Duodenal Mucosal Resurfacing
A New Procedural Therapy for Type 2 Diabetes

Safety and Proof-of-Principle
First In Human Clinical Study
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Disclosure

Manoel Galvao Neto MD, Leonardo Rodriguez MD, Patricia Rodriguez RN, Pablo Becerra MD, Paolina Vignolo MD

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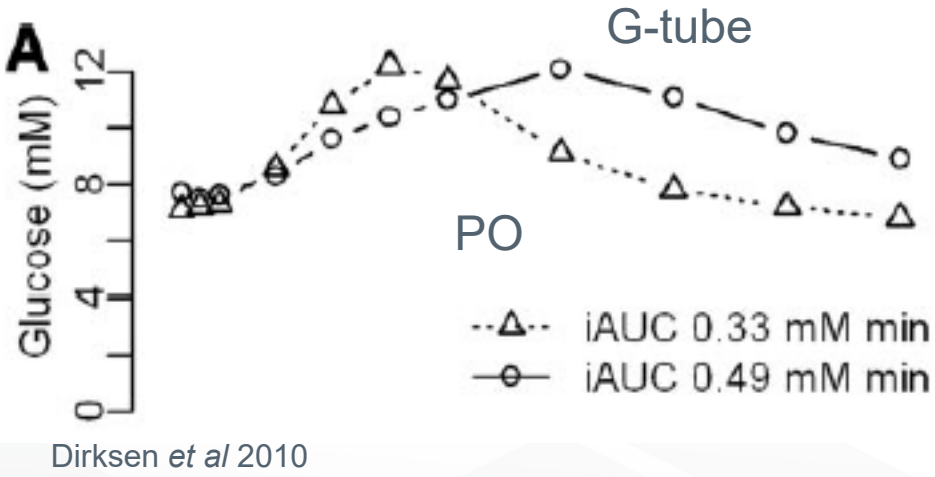
Nutrient stimulation of duodenum worsens glucose homeostasis in diabetics post-RYGB

