Study Title:	A resistance training program to improve physical function in sarcoma survivors
Protocol Number:	19942
Version Number:	4.0
Version Date:	16 APR 2020
Replaces:	version 3.0, dated 10 MAR 2020
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SUMMARY OF CHANGES

Protocol version 3.0 to 4.0 (16 APR 2020)

Section	Page(s)	Change	Justification
1.5.1	13	Include additional safety language for virtual sessions.	Added safety precautions.
3.1	15	Include remote assessment language.	Clarify remote visit implementation.
5.4	22	Include baseline assessment omissions for remote visit.	Removal of baseline assessments that will not be performed virtually.
6.1.1	27, 28	In-person training changed to initial training. Updated for virtual visits.	Clarify select testing measures to be adapted for virtual delivery.
6.1.3	28	Include that end of study assessment may be omitted, delayed, or delivered entirely virtually.	Clarify end of study updates for periods of hospital recommendations for decreased in-person contact.
12.3.1	37	Administrative edits.	Typographical errors corrected.

Protocol version 2.0 to 3.0 (10 MAR 2020)

Section	Page(s)	Change	Justification
Throughout	Throughout	Exercise physiologist via 1:1 videoconferencing has been updated for optional group videoconferencing.	Allow for participants to consent to optional group videoconferencing.
Study Design	6	Visits and assessments referenced in this protocol may refer to those performed both in-person or virtually through videoconferencing.	Allow for participant visits to be either in-person or virtual in nature.
1.3	15	Include optional group training.	To improve efficiency of training and to create peer support.
5.5	21	1:1 web-based videoconferencing for the first two weeks. After two weeks, the participant may decide to join a group videoconference with 1-2 other participants, or continue 1:1 with the EP.	To ensure initial training specifications have been outlined before providing option for group training.
12.3 & 12.3.1	34	Electronic or phone consent.	Allow for additional consenting modalities.

Protocol version 1.0 to 2.0 (17 SEP 2019)

Section	Page(s)	Change	Justification
1.5.1	12	Update DXA scans to include variance between baseline and follow-up.	Clarify imaging protocol; reduce radiation exposure for participants
5.8	22	Included DXA scan at follow-up footer.	DXA scan at follow-up will omit bone mineral density since there is no reasonable expectation for change over a 3 month period.

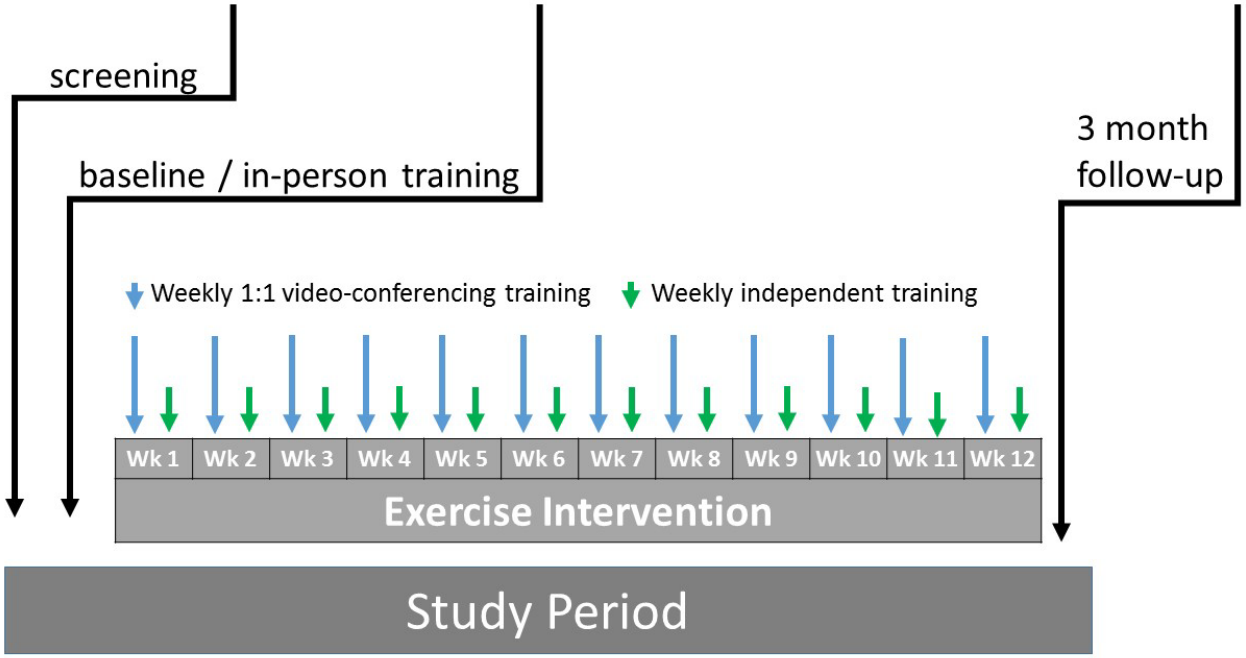
SYNOPSIS

Study Title	A resistance training program to improve physical function in sarcoma survivors
Protocol #	19942
Study Center	OHSU, single-site
Précis	Treatment of sarcomas can significantly affect physical function. Physical activity is an effective method to improve physical function and regain muscle performance; however, no effective approach has been routinely implemented that can improve physical function in sarcoma survivors. This study seeks to assess the feasibility of implementing a resistance training exercise regimen as a means to improve physical function in individual sarcoma survivors. In this study, eligible participants will be assigned a series of progressive training exercises that are to be performed biweekly for a total of 12 weeks. Each week, one training sessions will be performed independently by the participant, whereas the other will be monitored by a certified exercise physiologist in a videoconference with the participant. Video conferences may be in groups of 1-3 participants, depending on the preferences of the participant for 1:1 or a small group session. This "tele-exercise" approach allows the exercise physiologist to supervise exercise and adjust training programs to optimize safety and efficacy but reduces the patient burden by allowing the participant to exercise at home, which we expect will result in greater program adherence and study retention.
Primary Objective	The primary objective of this trial is to assess the feasibility of an individualized resistance training program in sarcoma survivors.
Secondary Objective	1. To assess secondary measures of feasibility of a home-based, individualized PRT program in sarcoma survivors 2. To determine if a 3-month resistance training program improves physical function in sarcoma survivors.
Exploratory Objective	To determine if a 3-month resistance training program improves body composition and bone mineral density in sarcoma survivors.
Primary Endpoints	The primary endpoint of feasibility will be measured by 3-month retention rate, exercise adherence rate and frequency of related serious adverse event.

