PROTOCOL INFORMATION

FULL/LONG TITLE OF THE TRIAL

Impact of minimally invasive surgery on Surgeon Health. A feasibility study

SHORT TRIAL TITLE / ACRONYM

ISSUE

PROTOCOL VERSION NUMBER AND DATE

Version 5.0 24.9.22

IRAS NUMBER: 300580

SPONSOR: University of Leicester

SPONSOR REFERENCE NUMBER: 0823

ISRCTN number / Clinicaltrials.gov Number: Not applicable

FUNDER(S): Grant provided by Intuitive Surgical

This protocol has regard for the HRA guidance

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the trial in compliance with the approved protocol and will adhere to the principles outlined in the Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031), amended regulations (SI 2006/1928) and any subsequent amendments of the clinical trial regulations, GCP guidelines, the Sponsor's (and any other relevant) SOPs, and other regulatory requirements as amended.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the trial publically available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the trial will be given; and that any discrepancies and serious breaches of GCP from the trial as planned in this protocol will be explained.

Sponsor:		
Signature: 		Date: 30/09/2022
Name (please print): Yasmin Godhania		
Position: Research Governance Officer		
Chief Investigator:		
Signature:		Date: ...../...../.....
Name: (please print): Professor Esther Moss		
Principal Investigator:		
Signature:		Date: ...../...../.....
Name: (please print):		

KEY STUDY CONTACTS

Chief Investigator & Supervisor	Dr Esther Moss FRCOG PhD Associate Professor Leicester Cancer Research Centre University of Leicester Room 4.27, 4th Floor, Robert Kilpatrick Building University of Leicester, Leicester LE2 7LX 0116 2523170 em321@le.ac.uk
Co-Investigator/Student	Dr Anumithra Amirthanayagam MBBS, BSc (Hons) Clinical Research Fellow in Minimally Invasive Surgery Registrar in Obstetrics and Gynaecology University of Leicester Leicester Cancer Research Centre Robert Kilpatrick Building Leicester LE 7LX aa1235@leicester.ac.uk
Trial Co-coordinator	N/A
Sponsor	University of Leicester Research & Enterprise Division Research Ethics, Governance & Integrity Office Leicester General Hospital Gwendolen Road Leicester LE5 4PW 0116 258 4867 RGOsponsor@le.ac.uk
Clinical Trials Unit	N/A
Collaborators	Professor Massimiliano Zecca Loughborough University M.Zecca@lboro.ac.uk Mr Baljit Singh Consultant Colorectal Surgeon University Hospitals of Leicester Honorary Associate Professor University of Leicester bs143@leicester.ac.uk
Funder(s)	Intuitive Surgical
Protocol Contributors	Dr Anumithra Amirthanayagam MBBS, BSc (Hons) Miss Yasmin Godhania (Research Governance Officer)
Statistician	N/A

CONTENTS

LIST OF ABBREVIATIONS

Define all unusual or 'technical' terms related to the trial. Maintain alphabetical order for ease of reference.

AE	Adverse Event
AR	Adverse Reaction
CI	Chief Investigator
CRF	Case Report Form
CTU	Clinical Trials Unit
GCP	Good Clinical Practice
ICF	Informed Consent Form
ISF	Investigator Site File
NHS R&D	National Health Service Research & Development
PI	Principal Investigator
PIC	Participant Identification Centre
PIS	Participant Information Sheet
QC	Quality Control
RCT	Randomised Control Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SOP	Standard Operating Procedure
TMF	Trial Master File
TMG	Trial Management Group
TSC	Trial Steering Committee

KEY WORDS

Work-related musculoskeletal symptoms (WMS)

State Trait Anxiety Inventory (STAI)

TRIAL SUMMARY

Trial Title	Impact of minimally invasive surgery on Surgeon Health.	
Trial Participants	Consultant Surgeons and Gynaecologists Patients	
Planned Sample Size	65 procedures for feasibility 100 procedures for validation	
Follow up duration	N/A	
Planned Trial Period	2 years	
	Objectives	**Outcome Measures**
Primary	1. The proportion of surgical procedures where all variables of the assessment tool are captured (continuous HR monitoring;; continuous movement sensor monitoring; STAI questionnaire; modified Nordic WMS questionnaire, interviews).	
Secondary	1. Analysis to combine the variables to give a single value of 'impact' (high/intermediate/low) per procedure 2. Validation of the combined impact values (subjective vs objective assessment) 3. Analysis of the impact of providing surgical training and supervision to surgical trainees using heart rate monitoring 4. Willingness of recruitment of patients/surgeons and sample size calculations for a future multi-centre study 5. Identification of primary/secondary outcomes for a future definitive multi-centre study 6. Optimisation/validation of patient data recording measures to capture anaesthetic/operative/clinical events and outcomes 7. Safety assessment of measurement tools and recording devices in the theatre environment 8. Optimisation of surgeon continuous heart rate monitoring during procedure, data collection and analysis 9. Optimisation of positioning and recording of muscle movement/activity sensors and streamlining of data-analysis 10. Optimisation/validation of WMS and State Trait Anxiety Inventory (STAI) questionnaires and data analysis	