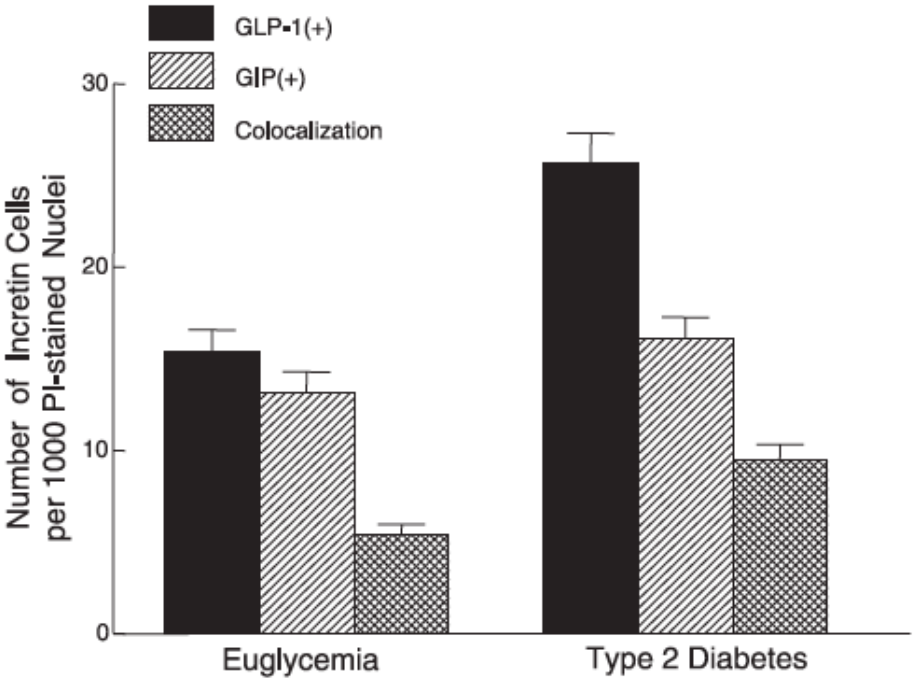


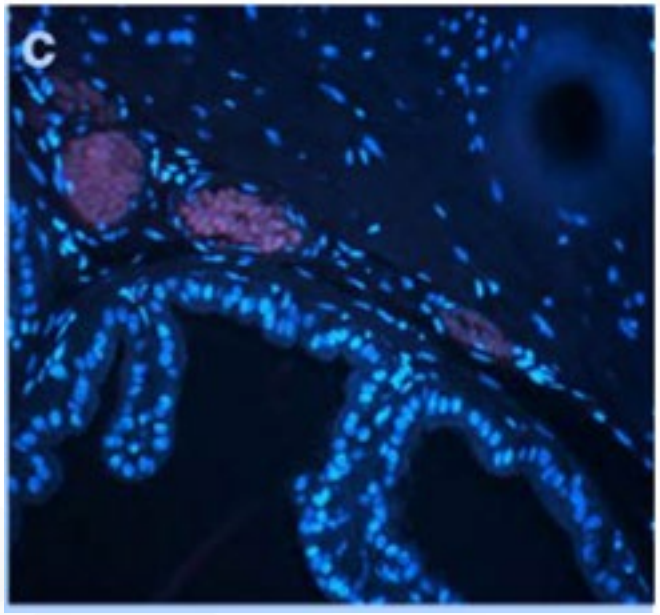
Dirksen *et al* 2010

What does this mean about mechanisms of RYGB-associated T2DM improvement?

- Glucose improvement not primarily due to diet, weight loss, or caloric restriction
- Must be mediated by some physiological change, perhaps in the duodenum

Human duodenal biopsies and animal models show diabetic duodenal mucosal changes





Duodenal biopsies from humans

Duodenal samples from diabetic rats

Theodorakis et al

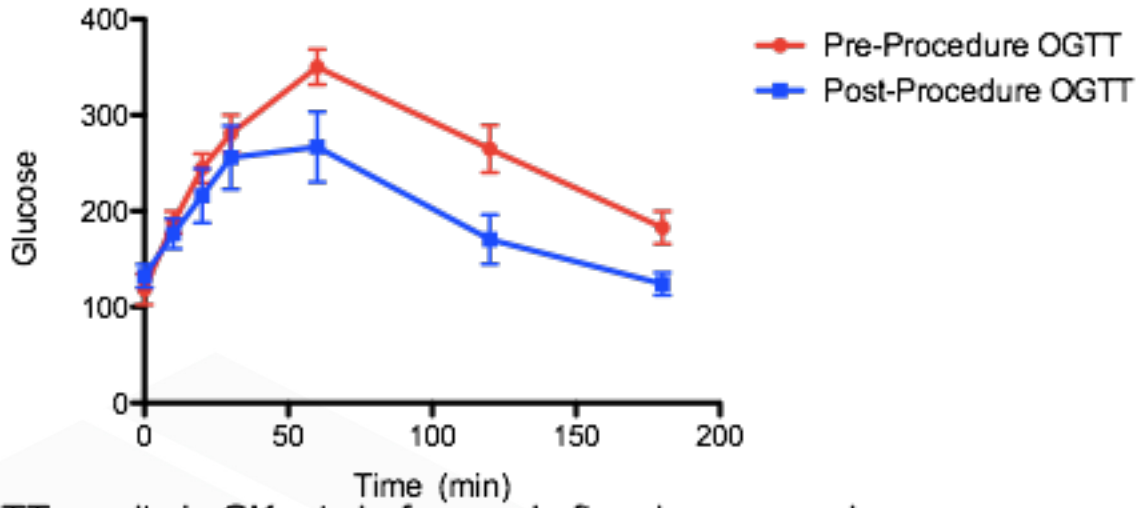
Gniuli *et al*

A model for Type 2 diabetes pathogenesis – intestinal hormonal changes may drive insulin resistance

