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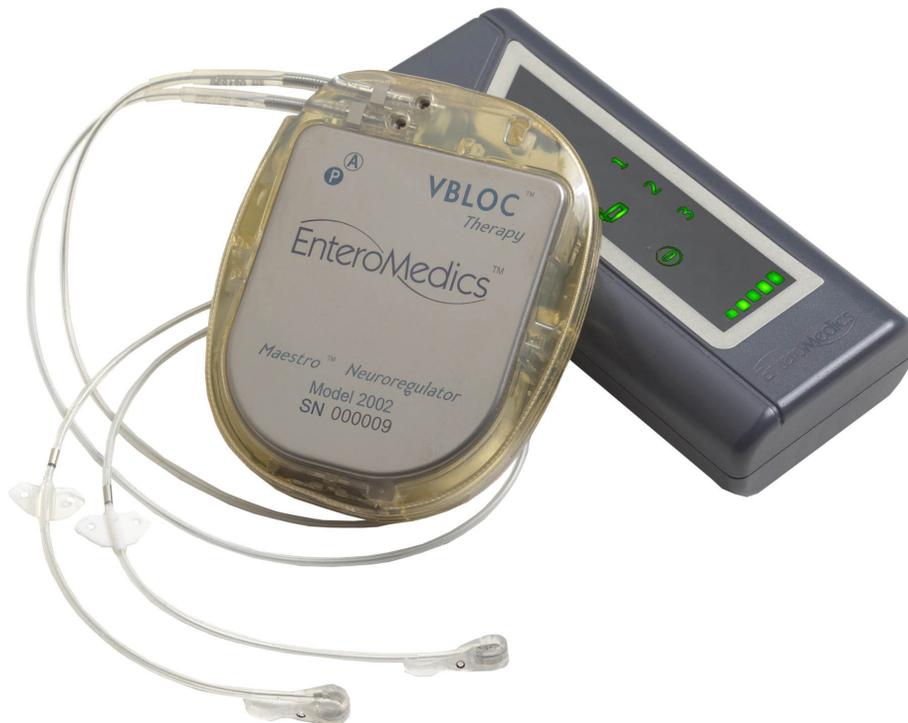
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Vagal Nerve Blockade for Obesity: VBLOC Therapy Using the Maestro RC2 Device



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Summary

- Alternative safe, effective, minimally invasive, and reversible weight-loss surgeries are needed to bring about sustained and clinically significant weight loss in patients for whom drug therapy or bariatric surgery are not indicated, or who do not want to undergo bariatric procedures that are invasive, irreversible, and bring a higher risk of short- and long-term adverse events.
- The Maestro RC2 device, a vagal nerve blocker positioned laparoscopically, could satisfy the need for such an alternative approach to inducing weight loss in obese patients.
- Compared with evidence concerning available bariatric surgeries, the combination of a better adverse event profile and significant but less striking weight loss observed in the first 24 months of the ReCharge trial suggests the promise of vagal nerve blockade therapy.

The Technology

EnteroMedics Inc. (St. Paul, MN, US) developed VBLOC, an intra-abdominal vagal nerve blocking (VNB) therapy that employs the second-generation pacemaker-like rechargeable Maestro RC2 device to target the vagus nerve to induce weight loss.¹⁻¹⁰ This technology is programmed to intermittently produce high-frequency, low-energy electrical pulses via implanted electrodes to block vagal nerve signals during waking hours.^{5,11,12} Vagal nerve signalling has been linked to the experiences of hunger and satiety, while at the same time playing a role in energy metabolism and upper gastrointestinal tract function. VBLOC's ability to influence these processes and events, including food intake, could represent a safer, less invasive, and reversible alternative to other weight-loss surgeries (e.g., irreversible vagotomy, laparoscopic gastric banding, sleeve gastrectomy, gastric bypass).^{2-5,7,11-15} However, VBLOC's mechanism of action is not completely understood — that is, all of the physiologic and anatomic factors that contribute to a decrease in body weight as well as improvements in obesity-related conditions, such as type 2 diabetes mellitus.^{4,12-14,16,17}

The Maestro device includes two internal electrodes, an integrated coil that serves as an antenna for telemetry and recharging, a rechargeable lithium ion battery with an estimated eight-year life, and an external battery-powered controller.²⁻⁷ The device is typically implanted during a 60- to 90-minute laparoscopic procedure. The electrodes are placed on the dissected anterior and posterior vagus nerve trunks to block both afferent and efferent signalling.^{2-5,11} The neuroregulator is placed in a subcutaneous pocket within the thoracic sidewall.

