Duodenal Resurfacing

& other gastro-duodenal procedures

Dr Adrian Sartoretto
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DISCLOSURES

Research funding from Endogenex for assessment of ReCET technology
Research funding from Erbe Elektromedizin GmbH
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Consulting honoraria for Intuitive Surgical
Previous research funding from BaroNova for the TransPyloric Shuttle
Previous consulting for Apollo Endosurgery

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- Type 2 Diabetes is a progressive condition that affects 536.6 million people worldwide with huge implications for healthcare resources
- Standard of care focuses on achieving glycemic goal and preventing micro- & macrovascular complications
- Despite an increasing number of available medications, over 50% of patients do not achieve adequate glycemic control

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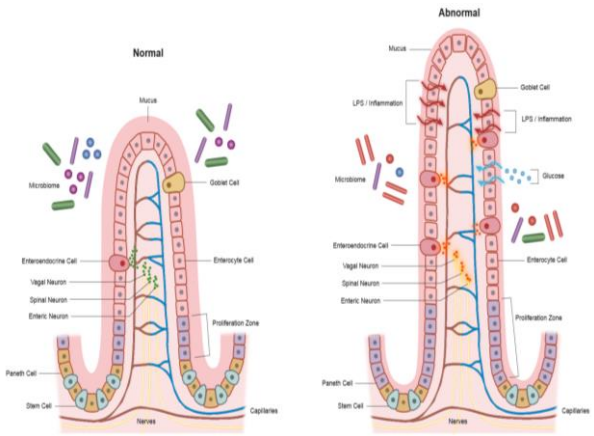
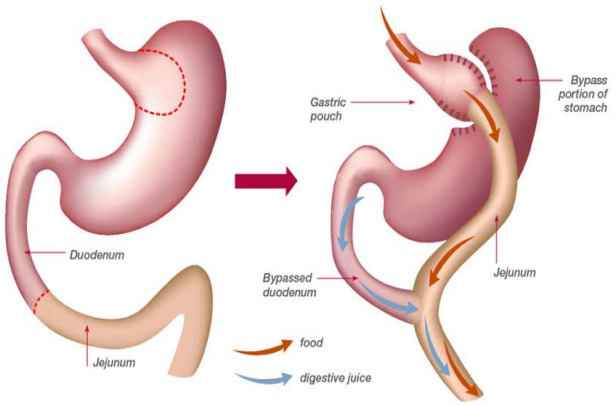
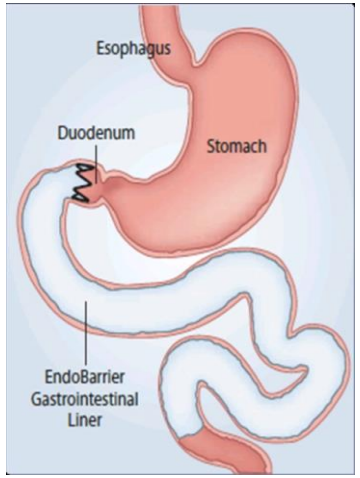
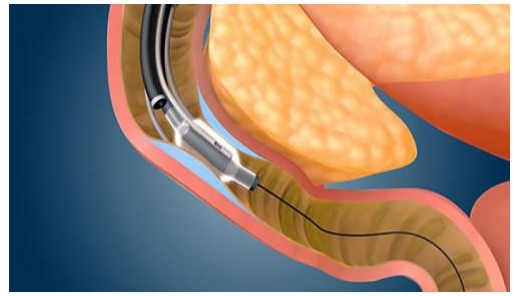
Duodenum as a Therapeutic Target for T2D









T2D is associated with duodenal mucosal maladaptation, increased intestinal permeability, and impaired nutrient sensing and incretin effect

Bypass surgery is the most effective treatment for T2D, resulting in diabetes remission in 30%-63% of patients at 1-5 yrs [1]

Exclusion of the duodenum via a duodenal-jejunal bypass liner improves glycemic control in patients with T2D

Duodenal mucosal resurfacing using thermal ablation improves glycemic control in patients with T2D

[1] Riddle et al. Standards of Diabetes Care. 2022; 45, Suppl 1

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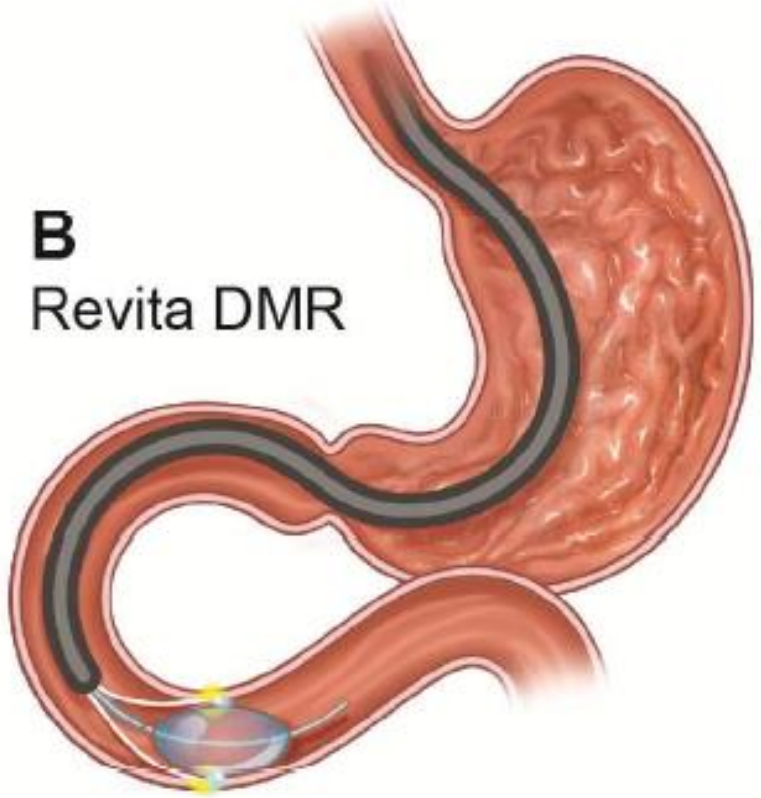
Revita® DMR, Fractyl

- Cauterises 10 – 15cm duodenal mucosa
  - Injects fluid to act as safety buffer to prevent full thickness burns & strictures
  - Circulates hot water via balloon to effect cuffs of mucosal burns
- First in Human results
  - Baseline G1 obese HbA1c 9.6±1.4%
  - Absolute reduction of 1.2±0.3% was seen in HbA1c at 6 months
  - Minimal weight loss of roughly 3% TBWL at 6 months
  - 2 strictures; treated with balloon dilatation
- Pivotal study currently recruiting