FUNDING AND SUPPORT IN KIND

FUNDER(S) (Names and contact details of ALL organisations providing funding and/or support in kind for this trial)	**FINANCIAL AND NON FINANCIALSUPPORT GIVEN**
Intuitive Surgical Grant	Project grant RM60G0742

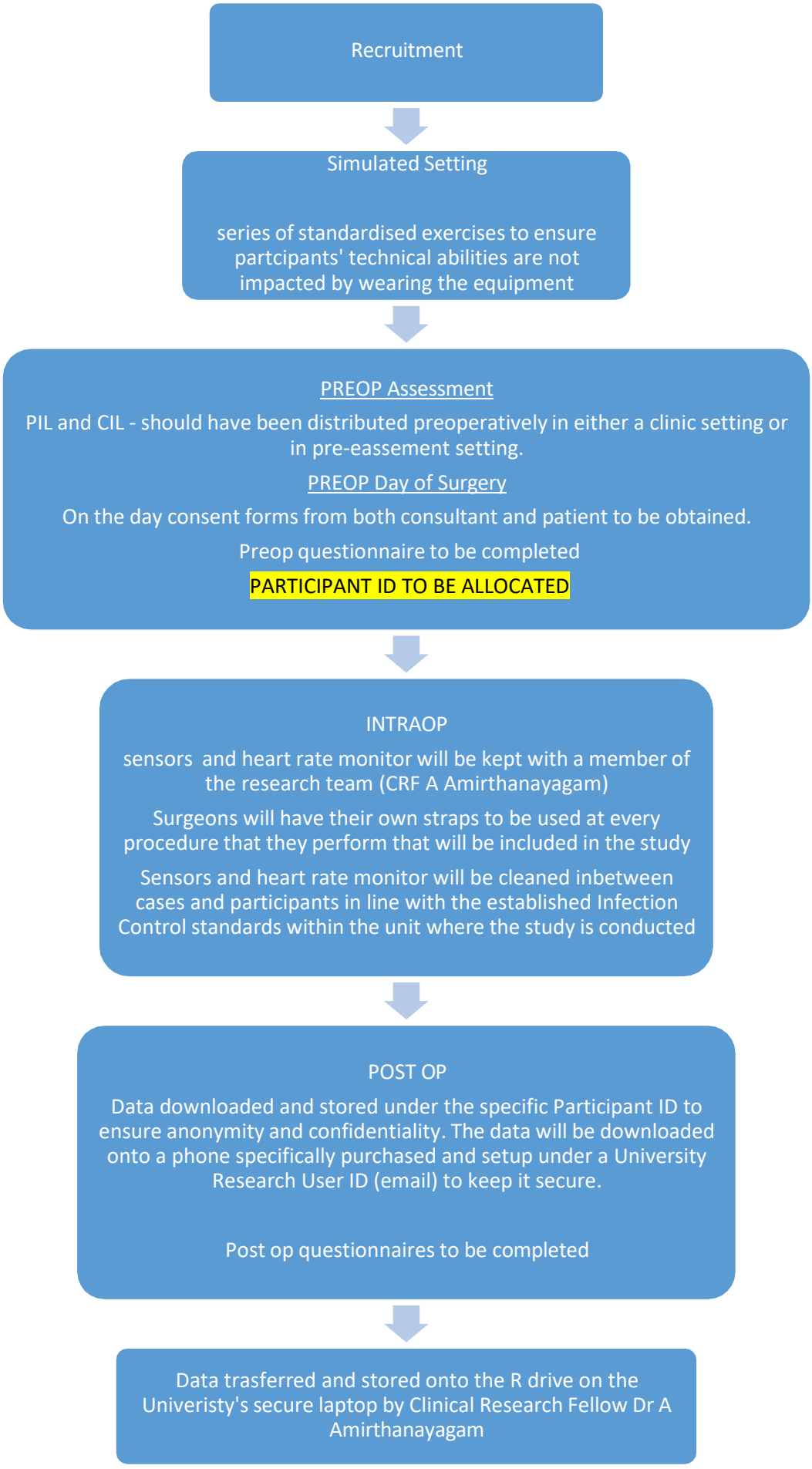
ROLE OF TRIAL SPONSOR

The sponsor of this research is the University of Leicester. The University of Leicester is registered as a research sponsor with the Department of Health and routinely takes responsibility as sponsor for research activities within the NHS.