Secondary Endpoints	Absence of related serious adverse events 1. Successful development of individualized PRT prescription based on functional limitations [100% of subjects receive individualized PRT prescription]. 2. Change in PROMIS-Cancer physical function score [at baseline and 3 months from start of planned exercise intervention] 3. Change in SF-36 physical function score [at baseline and 3 months from start of planned exercise intervention] 4. Change in GLTEQ physical activity score [at baseline and 3 months from start of planned exercise intervention] 5. Change in FACT-F fatigue score [at baseline and 3 months from start of planned exercise intervention] 6. Difference in 1-repitition maximum (1RM, kilogram) [at baseline and 3 months from start of planned exercise intervention] 7. Change in short physical performance battery (PPB) score [at baseline and 3 months from start of planned exercise intervention] 8. Change in grip strength (kilogram [Kg]) [at baseline and 3 months from start of planned exercise intervention] 9. Change in instrumented 6-minute walk test (i6MWT) [at baseline and 3 months from start of planned exercise intervention] 10. Change in instrumented postural sway (ISway) [at baseline and 3 months from start of planned exercise intervention] 11. Change in instrumented timed up and go test (iTUG) [at baseline and 3 months from start of planned exercise intervention]
Exploratory Endpoints	1. Change in weight [at baseline and 3 months from start of planned exercise intervention] 2. Change in total body fat mass [at baseline and 3 months from start of planned exercise intervention] 3. Change in fat free mass [at baseline and 3 months from start of planned exercise intervention] 4. Change in lean mass [at baseline and 3 months from start of planned exercise intervention] 5. Change in bone mass [at baseline and 3 months from start of planned exercise intervention]
Number of Participants	10
Duration of Intervention	12 weeks
Duration of Follow Up	3 months [from start of planned exercise intervention]

Inclusion Criteria	1. Age ≥15 years 2. History of histologically-confirmed sarcoma 3. History of treatment with surgery, radiation and/or chemotherapy for the sarcoma diagnosis 4. Completion of sarcoma treatment and no evidence of recurrent or residual disease on surveillance exam or imaging ≥2 years prior to study enrollment 5. Sarcoma location must have been in the extremities, body wall, pelvic/shoulder girdle or axial skeleton. 6. Currently engaging in <1 hour of resistance exercise per week by self-report. 7. Able and willing to commit to attending weekly video coaching sessions and independently completing weekly resistance training sessions. 8. Able and willing to commit to attending one initial in-person training session and one in-person follow-up assessment.
Exclusion Criteria	1. Medical contraindication(s) to any and all resistance training as determined by treating physician. 2. Non-English speaking. 3. Dependent on a mobility device (e.g., crutches, wheelchair) for independent activities of daily living (IADLs). Use of a cane is permitted. 4. Known psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the trial. 5. Any condition that, in the opinion of the investigator, would interfere with evaluation of study treatment or interpretation of participant safety or study results (e.g., pregnancy).
Statistical Considerations	This study has no formal hypothesis test but to assess the feasibility of the exercise intervention. The primary objective of feasibility will be determined by the study achieving 90% participant retention [i.e., 9 of 10 patients complete end-of-intervention assessments] with more than 75% exercise adherence rate [each participants completed end-of-intervention assessment also completed at least 18 of 24 prescribed training sessions] without related serious adverse events. Successful development of individualized PRT prescription based on functional limitations also be determined as a secondary feasibility measure [100% of subjects receive individualized PRT prescription]. The secondary endpoints of efficacy at baseline and 3 month follow-up will be summarized using descriptive statistics and compared using a paired t-Test.

SCHEMATIC OF STUDY DESIGN



This is a prospective study to assess the feasibility of implementing a resistance training regimen to improve physical function limitations of sarcoma survivors. In general, participants that previously received treatment for their sarcoma (any subtype), have no evidence of disease, and completed treatment at least 2 years prior to study enrollment are considered eligible. Participants will undergo visits and assessments throughout the protocol. Visits and assessments referenced in this protocol may refer to those performed both in-person or virtually through videoconferencing. Participants will undergo baseline assessments using a variety of survey tools and functional assessments to establish individual limits of physical function. Participants will subsequently be assigned a series of resistance training exercises and provided instructional guidance from a certified exercise physiologist. Participants will then perform their assigned exercises twice weekly during at-home training sessions. Each week, one of these training sessions will be conducted under the supervision of the exercise physiologist via videoconferencing. The other training session will be independently performed by the participant. Participants will undergo a repeat assessment of physical function using surveys and functional tests at a follow-up visit 3 months after initiating study intervention. Up to 10 participants will be recruited to this study.

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1. BACKGROUND INFORMATION AND SCIENTIFIC RATIONALE

1.1 EFFECTS OF EXERCISE ON POST-TREATMENT CANCER PATIENTS

While advancements in therapeutics continue to improve patient survivorship, the effects of treatment are not without adverse psychological and physical side effects, which can negatively impact quality of life.[1] Physical side effects experienced by cancer patients post-treatment include fatigue, decreased muscle strength and lean body mass, reduced bone mass, as well as diminished aerobic capacity.[2,3] Moreover, low skeletal muscle mass (i.e., sarcopenia) is shown to be an independent poor prognostic factor for survival among patients with various cancers.[4-6] Routine exercise, such as aerobic or progressive resistance training, allows for improving a patient's health status and counter these adverse side effects by increasing cardiopulmonary function, muscle strength, bone mineral density, while reducing body weight, fat mass, and fatigue.[7-9] Particularly, progressive resistance training appears to be most effective at counteracting muscle wasting.[7,8]

1.2 PROGRESSIVE RESISTANCE TRAINING

There is a strong association between lean body mass, muscle strength, and the ability to adequately perform functional measures of activities of daily living (e.g., chair rising, stair climbing).[10,11] Not surprisingly, sarcopenia following anticancer therapy often leaves cancer patients with diminished lean body mass, as well as decreasing muscle strength that together negatively impact the functional performance and independent lifestyle. Progressive resistance training (PRT) is particularly efficacious for adult and elderly cohorts given its efficacy in counteracting sarcopenia, abating osteoporosis, and reversing many physiological and functional impairments that accrue with age.[12]

The goal of PRT is to enhance the ability of muscles to generate force by using repetitive loads (i.e., training intensity).[13] In general, PRT involves challenging the skeletal muscles with some form of resistance (e.g., exercise machines, free weights, and elastic bands) that are lifted repetitively (~8–15 repetitions maximum [RM] per set) to the point of neuromuscular fatigue.[13] Optimal PRT sessions typical include a 48 to 72 hour recovery period that allows for physiological super-compensation (i.e., positive adaptation). Subsequent PRT sessions involve the incremental increase in the training intensity (i.e. load) and training volume (i.e. number of sets), as well as alterations/adjustments to the types of exercises, as well as time under tension for each repetition.[13]

1.3 SARCOMA AND POST-TREATMENT EXERCISE

Sarcomas are a collection of connective tissue cancers that make up nearly 20% of pediatric and ~1% of adult malignancies.[14,15] Sarcomas most often arise from bone, muscle or fat in the extremities. Treatment requires surgery at a minimum, and although current surgical approaches usually avoid amputation, surgery to remove a sarcoma of the extremity or limb girdle profoundly influences physical function. Additionally, sarcoma treatment frequently includes radiation and intense, multi-agent chemotherapy.[16-18]

Implementing a regimen of physical activity in patients with sarcoma is important to regaining muscle performance and enhancing recovery.[19] Muller et al[20] prospectively evaluated the impact of physical activity among pediatric cancer patients following a 4-week rehabilitation program consisting of land-based and aquatic exercises. Among the 150 study participants, 26 patients were part of the sarcoma cohort. The authors observed that following a 6-month period post-rehabilitation, patients exhibited a significant increase in physical activity volume and

cadence. Moreover, at the 12-month follow-up, participants in the sarcoma cohort showed a significant improvement in endurance compared to baseline.