A link between the internal and external components is established, and the device is programmed via a transmitter coil and proprietary software that can be loaded onto a laptop. Radiofrequency signals transmitted transcutaneously (≥ 5 cm away) permit the device's activation/deactivation, the retrieval of diagnostic data, and the modification of treatment parameters. The device can be recharged using either an external mobile unit worn by the patient or a standard, external AC charger. Therapy cannot be delivered during recharging. Patients typically perform daily battery checks and undertake recharging as needed. The device can be removed if necessary.

Regulatory Status

Toward the end of 2015, EnteroMedics will submit an application to Health Canada for regulatory approval of VBLOC therapy for adult obesity using the Maestro RC2 device (Dan Cohen, EnteroMedics Inc., St. Paul, MN: personal communication, 2015 March). The US Food and Drug Administration (FDA) recently approved this first-of-kind device to induce weight loss via vagal nerve blockade.^{6,7,19}

In March 2009, the device received Conformité Européenne (CE) Mark approval to be marketed to treat obesity within the European Union.²⁰ This approval was later expanded to include the management of type 2 diabetes mellitus via the improvement of glycemic control.²¹ The Maestro system was listed on the Australian Register of Therapeutic Goods in 2011.²²

Patient Group

Defined as a body mass index (BMI) of $\geq 30 \text{ kg/m}^2$,²³ obesity is a complex, multi-factorial problem with neuroendocrine, genetic, cultural-environmental, psycho-emotional-behavioural, socioeconomic, and metabolism-related components, and does not merely reflect an imbalance in the intake and expenditure of energy.^{9,16,24} The numbers of individuals with excess body weight and who are considered obese have increased steadily over the past 30 years, with perhaps a third of the world's current adult population being overweight.²⁵ Equally troubling is the rising obesity trend in children and adolescents.^{26,27}

As of 2011, 18.3% of adult Canadians were considered obese, with 71.6%, 19.7%, and 8.7% falling into obesity classes I, II, and III, respectively.²⁸ This 18.3% rate constituted a 200% increase

Table 1: VBLOC with the Maestro RC2 Device – Regulatory Status

COUNTRY (Initial Date)	LICENSED INDICATION(S)	CONTRAINDICATIONS	CONDITIONS OF APPROVAL
FDA, United States (January 14, 2015)	Patients 18 years of age or older who have a BMI of 40 to 45 kg/m ² or a BMI of 35 to 39.9 kg/m ² with one or more obesity-related conditions, and have failed at least one supervised weight management (diet, exercise) program within the previous five years	<ul style="list-style-type: none"> • Patients with cirrhosis of the liver, portal hypertension, esophageal varices, or an uncorrectable, clinically significant hiatal hernia • Patients for whom magnetic resonance imaging is planned • Patients at high risk for surgical complications • Patients who have a permanently implanted, electrically powered medical device, or gastrointestinal device or prosthesis (e.g., pacemaker, implanted defibrillator, neurostimulator) • Patients for whom shortwave, microwave, or therapeutic ultrasound diathermy (treatment using high-frequency electromagnetic radiation, electric currents, or ultrasonic waves to produce heat in body tissues) is planned 	To conduct a 5-year post-approval study to collect follow-up effectiveness and safety data (e.g., weight loss, adverse events, surgical revisions and explants, and changes in obesity-related conditions) on at least 100 patients who have received the device

BMI = body mass index; FDA = US Food and Drug Administration.

Source: FDA^{6,7,19}

from 1985. Other recent sources have suggested that obesity affects between one in four and one in five Canadian adults.^{29,30} Moreover, two-thirds of North Americans are either overweight or obese, and prevalence rates in most European countries range from about 40.0% to nearly 50.0%.³¹ By 2030, more than 36.0% of the population in developed countries could be overweight, with more than 22.0% potentially being considered obese.³²

For weight loss, these surgeries collectively have been found to be more effective than nonsurgical options.