ROLES AND RESPONSIBILITIES OF TRIAL MANAGEMENT COMMITEES/GROUPS & INDIVIDUALS

N/A

TRIAL FLOW CHART



1. BACKGROUND

The dramatic increase in obesity levels in the UK over the past two decades is having a sustained impact on all types of surgery. The impact on the surgeon of the change from open to MIS has been largely forgotten with the only benchmarking metrics considered being patient or financially focused. Obesity is a major risk factor for work-related musculoskeletal symptoms (WMS) experienced by surgeons, an issue that has the potential to reduce the working life and productivity of surgeons due to high rates of pain, stiffness and fatigue[1]. MIS, as compared to open surgery, is associated with significantly greater risk of WMS especially for neck, back, arm/shoulder and leg pain[1]. Indeed, WMS have anecdotally increased with 43-100% of surgeons from a wide range of specialties reporting symptoms after performing MIS when questioned. Several factors have been identified as increasing the risk of WMS with straight stick (SS) laparoscopy the most consistently reported being high volume work load and patient obesity[2]. WMS have also been reported to be significantly higher in female surgeons with significantly higher rates of shoulder/neck/upper back discomfort in women with smaller glove sizes compared to men ($p=0.004$)[3].

Impact of surgery on the surgeon is however not confined to musculoskeletal effects but also incorporates human factors issues such as cognitive load and psychological stress[4]. Stress can impair surgical performance[5], with laparoscopic procedures particularly triggering stress[6]. Measuring surgical stress is very challenging since it requires incorporation of subjective and objective perception of the situation,Thus a self-reported aspect is important when assessing cognitive workload, as is the need for simultaenous real-time assessment[7]. The Imperial Stress Assessment Tool (ISAT) was developed to measure surgeon stress and combines continuous heart rate monitoring with salivary cortisol and an objective questionnaire[8].

Since its introduction, robotic-assisted surgery (RA) has been reported to have greater benefits for surgeons' musculoskeletal health as compared to SS[9,10],although it is not without ergonomics issues typically from fixed position at the console[11,12], compared to SS[13], which instead has a greater impact on shoulder and arm movement[14]. RA however does appear to be associated with a lower rate of WMS compared to SS and open surgery when operating on obese patients[2,15]. RA has also been reported to be less stressful for the surgeon as compared SS[16].

Despite a randomised-controlled trial (RCT) reporting more favourable outcomes for RA as compared to SS [17] there is the view amongst UK healthcare commissioners that firm evidence supporting a significant advantage for RA over SS in gynaecology is still lacking. Discussions have taken place amongst the GO community in the UK (RCOG/BIARGS/BSGE/NCRI) as well as the general surgical community and currently the consensus is that a RCT of high-BMI EC patients would not be possible due to numerous objections, including lack of equipoise amongst RA surgeons preventing them from randomising patients to SS. A major theme that emerged from these discussions, however, was the high rate of WMS experienced by SS surgeons, since many surgeons report having to take time off for musculoskeletal surgery (shoulder/back) or having to reduce their surgical workload. Consequentially there is great concern as to future service delivery with a reduction in surgeons leading to greater waiting times or even high-BMI patients being denied surgery in favour of less curative non-surgical options, thereby impacting on survival rates.

2. RATIONALE

Minimally invasive surgery (MIS) has a significantly better peri-operative morbidity/mortality compared to open surgery and is the preferred surgical route for the management of numerous conditions. However, the impact of this change on surgeons has been largely forgotten. Obesity is a major risk factor for work-related musculoskeletal symptoms (WMS) experienced by surgeons, an issue that has the potential to reduce the working life and productivity of surgeons due to high rates of pain, stiffness and fatigue. Optimising surgeons' working conditions is vital for their own health and career longevity and also affects patients' safety and outcomes impact on surgical performance.

ISSUE is a feasibility study that aims to develop and validate a multi-faceted assessment tool that can objectively capture the real-time physical and psychological impact performing surgery has on the surgeon. We have previously shown that surgeons require significantly greater muscle movement/activity to complete exercises with standard laparoscopy versus robotic-assisted, and this difference is magnified in case of high BMI patients. The assessment tool will include continuous heart rate monitoring and upper-arm motion sensor monitoring during the procedure; and pre/post procedure WMS and State Trait Anxiety Inventory (STAI) questionnaires. This study has the support of the NCRI EC group and BIARGS.

The outcome of ISSUE will be a validated tool that can be used in a prospective, multi-centre study of open/laparoscopic/robotic surgery, which will provide objective evidence not only of patient outcomes but the impact of the different surgical routes on the surgeon.

3. RESEARCH QUESTION /OBJECTIVES AND OUTCOME MEASURES/ENDPOINTS

Hypothesis: The physical/psychological impact on surgeons is less with RA compared to SS and open surgery.

Aim: To develop and validate a 5-point assessment tool to objectively measure both the physical and psychological impact of complex surgical cases on a surgeon in order to give a single categorisation of impact: high, intermediate or low.

