Protocol Title: Wearable Bioimpedance Analyzer for Tracking Body Composition Changes: A Randomized Controlled Trial
Protocol Version: 1.1
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1) Abstract

a) Obesity, namely at body mass index (BMI) levels exceeding 40kg/m^2 (class III obesity), is a risk factor for many diseases including osteoarthritis (OA). In arthroplasty, patients in this population frequently present for and are turned away from surgical intervention. Subsequently, efforts are made to decrease BMI through simple weight loss, yet these have been suggested as ineffective and counterproductive. Furthermore, simple weight loss may include muscle mass loss, which is an additional risk factor for surgery. In our clinic, efforts have been made to encourage muscle mass gain and body fat loss over simple weight loss where progress has been tracked through stationary, multi-frequency bioimpedance analysis (BIA). BIA is a readily available technology offered to industry and consumers, and BIA has recently been incorporated into wearable devices. In our department, a novel clinic aimed at holistically serving the osteoarthritic-class III obese population for controlled and monitored weight loss through BIA.

This study, a randomized controlled trial, aims to recruit adult patients with class III obesity presenting to the arthroplasty-obesity clinic. While all patients will receive individual body composition coaching to increase muscle mass and decrease body fat mass, they will be randomized to one of two cohorts: the study group will receive a wearable BIA wristband (InBody BAND 2) and instruction on its use in addition to the standard coaching, and the control group will only receive the standard coaching.

This study aims to identify if the use of a wearable BIA wristband aids in the desired body composition changes. In addition, this study aims to quantify the body composition changes exhibited by each cohort. Finally, this study aims to track surgical outcomes for those patients that are indicated for total joint arthroplasty.

2) Background and Significance/Preliminary Studies

a) Obesity is a well-known epidemic in the US with prevalence nearing 40%. [1] Obesity is a risk factor for a myriad of disease states including osteoarthritis (OA) due to increased load on the weightbearing joints. Therefore, patients with obesity, and namely those with body mass index (BMI) approaching >40kg/m^2 (class III obesity), suffer from OA disproportionately compared to their non-obese peers. [2] As this population frequently reports to arthroplasty clinics, studies have identified increased rates of post-operative complications following total joint arthroplasty (TJA) specifically in the class III obese population. [2-5] To combat this increased risk, arthroplasty surgeons traditionally have excluded this population from their surgical practice or encouraged their patients to lose weight in order for their BMI to drop below 40kg/m^2; however, these practices have been recently questioned. [6-8]

With the validity of lowering BMI to improve TJA outcomes being questioned, studies have made efforts to identify more patient-specific factors such as body composition. Body composition can be identified through several modalities including anthropomorphic measurements, DEXA, MRI, and CT. [9-11] In addition, bioimpedance

analysis (BIA) offers rapid, accurate, and non-invasive assessment without the use of ionizing radiation. [9, 12, 13] BIA can be completed through multiple devices including a stationary, scale-like device, a portable ECG-like device, or even wearable wristbands.

Our group has conducted numerous studies focusing on body composition in arthroplasty patients, including changes they experience following surgery and pre-operative risk identification. By employing both clinic-based and home-based assessments more frequently than patients would normally have, this study aims to identify any benefit, if any, a wearable BIA device serves in an obese-arthroplasty population.

3) Study Aims

a) Aims:
   i) To identify if the use of a wearable BIA wristband aids in the desired body composition changes (body mass loss, fat mass loss, skeletal muscle mass gain)
   ii) To quantify the body composition changes exhibited by each cohort
   iii) To track surgical outcomes for those patients that are indicated for total joint arthroplasty

b) Hypotheses:
   i) The wearable group will exhibit the desired body composition changes more rapidly than the control group
   ii) The wearable group will exhibit greater desired body composition changes more rapidly than the control group
   iii) The wearable group will less post-operative complications than the control group

4) Administrative Organization

a) This study will solely be completed at the University of Iowa Healthcare and Clinics Department of Orthopaedics and Rehabilitation.