Obesity-related conditions such as hypertension, stroke, cardiovascular disease, dyslipidemia, metabolic syndrome, type 2 diabetes mellitus, obstructive sleep apnea, mood and self-esteem difficulties, osteoarthritis, and increased cancer risk are leading causes of morbidity, decreased life expectancy, and preventable death in developing countries.^{2,9,33-36} Moreover, in 2011, the risk of morbidity rose in adult Canadians as the severity of their obesity increased.²⁸ With the mounting incidence of obesity-related conditions, the cost burden on health care systems is rising, underscoring the need to develop effective and safe weight-loss treatments.^{35,37,38}

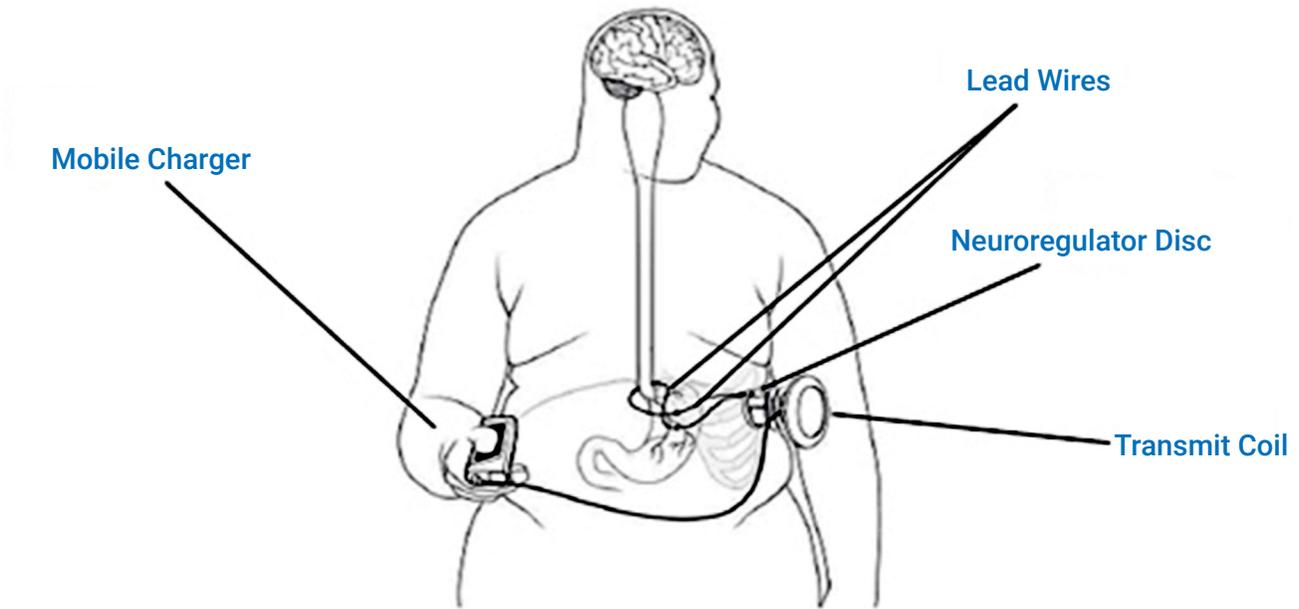
Current Practice

Current obesity treatments likely comprise two main approaches: conservative (e.g., dietary regimens and supplements; modifications of lifestyle/behaviour, such as physical activity); and invasive (e.g., bariatric surgery; gastrointestinal electrical stimulation; invasive endoscopic procedures, such as intragastric bezoars and balloons).³⁹ A recently published practice guideline recommends: lifestyle modification (e.g., food intake, activity levels) for individuals with a BMI \geq 25 kg/m²; pharmacotherapy potentially for those with a BMI \geq 30 kg/m² or a BMI \geq 27 kg/m² with at least one comorbid condition; and surgery as an option for those with a BMI \geq 40 kg/m² or a BMI \geq 30 kg/m² with one or more comorbidities.⁴⁰ To yield clinical benefits, a weight loss of 5.0% to 10.0% has been cited as the targeted minimum.⁴¹⁻⁴³