In an open non-randomized clinical trial, Winter et al[21] examined 31 pediatric patients with malignant bone tumors (22 osteosarcoma, 10 Ewing's sarcoma). All patients had received an endoprosthetic replacement and were treated with adjuvant chemotherapy and/or radiotherapy. Fifteen patients were assigned to the control group, which received symptom-specific physiotherapy. The other 16 patients were assigned to receive symptom-specific physiotherapy plus exercise intervention consisting of different exercises (i.e., strength, endurance, coordination, and flexibility exercises). The authors observed that following an 18-month follow-up, the volume and time spent in moderately intense activity was increased in both control and exercise groups, which was attributed to general recovery. Although not significant, patients in the exercise interventional group demonstrated a greater volume of physical activity compared to those in the control group.

1.4 **RATIONALE**

While essential for survival, treatment of sarcoma may lead to serious long-term health consequences, including decreased physical functioning[22-25]. Reduced joint range of motion, decreased muscle strength, lymphedema and marked deconditioning are frequent after completion of sarcoma therapy. Safe and adequate physical functioning requires dexterity, agility, flexibility, mobility and muscular strength, all of which are essential to performing independent activities of daily living and avoiding accidental injuries, such as falls. Reduced physical function leads to decreased overall physical activity, which in turn can contribute to the development of obesity, poor bone health, depression, and increased risk of falls or fracture that all can increase health care costs.

Despite the high risk for reduced physical functioning post-treatment, no strategies for improving physical function have been developed for sarcoma survivors and clinical guidelines are bereft of recommendations to manage functional consequences of treatment. Exercise has been shown to offer symptomatic relief from side effects of cancer treatment and improve quality of life among cancer survivors[26], but the potential benefits of exercise to improve physical functioning in sarcoma survivors are unknown.

This study seeks to investigate feasibility of implementing functional resistance training for sarcoma survivors as means to improve their physical function.

1.5 **POTENTIAL RISKS AND BENEFITS**

1.5.1 **KNOWN POTENTIAL RISKS**

Exercise and functional physical testing performed in this study can cause transient muscle soreness that typically resolves within 3 days. Participants may experience fatigue/tiredness related to exercise regimen. Participants are at possible, though slight, risk of injury from exercises; however, the exercise regimen will be taught to participants by a certified exercise physiologist (EP) that will guide and instruct participants on appropriate body mechanics to prevent or reduce risk of injury. Moreover, no significant injuries as a result of similar exercise regimens have been reported.[27]

This study involves the implementation of several survey tools to be administered to participants throughout the trial. Participants may be anxious about their ability to read surveys. To

minimize any undue stress, the study team will offer the option to have the survey questions verbally read (in person or over the telephone) to these individuals and help fill out the survey. If participants express anxiety regarding the ability to complete any of the physical tests (e.g., PPB, 1RM, grip strength) they will be given the option of discontinuing the test.

At baseline, participants will undergo imaging for total body fat mass, fat free or lean mass in kilograms, as well as bone mineral density for two clinically relevant sites (proximal femur and lumbar spine) to be determined by dual energy x-ray absorptiometry (DXA) (Hologic-QDR Discovery Wi; APEX software, v.4.02) scan. At follow-up, participants will undergo imaging for total body mass, fat free or lean mass in kilograms, to be determined by dual energy x-ray absorptiometry (DXA) (Hologic-QDR Discovery Wi; APEX software, v.4.02) scan. These scans include exposure to low-dose ionizing radiation. Participants may refuse DXA and remain eligible for the study. No pregnant women will undergo DXA and all women of childbearing potential will undergo urine pregnancy testing prior to DXA scan to minimize fetal risk. During periods of hospital recommendations for decreased in-person contact, imaging will be omitted.

During virtual sessions, additional safety precautions will include: 1) Providing safety recommendations specific to exercises and/or assessments (i.e., standing near a wall for balance activities) 2) Adapting the exercise protocol as necessary (ie. limit weight.) 3) Verifying address of remote exercise location (i.e., home address), should the study staff require the need to call 911 in an emergency 4) Ensuring that emergency contact information is up-to-date and readily available.

1.5.2 **KNOWN POTENTIAL BENEFITS**

An exercise regimen may improve physical function in sarcoma survivors. It cannot, however, be guaranteed that participants in this study will directly benefit from the intervention during study participation, as the clinical trial is designed to provide information about the safety and feasibility of this interventional approach.

Participants will receive the results of their DXA scans.

No compensation will be provided to participants for their involvement in this study. If participants are provided with resistance bands, handheld weights or weighted vests, they will be permitted to keep this equipment after successful completion of end-of-study assessments.

2. STUDY OBJECTIVES AND ENDPOINTS

2.1.1 **PRIMARY OBJECTIVE AND ENDPOINT**

Objective	Endpoint	Start	End

To determine the feasibility of a home-based individualized PRT program in sarcoma survivors.	1. Retention rate at 3 months end-of-intervention assessments 2. Exercise adherence rate 3. Frequency of related serious adverse events	Time of enrollment	Completion of 12 week exercise intervention

2.1.2 **SECONDARY OBJECTIVES AND ENDPOINTS**

Objective	**Endpoint**	**Start**	**End**
1. To assess secondary measures of feasibility of a home-based, individualized PRT program in sarcoma survivors	Successful development of individualized PRT prescription based on functional limitations for 100% of subjects.	Time of enrollment	Completion of 12 week exercise intervention
2. To determine if a 3-month PRT program improves physical function in sarcoma survivors.	1. Change in PROMIS-Cancer physical function score	Baseline	Completion of 12 week exercise intervention
	2. Change in SF-36 physical function score		
	3. Change in GLTEQ physical activity score		
	4. Change in FACT-F score		
	5. Difference in 1-repitition maximum (1RM, kilogram) from baseline		
	6. Change in Short physical performance battery (PPB) score from baseline		
	7. Change in grip strength (kilogram [Kg]) from baseline		
	8. Change in gait and balance as measured by mobile sensor		
	9. Change in instrumented 6-minute walk test (i6MWT)		
	10. Change in instrumented postural sway (ISway)		

	11. Change in instrumented timed up and go test (iTUG)		

2.1.3 EXPLORATORY OBJECTIVE AND ENDPOINTS

Objective	Endpoint	Start	End
To determine if a 3 month resistance training program improves body composition and bone mineral density	1. Change in weight	Baseline	Completion of 12 week exercise intervention
	2. Change in total body fat mass		
	3. Change in fat free mass		
	4. Change in lean mass		
	5. Change in bone mass		

3. STUDY DESIGN

3.1 DESCRIPTION OF THE STUDY DESIGN

Refer to Section 9 *for additional information regarding statistical methods used in this study.*

This is a prospective study to assess feasibility of implementing a resistance training regimen to improve the physical function limitations of sarcoma survivors. Participants must meet the inclusion criteria, have none of the exclusion criteria, and have provided written informed consent before the conduct of any screening tests not performed routinely in their treatment. All clinical evaluation and/or medical assessment pertaining to a participants' health that are required as part of this study will be performed by the principal investigator or qualified healthcare personnel.

