Clinical Investigation Plan (CIP)

Feasibility and safety of robotic bariatric surgery using the Senhance™ Surgical System: a pilot study

Short Title: RoboBar Study

Type of investigation:	Clinical investigation concerning medical devices (MD).
Categorisation:	Category A1
Registration:	www.ClinicalTrials.gov : follows Swiss National Clinical trial Portal : follows
Identifier:	Follows (institutional identifier)
Sponsor-Investigator:	PD Dr. med. Philipp C. Nett, Leitender Arzt Bariatrische Chirurgie Klinik für Viszerale Chirurgie und Medizin Inselspital – Universitätsspital Bern CH-3010 Bern philipp.nett@insel.ch Tel.+41 31 632 54 06
Sponsor representative (if the Sponsor is not located in Switzerland)	Not applicable
Medical Device:	Senhance™ Surgical System and Instruments from Asensus Surgical - Senhance Cockpit: (01)00815440020309 - Senhance Manipulator Arm: (01)00815440020293
CIP Version and Date:	V3.0 26.11.2021

Signature Page(s)

ID number of the investigation:	Investigation ID (follows)
Title:	Feasibility and safety of robotic bariatric surgery using the Senhance™ Surgical System: a pilot study

The Sponsor-Investigator has approved the CIP version 3.0 26.11.2021, and confirms hereby to conduct the investigation according to the CIP, the current version of the World Medical Association Declaration of Helsinki, ISO14155 norm, ICH-GCP as far as applicable, and the local legally applicable requirements.

Sponsor-Investigator:
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Place/Date _____ Signature _____

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SYNOPSIS

Sponsor-Investigator	Philipp C. Nett, MD
Title:	Feasibility and safety of robotic bariatric surgery using the Senhance™ Surgical System: a pilot study
Short title / Investigation ID:	RoboBar Study / follows
Clinical Investigation Plan, version and date:	Version 3.0 / 26.11.2021
Registration:	www.ClinicalTrials.gov : follows Swiss National Clinical trial Portal : follows
Category and its rationale:	Category A1 Clinical trial with a medical device representing only minimal risk for the investigated subject
Name of the MD, Unique Device Identification (UDI), name of the manufacturer	Senhance™ Surgical System and Instruments from Asensus Surgical - Senhance Cockpit: (01)00815440020309 - Senhance Manipulator Arm: (01)00815440020293
Stage of development:	Phase II: Evaluating feasibility and safety of the Senhance™ Surgical System with digital laparoscopy in bariatric surgery.
Background and rationale:	The introduction of laparoscopy in bariatric surgery in 1993 is considered a milestone to improve postoperative outcomes in terms of less complications and shorter hospital stay [1]. Furthermore, conversion into open surgery is associated with higher postoperative morbidity and mortality in bariatric surgery [2]. Nevertheless, the laparoscopic technique has several drawbacks as lack of tactile feedback, limited degrees of freedom of the laparoscopic instruments, bad depth perception and limited field of view and therefore a flat learning curve. Recently, robotic surgery has been introduced in bariatric surgery manly through the Da Vinci robotic system to overcome some of those drawbacks. Robotic surgery presents the advantage of a 3-dimensional visualisation with high definition, more ergonomics and facilitates some complex laparoscopic tasks such as suturing [3, 4]. These advantages are especially relevant in bariatric surgery were abdominal obesity is often a cause of uncomfortable and tedious position for the surgeon and restrains the exposure of the surgical field. Senhance™ Surgical System from Asensus Surgical is an innovative robotic technique which presents, additionally to the above mentioned advantages, haptic feedback, an eyetracker system, microinvasive surgery (with 3mm instruments), reusable instruments and a lower docking time when compared to usual robotic systems[5, 6]. The use of this new technology has not been systematically analysed in bariatric surgery. Nevertheless, its use is expected to be safe and efficient and may also present some advantages over conventional laparoscopic surgery.
Objective(s):	To evaluate feasibility and safety of Senhance™ Surgical System in bariatric surgery.

Outcome(s):	Primary outcomes (safety): intraoperative complications, postoperative morbidity, and postoperative mortality. Secondary outcomes (feasibility): Docking time, Operation time, conversion rate, length of hospital stay, and rehospitalisation rate.
Design:	Prospective single arm, two-stage phase II study
Inclusion / exclusion criteria:	Participants fulfilling all of the following <u>inclusion</u> criteria are eligible for the study: - Informed Consent as documented by signature (Appendix Informed Consent Form) - ≥ 18 years old - Capable of judgment - Patient eligible for laparoscopic bariatric surgery according to the SMOB (Swiss Study Group for Morbid Obesity) -Criteria and having a bariatric operation (including Sleeve gastrectomy, Y-Roux gastric bypass, Omega-loop gastric bypass) using Senhance™ Surgical System The presence of any one of the following <u>exclusion</u> criteria will lead to exclusion of the participant: - < 18 years of age - Participants incapable of judgment or participants under tutelage - Inability to follow the procedures of the study, e.g. due to language problems, psychological disorders, dementia, etc. of the participant, - No informed consent signed - Women who are pregnant - High risk patients (immunosuppression, myopathy, liver cirrhosis, severe heart or lung disease, renal failure) - Contra-indication for laparoscopic surgery - Prior upper gastro intestinal tract operations (such as hepatobiliary, pancreatic, gastrooesophageal, anti-reflux, bariatric surgery or splenectomy except cholecystectomy) or open surgery with incision above the umbilicus
Measurements and procedures:	Eligible patients for bariatric surgery are included into the study during the outpatient consultation used to plan the bariatric procedure (incl. signature of the informed consent + collection of clinicopathological data*). Perioperative data** are collected after the operation, on the hospital release day and during the postoperative consultation 30 days after surgery. <u>*Patient's clinicopathologic characteristics:</u> age, sex, ASA score, BMI, previous abdominal surgery (laparoscopic, laparotomy), comorbidity (cardiovascular, respiratory, renal, neurological, psychiatric disease, other relevant disease). <u>**Perioperative data:</u> type of procedure, docking time, operation time, intraoperative complication (bleeding, organ lesion, procedure interruption), conversion, postoperative complication at 30 day postoperatively (Clavien-Dindo Classification + type of complication: postoperative bleeding, anastomotic or staple line leakage, surgical site infection, cardiovascular complication, respiratory complication, thromboembolic complication, renal complication...) and need for re-intervention. Length of hospital stay and rehospitalisation rate at 30-day postoperatively.

Intervention:	The bariatric procedure will be done using the Senhance™ Surgical System. It is a robotic technology developed by Asensus Surgical aimed to assist in the accurate control of laparoscopic instrument for visualization and manipulation of tissue (grasping, cutting, blunt and sharp dissection and suturing) in laparoscopic and thoracoscopic surgery. This technic is provided with haptic feedback, eyetracker system, 3mm instruments and 3-dimensional visualization. The product bears a CE mark.
Control intervention (if applicable):	Not applicable
Number of subjects with rationale:	Treatment group: 39 patients should be included into the study as calculated for the Simon's two stage design of the study
Duration of the investigation:	12 months
Investigation schedule:	01.12.2021 First-Participant-In (planned) 30.11.2022 Last-Participant-Out (planned)
Investigator(s):	PD Dr. med. Philipp C. Nett, Leitender Arzt Bariatrische Chirurgie Klinik für Viszerale Chirurgie und Medizin Inselspital – Universitätsspital Bern CH-3010 Bern philipp.nett@insel.ch Tel.+41 31 632 54 06
Investigational Site:	Single centre, Inselspital (University hospital Bern)
Statistical considerations:	The primary endpoint of our study is the safety of this new robotic platform in bariatric surgery. Therefore our study is designed as a single arm, two-stage phase II study with a stopping rule for safety using the Simon's two-stage design. Considering that conventional laparoscopic bariatric procedures present a complication rate around 10%, we set the maximum acceptable threshold of complication at 25%. Type I error is assumed to be 0.05 and Type II error 0.8. Therefore a sample size of 39 patients is needed with an interim analysis at 22 patients. The stopping rule is 5 or more events at the interim analysis and robotic surgery is considered safe if less than 6 events occurred. Baseline characteristics and perioperative data will be presented as medians (IQ-range) for continuous variables or frequencies (percentages) for categorical variables. For statistical analysis SPSS Version 25 will be used. The docking time and operation time will be represented as a visual graphic with its evolution over time.
Compliance statement:	This investigation will be conducted in compliance with the CIP, the current version of the Declaration of Helsinki, ISO14155, ICH-GCP (as far as applicable) as well as all national legal and regulatory requirements.

