large volumes using thin section histology, there is a need for high resolution imaging and rendering of intact pancreatic tissue in 3D. **Aim:** To use optical clearing, whole organ imaging, and 3D rendering to quantify islets and innervation across the whole pancreas in healthy mice, in two mouse models of diabetes, and in pancreatic samples from nondiabetic and diabetic human donors. **Methods:** Whole-mount staining and clearing was performed using iDISCO+ to quantify innervation, defined by the neuronal marker NF200, and 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 4x or 12x magnification. Imaris was used to create digital surfaces covering the NF200+ innervation and islets to automatically determine innervation density and islet/nerve interactions. **Results:** Beta cell volumes were 1-4% in the human pancreas, and 1-2% in the healthy mouse pancreas, with regional variations in islet volume and insulin intensity. There were also significant differences in islet biology between the diabetes models. Innervation of the endocrine pancreas was significantly enriched compared to the surrounding exocrine pancreas, with regional variation. Islets were closely associated with pancreatic innervation and decreased in size with increasing distance from nerves in both mouse and human pancreatic tissue. Innervated islets were relatively preserved in models of diabetes. Finally, islet innervation and expression of neural markers were higher in human samples from diabetic patients and in mouse models of diabetes, with temporal and regional differences. **Conclusions:** 3D imaging and unbiased analysis across the whole pancreas provides comprehensive measurement of pancreatic nerve volumes and distribution. It allows detailed analysis of the anatomical relationship between nerves and islets, and reveals a close association that is maintained across species. The relative enrichment of innervated islets in diabetes and dynamic changes in islet innervation during the development of diabetes suggest further work is needed to examine the role of pancreatic nerves in preserving and protecting beta cells.

Diabetes Mellitus and Glucose Metabolism

CLINICAL AND TRANSLATIONAL GLUCOSE METABOLISM AND DIABETES

The Effects of a High Intensity Glycemic Program on Weight and BMI

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Background:
Multiple studies have shown that intensive glycemic control leads to improved HbA1c and delays the onset of complications in diabetes.[1] However, improvement in glycemic control has also been associated with weight gain.[1] The High A1C (HAC) program uses a multidisciplinary team to provide intensive therapy to patients with HbA1C ≥ 10% over 3 months to improve glycemic control. The aim of this retrospective study is to examine if the HAC program is associated with a significant change in weight and BMI.
Methods:
Patients enrolled in the HAC program were scheduled for frequent visits over the course of 3 months with an Endocrinologist, nurse practitioner, or diabetes educator. Data from patients with type 2 diabetes enrolled from March 2018 to June 2019 who attended at least 2 appointments was collected. Pre-enrollment HbA1c, weight, BMI, and total daily dose (TDD) of insulin (units/kg/day) were compared to post-enrollment using t-test analysis. Use of weight-lowering anti-hyperglycemic agents such as Metformin, GLP-1 agonists (GLP1A) and SGLT-2 inhibitors (SGLT2i) was collected.
Results:
44 patients were enrolled with 39/44 (88.6%) attending at least 2 visits and 5/44 (11.3%) who were lost to follow-up. The median HbA1c improved from 11.5% (9.7-14%) to 8.4% (5.9-14%), $p<0.001$.There was no significant change in mean weight (195lbs (110-360) vs 192lbs (114-358), $p=0.14$) or BMI (31 (20-49) vs 31 (21-49) kg/m^2, $p=0.86$). Pre-enrollment, 33/39 (84.6%) patients were on Metformin, 10/39 (25.6%) were on a GLP1A, and 3/39 (7.7%) were on a SGLT2i. At the end of the program, there were 34/39 (87%) patients on Metformin, 26/39 (66.6%) on a GLP1A, and 17/39 (43.5%) on a SGLT2i. There was no difference in the mean TDD of insulin at the start of the program of 0.63 units/kg/day (0-3.52 units/kg/day) compared to 0.60 units/kg/day (0-4.07 units/kg/day) at the end of the program ($p=0.97$).
Conclusions:
Patients enrolled in a high intensity glycemic control program had significant improvements in HbA1c without change in weight or BMI. Additional adjunctive non-insulin therapies and lifestyle management may be contributing factors for weight neutrality in our population. The significant improvement in HbA1c was not linked with increases in TDD of insulin.
Citation:
1."U.K. Prospective Diabetes Study Group: Intensive blood glucose control with sulfonylureas or insulin compared with convention treatment and risk of complications in patients with Type 2 Diabetes." *Lancet*, vol.353, 1998, pp.837-53.

Reproductive Endocrinology

MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES

Linking Gonadotropin-Regulated Testicular RNA Helicase (GRTH/DDX25) to Histone Ubiquitination Network and Acetylation During Spermiogenesis

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Gonadotropin Regulated Testicular Helicase (GRTH/DDX25), a testis specific RNA helicase essential for the completion of spermatogenesis. Our early studies