Although some studies show that comprehensive lifestyle modification (diet, exercise, behavioural therapy) can yield modest weight loss (7.0% to 10.0%) in obese adults,^{44,45} it often fails to produce long-term weight maintenance.^{39,46} FDA-approved pharmacotherapies (e.g., Belviq, Contrave, Qsymia, Saxenda) have also produced modest weight loss (3.0% to 9.0%) after 12 months,⁴⁷⁻⁵¹ but in some cases have also produced short- and long-term adverse events or side effects (e.g., blood pressure elevation, cardiovascular events, gastrointestinal problems, liver malfunction) that can lead some patients to stop treatment and regain up to all of their lost weight.^{39,52} Other key barriers to increasing the routine use of obesity medications include their failure to produce sustained/long-term weight loss, lapses in compliance, and in the US, the unwillingness of some insurance companies to provide coverage.^{3,39,53,54}

For those who do not respond to lifestyle modification and/or pharmacotherapy, several bariatric surgeries have been found to be efficacious and durable in significantly reducing weight loss while also affording secondary prevention, or even prophylaxis, for obesity's common comorbid conditions.^{9,55-58} For weight loss, these surgeries collectively have been found to be more effective than nonsurgical options.^{39,59} Historically, the six dominant procedures have been:

- jejunioleal bypass (all but 12 to 18 inches of small bowel is detached and set to side)
- Roux-en-Y gastric bypass ([RYGB] invasive and irreversible, to yield malabsorption of food, restrict size of stomach to create much smaller gastric pouch, then attach pouch to mid-jejunum)
- vertical banded gastroplasty (surgical stapling to partition stomach)
- biliopancreatic diversion (to limit oral intake, remove part of stomach) and its American version, the duodenal switch
- adjustable gastric banding (constricting ring placed around fundus of stomach)
- (irreversible) sleeve gastrectomy (to restrict food intake, remove greater fundus and curvature of stomach to create a smaller, tube-like stomach).^{10,17}



Source: US Food & Drug Administration

The choice of surgery depends on obesity severity, comorbidities, surgeon experience, individual patient preferences, and/or other contraindications.⁶⁰ Some are routinely performed in minimally invasive ways (e.g., laparoscopic adjustable gastric banding [LAGB], reversible).

These procedures vary in terms of speed, magnitude, and sustainability of excess weight loss (EWL) in morbidly obese patients (e.g., 45.0% and 66.0% at two years for LAGB and RYGB, respectively; 48.0% at six to eight years for laparoscopic sleeve gastrectomy). While they do have positive impacts on health status and quality of life, many are invasive and irreversible, carry a risk of serious adverse events — including death — and can produce distortions in anatomy that are unacceptable to some patients.^{9,15,39,61-68} For example, the primary bariatric surgeries (RYGB, LAGB) have exhibited an overall mortality rate of between 0.1% and 2.0%, and an overall risk of major complications of about 4.3% (e.g., surgical leaks, hernia, wound infection, bowel obstruction).^{15,39,61,69}

Other current, often irreversible yet minimally invasive surgeries include:

- gastric lumen reduction procedures that entail gastric plication/partitioning with sutures, staples, or implanted devices (e.g., transoral and vertical endoluminal gastroplasty)
- food malabsorption devices (e.g., duodenojejunal bypass sleeve)
- space-occupying devices (e.g., intragastric balloons)
- intraluminal placement of artificial bezoars (e.g., digestion-resistant polyethylene).^{10,39}

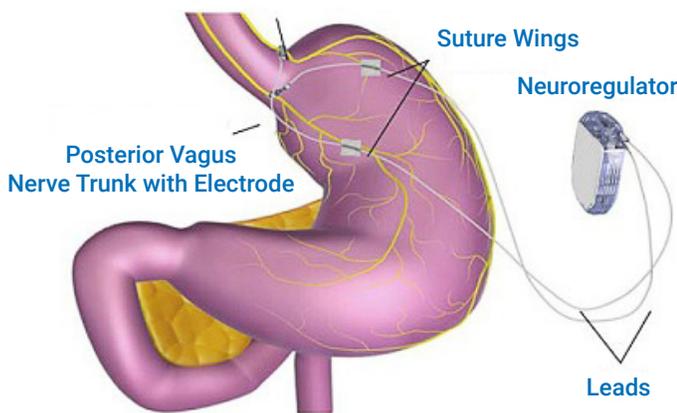
Many of these procedures and devices are poorly tolerated and their long-term effects have been less promising than expected.⁷⁰ Other laparoscopically implanted devices can be used to electrically stimulate the gastrointestinal tract.^{24,39,71}