ABBREVIATIONS

Provide a list of abbreviations used in the CIP – to be completed/adapted

AE Adverse Event

ADE	Adverse Device Effect
ASA score	American Society of Anesthesiology
ASADE	Anticipated Serious Adverse Device Effect
ASR	Annual Safety Report
BMI	Body mass index
CA	Competent Authority (e.g. Swissmedic)
CEC	Competent Ethics Committee
CIP	Clinical investigation plan
ClinO	Ordinance on Clinical Trials in Human Research (in German KlinV, in French Oclin, in Italian OSRUm)
ClinO-MD	Ordinance on Clinical Trials with Medical Devices (in German: KlinV-Mep, in French: Oclin-Dim, in Italian: OSRUm-Dmed)
CRF	Case Report Form (pCRF paper CRF; eCRF electronic CRF)
DD	Device Deficiency
DMC / DSMC	Data Monitoring Committee, Data Safety Monitoring Committee
Ho	Null hypothesis
H1	Alternative hypothesis
HRA	Federal Act on Research involving Human Beings (in German: HFG, in French: LRH, in Italian: LRUm)
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH-GCP	International Council for Harmonisation – guidelines of Good Clinical Practice
IFU	Instruction For Use
ISF	Investigator Site File
ISO	International Organisation for Standardisation
ITT	Intention to treat
MedDO	Medical Devices Ordinance (in German: MepV, in French: Odim, in Italian: Odmed)
MD	Medical Device
MDR	Medical Device Regulation (EU) 2017/745 of 5 April 2017
PI	Principal Investigator
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SDV	Source Data Verification
SNCTP	Swiss National Clinical Trials Portal
SOP	Standard Operating Procedure
USADE	Unanticipated Serious Adverse Device Effect

SUMMARY OF THE REVISION HISTORY IN CASE OF AMENDMENTS

Not applicable

INVESTIGATION SCHEDULE

Study Periods	Screening	Intervention Period	In-hospital follow-up	Follow-up
Visit	1	2	3	4
Time (day)	-5/14	0	2	30
Patient Information and Informed Consent	x			
Demographics	x			
Medical History	x			
In- /Exclusion Criteria		x		
Physical Examination			x	x
Vital Signs		x	x	
Laboratory Tests			x	
Pregnancy Test		x		
Operation with use of Medical Device		x		
Primary Variables		x	x	x
Secondary Variables		x	x	
Adverse Events		x	x	x

1. INVESTIGATION ADMINISTRATIVE STRUCTURE

1.1 Sponsor-Investigator

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1.2 Co- Investigators

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1.3 Statistician ("Biostatistician")

CTU Bern Dr. Brigitta Gahl
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3012 Bern
+41 031 684 33 72

1.4 Laboratory

Not applicable

1.5 Monitoring institution

Studynurse
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CH-3010 Bern
+41 31 632 59 00

1.6 Data Safety Monitoring Committee

Not applicable

1.7 Any other relevant Committee, Person, Organisation, Institution

Not applicable

2. ETHICAL AND REGULATORY ASPECTS

The final positive decision of the CEC on the conduct of the investigation will be made and given in writing to the Sponsor before the investigation can start.

2.1 Registration of the investigation

The study will be registered in ClinicalTrials.gov and in the Swiss National Clinical trial Portal (SNCTP via BASEC).

2.2 Categorisation of the investigation

Category A1: The treatment with Senhance™ Surgical System represents only minimal risk for the investigated subject.

Senhance™ Surgical System is a medical device in conformity with Medical Device Directive 93/42/EEC and subsequent amendments and integrations.

2.3 Competent Ethics Committee (CEC)

The Sponsor-Investigator will submit the investigation to the CEC and obtain ethical committee approval before the start of the investigation. The Co-investigators ensure that approval from the CEC is obtained and filed in the Investigator site file before the investigation starts.

2.3.1 Reporting duties to the Competent Ethics Committee

All changes in the research activity and all unanticipated problems involving risks to humans, planned or premature study end and the final report are reported to the CEC within the allowed time frames.

No changes to the protocol will be made without prior sponsor-investigator and CEC approval, except where necessary to eliminate apparent immediate hazards to study participants.

Amendments are reported according to Art. 15 ClinO-MD (see also 2.10).

The regular or premature end of the investigation as well as the interruption of the investigation is reported to the CEC within 15 days (within 24 hours if it is due to security reasons) (Art. 36 ClinO-MD). The reasons for a premature end or an interruption have to be explained.

A final report shall be submitted within one year after the regular end of the investigation and within 3 months after a premature end of the investigation (Art. 37 ClinO-MD).

2.4 Competent Authorities (CA)

2.4.1 Reporting duties to the competent authorities

Not applicable

2.5 Ethical Conduct of the Investigation

The investigation will be carried out according to the CIP and with principles enunciated in the current version of the Declaration of Helsinki, the European Regulation on medical devices 2017/745 (MDR), the Norms ISO14155 and ISO14971, the ICH-guidelines of Good Clinical Practice (GCP) as applicable, the Swiss Human Research Act (HRA) and its Ordinances and Swiss regulatory authority's requirements. The CEC will receive the Annual Safety Report (ASR) and interim reports and be notified about investigation stop/end in agreement with local requirements.

2.6 Declaration of interests

The Sponsor-Investigator (Philipp Nett) and the Co-Investigators (Gian Andrea Prevost and Pauline Aeschbacher) declare no conflict of interest.

2.7 Patient Information and Informed Consent

The Investigators explain to each subject the nature of the investigation, its purpose, the procedures involved, the expected duration, the potential risks and benefits and any discomfort it may entail. Each subject is informed that the participation in the investigation is voluntary and that he/she may withdraw from the investigation at any time and that withdrawal of consent will not affect his/her subsequent medical assistance and treatment. The subjects are informed that he/she can ask any question, and consult with family members, friends, their treating physicians or other experts before deciding about their participation in the investigation. Enough time is given to the subjects

The subjects are informed that authorised individuals other than their treating physician may examine his/her medical records.

All subjects are given a subject information sheet and a consent form describing the investigation and providing sufficient information for the subjects to make an informed decision about their participation in the investigation. The enrolment will be performed during the outpatient consultation used to plan the bariatric procedure. The bariatric procedure will be done at least five days after this consultation, and patients can until then retract their consent if they do not want to participate in this study. No participant will be included in an emergency situation.

The formal consent of a subject, using the approved consent form, is obtained before the subject is submitted to any investigation procedure.

The subject should read, understand, and voluntarily agree before signing and dating the informed consent form, and is given a copy of the signed document. The consent form is signed and dated by the subject and the Co-Investigators (or her/his designee). The signed consent form it is retained as part of the investigation records.

2.8 Subject privacy and confidentiality

The Sponsor-Investigator and Co-Investigators affirm and uphold the principle of the subjects' right to privacy and that they shall comply with applicable privacy laws. Especially, anonymity of the subjects shall be guaranteed when presenting the data at scientific meetings or publishing them in scientific journals.

Individual subject medical information obtained as a result of this investigation is considered confidential and disclosure to third parties is prohibited.

Subject confidentiality will be further ensured by utilising subject identification code numbers to correspond to treatment data in the computer files.

The Investigators will permit IEC review and investigation-related monitoring, providing direct access to source data/documents.

For data verification purposes, a CEC may require direct access to parts of the medical records relevant to the investigation, including subjects' medical history.

2.9 Early termination of the investigation

The Sponsor-Investigator may terminate the investigation prematurely according to certain circumstances, for example:

- ethical concerns,
- insufficient subject recruitment,
- when the safety of the subjects is doubtful or at risk, respectively,
- alterations in accepted clinical practice that make the continuation of the investigation unwise,
- early evidence of benefit or harm of the experimental intervention.

2.10 Clinical investigation plan amendments

Substantial amendments are only implemented after approval by the CEC (Art. 15 ClinO-MD). The use of waivers from the CIP is prohibited (Annex XV, Chapter 2, Art. 3.10 MDR).

Under emergency circumstances, deviations from the CIP to protect the rights, safety and well-being of the subjects may proceed without prior approval by the Sponsor-Investigator and the CEC. Such deviations shall be documented and reported to the Sponsor and the CEC within 2 days (Art. 34 ClinO-MD).

All non-substantial amendments are communicated to the CEC together with the Annual Safety Report (ASR) (Art. 15 ClinO-MD), as soon as possible (Art. 20 ClinO-MD). The ASR shall include any deviations from the CIP that may have affected the rights, safety or well-being of the subject or the scientific integrity of the investigation (ISO14155).

2.11 Deviation from the Clinical Investigation Plan

The use of waivers from the CIP is prohibited (Annex XV, Chapter 2, Art. 3.10 MDR).

The investigator is not allowed to deviate from the CIP, except as specified in 2.10.

3. BACKGROUND AND RATIONALE

3.1 Background and Rationale for the clinical investigation

The introduction of laparoscopy in bariatric surgery in 1993 is considered to be a milestone to improve postoperative outcomes in terms of complications and length of hospital stay [1]. Furthermore, conversion into open surgery is associated with higher postoperative morbidity and mortality in bariatric surgery[2]. Nevertheless, the laparoscopic technique has several drawbacks as lack of tactile feedback, limited degrees of freedom of the laparoscopic instruments, bad depth perception and limited field of view and therefore a flat learning curve.

Recently robotic surgery has been introduced in bariatric surgery manly through the Da Vinci robotic system to overcome some of those drawbacks. Robotic surgery presents the advantage of a 3-dimensional visualization with high definition, more ergonomics, and facilitates some complex laparoscopic tasks such as suturing [3, 4]. These advantages are especially relevant in bariatric surgery were abdominal obesity is often a cause of uncomfortable and tedious position for the surgeon and restrains the exposure of the surgical field.

