FACULTY OF MEDICINE AND HEALTH SCIENCES

DEPARTMENT OF HUMAN STRUCTURE & REPAIR - GROUP OF EXPERIMENTAL SURGERY

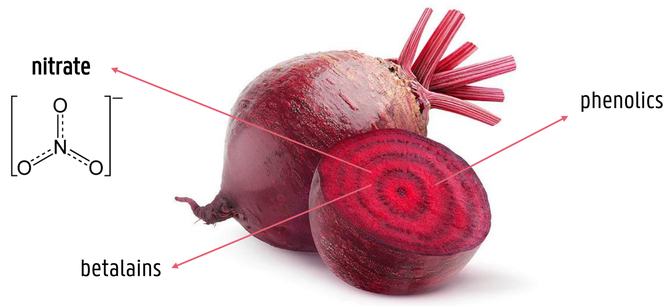
Barbara Cornillie (MSc), Wim Ceelen (MD, PhD), Kjell Fierens (MD), Guy Hubens (MD, PhD), Albert Wolthuis (MD, PhD), Sarah Cosyns (PhD)

USE OF BEETROOT JUICE TO PROTECT AGAINST POSTOPERATIVE ILEUS FOLLOWING COLORECTAL SURGERY: BEET IT STUDY

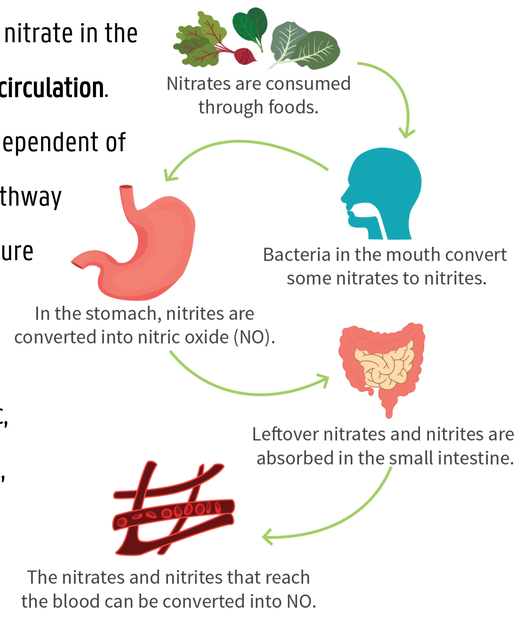
INTRODUCTION

BACKGROUND & RATIONALE

Beetroot is a rich source of **nitrate** (NO_3^-), serving as a **precursor of nitric oxide** (**NO**), which has multiple functions in the human body, including gastrointestinal (GI) motility. Apart from nitrate, beetroot contains many other beneficial compounds for human health. Many having anti-inflammatory and anti-oxidative effects.



The working mechanism of dietary nitrate in the body occurs via the **enterosalivary circulation**. This pathway of **NO synthesis** is independent of the endogenous L-arginine/NOS pathway and acts as a **backup system** to ensure NO supply when the endogenous is less effective or dysfunctional. This occurs with aging and in acidic, hypoxic and/or ischemic conditions, e.g. during a surgical procedure.



Symptoms
- nausea & vomiting
- no flatus & stool
- abdominal distention
- intolerance oral diet

Pathogenesis
- multifactorial etiology
- inflammation & oxidative stress
- sympathetic stimulation
- ↓ **NO synthases** (NOS)

Postoperative ileus
transient impairment of GI motility after abdominal surgery

Management
- mainly supportive
- multimodal approach
- ERAS® protocol

Consequences
- ↑ morbidity
- ↑ hospitalization
- ↑ healthcare costs

OBJECTIVE

The goal of the **BEET IT clinical study** (NCT05133024) is to examine if **preoperative intake of beetroot juice can improve recovery of GI function following colorectal surgery**, and thereby help to **reduce the duration of postoperative ileus (POI)** and **protect against prolonged POI (PPOI)**.