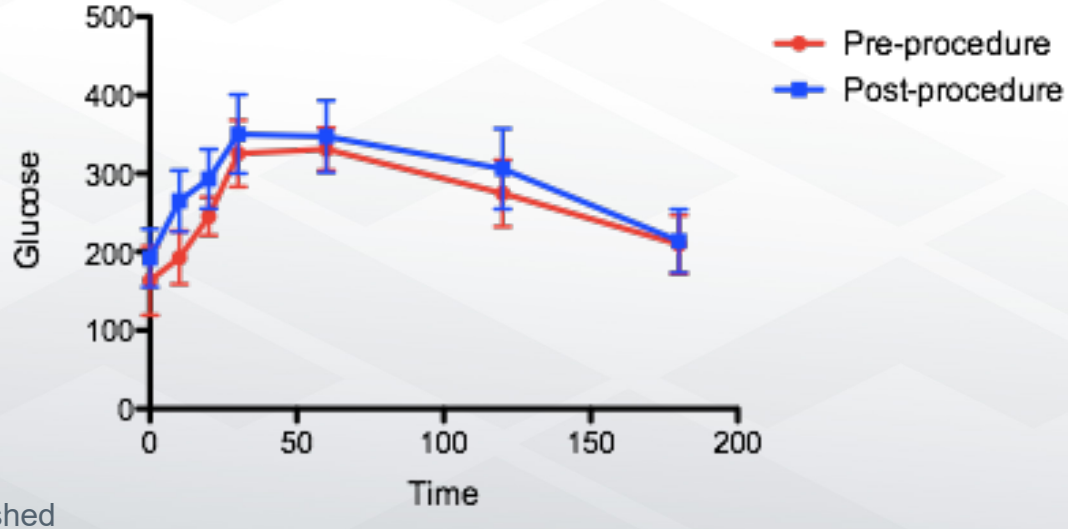
Fat Sugar → Mucosal hypertrophy/ hyperplasia change gut hormones → End-organ effects on muscle, liver, etc → Decompensation of pancreatic beta-cells → Hyperglycemia

Duodenal mucosal abrasion can improve glucose tolerance in diabetic rats

OGTT results in GK rats before and after duodenal abrasion



OGTT results in GK rats before and after sham procedure



34%

improvement in the OGTT after abrasion compared to sham treated rats

Unpublished

Revita FIH Clinical Trial

Trial Methodology:

- Open label first-in-human safety, feasibility, and proof-of-principle cohort study
- Dosimetric escalation (dose defined as axial length of circumferentially ablated duodenum)
- Efficacy analysis as a function of treated dose
- Dr. Leonardo Rodriguez, Clinica Indisa, Santiago, Chile

Procedural steps:

- Duodenal sizing
- Avoidance of papilla
- Circumferential saline expansion of submucosa
- Thermal ablation with a recirculating hot water-filled balloon
- Fully endoscopic
- No implant

Revita FIH Patient Characteristics

Enrollment criteria:

- T2DM < 10 yrs
- Age 28-75
- HbA1c 7.5-12%
- BMI 24-40
- No previous bariatric surgery
- Preserved pancreatic function