3.1 Primary objective

The proportion of surgical procedures where all 4 variables of the assessment tool are captured (continuous HR monitoring; continuous movement sensor monitoring; STAI questionnaire; WMS questionnaire).

3.2 Secondary objectives

1. Analysis to combine the 4 variables to give a single value of 'impact' (high/intermediate/low) per procedure
2. Validation of the combined impact values (subjective vs objective assessment)
3. To analyse the impact of providing surgical training and supervision to surgical traineeswith varying levels of experience within a live surgical setting using heart rate monitoring as objective measures (if the case has been deemed suitable by the Consultant for the trainee)
4. Willingness of recruitment of patients/surgeons and sample size calculations for a future multi-centre study
5. Identification of primary/secondary outcomes for a future definitive multi-centre study

6. Optimisation/validation of patient data recording measures to capture anaesthetic/operative/clinical events and outcomes
7. Safety assessment of measurement tools and recording devices in the theatre environment
8. Optimisation of surgeon continuous heart rate monitoring during procedure, data collection and analysis
9. Optimisation of positioning and recording of muscle movement/activity sensors and streamlining of data-analysis
10. Optimisation/validation of WMS and State Trait Anxiety Inventory (STAI) questionnaires and data analysis
11. To include the analysis of the cortisol samples collected at the feasibility stage within the preliminary analysis

3.3 Outcome measures/endpoints

To design and validate a 4-point assessment tool that can objectively measure the physical and psychological impact of complex surgical cases on a surgeon. The tool will then be taken forward and used in a large, multi-centre trial to determine whether a difference in surgeon impact exists between the different surgical modalities (open/laparoscopic/robotic) and if so to quantify the magnitude of the difference.

3.4 Primary endpoint/outcome

The proportion of cases where all the four components of the tool can be collected per case is the primary outcome.

3.5 Secondary endpoints/outcomes

1. Ergonomic analysis based on BMI including hip, waist ratio
2. Global measurements of surgeon including arm span, glove size and height to establish a potential association between ergonomics and anthropometric features of surgeon

4. TRIAL DESIGN

This is an observational study with the aim of investigating the impact that open and minimally invasive surgery (including robotic assist and straight stick laparoscopy) can have on surgeons' physical and psychological health.

The study will be using a monitoring tracking equipment called XSENS DOT Sensors, Actiheart heart rate monitor which are CE marked and will be used in its licensed indication. All equipment being used within the UHL operating theatres for the purpose of the study will have approval/authorisation from the medical physics department. The data collected will be downloaded on to a tablet using Bluetooth technology. Cortisol measurements were initially obtained at baseline (for each surgeon), preoperatively /intraoperatively (at time of the removal of specimen) and postoperatively as a biomarker to measure the cognitive impact of surgery. However, process evaluation within the feasibility stage has revealed it to be inconvenient and a potential disruption to theatre workflow especially if more than one case is recruited per list. The cortisol measurements obtained thus far will be included in the preliminary analysis but this biomarker will be omitted in the data collected at the validation stage. Surgeons will be expected to complete the STAI and modified Nordic WMS questionnaires as well. The WMS questionnaires have been further modified following the process evaluation carried out throughout the feasibility stage – to now include a numerical pain score to further objectively evaluate the intensity of the work related injuries sustained/ experienced.

XSENS DOT **ACTIHEART HEART RATE MONITOR**

The research involves working in collaboration with the wearable robotics team at Loughborough University.

5. TRIAL SETTING

Surgeons will attend for a session (before the surgery takes place) with the research team to familiarise themselves with the equipment to be worn during the planned surgery to ensure this does not affect their technical abilities. The session will consist of the surgeon performing a series of standardised tasks on a laparoscopic simulator (LapAR Innovus) with and without the monitoring equipment to ensure that their surgical performance (as determined by objective measurements) is not impaired by wearing the equipment. They will also provide feedback on the contents of the questionnaires (WMS and STAI) and a semi-structured interview. The day will be arranged at the convenience of the surgeon. Refreshments will also be provided and they'll be available to take breaks when needed.

The study will be taking place at secondary care hospitals and will initially involve University Hospitals of Leicester NHS Trust and will expand to other sites within England at a later date. Additional sites that are added, will be added through the amendment process.

The study will be recruiting surgeons and patients within Gynaecology and Surgical Directorates.

Surgeons will be invited to participate by the research team.

Members of the study team are experienced in working in theatres and are also part of the clinical care team. During R&I processes, permission will be sought from the Clinical Management Group about the study and observations during operations. Theatres management team will also be made aware of the study and of the surgeon's involvement ahead of the operation.