INTERVENTION (concentrated beetroot juice) → SURGERY (standard of care) → RECOVERY (GI function)

METHODS

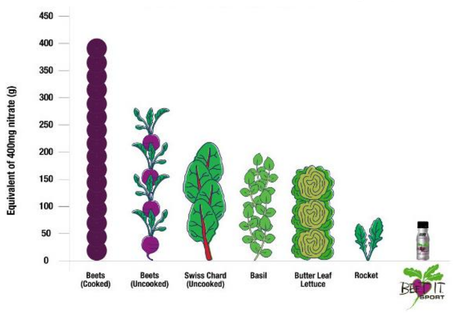
STUDY DESIGN

- phase II double-blind RCT
- 5 hospitals in Flanders (BE)
- 170 adult surgical patients
- 2 intervention arms 1:1
- recovery of GI function
- 3 months follow-up
- start 31 March 2021
- inclusion over 3-4 years

INTERVENTION

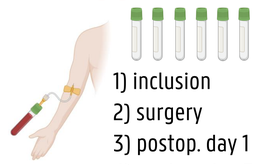
ACTIVE	PLACEBO
concentrated beetroot juice 400 mg nitrate / shot (70 mL)	concentrated beetroot juice **nitrate-depleted** shot (70 mL)

Patients consume **once daily a bottle** of juice in the **week before surgery**; in the morning before breakfast. This is 6 bottles on 6 consecutive days. The last one (7^{th}) is given in the hospital up to 2h before surgery.



STUDY PROCEDURES

BLOOD

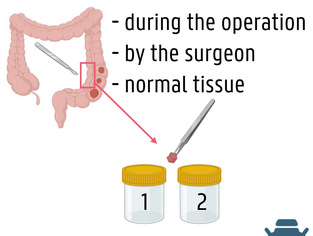


1) inclusion
2) surgery
3) postop. day 1
4) postop. day 3

→ same time, needle, posture, vein if possible

5' - 4000*g* - RT → storage at -80°C

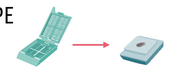
TISSUES



- during the operation
- by the surgeon
- normal tissue

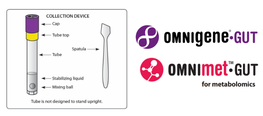
1) snap freezed, storage at -80°C

2) FFPE



FECES

- at home
- by the patient
- 2x (2x) before & after beet juice
- user-friendly collection kits (DNA Genotek Inc.)



temporary storage at RT
long-term storage at -80°C

→ Analysis of specific biomarkers related to inlammation, oxidative stress, NO bioavailability and intestinal barrier function & permeability

STUDY ENDPOINTS

Primary outcome:

Recovery of GI function, a **composite endpoint** requiring recovery of both upper GI (tolerance of a solid diet) and lower GI (passage of flatus and stool) functions.

Secondary outcomes:

- Time until 1st flatus
- Time until 1st stool
- Time until 1st tolerance liquids / semi-solid food / solid food
- Incidence and recovery of PPOI
- Length of hospital stay
- Postoperative complications

DATA COLLECTION

PREOPERATIVE (e.g. age, sex, weight) → INTRAOPERATIVE (e.g. blood loss, duration) → POSTOPERATIVE (e.g. first stool, analgesia)

Data are collected via the **Electronic Patient Dossier** (EPD) and **patient diary**. All data are subsequently entered in the Case Report Form (CRF) and electronic CRF via the **Research Electronic Data Capture** (REDCap) tool, a secure web-based application from which the study dataset is built. All data are **pseudonimized**.

EPD → DIARY → CRF → REDCap (Research Electronic Data Capture)

The diary includes **basic demographic** and **compliance information**, **postoperative findings** and a **movement** and **food questionnaire**. After study completion, **survival analysis** will be used to statistically analyze the data, using appropriate methods to account for competing risks, intercurrent events and missing data. An **interim analysis** is planned at 50% recruitment; i.e. data of 85 patients have been collected.

CURRENT INCLUSION STATUS

To date, 47 patients have been included. Of these, 63.8% are ♂, with a median age of 66 (56-72) years old (range: 32–89 years). Apart from the slow enrolment rate, compliance is excellent.

Center	*n* included	*n* to include
UZ Gent	10	60
UZ Leuven	24	50
UZ Antwerpen	11	40
AZ St-Lucas Gent	2	10
Ziekenhuis O-Limburg	-	10
TOTAL	**47**	**170**

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To be continued.....

Contact
barbara.cornillie@ugent.be
www.gihk.info/beet-it
Universiteit Gent
@ugent
Ghent University