate analysis. PGF was defined as non-fasted C-peptide ≥ 0.5 ng/ml 2 months after transplantation.

Results
We observed that total insulin synthesis of the islet cell graft and per beta cell were significantly associated with PGF in univariate (3.7 vs 4.8 nmol/graft/2h, p = 0.024 and 17.2 vs 25.2 fmol/10^3 beta cells/2h, p = 0.025 respectively) and multivariate analysis. ROC-AUC analysis was used to define a threshold of 4.0 nmol/graft/2h for total insulin synthesis (OR 4.4, p = 0.015) and 12.6 fmol/10^3 beta cells/2h for synthesis per beta cell (OR 7.0, p = 0.019). Increasing quantitative islet cell mass beyond thresholds for inclusion did not correlate with PGF. PGF after a first islet cell transplantation was significantly correlated to the duration of graft survival after completion of transplantation series (705 vs 1395 days, p = 0.026).

Conclusions:
In vitro insulin biosynthesis may serve as a functional biomarker of islet cell grafts with the potential to predict PGF and duration of graft survival. Our data indicate that qualitative markers can help improve outcomes in islet cell transplantation.

OP13 - CHEMICAL REPROGRAMMING OF TYPE 1 DIABETES PATIENT FIBROBLASTS INTO FUNCTIONAL AND CRYOPRESERVABLE B CELLS

Cecilia Masiero[1], Laura Monaco[1], Giorgia Fulgini[1], Manuela Marras[1], Chiara Ceriani[1 2], Giusy Di Giuseppe[3], Chiara Giacometti[3], Silvia Pellegrini[3], Hongkui Deng[4 5], Lorenzo Piemonti[1 2], Valeria Sordi[1]

[1]*IRCCS Ospedale San Raffaele, Diabetes Research Institute, Milan, Italy*
[2]*Università Vita-Salute San Raffaele, Milan, Italy*
[3]*IRCCS Ospedale San Raffaele, IPSC Factory, Centro Risorse Biologiche, Milan, Italy*
[4]*MOE Key Laboratory of Cell Proliferation and Differentiation, School of Life Sciences and MOE Engineering Research Center of Regenerative Medicine, School of Basic Medical Sciences, State Key Laboratory of Natural and Biomimetic Drugs, Peking University, Beijing, China*
[5]*Health Science Center, Peking-Tsinghua Center for Life Sciences, Peking University, Beijing, China*

Background
Induced pluripotent stem cells (iPSCs) can be differentiated into functional β cells, offering a promising strategy for cell replacement therapy in type 1 diabetes (T1D). A recent advance, chemical reprogramming, enables non-integrative conversion of adult somatic cells into pluripotent stem cells using small molecules that modulate signaling and epigenetic pathways (doi: 10.1038/s41586-022-04593-5). Compared with transcription factor–based methods, this strategy offers improved safety, reversibility, scalability, and compatibility with GMP manufacturing. Here, we applied this strategy to fibroblasts from a person with T1D, generated chemically induced iPSCs (ciPSCs), differentiated them into β cells, and assessed their functionality and cryopreservation potential for translational use.

Methods
Patient-derived fibroblasts were expanded from a skin biopsy, validated (karyotype, Short Tandem Repeats, Mycoplasma testing), and reprogrammed using the BeiCell™ Human Chemical Reprogramming Kit 2.0. ciPSC identity and pluripotency were confirmed by flow cytometry and trilineage differentiation. Beta cell differentiation followed a 7-stage protocol adapted from Barsby et al. (DOI: 10.1016/j.xpro.2022.101711), with spheroid aggregation at the pancreatic progenitor stage. Marker expression (OCT4, PDX1, NKX6.1, INS) was tracked by flow cytometry, and glucose-stimulated insulin secretion (GSIS) was evaluated by dynamic perifusion assays. Mature ciPSC-β cells were cryopreserved (CryoStor®), thawed, and analyzed for viability and reaggregation.

Results
Two stable ciPSC lines (DRI4#1, DRI4#2) were generated, exhibiting genomic stability, pluripotency, and efficient differentiation into definitive endoderm. Progressive expression of PDX1, NKX6.1, and insulin was observed throughout maturation, with glucose-responsive insulin secretion in both lines. Cryopreserved cells retained viability, reaggregated efficiently, and maintained glucose responsiveness with increased insulin expression three days post-thaw. DRI4#1 displayed slightly higher differentiation efficiency.

Conclusions
Chemical reprogramming of T1D fibroblasts yields stable, high-quality ciPSC lines

capable of differentiating into functional, glucose-responsive β cells. These cells can be cryopreserved without loss of function, supporting their suitability for scalable manufacturing and clinical translation. Ongoing studies are assessing in vivo functionality and exploring blood-derived chemical reprogramming as a faster, safer, and patient-specific route toward clinical-grade autologous β-cell therapy.

OP14 - METABOLOMIC PROFILING OF PANCREAS GRAFTS PRESERVED BY OXYGENATED HYPOTHERMIC MACHINE PERFUSION

Mohamed Elzawahry[1], Sadr Shaheed[1], John Fallon[1], Alexander Sagar[1], Peter Friend[1], Rutger Ploeg[1], James Hunter[1]

[1]*Nuffield department of Surgical Sciences, University of Oxford, Oxford, United Kingdom*

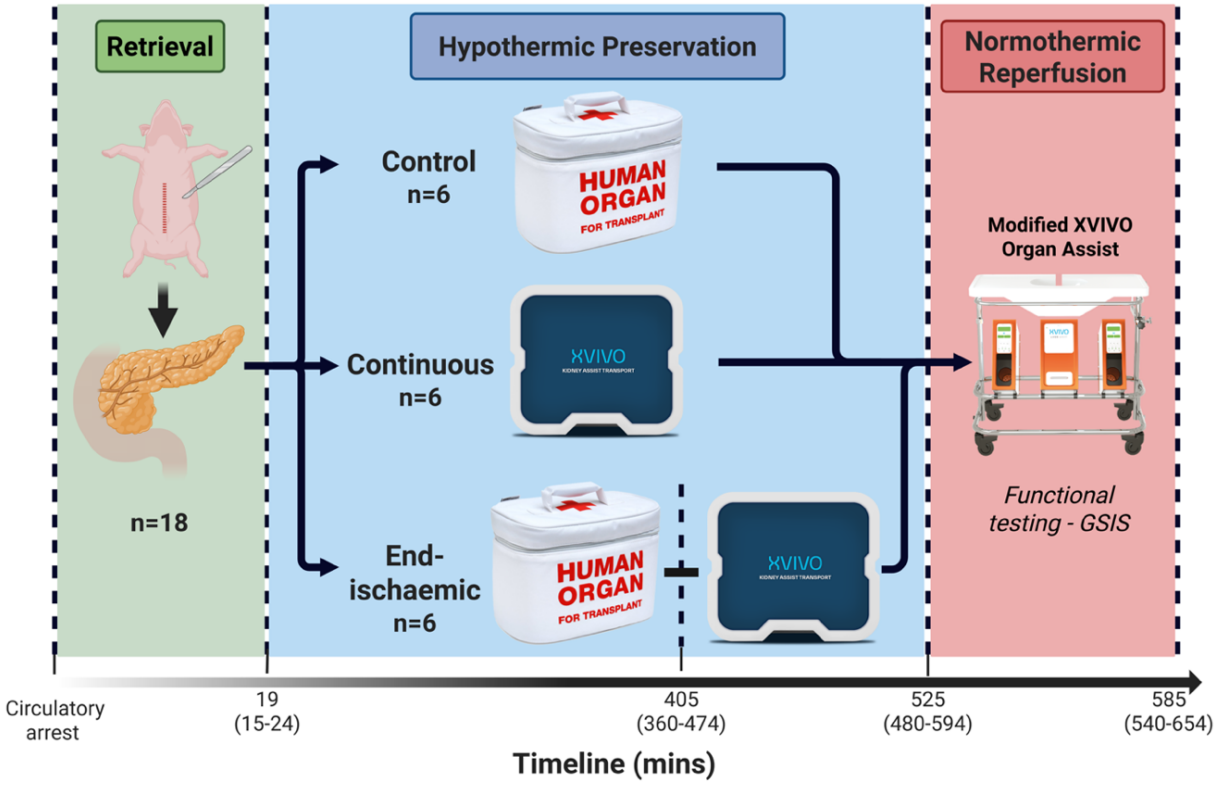
Background

Ischaemia–reperfusion injury (IRI) is a key factor in early morbidity and graft loss after pancreas transplantation and significantly affects the islet yield and quality after isolation. Oxygenated hypothermic machine perfusion ($HMPO_2$) has been shown to mitigate the consequences of IRI in liver and kidney preservation and is promising preclinically in pancreas preservation. The metabolic mechanisms underlying the benefit of $HMPO_2$ are poorly defined. This study aimed to highlight the key metabolites and pathways involved using metabolomic profiling.

Methods

18 porcine pancreases, with 19 minutes of warm ischaemia, were preserved in three groups (n=6): group 1: 8 hours of static cold storage (SCS), group 2: 6 hours of SCS followed by 2 hours of $HMPO_2$ and group 3: 8 hours of $HMPO_2$, and then all groups were assessed by 60-minute normothermic reperfusion (NR) with whole blood. (Fig 1A)

A.



B.

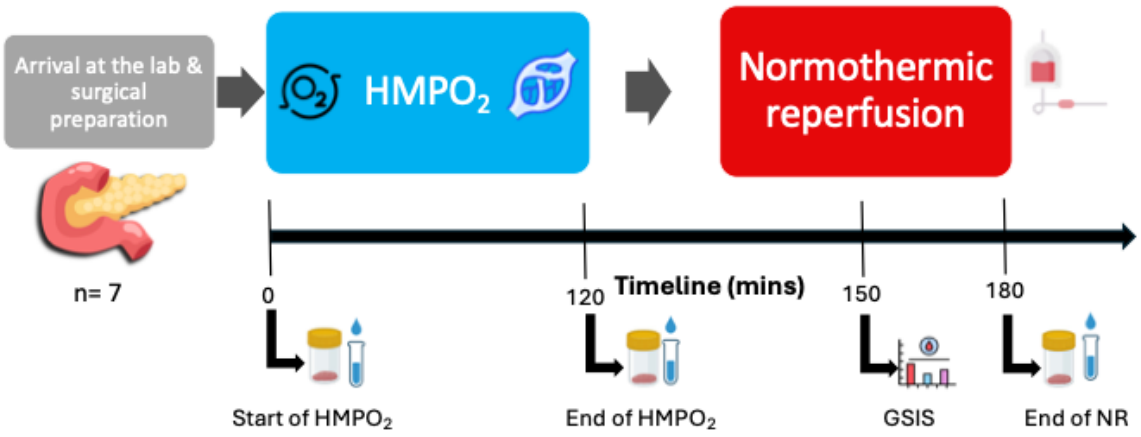


Figure 1 Flowchart of study design: **A**. Porcine. **B**. Human

Human validation cohort: seven pancreases declined for transplantation arrived in SCS, underwent 2h $HMPO_2$ followed by 60-minute NR. (Fig 1B)

Tissue samples were collected at start of cold preservation (T1), end of cold preservation (T2), and end of NR (T3) for untargeted metabolomics analysis using liquid chromatography-mass spectrometry (LC-MS).

Results

Key porcine tissue metabolic findings included:

Succinate, a mitochondrial marker of ischaemia, increased during SCS and decreased during $HMPO_2$.

Malate, a TCA metabolite, was consumed during $HMPO_2$ relative to SCS.

S-adenosylmethionine was lower in continuous $HMPO_2$ than SCS, indicating methylation demand.

L-cystine, a glutathione precursor, was lower in $HMPO_2$ than SCS.

Human graft metabolite trends mirrored the porcine $HMPO_2$ groups, supporting translational relevance.

Conclusion

Compared with SCS, $HMPO_2$ was associated with promising changes in key metabolites involved in energy metabolism and respiration. This supports that oxygen delivery during $HMPO_2$ sustains the residual metabolism under hypothermia and may mitigate IRI. Further targeted metabolomics analyses and larger human experiments can validate these findings.

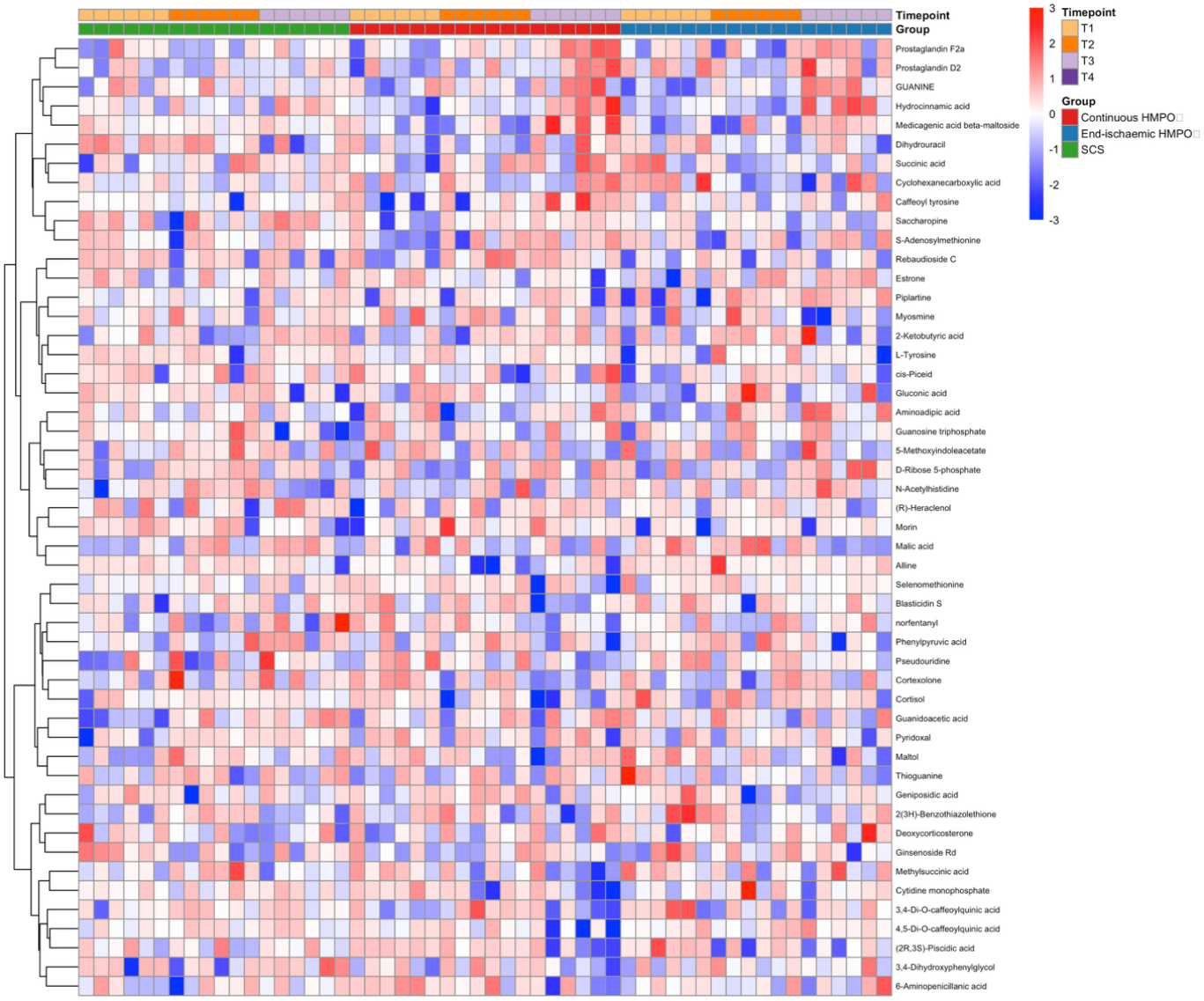


Figure 2 Heatmap of the top 50 metabolites in the porcine tissue samples.

OP15 - MHC-I DEFICIENCY GRAFTED ISLETS MIGHT NOT BE SUSCEPTIBLE TO MISSING SELF-INDUCED NK CELL REJECTION IN VIVO

Houying Cheng[1], Virginie Mathias[1 2], Luhan Revest[1], Thierry Walzer[1], Helena Paidassi[1], Olivier Thaunat[1 3]

[1]*CIRI, Centre International de Recherche en Infectiologie, Université de Lyon, Inserm U1111, Université Claude Bernard Lyon 1, CNRS UMR5308, ENS de Lyon, Lyon, France*
[2]*Établissement français du sang, Laboratoire HLA Rhône, Décines-Charpieu, France*
[3]*Hôpital Edouard Herriot, Service de transplantation, néphrologie et immunologie clinique, Lyon, France*

Background
Type 1 diabetes (T1D) results from the destruction of insulin-producing β cells by autoreactive $CD8^+$ T cells. Islet transplantation can restore glycaemic control, but its long-term success is limited by recurrent T1D and T cell–mediated rejection. To protect transplanted β cells from both auto- and allo-reactive $CD8^+$ T cells, MHC-I downregulation has been proposed. However, reducing MHC-I expression may expose the graft to natural killer (NK) cell–mediated damage. Indeed, our lab recently demonstrated that the failure of graft endothelial cells to deliver MHC-I dependent inhibitory signals (i.e. “missing self”), activates circulating NK cells and leads to microvascular rejection. However, transplanted islets are revascularized by the recipient’s endothelium and it remains unclear whether MHC-I–deficient β cells are also vulnerable to missing self-induced NK cell–mediated injury.

Methods
The human β-cell line EndoC-BH1 was genetically edited using CRISPR-Cas9 to suppress MHC class I (MHC-I) expression. To assess this phenomenon in vivo, streptozotocin-induced diabetic C57BL/6 mice were transplanted intraportally with islets isolated from either wild-type (WT) or MHC-I–deficient (B2MKO) syngeneic donors. Graft survival was monitored by measuring blood glucose levels.

Results
In co-culture experiments with primary human NK cells, MHC-I–deficient EndoC-BH1 cells were rapidly lysed, in contrast to wild-type (WT) cells, indicating heightened susceptibility to missing self-induced NK cell–mediated cytotoxicity in vitro.

Surprisingly, and in contrast to the in vitro findings, syngeneic B2MKO islets were not rejected, even after in vivo NK cell priming with poly(I:C).

Conclusions
Although MHC-I–deficient β cells are susceptible to missing-self–induced NK cell–mediated killing in vitro, this response does not appear to occur in vivo. Our findings suggest that cytotoxic NK cells remain largely confined to the circulation and do not efficiently access the interstitial niche where β cells engraft. Ongoing histological analyses and additional experiments are focused on elucidating the molecular mechanisms underlying this spatial restriction.

These insights contribute to a deeper understanding of innate immune surveillance in islet transplantation and may inform strategies to enhance graft survival and transplantation outcomes.

OP16 - A VASCULARIZED ISLET ON A CHIP (VIOC)

Ben Hansen[1], Luana Osório[2], Victoria Salem[1 2]

[1]*Department of Bioengineering, Imperial College London, London, United Kingdom*
[2]*Department of Diabetes, School of Cardiovascular and Metabolic Medicine and Sciences, King's College London, London, United Kingdom*

Background
Understanding islet biology is critical to the development of a cure for diabetes. However, as the pancreas cannot be biopsied nor functionally imaged, current experimentation largely occurs upon isolated islets, kept in static culture or fixed within microfluidic systems. These systems struggle to support the highly-metabolically-active islets for longer than 48 hours. Organ-on-Chip (OOC) technologies promise to support long term, complex tissue culture in controlled microfluidic environments. However, in vitro vascularisation of endocrine tissue remains a grand challenge. Here we present the development of a Vascularized Islet-on-Chip (VIOC) platform capable of supporting islet viability and maintaining function for longitudinal interrogation.

Methods
Chips were manufactured in-house from PDMS using 3D-printing. Perfusable microvessel networks were developed using a ratio of 5:1 human umbilical vein endothelial cells (HUVECs) to human adipose-derived mesenchymal stem cells (MSCs) in fibrin hydrogels. Microvessel networks were visualised over time using CMFDA dye, FITC dextran, and microbead perfusion. Chips were also loaded with mouse islets expressing GCaMP6f (ins-1 driven) as a proxy measure of insulin secretion. Subsequently bespoke computational analysis algorithms were applied to dextran images to generate vessel network morphological statistics and to islet calcium traces to determine intra islet beta cell connectivity and functionality.

Results
Perfusable microvessel networks are reproducibly formed with HUVEC/MSC mixes and reliably achieve perivascularisation of islets on chip. Functional readouts from islets within fibrin hydrogels alone decline at the same rate as those in static culture (<48 hours), but islets co-cultured within vascular networks on the chip retain healthy calcium readouts for 5 days. Furthermore, islets that have begun to degrade in static culture after 5 days regain healthy islet calcium and connectivity readouts when subsequently cultured on a vascularised chip. Vessel networks grown in the presence of islets are more richly vascularized (higher vessel area fraction) and feature thicker, more permeable vessels. Engineered tissue from the chip has been optimised into tissue slices for advanced histological and 'omics analyses.

Conclusions
We describe a vascularised islet on chip platform, demonstrating that reconstructed ECM in conjunction with a perfusable vascular microenvironment enhances islet viability, thereby prolonging their utility for longitudinal experimentation.