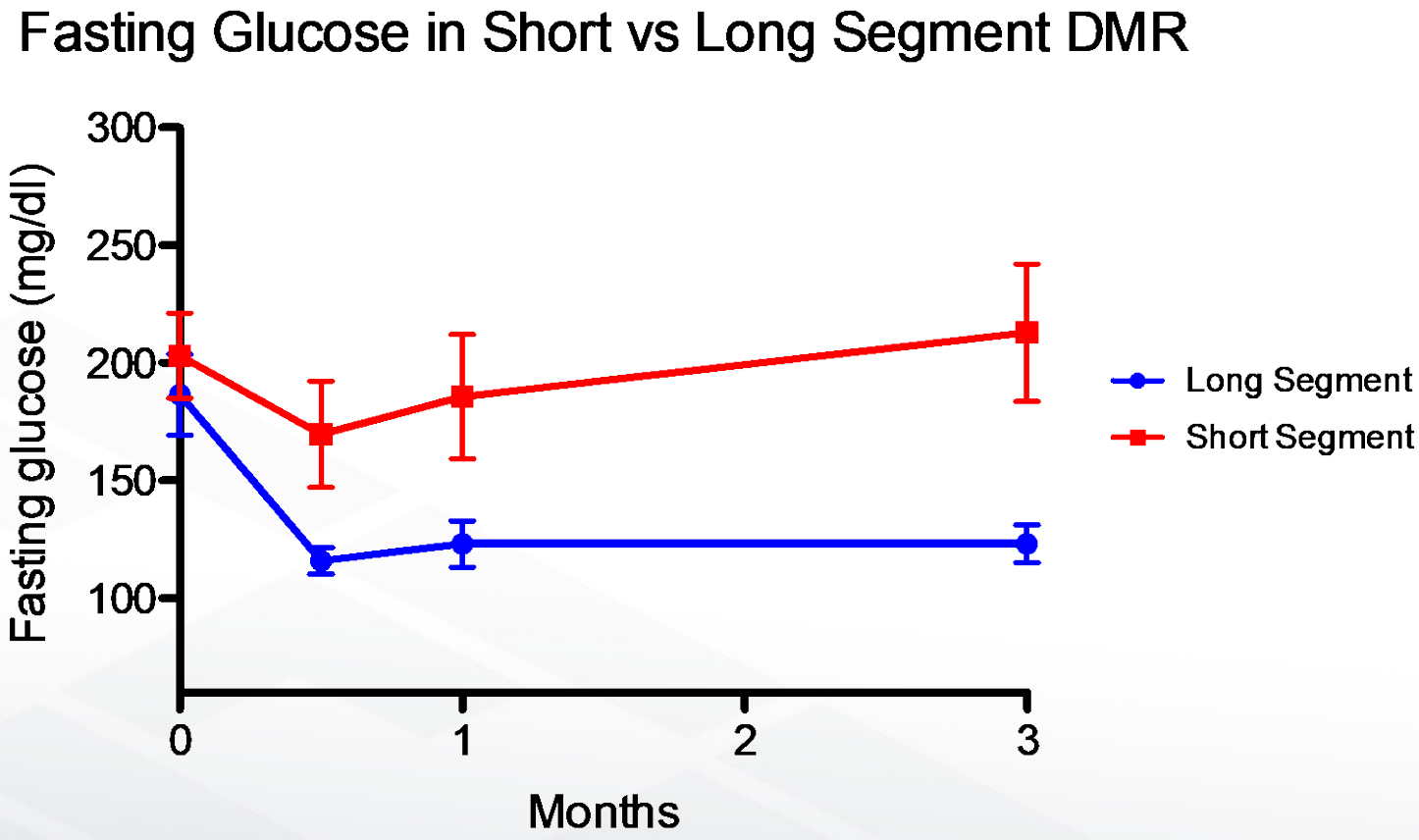
Characteristic	Value
Number	30
Female sex - N (%)	8 (38%)
Age - yr	53.7 +/- 8.2
BMI	31.3 +/- 3.5
Baseline HbA1c (%)	9.3 +/- 1.4
Duration diabetes - yr	5.7 +/- 3
Medications - N	1.8 +/- 0.7