DUODENAL RESURFACING AND OTHER GASTRO-DUODENAL THERAPIES

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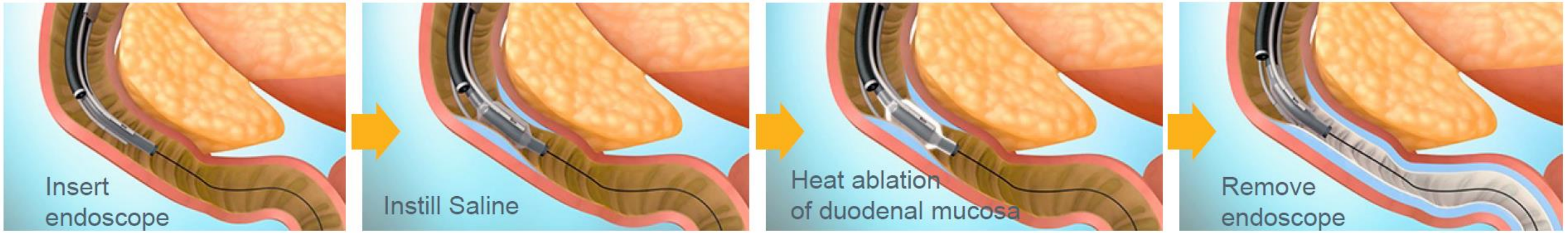
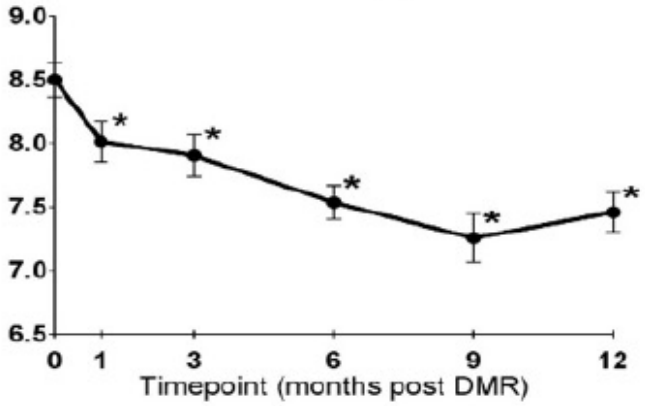
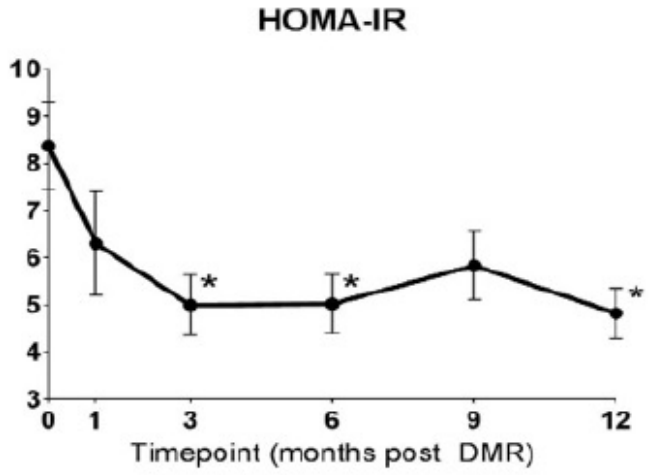


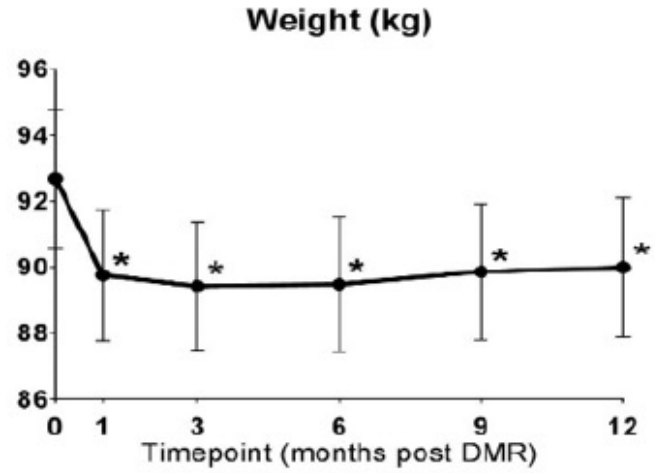
Revita-1: Impact on HBA1c and insulin resistance



Sustained HbA1c reductions in patients despite net medication reductions ($p<0.01$)



Sustained improvement in measures of insulin resistance (HOMA-IR) tie to core mechanism of action



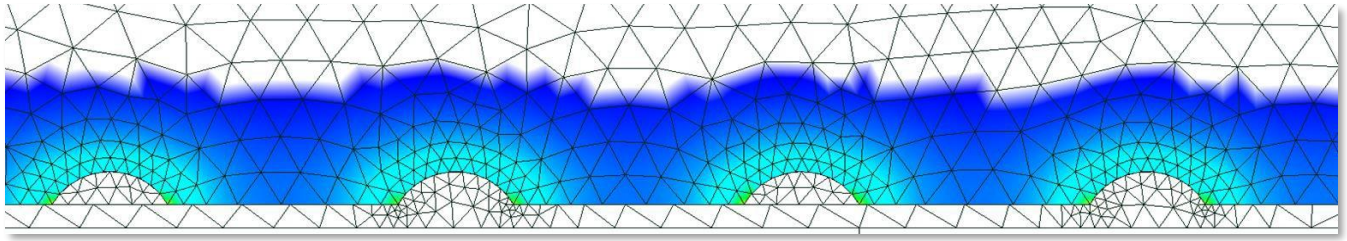
Sustained weight loss without any prescriptive lifestyle intervention program

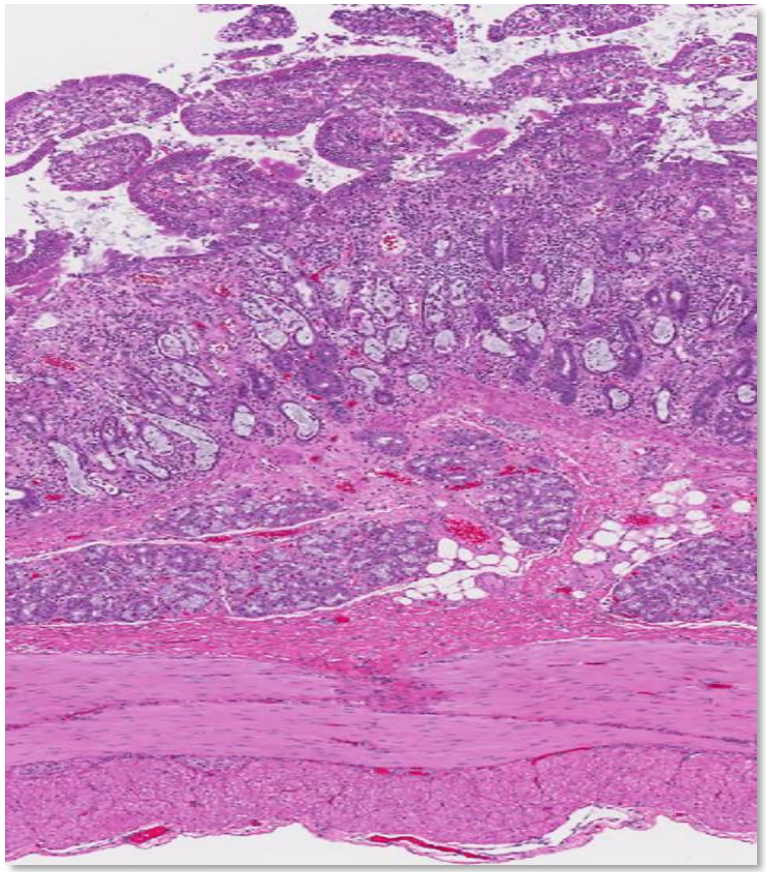
Van Baar et al ADA 2018 (manuscript in preparation)

Pivotal Study currently recruiting

ReCellularization via Electroporation Therapy (ReCET™)

- High voltage, ultra short pulsed electric field
- Increases cell permeability resulting in mucosal cellular apoptosis
- Preserves extracellular matrix and myocytes
- Rapid re-epithelialization due to preserved tissue architecture
- Non-thermal (< 4 °C average increase in probe temperature)
- Controlled depth of penetration





