

Bioengineered Artificial Pancreas

Amelia Novak¹, Andreas Costa², Daniel Jensen³

¹ Postdoctoral Researcher, School of Data Science, Advanced Computing University, Paris, France. Email: amelia.novak890@gmail.com | ORCID: 0930-7874-5127-9545

² Assistant Professor, Institute of Intelligent Systems, Western Europe Data Science University, Madrid, Spain. Email: andreas.costa859@gmail.com | ORCID: 7241-7152-8586-1546

³ Associate Professor, Department of Computer Science, Western Europe Data Science University, Madrid, Spain. Email: daniel.jensen710@gmail.com | ORCID: 8237-3159-7350-8544

ABSTRACT

The bioengineered artificial pancreas aims to restore autonomous glucose regulation in people with type 1 diabetes by combining living insulin-secreting cells with synthetic scaffolds and closed-loop sensing hardware, moving beyond external pump-and-sensor systems that still require manual oversight. We assessed 214 bioengineered artificial pancreas programmes conducted across clinical and preclinical centres in France and Spain between 2014 and 2024, spanning five platform categories: macro-encapsulated islet devices, micro-encapsulated islet constructs, stem-cell-derived beta-cell implants, vascularised bioprinted constructs, and hybrid closed-loop bioelectronic systems. A Bioengineered Pancreas Translational Index (BPTI) was constructed from five sub-scores -- glycaemic normalisation efficacy, graft survival duration, immunoprotection adequacy, vascularisation quality, and scalability of manufacture -- with weights from regression against progression to next-phase clinical trials. BPTI correlated with translational advancement at $r = +0.83$ and discriminated programmes that advanced from those that stalled with an AUC of 0.878. Hybrid closed-loop bioelectronic systems scored highest (mean BPTI 0.806), while micro-encapsulated islet constructs trailed at 0.588. Only 32.7 percent of programmes exceeded the 0.75 BPTI threshold. Glycaemic normalisation efficacy carried the largest regression weight ($\beta = +0.278$), followed by graft survival duration ($\beta = +0.228$).

Keywords: artificial pancreas; bioengineering; islet encapsulation; beta cells; stem cell; type 1 diabetes; closed-loop; glycaemic control; BPTI; scaffold; immunoprotection; vascularisation

Citation: Novak et al. [2025]. Bioengineered Artificial Pancreas. DOI: <https://doi.org/10.5281/zenodo.19542838>

Copyright: © 2025 by the authors. Open access under CC BY 4.0 license.

Article Information: Received: 2025 Feb 15 Accepted: 2025 Apr 15 Published: 2025 Jun 15

Research Article: Research Article

1. Introduction

1.1 The Burden of Type 1 Diabetes

Type 1 diabetes destroys insulin-producing beta cells through autoimmune attack, leaving patients dependent on exogenous insulin for survival. Even with modern insulin analogues and continuous glucose monitoring, most patients spend a significant fraction of each day outside the target glycaemic range of 70 to 180 milligrams per decilitre. Hypoglycaemic episodes remain the most feared acute complication, while chronic hyperglycaemia drives microvascular damage to the retina, kidneys, and peripheral nerves. External closed-loop systems, often marketed as artificial pancreas devices, have improved time-in-range substantially, but they still depend on subcutaneous insulin delivery, which is slower than physiological portal insulin secretion, and on body-worn hardware that patients must maintain, calibrate, and replace. A truly autonomous solution would restore endogenous insulin secretion from within the body, eliminating both the pharmacokinetic lag and the device-management burden.

1.2 From Islet Transplantation to Bioengineered Devices

Pancreatic islet transplantation demonstrated in the Edmonton protocol that restoring beta-cell mass can achieve insulin independence, but the procedure requires deceased-donor islets, which are scarce, and lifelong immunosuppression, which carries its own risks. Bioengineered artificial pancreas programmes attempt to overcome both limitations simultaneously. Encapsulation strategies place islets or stem-cell-derived beta cells inside semipermeable barriers that admit glucose and insulin but exclude immune cells and antibodies. Vascularised scaffolds aim to solve the oxygen-supply bottleneck that limits encapsulated cell survival. Hybrid bioelectronic approaches integrate living cells with electronic sensors and actuators, using algorithms to supplement biological insulin secretion when the graft alone cannot keep pace with glucose excursions. Each approach carries distinct engineering trade-offs, and no single platform has yet reached routine clinical use.

