PROTOCOL TITLE:

Does increased mobility assessed with 3D motion tracking technology lead to early post-operative recovery among patients undergoing oncologic surgeries

PROTOCOL NUMBER:

I 80918

NCT04000581

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VERSION NUMBER:

V3

DATE:

02/28/20

Confidentiality Statement

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1 OBJECTIVES

- To investigate objectively using evidence based randomized controlled trial the impact of early mobility (first day after the surgery) after any inpatient oncologic procedures on early recovery of postoperative course.
- Try to find out the minimum level of postoperative mobility that needed for early postoperative course recovery by objective assessment of range of movement for each participant using 3D motion tracking system (Xsens)

2 BACKGROUND

Early mobilization is considered an important element of postoperative care, however, it remains unclear how to best implement this intervention in clinical practice. One of the first surgeons to describe the concept of early mobilization after surgery was Dr. Emil Ries, a gynecologist in Chicago, in 1899 (1). Despite the report by Ries, the practice of early postoperative mobilization was slow to gain favor in North America and patients were still commonly kept on strict bed rest for several weeks after surgery to minimize pain and ensure adequate healing of wounds (2). It was not until the 1940s that early mobilization became accepted among surgeons after a number of observational studies suggested that this practice was not harmful to patients. Within the last 20 years, there has been significant progress in perioperative care with the development of standardized enhanced recovery pathways (ERPs). ERPs combine many different elements of care in the preoperative, intraoperative and postoperative periods, and aim to reduce morbidity, decrease hospital duration of stay, and improve patients' recovery after surgery (6). ERPs are comprised of up to 25 different interventions in the perioperative period; however, the relative contribution of each of these elements to the overall recovery process remains unclear.

Guidelines for perioperative care from the Enhanced Recovery after Surgery Society give early mobilization a strong recommendation grade, despite a very low level of evidence supporting its use. There is little evidence in the literature regarding strategies to promote compliance to early mobilization, and significant differences in mobilization goals exist between programs.

The use of 3D motion tracking technology in clinical practice started in 2017(10).This technology uses wireless inertial measurement units which could be used in clinical settings to objectively measure movement patterns (the joint range of movement and the distance of movement) during functional activities . These data analyzed by the software and yield further calculation representing the bio-kinematics of body movement.

3 INCLUSION AND EXCLUSION CRITERIA

Inclusion Criteria

To be included in this study, participants must meet the following criteria:

1. Age ≥ 18 years of age.
2. Ambulant inpatient with a stay of ≥ 2 days after any oncologic surgery.
3. ECOG scale of performance status of less than 3.
4. American Society of Anesthesiologist score (ASA) 3 or less

5. Participants who do not engage in regular exercise regimen before the surgery (other than regular occupational physical therapy).
6. Participant or legal representative must understand the investigational nature of this study and sign an Independent Ethics Committee/Institutional Review Board approved written informed consent form prior to receiving any study related procedure.

Exclusion Criteria

Patients with altered mental status, psychiatric illness, ECOG scale performance status 3 or more, ASA score of 4, participants who engage in regular exercise regimen before surgery (at least one session per week), restricted movement due to other diseases or those who require continuous monitoring will be excluded from this study.

Inclusion of Women and Minorities

Women and members of all races and ethnic groups are eligible for this study. Pregnant women are eligible for this study.

4 LOCAL AND STUDY-WIDE NUMBER OF SUBJECTS

80 patients will be included in this study. All data will be identified and the duration of the study will be 24 months. Participant recruitment will occur through written informed consent prior the start of the study after thorough description.

5 LOCAL AND STUDY-WIDE RECRUITMENT METHODS

Subjects will be identified from the Roswell Park Comprehensive Cancer Center Genitourinary (GU) clinic and in the inpatient wards when they are scheduled for inpatient oncological surgical procedures. All clinic staff will be informed about the study to help with recognizing patients. When a potential patient is identified in clinic, one of the study team members will be notified and will discuss the study aims, risks and benefits. The subject will then be asked to sign an informed consent after proper review.

6 MULTI-SITE RESEARCH

N/A

7 STUDY TIMELINES

The study duration is 24 months or until target accrual is reached. Subjects will be on study until they are discharged from the hospital. Subjects will be followed 30 days post discharge to note any complications or readmission. A post study questionnaire will be given to participants during one of their follow up visits which happen 2 weeks, 6 weeks, 3 months post discharge or over the phone if missed.