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REGENT-1 Study Overview

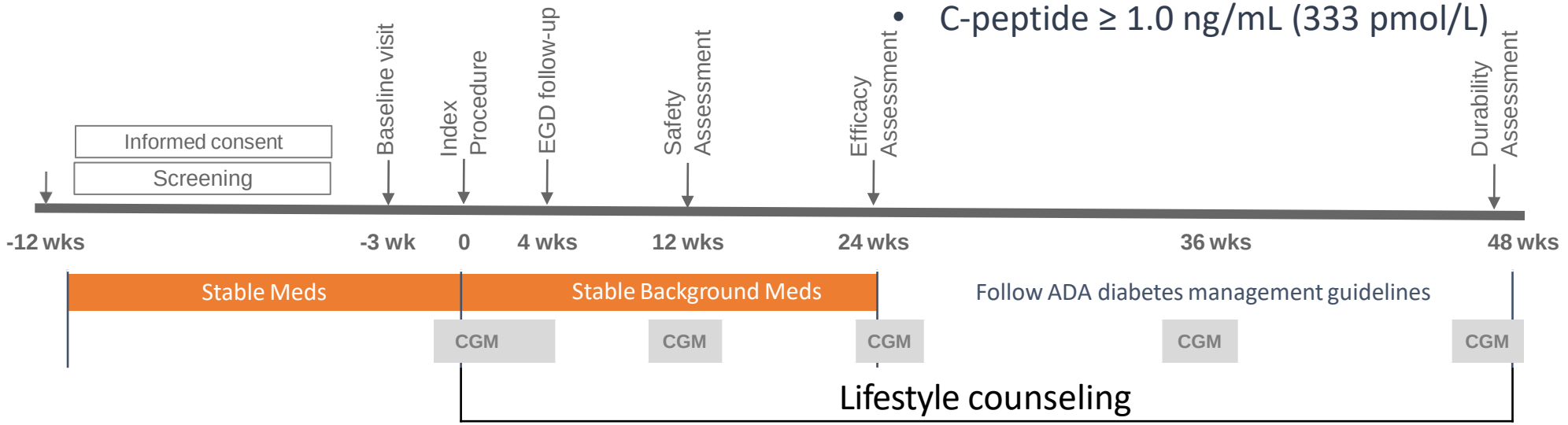
THE BMI CLINIC

Study Design

- Multicenter, open-label, single arm
- Stable background meds 12 w before and 24 w post procedure
- Treat to target after 24 w

Study Population

- Age: 18-70 yrs
- BMI: 24-40 kg/m^2
- T2D: ≤10 yrs, on 1-4 noninsulin glucose-lowering medications
- HbA1C: 7.5% – 11%
- C-peptide ≥ 1.0 ng/mL (333 pmol/L)



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Baseline Characteristics

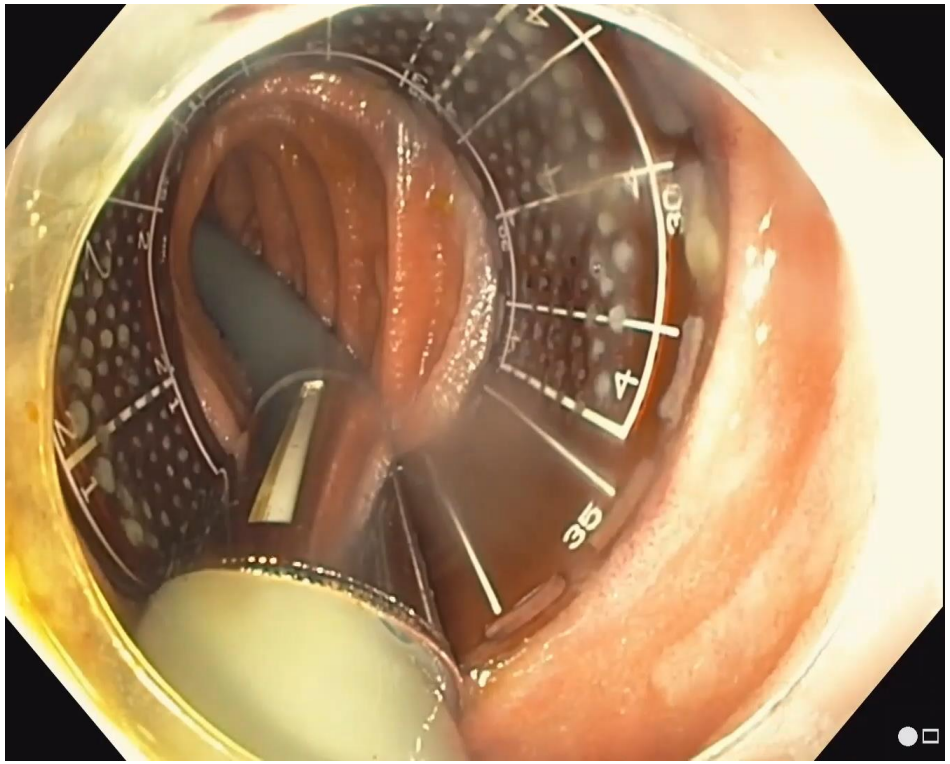
	Mean ± SD, %	Range
N	41	-
Age (years)	52.4 ± 8.6	30.0, 68.0
Male	78%	-
Weight (Kg)	93.7 ± 15.9	66.6, 130.0
BMI (Kg/m^2)	31.3 ± 3.7	24.1, 39.8
HbA1c (%)	8.7 ± 0.9	7.5, 10.5
FPG (mmol/L)	9.9 ± 2.2	6.8, 14.7
Insulin (IU/L)	12.5 ± 7.1	1.0, 35.0
HOMA-IR	5.5 ± 3.2	0.3, 13.2
C-peptide (pmol/L)	865 ± 355	440, 1900
Duration of T2D (years)	5.5 ± 2.6	<1, 9

	N (%)
Background GLMs	
Metformin	39 (95%)
Sulfonylureas	12 (29%)
SGLT2i	23 (56%)
GLP-1a	4 (10%)
DPP4	10 (24%)
No. of background GLMs	
1	11 (27%)
2	17 (41%)
3	9 (22%)
4	4 (10%)

Technical Feasibility

- N=41 enrolled
- Procedure success (≥ 6 cm of duodenum treated): 100%
- Mean treatment length: 11.1 ± 2.6 cm (range 6 -18 cm)

Device	Energy Level	No. of Patients N=41
Gen 1	600V Single Tx	12
	600V Double Tx	13
	750V Double Tx	5
Gen 2	750V Double Tx	11



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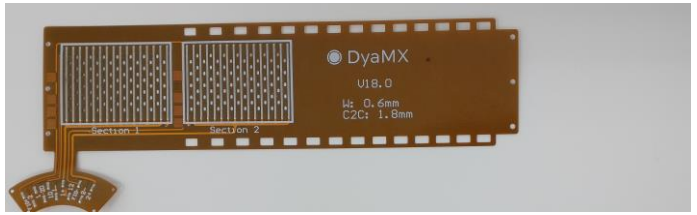
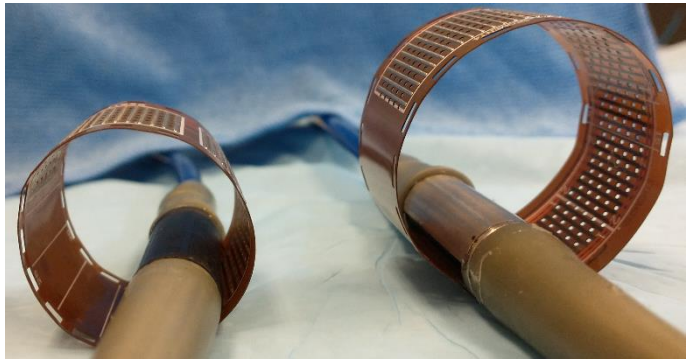
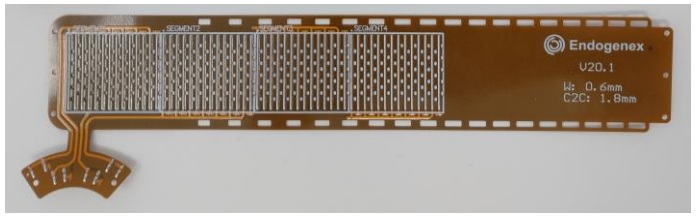
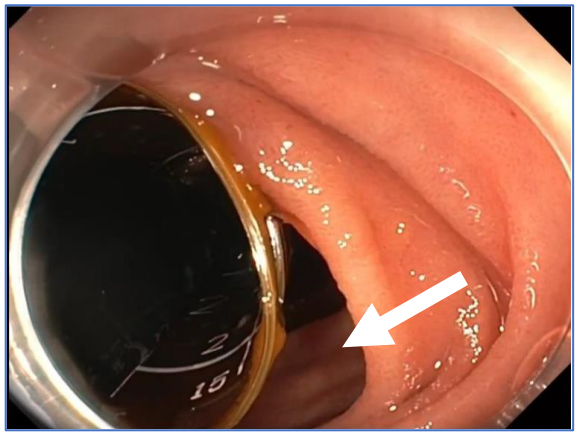
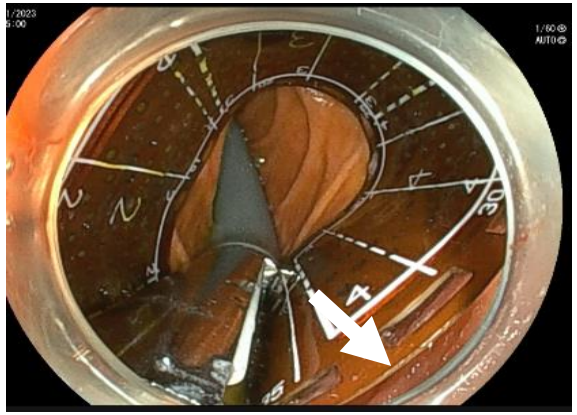
Technical Learning: Gen1 to Gen2