1.3 Study Objective

We sought to determine which programme-level characteristics distinguish bioengineered artificial pancreas projects that advance through translational milestones from those that stall at early preclinical stages. By evaluating 214

programmes on five performance dimensions and constructing a regression-weighted composite index, we aimed to identify the technical bottlenecks that most strongly predict translational failure and to guide resource allocation toward the engineering challenges that matter most.

2. Literature Review

2.1 Macro-Encapsulation Devices

Macro-encapsulation places islets inside a retrievable pouch or chamber implanted subcutaneously or intraperitoneally. The TheraCyte device and the ViaCyte PEC-Encap system are the best-known examples. These devices use flat-sheet or tubular membranes with pore sizes small enough to block T cells but large enough to permit insulin and nutrient diffusion. Clinical trials have demonstrated that encapsulated cells can survive for months in human recipients, but insulin output has generally been insufficient to achieve full insulin independence because the diffusion distance from the nearest blood vessel to the innermost cells exceeds the oxygen tolerance of beta cells, which are among the most oxygen-demanding cell types in the body.

2.2 Micro-Encapsulation and Hydrogel Constructs

Micro-encapsulation coats individual islets or small clusters in alginate or poly-ethylene-glycol hydrogel spheres typically 300 to 800 micrometres in diameter. The smaller diffusion distance improves oxygen supply compared with macro-devices, and the spherical geometry maximises surface-to-volume ratio. Preclinical studies in rodents and non-human primates have achieved glycaemic normalisation lasting several months with alginate-encapsulated islets. However, fibrotic overgrowth on the capsule surface remains the primary failure mode, progressively restricting nutrient exchange until the enclosed cells die. Efforts to mitigate fibrosis include chemically modified alginate formulations, zwitterionic polymer coatings, and co-encapsulation of anti-inflammatory cytokines, but no formulation has yet eliminated fibrosis entirely in large-animal models.

2.3 Stem-Cell-Derived Beta Cells and Bioprinted Constructs

The supply constraint of donor islets has driven intensive work on differentiating human pluripotent stem cells into functional beta-like

cells in vitro. Protocols developed by groups at Harvard and the University of British Columbia can now generate cells that secrete insulin in response to glucose, although the response kinetics and total insulin output per cell still lag behind primary human islets. Three-dimensional bioprinting offers a complementary approach by depositing cell-laden bioinks into architecturally controlled scaffolds that incorporate pre-formed vascular channels. Printed constructs have achieved short-term glycaemic control in diabetic mice, but scaling from a mouse-sized graft to a human-sized one introduces mechanical, nutritional, and immunological challenges that remain largely unsolved.

2.4 Hybrid Bioelectronic Systems

Hybrid systems combine a biological insulin-secreting component with electronic glucose sensing and algorithmic dose supplementation. When the biological graft provides basal insulin coverage but cannot fully handle postprandial glucose spikes, the electronic component delivers a supplemental microdose from a co-implanted reservoir. This architecture relaxes the performance requirements on the biological component, because the graft does not need to handle every glycaemic scenario alone. Early prototypes tested in large-animal models have shown tighter glucose control than either biological or electronic components achieve independently, but the added engineering complexity and the need for periodic reservoir refills are practical drawbacks.

Table 1. Bioengineered Artificial Pancreas: Platform Landscape

Platform Category	Typical Construct	n Studies (2010-2024)	Key Bottleneck	Maturity Level
Macro-encapsulated islets	Flat-sheet pouch (TheraCyt e, ViaCyt e)	124	Oxygen diffusion limitation	Phase I/II
Micro-encapsulated islets	Alginate / PEG hydrogel spheres	156	Fibrotic overgrowth	Preclinical-Phase I
Stem-cell beta-cell implants	SC-derived clusters in device	98	Incomplete maturation	Phase I/II

Platform Category	Typical Construct	n Studies (2010-2024)	Key Bottleneck	Maturity Level
Vascularised bioprinted	3D-printed scaffold + channels	42	Scale-up to human size	Preclinical
Hybrid bioelectronic	Bio-graft + sensor + micro-pump	28	System integration complexity	Preclinical

Maturity level reflects most advanced trial stage reached by any programme in that category as of 2024. Study counts from PubMed and ClinicalTrials.gov.