The Evidence

All results from the 12-month, double-blind (i.e., participants; outcome assessors) portion of ReCharge — a five-year, phase 3, pivotal, randomized controlled trial ([RCT] NCT01327976) — have been made public,² as have the 18-month⁷ and 24-month efficacy data (Dan Cohen, EnteroMedics Inc., St. Paul, MN: personal communication, 2015 March). Drawing participants from 10 sites (US, Australia), the trial randomly assigned (2:1) 239 morbidly obese adults to undergo laparoscopic implantation of either the Maestro RC2 device (n = 162) or a sham neuroregulator (n = 77) via the same five incisions. Participants were adults, aged 18 to 65 years, who had a BMI of 40 to 45 kg/m² (class III obesity) or 35 to 39.9 kg/m² (class II obesity) with one or more obesity-related conditions (e.g., hypertension, dyslipidemia, sleep apnea syndrome, obesity-related cardiomyopathy; up to 10.0% of patients with type 2 diabetes mellitus), and had failed at least one supervised weight management program in the previous five years. The sham did not include lead placement, and its current was dissipated into an electronic circuit within the device. Sham incisions did not result in peritoneal penetration. The “live” device was programmed to deliver VBLOC therapy for at least 12 hours daily. All patients received weight management education, but none were prescribed a diet or exercise regimen. Exclusion criteria included a known genetic cause of obesity, type 1 diabetes mellitus, and clinically significant hiatal hernias (> 5 cm) or other esophageal problems (e.g., varices or dissection).

The co-primary efficacy objectives were to clarify whether, in patients receiving VBLOC, mean per cent EWL was superior to sham by a 10-point margin, with at least 55.0% of VBLOC patients achieving a 20.0% EWL and 45.0% attaining a 25.0% EWL. The primary safety aim was to see whether VBLOC patients' serious adverse events rate (i.e., death; serious deterioration of health, including prolonged hospitalization or new in-patient hospitalization) related to the device, implantation or revision procedure, or therapy was less than 15.0%.²

Anterior Vagus Nerve Trunk with Electrode



Source: US Food & Drug Administration

The ReCharge trial remedied design limitations that had characterized the EMPOWER trial (see Benefits), a multi-centre (US, Australia), double-blind, 12-month RCT (NCT00521079) with 294 patients, mostly female (90.0%), aged 18 to 65 years with a BMI of 40 to 45 kg/m² or 35 to 39.9 kg/m² with one or more severe obesity-related conditions, and who had failed to achieve satisfactory or sustained weight loss with diet, behavioural intervention and/or pharmacotherapy. Patients were randomly assigned (2:1) to be implanted with an activated VBLOC system (n = 192) or an "inactive" control device (n = 102).^{4,72} Main outcomes were per cent EWL at 12 months, and serious adverse events. Patients controlled the duration of therapy using an external power source. Devices in both groups were subjected to regular, low-energy safety checks. After the initial 12-month period, patients were to be followed for another four years.

Twelve-month data have also been reported for an open-label, prospective yet uncontrolled study of obese patients (BMI of 30 to 40 kg/m²) with type 2 diabetes mellitus and elevated blood pressure (n = 28, 5 centres, NCT00555958).^{3,5,73-77} It investigated the

potential long-term impact (up to 60 months) of at least 12 hours of daily VBLOC — to a maximum of 15 hours — on EWL, glycemic control, blood pressure, and the occurrence of serious adverse events as well as unanticipated adverse effects. All patients received 17 individual weight management/counselling sessions.

Benefits

FDA approval was based on ReCharge 12- and 18-month data, even though neither of the primary efficacy objectives was met.² The mean between-group difference in per cent EWL in the intention-to-treat population was 8.5 points in favour of VBLOC (95% CI, 3.1 to 13.9), which failed to attain the target 10-point margin ($P = 0.71$); the mean per cent EWL in VBLOC and sham patients was 24.4% and 15.9%, respectively. Multiple imputation analysis revealed that the mean per cent EWL was 9.2 points higher in the VBLOC group (26.1% versus 16.9%; 95% CI, 2.7 to 15.6), and 52.5% of VBLOC patients achieved an EWL of 20.0% or more, with 38.3% exhibiting a loss of 25.0% or more. This compares with 32.5% of sham patients who achieved a loss of 20.0% or more and 23.4% who experienced a loss of 25.0% or more. Post-hoc analysis indicated that weight loss in VBLOC patients was statistically greater than in sham patients.