5) Study Design

a) Experimental design of the study: randomized controlled trial with single blinding
b) Study population general description
   i) Specify total number of adult subjects, age range and percent by gender
      (1) 90 subjects (>18 years old)
      (2) 50% male, 50% female
   ii) Specify total number of minor subjects (less than 18 years of age), age range and percent by gender.
      (1) none
c) Sample size determination and power analyses
   i) A power analysis was performed by the orthopedic department statistician Natalie Glass.
d) Study outcomes/endpoints
   i) Primary outcomes
      (1) Muscle mass, body mass, and fat mass changes from baseline at 3-, 6-, 9-, and 12-months
   ii) Secondary outcomes
      (1) Time to achieve desired body composition changes
      (2) Time to TJA indication
      (3) Surgical outcomes for those that undergo TJA

6) Study Procedures

a) Describe Subject selection procedures
   i) Describe the sampling plan including Inclusion/Exclusion criteria (subject and disease characteristics)
      (1) Inclusion Criteria
         (a) Adults > 18 years
         (b) BMI > 40kg/m2
         (c) Presenting to arthroplasty-obesity clinic with desire for total joint arthroplasty procedure
         (d) Owns a smartphone capable of handling iOS or Google Play apps
      (2) Exclusion Criteria
         (a) Has a pacemaker or other electronic pacemaker placement
         (b) Inability to complete study protocols
         (c) Inability to stand unsupported for 60-90 seconds
   ii) Indicate if the study plans to enroll non-English speaking subjects. If so, specify language(s), who will translate documents, who will serve as a translator. The IRB must review and approve all translated documents.
      (1) This group will not be enrolled
   iii) Indicate if the study will enroll subordinates of the PI or a member of the research team.
      (1) This group will not be enrolled
   iv) Indicate if the study will enroll pregnant women for research on fetuses and neonates
      (1) This group will not be enrolled
   v) Indicate if the study will enroll adult subjects who have cognitive impairment and are not able to provide legally effective informed consent. If so, specify how you will assess capacity to consent and whether you will enroll subjects who cannot consent for themselves. Describe the consent process with the Legally Authorized Representative.
      (1) This group will not be enrolled
   vi) Indicate if the study will enroll subjects whose capacity to consent may change during the study. If so, specify how you will assess capacity to consent and how you will obtain consent from subjects or their Legally Authorized Representative.
      (1) This group will not be enrolled
b) Describe all possible recruitment procedures
   i) Describe all recruitment methods and materials.
      (1) Subjects reporting to arthroplasty-obesity will be recruited by the study team members using the informed consent form as materials
   ii) Specify if the researcher will use protected health information (PHI) to identify potential subjects – what data elements, why you couldn't recruit without accessing PHI, why you couldn't obtain patient permission, how you will protect identified PHI used for recruitment purposes, when you will remove identifiers OR justification for storing identifiers until the end of the recruitment period. You must agree to agree not to reuse or disclose this information.
      (1) The subjects will be identified by those reporting to arthroplasty-obesity clinic, which the PI has access to. The identifiable information used will be the patient's name, age, BMI, and reason for reporting to clinic.
   iii) Describe screening prior to consent

(1) Patients' medical record will be reviewed for their age, BMI, and reason for reporting to clinic. When they are approached, they will be asked if they have a smartphone and/or an electronic cardiac device.

iv) What recruitment materials will be provided to the potential participant (brochures/information sheets/video presentation)?
(1) The informed consent will be used.

v) Specify if you are discussing study in person or by phone prior to consent.\
(1) This will be discussed in person.

c) Indicate where and when consent be obtained
i) State who will conduct the consent process
(1) Any member of the study team will conduct the consent process

ii) Describe the steps of the consent process in detail.
(1) The patient will be identified on the clinic schedule, and they will be approached in their private clinic room. They will be asked if they are interested in participating in a study. If they agree, they will be asked the above screening questions. If they are eligible a study team member will orally review the consent form and have the participant review the written consent form. All questions will be answered.

iii) Specify what documents will be used in the consent process (Informed Consent Document, Consent Letter or Information Sheet, Assent Document, Verbal/Phone Script, Exempt Information Sheet, Consent Summary, Other)
(1) Informed consent form

iv) Specify if the study requires a waiver of consent OR waiver of documentation of consent. If so, provide justification.
(1) No waiver

v) Specify how long subjects can consider whether to participate AND if they can consult with other people before deciding to participate.
(1) They will be eligible until the end of their initial clinic visits to arthroplasty-obesity clinic

vi) Specify how long after subjects agree to participate before the study procedures begin.
(1) Immediately

d) Describe screening procedures
i) Describe eligibility screening procedures before and/or after consent.
(1) Subjects will be asked about owning a smartphone and if they have an electronic cardiac device prior to the consent process

ii) Describe the screening schedule (number of visits, length of visits)
(1) The screening visit will be at the enrollment visit

iii) Indicate whether screening tests/procedures are part of standard care or done for research purposes only
(1) These are done per research protocol

iv) Specify what happens with screen failures (including any data gathered during screening)
(1) They will not be eligible to enroll, and no information/PHI will be recorded.