8 STUDY ENDPOINTS

The primary study endpoint is measuring early recovery of postoperative course by calculating early return of bowel motion (passing flatus and/or stool on which postoperative day), presence or absence of nausea and/or vomiting, presence or absence of chest symptoms (cough, sputum

and ability of using incentive spirometry), early discharge from the hospital and 30 days surgical related complications and readmissions.

The secondary study endpoint is measuring the range of joint movement in upper and lower joints of body, using the 3D motion tracking system (Xsens), to identify the minimum required level of mobility for better early postoperative course recovery.

A few other secondary endpoints concluded from the post experiment questionnaire include: assessing encouraged walking in the hospital setting subjectively improves their exercise habit outside of the hospital, how was the application of the sensors in a hospital setting as this is the first study to do so, and to assess the subjective impact of complications on quality of life.

9 PROCEDURES INVOLVED

This is a prospective randomized controlled trial comparing the early postoperative course of patients who undergo inpatient oncological procedures after assessment of their baseline physical activity before the surgery, using validated questionnaires in the clinic, to have a homogenized sample for the study. Participants will be randomized to the control arm (40 participants) and intervention group (40 participants). Control group participants will be asked to walk one to two laps around the ward twice per day, on the first day after the surgery following the usual clinical practice at Roswell Park Comprehensive Cancer Center-urology department (RPCCC). Their movement will be tracked with 3D motion tracking system (Xsens). The intervention arm participants will be asked to walk for minimum 30 minutes per day and their movement also will be tracked with Xsens. In both arms the patients will be asked to mobilize (walk out of the bed) on first day post-surgery under supervision and assistant of attending nurse in the floor if their clinical situation allowed. If patient cannot complete the walking tasks, they will be excluded from the study and they will be replaced by recruiting other patients.

Xsens is a wireless technology that makes use of sensors. The sensors are applied in a non-invasive manner and do not require the suit to be applied. There are various configurations of the sensors that can be utilized. The minimum number of sensors needed is 7. They are applied by using Velcro bands. The entire set-up takes about 5-10 minutes.

The study duration is 24 months or until target accrual is reached. In both arms their mobility will be tracked till they discharged from the hospital. In both arms we will assess the symptoms and signs of gastro-intestinal complications (nausea, vomiting, abdominal pain, passing flatus or stool) and chest symptoms (coughing, sputum, utilizing incentive spirometry) until they are discharged from the hospital. We will continue to follow them for 30 days post discharge to note any complications or readmission.

Patients at standard follow ups, 2 weeks, 6 weeks, 3 months or over the phone will complete a short post study questionnaire (Appendix B). The last three questions are taken from Woodfield et al., who assessed postoperative problems from the perspective of the patient on the identification of complications after surgery (11).

10 WITHDRAWAL OF SUBJECTS

N/A

11 RISKS TO SUBJECTS

Risk of fall is associated with mobility. This will be minimalized with standard procedures including; patient risk of fall stratification, supervised patient mobility and using balance assessment programs.

12 POTENTIAL BENEFITS TO SUBJECTS

There is no direct benefit to subjects.

13 DATA AND SPECIMEN BANKING

N/A

14 SAFETY REPORTING

N/A

15 DATA MANAGEMENT AND CONFIDENTIALITY

Data will be collected through computer logging, note taking, paper/pencil or computer forms. Demographic information (position title, years of experience, area of expertise) will be collected but names will not be associated with the data. Individual privacy will be maintained in all published and written data resulting from the study. Participants will be given a unique code/ID number. This number will be used instead of names to identify information collected during the study. De-identified data will be kept indefinitely, in paper and electronic form and on computers accessible to the investigators and their research assistants.

16 STATISTICAL PLAN

Demographics: Subject demographic and clinical characteristics will be reported by group using the appropriate descriptive statistics and graphical summaries. Comparisons will be made between groups using the Mann-Whitney U or Chi-square tests, as appropriate.

Randomization: Subjects will be randomized to the control and intervention groups in a 1:1 fashion using a permutation block design (block sizes = 4). The randomization list will be developed by the study statistician.