DMR Procedural Video

Revita FIH Results

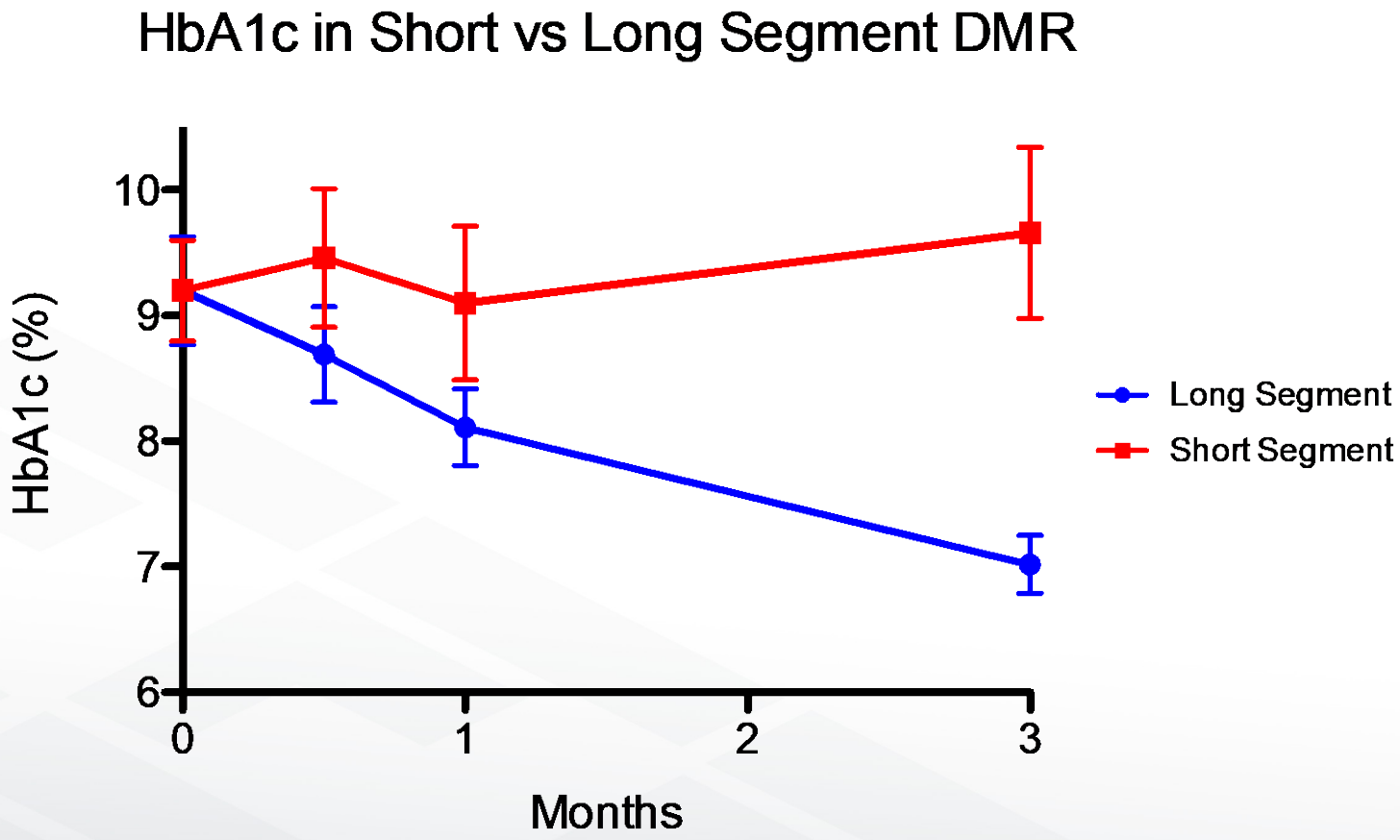
		Baseline	1 month	3 months
HbA1c	Long segment	9.20	8.11	7.02
	Short segment	9.19	9.10	9.66
Fasting glucose change	Long segment	186.5	-63.5	-67.2
	Short segment	193.3	-17.4	-16.4
Weight change	Long segment	85.0	-4.3	-5.6
	Short segment	86.6	-2.3	-0.6