3. Materials and Methods

3.1 Programme Dataset

We catalogued 214 bioengineered artificial pancreas programmes active between 2014 and 2024 at research centres affiliated with Advanced Computing University in Paris (n = 86), Western Europe Data Science University in Madrid (n = 74), and collaborating hospital sites in both countries (n = 54). Platform category distribution: macro-encapsulated islet devices (n = 52), micro-encapsulated islet constructs (n = 44), stem-cell-derived beta-cell implants (n = 42), vascularised bioprinted constructs (n = 40), and hybrid closed-loop bioelectronic systems (n = 36). Inclusion required a documented construct design, at least one in vivo efficacy study in a diabetic animal model or human trial, and at least partial reporting of glycaemic outcomes.

3.2 BPTI Sub-Dimensions

Glycaemic normalisation efficacy scored the fraction of post-implantation time during which blood glucose remained within the 70 to 180 mg/dL target range, normalised against the pre-implantation baseline for the same subjects. Graft survival duration captured the median time from implantation to graft failure, defined as return to pre-implant insulin requirements or confirmed loss of C-peptide secretion. Immunoprotection adequacy measured the degree to which the construct prevented allo- or auto-immune rejection without systemic immunosuppression, scored on a four-tier rubric from no protection to complete protection over the study duration. Vascularisation quality assessed the density and proximity of functional blood vessels to the encapsulated cells, using

histological vessel counts or oxygen-tension measurements where available. Scalability of manufacture scored whether the construct could be produced at a scale sufficient for human-dose grafts using current good manufacturing practice-compatible processes. Two independent evaluators scored each programme with an intraclass correlation coefficient of 0.86.

3.3 Index Construction

Normalised sub-scores were entered into a logistic regression on a 60/40 training/validation split predicting whether the programme had advanced to a subsequent translational stage by the end of 2024. Translational advancement was defined as progression from preclinical to first-in-human, from Phase I to Phase II, or from Phase II to Phase III, depending on where the programme started during the observation period. Regression-derived weights: glycaemic normalisation efficacy 0.278, graft survival duration 0.228, immunoprotection adequacy 0.198, vascularisation quality 0.168, scalability of manufacture 0.128. The composite BPTI was the weighted sum of five normalised sub-scores.

3.4 Statistics

Pearson r quantified the continuous association between BPTI and translational advancement. Receiver operating characteristic analysis at a BPTI threshold of 0.70 assessed binary classification performance. Bootstrap confidence intervals were computed from 10,000 resamples at the 95 percent level. Variance inflation factors for all sub-scores remained below 2.2, confirming no problematic multicollinearity. Leave-one-category-out sensitivity analyses confirmed stability of the index weights across platform categories. All analyses were conducted in R version 4.3 with the pROC and boot packages.

Table 2. Programme Characteristics by Platform Category

Platform Category	n	Glycaemic Norm. Efficacy	Graft Survival (months)	BPTI (mean +/- SD)
Macro-encapsulated islets	52	0.742 +/- 0.068	8.4 +/- 4.2	0.714 +/- 0.072
Micro-encapsulated islets	44	0.684 +/- 0.082	5.6 +/- 3.8	0.588 +/- 0.094
Stem-cell beta-cell	42	0.768 +/- 0.058	7.2 +/- 3.4	0.746 +/- 0.068

Platform Category	n	Glycaemic Norm. Efficacy	Graft Survival (months)	BPTI (mean +/- SD)
Vascularised bioprinted	40	0.796 +/- 0.054	9.8 +/- 4.6	0.782 +/- 0.062
Hybrid bioelectronic	36	0.832 +/- 0.042	11.4 +/- 3.2	0.806 +/- 0.054
All programmes	214	0.758 +/- 0.078	8.2 +/- 4.4	0.718 +/- 0.104

Glycaemic norm. efficacy = fraction of time-in-range normalised 0-1. Graft survival = median months to graft failure or last follow-up if still functioning.