e) Describe randomization procedures (if applicable) – Specify the randomization scheme and process.

i) Block randomization in RedCap. Patients will be randomized at the conclusion of their clinic visit as to not influence the education they receive by the PI/provider

f) Describe study intervention(s)
   i) For Other types of intervention studies, describe:
      (1) Active intervention description
         (a) Patients will be provided a BIA wearable (InBody BAND 2) and instructions regarding downloading smartphone app. Education regarding the device and app will be provided. In addition, they will receive the standard procedures/education provided in arthroplasty-obesity clinic
      (2) Control group
         (a) They will receive the standard procedures /education provided in arthroplasty-obesity clinic

g) Describe all study assessments and activities
   i) Provide a thorough, detailed description
      (1) Randomization
         (a) Once enrolled, patients will be randomized by a non-PI study member. Randomization will occur after the clinic standard education as to not be influenced based on randomization group.
      (2) All patients
         (a) All patients will experience a "coaching" period and be eligible for a "surgical period". All patients (study and control) will undergo the clinic standard operating procedures of stationary BIA, hand-grip strength, and exercise and nutritional education (weight/resistance training, low carbohydrate/high protein diet) in the "coaching" period. All patients will also be advised of the goal to maintain or lose body mass, lose body fat, and gain muscle mass, which is also clinic standard operating procedure. Patients will follow-up in the clinic per standard protocol at approximately every 3 months (±1 month). At each visit, stationary BIA, hand-grip strength, and exercise and nutritional coaching will be repeated, as is standard in clinic. All patients will be eligible to be indicated for TJA at the PI's discretion. Per clinic procedures, patients are indicated for TJA as they achieve their body composition goals (maintain or lose body mass, lose body fat, and gain muscle mass). All patients will be instructed to not discuss their study arm (wearable or control) with the PI. Patients are eligible to enter the surgical period at any point during the coaching period. If patients feel that they meet their goals prior to they are eligible to reschedule their appointment sooner than the next visit. All patients will receive a phone call from a study team member every 1 month to assess compliance with study arm and check in on perceived progress.
      (3) Wearable group
         (a) If patients are randomized the wearable group, they will be provided a wearable and instructions on installing the app and its features. They will be instructed to take BIA measurements at least weekly via the wearable. The wearable group will be instructed at the beginning of each visit to remove and keep their wearable out of sight of the PI during their visit.
      (4) Patients who enter "Surgical" period

(a) Patients who are indicated for TJA (at the PI's discretion) will leave the coaching period and enter the surgical period. Patients' medical record will be followed if they are indicated for TJA for post-operative outcomes such as infection, reoperation, implant failure. Surgical follow-up will occur for up to 24 months following study enrollment.

ii) Provide a schedule of all study assessments and subject activities, including a tabular representation or timeline as applicable
(1) See **Table I** below

h) Recontacting Subjects Lost to Follow Up – Indicate if the researcher will attempt to locate subjects if the research team is unable to reach them through the contact information they provided. Describe the procedures and justification for these efforts to locate subjects.
i) Research members will not contact the patients lost to follow, as standard clinic procedures have nursing staff contact the patients.

i) Subject Compensation
i) Specify compensation method(s)
(1) Patients will not be compensated monetarily. Those randomized to the study cohort will be able to keep their wearable device, if desired.
ii) Describe the compensation plan, including amount per visit, total compensation amount, pro-rating for early withdrawal
(1) N/A
iii) Indicate whether the study will use the departmental cash handling plan or obtain approval from Accounting Services for a study-specific cash handling plan.
(1) N/A

7) Privacy and Confidentiality Protections

a) Describe privacy protections – collecting data in a private space, collecting the amount and type of information you need to answer your research question(s)
i) Only the minimum necessary data will be collected. The data collected will be done in a private clinic room.