Several studies compare outcomes between laparoscopic and robotic intervention in bariatric surgery. Metanalysis shows that robotic bariatric surgery is associated with longer operative time and higher hospital costs when compared to laparoscopic bariatric surgery. However, comparable incidence of postoperative complications, postoperative mortality, conversion, reoperation, and length of hospital stay is reported [7-10]. Weight reduction also seems to be similar between laparoscopic and robotic bariatric surgery [7].

Senhance™ Surgical System from Asensus Surgical is an innovative robotic technic that presents, additionally, to the above mentioned advantages of robotic surgery: haptic feedback, an eye-tracker system, micro-invasive surgery (with 3m instrument), reusable instrument and a lower docking time when compared to usual robotic systems [5, 6].

This new technology has not yet been systematically tested in bariatric surgery. However, its use is expected to be safe and efficient and the new robotic platform may also present some advantages over laparoscopic surgery as well as other robotic technology. This new technology has already been proved safe and feasible in the field of gynecology, urology, colorectal surgery and general surgery [5, 11-15]. This platform has also been used in upper gastrointestinal surgery [16-18]. Furthermore, cholecystectomies performed with the Senhance™ Surgical robotic platform on patients with BMI above 48 kg/m2 have already been reported in the literature as feasible [15]. A pilot study was also performed for hysterectomy on obese patients (BMI up to 38kg/m2), and sigmoidectomy was reported for patients up to 38 kg/m2 [11, 19]. Therefore we believe that the Senhance™ Surgical platform is also safe and efficient in bariatric surgery.

The purpose of this study is to analyze the feasibility and safety of this new robotic plateform in bariatric surgery, which differs well from the Da Vinci robot of Intuitive Surgical with which all studies on robotic surgery in bariatrics have been performed. We believe that robotic surgery with a platform such as Asensus Surgical System allows a better ergonomics of the surgery while bringing a better precision in his gestures. This could also reduce postoperative pain and promote a faster recovery. The precision of the surgical gesture and the increased comfort of the surgeon could also positively influence the postoperative morbidity and the operative time.

3.2 Identification and description of the Investigational Medical Device

The Senhance™ Surgical System with Digital Laparoscopy from Asensus Surgical (formerly TransEnterix: TransEnterix Announces Name Change to Asensus Surgical and Introduces a New Category of Surgery, Performance-Guided Surgery | TransEnterix, Inc.).

Manufactured by:

Asensus Surgical Italia S.r.l.

Viale dell'Innovazione, 3

20126 Milano (MI), Italy

From Senhance Surgical System User Manual:

"The Senhance Surgical System is intended to assist in the accurate control of laparoscopic instruments for visualization and endoscopic manipulation of tissue including grasping, cutting, blunt and sharp

dissection, approximation, ligation, electrosurgery, suturing, mobilization, retraction, and sealing of vessels up to and including 5 mm in diameter in laparoscopic and thoracoscopic surgery. The system is indicated for adult and pediatric use. It is intended for use by trained physicians in an operating room environment in accordance with the Instructions for Use. Use of the device is limited to patients with a weight equal to or above 10 kg, who are suitable to be subjected to a conventional endoscopic technique.

In obese patients, stressed instruments may have a curved shaft. This curvature may cause abnormal forces on the haptic handles.

With obese patients, considering the loss of instrument range of motion, the movement may be uncomfortable. In some cases, the anatomical characteristics of the patient might make it necessary to use manual instruments.

In obese patients, it may be useful to repeat the docking in positions where the surgical instruments are stressed in order to reduce the forces that develop around the trocar and are transmitted to the handle. This procedure can only help, but not guarantee, correct transmission of the forces to the tip of the instrument. In fact, the feedback force to the handle increases proportional to the increase of the instrument inclination with respect to the angle at which you did the docking search. Therefore, this procedure can help only partially and may not be sufficient.

(…)

The Senhance system is contraindicated for use where endoscopic or laparoscopic surgical techniques are contraindicated.

(…)

Only physicians having adequate training and experience with endoscopic techniques should perform laparoscopic procedures with the Senhance system. Consult medical literature regarding techniques, complications, and hazards before performing any laparoscopic procedure. Only surgeons and staff who have received training provided by Asensus Surgical in the use of the Senhance system should use the system. Training provided by Asensus Surgical is limited to the use of the Senhance system and does not replace the necessary medical training and experience required to perform surgery. This device is intended to be used by: • Surgeons who have developed adequate robotic surgery skills to perform the tasks associated with each procedure and who have received specific training provided by Asensus Surgical in the use of this system. • Bedside scrubbed OR staff who are properly qualified to assist surgeons in the area of roboticallyassisted laparoscopic surgery and who have received specific training provided by Asensus Surgical in the use of this system. • OR staff (scrubbed and circulating) who are properly qualified to assist surgeons with preparing the sterile field and equipment for robotically-assisted laparoscopic surgery and who have received specific training provided by Asensus Surgical in the use of this system. Training is always offered upon installation of the device.

(…)

This device is covered by a declaration of conformity with Medical Device Directive 93/42/EEC or European Medical Device Regulation 2017/745 and subsequent amendments and integrations. The device is also covered by Radio Equipment Directive 2014/53/EU and RoHS 2 Directive 2011/65/EU. As required by law, the original of these declarations are available at Asensus Surgical Italia S.r.l."

3.3 Preclinical Evidence

Not applicable

3.4 Clinical Evidence to Date

This new technology has already been proved safe and efficient in the field of gynecology, urology, colorectal surgery and general surgery [5, 11-15]. This platform has also been used in upper gastrointestinal surgery [16-18]. Furthermore, cholecystectomies performed with the Senhance™ Surgical robotic platform on patients with BMI above 48 kg/m^2 have already been reported in the literature as feasible [15]. A pilot study was also performed for hysterectomy on obese patients (BMI up to 38kg/m^2), and sigmoidectomy was reported for patients up to 38 kg/m^2 [11, 19].

3.5 Justification for the design of the clinical investigation

Robotic surgery presents the advantage of better visualization with high definition, more ergonomics, and facilitates some complex laparoscopic tasks such as suturing [3, 4]. These advantages are especially relevant in bariatric surgery were abdominal obesity is often a cause of uncomfortable and

tedious position for the surgeon and restrains the exposure of the surgical field.

Our study will evaluate the feasibility and safety of Senhance™ Surgical System in bariatric surgery at a single center. Until now, this robotic system has not been investigated in bariatric surgery. The first step is to evaluate its feasibility and safety. Therefore, we propose a prospective pilot study during the introduction of this robot in our clinic. The aim initially is to analyze the feasibility and safety of this robot with a limited number of patients and this in a limited time to be able to highlight, if this new technology does not represent a risk for the patient in comparison to a conventional laparoscopic surgery. Therefore we plan to perform a prospective open observational single-center study with the advantage of less bias and confounding factors than in a retrospective study. To achieve a reasonable number of participants and to minimize selection bias we plan to offer robotic operation to all eligible patients. In view of the lack of data on this robot in bariatric surgery, a power analysis is not feasible. However, we have opted for a Simon's two stage design and thus perform an interim analysis with a stopping rule.

A randomized controlled trial with conventional laparoscopic is not yet feasible as we have to evaluate the feasibility and safety of this procedure first, as we recently introduced it in our centre. However subsequently and according to the results of this first study, a randomized study with a larger number of patients will be necessary to evaluate more precisely its outcome compared to bariatric surgery by conventional laparoscopy.

We started to operate with this new robotic platform on the 28.06.2021. On the planned starting date of the trial (01.12.2021) we expect still to be in the learning curve.

3.6 Explanation for choice of comparator

Not applicable

3.7 Risk evaluation (Risk-to-Benefits rationale)

Our study will analyze the safety of the use of the robotic platform of Asensus in bariatric surgery and will identify potential risks inherent to this technology. Possible adverse effects specific to the Senhance™ Surgical System are the same as in traditional laparoscopic surgery.

The most common complications after bariatric surgery are: anastomotic or staple line leakage, postoperative bleeding, pulmonary complications, thromboembolic complications and surgical site infection. We expect no adverse event specifically related to Senhance™ Surgical System that is not also part of classic laparoscopic bariatric surgery's complication. This study aims to observe the rate of these complications in robotic surgery compared to the laparoscopic technic. For other robotic platforms, literature reports a similar rate of postoperative morbidity and mortality between robotic and laparoscopic bariatric surgery [9, 21]. Thus the risks associated with the use of this robotic platform are expected to be similar to conventional laparoscopic bariatric surgery.

The potential benefits of this technology are a better postoperative outcome especially in terms of postoperative pain due to a better precision in the surgical gesture and a better ergonomics of the surgeon.