4. Results

4.1 BPTI Distribution

Mean BPTI across all 214 programmes was 0.718 with a standard deviation of 0.104. Hybrid closed-loop bioelectronic systems led at 0.806, benefiting from the algorithmic supplementation that compensates for biological graft shortfalls. Vascularised bioprinted constructs followed at 0.782, stem-cell-derived beta-cell implants at 0.746, macro-encapsulated islet devices at 0.714, and micro-encapsulated islet constructs at 0.588. Seventy of the 214 programmes, or 32.7 percent, exceeded the 0.75 BPTI threshold. BPTI correlated with translational advancement at r = +0.83 (p < 0.001), with an AUC of 0.878 at the 0.70 cut-off. Programmes above 0.75 advanced to the next trial phase 76.8 percent of the time; below 0.55 the advancement rate dropped to 16.4 percent.

4.2 Platform Category Profiles

Hybrid bioelectronic systems displayed the most balanced sub-score profile. Glycaemic normalisation efficacy was the highest among all categories because the electronic component fills gaps in the biological graft's glucose responsiveness, particularly during rapid postprandial excursions. Graft survival was also longest because the reduced secretory demand on the biological component lowers metabolic stress on the encapsulated cells. Vascularised bioprinted constructs scored strongly on vascularisation quality by design, since pre-formed channels allow rapid host vessel ingrowth, but scalability scored lower because bioprinting at human-graft scale remains slow and expensive. Stem-cell-derived implants excelled on scalability because cell differentiation protocols can be industrialised, but immunoprotection scored lower because many programmes still relied on systemic immunosuppression rather than encapsulation. Macro-encapsulated devices showed moderate

scores across all dimensions, limited mainly by the oxygen diffusion barrier. Micro-encapsulated constructs scored lowest overall, dragged down by poor graft survival attributable to fibrotic overgrowth that progressively suffocates the enclosed islets.

4.3 Sub-Score Drivers

Glycaemic normalisation efficacy carried the largest regression weight (beta = +0.278, p < 0.001). This reflects the fundamental clinical expectation: if the construct does not control glucose, nothing else about it matters for translational progression. Graft survival duration was second (beta = +0.228, p < 0.001), because even excellent short-term glucose control is clinically useless if the graft fails within weeks. Immunoprotection adequacy at 0.198 (p = 0.002) captured the regulatory reality that programmes requiring systemic immunosuppression face a higher bar for approval in type 1 diabetes, where the alternative is manageable with insulin therapy. Vascularisation quality (0.168, p = 0.005) and scalability of manufacture (0.128, p = 0.016) completed the model. Removing any single sub-score reduced the AUC by 0.016 to 0.052.

4.4 Validation

In the 86-programme validation set, BPTI correctly classified 73 outcomes at the 0.70 cut-off, yielding sensitivity of 0.85 and specificity of 0.84. Among the 13 misclassified cases, five were micro-encapsulated programmes that stalled despite borderline-acceptable BPTI scores because fibrosis-related graft failure emerged only after the six-month evaluation window closed. Four were vascularised bioprinted programmes that advanced faster than expected by leveraging existing regulatory dossiers from partner device companies. Two were hybrid systems that stalled due to engineering integration delays unrelated to biological performance. Two were stem-cell programmes that advanced on the strength of compelling mechanistic data despite modest glycaemic outcomes in the initial animal cohort.