Eligible participants enrolled into this study will undergo a set of baseline evaluations prior to the start of the intervention. Each participant will complete a free text self-report of physical limitations and their treating physician will identify recommended exercise limitations and modifications. Additional baseline standardized self-reported evaluations include: Patient-Reported Outcomes Measurement Information System (PROMIS) cancer-specific physical function assessment, 36-Item Short Form Health Survey (SF-36), Godin Leisure-Time Exercise Questionnaire (GLTEQ), and Functional Assessment of Cancer Therapy: Fatigue (FACT-F) scale. Physical assessments will be completed by a qualified exercise physiologist (EP) and include: 1-repitition maximum (1RM) test, short physical performance battery (PPB), grip strength test, and assessments of mobility using wearable sensors (postural sway (lSway), timed up and go (iTUG) and 6-minute walk test (6MWT)).

The EP will integrate results from baseline objective physical function assessments with patient-reported and physician-recommended limitations, and prescribe an individualized therapeutic resistance exercise plan. Each participant will undergo a one-time, in-person session with the EP, in which they will be provided a written exercise plan and receive training on how to perform the therapeutic resistance exercises at home. All subsequent exercise sessions will be conducted at home. During periods of hospital recommendations for decreased in-person contact, participants will perform all exercise sessions remotely (e.g., at home) using videoconferencing software. Specifically, participants are expected to complete a total of 24 exercise sessions over a 12-week period (i.e., 2 exercise training sessions per week for 12 weeks), with at least 1 full day of rest between each session (i.e., approximately 48 hours

between sessions). One home-based training session per week will be conducted via video-conferencing with the EP remotely supervising the participant. Training sessions may occur with up to three participants at a time, to improve efficiency of training and create peer support; however, if a participant does not want to or cannot be in a group, training will be delivered 1:1. The resistance training program utilized in this study is based on guidelines from the American College of Sports Medicine (ACSM).[27-32] The resistance exercise program will consist of upper and lower body exercises and may use free weights (i.e., dumbbells), weighted vests, and/or resistance bands. The resistance exercises employed in this study are common to activities of daily living and have been previously described.[27,30] Following the baseline assessment, the EP trainer will individualize the participant's training program; additional modifications to the exercise program may be introduced during video sessions as necessary based on the participant's physical limitations.

After completing the 12-week PRT program, participants will return to clinic for an end of study visit to evaluate physical function in relation to baseline performance. A total of 10 sarcoma survivors will be recruited for participation in this study. The total study duration for each participant is approximately 3 months, including the resistance training intervention and follow-up.

4. STUDY ENROLLMENT AND WITHDRAWAL

4.1 PARTICIPANT INCLUSION CRITERIA

To be eligible to participate in this study, an individual must meet all of the following criteria:

1. Eligible for the Sarcoma Survivorship Registry [IRB #12039]
    a. Age ≥15 years
    b. History of histologically-confirmed sarcoma
    c. History of treatment with surgery, radiation and/or chemotherapy for the sarcoma diagnosis
    d. Completion of sarcoma treatment ≥2 years prior to study enrollment
    e. No evidence of recurrent or residual disease on surveillance exam or imaging for at least 2 years prior to study enrollment
2. Sarcoma location must have been in the extremities, body wall, pelvic/shoulder girdle or axial skeleton. Intra-thoracic, intra-abdominal or cranial sarcomas are not eligible.
3. Currently engaging in <1 hour of resistance exercise per week by self-report. Examples of resistance exercise include: using free weights or weight machines, push-ups, sit-ups, lunges, plank, etc.
4. Able and willing to commit to attending weekly video coaching sessions and independently completing weekly resistance training sessions. This requires access to internet and a device with video and audio capabilities. A webcam may be provided by the study to the participant if needed.
5. Able and willing to commit to attending one initial in-person training session and one in-person follow-up assessment.
6. Ability to understand and willingness to sign a written informed consent document.

4.2 PARTICIPANT EXCLUSION CRITERIA

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Medical contraindication(s) to any and all resistance training as determined by treating physician.
2. Non-English speaking. At this time, we do not have resources to support translation of EP sessions.
3. Dependent on a mobility device (e.g., crutches, wheelchair) for independent activities of daily living (IADLs).
   a. Use of a cane is permitted.
4. Participant has known psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the trial.
5. Any condition that, in the opinion of the investigator, would interfere with evaluation of study treatment or interpretation of participant safety or study results (e.g., pregnancy).

4.3 STRATEGIES FOR RECRUITMENT AND RETENTION

Participants for this study may be identified through the existing Sarcoma Survivorship Registry (IRB#00012039), recruited through the Doernbecher Survivorship Program, or recruited from the OHSU Multidisciplinary Sarcoma Program. Potential study participants identified through the Sarcoma Survivorship Registry will be contacted by the study team using the preferred method of communication preselected by the registry participant (e.g., phone, email, mail). The participant will be provided information regarding the study and asked to provide a response indicating their (un)willingness to be contacted. Potential participants indicating interest in study will subsequently be contacted by mail, phone or email by a member of the study team.

Additional recruitment strategies may include direct community recruitment using newspaper advertisements, radio, announcements on websites, as well as presentations at cancer support groups and cancer-related conferences. Participants may also initiate contact with the investigator through information of this study posted on the clinicaltrials.gov website.

4.3.1 ACCRUAL ESTIMATES

No OHSU Knight Cancer Institute study will focus on any particular gender, racial or ethnic subset. No participant will be excluded from the study on the basis of gender, racial or ethnic origin. Male, female and minority volunteers will be recruited for this study from the general population and approximately 50% men and 50% women will be studied. Gender-nonconforming and gender-fluid individuals as members of the general population will also be recruited.

The projected gender, racial, and ethnic composition of the study will represent that of the state of Oregon (**Table 1**). An estimated 10 participants are to be recruited. Total accrual of all 10 participants is anticipated to take a total of 12 months.

Table 1. Projected accrual for Oregon population demographics						
Ethnic Category [OR]	**Sex/Gender**					
	Females		**Males**		**Total**	
	n	*%*	n	*%*	n	*%*
Hispanic or Latino	1	*6.6*	1	*6.5*	1	*13.1*
Not Hispanic or Latino	4	*43.8*	4	*43.1*	9	*86.9*
Ethnic Category: Total of all participants*	5	50.4	5	49.6	10	*100**
Racial Category						
American Indian or Alaskan Native	0	*0.9*	0	*0.9*	0	*1.8*
Asian	0-1	*2.4*	0-1	*2.3*	1	*4.7*
Black or African American	0	*1.1*	0	*1.1*	0	*2.2*
Native Hawaiian or other Pacific Islander	0	*0.2*	0	*0.2*	0	*0.4*
White	4	*43.9*	4	*43.2*	9	*87.1*
Two or more races	0	*1.9*	0	*1.9*	0	*3.8*
Racial Category: Total of all participants*	5	*50.4*	5	*49.6*	10	*100*
Source: Adapted from U.S. Census Bureau, 2017. *Totals may not equal 100 due to rounding.						

5. STUDY PROCEDURES/EVALUATIONS AND SCHEDULE

5.1 STUDY SPECIFIC PROCEDURES

5.1.1 DEMOGRAPHICS

Demographic variables, including race, ethnicity, education, marital status, employment, income, and (for females) childbearing potential will be measured at baseline by a questionnaire developed for this study. Health history and sarcoma-specific information (e.g., diagnosis, type and dates of cancer treatments, presence of other chronic conditions) will be obtained from participants' electronic health record.