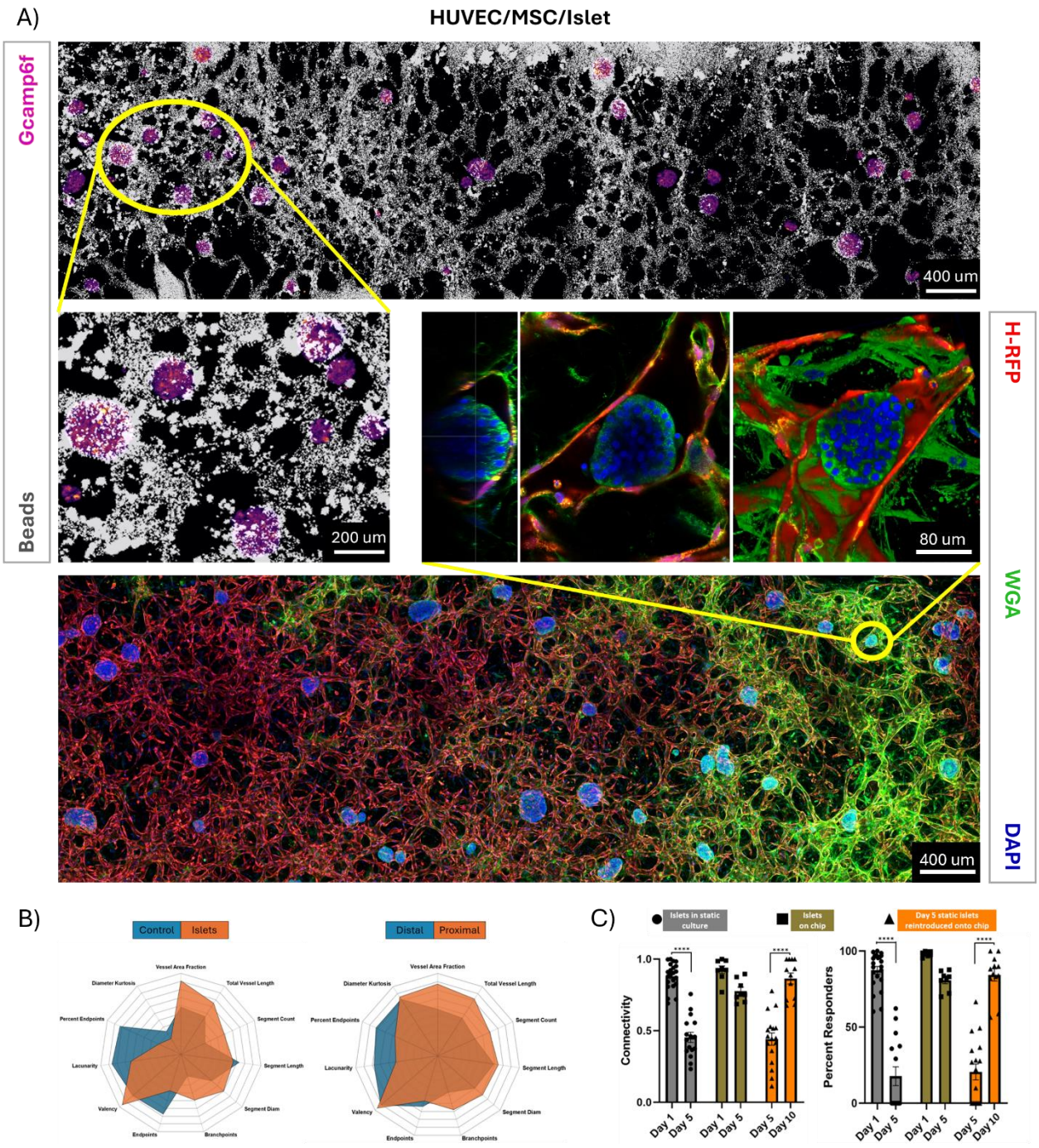


Figure 1. A) A vascularized islet-on-chip. B) Macro and micro-vascular changes in presence of islets. C) VIOC platform maintains and even restores islet functionality.

OP17 - SENOLYTIC PRECONDITIONING OF AGED DONOR PANCREAS IMPROVES ISLET ISOLATION AND TRANSPLANT OUTCOMES

Jan Kriz[1], Eva Fabryova[1], Lydie Plecita[2], Peter Girman[1], Blanka Holendova[2], Soňa Stemberkova-Hubackova[1]

[1]*Institute for Clinical and Experimental Medicine, Diabetes Center, Prague, Czech Republic*
[2]*Institute of Physiology, Czech Academy of Sciences, Prague, Czech Republic*

Background
Pancreatic islet transplantation is constrained by the limited availability of donor organs yielding sufficient numbers of high-quality islets. Appropriate therapeutic interventions may enable the use of additional, so-called marginal pancreases for islet isolation. Donor tissues from aged or inflamed pancreases, further affected by dysregulation following brain death and preservation, often accumulate senescent cells that impair regeneration and function. Treatment of islets with MitoTam, a novel senolytic compound, may improve tissue integrity and enable successful islet isolation from otherwise unsuitable pancreases.

Methods
17 month-old Lewis male rats were treated intraperitoneally with the senolytic drug MitoTam (MT; 2 mg/kg) or vehicle (corn oil; CO) twice weekly for four weeks. 3 month-old rats served as young controls. Islets (LO) were isolated, cultured overnight, and transplanted into diabetic Lewis recipients (3 months old; STZ 60 mg/kg, i.p.; 4 islets/g body weight). Recipients were divided into three groups: LO from treated donors (n = 4), LO from untreated donors (n = 4), and LO from young donors (n = 4). Animals were monitored for six months (blood glucose, weight, IVGTT).

Results
The number of senescent cells, along with markers of fibrosis and inflammation, was significantly elevated in islets from aged donors. Treatment with MitoTam reduced these markers to levels comparable to those in young grafts, whether applied in vivo to donors or in vitro to isolated islets. Consequently, recipients of MitoTam-treated islets achieved normoglycemia earlier and maintained better graft function for six months post-transplantation, whereas untreated aged islets exhibited a progressive decline in function over time.

Conclusions
Our findings suggest that senolytic therapy can rejuvenate aged pancreatic tissue and enhance the quality and yield of islets for transplantation, potentially expanding the donor pool for clinical islet transplantation.

Supported by
Czech Health Science Foundation (NW24-06-00021), Programme EXCELES-LX22NPO5104- Funded by the European Union – Next Generation EU, CZ-DRO (IKEM, IN 00023001).

OP18 - GENERATION OF HUMAN STEM CELL-DERIVED ALPHA CELLS WITH IMPAIRED GLUCAGON REGULATION IN TYPE 2 DIABETES

Shadab Abadpour[1 2], Chencheng Wang[1 3], Hanne Scholz[1 2]

[1]*Department of Transplant Medicine and Institute for Surgical Research, Oslo University Hospital, Oslo, Norway*
[2]*Hybrid Technology Hub, Center of Excellence, University of Oslo, Oslo, Norway*
[3]*Shanghai Longke Pharmaceutical Co, shanghai, China*

Background
Glucagon produced by pancreatic alpha cells is crucial in maintaining glucose homeostasis. However, individuals with type 2 diabetes (T2D) experience hyperglucagonemia both when fasting and after meals, leading to increased glucose production in the liver and exacerbating the hyperglycemia of this condition. Despite the longstanding awareness of this phenomenon, scientific inquiry into the functioning of alpha cells, particularly in the context of T2D, has historically received less attention compared to research on beta cells and insulin.

Methods
Here, we developed a protocol for generating alpha cells from human stem cells (SC-alpha) that exhibit impaired regulation of glucagon secretion while maintaining insulin secretion function, which may be useful for modeling type 2 diabetes (T2D) and drug development in vitro.

Results
In a 6-stage stepwise planar differentiation process, we obtained pancreatic progenitor cells (Stage 4), with over 50% positive for PDX1 and fewer than 10% positive for NKX6.1. The ARX protein that maintains alpha cell identity was activated and detectable at this stage. By targeting the cytoskeleton with latrunculin A at the first 24 hours of stage 5, we could generate >30% percent of Glucagon+ cells at day 7 of stage 5. Continuing differentiation until day 7 of Stage 6, and then suspending the cells in ultralow attachment cell culture plates, we obtained >55% of Glucagon+ cells, and >40% of cells were positive for C-peptide. Under 20 mM of glucose stimulation, these SC-alpha cell clusters showed a significant increase in insulin secretion (Insulin secretion index=1.14, $P<0.01$), and a significant increase in glucagon secretion (Glucagon secretion index=2.10, $P<0.05$). In contrast, the detected glucagon secretion from stem cell-derived beta cell clusters following the published protocol was negligible and nonsignificant (Glucagon secretion index=0.91, $P>0.05$).

Conclusions
Overall, the resulting SC-alpha cell clusters represented impaired regulation of glucagon secretion ability while still retaining a normal but inefficient insulin secretion ability, which might play a role in T2D research.

OP19 - GRADIENT SEPARATION OF HUMAN ISLETS OF LANGERHANS USING THE XTRA™ AUTOTRANSFUSION SYSTEM

Hanne Scholz[1 2], Arwa Saleh[3], Ragnhild Fjukstad[4], Marina Katavic[4], Lina Berglind[3], Kristin af Geijerstam[3], Sofie Ingvast[2], Olle Korsgren[2]

[1]*Department of Transplant Medicine and Section for Cellular Therapy, Oslo University Hospital, Department of Immunology, Genetics, and Pathology, Uppsala University, Uppsala, Sweden, Oslo, Norway*
[2]*Department of Immunology, Genetics, and Pathology, Uppsala University, Uppsala, Sweden*
[3]*Department of Clinical Immunology and Transfusion Medicine, Uppsala University Hospital, Uppsala, Sweden*
[4]*Department of Transplant Medicine and Section for Cellular Therapy, Oslo University Hospital, Oslo, Norway*

Background

The Nordic Network for Clinical Islet Transplantation (NNCIT) has conducted over 550 islet transplantations and 3,000 human islet isolations since 2002, contributing to both clinical applications[1-3], and research initiatives[4]. NNCIT operates two human islet isolation laboratories at Uppsala University Hospital and at Oslo University Hospital.

In 2008, we established a closed automated purification system for human islet separation[5], which successfully reduced isolation time while maintaining islet quality[6]. However, in 2020, Terumo Blood and Cell Technologies announced that the COBE 2991 cell processor would be phased out in EMEA countries (Europe, Middle East, and Africa) by the end of 2025.

Methods

We generated a purification step of the digestived pancreas tissue utilizing the Xtra™ Autotransfusion System (LivaNova) alongside computer-controlled pumps, as described in our earlier research[5]. In our procedures, we utilized an Optiprep working solution with a density of 1.1700 g/mL (heavy) and a UW working solution with a density of 1.045 g/mL mixed with the digestive tissue (light). These solutions were combined to create a density gradient in a 225 mL bowl during continuous centrifugation. This process facilitated tissue collection from light to heavy density, consequently achieving collections of high to low purity of islets.

Results

evaluate the new method, we compared the purifying effect of the gradient separation with that of the traditional COBE 2991 system. Results showed that dynamic glucose-stimulated insulin secretion indicated comparable stimulation indexes (SI > 5.8) and purity. No significant differences were observed in the outcomes of islet equivalents (IEQ) between the two systems.

Conclusions

In summary, we suggest that the new gradient separation method can effectively replace the purification step currently performed by the COBE 2991, offering a promising alternative for islet isolation processes moving forward.

OP20 - GRAFT PANCREATITIS AFTER PANCREAS TRANSPLANTATION: APPLICATION OF THE INTERNATIONAL STUDY GROUP FOR PANCREATIC SURGERY (ISGPS) DEFINITION OF POST-PANCREATECTOMY ACUTE PANCREATITIS

Valentina Andreasi[1], Stefano Partelli[2], Lucrezia Furian[3], Oriana Ciacio[4], Matteo Santangelo[3], Rossana Caldara[5], Valentina Tomajer[6], Arianna Bertuol[3], Davide Catarinella[5], Alessandra Ida[4], Antonio Sa Cunha[4], Paolo Rigotti[1], Lorenzo Piemonti[7], Massimo Falconi[1]

[1]*San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Pancreas and Transplant Surgery Unit, Milan, Italy*
[2]*IRCCS Ospedale San Raffaele, Chirurgia del Pancreas e dei Trapianti, Milan, Italy*
[3]*Padova University Hospital, Kidney and Pancreas Transplant Surgery Unit, Padova, Italy*
[4]*Hôpital Universitaire Paul Brousse, Université Paris-Saclay, Centre Hépato-biliaire, Villejuif, France*
[5]*San Raffaele Scientific Institute, Regenerative and Transplant Medicine Unit, Milan, Italy*
[6]*San Raffaele Scientific Institute, Pancreas and Transplant Surgery Unit, Milan, Italy*
[7]*San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Regenerative and Transplant Medicine Unit, Diabetes Research Institute, Milan, Italy*

Background

Despite graft pancreatitis being a clinically relevant complication after pancreas transplantation (PT), a universally accepted definition is lacking. Similarly, post-pancreatectomy acute pancreatitis was long undefined, until the International Study Group on Pancreatic Surgery (ISGPS) recently validated a definition based on clinical, biochemical and radiological criteria. Aim of this study was to apply the ISGPS definition to a multicenter cohort of PT recipients, to define post-transplant acute pancreatitis (PTAP) and assess its association with postoperative outcomes.

Methods

Consecutive patients who underwent PT at San Raffaele Hospital (Italy), Padova University Hospital (Italy) and Paul Brousse Hospital (France) between 2010 and 2024 were included. PTAP was defined according to ISGPS criteria as follows: 1) Postoperative hyperamylasemia for ≥48 hours; 2) Findings consistent with PTAP on contrast-enhanced CT performed within 30 days postoperatively. All multivariable analyses were adjusted for centre.

Results

Overall, 432 patients were included. The ISGPS definition was applicable to 416 patients, as 16 required graft pancreatectomy within postoperative day (POD) 1 for thrombosis. Prolonged POH occurred in 196 patients (47%) and CE-CT was performed in 371 cases (89%). PTAP was diagnosed in 86 cases (21%). POD1-2 amylase levels were significantly higher in patients with radiological pancreatitis compared to the remaining study cohort ($p<0.001$) (Fig. 1). Severe postoperative complications (Clavien-Dindo ≥3) occurred in 38% of patients with PTAP (n=33), compared to 24% of patients without (n=79) ($p=0.008$). PTAP was identified as the only independent predictor of severe postoperative complications (OR 2.482, $p=0.001$). The median length of hospital stay (LOS) was longer in the PTAP group (25 vs. 15 days, $p<0.001$). PTAP (OR 4.005, $p<0.001$) and graft rejection before discharge (OR 16.472, $p=0.001$) independently predicted a prolonged LOS (>23 days). Cold ischemia time (CIT) (OR 1.004, $p<0.001$) was the only independent determinant of PTAP. Death-censored graft survival was significantly worse in patients with PTAP ($p<0.001$) (Fig. 2). Independent determinants of graft loss included donor type (DCD, HR 8.207, $p=0.008$), CIT (HR 1.004, $p=0.005$), transplant type (PAK/PTA, HR 3.227, $p=0.001$), PTAP (HR 3.761, $p<0.001$), thrombosis (HR 2.731, $p<0.001$) and graft rejection (HR 3.763, $p<0.001$).

Conclusions

PTAP, as defined by the ISGPS, is a common clinical finding, occurring in nearly one-quarter of patients undergoing PT. This definition appears applicable in the PT setting, as it identifies a clinically relevant condition associated with prolonged hospitalization, major postoperative complications and worse graft survival.

Figure 1. Comparison of postoperative day (POD) 1 and 2 serum amylase levels, expressed as multiples of the institutional upper limit of normal (ULN), between patients with and without radiological graft pancreatitis.

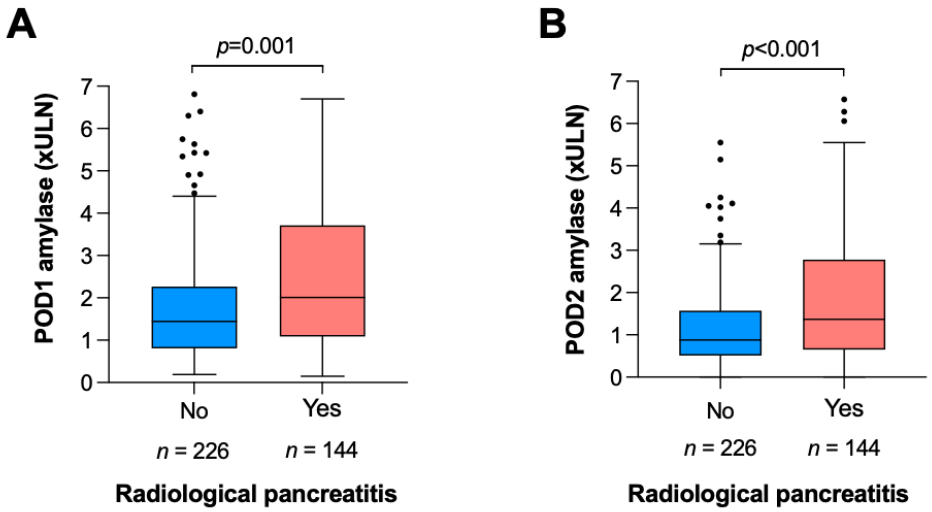
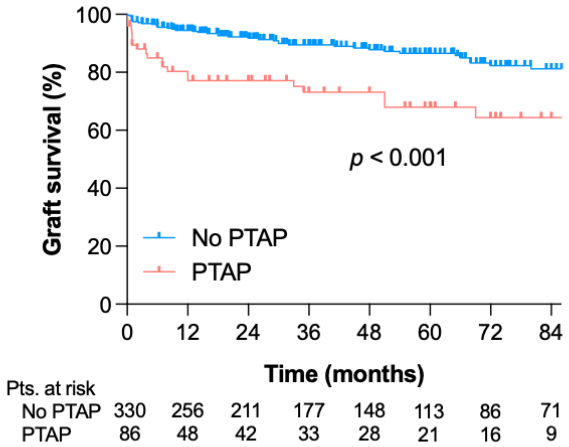


Figure 2. Comparison of death-censored graft survival between patients with and without post-transplant acute pancreatitis (PTAP



OP21 - THE IMPACT OF TIME TO DEATH IN CIRCULATORY DEATH DONORS AND PANCREAS ISLET ISOLATION OUTCOMES

Rhys Pook[1 2], Samuel Tingle[1 2 3], Abdullah Malik[1 2 3], Georgios Kourounis[1 2 3], Andrew Sutherland[4], Claire Counter[5], David Van Dellen[6], Angeles Maillo Nieto[3], James Shaw[1 3], Lora Irvine[7], Rebecca Spiers[8], Guo Cai Huang[9], Paul Johnson[10], John Casey[4], Steven White[2 3 5]

[1]*Translational and Clinical Research Institute, Newcastle University, Newcastle Upon Tyne, United Kingdom*
[2]*NIHR Blood and Transplant Research Unit, Newcastle University and Cambridge University, Newcastle Upon Tyne, United Kingdom*
[3]*Institute of Transplantation, Freeman Hospital, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, United Kingdom*
[4]*Royal Infirmary of Edinburgh, Edinburgh, United Kingdom*
[5]*NHS Blood and Transplant, Bristol, United Kingdom*
[6]*Manchester University NHS Foundation Trust, Manchester, United Kingdom*
[7]*Islet Cell Laboratory, Scottish National Blood Transfusion Service, Edinburgh, United Kingdom*
[8]*Islet Transplant Research Group, Nuffield Department of Surgical Sciences, University of Oxford, Oxford, United Kingdom*
[9]*Department of Diabetes, School of Life Course Sciences, Faculty of Life Sciences and Medicine, King's College London, London, United Kingdom*
[10]*Oxford Centre for Diabetes, Endocrinology and Metabolism, University of Oxford, Oxford, United Kingdom*

Background
Islet transplantation is an established treatment for a select cohort of patients with diabetes. Donation following circulatory death (DCD) entails varying agonal/ischemic times. We aimed to assess the impact of these time periods on the outcome of islet isolation.

Methods
Population cohort study of islet isolations from DCD pancreases (2009- 2023). Regression models with restricted cubic splines (RCS) for non-linear modelling, evaluated associations between ischemic intervals and islet outcomes, adjusted for key factors.

Results
153 pancreas isolations were included. Median islet yield was 235,000 IEQ (IQR: 138 – 347), with a median viability of 80.0% (IQR:75.0 – 85.0) and 50.3% met transplantation release criteria. Median time-to-death (TTD) was 14 minutes (IQR:10.5–18.5). No significant associations were observed between TTD, warm ischemia time or functional warm ischemia time and islet viability, yield or purity ($p>0.20$ for all). RCS analyses also showed no significant non-linear effects, $p>0.10$ for all (**Figure 1**). However, across all models pancreatectomy time consistently predicted lower islet viability ($p=0.009–0.012$), highlighting the significance of rapid retrieval. Increasing cold ischemia time was associated with a lower chance of the islet isolation reaching overall release criteria. Paradoxically, those with very short CIT had significantly inferior islet viability.

Conclusions
Consistent with our recent work in whole organ pancreas transplantation, TTD

does not impact on islet isolation outcomes and prolonged donor TTD should not be seen as a barrier to islet isolation. In contrast, prolonged pancreatectomy time was associated with inferior isolation outcomes, highlighting the importance of rapid retrieval.

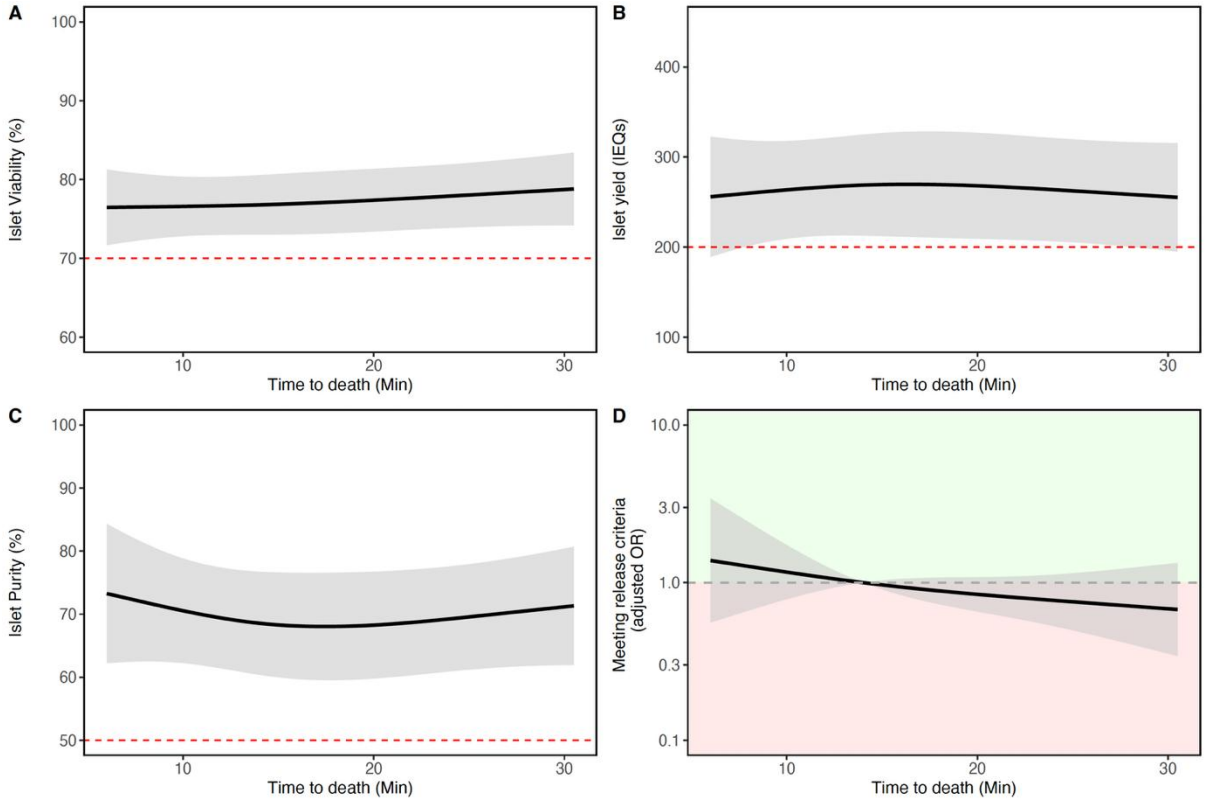


Figure 1 - Restricted cubic spline models of time to death's impact on islet isolation outcomes.