Revita FIH Results



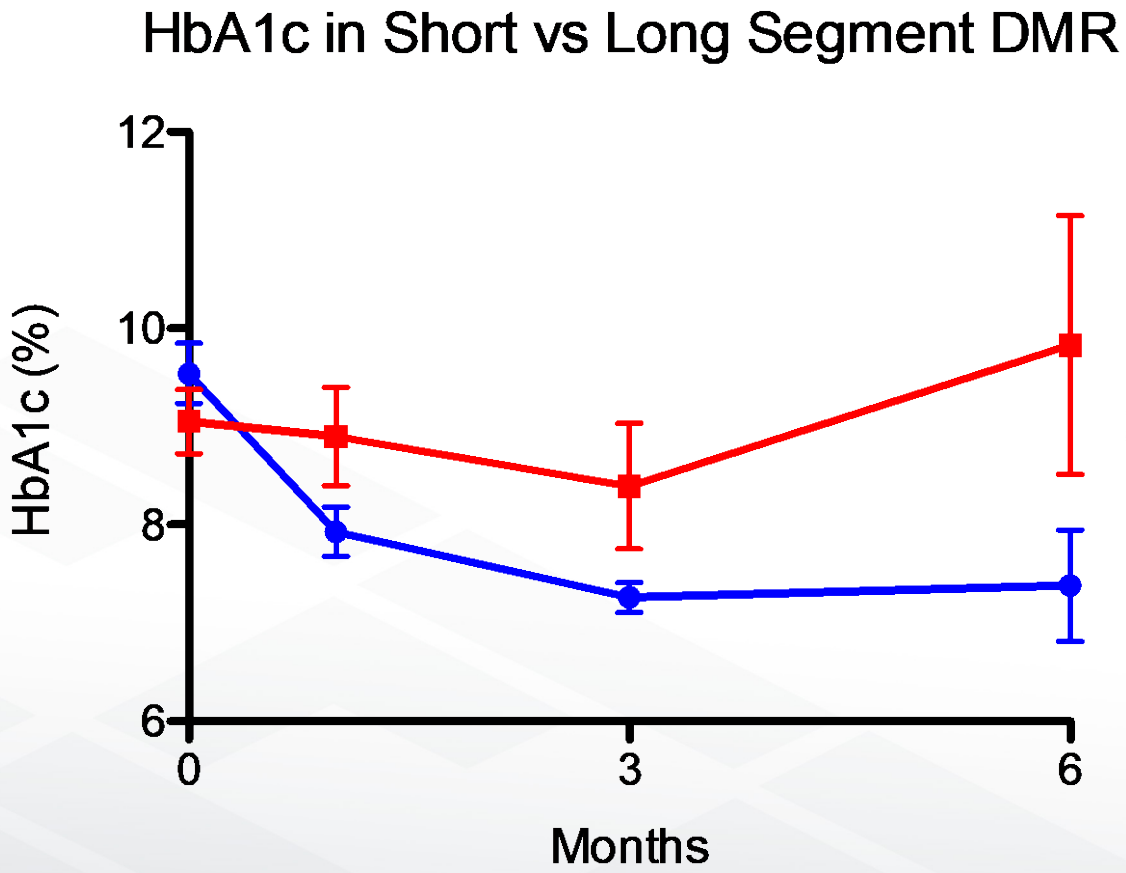
19 patients @ 1 month
10 patients @ 3 months