All subjects will also be offered participation in the Sarcoma Survivorship Registry [IRB #12039].

5.1.2 PHYSICAL LIMITATIONS

At baseline, each participant will complete a free text self-report of physical limitations. In addition, the treating physician will provide a written report identifying specific physical limitations and recommended modifications to physical activity.

5.1.3 ADVERSE EVENT EVALUATION

Adverse events will be monitored from the time the participant signs the Consent Form. Participants will be instructed to report all AEs during the study and will be assessed for the occurrence of AEs bi-weekly throughout the study by an in-house survey. All AEs (serious and non-serious) must be recorded on the source documents and CRFs regardless of the assumption of a causal relationship with the study intervention.

For details on AE collection and reporting, refer to Section 8.

5.1.4 SELF-REPORTED ADHERENCE TO ASSIGNED EXERCISE REGIMEN

For home-based sessions, participants are required to maintain a training log to assess adherence to the assigned intervention. Participants will be provided with a training log and are required to record the date, time, and duration of the exercise session, along with description of the exercise including intensity, number of repetitions, and number of sets.

5.1.5 SELF-REPORTED OUTCOME MEASURES

All self-reported assessments will primarily be administered electronically as an online survey, but may be administered on paper if requested by the participant. Study participants will complete each survey at baseline and at end of study visit.

5.1.5.1 *Godin Leisure-Time Exercise Questionnaire*

The Godin Leisure-Time Exercise Questionnaire (GLTEQ)[33] is a brief four-item query of usual leisure-time exercise habits. In this self-explanatory questionnaire, the study participant will be asked to respond to the question *"During a typical 7-Day period (a week), how many times on the average do you do the following kinds of exercise for more than 15 minutes during your free time?"*. The participants' responses will consist of entering the frequency of which the activity is performed in relation to its intensity (i.e., strenuous, moderate, or mild exercise).

5.1.5.2 *PROMIS-Cancer-Physical Function Measure*

The PROMIS-Cancer assessment[34] consists of 45 questions pertaining to physical function, each of which are designed as having five-point ordinal rating scales.

5.1.5.3 *36-Item Short Form Survey*

The 36-Item Short Form Health Survey (SF-36) consists of a set of generic, quality-of-life measures to survey physical function in the general population.[35]

5.1.5.4 *FACT-F*

The 13-item Functional Assessment of Cancer Therapy-Fatigue[36] (FACT-F) measurement system will be used to assess fatigue.

5.1.6 PHYSICAL FUNCTION ASSESSMENTS

During testing visits, if a participant experiences self-reported tiredness, or the participant's tiredness is observed by the EP (during 1:1 sessions), then they may be instructed to halt their participation in the physical function assessments, and begin again at a later time. Participants may rest as often as needed during the physical function assessments if tiredness occurs.

5.1.6.1 *Short Physical Performance Battery (PPB)*

The short PPB will be conducted as previously described[37], and consists of 3 timed performance tests: 1) 5 repeated chair stands, b) standing balance (semi-tandem stand; side-by side stand; tandem stand), and c) gait speed over 4 meters.

5.1.6.2 *One-repetition maximum (1RM) Strength Testing*

Maximal strength of the upper and lower body will be evaluated by a 1RM leg press and bench press (kg) according to established protocols.[30]

5.1.6.3 *Grip Strength*

Participant grip strength will be evaluated using a Lafayette Instruments using Hand Dynamometer Model 78010 (or equivalent device).

5.1.6.4 *Gait and Balance*

Postural stability and gait will be measured using standard and instrumented (i.e., wearable sensors) assessments. Participants will be fitted with elastic body straps designed to hold a number of wearable body sensors (iMobility, APDM, Inc.). Each wearable sensor weighs <25 grams (with battery), and houses an accelerometer, gyroscope, and magnetometer.

Study participants will be asked to conduct a 6-minute walk test (6MWT), a postural sway test, and the timed-up-and-GO (TUG) test. Each test will be conducted while wearing the iMobility sensors. For the 6MWT, each participant will walk as far as possible for 6 minutes along a defined walking course (e.g., hallway or corridor). Participants will be instructed to walk and not to run or jog. Postural way will be assessed during 30-seconds of quiet standing.[38] TUG will be evaluated by assessing measuring the time that it takes an individual to rise from a chair, walk 7 meters, turn around and return to the chair in a seated position.[39]

5.1.7 BODY COMPOSITION AND BONE MINERAL DENSITY

Total body fat mass, fat free or lean mass in kilograms, as well as bone mineral density for two clinically relevant sites (proximal femur and lumbar spine) will be determined by dual energy x-ray absorptiometry (DXA) (Hologic-QDR Discovery Wi; APEX software, v.4.02) scan. The DXA scan will be performed by trained research staff. Individual participant's height as well as weight using a physician scale, will also be recorded at time of each DXA scanning visit. Participants may refuse DXA and remain eligible for the study.

5.2 LABORATORY PROCEDURES AND EVALUATIONS

For women of childbearing potential, a urine pregnancy test will be checked prior to DXA scan. Women are considered of non-childbearing potential if they have had at least 12 months of amenorrhea at an age that is appropriate for menopause, or if they have had bilateral oophorectomy, hysterectomy or tubal ligation at least 6 weeks prior.

No other laboratory procedures are required as part of this study and should be performed only as clinically indicated. Results of any hematological (e.g., complete blood count [CBC]) or biochemical (e.g., complete metabolic panel [CMP]) laboratory testing performed as part of institutional standard of care practice may be recorded in appropriate CRF for the duration that an individual is participating in this study.

5.3 SCREENING ASSESSMENTS

All screening evaluations are to be conducted within 8 weeks prior to start of exercise intervention. Screening (consultation) visit may occur as part of standard of care. The following will be reviewed at screening:

- Eligibility criteria
- Informed consent obtained and documented

5.4 BASELINE ASSESSMENTS

All baseline assessments should be completed within 14 days before initiating the exercise intervention; however, these assessments may be performed during Week 1 prior to initiating exercise intervention.

Eligible participants enrolled into this study will be asked to provide response to four questionnaires: GLTEQ, PROMIS-Cancer-PF, SF-36 and FACT-F. Surveys will be completed online unless the participants prefer to complete using a paper version. Study staff will review surveys for completeness and follow-up with participants in person or by phone for missing data.

Participants should ideally complete initial physical function assessments (refer to Section 6.1.6) as well as body composition and bone mineral density (refer to Section 6.1.7) on same day. The exact order of the individual physical function assessments will be determined by the EP at the initial visit, but should be preferentially maintained for all subsequent time-points. This initial visit should take approximately 2 hours. If the visit is performed virtually, height, body composition and bone mineral density measures will be omitted.

At this visit, participants will receive study exercise equipment and instructions from the EP regarding their individualized PRT regimen. If this visit is performed virtually, participants will receive study exercise equipment via courier. Refer to Section 6.8, Schedule of Events for additional details.

5.5 ASSESSMENTS DURING TREATMENT

Participants will perform one weekly training under the supervision of an EP trainer via 1:1 web-based videoconferencing for the first two weeks. This first set of 1:1 videoconferencing will be used to observe and modify the PRT regimen for each participant. Any changes to an individual participant's PRT regimen (e.g., number of repetitions per set, number of sets, and/or mass of weights) should be recorded in the CRF. After two weeks, the participant may decide to join a group video conference with 1-2 other participants, or continue 1:1 with the EP. The weekly videoconferencing should ideally occur between Monday through Friday of each study week. Under certain circumstances (e.g., technical difficulties), videoconferencing may be rescheduled. The reason for rescheduling should be recorded in the CRF.

