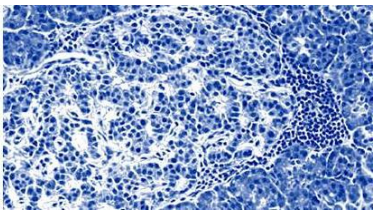
nPOD
Network for Pancreatic Organ Donors with Diabetes



3D Atlas of regional variation and dynamic changes in the islets of Langerhans in diabetes

AUTHORS

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PURPOSE

The pancreas is a highly heterogeneous organ, with regional anatomical, developmental and functional differences. Until now, laborious serial sectioning and reconstruction has been needed to deliver information about islet anatomy across the pancreas. There is a clear need for high resolution, organ-wide imaging to map regional variation and to assess the three-dimensional islet anatomy and distribution. Here, we used optical clearing, whole organ imaging, and 3D rendering to quantify insulin-producing beta cells across the whole pancreas in healthy mice, in two mouse models of diabetes, and in nondiabetic and diabetic human donors.

METHODS

Whole-mount staining and clearing was performed using iDISCO+ to determine the 3D volumes and distribution of insulin-producing beta cells in pancreata from C57Bl/6 mice, non-obese diabetic (NOD) mice, streptozotocin (STZ)-treated mice, and in pancreatic samples from nondiabetic and diabetic human donors. Z-stacked optical sections were acquired with an Ultramicroscope II at a 1.3x, 4x or 12x magnification. Imaris was used to create digital surfaces covering the insulin+ islets to automatically determine volumes and intensity data.

SUMMARY OF RESULTS

Tissue clearing, whole organ imaging and unbiased analysis provided straightforward measurement of beta cell volume across the whole pancreas. Beta cell volumes were 1-4% in the human pancreas, and 1-2% in the healthy mouse pancreas. There were regional variations in islet volume and insulin intensity. The majority of islets were between 1000 and 500,000 μm^3. There were significant differences in islet biology between the diabetes models. In NOD mice, insulin-positive islet numbers and beta cell volumes were dramatically reduced, with some islets exhibiting relatively preserved insulin intensities, and a striking shift to small islets. Islet number and volume were also reduced with STZ treatment with regional difference, but the insulin intensity was dramatically reduced and size distribution was minimally altered. The islet characteristics of the human samples were highly variable but the beta cell volume distribution was significantly altered in diabetes.

CONCLUSIONS

Whole organ 3D imaging allows quantification of beta cell volume and multiple parameters in animal models and human samples. There are significant regional differences in beta cell volume and islet size distribution in mouse models of diabetes. These regional variations emphasize the need for whole organ imaging for accurate quantification of pancreatic anatomy in animal models.