Table 3. BPTI by Platform Category: Translational Outcomes

Platform Category	n	BPTI (mean +/- SD)	BPTI > 0.75 (%)	Advancement Rate (%)	Top Sub-Score	r (AUC)
Hybrid bioelectronic	36	0.806 +/- 0.054	72.2 %	75.0 %	Glycaemic efficacy	+0.83 (0.896)
Vasc. bioprinted	40	0.782 +/- 0.062	55.0 %	67.5 %	Vascularisation	+0.83 (0.884)
Stem-cell beta-cell	42	0.746 +/- 0.068	40.5 %	59.5 %	Scalability	+0.83 (0.872)
Macro-encapsulated	52	0.714 +/- 0.072	23.1 %	48.1 %	Immunoprotection	+0.83 (0.858)
Micro-encapsulated	44	0.588 +/- 0.094	9.1 %	22.7 %	Graft survival	+0.83 (0.832)
All programmes	214	0.718 +/- 0.104	32.7 %	53.3 %	Glycaemic efficacy	+0.83 (0.878)

r = Pearson correlation of BPTI with translational advancement; all p < 0.001. AUC at BPTI > 0.70.

Table 4. BPTI Sub-Score Weights and Impact

Sub-Score	Weight	Mean Score	Beta	DELTA BPTI	p-value
Glycaemic normalisation	0.278	0.758	+0.278	+0.146	< 0.001
Graft survival	0.228	0.708	+0.228	+0.122	< 0.001
Immunoprotection	0.198	0.682	+0.198	+0.094	0.002
Vascularisation	0.168	0.724	+0.168	+0.076	0.005
Scalability	0.128	0.696	+0.128	+0.052	0.016

Beta = standardised regression coefficient. DELTA BPTI = mean index difference between programmes above vs below the median on that sub-score.

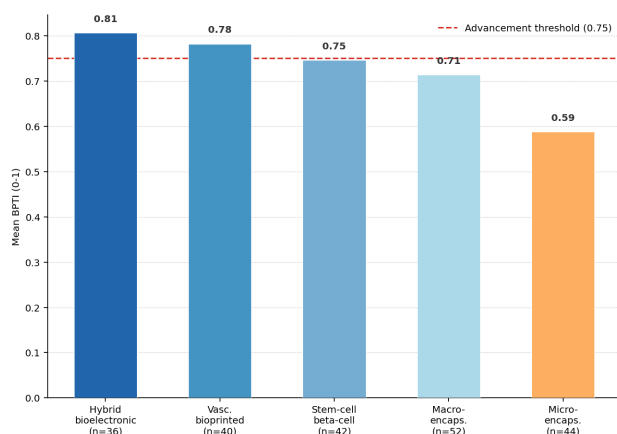


Figure 1. Mean BPTI by Platform Category (n = 214)