5.6 END OF STUDY VISIT AND EARLY TERMINATION VISIT

The end of study visit will occur as part of a scheduled follow up at 3 months from start of the protocol-directed PRT regimen. Specific assessments are listed in Section 5.8, Schedule of Events.

Any participant that completes or discontinues the study intervention must be evaluated within 30 days after termination or prior to the initiation of any other exercise intervention, if not

performed within the last 30 days. The early termination visit should include end of study assessments listed in Section 5.8, Schedule of Events.

5.7 **UNSCHEDULED VISITS**

Unscheduled study visits may occur at any time if medically warranted. Any assessments performed at those visits should be recorded in the eCRF.

5.8 SCHEDULE OF EVENTS

Procedures	Screening	Baseline†/W1	Intervention Period (12 weeks [W])											Follow Up*
			W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12	
Eligibility review	X													
Treating physician evaluation	X													
Informed Consent	X													
Questionnaires														
Physical Function: PROMIS-PF/Cancer		X												X
Quality of Life: SF-36		X												X
Exercise: GLTEQ		X												X
Fatigue: FACT-F		X												X
Baseline demographics		X												
Self-reported limitations		X												
Adverse Events		X	X		X		X		X		X		X	
Physical Tests														
BMI — height + weight		X												X
Strength – 1RM		X												X
Strength – grip														
Lower extremity function – short PPB		X												X
Gait – iTUG		X												X
Balance – lSway		X												X
Gait/Balance – i6MWT		X												X
DXA		X												X
Urine hCG**		X												X***
In-Person Training		X												
Videoconferenced PRT‡			X	X	X	X	X	X	X	X	X	X	X	
Independent PRT‡			X	X	X	X	X	X	X	X	X	X	X	

† Baseline assessments should occur within 14 days before initiating the exercise intervention; however, these assessments may be performed during Week 1 prior to initiating exercise intervention

‡ The PRT regimen will consist of 2 one-hour training sessions per week (1 videoconference, 1 independent) for a total of 12 weeks (i.e., a total of 24 training sessions).

*12-week assessments may occur ±14 days before or after completing the exercise intervention.

** Prior to DXA, for women of childbearing potential only.

*** DXA,at follow-up will omit bone mineral density.

5.8.1 INCLUSION OF CHILDREN

This study will include participants that are aged ≥15 years. (Note: individuals in Oregon aged ≥15 years are able to consent to medical and dental services without consent of a legally authorized representative (e.g., parent/legal guardian [ORS 109.640]).

5.9 OHSU PARTICIPANT REGISTRATION PROCEDURES

Participants will be required to give written informed consent to participate in the study before any screening tests or evaluations are conducted that are not part of standard care.

Registration from all consented participants must be entered into the OHSU electronic Clinical Research Management System (CRMS, e.g., eCRIS). At a minimum, registration of OHSU participants will include signed copies of the most recently Institutional Review Board (IRB)-approved, informed consent form and HIPAA authorization.

5.10 PARTICIPANT SCREENING AND ENROLLMENT

Potential participants will be screened using an IRB approved phone script. If eligible, an appointment will be made for consenting and initial testing. In order to participate in this study, signed informed consent must be obtained from the participant. The current IRB-approved informed consent must be signed and dated by each participant prior to undergoing any study procedures.

Baseline evaluations will begin once the participant has provided written informed consent to participate in the study and ends when the participant initiates the study exercise regimen. Study participants may be enrolled on to the study once all eligibility criteria are satisfied.

5.11 PARTICIPANT WITHDRAWAL OR DISCONTINUATION FROM STUDY INTERVENTION

Participants are free to withdraw consent and discontinue participation in the study at any time and without prejudice to further treatment. If a participant no longer wishes to participate in the interventional exercise regimen, but is willing to come for follow-up appointments, the participant's request should be honored, if possible. The following are examples demonstrating why a participant's exercise intervention might be discontinued.

- Adverse effects of the assigned exercise intervention precludes further study participation.
- Disease recurrence or progression.
- Investigator's discretion.

No further participant contact should be made if the participant withdraws consent for participation in the study. Information about the reason(s) for discontinuation and collection of any new or ongoing adverse events (AEs) should be collected at the time the participant withdraws consent.

5.11.1 HANDLING PARTICIPANT WITHDRAWAL AND DISCONTINUATION

Participants enrolled in this study that withdraw prior to initiating on-study exercise intervention will be replaced. Participants that initiate on-study exercise intervention and subsequently withdraw, will not be replaced.

5.12 CRITERIA FOR STUDY DISCONTINUATION

Criteria that can take a participant off-study include:
- Participant requests to be withdrawn from study without further follow-up,
- Any injury that prevents the participant from continuing with the assigned exercise intervention
- Completed study follow-up period,
- Progression of disease,
- Death,
- Investigator's discretion
- The participant becomes pregnant

5.13 STUDY SUSPENSION OR TERMINATION

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to funding agency, IRB, and other regulatory authorities. If the study is prematurely terminated or suspended, the Investigator will promptly inform the IRB and will provide the reason(s) for the termination or suspension.

Reasons for terminating the study may include the following:
- Incidence or severity of adverse events, in this or other studies, indicates a potential health hazard to participants.
- Demonstration of efficacy that would warrant stopping.
- Data that are not sufficiently complete and/or evaluable.
- Investigator(s) do not adhere to the study protocol, or applicable regulatory guidelines in conducting the study.
- Participant enrollment is unsatisfactory.
- Submission of knowingly false information from the study site to regulatory authorities.
- Upon instruction by local or other regulatory, or oversight authority.

Study may resume once concerns about safety, protocol compliance, data quality are addressed and satisfy the IRB or other regulatory authority.

6. TREATMENT PLAN

6.1 FUNCTIONAL RESISTANCE TRAINING REGIMEN

Participants enrolled in this study will be assigned an individualized resistance training regimen that is based on guidelines from the American College of Sports Medicine (ACSM).[28,29,31] The resistance exercise regimen consists of upper and lower body exercises and may use free weights (i.e., dumbbells), weighted vests, resistance bands and/or the participants' body weight. The resistance exercises employed in this study are all common to activities of daily living, and have been previously described.[27,30]

In this study, participants will be assigned an individualized regimen consisting of PRT exercises that are to be performed 2 times per week for a total of 12 weeks (**Table 2**). Each exercise session will consist of a maximum of 3 sets, with no more than 15 repetitions per set. A rest period of 1 to 2 minutes should be included between each set. Participants are required to rest at least one day between each exercise session.

Table 2. Example of PRT regimen.