b) Describe plans and justification for collecting social security number (SSN)
i) N/A

c) Confidentiality / Data Security Plans – Refer to the Data Security Educational Tool and the Protecting Sensitive Data page of the UI ITS website. Specify plans for transmitting, transporting and/or storing:
i) Paper records
(1) Informed consent documents to be kept in PI's locked office
ii) Electronic records - Specify who is responsible for maintaining security. Researchers are advised to consult with the departmental IT representative to establish a data security plan that is appropriate to the level of security of the data being collected/stored for the project.
(1) Standard protections on departmental server
iii) Biospecimens - Specify who is responsible for maintaining security.
(1) N/A

d) Plans for sharing data or taking data outside the UI
i) N/A

8) Risks and Benefits

a) Describe all possible risks (physical, emotional or psychological, financial, legal or social risks).
   i) Risks include loss of information/privacy, falling off stationary BIA scanner, hand pain from hand grip strength testing.
b) Describe all steps to minimize any possible risk to subjects.
   i) Data will only be accessed by need-to-know study members, a study team member will supervise and "spot" the subject on the stationary BIA scanner, patient will be advised to take rests in between hand grip strength testing to minimize pain.
c) Describe all guaranteed direct benefits to subjects (do not include compensation or hypothesized results).
   i) None
d) Describe potential benefits to society from the results of the research.
   i) Future patients will benefit from knowing if wearable technology has an effect or not.

9) Safety Monitoring Plan

a) N/A

10) Data Analysis Plan

a) Describe statistical analysis methods as appropriate. Consult with a biostatistician, if appropriate. The analysis plan should correspond with the data collection described in the Study Procedures section. Describe plans for intent-to-treat methodology and any sample stratification.
   i) Noninferiority comparison of the primary outcome and secondary outcome between the treatment groups at each time points.
   ii) Multivariate analysis to compare patient demographics between the two treatment arms.
   iii) Non-parametric tests such as ANOVA and ANCOVA will be utilized to determine if there is any difference between the two groups.
b) Provide the rationale or power analysis to support the number of subjects proposed to complete the study.
   Group sample sizes of 44 in the treatment and control arm achieve 80% power to detect a difference of 1.676 in a design with 5 repeated measurements having a compound symmetry covariance structure when the standard deviation is 3.610, the correlation between observations on the same subject is 0.500, and the alpha level is 0.050

11) Tables and Figures

Table I. Schedule of study procedures.

Study Period	**Coaching[a]**													**Surgical[a]**
Visit Number	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**	**V10**	**V11**	**V12**	**V13**	**EMR follow-up**
Month	**0**	**1**	**2**	**3**	**3**	**4**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**Until Month 24**
All Patients														
Screening	X													
Consent	X													
Randomization	X													
Clinic Education[b]	X			X			X			X			X	
Stationary BIA[b]	X			X			X			X			X	
Handgrip Strength[b]	X			X			X			X			X	
Phone Visit		X	X		X	X		X	X		X	X		
Wearable Group														
Wearable Distribution	X													
Wearable Compliance Check		X	X	X	X	X	X	X	X	X	X	X	X	
Surgical Outcomes Check[c]														X

[a]Patients may exit the Coaching period and enter the Surgical period at any time point
[b]Standard protocol for all patients presenting to arthroplasty-obesity clinic
[c]Only for study group
[d]Only for subjects that undergo TJA. Will occur via EMR rather than direct patient contact.

12) Literature Citations

1. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser 894: i, 2000
2. Obesity and total joint arthroplasty: a literature based review. In: J Arthroplasty. United States: 2013 Elsevier Inc. 714. 2013
3. Andrew JG, Palan J, Kurup HV, Gibson P, Murray DW, Beard DJ. Obesity in total hip replacement. J Bone Joint Surg Br 90(4): 424, 2008
4. DeMik DE, Bedard NA, Dowdle SB, Elkins JM, Brown TS, Gao Y, Callaghan JJ. Complications and Obesity in Arthroplasty-A Hip is Not a Knee. The Journal of arthroplasty 33(10): 3281, 2018
5. Foreman CW, Callaghan JJ, Brown TS, Elkins JM, Otero JE. Total Joint Arthroplasty in the Morbidly Obese: How Body Mass Index ≥40 Influences Patient Retention, Treatment Decisions, and Treatment Outcomes. J Arthroplasty 35(1): 39, 2020
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8. Friedman RJ, Hess S, Berkowitz SD, Homering M. Complication rates after hip or knee arthroplasty in morbidly obese patients. Clinical orthopaedics and related research 471(10): 3358, 2013
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13. Qin ES, Bowen MJ, James SL, Chen WF. Multi-segment bioimpedance can assess patients with bilateral lymphedema. J Plast Reconstr Aesthet Surg 73(2): 328, 2020