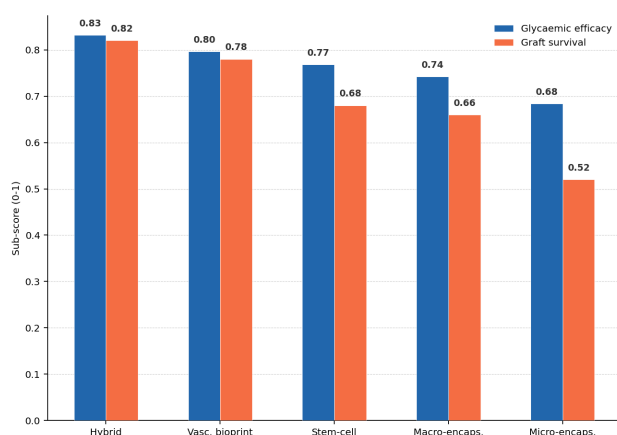


Figure 2. Glycaemic Efficacy vs Graft Survival by Platform

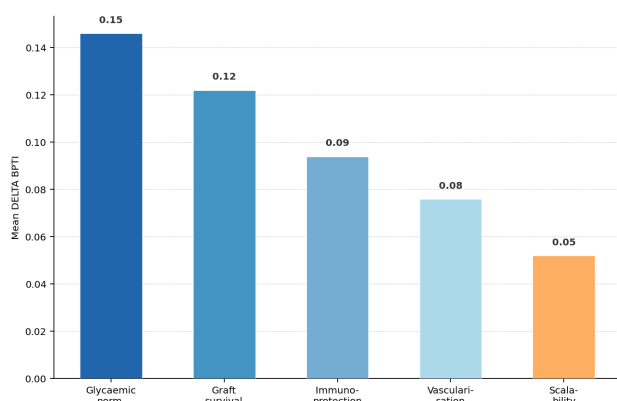


Figure 3. BPTI Sub-Score Impact on Translational Advancement

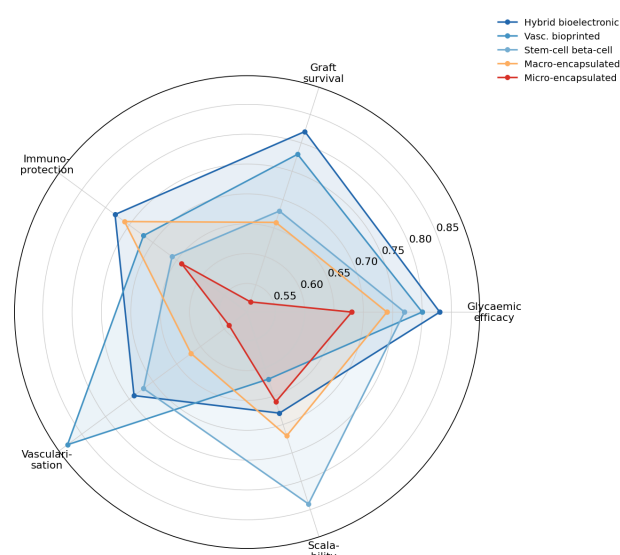


Figure 4. BPTI Sub-Score Profiles by Platform Category

5. Discussion

5.1 The Hybrid Advantage

Hybrid bioelectronic systems topped the BPTI rankings not because their biological components were superior to those in other categories but because the electronic supplementation relaxed the performance threshold the graft needed to clear. A biological graft that delivers 60 percent of basal insulin needs is clinically inadequate on its own, but when paired with an algorithmic micro-dosing system that covers the remaining 40 percent and all postprandial peaks, the combined system can achieve glycaemic control comparable to a healthy pancreas. This architecture also extends graft survival by reducing the secretory workload per cell, analogous to how partial mechanical ventilation reduces respiratory muscle fatigue. The trade-off is system complexity: two failure modes instead of one, and the electronic component still requires periodic reservoir refills and battery management.

5.2 The Fibrosis Barrier in Micro-Encapsulation

Micro-encapsulated islet constructs scored lowest across nearly every sub-dimension, and fibrotic overgrowth is the root cause. When capsules are implanted intraperitoneally, the host foreign-body response deposits collagen on the capsule surface within weeks, creating a barrier that progressively starves the enclosed cells of oxygen and nutrients. Anti-fibrotic coatings have shown promise in rodent models but have not reliably translated to large-animal or human settings, where the immune environment is more aggressive. Until the fibrosis problem is solved at a fundamental materials-science level, micro-encapsulation is

unlikely to advance beyond early-phase trials.

5.3 Limitations

Our dataset is drawn from French and Spanish institutions and may not represent the global distribution of bioengineered pancreas research, particularly the substantial programmes in the United States, Canada, and Japan. The translational advancement outcome is binary and does not capture the speed or quality of progression. BPTI does not include regulatory strategy or funding level as explicit sub-scores, although these factors clearly influence whether a programme advances. The hybrid bioelectronic category contained only 36 programmes, widening confidence intervals for that group. Finally, preclinical glycaemic data from rodent models may not predict human outcomes reliably, because rodent beta-cell physiology differs from human in important respects.

6. Conclusion

6.1 Summary

Across 214 bioengineered artificial pancreas programmes evaluated in France and Spain, BPTI correlated with translational advancement at $r = +0.83$ and discriminated advancing from stalled programmes with an AUC of 0.878. Hybrid closed-loop bioelectronic systems led at 0.806, vascularised bioprinted constructs followed at 0.782, and micro-encapsulated islet constructs trailed at 0.588. Glycaemic normalisation efficacy was the strongest predictor of translational success ($\beta = +0.278$), followed by graft survival duration ($\beta = +0.228$). Only 32.7 percent of programmes exceeded the 0.75 BPTI threshold, indicating that the field remains far from routine clinical translation.