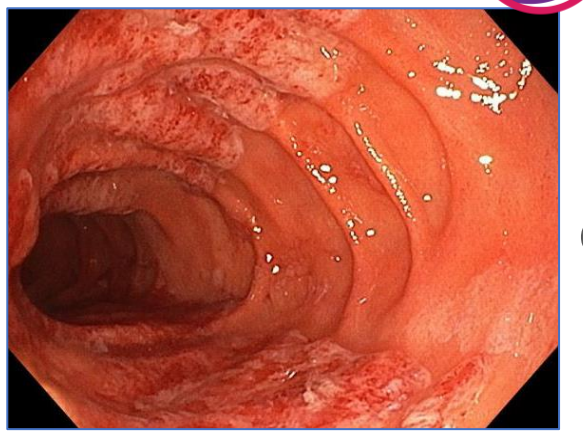












GEN 1

GEN 2

Improved duodenal wall apposition and circumferential coverage with the Gen 2 device.

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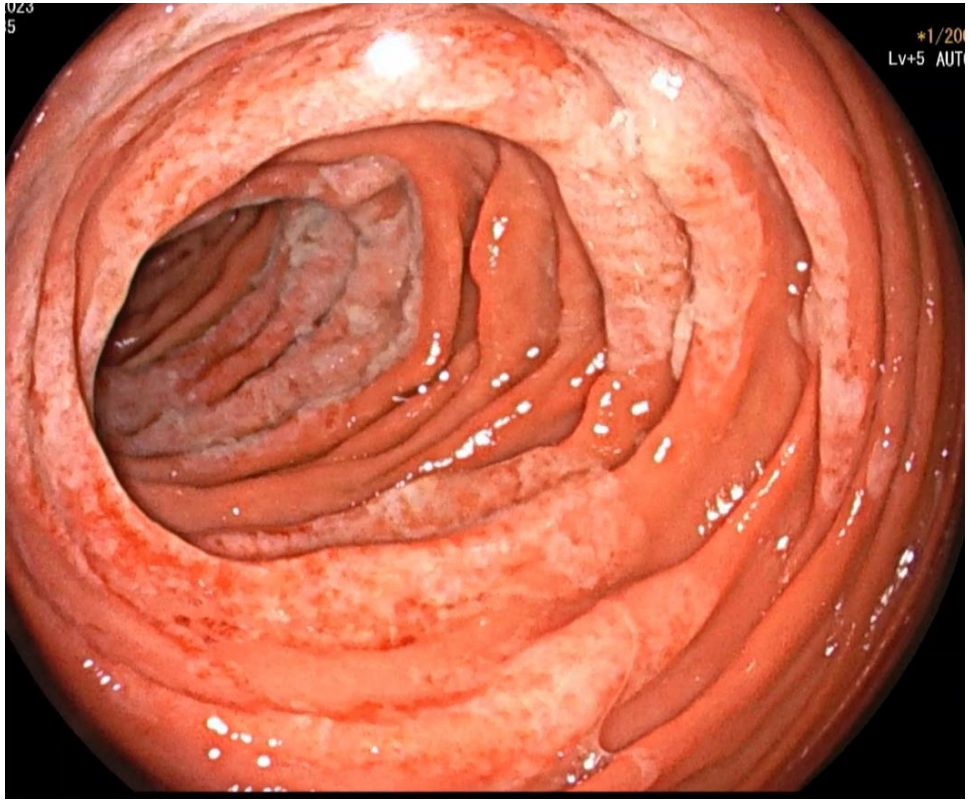
Safety

- No device/procedure-related SAEs
- Device/procedure-related AEs were mild to moderate, and mostly periprocedural
  - Mild: 75%
  - Moderate: 25%
  - Severe: 0%
- Incidence of diarrhea and GI symptoms decreased with modified transitional diet
- Treatment with higher energy doses were safe

Device/procedure-related AEs	600V single (n=12)	600V double (n=13)	750V double (n=5)	750V Double Gen 2 (n=11)	Grand Total
Abdominal discomfort		**1**			**1**
Abdominal distension	1	1			2
Abdominal pain	1	1			2
Constipation	1	1			2
Cough	1				1
Diarrhoea	6	3		1	10
Epigastric discomfort	1				1
Flatulence	2				2
Gastroenteritis		1			1
Gastrointestinal procedural complication		1			1
Gastrooesophageal reflux		1			1
Hepatic enzyme increased	1				1
Iron deficiency	1				1
Lethargy				1	1
Lip injury	1	1		1	3
Nausea	1	1		1	3
Oropharyngeal pain	11	5	1	2	19
Total	**28**	**17**	**1**	**6**	**52**