3.8 Justification of the choice of the investigation population

All patients eligible for a bariatric procedure meeting the inclusion criteria will be included in our study. The indication for the bariatric procedure is made according to the SMOB (Swiss Swiss Study Group for Morbid Obesity) -Criteria. High risk patients with relevant co-morbidities will not be included in our study. It is known that these patients are prompt to higher perioperative morbidity and mortality. However, the benefit of weight loss will present a relevant benefit to the course of their disease. Therefore bariatric procedures are not contraindicated in those cases. However, we believe that the introduction of the robotic system should not be experienced in these patients.

Patients under 18 years of age, incapable of judgment or under tutelage, will not be included in our study.

There will be no emergency enrolment of patients as bariatric surgery is usually performed as elective surgery.

4. CLINICAL INVESTIGATION OBJECTIVES

4.1 Overall Objective

This prospective study is performed to evaluate the feasibility and safety of the use of Senhance™Surgical System in bariatric surgery.

4.2 Primary Objective

The safety of the use of the Senhance™ Surgical System will be evaluated by monitoring intraoperative and postoperative complications, as well as postoperative mortality.

4.3 Secondary Objectives

The feasibility will be evaluated by monitoring the docking time, operation time, conversion rate (to conventional laparoscopy and open surgery), length of hospital stay and rehospitalisation rate.

4.4 Safety Objectives

See Chapter 4.2

5. CLINICAL INVESTIGATION OUTCOMES

5.1 Primary Outcome

The primary outcome will evaluate the safety of the use of the Senhance™ Surgical System in bariatric surgery.

Intraoperative complications such as bleeding, organ lesion, and procedure interruption will be monitored during the operation and reported postoperatively.

Postoperative complications and re-operation will be reported at discharge and at the 30-days follow up control. Complications will be classified according to its gravity by the Clavien-Dindo classification and by its type (postoperative bleeding, anastomotic or staple line leakage, surgical site infection, cardiovascular complication, respiratory complications, thromboembolic complication, renal complication...).

30-day postoperative mortality (= Clavien Dindo grade V) will be reported at discharge and at the planned 30-day-checkup.

5.2 Secondary Outcomes

As secondary outcomes feasibility of the use of the Senhance™ Surgical System in bariatric surgery will be evaluated.

Docking time and operation time, as well as conversion rate (into laparoscopic or open surgery), will be reported after the operation. This data will provide us some indirect information about the feasibility of such procedures.

The length of hospital stay will be reported at the discharge of the patient and the rehospitalisation rate at the 30-days follow up.

5.3 Other Outcomes of Interest

Not Applicable

5.4 Safety Outcomes

See paragraph 5.1 Primary Outcome.

6. CLINICAL INVESTIGATION DESIGN

6.1 General clinical investigation design and justification of design

Our study will evaluate the feasibility and safety of Senhance™ Surgical System in bariatric surgery at a single center. Therefore we plan to perform a prospective open observational single-center study with the advantage of less bias and confounding factors than in a retrospective study. To achieve a reasonable number of participants and to minimize selection bias we plan to offer robotic operation to all eligible patients. A randomized controlled trial with conventional laparoscopic is not yet feasible as we have to evaluate the feasibility and safety of this procedure first, as we recently introduced it in our centre.

The robot was introduced in June 2021 in our clinic and the first bariatric operation was performed on 28.06.2021. Due to a delay of our application to the CEC because of the new application procedure for medical devices, the approval for our study will come after the first operated patients. Nevertheless, deduced from other teams evaluating robotic operations we believe to still be in the learning curve at the beginning of the study.

No blinding is possible in our study. We plan to include 39 participant in our study which will be operated with our robot. The inclusion period will last 12 months and the follow-up 30 days.

6.2 Methods for minimising bias

6.2.1 Randomisation

Not applicable

6.2.2 Blinding procedures

Not applicable

6.2.3 Other methods for minimising bias

For minimization of selection bias, all consecutive patients eligible for laparoscopic bariatric surgery and meeting the inclusion criteria will be offered to participate in this study and will be prospectively included in the study.

6.3 Unblinding Procedures (Code break)

Withdrawal of informed consent will lead to participant's exclusion from the study.

Study or routine procedures will be stopped if safety concerns are raised.

7. CLINICAL INVESTIGATION POPULATION

7.1 Eligibility criteria

Intervention group (robotic surgery):

Subjects fulfilling all of the following inclusion criteria are eligible for the investigation:

- Informed Consent signed by the subject
- ≥ 18 years old
- Capable of judgment
- Patient eligible for laparoscopic bariatric surgery according to the SMOB-Criteria and having a bariatric operation (including Sleeve gastrectomy, Y-Roux gastric bypass, Omega-loop gastric bypass) using Senhance™ Surgical System

The presence of any one of the following exclusion criteria will lead to the exclusion of the subject

- < 18 years of age
- Participants incapable of judgment or participants under tutelage
- Inability to follow the procedures of the study, e.g. due to language problems, psychological disorders, dementia, etc. of the participant,
- No informed consent signed
- Women who are pregnant
- High risk patients (immunosuppression, myopathy, liver cirrhosis, severe heart or lung disease, renal failure)
- Contra-indication for laparoscopic surgery
- Prior upper GI operation (such as hepatobiliary, pancreatic, gastrooesophageal, anti-reflux or bariatric surgery or splenectomy except cholecystectomy) or open surgery with incision above the umbilicus

7.2 Recruitment and screening

Participants are recruited by the sponsor-investigator or the co-investigators present at the preoperative consultation.

For the female patient with potential pregnancy, a pregnancy-test will be performed on the day of the operation upon arrival at the hospital (see Chapter 9.3.2). Otherwise, no specific diagnostic investigations or screening is required for the study.

Patients meeting the inclusion criteria, in the absence of exclusion criteria, will be enrolled in our study.

No payment or compensation will be given to study participants.

7.3 Assignment to investigation groups

Not applicable

7.4 Criteria for withdrawal / discontinuation of subjects

Participants can, at any time of the study and for any reason, withdraw their informed consent in verbal or written form. This withdrawal will lead to participant's exclusion from the study.

Study or routine procedures will be stopped if safety concerns are raised.

8. CLINICAL INVESTIGATION INTERVENTION

8.1 Identity of the medical device under investigation

8.1.1 Experimental Intervention (medical device)

We plan to perform Sleeve gastrectomy, Y-Roux Gastric bypass and Omega-loop gastric bypass with the Senhance™ Surgical System.

According to our approach in laparoscopic bariatric surgery access to the intraabdominal space will be performed with a 12 mm self-cutting optical trocar under direct vision, which offers the visualization of different tissue layers to guarantee a safe entry to the intra-abdominal space. Pneumoperitoneum will be set to 12-15 mmHg. The following trocars will be placed under visual control. Placement and introduction of the robotic arm will be done by a trained surgeon or a trained surgical nurse under the supervision of the primary surgeon.

The planned procedure will be performed with the Senhance™ robotic system and, if required, assisted laparoscopically, for example, for the use of suction/irrigation devices, endoscopic staplers or for better exposure (liver retractor).

At the end of the procedure, the trocars will be retracted under visual control, and the skin closed with a skin stapler. As usual, in bariatric surgery in our center, abdominal wall closure will not be performed.

The Senhance™ robotic system will be used according to the manual instruction (see below). The operator and the assistant at the table have been trained before using the robot by Asensus Surgical (2 days of dry lab and 1 day of wet lab). A representative of Asensus Surgical is also present during the intervention in the operating room to supervise and offer technical support if necessary.

From Senhance Surgical System User Manual:

"The Senhance Surgical System is intended to assist in the accurate control of laparoscopic instruments for visualization and endoscopic manipulation of tissue including grasping, cutting, blunt and sharp dissection, approximation, ligation, electrosurgery, suturing, mobilization, retraction, and sealing of vessels up to and including 5 mm in diameter in laparoscopic and thoracoscopic surgery. The system is indicated for adult and pediatric use. It is intended for use by trained physicians in an operating room environment in accordance with the Instructions for Use. Use of the device is limited to patients with a weight equal to or above 10 kg, who are suitable to be subjected to a conventional endoscopic technique.

In obese patients, stressed instruments may have a curved shaft. This curvature may cause abnormal forces on the haptic handles.

With obese patients, considering the loss of instrument range of motion, the movement may be uncomfortable. In some cases, the anatomical characteristics of the patient might make it necessary to use manual instruments.

In obese patients, it may be useful to repeat the docking in positions where the surgical instruments are stressed in order to reduce the forces that develop around the trocar and are transmitted to the handle. This procedure can only help, but not guarantee, correct transmission of the forces to the tip of the instrument. In fact, the feedback force to the handle increases proportional to the increase of the instrument inclination with respect to the angle at which you did the docking search. Therefore, this procedure can help only partially and may not be sufficient.

(…)

The Senhance system is contraindicated for use where endoscopic or laparoscopic surgical techniques are contraindicated.