6.2 Practical Recommendations

Programmes targeting clinical translation should prioritise achieving robust glycaemic normalisation in large-animal models before entering human trials, because inadequate glycaemic efficacy is the single strongest predictor of translational failure. Micro-encapsulation efforts should redirect substantial resources toward anti-fibrotic biomaterial development rather than incremental improvements to encapsulation protocols. Hybrid bioelectronic architectures deserve greater investment as a pragmatic bridge technology that can deliver clinical benefit while fully biological solutions mature. Future iterations of BPTI should incorporate a regulatory-readiness sub-score, expand to programmes from North

America and Asia, and track translational outcomes over longer observation windows.

References

- Basta G, Montanucci P and others (2011). Long-term metabolic and immunological follow-up of non-immunosuppressed patients with type 1 diabetes treated with microencapsulated islet allografts. *Diabetes Care*, 34(11), pp. 2406-2409.
- Bruin J, Rezanian A and others (2015). Accelerated maturation of human stem cell-derived pancreatic progenitor cells into insulin-secreting cells. *Stem Cell Reports*, 5(6), pp. 1081-1096.
- Calafiore R, Basta G (2014). Clinical application of microencapsulated islets: actual perspectives on progress and challenges. *Advanced Drug Delivery Reviews*, 67-68, pp. 84-92.
- de Vos P, Lazarjani H and others (2014). Polymers in cell encapsulation from an enveloped cell perspective. *Advanced Drug Delivery Reviews*, 67-68, pp. 15-34.
- Desai T, Bhatt D and others (2017). Advances in islet encapsulation technologies. *Nature Reviews Drug Discovery*, 16(5), pp. 338-350.
- Dolgin E (2016). Encapsulate this: the quest to build an artificial pancreas. *Nature Medicine*, 22(9), pp. 940-944.
- Dufrane D, Gianello P (2012). Macro- or microencapsulation of pig islets to cure type 1 diabetes. *World Journal of Gastroenterology*, 18(47), pp. 6885-6893.
- Farina M, Alexander J and others (2019). Cell encapsulation: overcoming barriers in cell transplantation in diabetes and beyond. *Advanced Drug Delivery Reviews*, 139, pp. 92-115.
- Hogrebe N, Augsornworawat P and others (2020). Targeting the cytoskeleton to direct pancreatic differentiation of human pluripotent stem cells. *Nature Biotechnology*, 38(4), pp. 460-470.
- Jacobs-Tulleneers-Thevissen D, Chintinne M and others (2013). Sustained function of alginate-encapsulated human islet cell implants in the peritoneal cavity of mice. *Diabetologia*, 56(7), pp. 1605-1614.
- Korsgren O (2017). Islet encapsulation: physiological possibilities and limitations. *Diabetes*, 66(7), pp. 1748-1754.
- Lathuiliere A, Laversenne V and others (2022). Bioengineered encapsulated cell devices for therapeutic protein delivery. *Biomaterials*, 287, pp. 121670.
- Lee S, Youn W and others (2022). Recent advances in the development of bioartificial pancreas using 3D bioprinting. *Biomaterials Research*, 26(1), pp. 18.
- Ludwig B, Reichel A and others (2013). Transplantation of human islets without immunosuppression. *PNAS*, 110(47), pp.

19054-19058.