OP22 - EX-SITU MULTI-PARAMETRIC MAGNETIC RESONANCE IMAGING ASSESSMENT OF HUMAN PANCREAS GRAFTS AND THE EFFECTS OF OXYGENATED HYPOTHERMIC MACHINE PERFUSION

Mohamed Elzawahry[1], Aaron Axford[2], Alexander Daniel[3], Sadr Shaheed[1], Letizia Lo Faro[1], Jenny Collins[1], Christine Flaxman[4], Peter Friend[1], Rutger Ploeg[1], Nicola Dyson[5], James Shaw[5], Sarah Richardson[4], Damian Tyler[2], Susan Francis[3], James Hunter[1]

[1]*Nuffield department of Surgical Sciences, University of Oxford, Oxford, United Kingdom*
[2]*Oxford Centre for Clinical Magnetic Resonance Research, University of Oxford, Oxford, United Kingdom*
[3]*University of Nottingham, Nottingham, United Kingdom*
[4]*University of Exeter, Exeter, United Kingdom*
[5]*Diabetes Regenerative Medicine Group, Translational and Clinical Research Institute, Newcastle University, Newcastle, United Kingdom*

Background

About half of pancreases are declined for transplant after surgical retrieval. There is no validated objective pancreas graft assessment. Multiparametric magnetic resonance imaging (mp-MRI) is a non-invasive technique that can measure clinically-relevant parameters for pancreas grafts, such as steatosis and oedema. Oxygenated hypothermic machine perfusion ($HMPO_2$) is a novel method for pancreas preservation prior to transplantation or islet isolation. This study evaluated mp-MRI feasibility for donor pancreases preserved in static cold storage (SCS) and its ability to evaluate the effects of $HMPO_2$-preservation.

Methods

Eight human pancreases, declined for transplantation, were enrolled. After surgical preparation, two pancreases kept in SCS were used for protocol development (Fig 1) and six underwent 6 hours of $HMPO_2$ with mp-MRI assessment before and after $HMPO_2$ while in SCS (Fig 2). The mp-MRI protocol included: T_2* mapping to quantify residual blood; diffusion-weighted imaging to measure apparent diffusion coefficient (ADC) to assess oedema; and Dixon MRI to map fat fraction (FF). AI-driven histological quantification of fat and wet-to-dry ratio were used to quantify steatosis and oedema.

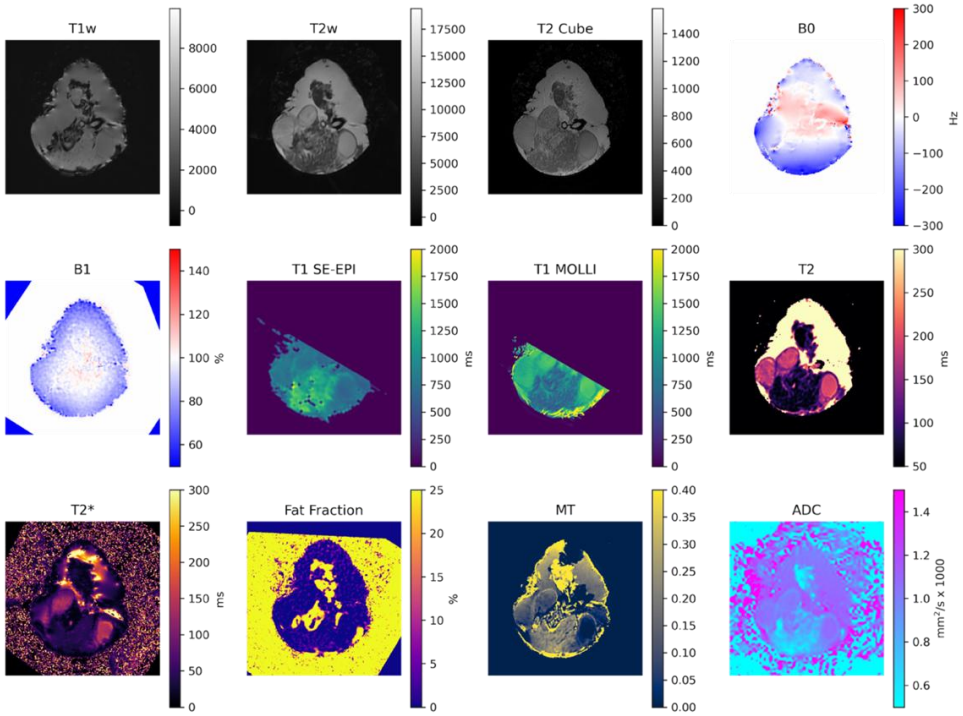


Figure 1 Representative example of the multi-parametric MRI protocol for an ex-situ human pancreas

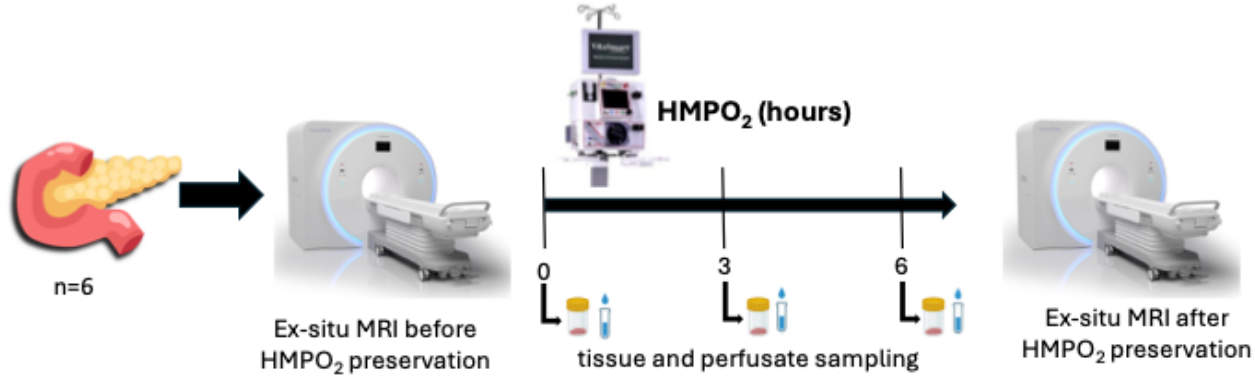


Figure 2 Flowchart of study design

Results

mp-MRI acquisition of *ex-situ* organs was feasible within 1 hour while maintaining clinical-standard hypothermia. In the six $HMPO_2$-preserved pancreases ADC and wet-to-dry ratio trended up but did not show a significant increase in tissue oedema. $HMPO_2$ improved microvascular flushing measured by increased T_2* indicating a reduction of residual blood. FF mapping revealed inter-organ variability, with good correlation between MRI and histological fat content.

Conclusion

Ex-situ mp-MRI of pancreases preserved in SCS is technically feasible and provides objective assessment of oedema, steatosis, and microvascular flushing and insights into $HMPO_2$ effects. These findings support the potential role of mp-MRI as a non-invasive pancreas graft assessment tool.

OP23 - DEVELOPMENT OF CELL-SURFACE FLOW CYTOMETRY ASSAYS FOR BENCHMARKING PLURIPOTENT STEM CELL-DERIVED ISLET THERAPIES

Jacqueline Schiesser[1 2 3], Meg Elliott[1 2 3], Nazneen Adenwalla[1 2], Edouard Stanley[1 2 3]

[1]*Murdoch Children's Research Institute, Melbourne, Australia*
[2]*The Novo Nordisk Center for Stem Cell Medicine (ReNEW), Murdoch Children's Research Institute, Melbourne, Australia*
[3]*Department of Paediatrics, University of Melbourne, Melbourne, Australia*

Background

Type 1 Diabetes (T1D) is an autoimmune disorder in which the insulin-secreting beta cells of the pancreas are destroyed, leaving people unable to regulate the level of glucose in their blood. Treatment with insulin replacement, whilst lifesaving, is burdensome to the individual, their family and the health care system. Near normal glycaemic control can be achieved by replacing the lost insulin-secreting beta cells using either whole pancreas or islet transplantation. However, the need for chronic immunosuppression, combined with a lack of donor organs, limit these treatments to a small group of T1D individuals with impaired hypoglycaemic awareness and/or severe hypoglycaemic events.

Stem cell-derived islets (sc-islets) generated from pluripotent stem cells (PSCs) are an alternative to donor-derived islets, potentially providing an unlimited number of insulin-producing cells for transplantation. Recent studies have demonstrated that transplantation of sufficient numbers of sc-islets allow for recipients to achieve insulin-independence. To date, recipients in these trials have been treated with extensive immunosuppression – potentially restricting the number of individuals that could benefit from this therapy. Alternatively, as PSC lines can be derived from any individual, this in theory provides a pathway to generate autologous sc islets for transplant – potentially reducing the need for immunosuppression. One hurdle for the use of autologous sc-islets is the widely recognised variability in the capacity of different PSC lines to differentiate towards specific fates. To address this, we are developing flow cytometric assays that can be used for both benchmarking differentiation outcomes and, in the future, as a basis for isolating target pancreatic cell types.

Methods

Using single-cell RNA sequencing data from differentiating PSCs, we identified novel cell surface markers that demarcate subpopulations of cells contained with pancreatic differentiation cultures. We have combined these novel markers with those previously reported by others to generate a more granular picture of pancreatic differentiation towards the formation of sc-islets.

Results

We have identified a suite of novel cell surface markers that facilitate the characterization of pancreatic differentiation towards the formation of sc-islets. We show how these markers can be used in combination with known markers of pancreatic differentiation to identify subpopulations of cells contained with pancreatic differentiation cultures using flow cytometry.

Conclusions

Novel cell surface markers used in combination with flow cytometry enable a more detailed picture of pancreatic differentiation towards sc-islets. In the future, such flow cytometry panels could be used to monitor the progress of pancreatic differentiation and could also underpin cell purification strategies to facilitate the development of autologous sc-islets as a treatment for T1D.

OP24 - EX VIVO BIOENGINEERED XENO-AVATAR FOR TRACKING IMMUNE RESPONSES TO ISLET SURVIVAL AND FUNCTION

Alessia Neroni[1], Cataldo Pignatelli[1], Matteo Monieri[1], Francesco Campo[1], Ilaria Marzinotto[1], cristina Olgasi[2], Antonia Follenzi[2], Lorenzo Piemonti[1 3], Antonio Citro[1]

[1]*Diabetes Research Institute,IRCCS Ospedale San Raffaele, Milan, Italy*
[2]*Department of Health Sciences, School of Medicine, University of Piemonte Orientale, Novara, Italy*
[3]*Università Vita-Salute San Raffaele, Milan, Italy*

Background

Pancreatic endocrine disorders, including T1D and T2D, are rapidly increasing worldwide, emphasizing the need for advanced human-based models to investigate mechanisms and develop targeted interventions. However, the pancreas remains an inaccessible organ, limiting the ability to directly monitor disease progression. Current experimental models are insufficient, as they lack the complexity of the native human islet microenvironment, particularly the vascularized niche essential for physiological endocrine function. A major unmet need is the ability to monitor graft rejection. In this context, there is a pressing demand for an ex vivo, patient-specific platform that can serve as a functional “avatar” to simulate islet allo-xenotransplantation in diabetic patients. Such a model could enable the real-time assessment of immune cell infiltration, β-cell injury, and graft viability, serving as a predictive tool to personalize immunosuppressive strategies and improve transplant outcomes.

Methods

Vascularized Islet Organs (VIOs) were engineered using decellularized left lung lobes from rats, repopulated with neonatal pig islets (NPIs) and blood outgrowth endothelial cells (BOECs). Cell seeding was performed via the trachea, pulmonary artery, and pulmonary vein to ensure appropriate distribution and vascular integration. Customized bioreactors provided dynamic perfusion for a total of 14 days. The first 7 days (maturation phase, MP) were dedicated to cell engraftment and tissue maturation, while the following 7 days (testing phase, TP) were used to assess endocrine and vascular function under various experimental conditions. To model immune-mediated β-cell injury, VIOs were perfused with PBMCs syngeneic with BOECs, pre-activated through co-culture with pig splenocytes to mimic a xenogeneic immune response. β-cell damage was monitored by quantifying circulating levels of miR-375, a known surrogate marker of β-cell death. Immunofluorescence (IF) and confocal microscopy were employed to evaluate leukocyte trafficking and spatial interactions with the endothelial and islet compartments within the VIOs.

Results

Preliminary results indicated increased β-cell stress and death in VIOs co-cultured with pre-activated PBMCs, as suggested by a rapid increase in miR-375 levels immediately following leukocyte infusion. Confocal microscopy, at the end of the experimental period, showed evidence of leukocyte trafficking through the vascular network and infiltration into peri-islet zones. Human $CD3^+$ T cells were detected

within the tissue, and histological observations suggested early immune–islet interactions.

Conclusions

The ex vivo VIO model recapitulates key features of the physiological vascularized islet microenvironment, providing a perfused avatar system to assess immune responses against its endocrine counterpart. It may serve as a clinically relevant platform to investigate β-cell replacement strategies, screen therapeutic compounds, and guide immune-modulatory strategies in a preclinical setting.

OP25 - PANCREAS TRANSPLANTATION AFTER EUTHANASIA: COMPARATIVE ANALYSIS OF DCD-V, DCD-III AND DBD DONORS

Noor Alkemade[1], Paul van der Boog[1], Dries Braat[1], Sijbrand Hofker[2], David Lam[1], Robert Pol[2], Volkert Huurman[1], Andrzej Baranski[1]

[1]*Leiden University Medical Center, Leiden, Netherlands*
[2]*University Medical Center Groningen, Groningen, Netherlands*

Background
Pancreas transplantation remains a rare but important treatment option for patients with complicated diabetes. Given the shortage of viable donor organs, Donation after Circulatory Death (DCD) donors have shown to be a viable source. This study provides the first comparative analysis of pancreas transplantation between DCD Type III (controlled cardiac arrest), DCD Type V (euthanasia) and Donation after Brain Death (DBD).

Method
We conducted a retrospective cohort study using data from the Dutch Transplant Registry, including all pancreas transplantations from DCD-V, DCD-III and DBD donors between 2002 and 2024. Evaluated outcomes included organ allocation and utilization, transplant type, graft and patient survival, surgical complications, and metabolic function.

Results
Over a 22-year period in the Netherlands, 4,755 pancreases were offered, of which 517 were transplanted (DCD-III: 98; DCD-V: 19; DBD: 398). Donor age and BMI differed between groups ($p<0.01$). The utilization rate was higher for DBD (20.7%), and DCD-V donors (18.4%) compared with DCD-III donors (4.0%) ($p<0.01$). No significant differences were observed in 5-year graft or patient survival ($p=0.11$ and $p=0.52$, respectively). The first warm ischemia time was comparable between the DCD-III and DCD-V cohorts ($p=0.09$), whereas the second warm ischemia time differed ($p<0.01$). In simultaneous pancreas–kidney (SPK) transplants, dialysis post transplantation occurred more often in de DCD-III cohort, but no differences in creatinine levels, rejection rates, chronic transplant glomerulopathy, or chronic damage were observed. Interestingly, thrombosis occurred most frequently among DBD donors ($p<0.01$). HbA1c levels at 3-, 12-, and 36-months post-transplantation did not differ significantly between groups.

Conclusions
Pancreas transplants from DCD-V donors demonstrate comparable utilization and outcome to those from DCD-III and DBD donors. Further studies with larger cohorts are needed to confirm these findings.

OP26 - IMPLEMENTING BEST PRACTICE GUIDELINES IN AUTOLOGOUS ISLET TRANSPLANTATION THROUGH AN INTERNATIONAL SURVEY

Gioia Sgrinzato[1], Arianna Bertuol[1], Joana Ferrer-Fàbrega[2], Steven White[3], Marta Zanoletti[1], Charlotte Leseman[4], Caterina Di Bella[1], Lucrezia Furian[1]

[1]*Kidney and Pancreas Transplantation Unit, University Hospital of Padova, Padova, Italy*
[2]*Hepato-Biliary-Pancreatic Surgery and Liver and Pancreas Transplant Unit. Department of Surgery. Hospital Clinic of Barcelona, Barcelona, Spain*
[3]*Department of Hepatopancreatobiliary and Transplantation Surgery, Freeman Hospital, Newcastle upon Tyne, Tyne and Wear, United Kingdom*
[4]*Department of Surgery, Amsterdam UMC, Location University of Amsterdam, Amsterdam, Netherlands*

Background
Islet autotransplantation (IAT) following pancreatic surgery is an effective strategy to mitigate postoperative diabetes with good functional outcomes. Despite nearly five decades of clinical practice, consensus guidelines for IAT remain lacking with significant variations in islet isolation techniques and transplantation strategies. However, the expected rise in IAT indications and its broader implementation in the coming years highlights the need for standardized protocols. The aim of the present study was to assess current practices and indications for IAT across international expert centers.

Methods
A research group from the University of Padua, in collaboration with the Leiden University Medical Center (LUMC), developed a standard-of-care survey distributed to world-wide islet transplantation centers. The survey included 28 questions evaluating current IAT indications, pancreas processing methods, islet purification technique and protocols for islet infusion. The questionnaire was created using Microsoft Forms and distributed via email. The European Pancreas and Islet Transplant Association (EPITA) endorsed facilitated the dissemination of the survey in Europe, while the LUMC study group facilitated outreach worldwide. The survey was open for response from April 30th, 2025 to May 25th, 2025. Subsequently, the analysis of the collected data was conducted.

Results
Fifteen islet transplant centers completed the survey, with fourteen actively performing IAT. Topics of concordance were the procedural intervention, the presence and the use of on-site isolation islet laboratory, the average cold ischemia time for IAT procedure, the need of cold preservation solution, the pancreatic perfusion of collagenase in the reference specialized laboratory rather than in the OR, the intra-operative and post-operative heparin administration, and the monitoring of portal pressure. There was disagreement with respect to indications for IAT (except for chronic pancreatitis), the timing of islet infusion, the type of vascular flush utilized prior to islet processing, the need for islet purification, minimum and maximum volumes of islet infusion in a single procedure, heparin dosage and techniques of administration and finally splenic preservation at the time of TP.

Conclusions
Despite the limited sample size, this international survey reveals considerable

variability in clinical practice, highlighting a significant lack of standardized guidelines for IAT. These findings emphasize the need, through the expansion of IAT programs to identify areas of disagreement and to implement large-scale multi-center studies. The future development of international guidelines is essential to increase safety and quality control as well as procedural standardization in order to promote the broader adoption of IAT techniques for our patients to enhance high-quality outcomes.

OP27 - PORTAL PRESSURE CHANGES AND PROCEDURAL COMPLICATIONS: 14 YEARS AT THE SCOTTISH ISLET TRANSPLANT UNIT

Kaylan Coetser[1 2], Kirsty Duncan[1], Shareen Forbes[1], Andrew Sutherland[1], John Casey[1], Rachel Thomas[1]

[1]*Edinburgh Transplant Centre, Edinburgh, United Kingdom*
[2]*Edinburgh Medical School, University of Edinburgh, Edinburgh, United Kingdom*

Background

Islet transplantation can improve glycaemic control and insulin independence in select type 1 diabetes patients with glycaemic instability and severe hypoglycaemia. Islets may be transplanted alone or as part of a simultaneous islet-kidney (SIK) transplant. Combined islet-kidney transplantation in patients with type 1 diabetes and end-stage renal disease provides better glycaemic control and superior patient graft survival than kidney transplantation alone and improves overall survival and cardiovascular outcomes. The standard islet infusion technique is via the portal vein. Portal pressures rise during infusion proportional to packed cell volume, usually returning to baseline post-procedure. Studies on repeated islet infusions show inconsistent results, with some reporting incremental increases in peak post-infusion portal pressures and others finding no significant cumulative effect. There is limited data on the effects of sequential portal pressure elevations. Excess packed cell volume and acute rises in portal venous pressure are key risk factors for portal thrombosis, with recommended limits of <5 mL and <5 mmHg, respectively. This audit was conducted to evaluate the safety of islet transplantation at the Scottish Islet Transplant Unit by reviewing portal pressure changes, procedural complications, and their associations over a 14-year period.

Methods

A retrospective audit was conducted at our single centre, using data from February 2011 to February 2025. Records of all patients who underwent islet transplant were analysed. Data extracted included cold ischaemic time, islet yield, purity, and viability. Patient records were reviewed to find portal pressure changes and procedural complications. Complications were categorised using Clavien–Dindo Classification.

Results

In 14 years, 87 patients underwent 152 islet transplants: 85 had 1 transplant, 58 had 2 transplants, 7 had 3 transplants, and 2 had 4 transplants. Cold ischaemic time ranged from 212 to 1,236 minutes. Islet viability ranged from 68% to 88% and islet purity from 18% to 95%. Median number of islets transplanted: 310,689 (IQR 144,945) IEQs. The mean rise in portal pressure was 0.27 mmHg (range –3 to 8 mmHg); only 2 patients exceeded the 5-mmHg recommended threshold. 20 complications were recorded across 152 transplants which were categorised as Grade I (n = 12), Grade II (n = 6), and Grade IIIa (n = 2). No correlation was observed between portal pressure rise and complication severity or number of transplants.

Conclusions

Over 14 years of islet transplantation at the Scottish Islet Unit, complications were predominantly minor and within accepted limits. Portal pressure changes were minimal during islet transplants reproducibility of the procedure with no differences seen between the infusion number. The risk of post procedure bleeding was low. This is likely due to the high level of procedural safety achieved under the expertise of our specialist HPB interventional radiology team.