Somewhat longer-term ReCharge data suggest that the weight loss seen at 12 months was maintained. At 18 months, the mean per cent EWL in the VBLOC and sham groups was 25.2% (95% CI, 20.6 to 29.8) and 11.7% (95% CI, 5.4 to 18.0), respectively, with a difference of 13.5% (95% CI, 5.7 to 21.3).⁷ The mean per cent EWL at 24 months was 21.0 ± 25.1% (95% CI, 16.1 to 25.9) and 3.9 ± 14.3% (95% CI, -2.3 to 10.1) in the VBLOC (n = 103) and sham groups (n = 23), respectively, with a difference of 17.0 ± 23.6% (95% CI, 9.3 to 24.8; $P < 0.001$) (Dan Cohen, EnteroMedics Inc., St. Paul, MN: personal communication, 2015 March).

Twelve-month per cent EWL did not differ significantly for the two groups in EMPOWER: 17 ± 2% and 16 ± 2% for VBLOC and control patients, respectively.^{4,72} But, clinically important weight loss was related linearly to hours of device use; VBLOC and control patients with at least 12 hours of daily use achieved 30 ± 4% and 22 ± 8% EWL, respectively. Treatment group patients who received at least 12 hours daily of VBLOC therefore achieved the level of weight loss anticipated in the design. Even so, the significant dose response of weight loss in relation to hours of device use for both groups, coupled with the possibility that control patients may have received some degree of VNB as a result of low-energy safety or device checks, confounded

the interpretation of the trial results. This scenario necessitated conducting what became the ReCharge RCT, in which the device consistently delivered at least 12 hours of VBLOC daily, while the sham could not deliver any VNB therapy.

Adverse events appeared to be less severe than those linked to conventional bariatric surgeries (e.g., LAGB).

Twenty-six (of 28) patients (17 female, 9 male; 51 ± 2 years of age; BMI of 37 ± 1 kg/m²) completed the one-year follow-up in the uncontrolled study.^{3,5,73-77} At 12 months, mean per cent EWL was $25 \pm 4\%$ ($P < 0.0001$), and glycated hemoglobin (HbA_{1c}) declined by $1.0 \pm 0.2\%$ ($P = 0.02$). In patients with type 2 diabetes mellitus and elevated blood pressure ($n = 15$), mean arterial blood pressure decreased by 8 ± 3 mm Hg ($P = 0.04$) at 12 months. All patients' mean arterial blood pressure decreased by 3 ± 2 mm Hg at 12 months. VBLOC was associated with meaningful weight loss, improvements in HbA_{1c}, and reductions in blood pressure. Clinically significant weight loss was sustained at 18 months (mean EWL = $26.0 \pm 4.0\%$; $P < 0.001$; $n = 21$; 12 hours daily of VBLOC) and 36 months (mean EWL = $24.3 \pm 3.9\%$; $P < 0.0001$; $n = 18$), as were positive changes in glycemic control. Improved mean arterial pressure was sustained at 18 months ($P = 0.008$; $n = 12$), but not at 36 months ($P < 0.14$; $n = 10$). Earlier clinical evaluations of VBLOC in typically small samples of patients with type 2 diabetes mellitus or elevated blood pressure had likewise revealed improvements in glycemic control and blood pressure levels, in addition to weight loss.^{78,79}

It is likely that the sham group's initial weight loss of 6.0% in the ReCharge RCT was the result of a placebo effect of surgery, daily self-monitoring that was reinforced by interaction with the sham device when recharging its battery, and participation in the weight management program.^{2,80} Ongoing self-monitoring of behaviour and weight for some patients can constitute a notable behavioural change.⁸¹ This effect of mindful attention was similar to what was observed in both the EMPOWER⁴ and SHAPE trials, with the latter involving implantation of a gastric stimulator.⁷¹ Notable placebo effects in surgery trials are also not uncommon.⁸²⁻⁸⁴ Finally, as ReCharge participants were mostly Caucasian women with a BMI of 35 to 45 kg/m², with a low probability of type 2 diabetes

mellitus – a common comorbidity of significant obesity – and a low rate of other metabolic complications (e.g., hypertension, dyslipidemia), extrapolation of their results to other populations should be undertaken with caution.²