(…)

Only physicians having adequate training and experience with endoscopic techniques should perform laparoscopic procedures with the Senhance system. Consult medical literature regarding techniques, complications, and hazards before performing any laparoscopic procedure. Only surgeons and staff who have received training provided by Asensus Surgical in the use of the Senhance system should use the system. Training provided by Asensus Surgical is limited to the use of the Senhance system and does not replace the necessary medical training and experience required to perform surgery. This device is intended to be used by: • Surgeons who have developed adequate robotic surgery skills to perform the tasks associated with each procedure and who have received specific training provided by Asensus Surgical in the use of this system. • Bedside scrubbed OR staff who are properly qualified to assist surgeons in the area of roboticallyassisted laparoscopic surgery and who have received specific

training provided by Asensus Surgical in the use of this system. • OR staff (scrubbed and circulating) who are properly qualified to assist surgeons with preparing the sterile field and equipment for robotically-assisted laparoscopic surgery and who have received specific training provided by Asensus Surgical in the use of this system. Training is always offered upon installation of the device.

(…)

This device is covered by a declaration of conformity with Medical Device Directive 93/42/EEC or European Medical Device Regulation 2017/745 and subsequent amendments and integrations. The device is also covered by Radio Equipment Directive 2014/53/EU and RoHS 2 Directive 2011/65/EU. As required by law, the original of these declarations are available at Asensus Surgical Italia S.r.l."

Figure 4-1 shows images of the key Senhance system components. These components are described in more detail in the following sections.

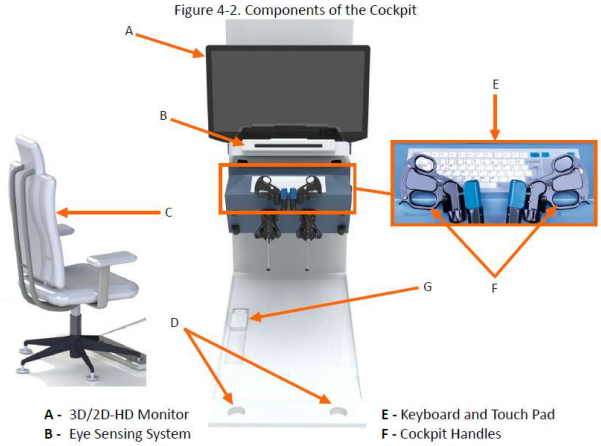
Figure 4-1. Senhance System Key Components

The cockpit is the control center of the Senhance system. The surgeon logs into and out of the system from the cockpit, configures the cockpit settings, assigns instruments to handles, views the operative site, and controls the movement of the manipulator arms.

The cockpit is comprised of the following components (See Figure 4-2. Components of the Cockpit):

- **Keyboard and Touch Pad:** Enable the surgeon to log in and out of the cockpit, and perform other actions during Setup and the surgical procedure. Many of the functions of the eye sensor can also be performed using the keyboard.
- **Handles (Laparoscopic Telescoping Masters):** Enable the surgeon to manipulate and control the surgical instruments (when the clutch pedal is pressed).
- **Monitor:** Displays the surgical image from the endoscope as well as informational icons and messages.
- **Eye Sensor:** Moves the endoscope's field of view (pan) and moves the camera closer or farther from the object (zoom).
- **Clutch pedal:** Activates the manipulator arm(s) when pressed, and deactivates the manipulator arm(s) when released.
- **Ergonomic chair:** Provides comfortable seating for the surgeon. Chair capture ports are built into the cockpit to ensure the proper positioning of the cockpit chair.

Figure 4-2. Components of the Cockpit

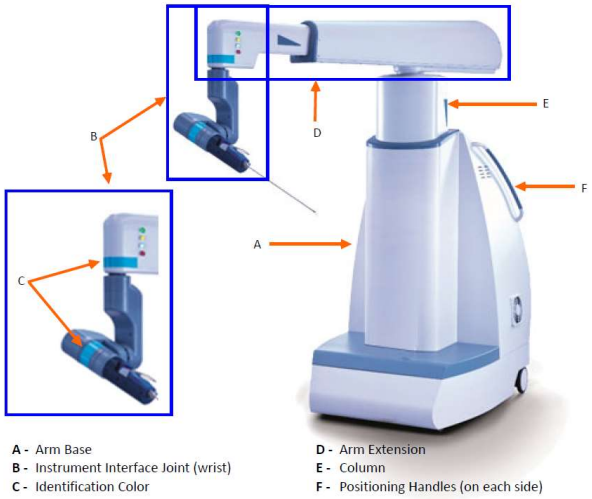


A - 3D/2D-HD Monitor
B - Eye Sensing System
C - Ergonomic Chair
D - Chair Capture Ports
E - Keyboard and Touch Pad
F - Cockpit Handles
G - Clutch Pedal

The Senhance system supports up to four manipulator arms, which are interchangeable and identical except for the identification colors on the arm extension and instrument interface (LIA) joint of each arm. Each manipulator arm is comprised of the following components as shown in Figure 4-17:

- **Arm base:** The wheel-mounted lower section of the manipulator arm, which contains the electrical cabinet, rear control panel, power and arm cable connectors, and positioning handles.
- **Arm extension:** The upper section of the arm which swivels around the pivot joint (J2) and can be extended or retracted via the extension joint (J3).
- **Instrument interface joint (wrist):** The portion of the arm that contains three joints (J4, J5, J6) which help position the instrument within the operating field.
- **Laparoscopic Instrument Actuator (LIA):** The Laparoscopic Instrument Actuator (LIA), hereafter called the *instrument interface*, is the portion of the arm that holds the surgical instrument. It contains a catch mechanism for the adapter alignment pin, magnets that help with instrument attachment, push buttons to enable manipulator arm movement, and sensors to identify the attached instrument.

Figure 4-17. Manipulator Arm



A - Arm Base
B - Instrument Interface Joint (wrist)
C - Identification Color
D - Arm Extension
E - Column
F - Positioning Handles (on each side)

Figure 4-37 shows examples of the instruments with their adapters.

Figure 4-37. Senhance Surgical Instruments and Adapters

From Senhance Surgical System User Manual, For a complete list of Senhance™ instrument please see the Appendix: Senhance Surgical System User Manual

8.1.2 Control Intervention (standard/routine/comparator)

Not applicable

8.1.3 Labelling and Supply (re-supply)

Not applicable

8.1.4 Storage Conditions

Not applicable

8.2 Discontinuation or modifications of the intervention

Conversion from a robotic procedure to a laparoscopic procedure can be done for the following reason:

- Technical problem with the robotic system which does not prevent safe use of the laparoscopic technic
- Surgeon choice: at any time of the operation the surgeon can decide to perform a conversion in laparoscopy if he esteems the use of the robotic platform not appropriate or too risky

Conversion from a robotic procedure to an open procedure can be done for the following reason:

- Technical problem with the robotic system which also prevents a safe use of the laparoscopic technic
- Surgeon choice: at any time of the operation the surgeon can decide to perform a conversion in open surgery if he esteems the use of the robotic platform not appropriate or too risky
- Anesthesiological reason: if the patient does not tolerate the pneumoperitoneum

Each conversion to laparoscopic or open surgery will be reported in the secondary outcome.

8.3 Compliance with clinical investigation intervention

Not applicable

8.4 Data Collection and Follow-up for withdrawn subjects

Participants can, at any time of the study and, for any reason, withdraw their informed consent in verbal or written form. This withdrawal will lead to participant's exclusion from the study.

If the bariatric operation is already performed, the follow-up will be performed as usually done in our bariatric center (with clinical control at 1, 3, 6, and 12 months during the first year, then each 6 to 12 months during the following years). The clinicopathological data and outcome until withdraw will be collected for safety reasons and will be included in the study.

If the bariatric operation has not yet been performed, but the patient still wants to benefit from a bariatric procedure, bariatric procedure will be performed by laparoscopic technique and the follow-up will be performed in our bariatric center as usual. The clinical data collected before withdrawal will be included in the study.

If the bariatric operation has not yet been performed, and the patient does not wish to benefit from it, he will be redirected to a conservative weight loss program according to the situation. The clinical data collected prior to the withdrawal will be used in the study.

The medical follow-up of withdrawn subjects, or of subjects that drop out from the investigation prematurely is described in chapter 9.2.5 and chapter 9.2.6.

No further data is collected after patients' withdrawal. Health-related personal data will be stored in an anonymized manner after completion of data evaluation.

8.5 Clinical investigation specific preventive measures

No specific preventive measures has to be taken during the study that is not also recommended for standard bariatric procedure such as cessation of therapeutic anticoagulation.