CS01 - MANAGEMENT OF EXTENSIVE VASCULAR THROMBOSIS FOLLOWING SPK TRANSPLANTATION

Rongrong Hu Zhu[1], Marc Martin[2], Alejandro Pascagaza[2], Maria Arantzazu Gelabert[2], Rocío García[1], Enrique Montagud-Marrahi[3], Pedro Ventura-Aguiar[3], Anna Darnell[2], Mª Angeles Garcia-Criado[2], Ramón Rull[1], Joana Ferrer-Fàbrega[4]

[1]*Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (ICMDiM), Hospital Clínic, University of Barcelona, Network for Biomedical Research in Hepatic and Digestive Diseases (CIBERehd), August Pi i Sunyer Biomedical Research Institute (IDIBAPS), Barcelona, Spain*
[2]*Department of Radiology, Hospital Clínic, University of Barcelona, Barcelona, Spain*
[3]*Renal Transplant Unit, Nephrology and Kidney Transplant Department, Hospital Clínic, University of Barcelona, Barcelona, Spain*
[4]*Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (ICMDiM), Hospital Clínic, University of Barcelona, Barcelona, Spain*

Background

A comprehensive preoperative assessment is essential in pancreas transplantation, as recipient comorbidities may increase the risk of postoperative complications. Vascular complications remain a major cause of early graft loss. In this context, interventional radiology has become a key therapeutic tool, offering minimally invasive strategies -such as thrombectomy and angioplasty- for graft salvage.

Methods

We report a case of a 45-year-old female with a medical history of hypertension, dyslipidemia, monoclonal gammopathy of undetermined significance, type 1 diabetes mellitus diagnosed at age 15 and chronic kidney disease on hemodialysis since 2022. The patient presented positive anticardiolipin and anti-β2 glycoprotein I IgM antibodies without prior thrombotic events. After evaluation by the Hemostasis team, the result was deemed false positive and the patient underwent an SPKT in August 2025, with a prompt discharge. In alignment with the Hemostasis team's recommendations, a 4-week course of antithrombotic prophylaxis was administered using low molecular weight heparin (LMWH) at a dose of 20 mg every 12 hours. This approach deviated from the standard protocol, which typically limits anticoagulation to the duration of hospitalization.

One month later, after completing anticoagulation therapy, the patient presented to her local emergency department with nausea, vomiting and oral intolerance. Laboratory tests showed mild elevation of inflammatory markers but renal and pancreatic graft function remained preserved, with normoglycemia.

A CT scan revealed extensive thrombosis from the splenic vein to the inferior vena cava, along with two ureteral stones causing hydronephrosis of the renal graft. Upon referral to our centre, a repeat CT scan demonstrated progression of thrombosis involving the inferior vena cava (extending to the accessory right suprahepatic vein), both renal veins, bilateral iliac-femoral axes and complete thrombosis of the pancreatic graft venous outflow (portal, superior mesenteric, and splenic veins). The pancreatic graft showed mild inflammatory changes and the renal graft exhibited moderate hydronephrosis due to two ureteral calculi (3 mm and 8 mm), for which a double-J stent was placed.

Interventional radiology performed thrombectomy of the inferior vena cava and pancreatic graft vein, along with angioplasty of an intrahepatic vena cava stenosis, successfully restoring vascular patency. No procedural complications were reported.

Results

Follow-up imaging at 48 hours confirmed patency of the inferior vena cava and graft vasculature. Pancreatic and renal graft function remained stable throughout hospitalization while under treatment with 60 mg of LMWH every 12 hours.

Conclusions

Despite thorough preoperative evaluation, unforeseen complications may still arise. This case highlights the importance of early recognition and multidisciplinary management of extensive vascular thrombosis following SPKT. Interventional radiology can play a critical role in preserving graft function and improving patient outcomes in complex vascular complications.

CS02 - EXPANDING THE BOUNDARIES OF PANCREAS TRANSPLANTATION: A NOVEL APPROACH TO PARTIAL PANCREAS TRANSPLANTATION

Inês Barros[1], Beatriz Chumbinho[1], Sofia Corado[1], Ana Marta Nobre[1], Edite Filipe[1], Luís Bicho[1], Luís Ramalhete[2], Sofia Carrelha[1], Ana Pena[1], Emanuel Vigia[1], Aníbal Ferreira[1], Hugo Pinto Marques[1]

[1]*ULSSJosé, Hospital Curry Cabral, Unidade Hepato-bilio-pancreática e de Transplantação, Lisbon, Portugal*
[2]*IPST - Instituto Português do Sangue e Transplantação, Lisbon, Portugal*

Background

Pancreatic transplantation remains the definitive treatment for restoring endogenous insulin secretion in patients with insulin-dependent diabetes mellitus. While whole-organ and segmental pancreas transplants have been performed for decades, all reported cases to date have involved either the body and tail of the pancreas or a complete graft. To our knowledge, no successful transplantation of the pancreatic head alone has been previously described. This innovative approach may offer new opportunities for expanding the donor pool and optimizing graft utilization.

Recent morphometric and histological studies have demonstrated that islet (β-cell) distribution in the human pancreas is relatively uniform, challenging the earlier belief that β-cells are predominantly located in the body and tail. Here, we present what we believe to be the first reported case of a partial pancreatic transplantation involving exclusively the head of the pancreas.

Case report

We report the case of a 38-year-old male patient with long-standing type 1 diabetes mellitus and end-stage renal disease on dialysis. During multiorgan procurement, an accidental injury to the splenic artery occurred. Despite attempted reconstruction, adequate perfusion to the distal pancreas could not be restored. Consequently, a distal pancreatectomy (body and tail) was performed, leaving only the pancreatic head in situ (Fig. 1 and 2). The postoperative course has been remarkably favorable. The patient achieved stable glycemic control without the need for exogenous insulin, maintaining normal glucose levels throughout follow-up.

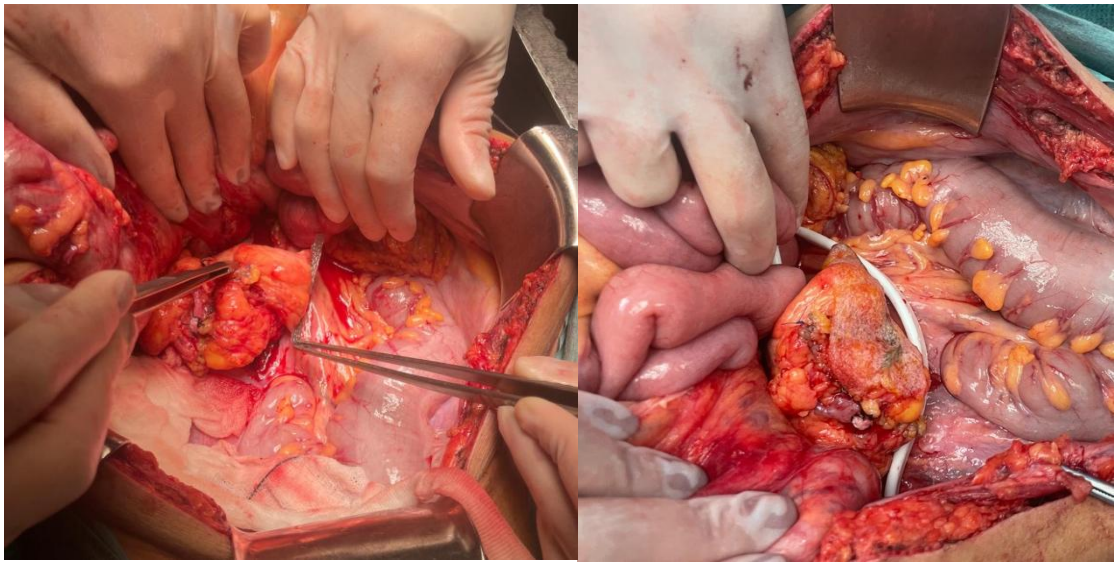


Fig 1, 2 – Pancreatic head graft

Discussion/Conclusion

Traditionally, pancreas transplantation involves the entire organ or a segment comprising the body and tail. The successful engraftment and metabolic function observed in this case demonstrate that the pancreatic head alone can sustain sufficient endocrine activity to achieve insulin independence. This observation is consistent with anatomical evidence showing uniform β-cell distribution throughout the pancreas, suggesting that the head possesses adequate islet mass to maintain glucose homeostasis.

The possibility of using a pancreatic-head-only graft broadens the applicability of pancreas transplantation, particularly when vascular injury or anatomical limitations preclude the use of the whole organ. This case adds to the evolving evidence that partial or technically modified grafts can achieve satisfactory metabolic outcomes. Looking forward, this approach raises the intriguing possibility that a single graft could be shared between two recipients.

In conclusion, this innovative approach challenges conventional paradigms in pancreas transplantation, showing that a pancreatic-head- graft can restore insulin independence. Continued follow-up and additional reports are warranted to confirm long-term metabolic stability and to define the role of this strategy within modern transplant practice.

This case represents, to our knowledge, the first reported transplantation of the pancreatic head alone.

PP01 - DEVELOPMENT OF AN ALL-HUMAN VASCULARIZED MODEL OF PANCREATIC ISLETS ON-CHIP: TOWARDS PERSONALIZED MEDICINE FOR TYPE 1 DIABETES

Mélanie Lopes[1], Emily Tubbs[1], Clara Pirlian[1], Priscille De GEA[1], Stéphanie Combe[1], Joris Kaal[2], Fabrice Navarro[2], Sandrine Lablanche[3], Xavier Gidrol[1]

[1]*Univ. Grenoble Alpes, INSERM, CEA, IRIG, Biomics,, Grenoble, France*
[2]*Univ. Grenoble Alpes, INSERM, CEA, LETI, DTIS, Grenoble, France*
[3]*Univ. Grenoble Alpes, INSERM, Diabetology and endocrinology department, Grenoble Alpes University Hospital, Grenoble, France*

Background

Islet transplantation is a promising cell replacement therapy, but the loss of graft efficacy after 5–10 years suggests that this approach could still be further optimized. Therefore, the development of a vascularized human pancreatic islet model for the study of diabetes appears essential.

Our project proposes an innovative alternative: a microfluidic islet-on-chip model (Figure 1), designed to mimic human physiological conditions, including vascularization and the specific microenvironment of pancreatic islets.

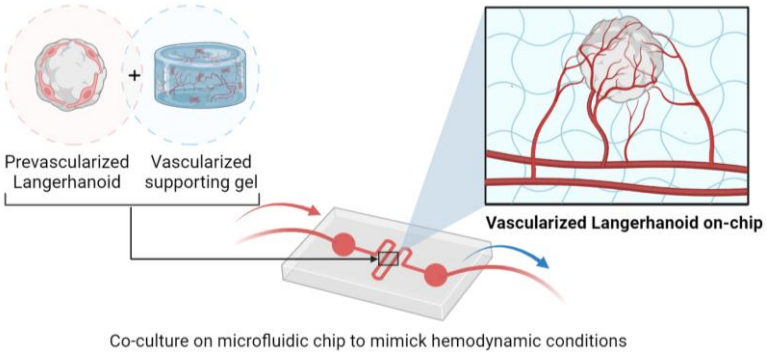


Figure 1: Schematic representation of the vascularized Langerhanoid on a microfluidic chip.

Methods

This model relies on a microfluidic chip integrating pre-vascularized human Langerhans islet spheroids (hereafter referred to as Langerhanoids), composed of three self-organized human cell types: endothelial, stromal, and insulin-secreting cells. The chip incorporates a bioactive hydrogel seeded with endothelial cells to promote vascular network formation, while perfusion ensures physiological nutrient and oxygen flow. Cell ratios, cell types, and hydrogel composition were optimized to establish a permissive microenvironment for vascular sprouting and functional anastomosis between Langerhanoid sprouts and the surrounding endothelial network within the chip.

Results

A human-derived hydrogel enriched in growth factors was developed to support endothelial network formation and pancreatic islets' function. At day 10 of culture in

this hydrogel, endothelial cells network significantly increased compared to the bovine-fibrin control, especially regarding total network length (182 475 µm vs. 163 369 µm), number of segments (4 031 vs. 3 018), and number of nodes (9792 vs. 7618), **($p < 0.05$, n=4,** Angiogenesis Analyzer**).**

In these cell culture conditions with the developed hydrogel, we observed a pro-angiogenic response, with increased mRNA levels of CD31, PDGFRβ, VEGFR1, integrin, and VE-cadherin by at least 10-fold relative to controls ($p<0.05$, n=3). Native human pancreatic islets embedded in the human-derived hydrogel developed seem viable (based on Syto13/Propidium Iodide staining) and functional (regarding insulin secretion in response to glucose stimulation) (n=2, ongoing). Optimized cell ratios improved the development of endothelial network within the Langerhanoid and the microenvironment (n=3, ongoing).

Conclusions

Ultimately, this all-human vascularized islet-on-chip model represents a versatile platform for studying the interactions between pancreatic islets, vasculature, and their microenvironment. Beyond providing mechanistic insights into islet survival and function, its compatibility with a possible immune system perfusion also makes it a valuable tool for drug testing and patient-specific applications, paving the way toward personalized medicine in type 1 diabetes.

PP02 - COMPUTATIONAL DESIGN AND BIOFABRICATION OF A XENOGENIC VASCULARIZED ISLET ORGAN (BIOVIO) FOR TYPE 1 DIABETES

Matteo Monieri[1], Alice Chirichelli[1], Francesco Campo[1], Sofia Cochi[1], Alessia Neroni[1], Cataldo Pignatelli[1], Elisabeth Kemter[2 3 4], Eckhard Wolf[2 3 4], Lorenzo Piemonti[1 5], Antonio Citro[1]

[1]*Diabetes Research Institute, IRCCS Ospedale San Raffaele, Milan, Italy*
[2]*Chair for Molecular Animal Breeding and Biotechnology, Gene Center and Department of Veterinary Sciences, LMU, Munich, Germany*
[3]*Center for Innovative Medical Models (CiMM) LMU, Munich, Germany*
[4]*German Center for Diabetes Research (DZD), Neuherber, Germany*
[5]*University Vita-Salute San Raffaele, Milan, Italy*

Background

Intrahepatic islet transplantation is the current β-cell replacement approach in severe Type 1 Diabetes (T1D) patients. However, its application is limited due to shortage organ donor and islets loss after implant due peritransplant damage. To overcome these issues, we develop ex vivo a bioengineered vascularized islet organ (BioVIO) integrating immature neonatal porcine islets (NPIs) into a revascularized decellularized neonatal pig lung left lobe scaffold to efficiently deliver β-cell to T1D patients.

Methods

Lungs were decellularized by vascular perfusion of 0,1% SDS and 1% Triton X-100, then validated by HE staining and DNA analysis. 3D-CAD models were obtained through pig lungs perfusion with a contrast agent and X-Ray scanned. 3D renderings were analyzed in geometrical terms to estimate the number of cells needed to fully cover BioVIO's vascular network. Computational fluid-dynamics (CFD) simulations were performed on COMSOL Multiphysics to evaluate fluid velocity and wall shear stress (WSS) experienced by BOECs. Bio-VIOs were engineered by repopulating the vascular compartment with predicted blood outgrowth endothelial cells (BOECs) and the alveolar space with NPIs. After 7 days of dynamic culture, vascular function was assessed via fluorangiography (IF), while endocrine performance through dynamic glucose perifusion (ELISA, IF). β-cell death was estimated by droplet digital PCR analysis of released miR-375. BioVIO's fragments were transplanted subcutaneously in immunodeficient diabetic mice and compared to NPIs implanted in kidney capsule. Explanted fragments were used for histological evaluation of in vivo integration and function (IF).

Results

Neonatal pig lung have been successfully decellularized as demonstrated by histological analysis and DNA content (< 50 ng/mg) while preserving intact matrix protein (collagen I+, IV+). 3D reconstructions revealed that approximately 100 million BOECs are required to engineer BioVIO's vascular bed. WSS in the structure was analyzed through CFD simulations: maximum values of 1.25 ± 0.28 Pa were observed when a flow rate of 4 mL/min was imposed. Ex vivo confocal images confirmed that the vascular bed was entirely covered with HUVECs ($CD31^+$, vWF^+) and 0.2 μm microspheres were confined within the vasculature confirming the

structural integrity. After 7 days of BioVIO's culture, NPIs engrafted inside the alveolar space (Insulin+, CHGA+) and surrounded as predicted by simulation data by a functional endothelium (hVWF+). BioVIO showed an improved insulin secretion (4.7 mU/min) coupled to an overall survival of β-cell mass around 80% during culture compared to NPIs alone. Preliminary in vivo results confirmed BioVIO's ability to engraft and restore normoglycemia.

Conclusions
we engineered a BioVIO device able to harbour a therapeutic dose of insulin producing cells both in vitro and in vivo. Ongoing studies in humanized NSG diabetic mice with edited NPIS will confirm BioVIO's translational potential.

PP03 - TOWARDS PHYSIOLOGICALLY RELEVANT ENGINEERED VASCULATURE: THE IMPACT OF CELL SOURCE SELECTION IN MICROFLUIDIC PLATFORMS

Luana Osório[1], Benjamin Hansen[2], Xiang Xu[2], Victoria Salem[1 2]

[1]*King's College London, London, United Kingdom*
[2]*Imperial College London, London, United Kingdom*

Background

Endothelial cells (EC) are key to graft integration. In islet transplantation, rapid and functional vascularization maintains oxygen and nutrients supply, promoting graft survival. Organ-specific EC differentiation and vascular bed formation are not well understood. While EC share core traits, their phenotype and behavior is highly tissue dependent, challenging the recreation of physiologically relevant vasculature from patient-derived EC of varied sources. We present a microfluidic model that interrogates the validity of sourcing EC and stromal cell (SC) co-cultures towards the study of organotypic pancreatic vasculature.

Methods

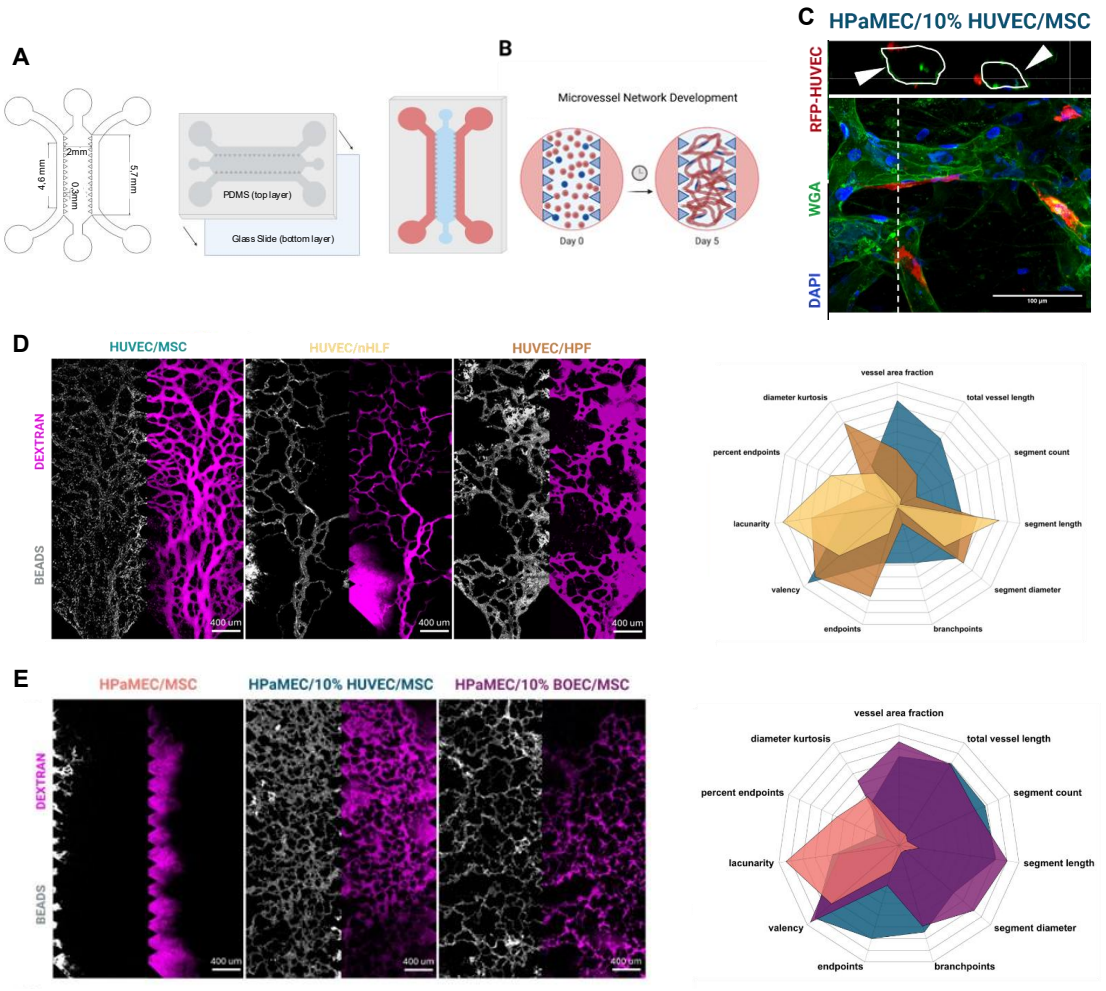
Microfluidic chips were cast from PDMS, using SU-8 photolithography and 3D printing molds. Chips were loaded with EC and SC embedded within a fibrin hydrogel at a 5:1 ratio. EC human subpopulations tested were umbilical vein endothelial cells (HUVEC), pancreatic microvascular endothelial cells (HPaMEC), and patient-derived blood outgrowth endothelial cells (BOEC). SC human subpopulations tested were adipose mesenchymal stromal cells (MSC), normal lung fibroblasts (NHLF) and pancreatic fibroblasts (HPF). Chips were cultured for five days with controlled pressure gradients to produce perfusable vessels, prior to either live imaging or fixed immunofluorescence imaging. Network morphology was analysed using in-house algorithms to generate network morphology readouts. Bulk RNA Sequencing analysis was performed on extracted chip samples using DESeq2, DAVID, and GSEA.

Results

Microvessel networks with different SC showed distinct SC-dependent morphologies. MSC generated densely vascularised networks with wide vessels whilst NHLF created thinner and sparse networks. Principle component analysis performed on sequenced samples revealed tightly clustered replicates with distinct pseudotemporal trajectories. Differential gene expression of ECM factors in each network reflected that of network's stromal cell and native tissue type. HPaMEC only networks failed to self-assemble on chips. Upon the addition of a small (10%) sub-population of less terminally differentiated ECs (HUVEC or BOEC), the self-assembly capability of pancreatic ECs is rescued. Imaging and transcriptomic readouts revealed that the HUVECs do not form the HPaMEC networks but transdifferentiate into a supporting cell phenotype. These networks revealed sweeping upregulation of pro-vasculogenic genes - CD248, SDC4, and XBP1 - and downregulation of anti-vasculogenic genes - IGFBP4, PTX3, and TIMP-2.

Conclusions

Microfluidic platforms offer the opportunity to engineer and study tissue using patient-derived cells. Here we show that careful manipulation of cell mixes can tune organotypic features. Terminally differentiated, primary EC can be prompted to develop perfusable networks with the addition of small populations of more immature EC, displaying plasticity to support vascularization. Advanced tissue engineered platforms hold great promise for disease modelling and regenerative medicine.