Primary Analysis: The primary objective is to evaluate changes in mobility between the control (standard of care) and intervention (additional activity) groups. The primary outcomes are measures of mobility (i.e. range of movement), which are treated as continuous measures and will be summarized by group and time-point using the mean, median, and standard deviation. The measures of mobility will each be modeled as a function of treatment group, time post-surgery, their two-way interaction, and random subject effects using a linear mixed model. Within each group, the effect of time on the mean will be evaluated using tests about the appropriate contrasts of model estimates. The effect of the two groups on the time-mobility relationship will be evaluated using an F-test about the interaction term. All model assumptions will be evaluated graphically and transformations will be applied as necessary.

Secondary Analyses: The secondary objective is to evaluate the impact on post-surgical complications. The complication status (present/absent) and grades will be summarized by group and compared using Fisher's exact test or the chi-square test, as appropriate.

The association between complication status and changes in measures of mobility may be evaluated using logistic regression models.

Sample Size Determination: The power calculations are based on the primary analysis, which compares the changes in measures of mobility between the two groups. Since the form of the models is unknown beforehand, a simplified and conservative power calculation is based on comparing the mean change (baseline to discharge) in a given mobility measure between groups using a two-sided, two-sample t-test. With a sample size of n=40 per group, we have 80% power (at $\alpha = 0.05$) to detect a difference of at least 0.63 standard deviations. Such a moderate effect size would be considered clinically relevant.

17 VULNERABLE POPULATIONS

N/A

18 COMMUNITY-BASED PARTICIPATORY RESEARCH

N/A

19 SHARING OF RESULTS WITH SUBJECTS

N/A

20 SETTING

The potential subjects will be identified in the genitourinary clinic at Roswell Park Comprehensive Cancer Center where they will meet with one of the research team members and in the inpatient wards. The research procedure will be performed at Roswell Park Comprehensive Cancer Center inpatient wards.

21 PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF SUBJECTS

Participants will be free to determine whether to respond to requests for participation. All participants, even after providing consent, are free not to answer any questions, or choose to end their participation and thus can privately maintain control over the level of information provided to us. No PHI will be recorded.

Data will be stored on a secured, password protected RPCI server in the Urology department that is maintained by the information technology department. Access will be limited to the PI and Coinvestigator's.

22 RESOURCES AVAILABLE

Our research team comprises of surgeons, clinical and research fellows, research assistants and coordinators. Our diverse team has worked on similar projects and has extensive experience in undergoing clinical trials. Dr. Khurshid Guru's laboratory, the Advanced Technologies Laboratory for Advanced Surgery (ATLAS) is located at Grace Cancer Drug Center is approximately 1400 sq. feet. A major portion of the lab is dedicated for industrial and human factor engineering researches and sciences. The laboratory is fully equipped to safely carry out and develop the proposed work. The laboratory personnel comprised of surgeons, clinical and research fellows, medical illustrators and engineers are highly experienced in conducting clinical research. The innovative multidisciplinary team utilizes the lab space for equipment storage and

data analysis. Space and network access are readily available throughout the study period. The PI, Dr. Khurshid Guru, and the research team members have their dedicated equipped work space with secretarial support. All participating research members will receive an in-service that adequately explains the research protocol, procedures and individual duties.

23 PRIOR APPROVALS

N/A

24 ECONOMIC BURDEN TO SUBJECTS

There are no costs to the subjects.

25 CONSENT PROCESS

This study will not be initiated until the protocol and informed consent document(s) have been reviewed and approved by a properly constituted Institutional Review Board (IRB) or Independent Ethics Committee (IEC). Each participant (or legal guardian) shall read, understand, APPROVED RPCI IRB Protocol and sign an instrument of informed consent prior to performance of any study-specific procedure. It is the responsibility of the investigator to ensure that the participant is made aware of the investigational nature of the treatment and that informed consent is given. The Investigator is responsible for the retention of the participant log and participant records; although personal information may be reviewed by authorized persons, that information will be treated as strictly confidential and will not be made publicly available. The investigator is also responsible for obtaining participant authorization to access medical records and other applicable study specific information according to Health Insurance Portability and Accountability Act regulations (where applicable). This study will be conducted in compliance with all applicable laws and regulations of the state and/or country and institution where the participant is treated. The clinical trial should be conducted in accordance with the ethical principles embodied in the Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, consistent with good clinical practice and the applicable regulatory requirements and according to the guidelines in this protocol, including attached appendices. The RPCI SOP: Informed Consent Process for Research (HRP-090) will be followed.