8.6 Concomitant Interventions (treatments)

Not applicable

8.7 Medical Device Accountability

Not applicable

8.8 Return, Analysis or Destruction of the Medical Device

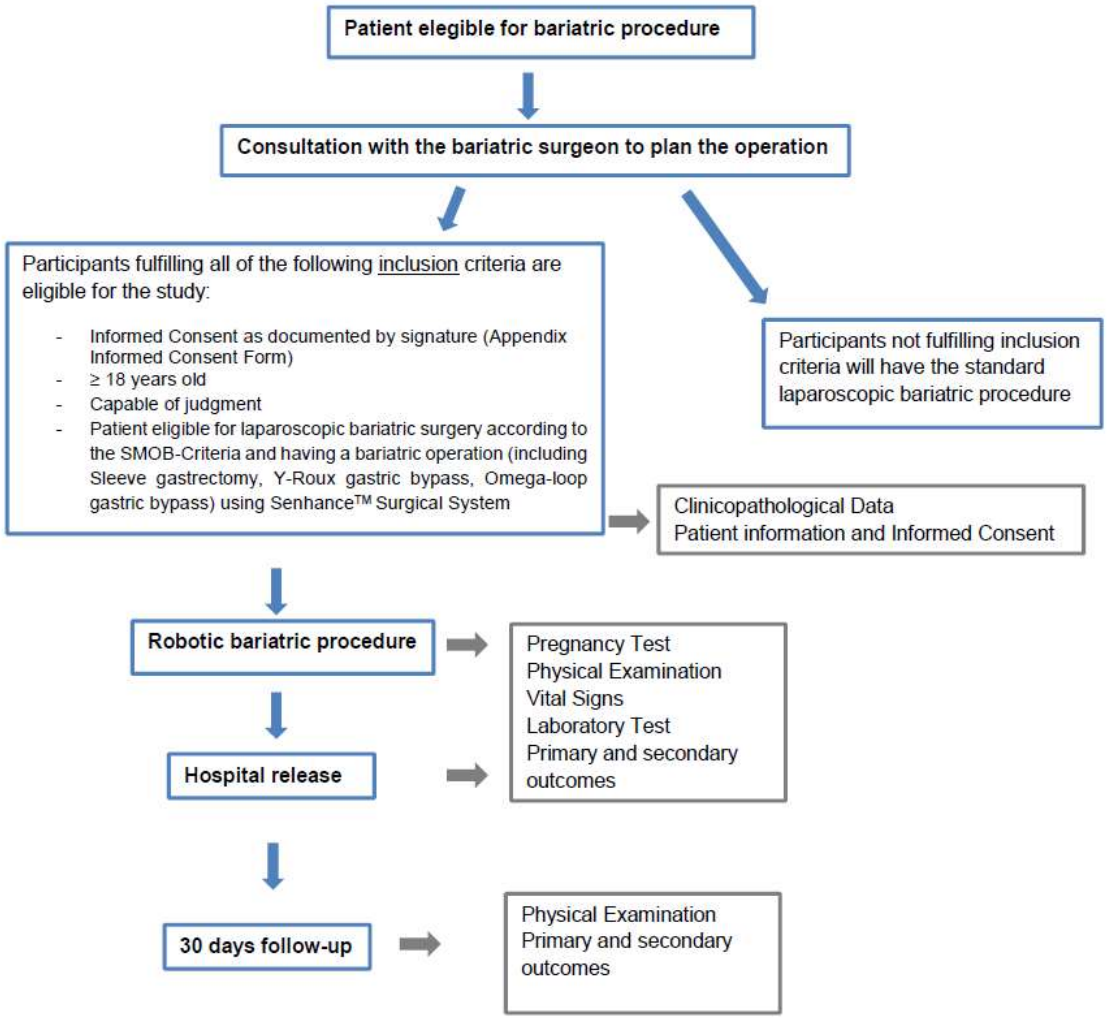
The majority of the instruments used are reusable after sterilization. The rest of the instruments like sterile draping or single-use instruments will be disposed.

In case of device deficiencies, including malfunction, usability issues, or inadequacy in the information supplied by the manufacturer including labelling, the devices will be returned to the sponsor for analysis.

The Sponsor-Investigator will contact the Swiss representative of Asensus Surgical and send him directly the photo, description of the dysfunction and the dysfunctional device.

9. CLINICAL INVESTIGATION ASSESSMENTS

9.1 Clinical investigation flow chart(s) / table of clinical investigation procedures and assessments



9.2 Assessments of outcomes

See Chapter 5

9.2.1 Assessment of primary outcome

Intraoperative complications such as bleeding, organ lesion, and procedure interruption will be monitored during the operation and reported postoperatively in the CRF

Postoperative complications and re-operation will be reported at discharge and at the 30-days follow up control the CRF.

Complications will be classified according to its gravity by the Clavien-Dindo classification and by its type (postoperative bleeding, anastomotic or staple line leakage, surgical site infection, cardiovascular complication, respiratory complications, thromboembolic complication, renal complication...).

30-day postoperative mortality (= Clavien Dindo grade V) will be reported at discharge and at the planned 30-day-checkup in the CRF.

Significant bleeding is defined as a drop in haemoglobin level > 3 g/dl post-operatively compared with

the post-operative baseline level and/or any post-operative transfusion of packed red blood cells for a falling haemoglobin and/or the need for radiological intervention (such as embolization) and/or re-operation to stop bleeding [20].

Any injury to other intraabdominal organ is either documented in the intraoperative CRF sheet filled by the primary surgeon if realized intraoperatively or documented in the electronic CRF if realized postoperatively and confirmed by imaging (CT) or during a re-operation or a gastroscopy.

Anastomotic or stapple leakage is define as a discharge of gastric or intestinal fluid or air from the bowel or stomach into the abdominal cavity and is diagnosed by imaging (CT) or during a re-operation or a gastroscopy.

SSI are defined by the United States Centers for Disease Control and Prevention (CDC) as “an infection that occurs after surgery in the part of the body where the surgery took place”[21]. Superficial SSI involve only the skin and subcutaneous tissue, deep SSI affect tissues under the skin like muscle, fascia, and adjacent organs/space SSI affect organs/space opened or manipulated during the operation or foreign body [21, 22].

Pneumonia is diagnosed by the prevalence of an infiltrate on imaging (either conventional radiography or CT-scan) in a patient with a clinically compatible syndrome (eg, fever, dyspnea, cough, and sputum production).

9.2.2 Assessment of secondary outcomes

Docking time and operation time, as well as conversion rate (into laparoscopic or open surgery), will be reported after the operation in the CRF.
The length of hospital stay will be reported at the discharge of the patient in the CRF and include the day of admission to the hospital and including the day of discharge from the hospital. Re-admission rate will be reported at the 30-days follow-up.

9.2.3 Assessment of other outcomes of interest

See Chapter 5.2

9.2.4 Assessment of safety outcomes

See Chapter 5.1

9.2.4.1 Adverse events

Any adverse event during the operation or until 30 days after the operation will be reported with its time of onset, duration, resolution, action to be taken, assessment of intensity, and relationship with the medical device. After the operation and during its hospital stay, each patient will be visited at least one time a day from the surgical resident. Vital signs, laboratory parameters, and clinical evaluation will help us to identify adverse events and treat them appropriately. During the postoperative control at 30 days postoperative, the surgeon will perform an anamnesis and clinical evaluation of the patient to identify adverse events. If required, further examination such as laboratory parameters, vital signs measurement, or diagnostic (CT-Scan, Gastroscopy, Reoperation) may be requested by the surgeon. Laboratory measurement will be performed by the laboratory of the Inselspital.

The most common complications after bariatric surgery are: anastomotic or staple line leakage, postoperative bleeding, pulmonary complications, thromboembolic complications and surgical site infection.

9.2.4.2 Laboratory parameters

A pregnancy test (urine sample) will be performed on the day of the operation upon arrival at the hospital (see Chapter 9.3.2).

At days 1 and 2, after the operation, a blood sample is performed to measure the blood count, CRP, kidney value, sodium, and potassium.

More tests are effectuated according to the clinic of the participant.

These blood tests correspond to the standard performed in laparoscopic bariatric surgery and no additional blood tests are planned in robotic bariatric surgery.

9.2.4.3 Vital signs

Vital signs will be taken when the participant arrives in its room on the day of the operation. During the induction phase, the operation and the waking phase, the participant is monitored (ECG, Blood pressure, oxygen saturation, heart rate) under the surveillance of an anaesthesiologist and a nurse anesthetist. When the participant is stable, he will be transferred to the regular station. Vital signs will be measure three times a day until its release from the hospital. If indicated, vital signs will be measured during the postoperative consultation at 30 days.

This surveillance correspond to the standard performed in laparoscopic bariatric surgery and no additional surveillance are planned in robotic bariatric surgery.

9.2.5 Assessments in subjects who prematurely stop the clinical investigation

If the bariatric operation was already performed, the follow-up would be performed as usually done in our bariatric center (with clinical control at 1, 3, 6, and 12 months during the first year, then each 6 to 12 months during the following years). The clinicopathological data and outcome will be collected for safety reasons but will not be included in the study.

If the bariatric operation has not yet been performed, but the patient still wants to benefit from the bariatric procedure, and if there is no contraindication, this one will be performed with the usual laparoscopic technic and the follow-up will be performed as usually done in our bariatric center. The clinical data collected will be used for the study up to the point of withdrawal only.

If the bariatric operation has not yet been performed and the patient does not wish to benefit from it or if the procedure is contraindicated, he will be redirected to a conservative weight loss program according to the situation. The clinical data collected will be used for the study up to the point of withdrawal only.

The number of patients who prematurely stop the study will be reported.

9.2.6 Follow-up of the subjects after the regular termination of the clinical investigation

As in laparoscopic bariatric surgery, patients are checked after the 3-month follow-up, in a standard way at 3, 6, 12 and 18 months after the operation and then annually with a blood test and a clinical check-up. This follow-up will be done in a similar way for patients who have had robotic bariatric surgery.