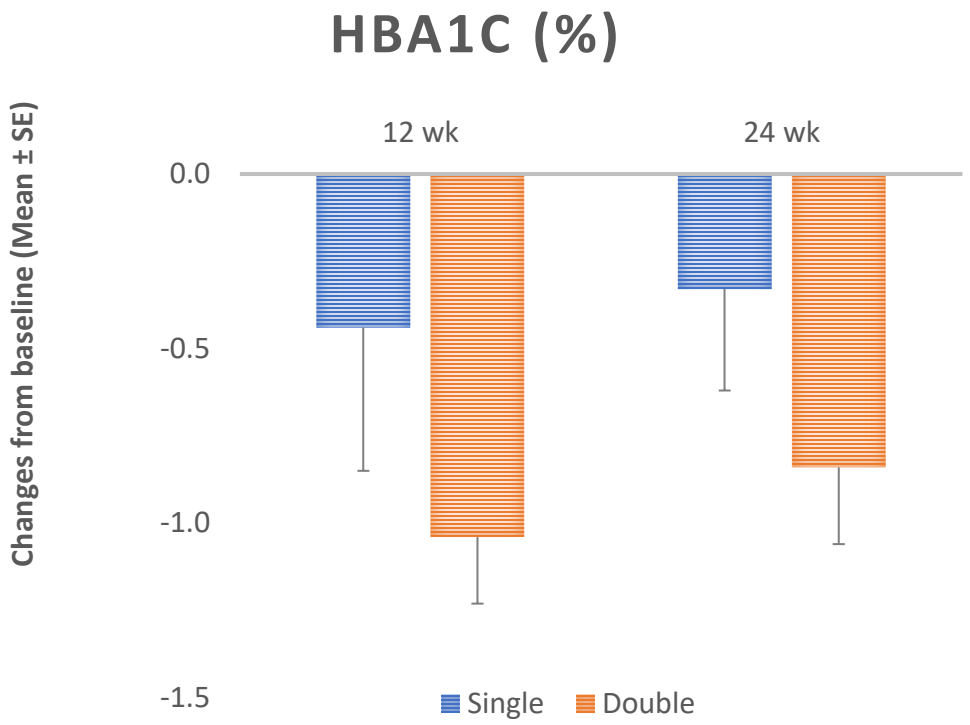
Complete Healing by Week 4

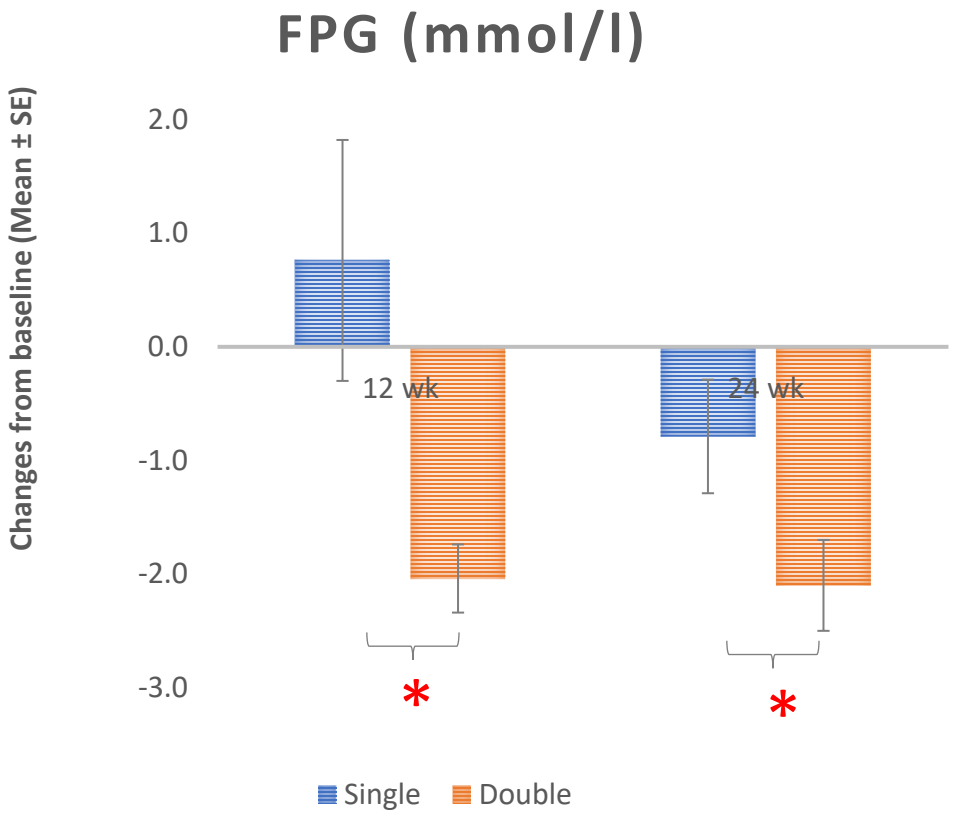


Immediately post treatment

4 weeks post treatment

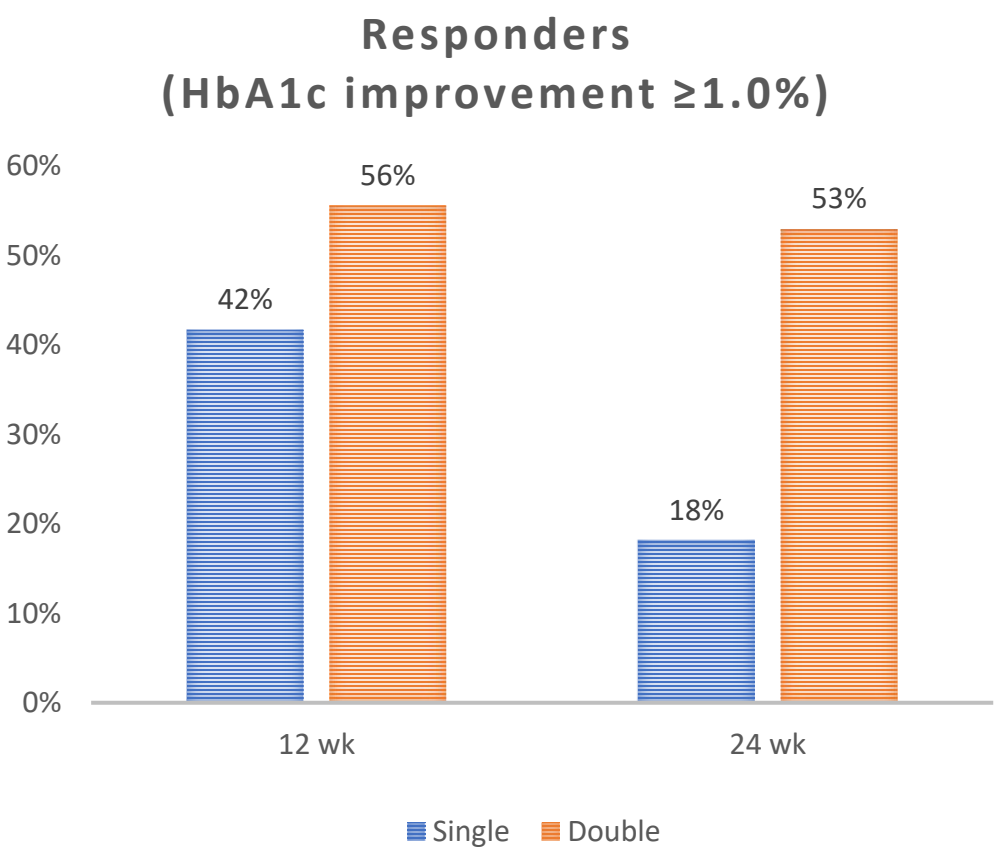
Glycemic Improvement by Energy Doses

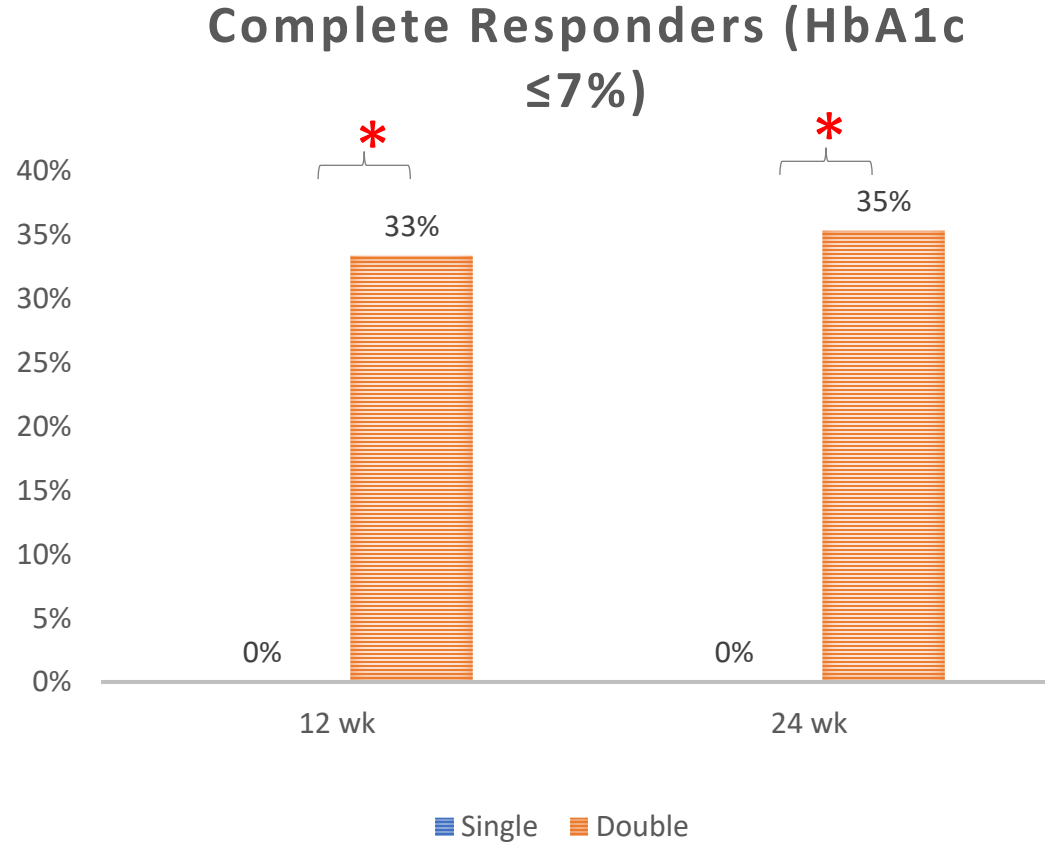




* p<0.05

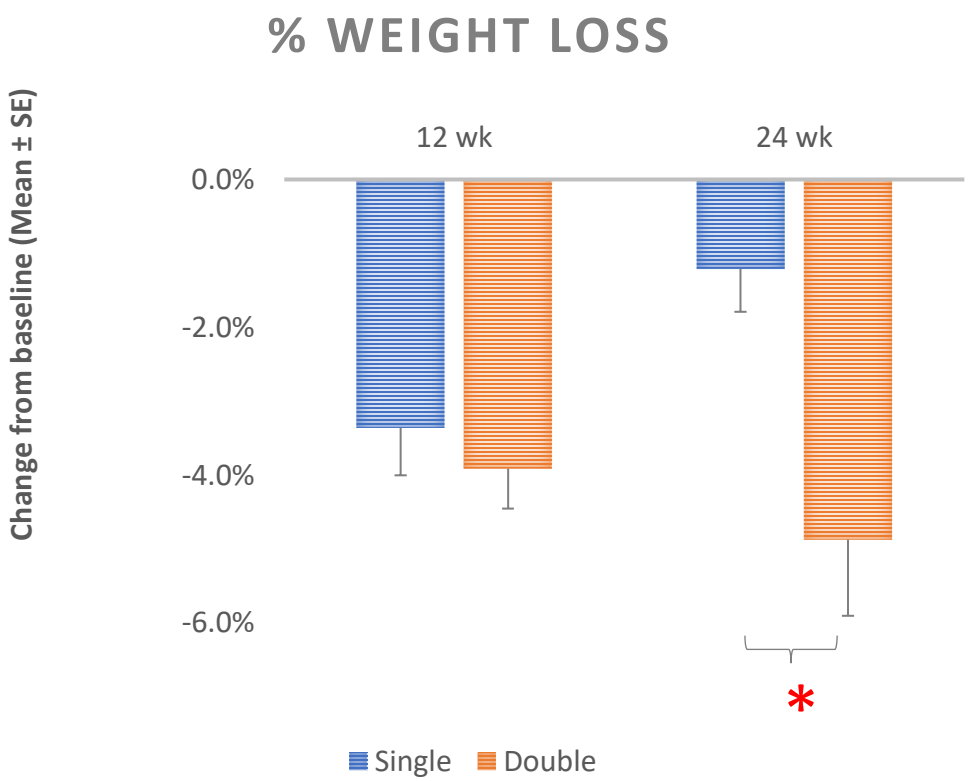
Responder Rate by Energy Doses