Activity Type	Prescription				Schedule
	Sets	*Reps*	*Time*	*Resistance*	
• Warm-up			10min		2 times per week**
• Posture Squat	2-3	10-15		Body weight	
• Band Chest Press	2-3	10-15		Body weight	
• Band Deadlift	2-3	10-15		Band	
• Band Side Step	2-3	10-15		Band	
• Lunging One Arm Row	2-3	10-15		Band	
• Reverse Lung with Kick	2-3	10-15		Body weight	
• Push Up (modified)	2-3	10-15		Body weight	
• Plank	2-3	10-15	20s-1min	Body weight	
• Glute Bridge	2-3	10-15		Body weight	
• Cool down			8-10min		
** Once during video-conference with EP and once independently					

Following the baseline assessment, the EP trainer will individualize the participant's training program; additional modifications to the exercise program may be introduced during video sessions as necessary.

The individualized training regimen will be progressive, and the intensity of each exercise will be dependent on the resistance relative to the participant's capability.

6.1.1 **INITIALTRAINING SESSION**

If the initial visit is performed in-person, participants will be provided with the necessary equipment (i.e., resistance bands, weights, weighted vest as appropriate) and receive in-person verbal and written instruction from an EP trainer on how to use the equipment and perform each assigned exercise.

During periods of hospital recommendations for decreased in-person contact, the initial study visit may be omitted, delayed, or delivered entirely virtually. If the initial visit is delivered virtually, participants will receive study exercise equipment via courier, verbal instruction from an EP trainer on how to use the equipment and perform each assigned exercise by phone or teleconference, and written instruction from an EP trainer on how to use the equipment and perform each assigned exercise by email and/or courier. Select testing measures will be adapted to this type of delivery. These testing measures include:

- Weight
- Physical Performance Battery (PPB)
- All surveys will continue to be sent out electronically as previously described. If a participant needs a paper survey to complete the survey, one will be provided or their data will be marked as "missed" if study staff are unable to mail a paper survey to the participant during their outlined testing window.

To assess upper body strength remotely, novel assessments to this trial will include:

- Push-up (modified) test (if applicable): Measured by the number of push-ups completed in one continuous bout until fatigue
- Plank test (if applicable): Measured by the amount of time in seconds that the participant

is able to hold a plank position.

To assess lower body strength remotely, novel assessments to this trial will include:

- Posture squat (if applicable): Measured by the amount of time in seconds that the participant is able to hold a posture squat position.

6.1.2 VIDEOCONFERENCING & INDEPENDENT EXERCISE

Each participant must have access to a device with internet connection and audio/video capability in order to be eligible for this study. A webcam may be provided if needed, but should be returned at the end of study. Participants will receive written instructions for installing and using the OHSU-approved videoconferencing software.

Participants will perform all exercise sessions remotely (e.g., at home). One exercise session per week will be conducted under the supervision of an EP trainer using videoconferencing software. During these web-based video conferences, the EP trainer will observe the participant and provide feedback on technique, as well as implement progressive resistance (e.g., increase number of repetitions or increase weight). Each participant will also complete one-hour of prescribed resistance exercise independently each week and record their effort in a training log.

6.1.3 END-OF-STUDY 3 MONTH FOLLOW-UP

The exercise intervention will be conducted for a total of 12 weeks; however, participants will be encouraged to continue resistance training after completing the study intervention. An end of study visit will occur approximately 3 months (±14 days) after first home PRT session. During periods of hospital recommendations for decreased in-person contact, the end of study visit may be omitted, delayed, or delivered entirely virtually.

After successful completion of the end-of-study assessments, participants will be allowed to keep all study-related exercise equipment provided (e.g., resistance bands, dumbbells, weighted vests). Participants will be required to return the webcam if one was provided.

6.2 EXERCISE MODIFICATIONS

Between the initial assessment & first video-conferenced session, the EP trainer may further individualize each participants' training program. These modifications will be introduced during the first videoconference training session. Alterations (individualization) of the exercise regimen will be based on the participant's limitations. These will primarily be related to decreased range of motion in a specific joint or reduced weight bearing potential in a muscle group. Exercises involving that specific joint/muscle group will proceed *"as tolerated."* Exercises on the contralateral side will continue unaltered. Any modifications to the exercises will be recorded in the participants' training log.

If necessary, and at the discretion of the EP, the intensity of one or all exercises may be increased or decreased by altering the number of sets, lower band resistance, or time held for each exercise. All changes will be recorded in the participants' training log.

6.2.1 EXERCISE DELAYS

In general, interruptions to scheduled exercise sessions are permitted in the case of medical /

surgical events or logistical reasons (e.g., elective surgery, unrelated medical events, vacation, and holidays) not related to study intervention. Participants should resume exercise intervention within 2 weeks of the scheduled interruption, unless otherwise discussed with the investigator. The reason for interruption should be documented in the CRF.

Missed exercise sessions (including videoconferencing) may be completed within the same scheduled week as long as there is at least 1 day of rest between sessions.

7. EFFICACY MEASURES

7.1 GLTEQ

To score the GLTEQ, the weekly frequencies of strenuous, moderate, and light activities are multiplied by nine, five, and three, respectively. Total weekly leisure activity is calculated in arbitrary units by summing the products of the separate components, as shown in the following formula:

$$\text{Weekly leisure activity score} = (9 \times \text{Strenuous}) + (5 \times \text{Moderate}) + (3 \times \text{Light})$$

The same method of score is applied for each specific question.

7.2 PROMIS-CANCER PHYSICAL FUNCTION ASSESSMENT

For adults, each question in the PROMIS-Cancer survey has five response options ranging in value from one to five. The total raw score for the survey with all questions answered is derived by calculating the sum of the values of the response to each question. Once calculated, a conversion table translates the raw scores into a T-score. The T-score rescales the raw score into a standardized score with a mean of 50 and a standard deviation (SD) of 10. The standardized T-score is reported as the final score for each participant as follows:

- Scores 0.5 – 1.0 SD worse than the mean = mild symptoms/impairment
- Scores 1.0 – 2.0 SD worse than the mean = moderate symptoms/impairment
- Scores 2.0 SD or more worse than the mean = severe symptoms/impairment

7.3 QUALITY OF LIFE (SF-36)

Scoring and analysis of the SF-36 survey will be performed as previously described.[35] All items in this survey are scored so that a high score defines a more favorable health state.

7.4 FATIGUE (FACT-F)

Fatigue was assessed using the Functional Assessment of Chronic Illness Therapy – Fatigue (FACT-F) scale. This is a 13 item, uni-dimensional, 5-point Likert scale, measuring physical fatigue over the past week. The scale has high internal consistency[36] and is widely used in the literature.

7.5 SHORT PHYSICAL PERFORMANCE BATTERY (PPB)

The short PPB consists of three timed tests: 5 repeated chair stands, standing balance, and gait speed over 4 meters. Each test is scored 0 (unable) to 4, based on quartiles of performance,[40] then scores are summed. Higher scores indicate better physical function.

7.6 1RM STRENGTH TEST

The 1RM is defined as the maximal weight (kg) an individual can lift for only one repetition.

7.7 GRIP STRENGTH

To measure hand grip strength, participants are to apply as much force as possible with one hand to the dynamometer. Three separate tests should be conducted, with a rest of 10-20 seconds between each squeeze to avoid muscle fatigue. The force exerted is measured to the nearest kg.