Adverse Effects

The VBLOC intervention in the ReCharge RCT was well tolerated, and the primary safety objective was achieved.² The rate of serious adverse events linked to the device, implantation/revision or therapy in VBLOC patients at 12 months was 3.7% (95% CI, 1.4 to 7.9), which was significantly lower than the 15.0% target ($P < 0.001$). Adjudicated causes included: neuroregulator malfunction ($n = 2$), pain at neuroregulator site ($n = 1$), atelectasis (lung collapse/closure, $n = 1$), emesis ($n = 1$), and gallbladder disease ($n = 1$). Various events ($n = 9$) followed the general surgery: nausea ($n = 6$ of 9), intra-operative oozing, complicated liver biopsy, and moderate ileus of the stomach. When these two classes of serious adverse events are combined, the rate is 8.6% (95% CI, 4.8 to 14.1); this contrasts with no such events in the sham group. The most common therapy-related adverse event was pain at the neuroregulator site. Ninety-six per cent of the pain-related events in VBLOC participants were mild or moderate; yet in three cases, pain required a revision and in one case, an explant. VBLOC participants reported mild or moderate heartburn and dyspepsia, abdominal pain, dysphagia, and belching more often than sham participants. Typically mild or moderate nausea also occurred more frequently in the VBLOC group.

Adverse events appeared to be less severe than those linked to conventional bariatric surgeries (e.g., LAGB).^{85,86} The implications of the 8.6% rate of serious adverse events in the ReCharge trial, which was linked to either the therapy, device, or the surgery, remain uncertain.⁸⁰

In the EMPOWER RCT, the use of VBLOC to treat morbid obesity proved to be safe.^{4,72} Few serious adverse events were associated with the device ($n = 4$), or its implantation or revision procedure ($n = 5$). No serious adverse events were linked to the therapy, and few were related to the surgery/anesthesia ($n = 4$).

In the open-label, uncontrolled study of patients with type 2 diabetes mellitus and elevated blood pressure, VBLOC use was safe; no surgical complications were observed, and the one serious adverse event (pain at implant site) was easily

resolved.^{3,5,73-77} No unanticipated adverse effects were observed. To date, across all Maestro RC2 trials, surgical revision has been linked most often to implantation site pain and device malfunction, and no deaths have been recorded.^{2-6,72-77}

Administration and Costs

It has been assumed that the reliable and effective administration of VBLOC within hospital or specialist care settings requires appropriate preparation and oversight. Surgeons must receive special training and certification to reliably and safely implant and explant the Maestro device.⁷ Other implementation-related issues are raised in the following paragraphs.

Pricing for VBLOC therapy using the Maestro RC2 device has not yet been determined for Canada. In the US, it has been set at US\$15,000 for the device and US\$4,000 for the patient “kit” (Dan Cohen, EnteroMedics Inc., St. Paul, MN: personal communication, 2015 March). Neither figure includes hospital costs or physician fees. Excluding the device’s implantation-related cost, this compares favourably with the average price of US\$20,000 for a vagal nerve stimulation device that has been approved to treat refractory epilepsy and treatment-resistant depression.⁹ In the European Union, the Maestro device costs an estimated US\$20,000.⁸

An independent panel of experts recently estimated that VBLOC would likely have a small financial impact in the US (level 2/5 rating), and that its cost would likely be comparable to other weight-loss surgeries.⁸⁷ The cost for LAGB placement can range from US\$17,000 to US\$30,000, from US\$20,000 to US\$35,000 for an RYGB,⁸⁸ and about US\$30,000 for a gastric bypass⁸⁹ (although it is unclear whether this third figure includes both the device and the surgery).⁸⁷ An EnteroMedics representative has said that the Maestro device’s laparoscopic implantation in the US should cost less than an LAGB or gastric sleeve procedure, yet would be more expensive than lap-band surgery (Dan Cohen, EnteroMedics Inc., St. Paul, MN: personal communication, 2015 March).

