In addition, the requirement for placing allogeneic islet cells near the bloodstream to rapidly respond to blood glucose levels as described above, coupled with the high oxygen requirements of pancreatic islet cells, especially during insulin secretion (Sato *et al.*, 2011), adds additional challenges to recapitulating normal pancreatic function at the scale of the whole organ. Although these vascularization challenges are clearly defined, biomaterials technologies which could be used to develop vascularized devices have remained elusive.

SUMMARY

Briefly, the present disclosure describes vascularizing devices and methods for implanted diagnostics and therapeutics. The inventors have applied the latest in 3D bioprinting technology to direct vascularization of immunoisolated therapeutic cell constructs for long-term viability and functionality, and to permit engraftment of higher densities of therapeutic cells.

In light of the requirements for an effective vascular network, the design criteria for fabricated tissues which mimic blood vessel geometry include, but are not limited to, a plurality of branched vessels ranging in size from tens to hundreds of micrometers in diameter and substantially smooth inner walls that may minimize frictional drag and turbulence during fluid flow.

The present disclosure describes, in certain examples, a device containing a degradable shell and a non-degradable core. In certain examples, the non-degradable core can include encapsulated therapeutic cells and/or biosensors, wherein the degradable shell serves as a scaffold for blood vessel growth, resulting in enhanced blood flow to the cells and/or biosensors.

In one aspect, the present disclosure refers to an implantable device comprising a degradable polymer, and an inner non-degradable portion comprising a non-degradable polymer, wherein the degradable outer housing comprises a patterned architecture that promotes vascularization of said implantable device, wherein the patterned architecture comprises blood vessel geometries. More specifically, there is described an implantable device comprising a degradable outer housing comprising a degradable polymer, and an inner non-degradable portion comprising a degradable polymer. The degradable outer housing may comprise a patterned architecture that promotes vascularization of said implantable device, *i.e.*, a vascularization bed, and/or the non-degradable portion may comprise a natural or synthetic hydrogel. The synthetic hydrogel may be poly(ethylene glycol) diacrylate (PEDGA). The device may further comprise gel methacrylate (GelMA), natural and chemically modified hyaluronic acid, and natural and chemically modified alginate.

The hydrogel may comprise more than 80% water. The hydrogel may comprise about 10% GelMA and about 3% PEDGA. The hydrogel may comprise monomers of acrylate-(PEG-protein)$_n$-PEG-acrylate, optionally wherein PEG is 2–35 kDa, protein is greater than 100 Da,

WHAT IS CLAIMED:

1. An implantable device comprising a degradable outer housing comprising a degradable polymer, and an inner non-degradable portion comprising a non-degradable polymer, wherein the degradable outer housing comprises a patterned architecture that promotes vascularization of said implantable device, wherein the patterned architecture comprises blood vessel geometries.

2. The implantable device of claim 1, wherein the non-degradable portion comprises a natural or synthetic hydrogel.

3. The implantable device of claim 2, wherein the synthetic hydrogel is poly(ethylene glycol) diacrylate (PEGDA).

4. The implantable device of claims2-3, further comprising gel methacrylate (GelMA).

5. The implantable device of claims 2-4, wherein the hydrogel comprises more than 80% water.

6. The implantable device of claims 3-5, wherein the hydrogel comprises about 10% GelMA and 3-4% PEGDA having a molecular weight of about 3.4 kDa.

7. The implantable device of claims 12, wherein said hydrogel comprises monomers of acrylate-(PEG-protein)$_n$-PEG-acrylate, optionally wherein PEG is 2–35 kDa, protein is greater than 100 Da, and total MW is at least 500 kDa or n = 2-500 repeat units.

8. The implantable device of claims 1-2, wherein the hydrogel comprises acrylamide, vinyl-sulfone, norbornene replace the acrylate groups, alginate, silk, dextran, chondroitin sulfate, hyaluronic acid, cellulose, heparin, poly(caprolactone) or multi-component versions thereof.

9. The implantable device of claims 1-2, wherein the inner non-degradable portion is loaded with cells, drugs, *i.e.*, small molecule therapeutics or biological therapeutics (peptides, antibodies, *etc.*), or crystals.

10. The implantable device of claim 9, wherein the cells comprise cells from xenotissue, cells from a cadaver, stem cells, cells derived from stem cells, cells from a cell line, primary cells, reprogrammed cells, reprogrammed stem cells, cells derived from reprogrammed stem cells, genetically engineered cells, or combinations thereof.

11. The implantable device of claim 9, wherein the cells are human cells.

12. The implantable device of claim 9, wherein the cells are insulin-producing cells.

13. The implantable device of claim 9, wherein the cells are pancreatic islet cells.

14. The implantable device of claims 1-13, wherein the degradable outer housing or inner non-degradable portion is loaded with oxygen-releasing compounds, such as CaO_2.

15. The implantable device of claims 1-14, wherein the degradable outer housing or inner non-degradable portion is loaded with drugs, *i.e.*, small molecule therapeutics or biological therapeutics (peptides, antibodies, *etc.*), crystals, with non-crystallized, crystallized, and/or encapsulated pro-angiogenic factors, such as VEGF, cells, such as pro-angiogenic cells, such as endothelial cells, mesenchymal stem cells, endothelial progenitors, proangiogenic macrophages.

16. The implantable device of claims 1-8, wherein the inner non-degradable portion is loaded with a biosensor.

17. The implantable device of claim 16, wherein the biosensor can measure blood oxygen, blood glucose, tumor antigens, cholesterol, creatinine, hemoglobin A1C, insulin, glucagon, hormone levels, levels of small molecule drugs, DNA, RNA, cytokines, circulating tumor cells, among other possible diagnostic indicators.

18. The implantable device of claims 1-17, wherein the degradable outer housing and/or the inner non-degradable portion is/are patterned, such as where the inner non-degradable portion is patterned to permit vascularization once implanted.

19. The implantable device of claim 18, wherein the patterned portion comprises blood vessel geometries, such as a plurality of branched vessels ranging in size from tens to hundreds of micrometers in diameter and having substantially smooth inner walls to minimize frictional drag and turbulence during fluid flow.

20. The implantable device of claims 1-19, wherein the device comprises multiple layers of hydrogels.

21. The implantable device of claims 1 to 20, wherein the device comprises a therapeutic agent.