On the day of the operation, members of the study team will take care to introduce themselves and request permission to observe the surgery. The Senior Theatre Nurse will be provided with evidence of informed consent and will be asked for confirmation of the patient's identity. At the start and end of the procedure, all the equipment that was used for the study will be signed in and out by two members of the research/clinical team. As part of this study, we will also ask the Surgeon to explain our presence to the wider theatre team and to ask if anyone has any objections. In the event that the case had been deemed suitable for the assisting trainee as per the Consultant (lead for the clinical team) we will then monitor their heart rate with their consent to analyse the impact of training on the trainer (Consultant Surgeon).

It will be detailed in the patient's medical records that they consented to the study as they will also be completing a separate consent form. Patient measurements (waist/hip) will be taken on the morning of surgery.

The sensors will be safety assessed by the medical physics team at the hospital before being used by the surgeons in the theatre setting.

6. PARTICIPANT ELIGIBILITY CRITERIA

The study involves 2 cohorts: surgeons and patients.

6.1 Inclusion criteria

Surgeons:

- Consultant Surgeons and Gynaecologists
- Able to consent
- Patient consents to their surgeon participating in the study

Patients:

- All patients
- Able to consent
- Undergoing intra-abdominal surgery with a procedure expected to last less than 2 hours in duration
- >18 years

6.2 Exclusion criteria

Surgeons:

Besides the inverse of the inclusion criteria, patients who do not consent for their surgeon to participate.

Patients:

Inverse of the inclusion criteria.

7. TRIAL PROCEDURES

Schedule of Procedures

Procedures	**Visits (insert visit numbers as appropriate)**						
	Screening	**Baseline**	**Visit 1 (before the operation)**	**Pre-Op**	**During Op**	**After Op**	**Follow Up & post interview**
Surgeons:							
Approached by Research team	x						
Informed consent		x					
Attendance at Leicester University			x				

• Monitoring of the equipment • Laparoscopic simulator tasks • Feedback on questionnaires • Semi structured interview •							
Subjective assessment about the complexity of the procedure						x	
Sensor monitoring					x		
Pre-op questionnaire				x			
Post-op questionnaire						x	
Interview							X2
Patients:							
Eligibility check	x						
Informed consent		x					
Information collected from medical records		x		x		x	

7.1 Recruitment

Surgeons

An email invite attaching the PIS will be circulated to the surgeons by the Research Team at the hospital site. Surgeons who wish to participate can then contact the research team (who are also part of the clinical care team) to discuss the study further and for consent to take place.

Patients

Surgeons will be given an eligibility criteria list to decide which patients should be invited to participate in the study. Patients will be provided with the PIS at one of the routine appointments by their clinical care team. The patient will also have at least 24 hours to decide if they wish to take part or not. The researcher will also be available to answer any queries. They will need to contact the research team to let them know if they wish to participate. The researcher will consent the patient to study on the day of the operation. All due care will be taken into consideration to ensure that the consenting process does not coincide or interrupt clinical care on the day of the operation.

7.1.1 Participant identification

The research team will not be identifying patients, this will be conducted by the direct clinical care team.

7.1.2 Screening

The surgeons will be screening suitable patients.

7.1.3 Payment

No payments will be made to participants since no additional visits will be required.

7.2 Consent

Prior to participation in the study, participants (surgeons and patients) will be required to give written informed consent.

Consent will be required from the patient in order for the surgeon to participate in the study.

Consent will be taken on the day of the surgery by a member of staff from the research team. All due consideration will be taken to ensure that the consent process does not coincide with the clinical day to day activities on the ward.

Written and verbal versions of the participant information and informed consent will be presented to the participants detailing no less than: the exact nature of the study; the implications and constraints of the protocol; the known side effects and any risks involved in taking part. It will be clearly stated that the participant is free to withdraw from the study at any time for any reason without prejudice to future care, and with no obligation to give the reason for withdrawal.

The participant will be given sufficient time to consider the information leaflets, and the opportunity to question the Investigator, their GP or other independent parties to decide whether they will participate in the study. They will be allowed, at least 24 hours to make their decision. Written Informed Consent will then be obtained by means of participant dated signature and dated signature of the person who presented and obtained the informed consent. The person who obtained the consent must be suitably qualified and experienced, and have been authorized to do so by the Chief/Principal Investigator as detailed on the Delegation of Authority and Signature log for the study. The original signed form will be retained at the study site within the Trial Master File (TMF) or Investigator Site File (ISF). A copy of the signed Informed Consent will be given to participants and a copy retained in the participant medical notes.

Patient information sheets, consent forms and any amendments will be approved by Research Ethics Committee (REC), Health Research Authority (HRA), Study Sponsor and the local trust R&I department prior to implementation. The process of consent requires individual discussion with the p*articipants*.

7.3 Randomisation

N/A

7.4 Blinding

N/A

7.5 Unblinding

N/A

7.6 Trial assessments/procedures

Surgeons

Pre-study assessment will be conducted as detailed in section 5 prior to surgery.