Concurrent Developments

Other obesity-targeting, minimally invasive health care technologies are currently being developed.⁸⁻¹⁰ These include:

- ReShape Duo (nonsurgical, dual-intragastric balloon for rapid weight loss)⁹⁰
- EndoBarrier endoluminal sleeve (nonsurgical, temporary gastric bypass)⁹¹
- Vibrynt Prevail Implant System (restricts food consumption by limiting the stomach’s ability to expand)
- various gastric stimulators.^{10,24,39,71}

Data relating to the first-generation Maestro VNB device¹¹ continue to be published.^{13,14} Other emerging products include various pharmacotherapies, some of which have been used to treat migraine and seizure disorders, depression, epilepsy, or to produce smoking cessation; some are opioid antagonists, while others target leptin, ghrelin, or hormones that exhibit both glucose-regulating and anorexigenic actions.^{39,92-94} As lifestyle management strategies are routinely being developed, none are highlighted here.

Rate of Technology Diffusion

In announcing the FDA’s approval, EnteroMedics said it expected the Maestro device would be available on a limited basis at select Bariatric Centers of Excellence in the US in 2015.⁹⁵ A panel of experts recently estimated its potential for adoption as “moderate” (level: 3/5),⁸⁷ which may reflect the view that few obesity treatments exist that are both reliably effective and safe (e.g., less surgical risk, less likely to notably alter anatomy).^{9,65,80,96}

To address a significant unmet need in obese patients who have exhausted other weight-loss methods (e.g., medical therapy; behaviour therapy) and are ineligible for other bariatric surgery, VBLOC’s potential utility was situated at the lower end of the high-impact range.⁹ It might even be considered a low-risk option for morbidly obese patients who need to lose weight (i.e., 10.0% EWL) before undergoing invasive bariatric surgery (e.g., gastric banding),^{9,51,87} or it could be added to lifestyle modification and/or pharmacotherapy to induce weight loss in patients with a BMI of ≥ 35 kg/m² and who have been unable to lose enough weight solely via a supervised weight-loss program.^{45,80,87} Further, longer-term RCTs focusing on safety and efficacy will likely be required

to dispel concerns on the part of patients, physicians, and third-party payers that VBLOC is no more than an investigational or experimental therapy for obesity.^{2,9,12,80,87}

In the US, VBLOC is expected to diffuse slowly into clinical practice, with early adoption occurring in up to 25.0% of facilities, and projected use in up to 20.0% of eligible patients (anticipated utilization level: 1/5).⁸⁷ Its diffusion in the US could depend largely on its level of insurance coverage, as most patients would be unlikely to afford the device as well as the cost of its placement and maintenance.⁹ To address this situation, EnteroMedics has entered into a partnership with American HealthCare Lending — a patient financing company for health care providers in the cosmetic dentistry, bariatric surgery, fertility, plastic surgery, and other industries — to provide funding to increase patient access to VBLOC.⁹⁷

Implementation Issues

It has been estimated that, while the addition of VBLOC to the obesity armamentarium could slightly increase the volume of obesity procedures in existing bariatric centres because of their experience with other bariatric surgeries, the introduction of VBLOC would likely have little impact on the infrastructure/personnel or protocols needed for its delivery or patient management.^{9,87} Two potential minor impacts are the additional post-operative efforts needed to monitor and adjust the device or its parameters, and the possibility that laparoscopic placement could eventually allow the surgery to be done on an outpatient basis.⁹

To facilitate implementation, EnteroMedics has developed a training and certification program, with guidelines, to identify facilities that are qualified to deliver VBLOC.⁷ The program includes: classroom training, observation, and supervised implantation; device setup; and a focus on intra-operative and post-operative care. Annual recertification is required.

EnteroMedics has announced that, by the end of March 2015, 15 US centres had been certified and 19 physicians trained to implant the Maestro device and administer VBLOC therapy. The company's aim is to establish 20 to 25 VBLOC therapy centres and trained physicians by the end of 2015.⁹⁸

Methods

Literature Search Strategy

A peer-reviewed literature search was conducted using the following bibliographic databases: MEDLINE, PubMed, Embase, and The Cochrane Library. Grey literature was identified by searching relevant sections of the CADTH Grey Matters checklist (<http://www.cadth.ca/resources/grey-matters>). No methodological filters were applied, but a human filter was applied. The search was limited to English language documents published between January 1, 2010 and March 10, 2015. Regular alerts were established to update the search until July 7, 2015.

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