9.3 Procedures at each visit

9.3.1 Peroperative consultation

All patients where bariatric surgery is indicated and desired are seen at this consultation to plan the operation. During this visit, and for those who meet the inclusion criteria, the possibility of participating in the study will be discussed. The patient will receive oral and written information about the study. If the patient meets the inclusion criteria for the study and is willing to participate, he will be included.

The operation will be planned and explained to the patient. A consultation with the anesthesiologist will be organized.

9.3.2 Operation and Hospital stay 3-4 days

Day 0:

Pregnancy test (urine)
Exclusion and Inclusion criteria will be tested
Operation

Hospital stay of 3-4 days.

After the operation and during its hospital stay, each patient will be visited at least once a day from the surgical resident. Vital signs, laboratory parameters, and clinical evaluation will help us to identify adverse events and treat them appropriately. If required, further examination such as laboratory parameters, vital sign measurements, or diagnostic (CT-Scan, Gastroscopy, Reoperation) may be requested by the surgeon.

9.3.3 Postoperative consultation (30 day after the operation)

During the postoperative control at 30 days postoperative, the surgeon performs an anamnesis and

clinical evaluation of the patient to identify adverse events. If required, further examination such as laboratory parameters, vital sign measurements, or diagnostic (CT-Scan, Gastroscopy, Reoperation) may be requested by the surgeon.

10. SAFETY

10.1 Definition and Assessment of (Serious) Adverse Events and other safety related events

Adverse Event (AE) (Art. 2 Abs 57 MDR)

Any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons whether or not related to the MD.

Serious Adverse Event (SAE) (Art. 2 Abs 58 MDR)

Any adverse event that led to any of the following:

(a) death,
(b) serious deterioration in the health of the subject that resulted in any of the following:
  (i) life-threatening illness or injury,
  (ii) permanent impairment of a body structure or a body function,
  (iii) hospitalisation or prolongation of patient hospitalisation,
  (iv) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
  (v) chronic disease,
(c) foetal distress, foetal death or a congenital physical or mental impairment or birth defect.

Note: planned hospitalization for pre-existing condition, or a procedure required by the CIP, without a serious deterioration of the health status of the subject, is not considered an SAE

Device deficiency (Art. 2 Abs 59 MDR)

Inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, of an investigational device, including malfunction, user errors and inadequate information supplied by the manufacturer.

Malfunction (ISO14155)

Failure of an investigational device to perform in accordance with its intended purpose when used in accordance with the instructions for use or the CIP.

Device deficiency with Serious Adverse Device Effect (SADE) potential (Art. 80 Abs 1 letter c MDR; ISO14155)

Any device deficiency that might have led to a serious adverse event if appropriate action had not been taken, intervention had not occurred, or circumstances had been less fortunate.

Adverse Device Effect (ADE) (ISO14155)

Adverse event possibly, probably or causally related to the use of an investigational device or procedures.

Serious Adverse Device Effect (SADE) (ISO14155)

Adverse device effect (ADE) that has resulted in any of the consequences characteristic of a serious adverse event.

Unanticipated Serious Adverse Device Effect (USADE) (ISO14155)

Serious adverse device effect (SADE) which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

Causal Relationship of SAE (MDCG 2020-10/1)

A causal relationship towards the medical device or the procedure of the investigation should be rated

by the Co-Investigators and the Sponsor-Investigator as follows:

- **Not related:** The relationship to the device or procedures can be excluded.
- **Possible:** The relationship with the use of the investigational device is weak but cannot be ruled out completely. Alternative causes are also possible.
- **Probable:** The relationship with the use of the investigational device seems relevant and/or the event cannot reasonably be explained by another cause.
- **Causal relationship:** The serious event is associated with the investigational device or with procedures beyond reasonable doubt.

10.2 Adverse events categorization

The adverse events are categorized by the PI and the Sponsor using the following algorithm:

Does the AE meet the seriousness criteria?

- No, it is not serious
  - Is the relationship to the device or the procedure possible, probable or causal?
    - No: non-related AE
    - Yes: ADE
- Yes, it is serious: SAE
  - Is the relationship to the device or the procedure possible, probable or causal?
    - No: non-related SAE
    - Yes: SADE
- Is it anticipated (within expected type, severity and frequency of the complications)?
    - No: unanticipated SADE (USADE)
    - Yes: anticipated SADE (ASADE)

10.3 Documentation and reporting in Medical Device Category C clinical investigations

Not applicable

10.4 Documentation and reporting in Medical Device Category A clinical investigations

Device deficiencies (DD) and all **adverse events (AE)** including all **serious adverse events (SAE)** are collected, fully investigated and documented in the source document and appropriate case report form (CRF) during the entire investigation period, i.e. from patient's informed consent until the last CIP-specific procedure, including a safety follow-up period.

- Documentation of AEs (including SAEs) by the Co-Investigators includes diagnosis or symptoms, start and stop dates of event, event treatment, event resolution, assessment of seriousness and causal relationship to MD and/or investigation procedure (Art. 32 ClinO-MD, ISO14155).
- Documentation of DDs by the Co-Investigator includes description of event, start date, investigational device information, action taken with regard to the investigational device, and whether the DD led to an AE. The Sponsor-Investigator shall review all DDs and determine and document in writing whether they could have led to a SAE (DD with SADE potential) (Art 32. ClinO-MD, ISO14155).

Information on AEs is systematically collected during the hospitalization after the operation (2-3 days) and at the regular study visits 30-days after to the procedure, as applicable and clinically justified in the context of the specific protocol. In case of premature study withdrawal of a participant after the operation, he will still benefit of a 30-days visit as it is the case for all patients after bariatric surgery in our center.

10.4.1 Foreseeable adverse events and anticipated adverse device effects

Possible adverse effects specific to the Senhance™ Surgical System are the same as traditional laparoscopic surgery. Due to a learning curve, the operation time will probably be, in the beginning,

longer than in general laparoscopic bariatric surgery.

Mortality at less than 30 days after a Sleeve Gastrectomy is estimated at 0.29% (95% CI : 0.11 to 0.63%) and for Roux-en-Y gastric bypass at 0.38% (95% CI: 0.22-0.59%). The reoperation rate after a Sleeve Gastrectomy is estimated at 2.96% and for Roux-en-Y gastric bypass at 5.34%. The postoperative complication rate after a Sleeve Gastrectomy is estimated at 8.9% and for Roux-en-Y gastric bypass at 12.0%. [23]

The most common complications after bariatric surgery and their treatments are:

- anastomotic or staple line leakage → endoscopic or surgical closure / drainage
- postoperative bleeding → blood transfusion, coagulation optimization, reoperation
- pulmonary complications → antibiotics, invasive ventilation
- thromboembolic complications → anticoagulation
- surgical site infection → local treatment, VAC therapy, antibiotics

We expect no adverse events specifically related to Senhance™ Surgical system. Expected possible adverse events are the same as in traditional laparoscopic bariatric surgery. For other robotic platforms, literature reports a similar rate of postoperative morbidity and mortality between robotic and laparoscopic bariatric surgery [9, 24].

10.4.2 Reporting of Safety related events

Reporting to the Sponsor:

All SAEs, device deficiencies and health hazards that require measures are reported to the Sponsor-Investigator by the Co-Investigators (or authorized designee) within 24 hours after becoming aware of the event. Device deficiencies are assessed regarding their potential to lead to an SAE. DD are assessed regarding their potential to lead to an SAE.

Pregnancies

On the day of the operation each female participant that can be pregnant (except hysterectomy, postmenopausal) will have a pregnancy test. If the test is positive, the operation will be reported and the participant excluded from the study.

Reporting of pregnancies after the operation is not necessary.

Reporting to the Competent Ethics Committee:

The Sponsor-Investigator reports to the CEC promptly any serious adverse event which has a causal relation with the MD, comparator or procedure/test method or where a causal relation appears to be possible (Art. 33 ClinO-MD).

In order to ensure prompt notification, the Sponsor-Investigator may initially submit an incomplete notification.

If safety and health hazards that require measures must be taken immediately during the conduct of the investigation, the Sponsor notifies the CEC within 2 days of these measures and the circumstances which made them necessary (Art. 34 ClinO-MD).

Periodic safety reporting (Art. 35 ClinO-MD):

An Annual Safety Report (ASR) is submitted by the Sponsor-Investigator to the CEC, yearly. The ASR contains a list of all SADEs and DDs and a report on their degree of seriousness, causal relationship with the MD and procedure and on subjects' safety.

Other reporting is done according to provisions of MD vigilance as per Art. 87-90 MDR (Art. 33 abs 4.b ClinO-MD) and Art. 67 MedDO.

10.5 Assessment, notification and reporting on the use of radiation sources

Not applicable

11. STATISTICAL METHODS

11.1 Hypothesis

The investigator's hypothesis is that, robotic in bariatric is a safe and efficient way to perform bariatric surgery.