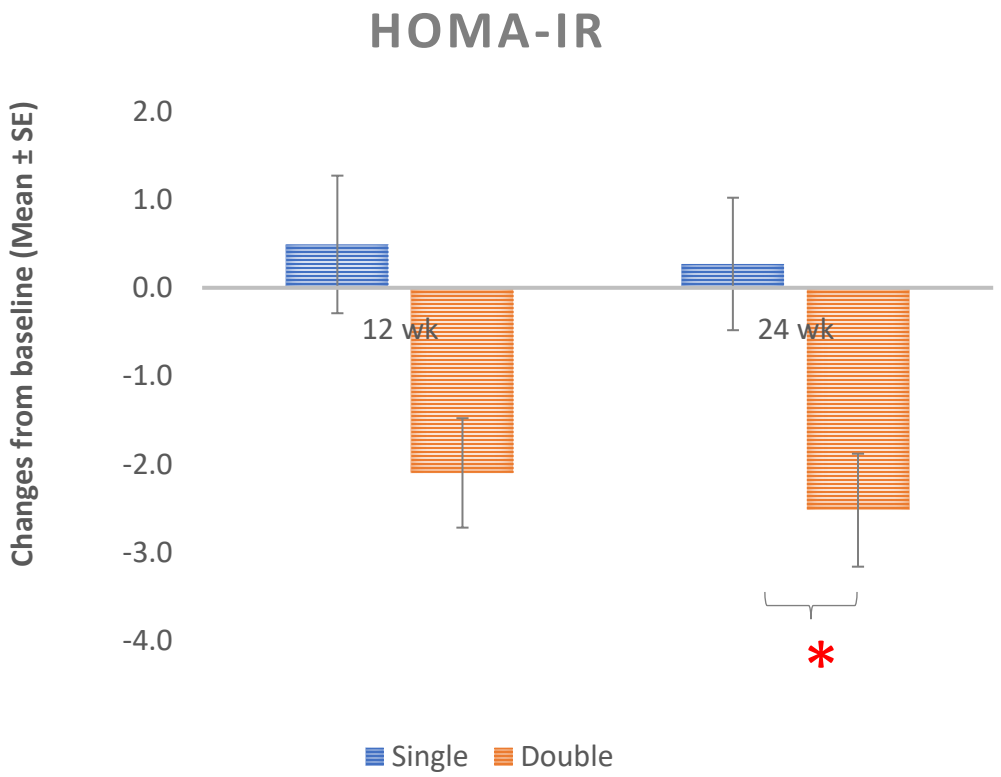




* p<0.05

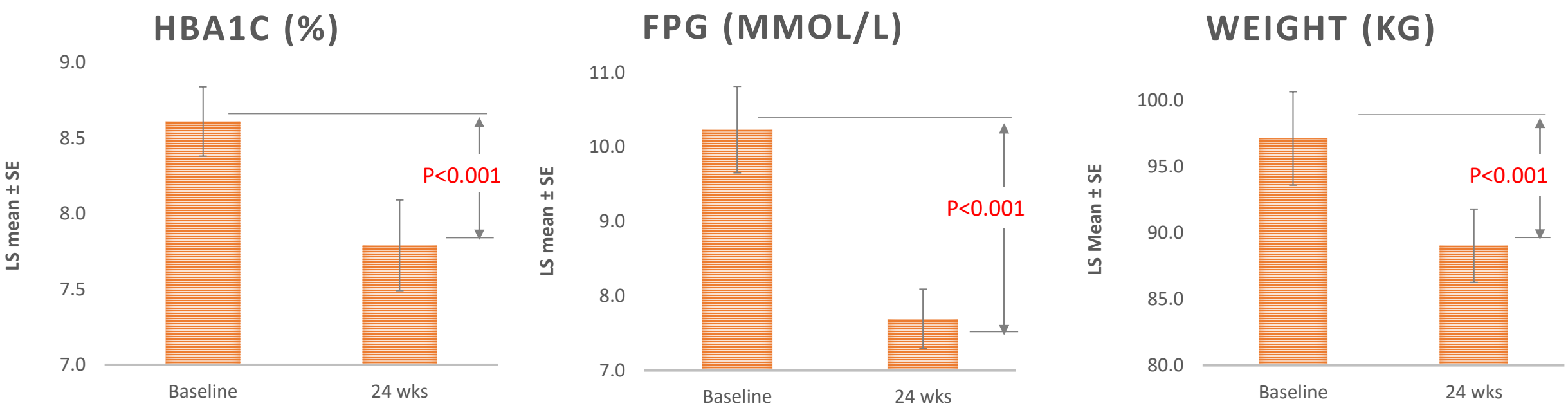
Improvement in Weight and Insulin Resistance by Energy Dose





*p<0.05

Improvement in Glycemic Control



N=16, double Tx, stable background medications, except 2 patients had reduction of sulfonylurea doses, and 2 patients discontinued SGLT2i.