Microvessel self-assembled networks with small sub-populations of patent EC.

PP04 - HUMAN VASCULARIZED ISLET ORGAN (HVIO) AS A MODEL PLATFORM FOR DRUG TESTING

Cataldo Pignatelli[1], Alessia Neroni[1], Ilaria Marzinotto[1], cristina Olgasi[2], Antonia Follenzi[2], Vito Lampasona[1], Lorenzo Piemonti[1], Antonio Citro[1]

[1]*IRCCS San Raffaele Research Institute, Diabetes Research Institute (DRI), Milan, Italy*
[2]*University of Piemonte Orientale, Department of Health Sciences, Department of Health Sciences, Novara, Italy*

Background
Reliable *in vitro* models of the endocrine pancreas are crucial for studying diabetes pathophysiology and screening therapeutics. However, current models often lack physiological complexity, including features of the native pancreatic islet microenvironment, thereby limiting their predictive accuracy. Here, we bioengineered human vascularized islet organs (hVIOs) using human islets (HIs) and blood-outgrowth endothelial cells (BOECs) and tested it as a drug-testing platform. To this end, titration of hVIO platform was performed using a well-known drug, exendin-4 (Ex4), a widely used GLP-1 receptor agonist known to stimulate insulin secretion and improve β-cell function.

Methods
Before hVIO engineering, individual cellular components (HI and BOEC) were incubated with different concentrations of Ex4 for 7 days, and the effects on each cell type were analyzed. Successively, hVIOs were generated by reseeding decellularized rat lung lobes with HIs and BOECs, respectively delivered through the trachea and the pulmonary artery and vein. The hVIOs were cultured in custom-designed bioreactors under dynamic perfusion for 14 days. β-cell mass and endothelial function were monitored by assessing MiR-375 expression (a marker of β-cell death), insulin secretion, fluorangiography, and a dextran permeability assay to evaluate endothelial barrier integrity, as well as by immunofluorescence analysis. The hVIO platform protocol was established to include a 7-day maturation phase (MP) followed by a 7-day testing phase (TP). Once the platform was fully characterized, matured hVIOs and hVIOs lacking BOECs were treated with Ex4 during the final 7 days of culture (TP).

Results
Ex4 showed no significant effect on either the proliferation or viability of BOECs. Conversely, the compound enhanced the insulin secretion capacity of His. Fully engineered hVIOs exhibited complete revascularization and functional integration between the endocrine and vascular components within 7 days, with insulin secretion levels higher than those of conventionally cultured HIs; this performance was maintained after 14 days. During the TP, hVIOs were chronically treated with Ex4. Treated hVIOs demonstrated improved insulin secretion while maintaining both an intact endocrine phenotype and vascular structure. In contrast, hVIOs engineered without BOECs showed a reduced insulin secretion, even upon Ex4 treatment, highlighting the essential role of the endothelial compartment in supporting β-cell function.

Conclusions
Taken together, these preliminary results indicate that the hVIO platform can recapitulate the functional crosstalk between the vascular and endocrine compartments and is responsive to pharmacological stimulation. Although Ex4 was used as a proof-of-concept molecule, further studies are required to strengthen the significance of these findings. Additionally, testing a broader range of compounds will be essential to validate the platform as a reliable and scalable *in vitro* model for drug screening and β-cell–targeted therapy development.

PP05 - VALIDATION OF REFERENCE GENES FOR RT-QPCR NORMALISATION IN DONOR PANCREATIC TISSUE

Rhys Pook[1 2], Nafi Pringgodigdo[1], Rachel Botting[1], Minna Honkanen-Scott[1], James Shaw[1 2 3], Simi Ali[1 2], William E Scott Iii[1 2]

[1]*Translational and Clinical Research Institute, Newcastle University, Newcastle Upon Tyne, United Kingdom*
[2]*NIHR Blood and Transplant Research Unit, Newcastle University and Cambridge University, Newcastle Upon Tyne, United Kingdom*
[3]*Institute of Transplantation, Freeman Hospital, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, United Kingdom*

Background

Accurate normalisation of reverse-transcription quantitative polymerase chain reaction (RT-qPCR) is essential for reliable measurement of bench top pancreatic gene expression studies. The validity of RT-qPCR depends on stable reference genes (RGs), yet traditional housekeeping genes (HKG) such as GAPDH, ACTB and RPLP0 often show variable expression. Inappropriate reference-gene selection risks introducing substantial bias and with 15% of published studies reporting reference gene validation[1], it highlights the need for systematic evaluation within experimental contexts.

Methods

RNA sequencing (RNA-seq) was performed on 13 non-diabetic human donor pancreatic biopsies selected from the MRC Newcastle Quality in Organ donation biobank. Donors were selected and stratified into <10 hours and >20 hours cold ischemia time to capture clinically relevant variation. RNA was extracted, quality checked and sequenced (Illumina NovaSeq 600, PE150). Reads were aligned to the human reference genome (GRCh38/hg38) and raw counts were normalised using DESeq2. Genes with low abundance (mean counts ≤10) or non-coding were excluded. Remaining genes were assessed using coefficient of variation (CV) with a threshold of CV<0.1 and mean counts between 500-3000. Candidate RGs were then ranked and cross-referenced with established HKGs.

Results

14,845 genes were sequenced which was reduced to 5,571 genes after QC and 16 out of the 32 commonly used HKGs remained. The most stable filtered HKGs were MRLP19, PGK1 and EIF2B1. Common housekeeping genes such as RPLP0 were excluded off high expression and large CV values compared to novel genes. Three genes, CDS2, PSMD2 and SNX1 emerged as the most stable novel candidate genes. Demonstrating high stability across ischaemia conditions. CDS2 encodes a key enzyme in phospholipid biosynthesis, PSMD2 a core subunit of the 26s proteasome and SNX1 a regulator of endosomal trafficking and lysosomal sorting.

Conclusions

This study utilised transcriptome-wide stability evaluation of genes from human pancreas tissue. CDS2,PSMD2, and SNX1 were identified as novel reference genes for RT-qPCR studies in our experiment conditions. These genes combine low

variability and good expression with backed mechanistic justification. MRLP19,PKG1 and EIF2B1 presented with higher stability compared to commonly used HKGs and will be taken to RT-qPCR stability validation to aid in normalisation of gene expression in human pancreas ischemia studies.

PP06 - INSULIN-SECRETING SPHEROIDS ENGINEERED FROM ISLET AND EXTRAVILLOUS TROPHOBLAST CELLS TO TREAT TYPE 1 DIABETES

Hiba Msheik[1], Emilie Derisoud[1], Fanny Lebreton[2], Kevin Bellofatto[2], Marie Cohen[1], Ekaterine Berishvili[2]

[1]*Department of Pediatrics, Gynecology and Obstetrics, Faculty of Medicine, Geneva, University Hospitals and University of Geneva, Geneva, Switzerland*
[2] *Cell Isolation and Transplantation Center, Department of Surgery, Geneva University Hospitals and University of Geneva, Geneva, Switzerland*

Background
Successful intraportal transplantation of pancreatic islets in type 1 diabetes (T1D) patients is impaired by poor vascularization, inflammation, and immunosuppressive drug toxicity. Approaches that co-assemble insulin-secreting cells with supportive cells have been explored experimentally, but their translational value remains uncertain. Extravillous trophoblast (EVT) cells exhibit vasculogenic and immunoregulatory features in vitro, suggesting they could modulate the peri-graft milieu; however, suitable models to rigorously test EVT–islet interactions are lacking.

Methods
We generated seven proliferative EVT populations from first-trimester trophoblast organoids using a protocol developed in our lab. Phenotyping across passages used qPCR, immunofluorescence (IF), and flow cytometry. To generate insulin-secreting organoids, EVT cells were combined with EndoC-βH5 cells either by direct co-aggregation or by peripherally layering (shielding) EVT around pre-formed EndoC-βH5 spheroids. Function was assessed by glucose-stimulated insulin secretion (GSIS) assay; viability by fluorescein diacetate/propidium iodide staining (FDA/PI); and cellular spatial organization by IF staining for β-cell and EVT markers. To avoid artifacts from islet dissociation, we initiated co-culture of EVT with intact rat islets and evaluated viability and insulin release.

Results
All EVT populations maintained EVT identity and expression of key immunomodulatory molecules over passages. EndoC-βH5- and mixed EndoC-βH5-EVT cultures formed round spheroids within five days of with comparable viability. Incorporation of 30% of EVT did not diminish glucose-responsive insulin secretion by EndoC-βH5 cells. IF revealed predominant EVT localization to spheroid core irrespective of assembly method, a configuration that may limit paracrine interactions with the external microenvironment and thereby temper putative vasculogenic or immunomodulatory effects. In preliminary co-cultures with intact rat islets, EVT did not impair islet viability or insulin secretory responses.

Conclusions
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 cell-based therapies targeting other diseases.

PP07 - ENHANCING RNA INTEGRITY: OPTIMISED PRESERVATION STRATEGIES FOR HUMAN PANCREATIC TISSUE

Rhys Pook[1 2], Abbie Hearne[2], Rachel Botting[2], Minna Honkanen-Scott[2], James Shaw[1 2 3], Simi Ali[1 2], William E Scott Iii[1 2]

[1]*NIHR Blood and Transplant Research Unit, Newcastle University and Cambridge University, Newcastle Upon Tyne, United Kingdom*
[2]*Translational and Clinical Research Institute, Newcastle University, Newcastle Upon Tyne, United Kingdom*
[3]*Institute of Transplantation, Freeman Hospital, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, United Kingdom*

Background
Unlike other organs, the secretory and enzyme-rich nature of the pancreas results in rapid post-mortem tissue degradation at the cellular level through RNase/enzyme activation; limiting the utility of pancreatic biopsies for transcriptomic analysis.

This study compares four methods of tissue-preservation reported for animal studies to optimise collection and storage of human pancreatic tissue for gene expression analysis[1].

Methods
Human research pancreata were transported to our labs, dissected and regionally biopsied (36 samples/pancreas from 4 donors). Tissue was preserved using four methods: immediate RNA isolation, snap frozen, RNA*later* submerged and RNA*later* injected. All *RNAlater* treated tissue underwent a freeze-thaw prior to extraction using a spin column technique. Yield and purity were measured by Nanodrop and RNA Integrity Number (RIN) score assessed by TapeStation analysis. Statistical analysis consisting of Kruskal-Wallis followed by post-hoc Dunn's test.

Results
RNA yield (25-500 ng/µL) and concentration (260/280 ratio ~ 2.00 & 260/230 ratio 2.00-2.20) was acceptable for all samples . Significantly higher RIN scores were observed for RNA*later* injection (Mean: 7.1 ± SEM 0.18; p=0.03) and RNA*later* submerged (Mean: 7.1 ± SEM 0.19; p=0.03) compared to snap frozen (Mean: 3.7 ± SEM 0.20). Notably, all RNA*later* treated samples met quality thresholds (RIN ≥ 4.00) and no significant difference between injected and submerged methods was observed.

Conclusions
Preserving pancreas biopsies with RNA*later* followed by snap freezing preserves the transcriptome at the moment of sampling, preventing molecular degradation. This ensures downstream molecular analyses truly reflects tissue status during the peri-transplant period. This work demonstrates an optimal method for preserving high-quality RNA in pancreatic biopsies which can improve the consistency in RNA quality for analysis enabling deeper understanding of pancreatic biology.

PP08 - BALANCING METABOLIC VIABILITY AND VASCULAR INTEGRITY IN CULTURED PANCREATIC ISLETS

Lydie Plecita[1], Stepanka Benakova[1], Eva Fabryova[2], Veronika Tomsovska[2], Blanka Holendova[1], Jan Kriz[2]

[1]*Institute of Physiology, CAS, Praha, Czech Republic*
[2]*Institute of Clinical and Experimental Medicine, Praha, Czech Republic*

Background
The identification of new sites for pancreatic islet transplantation requires a solid system for *in vitro* islet cultivation. Extended culture has been reported to disrupt and eliminate the intra-islet vasculature, which is essential for oxygen and nutrient delivery after transplantation. Impaired revascularization is a major cause of reduced graft survival and function.

Methods
We used confocal microscopy, transcriptomic profiling, respirometry, and ELISA for a glucose-stimulated insulin secretion assay.

Results
In this study, we evaluated the condition of the endothelial capillary network during 5 days of incubation in standard CMRL medium. Islets from transgenic Tie2-GFP mice enabled direct three-dimensional visualization of endothelial structures within the islet volume. We observed that the endothelial network became progressively disintegrated rather than completely lost, and this effect showed no correlation with islet volume. Transcriptomic profiling of selected endothelial and pericyte genes indicated a partial tendency toward recovery after 5 days, suggesting that vascular support mechanisms remain active. To further assess islet fitness, we analyzed energy metabolism and insulin secretory capacity. Mitochondrial oxidative function was preserved throughout the culture period. Glucose-stimulated insulin secretion remained detectable but was attenuated, largely due to increased basal insulin release on day 5.

Conclusions
Together, these findings demonstrate that short-term culture maintains overall metabolic viability but compromises vascular integrity and insulin responsiveness. Supporting endothelial cell stability during in vitro cultivation may therefore be essential to improve revascularization, enhance long-term graft performance, and promote better integration of islet transplants at recipient sites.

Output of project no. NW25-01-00221 funded by the Czech Health Research Council

PP09 - LOW RESPONSIVENESS OF MACRO-ENCAPSULATED HUMAN ISLETS TOWARDS GLUCOSE CHALLENGE DESPITE EXCELLENT SURVIVAL IN SILICONE-BASED OXYGEN-DELIVERING DEVICES

Daniel Brandhorst[1], Heide Brandhorst[1], Rebecca Spiers[1], Daniel Domingo-Lopez[2], Eoin O'Cearbhaill[3], Fergal Coulter[3], Stefano Deotti[2], Lucy Crawford[1], Katarzyna Marszalek[1], Anthony Cornu[1], Helena Kelly[4], Garry Duffy[5], Paul Johnson[1]

[1]*Islet Transplant Research Group, Nuffield Department of Surgical Sciences, John Radcliffe Hospital, University of Oxford, Oxford, United Kingdom*
[2]*Anatomy and Regenerative Medicine Institute (REMEDI), College of Medicine, Nursing and Health Sciences, National University of Ireland, Dublin, Ireland*
[3]*School of Mechanical Engineering, Centre for Biomedical Engineering, University College of Dublin (UCD), Dublin, Ireland, Dublin, Ireland*
[4]*School of Pharmacy & Biomolecular Sciences, Royal College of Surgeons in Ireland (RCSI), Dublin, Ireland*
[5]*Anatomy and Regenerative Medicine Institute (REMEDI), College of Medicine, Nursing and Health Sciences, National University of Ireland, Galway, Ireland*

Background

The ultimate goal for islet transplantation is to transplant islets from any source without the need for life-long immunosuppression. Islet macroencapsulation is one approach being investigated extensively to achieve this goal, offering the additional benefits of cell containment and removability. However, to date, attempts to translate this clinically have been hampered by the vulnerability of encapsulated islets to damage from hypoxia. In this study, we compared the efficiency of different components of a novel oxygen-delivering matrix to reduce inflammation, necrosis and apoptosis in human islets.

Methods

Isolated human islets (n = 10) were mixed with different matrices: (A) supplemented CMRL, (B) Hyaluronic acid (HA)-based Gel, (C) Beta-Gel (HA-Gel+PFC-emulsion) or (D) Beta-Gel+O2. Afterwards, silicone-based macrodevices were loaded with 600 matrix-immersed IEQ and cultured for 4 – 5 days. Islet characterisation included yield, counted as islet particle number (IN) and IEQ; necrosis (PI); apoptosis (Annexin V-PI) and reactive oxygen species (ROS) production (DCFH-DA). The glucose-stimulation index (SI) was measured after 24 hours of culture by injecting glucose into the devices to obtain a final internal concentration of 25 mmol/L and normalised to the baseline insulin level at 5.5 mmol/L glucose after 0 and 150 min of incubation. Parameters were related to IEQ and normalised to preculture data if appropriate (mean ± SEM).

Results

Results are shown in Table 1. After culture, a massive islet loss was noted when using CMRL which could be prevented by Beta-Gel and oxygenated Beta-Gel. Reduction of islet yield correlated with enhanced fragmentation (IN/IEQ ratio) that was highest in CMRL and lowest in Beta-Gel and Beta-Gel+O_2. ROS was highest in CMRL and substantially lower in Beta-Gel or Beta-Gel+O_2. In contrast, necrosis was similar in HA-Gel and Beta-Gel whilst Beta-Gel+O_2 provided most efficient reduction of necrosis. Postculture apoptosis was massively enhanced in CMRL compared with Beta-Gel and Beta-Gel+O_2 showing lowest increase of apoptosis. Glucose

stimulation resulted in an extremely low insulin release varying between 0.02 µU/IEQ in CMRL and 1.46 µU/IEQ in Beta-Gel+O_2. As shown in Table 1, the corresponding SI was significantly lowest in CMRL and highest in Beta-Gel+O_2.

TABLE 1 Characterisation of islets cultured in silicone-based macrodevices loaded with different matrices as indicated by the experimental groups. The macrodevices were incubated for 4 – 5 days in normoxic atmosphere at 37°C (n = 10).

Exp. Groups	Islet Yield (IEQ)	Fragmentation (IN/IEQ)	ROS (FI/IEQ)	Necrosis (FI/IEQ)	Apoptosis (FI/IEQ)	SI (150 min) (25/5.5 mM)
Preculture	600 ± 0	0.45 ± 0.05	39.6 ± 6.7	33.0 ± 1.0	24.4 ± 1.7	n.d.
	(100 ± 0%)	(100 ± 0%)	(100 ± 0%)	(100 ± 0%)	(100 ± 0%)	
CMRL	67.5 ± 12.8[c]	1.76 ± 0.2[c]	258.2 ± 78.6[c]	128.9 ± 12.7[c]	208.2 ± 27.0[c]	0.37 ± 0.09
	(11.3 ± 2.1%)	(412.1 ± 49.5%)	(729.7 ± 232.4%)	(384.7 ± 30.4%)	(899.2 ± 145.8%)	
HA-Gel	201.0 ± 32.3[c,h]	1.18 ± 0.18[b,g]	165.4 ± 53.7[b,h]	77.9 ± 8.9[b,d,g]	139.7 ± 24.7[c,g]	5.42 ± 1.34[d]
	(33.5 ± 5.4%)	(284.7 ± 58.3%)	(475.3 ± 159.2%)	(233.9 ± 23.8%)	(599.2 ± 130.3%)	
Beta-Gel	367.8 ± 21.3[b,e]	0.65 ± 0.03[a,e]	73.9 ± 11.5[a,d,g]	71.0 ± 7.5[c,d,g]	79.6 ± 15.3 [b,e]	1.46 ± 0.33[g]
	(61.3 ± 3.6%)	(159.3 ± 14.5%)	(208.4 ± 28.2%)	(213.2 ± 18.1%)	(339.6 ± 63.4%)	
Beta-Gel+O_2	486.7 ± 30.1[f]	0.64 ± 0.04[f]	46.2 ± 5.9[f]	46.5 ± 4.8[f]	60.1 ± 7.7[f]	8.22 ± 0.83[f]
	(81.1 ± 5.0%)	(159.6 ± 18.6%)	(132.9 ± 20.3%)	(140.1 ± 11.6%)	(259.0 ± 36.5%)	

Figures normalised to islets preculture are shown in parentheses.

[a]$P < 0.05$, [b]$P < 0.01$, [c]$P < 0.001$ vs preculture; [d]$P < 0.05$, [e]$P < 0.01$, [f]$P < 0.001$ vs CMRL; [g]$P < 0.05$, [h]$P < 0.01$ vs Beta-Gel+O_2;

Conclusions

Our study demonstrates that the use of a suitable bio-compatible matrix can reduce inflammation and apoptosis and to protect the integrity of macro-encapsulated human islets. As hypoxia is the most decisive factor for islet survival, the efficient delivery of oxygen, even for a limited time, promotes islet early graft survival within macrodevices. Further studies are required to address the time-gap between implantation and completed revascularisation in order to fully restore normal physiological kinetics of insulin release from macro-encapsulated islets.

PP10 - LEVERAGING THE ANTIOXIDANT AND IMMUNOMODULATORY PROPERTIES OF FUCOIDANS IN ISLET ENCAPSULATION

VIJAYAGANAPATHY VAITHILINGAM[1], Sami Gemal Mohammed[1], Aart van Apeldoorn[1]

[1]*MERLN Institute for Technology Inspired Regenerative Medicine, Maastricht, Netherlands*

Background

Hydrogel microencapsulation of islets is an effective strategy to protect transplanted donor islets from immune cell attack; however, those islets remain susceptible to pro-inflammatory cytokines, radicals and reactive oxygen species that induce oxidative stress and thereby poor islet survival and function. Hydroogels can be supplemeted with compounds having antioxidant and immunomodulatory properties to mitigate the oxidative stress and the cytotoxic effects of cytokines on encapsulated islets. In this study, we explored the redox and immunomodulatory properties of fucoidan from an algae species namely Fucus vesiculosus and its potential application in hydrogel formulation.

Methods

The free radical scavenging activity and cytotoxicity of fucoidan was assessed using DPPH and viability assays, respectively. Fucogel was made by blending fucoidan with alginate and its rheological and viscoelastic properties were assessed. Fucocaps (fucoidan microcapsules) were then generated and and their fucoidan release kinetics were assessed. Primary human islets encapsulated in Fucocaps were exposed to pro-inflammatory cytokines or H_2O_2 and assessed for their viability and function. Finally, using the capsule-in-capsule technology, a dual encapsulation strategy with fucoidan hydrogel being in the core surrounded by alginate hydrogel for creating a redox and immunomodulatory niche for human islets were explored.

Results

Fucoidans exhibited a dose response increase in their DPPH free radical scavenging activity with a maximum inhibition of ~90% and an IC50 of 541.6 µg/ml. Fucoidans were found to be non-toxic to cells at concentrations up to 10 mg/ml. Both alginate and Fucogel had similar viscoelastic properties with no differences in their hydrogel mesh sizes. The osmotic pressure test shows that both alginate and Fucocaps had similar physical and mechanical characteristics including microcapsule stability. Viability and ATP levels of human islets in Fucocaps at days 1 and 5 were significantly higher compared to those in alginate. Furthermore, islets in Fucocaps functioned better in response to high glucose exposure with approximately 2-fold higher stimulation index at day 5 compared to alginate microcapsules. When exposed to pro-inflammatory cytokines or H_2O_2, islets encapsulated in Fucocaps showed significantly higher viability, ATP and stimulation index compared to those encapsulated in alginate. Finally, dual encapsulation of human islets was successfully achieved where islets maintained their viability and function for up to 5 days in culture.