11.2 Determination of Sample Size

The study is designed as single arm, two-stage phase II study with a stopping rule for safety using the Simon's two-stage design.

Literature shows a complication rate for conventional laparoscopic bariatric surgery of 10%. We expect to have similar complication rates with bariatric surgery. For calculation of the safety stopping point we set the maximum acceptable threshold of complications at 25%.

We used Simon's 2 stage design to derive the time point of an interim analysis and a stopping rule for safety, assuming Type I error to be 0.05 and Type II error 0.8.

Simon's optimal two-stage design yielded the following numbers with respect to a 25% threshold:

- Interim analysis will be done at 22 patients. If there are 5 or more events, the study will stop fo r safety.
- Final analysis will be done at 39 patients. Robotic surgery can be regarded as successful if les s than 6 events occurred.

11.3 Statistical criteria of termination of the investigation

See 11.2

11.4 Planned Analyses

11.4.1 Datasets to be analysed, analysis populations

In the absence of contraindication (see exclusion criteria below) we will include consecutive patients which are eligible for bariatric surgery according to the SMOB-Criteria and having a robotic bariatric operation (including Sleeve gastrectomy, Y-Roux gastric bypass, Omega-loop gastric bypass) at our Adiposity Center at the Inselspital, University Hospital Bern, Switzerland.

11.4.2 Primary Analysis

In this pilot trial, feasibility and safety of the robotic platform in bariatric surgery will be assessed.

For the primary outcome (safety), following variable will be reported: intraoperative complications, postoperative morbidity, and postoperative mortality.

For the secondary outcomes (feasibility) following variable will be analysed: Docking time, Operation time, conversion rate, length of hospital stay and rehospitalisation rate.

Baseline characteristics and perioperative data will be presented as medians (IQ-range) for continuous variables or frequencies (percentages) for categorical variables.

Operation and docking time will be represented as a visual graphic with its evolution over time.

Descriptive statistics, graphs will be performed with SPSS Version 25.

For the primary outcome (safety), the analysis will be done after the 30-day follow-up of the last participant.

For the secondary outcome (feasibility), the analysis will be done after the 30-day follow-up of the last participant.

11.4.3 Secondary Analyses

Not applicable

11.4.4 Interim analyses

To guarantee the procedure's safety, the intraoperative and postoperative complications, as well as the postoperative mortality, will be analyzed after inclusion of 22 participant and will be presented as frequencies (percentages). The analysis will be done by the Sponsor-Investigator. If there are 5 or more events, the Sponsor-Investigator will terminate the study for safety.

11.4.5 Deviation(s) from the original statistical plan

No deviation is planned.

11.5 Handling of missing data and drop-outs

There will be no imputation for missing values. Missing values are reported and only available data are used for descriptive analysis.

Drop-outs will not be replaced.

12. QUALITY ASSURANCE AND CONTROL

The Sponsor-Investigator is responsible for implementing and maintaining quality assurance and quality control systems with written SOPs and Working Instructions. The co-investigators are responsible for proper training of all involved study personnel.

12.1 Data handling and record keeping / archiving

12.1.1 Case Report Forms

Data are recorded on paper by the primary surgeon conducting the procedure after the operation, by the attending surgical resident releasing the patient at the end of the hospital stay and by the surgeon performing the bariatric consultation prior to the operation during the enrollment of the participant and at 30 days postoperative. The paper CRF's are provided with the name of the Sponsor-Investigator or the co-investigators and their signature. These data will be scanned in an electronic Case Report Forms (p-/e-CRF). For each enrolled study participant, a CRF is maintained. CRFs will be kept current to reflect the subject status at each phase during the course of study. Participants will be coded in the CRF with a code identification (participant number in combination with the year of birth). The information on the paper CRF's is entered into an electronic database anonymously by the Co-Investigator.

12.1.2 Specification of source data and source documents

Source data are available at the site to document the existence of the study participants. Source data include the original documents relating to the study, as well as the medical treatment and medical history of the participant. The last one is found in the hospital information system (IPDOS).

The source documents in the study are:

- Eligibility form CRF
- Intra-operative CRF
- Post-operative CRF
- 30-day control CRF
- SAEs, AEs

Paper data will be kept under lock in the study nurses' offices at the Inselspital.

Electronic data will be stored on the Inselspital's Sharepoint server and protected by a password.

Access to the data is restricted to the persons involved in the study. No other persons have access to the data, and no data is passed on to others.

12.1.3 Archiving of essential clinical investigation documents

All study data must be archived for a minimum of 10 years after study termination or premature termination of the clinical trial.

Paper data will be kept under lock in the study nurses' offices at the Inselspital.

Electronic data will be stored on the Inselspital's Sharepoint server and protected by a password.

12.2 Data management

12.2.1 Data Management System

Data are extracted from the hospital information system (ipdos) and from the paper CRF's by the co-investigator (Pauline Aeschbacher) and entered in an Excel sheet. The Excel document is stored on a SharePoint platform that was centrally set up by the Inselspital. It fulfills all requirements of the Human Research Act (HRA). The physical location of the servers is in Zollikofen BE. Sharepoint stores the following versions of the document allowing for tracking changes. The Sharepoint database is accessible only by the Sponsor-Investigator and the co-investigators.

All identifying data (only PID and FID) will be kept separate from the actual study data. All digital documents are password protected. No identifying paper data will be made.

12.2.2 Data security, access and back-up

Unencrypted data is only viewed by the Sponsor-Investigator and the co-investigators.

Project data will be handled with uttermost discretion and is only accessible to authorized personnel who require the data to fulfil their duties within the scope of the research project. On the CRFs and other project specific documents, participants are only identified by a unique participant number.
Study-related data of the patient will be collected in a coded manner.

The SharePoint server is kept in a locked server-room. Only the system administrators have direct access to the server and back-up tapes. Each access on the platform occurs only with personal credentials (user name and password). The credentials are managed centrally in the Active Directory System of the Inselspital. An anonymous access to the SharePoint platform is not possible. A role concept (read, read/write and administrator) is realized using SharePoint groups and regulates permission for each user and each research project in order to use the system as he/she requires. Every access to the SharePoint server is recorded by the audit function of the SharePoint Server. This audit trail contains information about the accessing user, date and time of access and the name of the document that was accessed. The tracking of the actual data changes are not included in this audit trail. Therefore, the SharePoint versioning functionality is at all times switched on. The backup of the server and the database instances is done once a week by 1 full and 6 incremental backups. The retention time is 30 days.

In case of withdraw the data and samples collected up to that point will still be evaluated in encrypted form. The key allocation will be then destroyed so that the data remain anonym.

12.2.3 Analysis and archiving

At final analyses data files will be extracted from the SharePoint platform into statistical packages to be analyzed.

Coded data are stored digitally on a password protected SharePoint-database on the Insel-server for ten years.

The key document to decode data is stored separately in a specific folder on the Insel-server protected by a password with access by our study nurses only (for ten years). Our study nurses are not participating in the study and, therefore, capable of storing the key document (HFG Art. 26.)

12.2.4 Electronic and central data validation

Data are validated by visual control using graphs to detect possible misentries.

12.3 Monitoring

In order to guarantee a high study quality and data retrieval, on-site monitoring will be performed by a Studynurse from the Inselspital not participating in the study. Regular monitoring visits at the Inselspital will take place prior to the start and during the interim analysis and are organised by the Sponsor-Investigator.

Following documents will be monitored: informed consents and informed consent process, source data verification, inclusion and exclusion criteria, processing of subjects' data, preservation of subject's confidentiality.

2 visits will take place during the study (one before the beginning of the study, one during the interim analysis).

12.4 The source data/documents are accessible to monitors and questions are answered during monitoring by the Sponsor Investigator and the site staff.Audits and Inspections

There are no planned procedures for auditing trial conduct other than the internal inspection and control of the principal investigator.

However, the study documentation and the source data and documents are accessible to the CEC, and questions are answered during every surprise inspection. Of course, all involved parties must keep the

participant data strictly confidential.

12.5 Confidentiality, Data Protection

Direct access to source documents will be permitted for purposes of inspections and monitoring (12.4) (ICHE6, 6.10).

During and after the study the Investigators as well as the people involved in the publication and dissemination of the study related paper will have access to protocol, dataset and statistical code.

12.6 Storage of biological material and related health data

See 12.2.3

13. PUBLICATION AND DISSEMINATION POLICY

The results of the study will be published via oral communications during national and international meetings and via a written publication. The principal investigator will provide the Ethics Committee with a summary of the study's findings. The publication of the study results will be authored by Pauline Aeschbacher. The senior author will be Philipp Nett. Co-authorship on any of the publications will be based on a conceptual contribution to the study according to the criteria of the International Committee of Medical Journal Editors.

14. FUNDING AND SUPPORT

14.1 Funding

There is no funding for this study.

14.2 Other Support

Not applicable

15. INSURANCE

Not applicable (The category A study entails only minimal risk.)

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17. APPENDICES

1. Medical Devices: CE Certificate

2. Medical Devices: List of norms (vollständig eingehaltene, teilweise eingehaltene)

3. Patient Information and informed consent, General consent