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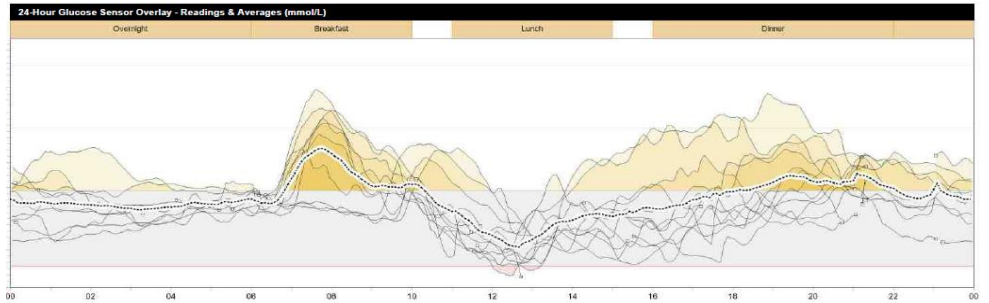
Case Example #1

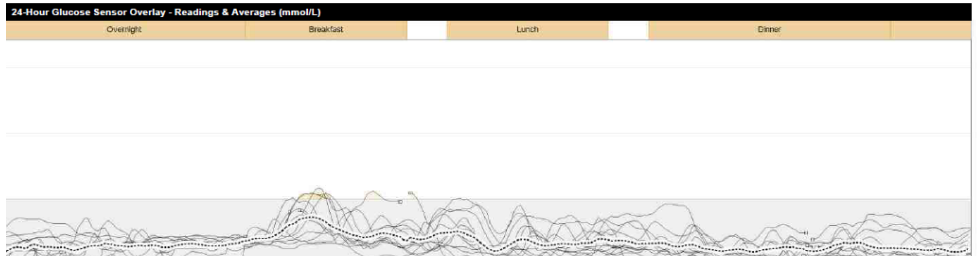
- 58 yr, male, BMI 34.3 kg/m^{2,} T2D duration 5 yrs, hypertension
- Baseline Meds: MF, SU, SGLT2i
- C-peptide 667pmol/L
- Procedure: 600V double, 10cm
- Post procedure: mild diarrhea for <1 day

	Baseline	12 wk	24 wk
HbA1c (%)	8.0	6.0	6.1
FPG (mmol/L)	8.0	6.1	5.6
Insulin (mU/L)	14.0	5.0	7.0
TIR (%)	68	99	100
Weight (kg)	100.4	96.1	84.2

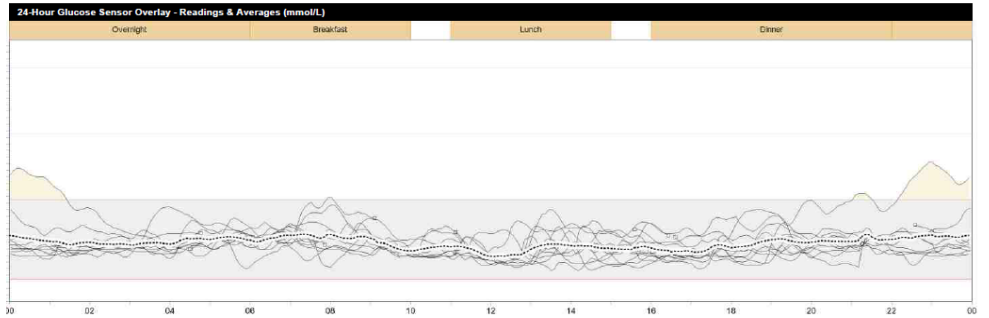
Baseline



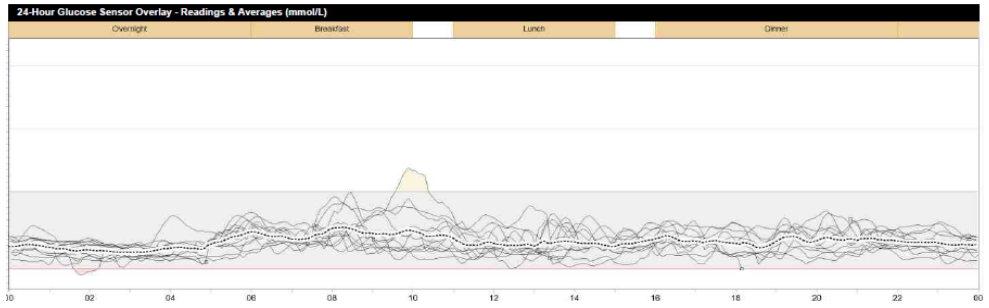
Week 4



Week 12



Week 24



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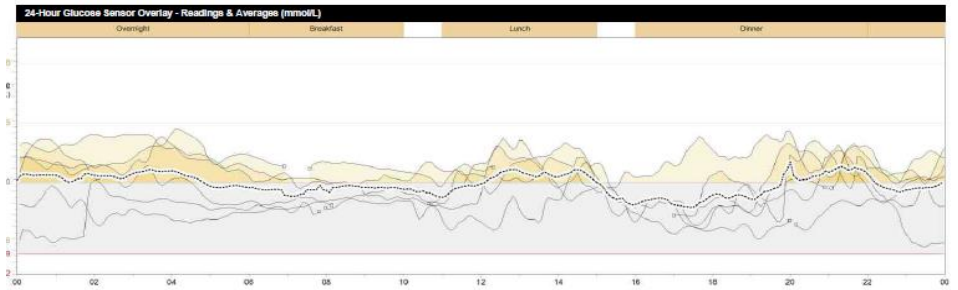
Case Example #2

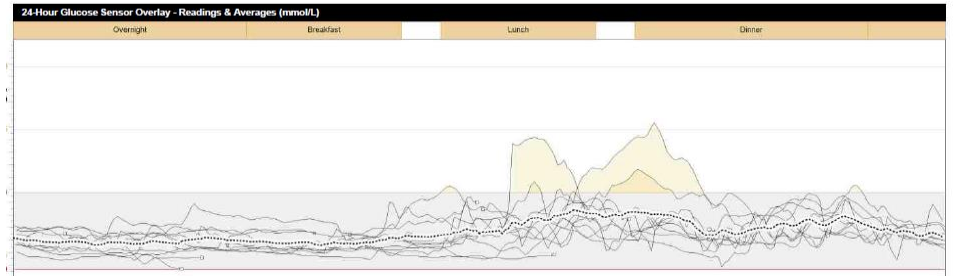
- 68 yr, male, BMI 34.0 kg/m^2, T2D duration 5 yrs, dyslipidemia
- C-peptide 471 pmol/L
- Baseline Meds:DPP4, SGLT2i
- Procedure: 600V double, 14cm
- Post procedure: moderate sore throat

	Baseline	12 wk	24 wk
HbA1c (%)	8.4	6.5	6.8
FPG (mmol/L)	9.4	5.8	6.8
Insulin (mU/L)	6	5	5
TIR (%)	51	100	96
Weight (kg)	98.3	91.2	91.5