This study will be conducted in compliance with all applicable laws and regulations of the state and/or country and institution where the participant is treated. The clinical trial should be conducted in accordance with the ethical principles embodied in the Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, consistent with good clinical practice and the applicable regulatory requirements and according to the guidelines in this protocol, including attached appendices.

26 PROCESS TO DOCUMENT CONSENT IN WRITING

The Investigator (or IRB specified designee) is responsible for obtaining written consent from each participant or the participant's legally authorized representative in accordance with GCP guidelines using the approved informed consent form, before any study specific procedures (including screening procedures) are performed. The informed consent form acknowledges all information that must be given to the participant according to applicable GCP guidelines, including the purpose and nature of the study, the expected efficacy and possible side effects of

the treatment(s), and specifying that refusal to participate will not influence further options for therapy. Any additional information that is applicable to the study must also be included. Additional national or institutionally mandated requirements for informed consent must also be adhered to. The participant should also be made aware that by signing the consent form, processing of sensitive clinical trial data and transfer to other countries for further processing is allowed. The Investigator shall provide a copy of the signed consent form to the participant and the signed original shall be maintained in the Investigator File. A copy of the signed consent form must be filed in the participant file. At any stage, the participant may withdraw from the study and such a decision will not affect any further treatment options. The RPCC "SOP: Written Documentation of Consent (HRP-091)" will be followed.

27 DRUGS OR DEVICES

3D motion tracking system (Xsens) is commercially available device used in research, especially sport medicine. These devices will not be used for any off label purposes. They will be stored in the ATLAS lab (G-401).

28 REFERENCES

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29 APPENDICES/ SUPPLEMENTS

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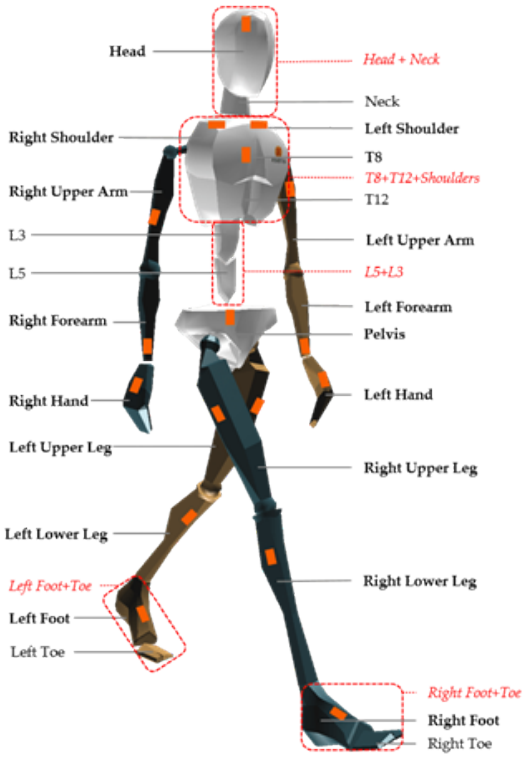
Appendix A:

Xsens Motion Tracking Technology



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Appendix B.

Post study questionnaire documenting postoperative problems from the perspective of the patient and study feedback

Post Experiment Questionnaire

Participant ID:
Date of Surgery:
Date of Questionnaire Completion:

How satisfied were you with the process of applying of sensors?

Very Unsatisfied	Unsatisfied	Neutral	Satisfied	Very Satisfied

Were the sensors comfortable throughout your wear?

Very Uncomfortable	Uncomfortable	Neutral	Comfortable	Very Comfortable

Did having the sensors on push you to walk more?

Very Unlikely	Unlikely	Neutral	Likely	Very Likely

How much of your previous mobility have you regained since the operation?

0%	25%	50%	75%	100%

Have you been pushing yourself to exercise since the operation?

Never	Rarely	Sometimes	Often	Always

How Much Pain Do You Feel Day to Day?

Not At All	A Little Bit	Moderately	Quite A Bit	Extremely

Your quality of life now compared to the month before the surgery?

A lot worse	Somewhat Worse	About the Same	Somewhat Better	A Lot Better

How Do You Feel About Yourself as A Result Of Your Surgery?

A lot worse	Somewhat Worse	About the Same	Somewhat Better	A Lot Better