Conclusions

Encapsulation of human islets in fucoidan hydrogels can alleviate oxidative stress, provide protection against pro-inflammatory cytokines, and as a result enhance islet viability and function. Fucogels can, therefore, be a promising biomaterial for bioengineered immunoprotective beta cell replacement devices with an added redox- and immunomodulatory properties.

PP11 - CRYOGEL-BASED, PREVASCULARIZED BIOLOGICAL PLATFORM FOR ISLET TRANSPLANTATION

Nicerine Krause[1], Ekaterine Berishvili[1], Fanny Lebreton[1], Kevin Bellofatto[1]

[1]*Faculty of Medicine, University of Geneva, Geneva, Switzerland*

Background
Intrahepatic islet transplantation can restore insulin independence but is hindered by donor scarcity, lifelong immunosuppression, and poor engraftment due to IBMIR and inadequate vascularization. Subcutaneous transplantation offers accessibility and safety but exposes to hypoxia and slow revascularization. Regenerative approaches using hydrogels provide scaffolds for islet support but limit cellular movement. Cryogels, with large, interconnected pores, improve cell transplantation but struggle to mimic native extra-cellular matrix (ECM) and support vascularization. Placenta-derived cryogels, can mimic ECM, enhance islet survival under hypoxia, while blood outgrowth endothelial cells (BOECs) can improve neovascularization and graft function, offering promising advances.

Method
Collagen I hydrogels and human placenta–derived basement membrane extract (BME) were mixed at various ratios and crosslinked to form cryogels. Matrix protein composition was analyzed by LC-MS/MS. Biophysical properties (porosity, pore interconnectivity, density, and water-swelling capacity) were measured across hydrogel/BME ratios. Cytocompatibility with pancreatic islets and BOECs was assessed by MTT and Live/Dead assays. GFP-labeled BOEC growth in the different cryogels was evaluated at multiple timepoints by fluorescence microscopy (Leica LAS X, spectral mode). Static incubation assays were performed after seeding rat islets (100 IEQ) and human islets (50 IEQ) onto each cryogel.

Results
LC-MS/MS revealed collagen and glycoprotein profiles comparable to commercial Matrigel. Varying hydrogel/BME ratios produced cryogels with optimal porosity and interconnectivity suitable for cell seeding across all conditions; higher Collagen I content correlated with markedly increased water uptake (4766% vs 1728%, p = 0.0419). MTT and Live/Dead assays with pancreatic islets and BOECs showed no significant cytotoxicity versus controls. GFP-BOECs formed extensive tubular networks on cryogel surfaces, indicating pro-angiogenic properties. By Day 14, islets on cryogels maintained or improved stimulation index (SI) values (1.54 ± 0.57 to 2.18 ± 0.40), whereas conventional cultures declined (1.15 to 0.90) and Cultrex decreased sharply (2.12 to 0.60).

Conclusions
Placenta-derived Collagen I/BME cryogels maintain structural integrity, support islet survival, promote neovascularization, and improve graft function, representing a promising strategy to enhance outcomes of islet transplantation.

PP12 - ESTABLISHING A CROSS-BORDER PANCREATIC ISLET TRANSPLANTATION PROGRAM BETWEEN THE CZECH REPUBLIC AND SLOVAKIA: EARLY CLINICAL OUTCOMES

Alžběta Vojtíšková[1], Martina Dolečková[2], Michaela Kudláčková[2], Zuzana Berková[1], Veronika Tomšovská[1], Eva Fabryová[1], Klára Zacharovová[1], Ivan Leontovyč[1], Kateřina Bittenglová[2], Jan Kříž[2], František Saudek[2], Tatiana Baltesová[3], Ingrid Dravecká[3], Stefan Hulík[3], Igor Gala[3], Juraj Miklušica[4], Ivana Dedinska[4], Martina Konkolová[5], Zuzana Žilinská[6], Peter Girman[2]

[1]*Institute for Clinical and Experimental Medicine; Department of Experimental Medicine, Laboratory of Pancreatic Islets, Czechia, Prague, Czech Republic*
[2]*Institute for Clinical and Experimental Medicine; Diabetes Center; Department of Diabetes, Czechia, Prague, Czech Republic*
[3]*L. Pasteur University Hospital, Košice, Slovakia*
[4]*Jessenius Faculty of Medicine in Martin, Martin, Slovakia*
[5]*F.D. Roosevelt University Hospital, Banska Bystrica, Slovakia*
[6]*University Hospital, Bratislava, Slovakia*

Background
To expand access to pancreatic islet transplantation (PITx) in Slovakia, a cross-border collaboration was established involving four Slovak transplant centers (Košice, Martin, Banská Bystrica, and Bratislava) and the islet isolation tissue facility at IKEM in Prague, Czech Republic. Donor pancreases are procured in Slovak hospitals and transported to IKEM for islet isolation. The islets are then returned and transplanted locally in Slovakia. This case series presents the early clinical outcomes of this collaborative program.

Methods
A retrospective analysis was conducted on eleven patients who received PITx within this cross-border model between October 2022 and July 2025**:** nine allogeneic and two autologous transplants. Allogeneic transplant types included islet-after-kidney and simultaneous islet–kidney procedures. Recipients of allogeneic PITx received 180,000–502,000 islet equivalent units (IEQ), and autologous recipients 38,000–165,000 IEQ. Mean cold ischemia time was 5,1 ± 1,0 hours. Clinical follow-up included assessment of insulin requirements, HbA_1c, fasting C-peptide, and hypoglycaemia events at baseline and at 1, 3, 6, 12, and 24 months post-transplantation, where available.

Results
Most patients (55%) demonstrated robust graft function, with sustained C-peptide production (0,61 ± 0,51 nmol/l) and improvements in HbA_1c (46 ± 8 mmol/mol). Mean daily insulin dose decreased from 53 ± 21 IU pre-transplant to 27 ± 18 IU post-transplant and 1 patient achieved insulin independence. In a subset of patients (18%), meaningful reductions in insulin usage occurred (−40%) despite weak or absent C-peptide levels. Notably, two patients (18%) reported a complete resolution of hypoglycaemic episodes, while others (67%) experienced improved hypoglycaemia awareness. No procedure-related mortality or severe complications were observed.

Conclusions

This cross-border islet transplantation model has proven feasible and effective, facilitating the shared use of specialized transplant services between countries. Initial clinical outcomes are encouraging, with multiple patients achieving excellent graft function and glycaemic control. Continued monitoring and further expansion of the network are warranted.

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

PP13 - PATIENT-REPORTED OUTCOME MEASURES FOR KIDNEY TRANSPLANT WITH BETA CELL REPLACEMENT: A REVIEW

Adam O'Connor[1] [1], Rachel Thomas[1]

[1]*Edinburgh Transplant Centre, Edinburgh, United Kingdom*

Background

It is well known that kidney transplant with beta cell transplant (including simultaneous pancreas–kidney (SPK), simultaneous islet kidney (SIK), or islet after kidney (IAK)) improves glycaemic stability and renal graft survival. SPK should be offered to all patients with renal failure secondary to type 1 diabetes. Generally, the decision to proceed is based on fitness, and SIK is a viable option for patients who are not considered fit enough or willing to take on risks of SPK. IAK is usually preferred when a recipient has a live donor due to waiting list times with option for islet transplant later. However, little is known about the potential recipient experience when deciding what type of transplant to pursue.

Patient-reported outcome measures (PROMs) including quality of life (QoL) measurement try to quantify well-being and treatment-satisfaction and are increasingly used to inform patients and ensure holistic care. A review published over 20 years ago advocated for increased utilization of QoL measures in organ transplantation but remains difficult. This study aimed to systematically summarise existing PROMs data in SPK, SIK, and IAK recipients.

Methods

We searched MEDLINE, PMC, Embase, Web of Science, and CENTRAL (2015–present), plus citation tracking, for adult studies reporting PROMs after SPK, SIK and IAK. Inclusion required extractable data for at least one target domain: generic QoL (e.g., SF-36 domains/PCS/MCS or W-BQ12), treatment satisfaction (RTSQ/DTSQ), renal-specific QoL (KDQOL- SF™/RDQoL), or health utility (EQ-5D index or VAS).

Results

Fifteen suitable papers fit criteria. There is no standard transplant QoL measure and therefore results were scattered across generic, diabetic-specific, renal-specific, and treatment-experience domains. Generally, QoL improved after SPK including pain, treatment satisfaction, general health and social functioning. Positive results were also seen after IAK but to a lesser extent than SPK. Islet alone and kidney alone patients also reported benefits.

There were no studies with PROM data for SIK.

Conclusions

SPK and IAK improve QoL for type 1 diabetics with renal failure. However, findings are heterogeneous and, in keeping with the acknowledged difficulty in conducting this type of research, often reported without comparable effect sizes. Although PROM evidence from transplant recipients is rare, it does appear to confer considerable emotional benefit. No studies specifically looked at SIK recipients either

alone or compared to other transplant types. This will be increasingly important as islet cell transplant becomes more widespread and available to those that are not considered fit for SPK and with less pancreases available for whole organ transplant. We propose to collect and report outcomes from SIK recipients using a pre-specified PROM measure as data mapped to domains patients value (general health, pain, function, sleep, work, treatment burden, and health utility) would fill an important evidence gap. This will provide better information for patients and clinicians to help decision making and future trial design.

PP14 - OUTCOMES OF TOTAL PANCREATECTOMY WITH ISLET AUTOTRANSPLANTATION IN HEREDITARY CHRONIC PANCREATITIS: A SINGLE-CENTRE UK EXPERIENCE

Javed Latif[1], Cristina Pollard[1], Giuseppe Garcea[1], Ashley Dennison[1]

[1]*Department of Hepatopancreatobiliary Surgery, University Hospitals of Leicester, Leicester, United Kingdom*

Background
Hereditary chronic pancreatitis (CP), most commonly associated with PRSS1, SPINK1 and CFTR mutations, presents early in life, carries a prolonged disease burden, and confers a ~40% lifetime risk of pancreatic cancer. Total pancreatectomy with islet autotransplantation (TPIAT) is increasingly performed in this group, but outcomes remain underreported. This study evaluates perioperative, metabolic, and functional outcomes of TPIAT in hereditary CP patients at a single UK specialist centre.

Methods
A retrospective review was conducted of all hereditary CP patients undergoing TPIAT between 1994–2024. Demographic, operative, metabolic, and postoperative outcomes were analysed. Genetic diagnoses were confirmed by accredited genomic testing (PRSS1, SPINK1, CFTR).

Results
Nineteen patients with hereditary CP were included. Median (IQR) age was 30 (21 – 41) years. Median (IQR) disease duration was 108 (87 – 123) months. Median (IQR) operative duration was 657 min (645 – 681), although blood loss remained low (median 500 mL). No Clavien-Dindo grade III–V complications or mortality occurred. Median (IQR) hospital stay was 15 (14 – 20) days. Median (IQR) islet yield was 48,070 (20,392 – 107466) IEQ). Median (IQR) islet viability was 90 (85 – 96) %. At one year, insulin independence was achieved in 12% of patients and 53% of patients had discontinued opiates.

Conclusions
Hereditary CP patients undergoing TPIAT are younger and physiologically robust, resulting in fewer complications and faster recovery despite technically complex surgery. However, long-standing disease and pancreatic fibrosis contribute to reduced islet yields, limiting insulin independence. Early consideration of TPIAT in this cohort may preserve islet mass and optimise metabolic outcomes, while also mitigating cancer risk.

PP15 - DETERMINANTS OF ISLET YIELD AND CLINICAL IMPACT FOLLOWING TOTAL PANCREATECTOMY WITH ISLET AUTOTRANSPLANTATION

Javed Latif[1], Cristina Pollard[1], Giuseppe Garcea[1], Ashley Dennison[1]

[1]*Department of Hepatopancreatobiliary Surgery, University Hospitals of Leicester, Leicester, United Kingdom*

Background

Chronic pancreatitis often leads to intractable pain requiring total pancreatectomy, which eliminates pain but causes brittle diabetes. Total pancreatectomy with islet autotransplantation (TPIAT) mitigates this by reinfusing isolated islets, yet metabolic outcomes remain variable. Insulin independence depends strongly on islet yield, but the long-term durability of graft function and the impact of clinical factors such as prior surgery or disease duration remain incompletely defined. This study analyses a large UK single-centre cohort to evaluate determinants of islet yield and their association with long-term glycaemic outcomes.

Methods

An analysis of a retrospective single-centre cohort study of 80 patients undergoing TPIAT from 1994–2024 was performed. Islet equivalents (IEQ) were quantified post-enzymatic digestion and stratified as low (<150,000 IEQ), intermediate (150,000–300,000 IEQ), or high (>300,000 IEQ). Clinical factors (prior pancreatic surgery, symptom duration) and glycaemic outcomes (insulin independence at one year and last follow-up, median 36 months) were extracted from patient records. Associations were assessed using Mann-Whitney U tests for continuous variables and chi-square tests for categorical variables.

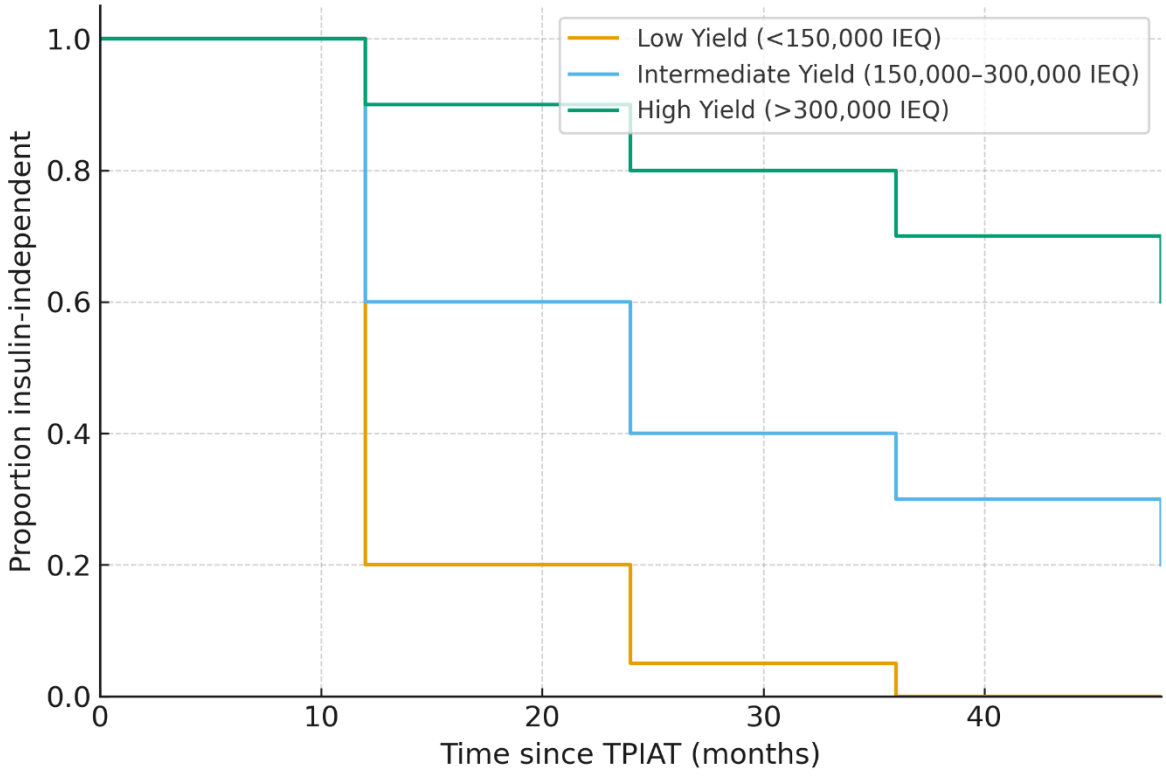
Results

Median (IQR) islet yield was 202,991 (118,000–356,000) IEQ. High yields (>300,000 IEQ) were achieved in 28% of patients, of whom 73% were insulin independent at last follow-up (median 36 months). In contrast, insulin independence was achieved in 31% of intermediate-yield patients and 10% of low-yield patients. Compared with low yield, high yield was associated with markedly greater odds of insulin independence (OR 7.8, 95% CI 2.6–23.5). Prior pancreatic surgery significantly reduced yields (median 155,000 vs 256,000 IEQ, p=0.004). Shorter symptom duration and younger age were also associated with higher yields. Subgroup analyses were performed to assess long-term metabolic outcomes. Amongst patients who achieved insulin independence, the median duration of insulin-free survival was 36 months in the high-yield group compared with 18 months in the intermediate-yield group. By three years after surgery, only 10% of the low-yield group remained insulin independent compared with 70% of the high-yield group (Figure 1).

Conclusions

Islet yield is the key determinant of metabolic outcome after TPIAT, with higher yields favouring insulin independence and partial graft function enhancing glycaemic stability. Early referral, surgical optimisation, and improved isolation techniques are essential to maximise yield and outcomes.

Figure 1: Kaplan–Meier Estimates of Insulin Independence Stratified by Islet Yield



PP16 - INFLUENCE OF PERFUSION STRATEGY ON PANCREATIC GRAFT VIABILITY IN CONTROLLED DCD: ABDOMINAL VERSUS THORACOABDOMINAL NRP

Rongrong Hu Zhu[1], Ramón Rull[1], Rocío García[1], Carlos Perez Serrano[2], CLARA Bassaganyas Vancells[2], Alba Torroella[1], Maria Magdalena Llompart[1], Emma Folch Puy[3], Víctor Emilio Holguin[1], Enrique Montagud-Marrahi[4], Pedro Ventura-Aguiar[4], Antonio J Amor[5], Fritz Diekmann[4], Mireia Gispert[6], Angel Ruiz[7], Mª Angeles Garcia-Criado[2], Josep Fuster[8], Joana Ferrer-Fàbrega[8]

[1]*Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (ICMDiM), Hospital Clínic, University of Barcelona, Barcelona, Spain*
[2]*Department of Radiology, Hospital Clínic, University of Barcelona, Barcelona, Spain*
[3]*Experimental Pathology Department, Institut d'Investigacions Biomèdiques de Barcelona (IIBB). Consejo Superior de Investigaciones Científicas (CSIC), Barcelona, Spain*
[4]*Renal Transplant Unit, Nephrology and Kidney Transplant Department, Hospital Clínic, University of Barcelona, Barcelona, Spain*
[5]*Diabetes Unit, Department of Endocrinology and Nutrition, Hospital Clínic, University of Barcelona, Barcelona, Spain*
[6]*Perfusionist Nurse. Surgical Area. Hospital Clínic, Barcelona, Spain*
[7]*Donation and Transplantation Coordination Unit, Hospital Clinic,, Barcelona, Spain*
[8]*Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (ICMDiM), Hospital Clínic, University of Barcelona, Network for Biomedical Research in Hepatic and Digestive Diseases (CIBERehd), August Pi i Sunyer Biomedical Research Institute (IDIBAPS), Barcelona, Spain*

Background
Pancreas transplantation from controlled donation after circulatory death (cDCD) donors is increasingly being explored as a viable option. This study evaluates outcomes of pancreas transplants using abdominal normothermic regional perfusion (A-NRP) and thoracoabdominal normothermic regional perfusion (TA-NRP) protocols.

Methods
A retrospective observational study was carried out including all pancreas transplants from cDCD donors using TA-NRP and A-NRP from November 2019 to August 2025 at our center. Donor and recipient characteristics, ischemia times, surgical complications, and 1-year graft and patient survival were analyzed.

Results
A total of 34 pancreas transplants from cDCD donors were analyzed, with 12 performed under A-NRP and 22 under TA-NRP.

All TA-NRP cases were simultaneous pancreas-kidney (SPK) transplants, while the A-NRP group included 91.6% SPK and 8.3% pancreas-after-kidney (PAK) procedures. Donors in the A-NRP group were younger, with a median age of 30 years [19–43] compared to 44 years [33–49] in the TA-NRP group (p=0.01). Male donor prevalence was slightly higher in the TA-NRP group (68.2% vs. 58.3%, p=0.71). BMI was comparable between groups (24.1 vs 23.6 kg/m^2, p=0.42).

Cause of death distribution differed: A-NRP donors showed equal proportions of cardiovascular disease (CVD), trauma, and anoxia (33.3% each), whereas TA-NRP donors had a predominance of CVD (50%), followed by trauma (22.7%), euthanasia (18.2%), and anoxia (9.1%). CPR was more frequent in A-NRP donors (41.7% vs. 13.6%).

Median ICU stay was longer in A-NRP donors (7.5 vs. 5 days, p=0.11), and serum amylase levels were lower (55.5 vs. 96 U/L, p=0.11). IGL-1 was the primary preservation solution in both groups, with similar usage rates (83.3% vs 81.8%). Premortem cannulation was performed in all TA-NRP cases and in 83% of A-NRP cases (p=0.04).

Warm ischemia times were comparable between groups (median WIT: 18 minutes, p=0.91), although functional WIT was shorter in A-NRP (11.5 vs. 14 minutes, p=0.21). Postmortem NRP duration was slightly longer in TA-NRP (115.5 vs. 100.5 minutes, p=0.89), and cold ischemia time was marginally higher (6.3 vs. 5.8 hours, p=58).

Recipient characteristics showed older age in the A-NRP group (48.5 vs. 44 years, p=0.23), with similar gender distribution and BMI (p=0.71). Hospital stay was slightly longer for TA-NRP recipients (13.5 vs. 12 days, p=0.89).

Pancreas-related surgical complications were more frequent in the A-NRP group (75% vs. 59%, p=0.465). Clavien-Dindo grade IIIB complications were more prevalent in TA-NRP (27.3% vs. 16.7%). Specific complications varied, with venous thrombosis being the most common in both groups.

One-year graft survival was slightly higher in the A-NRP group (82.5% vs. 80.6%, p=0.804), while patient survival was 100% in both cohorts.

Conclusions
These results support the feasibility and safety of pancreas transplantation from cDCD donors using both A-NRP and TA-NRP.

PP17 - OUTCOMES OF SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANT IN PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION. A SINGLE CENTRE EXPERIENCE.