The LapAR (Inovus) comes with its own established system of data capture and analysis that provides objective and comparable metrics when the surgeon undertakes different simulated tasks. The software will include both general surgical and gynaecological relevant exercises. The data obtained will be used to establish that the sensors and heart rate monitor will not have a negative impact on the surgical tasks itself in the live setting.

Day of surgery

A member of research team will meet with the surgeon (this will be arranged in advanced so that it does not coincide with clinical processes) for the following assessments:

Before surgery:

- Completion of the questionnaire which will take about 10 minutes to complete
- Wearing of sensors

After surgery:

- Completion of the questionnaire which will take about 10 minutes to complete

Surgeons will be invited to participate in an interview with the researcher to discuss their experience of the measurement tool and challenges they have experienced when collecting the data. This will be two interviews per participant to gather their views on the various aspects of the study as a whole as well as their potential ongoing musculoskeletal symptoms.

Patients

Access to medical records to obtain data:

- Medical co-morbidities
- Body habitus (BMI)
- Intra/post-operative events/recovery
- Waist/hip measurements will be taken by the researcher on the morning of surgery.
- Subjective assessment from the patient's healthcare professional regarding the level of complexity of the procedure.

There are no research trial specific assessments for patients but consent will be sought to access their medical records to obtain data from their medical records. The data collected will be pseudonymised at the site before being transferred to the University of Leicester. There will be no personal data being transferred.

7.8 Withdrawal criteria

It will be clearly stated that the participant is free to withdraw from the study at any time for any

reason without prejudice to future care, and with no obligation to give the reason for withdrawal.

If the data has already been anonymised, this cannot be removed. However there will be no further data capture following withdrawal of consent.

7.10 Assessment and management of risk

The monitoring equipment to be used, are CE marked and are being used in its licensed indication. This research does not involve the testing of the monitoring equipment. The safety and suitability of the monitoring equipment will be confirmed prior to study being conducted by the Medical Physics team.

Infection control procedures for the equipment will be conducted in line with organisational (University and NHS) policies and procedures due to the COVID pandemic.

We will be using a University of Leicester tablet linked to a University of Leicester email address to collect data from the sensors. Only the participant ID number will be stored when the sensors are being used. Once the data has been transferred onto the University's server, the data from the tablet will be deleted.

Interviews will be recorded on an encrypted USB voice recorder. The surgeon's ID number will be mentioned at the beginning of the recording to maintain anonymity. The voice recorder will be stored securely at the University of Leicester, in secure cupboard in a locked room. Once the recordings have been transferred to the servers, they will be deleted from voice recorder. Voice recordings will be transcribed by the research team or by a transcribing company. If a transcribing company is used, a confidentiality agreement will be executed. Any quotes used in publications will be anonymised and the participant will not be identified from them.

7.11 End of trial

As soon as data has been collected and analysed.

8. Storage and analysis of samples

Samples will be stored at the RKCSB. The saliva samples will then be sent to a commercial organisation for analysis and an agreement will be in place for the services that is provided. Samples will then be destroyed in line with the HTA's guidance. At the validation stage this is no longer applicable as no salivary cortisol swabs will be taken / stored following this amendment. The previously obtained salivary samples (ie prior to the amendment) will be sent to a commercial organisation for analyse and agreement will be in place for the services that is provided. Samples will then be destroyed in line with the HTA's guidance

9. Recording and reporting of SAEs

9.1 Definitions

Term	Definition

Adverse Event (AE)	Any untoward medical occurrence in a patient or clinical investigation participants, which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the the study, whether or not considered related to the study.

Adverse Reaction (AR)	An untoward and unintended response in a participant to an investigational medicinal product which is related to any dose administered to that participant. The phrase "response to an investigational medicinal product" means that a causal relationship between a trial medication and an AE is at least a reasonable possibility, i.e. the relationship cannot be ruled out. All cases judged by either the reporting medically qualified professional or the Sponsor as having a reasonable suspected causal relationship to the trial medication qualify as adverse reactions. It is important to note that this is entirely separate to the known side effects listed in the SmPC. It is specifically a temporal relationship between taking the drug, the half-life, and the time of the event or any valid alternative aetiology that would explain the event.
Serious Adverse Event (SAE)	A serious adverse event is any untoward medical occurrence that: • results in death • is life-threatening • requires inpatient hospitalisation or prolongation of existing hospitalisation • results in persistent or significant disability/incapacity • consists of a congenital anomaly or birth defect Other 'important medical events' may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the above consequences. NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.
Serious Adverse Reaction (SAR)	An adverse event that is both serious and, in the opinion of the reporting Investigator, believed with reasonable probability to be due to one of the trial treatments, based on the information provided.
Expected Serious Adverse Events/Reactions	There are none expected for this type of research study but if any are identified, these will be reported in line with Sponsor's SOPs.
Suspected Unexpected Serious Adverse Reaction (SUSAR)	A serious adverse reaction, the nature and severity of which is not consistent with the information about the medicinal product in question set out in the reference safety information: • in the case of a product with a marketing authorisation, this could be in the summary of product characteristics (SmPC) for that product, so long as it is being used within it's licence. If it is being used off label an assessment of the SmPCs suitability will need to be undertaken. • in the case of any other investigational medicinal product, in the investigator's brochure (IB) relating to the trial in question

9.2 Reporting procedures for All Adverse Events

There are none expected for this type of study but if any are expected to be reported, sponsor processes will be followed.

