Reduction in Liver Fat in Patients with Type 2 Diabetes Following Treatment with Duodenal Mucosal Resurfacing

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Introduction
- Duodenal Mucosal Resurfacing (DMR) is currently being investigated as a treatment for insulin-resistant metabolic disease including Type 2 diabetes (T2D) 1, 4.
- Data from recent multicenter, single-arm Revita-1 study in T2D patients demonstrated sustained reductions (12 months) in HbA1c, fasting plasma glucose (FPG), and Insulin Resistance Model Assessment Index (HOMA-IR) as well as a lowering of liver transaminases.7

Objective
- Revita-2 (clinical trial NCT02879383) is a randomized, sham-controlled, single-blinded study to evaluate the effects of DMR on glycemic and liver metabolic parameters in 120, including measures of fat fraction in the liver through magnetic resonance imaging (MRI).
- Trials involve a training phase in which the study sites familiarize themselves with the intervention procedure before beginning the randomized phase of the protocol. Sites were required to conduct a total of 3 (open-label training cases) for a maximum of 10 total cases and this created an open-label cohort distinct from the randomized cohort.
- We report here preliminary data from the open-label cohort.

Methods
- Eligible subjects participated in 4 weeks oral anti-diabetic medication run-in period to establish stable baseline glycemia, and medication and nutritional compliance.
- Metabolic data (e.g. HbA1c, lipid and hepatic parameters) were collected at baseline and 12 weeks.
- Liver MRI was performed at selected sites at baseline and 12 weeks on the same MRI scanner for each subject. MRI at baseline and 12 weeks using vendor-derived proton density fat fraction (PDF) sequences were acquired for each subject.
- All subjects enrolled in the open-label cohort were treated with the DMR procedure and weighed follow-up visits for 48 weeks.
- Key Inclusion criteria include:  
  - Aged 26-75 years
  - T2D diagnosis (WHO criteria) 10 years
  - Known active hepatitis or active liver disease
  - Previous GI surgery that could affect the ability to treat the duodenum

Key Exclusion criteria include:
- Diagnosis with Type 1 Diabetes or with a history of ketonemia
- Current use of insulin or insulin-like analogues
- Hypoglycemia unawareness or history of severe hypoglycemia
- Known autoimmune disease, as evidenced by a positive ANA test
- Active in situ infection
- Previous bariatric surgery that could affect the ability to treat the duodenum
- History of chronic or acute pancreatitis
- Known active hepatitis or active liver disease

Subjects received DMR treatment under deep sedation in a left lateral position. Known active hepatitis or active liver disease

Results
- Initial data from the open-label training cohort are available for 24 subjects through 3 months (12 weeks). We also report preliminary data from a subset of 14 subjects (n=22) who underwent MRI study at baseline and 12 weeks.

Subjects enrolled had a mean age of 58 yrs with a mean duration of T2D of 8 yrs. All but one subject was receiving metformin and the majority (64%) were taking a sulfonylurea.

Table 1. Subject Demographics and Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Baseline (n=24)</th>
<th>12 weeks (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>58 (±4.8)</td>
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</tr>
<tr>
<td>Sex</td>
<td>Male 13 (54%)</td>
<td>Male 10 (83%)</td>
</tr>
<tr>
<td>Duration of T2D, years</td>
<td>142 (±17)</td>
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</tr>
<tr>
<td>Weight (kg)</td>
<td>88.2 (±1.9)</td>
<td>86.7 (±1.9)</td>
</tr>
</tbody>
</table>

Oral anti-diabetic medications:
- Metformin 22 (91%)  
- SGLT-2 inhibitor 9 (37%)  
- DPP-4 inhibitor 15 (63%)  
- Meglitinide 15 (63%)  

Side effects included immediate post-procedure pain. Subjects were administered oral analgesia (paracetamol) immediately post-procedure.  

Medication adherence and dietary intervention were not assessed.

Conclusions
- Compared to baseline, significant improvement in all parameters of glycemia and broader metabolic parameters were observed (Table 1).
- Available MRI data from a subset of 13 subjects revealed a mean reduction of 11.2% (p = 0.001) in absolute hepatic fat fraction at 12 weeks (Figure 1B).

Table 3. Baseline and 12 Week Metabolic Values

<table>
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<th>Metabolic Parameter</th>
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<tr>
<td>Fasting Total Cholesterol</td>
<td>197 ± 28</td>
<td>206 ± 32</td>
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<td>Fasting HDL (mg/dl)</td>
<td>47.3 ± 2.8</td>
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Efficacy
- Key procedural metrics including procedure time, defined as catheter in to catheter out, and number of ablations completed are illustrated in Table 2.

Table 2. Key Procedural Metrics

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<td>Median Procedure Time (minutes)</td>
<td>45 (18)</td>
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<td>Number of procedures completed</td>
<td>9 (6-12)</td>
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Safety
- Mild gastrointestinal symptoms immediately post-procedure were the most commonly reported adverse event (AE), including abdominal pain, constipation, diarrhea, and dyspepsia.
- No device or procedure related serious AEs were reported.
- No unexpected adverse device effects were reported.

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