Dimitrios Chatziisaak[1], Ashley Lau[1], Chris Callaghan[1], Martin Drage[1], Rachel Hilton[1], Nicos Kessaris[1], Georgios Papadakis[1]

[1]*Guy's and St. Thomas' NHS Foundation Trust, Department of Transplant Surgery, London, United Kingdom*

Background

The advent of highly active antiretroviral therapies (HAART) has altered the natural history of HIV infection into a chronic condition. As survival improves, non–HIV-related comorbidities such as diabetes mellitus and end-stage kidney disease have become increasingly prevalent among these patients. Solid organ transplantation, once contraindicated in this population, is now an established therapeutic option, with kidney and liver transplants demonstrating outcomes comparable to HIV-negative recipients under effective viral suppression. However, experience with simultaneous pancreas–kidney (SPK) transplantation in HIV-positive patients remains scarce, primarily due to concerns regarding immunosuppression, infection risk, and potential interactions between antiretroviral and immunosuppressive agents. Expanding evidence from current literature, SPK transplantation can restore metabolic control without compromising HIV stability. The present study evaluates the feasibility, safety, and outcomes of SPK transplantation in HIV-positive recipients within a high-volume transplant centre.

Methods

A retrospective analysis was conducted of HIV-positive patients undergoing SPK transplantation between 2007 and 2025. Data were extracted from prospectively maintained records, including demographics, immunosuppressive regimens, HAART compatibility, rejection episodes, infections, and graft function. Primary outcomes were patient, kidney, and pancreas graft survival; secondary outcomes included postoperative infection and maintenance of HIV control.

Results

Three male recipients (mean age 44.5 years) underwent SPK transplantation while on stable HAART with undetectable viral loads and preserved CD4 counts. Immunosuppression consisted of tacrolimus, mycophenolate mofetil, and prednisolone, with early steroid withdrawal in one case; tacrolimus doses were individualized due to HAART interactions. Median follow-up was 3 years. Patient, kidney, and pancreas graft survival were 100%. No biopsy-proven acute rejection occurred.

The mean serum creatinine was 174.5 µmol/L at 1 month post-transplant (95% CI: 53.8–295.2), 138.5 µmol/L at 6 months (95% CI: 30.5–246.5), and 128.5 µmol/L at 1 year (95% CI: 81.2–338.2). By year 3, the mean creatinine was 137.5 µmol/L (95%

CI: 67.6–207.4), indicating stable long-term renal function. All patients remained insulin-independent with preserved pancreatic function. Two patients developed bacterial infections, successfully treated with antibiotics. Outcomes were comparable to HIV-negative SPK recipients.

Conclusions
SPK is feasible in selected HIV-positive recipients. In the context of effective HAART and tailored immunosuppression, outcomes demonstrate excellent patient and graft survival, minimal rejection, and controllable infection risk. These results reinforce that HIV infection should not be considered a contraindication to SPK transplantation. Further multicentre studies are warranted to optimize immunosuppressive strategies and expand equitable access for this growing patient population.

PP18 - IMPACT OF EXOCRINE DRAINAGE TECHNIQUE ON HEMORRHAGIC COMPLICATIONS AFTER PANCREAS TRANSPLANTATION

Rongrong Hu Zhu[1], Ramón Rull[1], Rocío García[1], CLARA Bassaganyas Vancells[2], Carlos Perez Serrano[2], Emma Folch Puy[3], Víctor Emilio Holguin[1], Enrique Montagud-Marrahi[4], Pedro Ventura-Aguiar[4], Antonio J Amor[5], Fritz Diekmann[4], Mª Angeles Garcia-Criado[2], Josep Fuster[6], Joana Ferrer-Fàbrega[6]

[1]*Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (ICMDiM), Hospital Clínic, University of Barcelona, Barcelona, Spain*
[2]*Department of Radiology, Hospital Clínic, University of Barcelona, Barcelona, Spain*
[3]*Experimental Pathology Department, Institut d'Investigacions Biomèdiques de Barcelona (IIBB). Consejo Superior de Investigaciones Científicas (CSIC), Barcelona, Spain*
[4]*Renal Transplant Unit, Nephrology and Kidney Transplant Department, Hospital Clínic, University of Barcelona, Barcelona, Spain*
[5]*Diabetes Unit, Department of Endocrinology and Nutrition, Hospital Clínic, University of Barcelona, Barcelona, Spain*
[6]*Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (ICMDiM), Hospital Clínic, University of Barcelona, Network for Biomedical Research in Hepatic and Digestive Diseases (CIBERehd), August Pi i Sunyer Biomedical Research Institute (IDIBAPS), Barcelona, Spain*

Background

Pancreas transplantation is a well-established treatment for selected patients with diabetes mellitus, offering improved glycemic control and quality of life. Postoperative hemorrhagic complications remain a significant concern, potentially affecting graft and patient survival. This study aims to evaluate hemorrhagic complications following pancreas transplantation depending on the type of exocrine drainage technique.

Methods

A retrospective cohort study was conducted including 525 pancreas transplantations at our center between January 2000 and July 2025. Patients were categorized by exocrine drainage type: duodenojejunostomy (DJ) or Duodenoduodenostomy (DD). Donor and recipient characteristics, postoperative complications and long-term outcomes were assessed.

Results

Among the donors, 93.9% (n=493) were from donation after brain death (DBD), with all donors in the DJ group (n=337) and 83% (n=156) in the DD group. Controlled donation after circulatory death (cDCD) accounted for 17% (n=32) of donors, exclusively in the DD group. The median donor age was 33 years (31 in DJ vs 36 in DD, $p < 0.05$), with a median BMI of 23.4 kg/m² (23.4 in DJ vs 23.5 in DD), and 59.6% were male (61.1% in DJ vs 56.9% in DD). Causes of death included trauma (47.8%; 54% in DJ vs 36.7% in DD), cerebrovascular accident (39.4%; 36.9% in DJ vs 45.7% in DD), anoxia (7.8%; 5.6% in DJ vs 11.7% in DD), and euthanasia (4%; all in DD). Median ICU stay was 2 days (3 in DJ vs 2 in DD), and cold ischemia time (CIT) averaged 10 hours (10.3 in DJ vs 7.5 in DD, $p < 0.05$).

Recipient demographics showed 62.3% male (63.3% in DJ vs 58.5% in DD), with a median age of 41 years (40 in DJ vs 43 in DD, $p < 0.05$) and a BMI of 23 kg/m² in both groups. The median duration of diabetes mellitus was 26 years (26 in DJ vs 28

in DD, $p < 0.05$), and dialysis duration was 24 months (27 in DJ vs 18 in DD, $p < 0.05$).

Out of 525 pancreas transplant recipients, 54 (10.3%) developed hemorrhagic complications. These were distributed according to the type of exocrine drainage: 28 cases in the DJ group and 26 in the DD group. In the DJ group, the severity of complications based on the Clavien-Dindo classification was: Grade I – 3.6% (n=1), Grade II – 3.6% (n=1), and Grade IIIB – 92.3% (n=26). In the DD group, complications were classified as: Grade I – 7.7% (n=2), Grade II – 34.6% (n=9), Grade IIIA – 3.8% (n=1), and Grade IIIB – 54.8% (n=14). Reintervention rates due to hemorrhagic complications were higher in the DJ group compared to DD.

Among patients with hemorrhagic complications, the DD group demonstrated superior 5-year outcomes, with graft survival reaching 87% compared to 70.6% in the DJ group ($p = 0.352$).

Similarly, 5-year patient survival was also higher in the DD group, at 95.2% versus 92.9% in the DJ group ($p = 0.628$).

Conclusions
Duodenoduodenostomy drainage was associated with fewer severe hemorrhagic complications and better long-term graft and patient survival compared to duodenojejunostomy, suggesting a potential advantage in surgical technique selection.

PP19 - EARLY SURGICAL COMPLICATIONS OF PANCREAS TRANSPLANT

Karol Sutoris[1], Peter Girman[1], Frantisek Saudek[1], Jan Kriz[1], Radomira Koznarova[1], Terezia Havrdova[1], Jiri Veleba[1], Barbora Hagerf[1], Sara Sabolova[1], Tomas Marada[1], Jaroslav Chlupac[1], Jiri Fronek[1], Kvetoslav Lipar[1]

[1]*Institute for Clinical and Experimental Medicine, Prague, Czech Republic*

Background
Pancreas transplantation provides definitive metabolic control in patients with diabetes mellitus, particularly in those with end-stage renal disease when performed in combination with kidney transplantation. Despite technical advances, early surgical complications continue to compromise graft survival and patient outcomes. This study aimed to analyze the incidence, types, and impact of early surgical complications following pancreas transplantation over a five-year period at a single high-volume transplant center.

Methods
A retrospective single-center study was conducted at the Institute for Clinical and Experimental Medicine (IKEM) in Prague, Czechia, including all pancreas transplants performed between 2000 and 2024. Early surgical complications were defined as events occurring within 30 days postoperatively and included bleeding, graft thrombosis, intestinal anastomotic leakage, pancreatitis, abscess formation, and bowel complications. Demographic data, donor and recipient characteristics, operative techniques, timing, and outcomes were collected and statistically analyzed.

Results
A total of 177 pancreas transplants were performed during the study period: 81% simultaneous pancreas–kidney transplants (n=147), 9% pancreas-after-kidney transplants (n=16), 4% pancreas transplants alone (n=7), 4% multi-organ transplants (n=7), and 6% pancreas retransplantations (n=10). In the majority of cases (93%), the graft was placed intraperitoneally.
Early surgical complications occurred in 47% of cases. Intra-abdominal bleeding was the most frequent (15%), originating from the pancreas graft in 10% and from the kidney graft in 5%. Pancreas graft thrombosis occurred in 5% of cases (with venous thrombosis being three times more common than arterial), and duodenal anastomotic leakage was observed in 1%. Reperfusion pancreatitis was observed in fewer than 5% of recipients, and controlled pancreatic fistula only in 1% – all of which were successfully managed conservatively. A peripancreatic abscess developed in 5% of cases, and early mechanical ileus required surgical intervention in only three patients in the entire cohort.
The incidence of early relaparotomy after pancreas transplantation in our study group was 18%. Pancreas graft loss due to surgical complications occurred in 6% of recipients, while kidney graft loss was recorded in only one case.

Conclusions
Although the incidence of early surgical complications of pancreas transplant is not negligible, the number of required reoperations does not mirror this frequency.

Nevertheless, early surgical complications remain a major cause of early graft loss following pancreas transplantation. Continuous refinement of surgical technique, prompt recognition, and timely intervention are essential to preserve graft function and improve patient outcomes. Findings from this five-year single-center experience at IKEM underscore the importance of meticulous surgical management and multidisciplinary care in minimizing technical failures.

PP20 - THE IMPACT OF THE PANCREAS DONOR RISK INDEX SCORE ON OUTCOMES AFTER SOLID ORGAN PANCREAS TRANSPLANTATION

Ruth Owen[1], Sean Pattinson[1], Emily Thompson[1], Abdullah Malik[1], Lewis Simmonds[2], Claire Counter[2], John Casey[3], Colin Wilson[1], Steven White[1]

[1]*Institute of Transplantation, Freeman Hospital, Newcastle Upon Tyne, United Kingdom*
[2]*NHS Blood and Transplant Statistics, Bristol, United Kingdom*
[3]*Edinburgh Royal Infirmary, Edinburgh, United Kingdom*

Background
The UK pancreas transplant waiting list is growing and rates of pancreas transplantation are falling. Factors thought to have contributed to this change are lower rates of consent for organ donation alongside an increasing number of DCD organ donors. The PDRI was developed using SRTR data to help assess donor risk and guide pancreas utilization and has been validated in a UK cohort but it is not known what impact this has had on overall pancreas utilization or graft survival rates. The aim of this study was to identify whether the PDRI has led to changes in both the risk profile and what impact this has had on overall pancreas graft failure rates.

Methods
Retrospective data on all UK solid organ pancreas transplants from 2015 - 2023 were obtained from the NHSBT UK Transplant Registry. Cases missing survival data, retransplants and multi-organ transplants were excluded, resulting in a final cohort of n=1417. Graft survival analyses were conducted using Kaplan-Meier plots and Cox regression models at ninety-days, one-year and three-years. Data analyses were performed during 3 consecutive eras: 2015-2017, 2018-2020, 2021-2023.

Results
Higher PDRI scores were associated with lower graft survival rates, though this did not reach statistical significance at 90 days (p=0.0627), one-year (p=0.084) or three-years (p=0.32). Three-year graft survival was significantly lower for grafts from high-risk donors (PDRI>1.848) compared with lower risk donors (PDRI<1.848) during 2015–2017 (79.2% vs. 86.4%, p=0.0381), but not in later eras (2018–2020: p=0.8431; 2021–2023: p=0.9178). The proportion of high-risk donors transplanted decreased from 30% in 2015–2017 and 22% in the remaining eras.

Conclusions
The PDRI remains a valuable tool for pancreas graft selection and risk assessment. Despite the use of more marginal donors with higher donor risk scores this does not appear to have changed overall graft survival rates during different eras. The improved outcomes in later years also suggests better management of higher-risk grafts. These findings need to be confirmed in a more detailed analysis between SPK and solitary pancreas transplant groups.

PP21 - GLUCOSE METABOLISM AFTER PANCREAS-KIDNEY, ISLET-KIDNEY AND KIDNEY-ALONE TRANSPLANTATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

Arnold Marchis[1,2], Mahmoud Obeidat[1], Yoon Kee Beck[1], Sándor Orbán[1,2], Georgiosz Kukumzisz[1], Devarajulu Mariyappan[1], Orsolya Dohán[1,2], Reka Toth[1], Peter Fehervari[1], Titus Augustine[4,5], Péter Hegyi[1,2,3,6], Szilárd Váncsa[1,2†], Bálint Erőss[1,2,3†]

† authors contributed equally

[1]*Centre for Translational Medicine, Semmelweis University.,*
[2]*Institute for Pancreatic Diseases, Semmelweis University., Budapest, Hungary*
[3]*Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary*
[4]*Manchester University Hospitals NHS Foundation Trust, Manchester, UK*
[5]*University of Manchester, Manchester, UK*
[6]*Translational Pancreatology Research Group, Interdisciplinary Centre of Excellence for Research Development and Innovation, University of Szeged, Szeged, Hunga*

Background
Type 1 diabetes (T1D) is an autoimmune disease which severely affects life expectancy. Diabetic nephropathy is a leading cause of end-stage renal disease (ESRD), and patients require dialysis or renal transplantation (RT). Options for therapy to achieve adequate glucose metabolism are pancreas transplantation, islet transplantation or insulin therapy. This systematic review and meta-analysis assesses glucose metabolism, cardiovascular risk parameters, kidney function, overall patient and graft survival and hazard ratios comparing individual patient data between different transplantation methods.

Methods
Our systematic search was performed in three databases (Pubmed, Embase, and Cochrane Library) on the 16th of November 2024. Both single-arm and two-arm studies reported on PKT (pancreas-kidney transplant), islet-kidney transplant (IKT) and kidney transplant alone and insulin therapy (KTA-I) were included. Our primary outcome was the change in HbA1c levels from baseline to 12 months of follow-up. Mean differences (MD) and their 95% confidence interval (CI) were calculated using a random-effect model. The protocol was registered in PROSPERO (CRD42024610944).

Results
Pancreas transplantation significantly decreases HbA1c levels by 2.93% (95% CI -3.33, -2.54) after 12 months of transplantation (Figure 1). SPKT could decrease the HbA1c by 2.59% (95% CI: 5.43, 0.25) more compared to KTA-I after 12 months of follow-up.

Conclusions
Pancreas transplantation significantly improves glucose metabolism, kidney function and blood pressure in patients with T1D undergoing renal transplantation. SPKT is superior to KTA-I therapy in improving glucose metabolism.

PP22 - RETHINKING VASCULAR ANASTOMOSIS: THE IMPACT OF ACCESSORY ARTERIAL GRAFTS IN PANCREAS TRANSPLANT SURGERY

Rongrong Hu Zhu[1], Ramón Rull[1], Rocío García[1], CLARA Bassaganyas Vancells[2], Carlos Perez Serrano[2], Emma Folch Puy[3], Víctor Emilio Holguin[1], Enrique Montagud-Marrahi[4], Pedro Ventura-Aguiar[4], Antonio J Amor[5], Fritz Diekmann[4], Mª Angeles Garcia-Criado[2], Josep Fuster[6], Joana Ferrer-Fàbrega[6]

[1]*Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (ICMDiM), Hospital Clínic, University of Barcelona, Barcelona, Spain*
[2]*Department of Radiology, Hospital Clínic, University of Barcelona, Barcelona, Spain*
[3]*Experimental Pathology Department, Institut d'Investigacions Biomèdiques de Barcelona (IIBB). Consejo Superior de Investigaciones Científicas (CSIC), Barcelona, Spain*
[4]*Renal Transplant Unit, Nephrology and Kidney Transplant Department, Hospital Clínic, University of Barcelona, Barcelona, Spain*
[5]*Diabetes Unit, Department of Endocrinology and Nutrition, Hospital Clínic, University of Barcelona, Barcelona, Spain*
[6]*Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Clinic Institute of Digestive and Metabolic Diseases (ICMDiM), Hospital Clínic, University of Barcelona, Network for Biomedical Research in Hepatic and Digestive Diseases (CIBERehd), August Pi i Sunyer Biomedical Research Institute (IDIBAPS), Barcelona, Spain*

Background

Vascular anastomosis is a critical component of pancreas transplantation, directly influencing graft perfusion and postoperative outcomes. Traditionally, arterial reconstruction has relied on splenomesenteric or Y graft techniques to establish adequate blood flow. However, these approaches may be limited by anatomical variability and technical complexity. This study explores the use of accessory arterial grafts as an alternative strategy, aiming to optimize vascular supply.

Methods

A descriptive study will analyze three arterial anastomosis configurations used in pancreas transplantation performed at a single-center from May 2016 to July 2025: (1) splenomesenteric anastomosis with an interposed iliac graft between the splenic and superior mesenteric arteries, (2) splenomesenteric anastomosis with an iliac graft to the recipient's common right iliac artery, and (3) a combined technique using both an interposed iliac graft and an additional iliac graft to the recipient's common right iliac artery.

Results

A total of 188 pancreas transplantations were carried out in a period of 9 years. Among these, there were 15 cases utilizing alternative vascular configurations with accessory arterial grafts, 6 involved splenomesenteric anastomosis with an interposed iliac graft between the splenic and superior mesenteric arteries. This first group —in which all cases were Simultaneous Pancreas-Kidney (SPK) transplants— experienced three notable complications: one case of pancreatitis accompanied by distal splenic artery thrombosis (with the graft remaining functional), one conservatively managed hemoperitoneum, and one transplantectomy due to intestinal anastomotic dehiscence.

In another 8 cases —comprising 4 SPK transplants and 4 Pancreas Retransplantations (PRT)— a splenomesenteric anastomosis was performed using

an iliac graft connected to the recipient's common right iliac artery. This second group presented one venous thrombosis, one case of pancreatitis in a PRT, and one abdominal hematoma—all with functioning grafts—and one transplantectomy.

A single PRT case employed a combined technique using both an interposed iliac graft and an additional iliac graft to the recipient's common right iliac artery, which also resulted in transplantectomy.

Despite these complications, one-year patient survival was 100% across all configurations.

Conclusions

Accessory arterial grafts may offer enhanced flexibility in complex vascular anatomies, facilitate tension-free anastomoses and improve arterial alignment, potentially improving graft perfusion.

Despite isolated complications, alternative vascular techniques are a viable option to complement or replace classical anastomosis strategies in selected cases.

PS01 - NOVEL GASEOUS ORGAN BIOPSY TECHNOLOGY TO PREDICT ORGAN STATUS DURING PRESERVATION

Rhys Pook, Claire Batty, Aimen Amer, Simi Ali, William E Scott Iii

What is the problem you are trying to address (Background)?

Pancreas transplantation is constrained by the absence of real-time tools to evaluate graft viability. Current assessment depends on surgical inspection and subjective judgement, leading to the discard of potentially viable organs. To safely increase utilisation, the field needs a non-invasive, real-time prognostic biomarker to assess organ condition.

What are your solutions to address problems (Aims)?

This project aimed to establish initial proof-of-concept that volatile organic compounds (VOC) are potential biomarkers of pancreas viability during organ preservation by gaseous oxygen persufflation (PSF). These VOCs can be linked to known biological pathways and compared with established tissue evaluation methodologies.

How are you going to solve the problems? (What methods are you going to use, and if you have any data supporting your hypothesis/methods)

Human donor pancreata (n=3) were prepared and gas delivery assessed (using N_2) prior to 24h PSF (40% O_2 at 4°C) using the ScubaTx device. VOCs were collected via a bespoke headspace collection device at baseline, 5min, 12h and 24h. Effluent gas was collected in thermal desorption tubes and profiled by gas chromatography mass spectrometry. 267 compounds have been identified so far. This was reduced to 97 after filtering to eliminate compounds observed only once. Results revealed clear temporal shifts across time points. Further proof-of-concept of the experimental design was achieved by identifying a donor-specific anaesthetic compound – Sevoflurane. Thus, validating both the sensitivity of the system and feasibility of the monitoring set up.

What do you need for further investigation? What do you want to do in the future?

Parallel analyses of tissue biopsies including histology, ultrastructural evaluation and transcriptomics are underway to correlate markers of cellular injury and stress responses which may be linked to VOC signatures. The next phase will expand donor cohorts to include organs subjected to both short and prolonged cold ischaemia. These profiles will be correlated with cellular injury and metabolic stress markers to define signatures of a health. Longer-term, this work provides the

foundation for translational development of VOC-based sensors for temporal, non-invasive monitoring during the peri-transplant period

Why is this work important and relevant to the future of beta cell replacement therapy?

This work represents the first demonstration of volatile organic compound analysis for *ex vivo* monitoring of donor-organs. Here we establish proof-of-concept for real-time sensing technologies that could help future graft selection for beta-cell replacement therapy.

PS02 - FEASIBILITY STUDY OF AUTOMATED PANCREATIC ISLET ISOLATION USING ROBOTIC AND MODULAR BIOPROCESSING SYSTEMS

Rami Aljaberi, Mekhola Hoff

Background
Pancreatic islet transplantation can restore insulin independence in selected type 1 diabetes patients, yet current islet isolation methods are highly manual, variable, and inefficient. Up to half of the islets can be lost during purification due to open handling and complex multi-step processes, limiting scalability and access to this curative therapy.

Aims
This study aims to develop and evaluate a fully automated, robotic, and closed-system bioprocessing platform for pancreatic islet isolation. The goal is to reduce operator dependency, contamination risk, and variability while improving yield, reproducibility, and efficiency.

Methods
The automated system will integrate enzymatic digestion, purification, and washing in a modular workflow. It will replicate standard manual steps—collagenase perfusion, Ricordi chamber digestion, and density gradient centrifugation—within a sterile robotic platform. Validation will compare islet yield, viability, purity, and functionality against manual controls. Exploratory endpoints include process duration, sterility, and operator intervention frequency.

Future work
Further work will focus on optimizing robotic parameters for different donor conditions, integrating real-time monitoring sensors, and testing compatibility with stem cell–derived islets. Scaling the platform for clinical-grade production and regulatory validation will be essential for translation.