All AEs occurring during the study observed by the investigator or reported by the participant, whether or not attributed to study, will be recorded on the CRF.

The following information will be recorded: description, date of onset and end date, severity, assessment of relatedness to study, other suspect device and action taken. Follow-up information should be provided as necessary.

AEs considered related to the study as judged by a medically qualified investigator or the sponsor will be followed until resolution or the event is considered stable. All related AEs that result in a participant's withdrawal from the study or are present at the end of the study, should be followed up until a satisfactory resolution occurs.

It will be left to the investigator's clinical judgment whether or not an AE is of sufficient severity to require the participant's removal from treatment. A participant may also voluntarily withdraw from treatment due to what he or she perceives as an intolerable AE. If either of these occurs, the participant must undergo an end of study assessment and be given appropriate care under medical supervision until symptoms cease or the condition becomes stable.

The severity of events will be assessed on the following scale: 1 = mild, 2 = moderate, 3 = severe.

The relationship of AEs to the study will be assessed by a medically qualified investigator.

10 STATISTICS AND DATA ANALYSIS

10.1 Sample size calculation

A key unknown for the feasibility of the full trial is whether it is possible to capture all 5 components of the tool for objective assessing stress of surgery therefore the proportion of surgeries with all 5 variables completely captured will be our primary feasibility outcome.

We believe this will be high, at around at least 90%. A sample size of 65 produces a two-sided 95% confidence interval with a width equal to 0.16 when the sample proportion is 0.90, with lower limit 0.80 and upper limit 0.96. This data will be used to determine the parameters to classify cases into low, intermediate and high impact depending on the physical/psychological impact on the surgeon.

A further 100 cases have been included as validation of the tool. This is based on a 50% prevalence of 'high' impact procedure and 95% confidence level and a sensitivity of 0.90 (0.772-0.970).

10.2 Planned recruitment rate

Development of tool - 65 operations.

Validation of tool – 100 operations

10.3 Statistical analysis plan

10.3.1 Summary of baseline data and flow of patients

Data to be analysed includes:

- Heart rate
- Motion tracking data from XSens DOT
- Questionnaires completed
- Semi structured Interviews
- Information from medical records including (BMI, waist/hip measurements and ratio)

10.3.2 Primary outcome analysis

Multi-variate analysis will be performed to identify factors increasing surgeon impact and statistical modelling will be used to calculate a single value that is representative of the cumulative 'impact' of the case on the surgeon so that cases can be categorised as 'high', 'intermediate' or 'low' impact. Case complexity (for example BMI, previous surgery) and subjective surgeon opinion will be compared with the impact classification to determine internal consistency (Cronbach alpha) and content validity.

Following the development of the impact classification, geographical external validation will be conducted at additional sites, and surgeons recruited to confirm the accuracy of the 5-point assessment tool.

Data gathered from the interviews will undergo qualitative analysis

11.3.3 Secondary outcome analysis

Analysis of surgeon ergonomic data in light of case complexity and patient BMI in relation to surgeon's anthropometric measurements.

10.5 Procedure(s) to account for missing or spurious data

As this is a feasibility study looking at how feasible it is to collect this data, the trend of missing data i.e (which aspect is most frequently difficult to obtain) will be monitored. This will help understand whether or not all aspects of the tool are key to classifying the cases appropriately.

11. DATA MANAGEMENT

11.1 Data collection tools and source document identification

Surgeons

- Demographic information
- State Trait Anxiety Inventory and modified Nordic Work-related musculoskeletal Symptoms questionnaires.
- Data from sensors – XSENS DOT and Actiheart heart rate monitor
- Interviews will be recorded on an encrypted voice recorder and we will state the participant's number at the beginning of the recording so that they are not identifiable. The recording will then be transferred to the University of Leicester and will be deleted from the recorder. The recording will be transcribed by the researcher or by a

transcribing company. If a transcribing company is to be used, there will be confidentiality agreement in place with the company.

Patients

Access to medical records to obtain data:

- Medical co-morbidities
- Body habitus (BMI, waist-hip measurements and ratio)
- Intraoperative events
- Subjective assessment from the patient's surgeon regarding the level of complexity of the procedure.

11.2 Data handling and record keeping

All data handling and record keeping will be kept in adherence to University of Leicester's and NHS Organisation(s) policies.