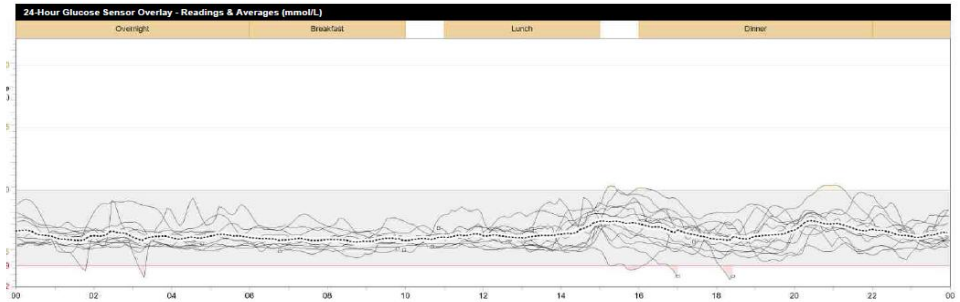
Baseline



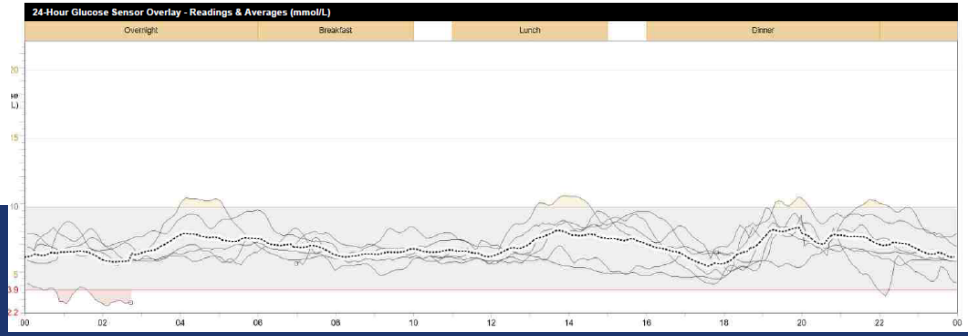
Week 4



Week 12



Week 24



Conclusions

- ReCET™ represents the first non-thermal endoscopic ablative therapy, and thus the only therapy to selectively ablate cells
- ReCET ™ was technically feasible with technical success in 100% of subjects
- ReCET™ appears safe & well tolerated: No Serious Adverse Events; all AEs were mild to moderate and transient
- ReCET™ applied to the duodenum resulted in durable and clinically meaningful improvement in glycemic control
- Dose response observed; higher energy doses were more effective without increased risk of AEs

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Article published online: 2023-08-21

E-Videos Thieme

Application of radiofrequency ablation in duodenal mucosal reconstruct

OPEN ACCESS

A 63-year-old woman was diagnosed with type 2 diabetes 8 months ago and was scheduled for duodenal mucosal reconstruction. The patient took metformin orally to control blood sugar. Before the operation, fasting blood glucose was 7.0 mmol/L (15.7 mmol/L 2 hours after a meal), and glycosylated hemoglobin was 7.1%. A single-channel flexible endoscope (EVIS GIF-N170; Olympus, Tokyo, Japan) was introduced into the horizontal part of the duodenum, and the Endoscopic Catheter (Barrx Channel; Medtronic, Minneapolis, USA) was inserted into the biopsy channel of the endoscope

▶ **Fig. 1** The endoscopic catheter was inserted into the biopsy channel of the endoscope.

▶ **Fig. 2** Radiofrequency ablation of the duodenal mucosa was performed from the horizontal part of the duodenum.

Li Zhengqi et al. Application of radiofrequency … Endoscopy 2023; 55: E959–E960

Sleeve Liners

Devices which form a barrier between duodenal mucosa and chyme and delay admixture of chyme with biliopancreatic juices

Reset®, Morphic Medical (formerly EndoBarrier)

Endosleeve®, Metamodix

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ACG CASE REPORTS JOURNAL

CASE REPORT | ENDOSCOPY

Concurrent Placements of a Duodenal-Jejunal Bypass Liner and an Intragastric Balloon Among Severely Obese Patients: A Case Series

Adrian Sartoretto, BMedSC, MBBS, FRACP[1,2], George Marinos[1], and Zhixian Sui, PhD, MHlSc[1,3]

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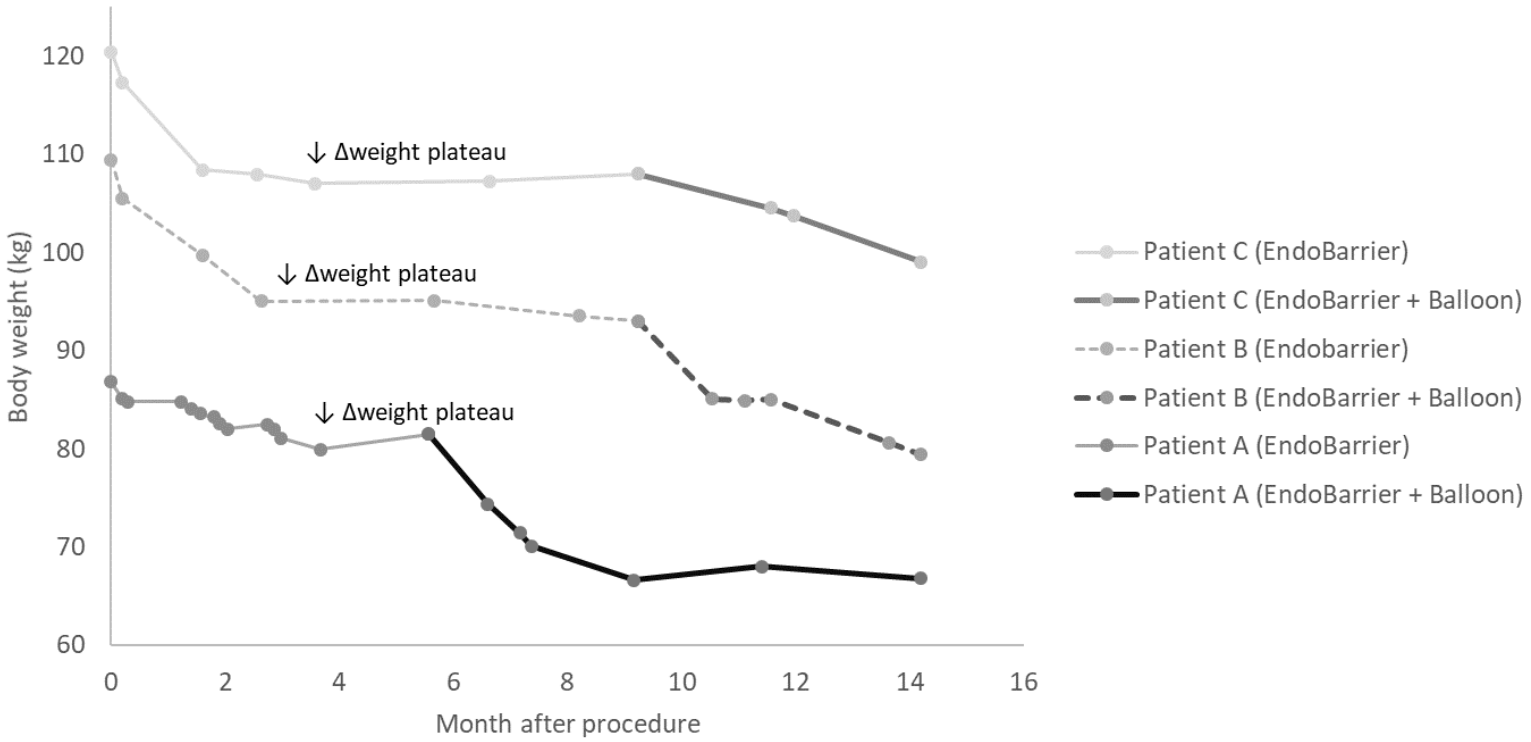

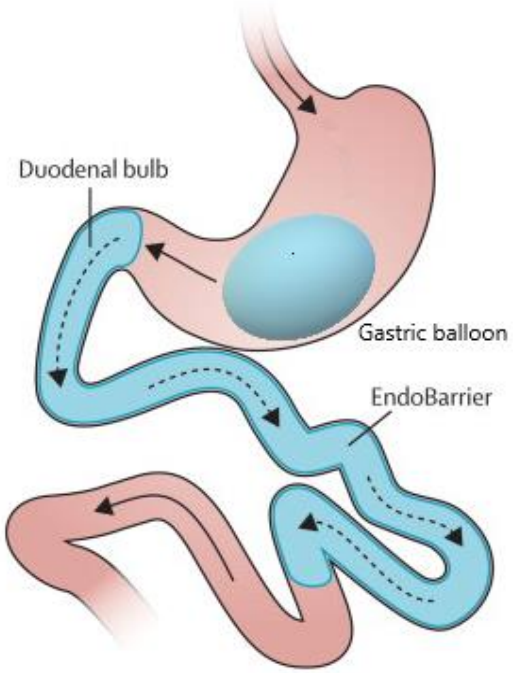

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