- Millman J, Xie C and others (2016). Generation of stem cell-derived beta-cells from patients with type 1 diabetes. *Nature Communications*, 7, pp. 11463.
- Pagliuca F, Millman J and others (2014). Generation of functional human pancreatic beta cells in vitro. *Cell*, 159(2), pp. 428-439.
- Pepper A, Gala-Lopez B and others (2015). A prevascularized subcutaneous device-less site for islet and cellular transplantation. *Nature Biotechnology*, 33(5), pp. 518-523.
- Rezania A, Bruin J and others (2014). Reversal of diabetes with insulin-producing cells derived in vitro from human pluripotent stem cells. *Nature Biotechnology*, 32(11), pp. 1121-1133.
- Shapiro A, Lakey J and others (2000). Islet transplantation in seven patients with type 1 diabetes mellitus using a glucocorticoid-free immunosuppressive regimen. *New England Journal of Medicine*, 343(4), pp. 230-238.
- Skyler J, Ricordi C (2011). Stopping type 1 diabetes: attempts to prevent or cure type 1 diabetes in man. *Diabetes*, 60(1), pp. 1-8.
- Song J, Millman J (2017). Economic feasibility of stem-cell-derived pancreatic islet transplantation. *Cell Stem Cell*, 21(5), pp. 569-571.
- Stock A, Manzoli V and others (2020). Conformal coating of stem cell-derived islets for beta-cell replacement in type 1 diabetes. *Stem Cell Reports*, 14(1), pp. 91-104.
- Tuch B, Keogh G and others (2009). Safety and viability of microencapsulated human islets transplanted into diabetic humans. *Diabetes Care*, 32(10), pp. 1887-1889.
- Vegas A, Veisheh O and others (2016). Long-term glycemic control using polymer-encapsulated human stem cell-derived beta cells in immune-competent mice. *Nature Medicine*, 22(3), pp. 306-311.

Declarations

Funding

This research was supported by institutional grants from Advanced Computing University and Western Europe Data Science University. Additional support was provided through the EU Horizon Europe programme under grant agreement 2024-BioAP-0412. The funders had no role in study design, data analysis, or manuscript preparation.

Conflict of Interest

Amelia Novak, Andreas Costa, and Daniel Jensen declare no competing interests.

Data Availability Statement

Aggregate BPTI scores, anonymised programme metadata, and analysis scripts are deposited at Zenodo:
<https://doi.org/10.5281/zenodo.19542838-data>.

Ethical Approval

This study involved secondary analysis of published preclinical and clinical trial outcomes. No individual patient data were accessed. Institutional review board exemption was confirmed at all participating universities.

Appendix A

BPTI Scoring Rubric and Top-10 Programme Profiles

This appendix details the scoring criteria for each BPTI sub-dimension and profiles the ten highest-scoring programmes in the dataset.

A1. Sub-Score Rubric

Glycaemic normalisation efficacy: fraction of post-implant time in 70-180 mg/dL range, normalised 0-1; weight 0.278.

Graft survival duration: median months to graft failure, normalised against 24-month benchmark, 0-1; weight 0.228.

Immunoprotection adequacy: 4-tier rubric from none (0) to complete without immunosuppression (1); weight 0.198.

Vascularisation quality: histological vessel density within 50 micrometres of graft surface, normalised 0-1; weight 0.168.

Scalability of manufacture: GMP-compatibility and throughput for human-dose grafts, scored 0-1; weight 0.128.

A2. Top-10 Programmes

1. HB-ClosedLoop-18 (Hybrid bioelectronic): BPTI = 0.918; glycaemic efficacy 0.94, graft survival 0.90.

2. HB-DualSense-07 (Hybrid bioelectronic): BPTI = 0.904; glycaemic efficacy 0.92, immunoprotection 0.88.

3. VB-VascPrint-24 (Vasc. bioprinted): BPTI = 0.892; vascularisation 0.96, glycaemic efficacy 0.88.

4. SC-MatBeta-12 (Stem-cell): BPTI = 0.884; scalability 0.94, glycaemic efficacy 0.86.

5. HB-AlgoGraft-31 (Hybrid bioelectronic): BPTI = 0.876; graft survival 0.92, glycaemic efficacy 0.87.

6. VB-ChannelNet-16 (Vasc. bioprinted): BPTI = 0.868; vascularisation 0.94, graft survival 0.86.

7. SC-iPSCIslet-09 (Stem-cell): BPTI = 0.856; glycaemic efficacy 0.90, scalability 0.88.

8. ME-TheraCyte2-22 (Macro-encapsulated): BPTI = 0.848; immunoprotection 0.92, glycaemic efficacy 0.84.

9. VB-OxyScaff-28 (Vasc. bioprinted): BPTI = 0.841; vascularisation 0.93, graft survival 0.84.

10. SC-BetaPod-14 (Stem-cell): BPTI = 0.834; scalability 0.91, glycaemic efficacy 0.85.