11.3 Access to Data

Direct access will be granted to authorised representatives from the Sponsor, host institution and the regulatory authorities to permit trial-related monitoring, audits and inspections- in line with participant consent.

11.4 Archiving

Research data will stored for 6 years and storage will comply with the University of Leicester archiving Standard Operating Procedure. Details can be found at: http://www2.le.ac.uk/offices/ias.

12. MONITORING, AUDIT & INSPECTION

Direct access will be granted to authorised representatives from the Sponsor and host institutions for monitoring and/or audit of the study to ensure compliance with regulations.

13. ETHICAL AND REGULATORY CONSIDERATIONS

13.1 Research Ethics Committee (REC) review& reports

Once the initial sponsor review process is complete and a sponsor reference number has been allocated, and all requested documentation has been received and checked, authorisation from the University of Leicester's Research Governance Office will be received to book further review of the proposed research. The University of Leicester's Ethics Committee or NHS Research Ethics Committee and the Health Research Authority will then review the proposal. Agreement in principle is subject to the research receiving all relevant regulatory permissions. Submission for regulatory approvals will be submitted via Integrated Research Application System (IRAS). The Chief Investigator will ensure that all regulatory approvals, confirmation of capacity and capability from NHS sites and sponsor greenlight are in place before participants are approached.

For any required amendment to the study, the Chief Investigator, in agreement with the sponsor will submit information to the appropriate body in order for them to issue approval for the amendment. Amendments will be implemented upon receiving Sponsor Green Light.

The Research Governance Office's Standard operational procedures will be followed for the duration of the trial.

Amendments will be submitted to the sponsor in the first instance for approval.

Annual progress reports will be submitted to the Ethics Committee annually on the anniversary date of when favourable opinion is given by the Chief Investigator.

The Chief Investigator will notify the REC when the study has ended by completing the end of study notification form and will submit a final report of the results within one year after notifying REC.

A trial master file will be maintained for the duration of the study and will be stored for 6 years after the study has ended.

13.2 Peer review

Peer reviewed as part of the competitive surgical grant process by Intuitive Surgical

13.3 Public and Patient Involvement

The study has been designed with the support of the members of gynaecological oncology and general surgical community. When the study is complete, patients will have been signposted at the time of consent to refer to the relevant webpage associated with the study for dissemination of findings on a public platform.

For the surgical community, the findings will be presented at conferences and published when study is complete.

13.4 Regulatory Compliance

Not applicable, the monitoring equipment to be used, is CE marked and being used in its licensed indication. This research does not involve the testing of the monitoring equipment.

13.5 Protocol compliance

If a protocol breach occurs, then the CI will document this in adherence to the University's Standard Operational Procedure SOP Identifying and Reporting Deviations and Serious Breaches of GCP and/or the Protocol for Trials. The CI will seek advice from the research supervisors and the sponsor.

13.6 Data protection and patient confidentiality

All information collected in the study will be kept strictly confidential.

The Chief Investigator will have access to the trial documentation and will be the data custodian.

The investigator will comply with the requirements of the General Data Protection Regulation (and other applicable regulations) with regards to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles.

Analysis of the generated will be undertaken by the chief investigator on University of Leicester premises. All collected data will be saved on the R-drive at the University of

Leicester. Any printed confidential material will be kept in a folder in a locked drawer in a secured room in a secure office environment office at the University of Leicester.

Anonymised research data will be stored for six years after the study has ended. Long-term storing will comply with the University of Leicester archiving Standard Operating Procedure. Details can be found at: http://www2.le.ac.uk/offices/ias.

13.7 Financial and other competing interests for the chief investigator, PIs at each site and committee members for the overall trial management

N/A.

13.8 Indemnity

The University of Leicester insurance applies for this study.

13.9 Post trial care

N/A.

13.8 Access to the final trial dataset

The Chief Investigator will have access to the full dataset.

Direct access will be granted to authorised representatives from the Sponsor and host institutions for monitoring and/or audit of the study to ensure compliance with regulations.

14. DISSEMINIATION POLICY

Any data arising from this study will be published and presented in a peer-review journal, if possible an open access journal. The manuscript will be deposited with the University of Leicester, according to the University of Leicester's policies (see http://www2.le.ac.uk/library/downloads/open-access/open-access-policy) and data sharing policies.

A summary of results will also be sent to participants who wish to receive a copy.

15. REFERENCES

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16. Appendix 1 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made
	V4	11.8.2022	A Amirthanayagam	Removal of salivary cortisol measure from protocol
	V5	24.09.2022	A Amirthanayagam /E Moss	Modification of the WMS Nordic questionnaire to include a numerical pain score system and description of the usage of previous samples of cortisol for analysis

List details of all protocol amendments here whenever a new version of the protocol is produced.

Protocol amendments must be submitted to the Sponsor for approval prior to submission to the REC committee/HRA.