Why is this work important and relevant to the future of beta cell replacement therapy?
This work lays the foundation for automated, standardized islet processing—a critical step toward scalable beta cell replacement. As stem cell–derived and bioengineered islets become clinically viable, a robotic closed-system platform will ensure consistent quality, safety, and efficiency, accelerating the adoption of islet transplantation as a mainstream therapy for type 1 diabetes.

PS03 - DEVELOPMENT OF AN ALL-HUMAN VASCULARIZED MODEL OF PANCREATIC ISLETS ON-CHIP: TOWARDS PERSONALIZED MEDICINE FOR TYPE 1 DIABETES

Mélanie Lopes, Emily Tubbs, Fabrice Navarro, Sandrine Lablanche, Xavier Gidrol

What is the problem you are trying to address (Background)?

Islet transplantation is a promising cell replacement therapy, but the loss of graft efficacy after 5–10 years suggests that this approach could still be further optimized. Therefore, the development of a vascularized human pancreatic islet model for the study of diabetes appears essential.

What are your solutions to address problems (Aims)?

Our project proposes an innovative alternative: a microfluidic islet-on-chip model (Figure 1), designed to mimic human physiological conditions, including vascularization and the specific microenvironment of pancreatic islets.

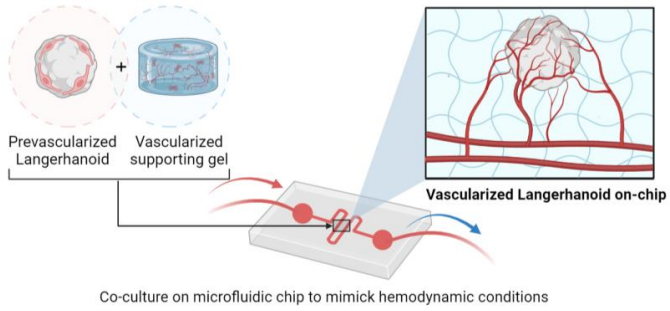


Figure 1: Schematic representation of the vascularized Langerhanoid on a microfluidic chip.

How are you going to solve the problems? (What methods are you going to use, and if you have any data supporting your hypothesis/methods)

This model relies on a microfluidic chip integrating pre-vascularized human Langerhans islet spheroids aka Langerhanoids, composed of three types of self-organized human cells. The chip incorporates a bioactive hydrogel seeded with endothelial cells to promote vascular network formation, while perfusion ensures physiological nutrient and oxygen flow. Cell ratios, cell types, and hydrogel composition were optimized to establish a permissive microenvironment for vascular sprouting and functional anastomosis between Langerhanoid sprouts and the surrounding endothelial network within the chip.

What do you need for further investigation? What do you want to do in the future?

A human-derived hydrogel enriched in growth factors was developed to support endothelial network formation. At day 10, a significant increase was observed with the developed hydrogel regarding total length, segment, nodes and pro-angiogenic genes expression compared to bovine fibrin controls (n=4). Pancreatic islets embedded in this matrix preserved their viability and insulin secretion upon glucose stimulation (n=2,

ongoing). Optimized cell ratios improved the development of endothelial network within the Langerhanoid and the microenvironment (n=3, ongoing).

Why is this work important and relevant to the future of beta cell replacement therapy?

Ultimately, this all-human vascularized islet-on-chip model represents a versatile platform for studying the interactions between pancreatic islets, vasculature, and their microenvironment. Beyond providing mechanistic insights into islet survival and function, its compatibility with a possible immune system perfusion also makes it a valuable tool for drug testing and patient-specific applications, paving the way toward personalized medicine in type 1 diabetes.

PS04 - A VASCULARISED ORGAN-ON-CHIP PLATFORM TO MODEL IMMUNE–ISLET INTERACTIONS AND TEST IMMUNOMODULATORY STRATEGIES FOR TYPE 1 DIABETES

Xiang Xu, Maja Witowska, Benjamin Hansen, Luana A De Abreu Queiros Osorio, Victoria Salem

Type 1 diabetes (T1D) results from the autoimmune infiltration and destruction of insulin-producing β-cells in the pancreatic islets. The islet microvasculature plays a pivotal role in this process, under inflammatory stress, it becomes adhesive and chemotactic, guiding immune cells across the endothelium and into the islet niche. Current in vitro and animal models fail to capture this complex vascular–immune dynamic.

We have engineered a vascularised organ-on-chip (OoC) model that recapitulates the human islet microenvironment, enabling quantitative study of immune cell trafficking to provide a preclinical testing platform for anti-inflammatory drugs, immunomodulatory biomaterials, and local immunosuppressive coatings. Our microfluidic platform supports the self-assembly of perfusable human microvascular networks (MVNs) within a fibrin matrix. Controlled flow via a custom-built pressure-driven system that establishes physiological shear and vessel maturation, fluorescently labelled PBMCs are perfused to quantify adhesion and transendothelial migration (TEM) using both endpoint imaging (24–48 h) and live 4D confocal microscopy (90 min; xyzt).

To emulate the inflamed islet niche, we integrate cytokine priming (TNF-α, IL-1β, IFN-γ) for endothelial activation and chemokines (CCL2, CXCL12, CXCL10) embedded in fibrin to create tissue-side chemokine gradients. This drives significantly increased TEM vents and PBMC movement. Future iterations will incorporate antigen-tethered hydrogels and primary human islets to recreate β-cell autoantigen presentation. The system will be used to screen candidate immunosuppressive agents and immune-modulating biomaterials for their ability to prevent immune infiltration while preserving vascular integrity.

This vascularised OoC bridges immunology and tissue engineering, providing a human-relevant testbed for next-generation T1D therapies. By enabling controlled, quantitative analysis of immune–islet interactions, it offers a pathway toward personalised screening of immunosuppressive strategies that could improve the long-term survival of transplanted or stem-cell–derived β-cells in future replacement therapies.

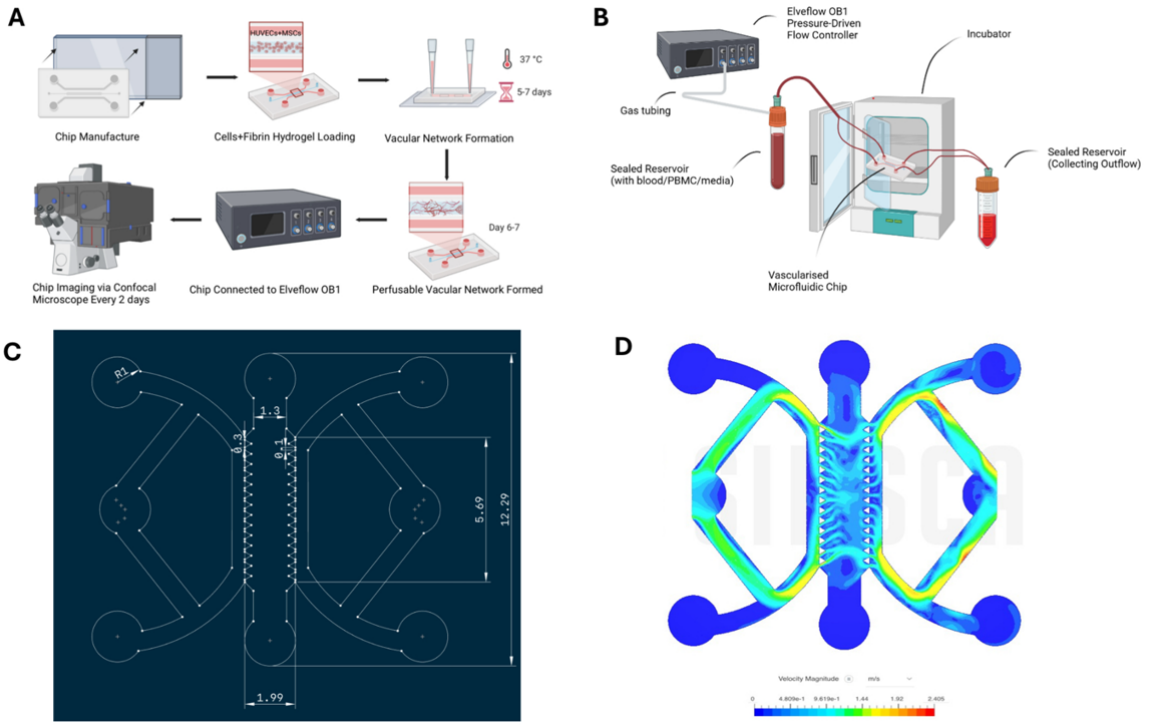


Figure 1 Pressure-driven perfusion workflow and chip design for vascular remodeling experiments.

(A) Stepwise schematic of the experimental workflow, including chip fabrication, cell-hydrogel loading (HUVECs + MSCs), vascular network formation under static conditions, and connection to the Elveflow OB1 system for pressure-driven perfusion.

(B) Diagram of the Elveflow OB1 pressure controller setup. Media or PBMCs are pressurized in a sealed reservoir, flow through the chip inside the incubator, and exit via a secondary sealed reservoir.

(C) Engineering blueprint of the microfluidic chip showing dimnsions of side and central channels and outlet ports.

(D) Computational fluid dynamics (CFD) simulation displaying flow velocity profiles throughout the chip, confirming uniform perfusion with central flow concentration. Velocity magnitudes range from 0 to 2.4 mm/s.

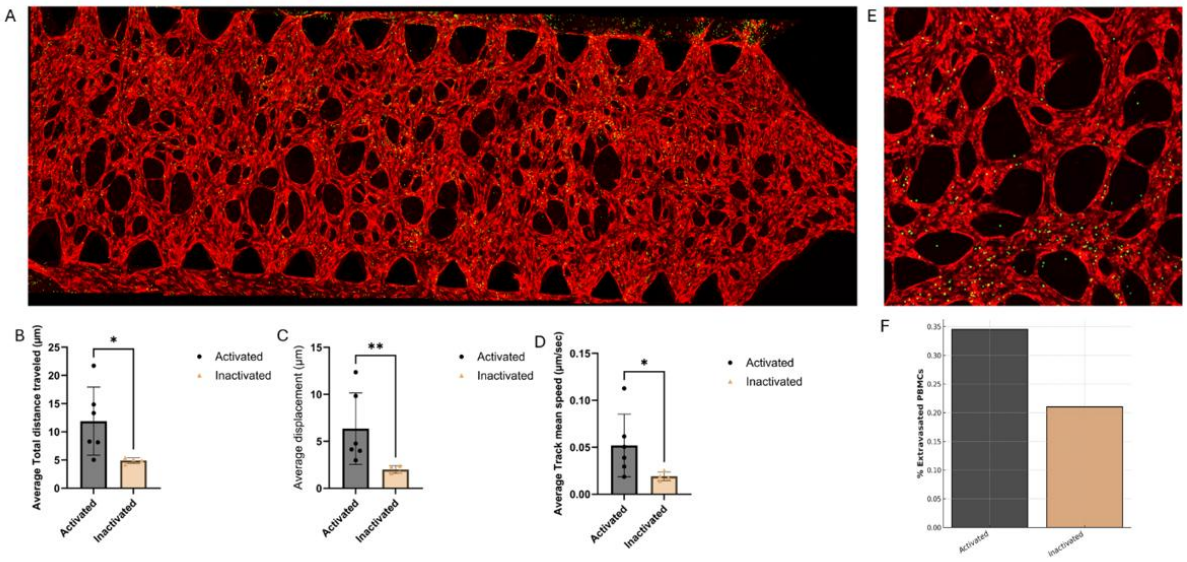


Figure 2 Preliminary quantification of PBMC motility and extravasation in vascularized microfluidic chips.
(A) Maximum intensity projection of the central chamber of a vascularized microfluidic chip showing self-assembled perfusable RFP–HUVEC (red) and MSC co-cultured microvessel networks supporting perfused CMFDA-labelled PBMCs (green). The network demonstrates extensive lumen formation across the central gel channel.
(B–D) Quantitative analysis of PBMC motility parameters obtained from 3D time-lapse imaging (xyzt). Activated PBMCs display significantly higher total distance travelled (B), net displacement (C), and mean track speed (D) compared to inactivated PBMCs, indicating increased motility and potential for transendothelial migration (TEM). Bars represent mean ± SD; each point corresponds to an individual tracked PBMC; $p < 0.05$, $p < 0.01$, Student's t-test.
(E) Representative confocal projection of an ROI within the vascularized network showing adherent and transmigrated PBMCs in close association with the vessel wall.
(F) Preliminary quantification of PBMC extravasation rates per ROI based on endpoint analysis of 24–48 h perfusions. Activated PBMCs demonstrated a higher proportion of extravasated cells (0.345%) compared to inactivated PBMCs (0.210%), consistent with enhanced migratory activity observed in live imaging.

PS05 - DIETARY GUIDELINES POST KIDNEY TRANSPLANT – IS THIS THE MISSING LINK IN GRAFT SURVIVAL?

Suzanne Schneider, Deborah Biggerstaff, Thomas Barber

BACKGROUND

The physiology of a transplanted kidney is affected from the moment it is separated from the donor. The risk of complications arising from surgery are highly associated with ischemic-reperfusion injury (IRI) due to the effects of hypoxia and oxidative stress during the procurement, preservation and reperfusion procedures. Hypoxia promotes the formation of reactive oxygen species, and it seems apparent that finding ways of optimising the metabolic milieu for the transplanted kidney would improve recovery and graft survival. Emerging research highlights the potential benefits of nutritional interventions—particularly antioxidant and energy-supporting nutrients—in reducing IRI-related damage and enhancing graft survival. These benefits are especially relevant for transplant recipients who are often nutritionally compromised due to prolonged dialysis and stringent diets. Despite the high incidence of allograft failure, a search of the literature and grey literature reveals no medical nutrition therapy guidelines for post-transplant recovery and survival.

AIMS

Review current evidence on the impact of specific macro- and micronutrients on IRI and allograft survival in the perioperative period, highlighting targeted nutrition as a critical yet overlooked component of post-transplant care.

METHOD

A comprehensive MEDLINE and Embase search (English only, no date limits) identified 68 papers, none. Grey literature from major transplant organizations likewise revealed no nutrition guidance. Consequently, a narrative review and systematic synthesis of available evidence was undertaken.

FURTHER INVESTIGATION

1. The effect of a Therapeutic Carbohydrate Restricted diet versus a standard diet on post-surgical recovery.
2. Reduction of New Onset Diabetes After Tx through dietary intervention.

IMPACT STATEMENT

Transplant patients have unique nutritional needs, and many kidney recipients are already deficient at the time of surgery, which increases the risk of IRI, graft failure, and mortality. With over a third of grafts failing within 10 years, clear post-transplant dietary guidelines are essential to improve outcomes and support long-term.

PS06 - CELL-BASED IMPLANT FOR BETA CELL REPLACEMENT THERAPY

Carolin Hermanns, Aylin Seedorf, Sami Gemal Mohammed, Julie Kerr-Conte, Aart van Apeldoorn

What is the problem you are trying to address (Background)?

Beta cell delivery devices are currently considered the preferred method for beta cell replacement therapy, offering safe implantation and support for cell function.

What are your solutions to address problems (Aims)?

While synthetic devices improve the islet environment, they still risk triggering foreign body responses. Creating cell-based implants may address this issue and enhance engraftment.

How are you going to solve the problems? (What methods are you going to use, and if you have any data supporting your hypothesis/methods)

Commercially available NUNC UpCell dishes were used to culture immortalized mesenchymal stem cells into cell sheets. Cell sheets of MSCs and HUVECs were layered on top of each other to encapsulate β-cells. The construct was transferred to decellularized ECM. Functionality of the construct was assessed.

Stacking cell sheets with one ECM support improves stability and handling of constructs. A multilayered construct integrates insulin-producing cells well. HUVECs and iMSCs cultured together form a vascular-like network within the cell sheets. Encapsulated β-cells stay functional for several days.

What do you need for further investigation? What do you want to do in the future?

The next step involves replacing primary islets with stem cell-derived beta cells, followed by evaluating their functionality and engraftment. Additional in vivo testing of the construct is required to evaluate engraftment and long-term function.

Why is this work important and relevant to the future of beta cell replacement therapy?

The advancement of iPSCs and a cell-based delivery method has the potential for a fully personalised treatment for type 1 diabetes. Such an approach promises reduced immune rejection, may eliminate the necessity for

immunosuppression, long-term graft survival, and a tailored therapy that adapts to individual patient needs, thereby improving the patient's quality of life.

BOARD OF REVIEWERS

Shadab Abadpour, Norway
John Casey, UK
Antonio Citro, Italy
Jason Doppenberg, Netherlands
Joana Ferrer-Fabrega, Spain
Peter Girman, Czech Republic
Paul Johnson, UK
Julie Kerr-Conte, France

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:

P. Friend
R. Ploeg

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

S. Abadpour
N. Adenwalla
K. af Geijerstam
I. Akerman
S. Ali
R. Aljaberi
N. Alkemade
I. Alwayn
C. Amayene Amassogo
A. Amer
A. Amor
V. Andreasi
A. Axford
T. Baltesová
A. Baranski
T. Barber
I. Barros
C. Bassaganyas Vancells
C. Batty
N. Belavina
K. Bellofatto
S. Benakova
L. Berglind
E. Berishvili
Z. Berková
A. Bertuol
L. Bicho
D. Biggerstaff
K. Bittenglová
M. Boermeester
A. Bolla
B. Bonsing
E. Bosi
R. Botting
D. Braat
H. Brandhorst
D. Brandhorst
O. Busquets Carrera
L. Cabedo
R. Caldara
C. Callaghan
F. Campo
A. Caretto
S. Carrelha
J. Casey
D. Catarinella
C. Ceriani
D. Chatziisaak
H. Cheng
M. Chetboun
A. Chirichelli
J. Chlupac
B. Chumbinho
O. Ciacio
A. Citro
S. Cochi
K. Coetser
J. Collins
S. Combe
S. Corado
A. Cornu
F. Coulter
C. Counter
L. Crawford
A. Daniel
A. Darnell
L. De Abreu Queiros Osorio
P. De Gea
E. de Koning
D. De Paep
W. de Vos
I. Dedinska
F. Defrance
H. Deng
A. Dennison
S. Deotti
L. DETEVE
C. Di Bella
G. Di Giuseppe
F. Diekmann
M. Dolečková
D. Domingo-Lopez
M. Drage
I. Dravecká
G. Duffy
K. Duncan
N. Dyson
N. Eggebeen
M. Elliott
M. Elzawahry
M. Engelse
E. Fabryova
E. Fabryová
M. Falconi
J. Fallon
A. Ferreira
J. Ferrer-Fàbrega
E. Filipe
R. Fjukstad
C. Flaxman
S. Florman
E. Folch Puy
A. Follenzi
S. Forbes
S. Francis
J. Fronek
G. Fulgini
L. Furian
J. Fuster
I. Gala
G. Garcea
R. García
M. Garcia-Criado
M. Gelabert
C. Giacometti
X. Gidrol
A. Gil-Ordoñez
P. Gillard
P. Girman
M. Gispert
B. Hagerf
B. Hansen
T. Havrdova
A. Hearne
C. Hermanns
R. Hilbrands
R. Hilton
M. Hoff
S. Hofker
B. Holendova
V. Holguin
M. Holzner
M. Honkanen-Scott
R. Hu Zhu
G. Huang
S. Hulík
J. Hunter
V. Huurman

A. Ida
A. Inderson
S. Ingvast
L. Irvine
Y. Issa
D. Jacobs-Tulleneers-Thevissen
S. Jimenez-Serrano
P. Johnson
J. Kaal
M. Katavic
H. Kelly
R. Kempeneers
E. Kemter
J. Kerr-Conte
N. Kessaris
M. Khubutia
N. Klochkova
A. Kondrashkin
S. Kondrashkina
M. Konkolová
O. Korsgren
G. Kourounis
R. Koznarova
N. Krause
J. Kriz
J. Kříž
M. Kudláčková
S. Lablanche
D. Lam
V. Lampasona
J. Latif
A. Lau
F. Lebreton
I. Leontovyč
C. Leseman
Z. Ling
K. Lipar
M. Llompart
L. Lo Faro
M. Lopes
M. Lysenko
M. Maanaoui
P. Magistretti
A. Maillo Nieto
A. Maillo-Nieto
A. Malik
T. Marada
A. Marchis
T. Markova
M. Marras
K. Marszalek
M. Martin
I. Marzinotto
C. Masiero
V. Mathias
M. Matute-Gonzalez
R. Melzi
A. Mercalli
S. Mieog
J. Miklušica
S. Mohammed
L. Monaco
M. Monieri
E. Montagud-Marrahi
P. Monti
J. Moreno-Rojas
H. Msheik
F. Navarro
A. Neroni
M. Niesters
M. Nijhoff
A. Nobre
E. O'Cearbhaill
A. O'Connor
c. Olgasi
L. Osório
R. Owen
H. Paidassi
L. Panariello
G. Papadakis
S. Partelli
A. Pascagaza
C. Patel
S. Pattinson
F. Pattou
M. Pavesi
D. Peeler
S. Pellegrini
A. Pena
C. Perez Serrano
L. Piemonti
C. Pignatelli
H. Pinto Marques
C. Pirlian
L. Plecita
R. Pol
C. Pollard
R. Pook
N. Pringgodigdo
G. Rafart-Martínez
L. Ramalhete
D. Reumann
L. Revest
S. Richardson
P. Rigotti
A. Ruiz
R. Rull
A. Sa Cunha
S. Sabolova
M. Sachdeva
A. Sagar
A. Saleh
V. Salem
M. Santangelo
F. Saudek
J. Schiesser
S. Schneider
H. Scholz
W.E. Scott III
W. Scott Iii
A. Seedorf
G. Sgrinzato
S. Shaheed
J. Shaw
N. Sheerin
L. Simmonds
V. Sordi
R. Spiers
E. Stanley
S. Stemberkova-Hubackova
M. Stevens
A. Sutherland
K. Sutoris
O. Thaunat
R. Thomas
E. Thompson
S. Tingle
M. Tol
V. Tomajer
V. Tomsovska
V. Tomšovská
A. Torroella
R. Tresa
E. Tubbs
D. Tyler
V. Vaithilingam
A. van Apeldoorn
D. Van Dellen
L. Van den Berghe
P. van der Boog
J. van Hooft
L. van Leeuwen
M. Vantyghem
J. Veleba
P. Ventura-Aguiar
E. Vigia
A. Vojtíšková
V. Wadhera
T. Walzer
C. Wang
S. White
C. Wilson
M. Witowska
J. Wojciechowski
E. Wolf
X. Xu
K. Zacharovová
M. Zanoletti
M. Zeeshan Akhtar
E. Zeltyn-Abramov
Z. Žilinská