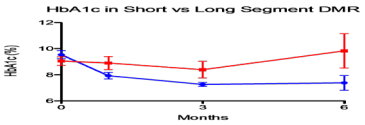
Revita FIH Results



19 patients @ 1 month
10 patients @ 3 months

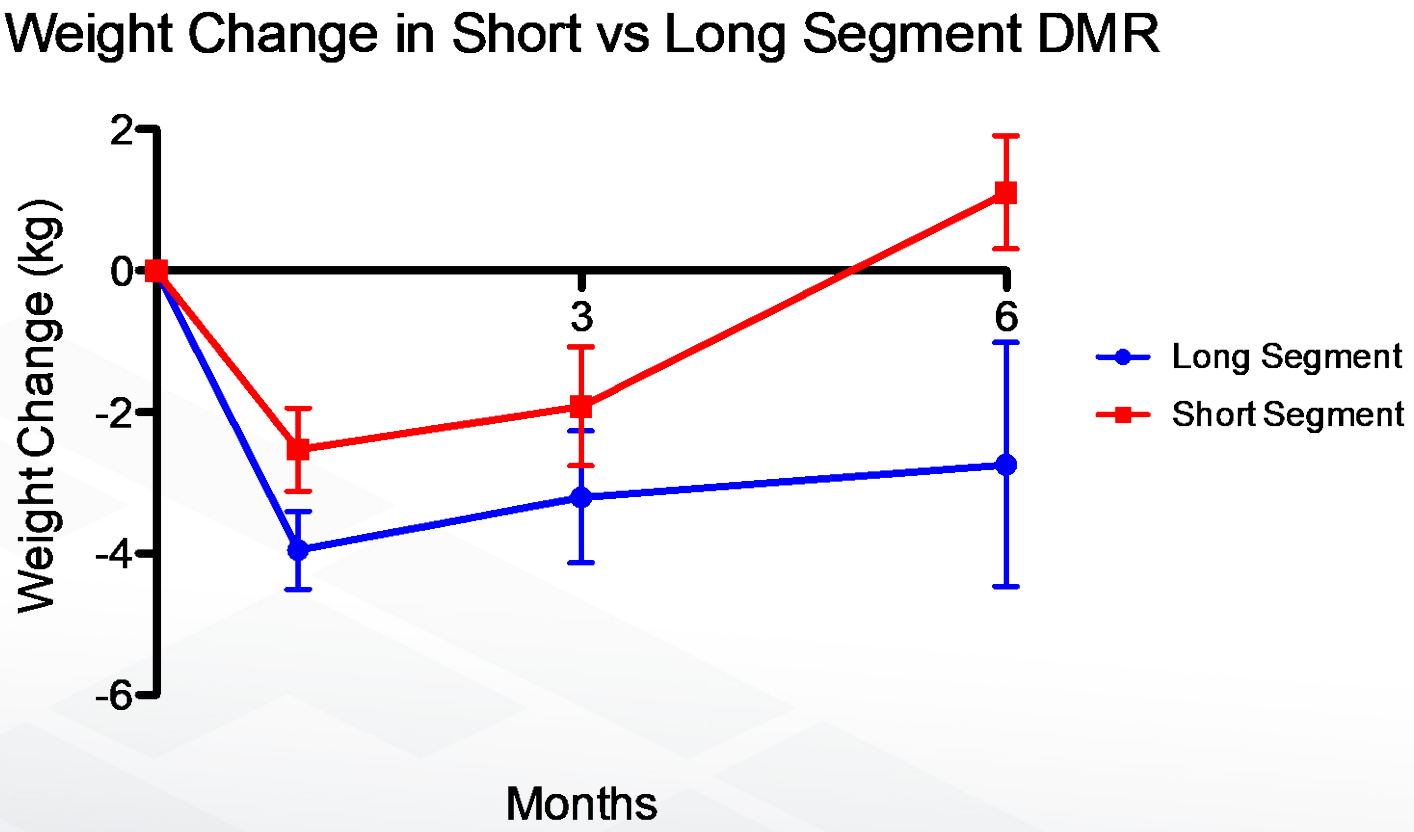
Revita FIH Results / Up-to-Date Data





30 patients @ 1 month
24 patients @ 3 months
8 patients @ 6 months

Revita FIH Results / Up-to-Date Data



Adverse Events

- 1 patient experienced a duodenal stenosis that was easily dilated with TTS CRE balloon. Now doing well
- No bleeding, pancreatitis, duodenal ulcers, malabsorption, perforation, infection, or death

Adverse Events (all transient)	Number
Abdominal bloating	5
Sore throat	2
Asymptomatic Duodenitis	2
Abdominal muscle pain	2
Right hip pain	1
Diarrhea	1
GI virus	1
Gastric ulcer	1
Back pain	1
Molar pain	1
Rash	1
Cold	1

Conclusions

- Intriguing early data to support concept of duodenal mucosal resurfacing as a treatment for Type 2 Diabetes
- Safety profile is remarkably good
- Additional studies are warranted