

*ASSESSMENT OF GASTRIC FUNCTION
USING BODY SURFACE GASTRIC
MAPPING IN PATIENTS ON
SEMAGLUTIDE (OZEMPIC)*

NCT06401746

Study Protocol

February 20 2024

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Title	ASSESSMENT OF GASTRIC FUNCTION USING BODY SURFACE GASTRIC MAPPING IN PATIENTS ON SEMAGLUTIDE (OZEMPIC)
Study Design	Observational prospective cohort pilot
Study Population	Adult patients diagnosed with or without type 2 diabetes mellitus (T2DM)
Brief Summary	Gastric motility is controlled by an underlying myoelectrical activity, however reliable methods for measuring gastric motility have been lacking. We recently developed and introduced Body-Surface Gastric Mapping (BSGM) as a novel non-invasive diagnostic tool to assess gastric myoelectrical activity, to aid with the diagnosis of functional gastrointestinal disorders. It is an FDA-approved medical device called Gastric Alimetry that incorporates high-resolution electrogastrography and a validated patient-reported symptom tracking App in order to achieve accurate non-invasive biomarkers of gastric dysfunction (1–3). GLP-1 receptor agonists (GLP-1 RAs) such as semaglutide (brand name: Ozempic) profoundly alter gastric function (4), which is likely to be a key mechanism of action, however this has been poorly defined due to a lack of available clinical tools. Alterations in gut function, including myoelectrical activity, is also likely to be a mechanism of gastrointestinal side effects. A proof-of-principle case study of semaglutide using BSGM (Gastric Alimetry) showed abnormal gastric myoelectrical activity along with the development of severe bloating following the meal after 5 weeks of semaglutide use. We will extend on this initial finding by conducting an exploratory pilot study to investigate the effects of semaglutide on gastric motility.
Study Aims	1. To measure the effects of semaglutide on gastric function using BSGM. 2. To assess the correlation between gastric function and symptoms/side effect profiles after semaglutide.
Study Duration	6-9 months, including recruitment, pre-semaglutide test and post-semaglutide test
Hypothesis	1) BSGM will identify changes in gastric function, which will provide novel insights into the mechanism of GLP-1RAs and their side effects. 2) Changes in gastric electrical activity will be associated with symptom severity.

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Study Procedure	Patients will be recruited from metabolic clinics in Campbelltown and Camden. If a suitable patient is identified and they have at least one month's supply of semaglutide, the patient will be directed to the study coordinator who will organise for the pre- semaglutide BSGM test. Informed consent will be obtained prior to participation. ● Pre- semaglutide: BSGM using Gastric Alimetry BSGM will be undertaken as per standard protocol (4.5 hr recording). They will be asked to fill out questionnaires about their demographics, medical history, and symptoms (GCSI, PAGI-SYM). Blood glucose levels will be monitored before the meal and every hour after the meal using a finger prick, or a continuous glucose monitor. ● Semaglutide use Patients will take semaglutide (subcutaneous once weekly injection), as prescribed. The standard dosing is as follows: 0.25 mg for 4 weeks, 0.5 mg for 4 weeks and 1 mg maintenance dose after (or when maximum tolerated dose is reached). ● Post- semaglutide: BSGM using Gastric Alimetry After reaching the maintenance dose or maximum tolerated dose, patients will return to repeat the BSGM test (ideally 24-48 hrs after injection). They will be asked to complete the same questionnaires. If the patient does not have continuous administration of semaglutide from pre-test until they reach this dose, a post- semaglutide BSGM test will not be undertaken. However, if the patient does have continuous administration in the future, a post- semaglutide BSGM test will be considered. Consented patients will have their clinical records reviewed for their most recent endoscopy test result (if available) to check for any structural abnormalities in the upper GI.
Site	MacArthur Clinical School, Western Sydney University
Inclusion Criteria	● >18 years old ● No gastrointestinal symptoms based on Rome IV criteria ● Can give informed consent ● Can understand risks/benefits of study For diabetics: ● Diagnosed T2DM (defined as HbA1c levels > 7%) ● Fasting blood glucose level < 15 mmol/L (since hyperglycaemia may delay gastric emptying, as recommended by the Consensus Recommendations for Gastric Emptying Scintigraphy) (5)

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Exclusion Criteria	• Current use of semaglutide, similar GLP-1 RAs or regular insulin in the last 3 months • Confirmed gastroparesis on gastric emptying scintigraphy • Pregnant or breast-feeding • Inability to perform BSGM test: history of severe skin allergies or sensitivity to adhesives, cosmetics or lotions; chronically damaged or vulnerable epigastric skin (fragile skin, wounds, inflammation); unable to remain in a relaxed reclined position for the test duration.										
Method	<table><tr><th>Day 0</th><th>Day 1-28</th><th>Day 28-56</th><th>Day 57</th><th>Day 58-59 (+ 28)</th></tr><tr><td>BSGM</td><td>0.25 mg dose</td><td>0.5 mg dose</td><td>1 mg dose (or maximum tolerated dose)</td><td>BSGM</td></tr></table>	Day 0	Day 1-28	Day 28-56	Day 57	Day 58-59 (+ 28)	BSGM	0.25 mg dose	0.5 mg dose	1 mg dose (or maximum tolerated dose)	BSGM
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Outcome Measures	Primary outcome: Change in BSGM metrics after semaglutide use compared to baseline. Secondary outcome: Change in symptom scores after semaglutide use compared to baseline.										
Analysis Plan	Data sources: • Body Surface Gastric Mapping (BSGM) Metrics: - Principal Gastric Frequency (PGF) - Gastric Alimetry® Rhythm Index (GA-RI) - BMI-adjusted amplitude - Fed:Fasted Amplitude Ratio (ffAR) - Meal Response Ratio (MRR) • Symptom Data: - Total symptom burden score (from Gastric Alimetry® app) - Rome IV criteria (for gastroduodenal disorders diagnosis) - Patient Assessment of Upper Gastrointestinal Disorders-Symptom Severity Index (PAGI-SYM) and its subscales (e.g., fullness/early satiation) - Gastroparesis Cardinal Symptom Index (GCSI) Data will be collected at two time points: baseline and after reaching a 1 mg semaglutide dose (or maximum tolerated dose). Metric and symptom data are treated as continuous variables and compared using paired t tests. A p-value of < 0.05 was considered significant.										

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Sample Size	This is an observational cohort trial that will not affect the clinical management of participants. Given this is a pilot study, there are no pre-existing indicators to determine optimal sample size. As per the recommendations for pilot studies (6), we aim to recruit 10-15 patients. These results will inform the clinical decision rule on patient outcomes in order to estimate the required parameters in a future clinical trial.
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