7.8 GAIT AND BALANCE

Balance and gait will be measured using body worn sensors (iMobility, APDM, Inc.), which continuously and wirelessly record 3D linear accelerations and angular velocity. An instrumented postural sway test (ISway) will record center of pressure displacement and acceleration signals during 30-seconds of quiet standing.[41] iMobility is also used for an instrumented version of the timed-up-and-GO (TUG) test, iTUG, to detect changes in mobility in patients that may not be not apparent from a stopwatch score.[42] For each study participant, standard TUG will also be evaluated by measuring the time that it takes an individual to rise from a chair, walk 7 meters, turn around and return to the chair in a seated position. Finally, study participants will be asked to complete a 6-minute walk test (i6MWT) while wearing the iMobility sensors. In addition to the standard metrics obtained from iMobility, the number of meters walked during the 6-minutes will also be recorded.

7.9 BODY COMPOSITION AND BONE MINERAL DENSITY

Body composition will be expressed as % whole-body lean mass and leg lean mass (kg). Coefficients of variation (CV) for lean and fat mass in our laboratory are <1.0%. DXA scans will be analyzed following standard procedures (Hologic Inc). Visceral (VAT) and subcutaneous (SAT) adipose tissue will also be quantified from the whole body scans.

Trained research staff will utilize the DXA manufacturer software (Apex, Hologic Inc.) to analyze each scan by loading it onto the DXA analysis workstation where it can be assessed using the appropriate DXA software. The trained research staff member will analyze the scan by reviewing and modifying the bone edges and positioning markers to define the necessary regions of interest. In general, the software will automatically detect bone edges; however, if needed, a trained research staff can intervene to manually identify the bone edges. Once analyzed, the scan will be saved and archived with the results of the analysis included.

8. SAFETY

8.1 SPECIFICATION OF SAFETY PARAMETERS

The Investigator is responsible for monitoring the safety of participants who have enrolled in the study. Safety assessments will be based on medical review of adverse events and the results of safety evaluations at specified time points as described in Section **1.1**. Any clinically significant adverse events persisting at the end of treatment visit will be followed by the Investigator until resolution, stabilization, or death, whichever comes first.

8.2 REPORTING PROCEDURES

Adverse events during exercise sessions will be graded according to their significance for severe consequences, such as injury or death, using the following grades determined by the OHSU IRB. In this study we do not anticipate moderate or serious adverse events.

- A serious adverse event is defined as any event that is life-threatening or disabling and requiring medical attention. Serious adverse events that may occur during exercise in this study include death and cardiovascular events, though these are extremely rare in the absence of significant cardiac pathology.

- A moderate adverse event is defined as any event that resolves with treatment. Moderate adverse events that may occur during exercise include symptoms, such as shortness of breath and orthostatic intolerance.

- A mild adverse event is defined as any event that does not require treatment. Reports of side effects, such as muscle soreness, moderate tiredness while exercising, and similar discomforts are mild adverse events.

- An unexpected adverse event is defined as any event that does not include physical harm. Examples of unexpected adverse events may include breaches of confidentiality, emotional harms, or complaints about study procedures or conduct of investigators.

A survey (Adverse Events Survey) was created by the study team to be administered electronically every other week during the participants' 12-week long participation in the study. Adverse events reported through this survey will be followed-up by study staff with a phone call when the self-reported severity is a 5 (moderate) or greater or if more information is needed to determine reportability. Participants will also have the opportunity to report adverse events during the home-program video calls.

Serious adverse events will be reported immediately to the Principal Investigator (PI), who will immediately notify all other investigators. The PI will file a full written report to the OHSU Institutional Review Board (IRB) within 24 hours of notification of the serious event, as required by the OHSU IRB. Specifically, the following will be reported, in writing:

1. All deaths in study participants, during the intervention period, regardless of cause,
2. All serious adverse events associated with the study procedures

Cardiac events or deaths are very rare in persons engaging in low or moderate intensity exercise, though it is possible that a person with previously undisclosed cardiovascular disease may experience a cardiac event or death during exercise. Regardless of cause, we are required to notify the OHSU IRB within 24 hours if a participant dies during this study.

Moderate adverse events will be tabulated by the PI, who will notify members of the research team if trends are identified. If trends are noted, preventive measures will be implemented, such as providing education of participants in the study to emphasize prevention of the adverse event. Moderate adverse events will be included in annual reports to the OHSU IRB.

Mild adverse events will be entered in progress notes. Participants will receive advice on avoiding such events.

Unexpected adverse events that do not include physical harm, usually having to do with study procedures, will be reported within 10 days to OHSU IRB, using a written report form.

9. STATISTICAL CONSIDERATIONS

Refer to Section 3.1, Description of the Study Design for a detailed description of the study design and endpoints.

9.1 ANALYSIS POPULATIONS

Participants evaluable for analysis includes all enrolled participants that completed baseline physical function assessment and completed at least one day of exercise intervention.

9.2 DESCRIPTION OF STATISTICAL METHODS

9.2.1 GENERAL APPROACH

This is a single-arm, prospective study to assess feasibility of implementing a resistance training regimen in sarcoma survivors.

9.2.2 ANALYSIS OF PRIMARY AND SECONDARY FEASIBILITY ENDPOINTS

Among evaluable participants, the retention rate, exercise adherence rate and rate of PRT prescriptions provided will be estimated using percentage and 95% confidence interval. The incidence of exercise-related serious adverse events will be evaluated using descriptive statistics. The primary objective of feasibility will be determined by the study achieving 90% participant retention [i.e., 9 of 10 patients complete end-of-intervention assessments] with more than 75% exercise adherence rate [each participants completed end-of-intervention assessment also completed at least 18 of 24 prescribed training sessions] without related serious adverse events. Successful development of individualized PRT prescription based on functional limitations also be determined as a secondary feasibility measure [100% of subjects receive individualized PRT prescription].

9.2.3 ANALYSIS OF THE SECONDARY EFFICACY ENDPOINTS

The efficacy measurements, including four questionnaires (GLTEQ, PROMIS-Cancer-PF, SF-36 and FACT-F) and physical assessments (short PPB, 1RM, grip strength, i6MWT, iTUG, ISway) wearable mobility sensor) at baseline and at end of exercise intervention (i.e., 3 months from start of PRT regimen) will be summarized as mean and standard deviation. We also compare scores at baseline and at 3 months using paired t-Test to determine if a 3-month resistance training program improves physical function. As standard practice, we will initially examine distribution of each outcome variable using Shapiro-Wilk test, as well as data visualization techniques. If normality assumption is violated, we will consider transforming the data or adopting non-parametric approaches.

9.2.4 ANALYSIS OF THE EXPLORATORY ENDPOINTS

Body composition and bone mineral density at baseline and end of exercise intervention (i.e., 3 months from start of PRT regimen) will be summarized as mean and standard deviation. They are also be compared using paired t-Test to determine if a 3-month resistance-training program improves body composition and bone mineral density in sarcoma survivors.

9.3 SAMPLE SIZE, POWER, ACCRUAL RATE AND STUDY DURATION

9.3.1 SAMPLE SIZE AND POWER

Up to 10 participants will be recruited to this study. This is a feasibility study with no formal hypothesis test but to assess the preliminary estimate of feasibility.

9.4 HANDLING OF MISSING DATA

Every attempt will be made to obtain data at the defined time points as described in the primary and secondary endpoints. We will examine dropout and patterns of missing data to determine mechanisms (MCAR, MAR or not ignorable). In the case of data missing MCAR or MAR, mixed-effect model will allow unbiased parameter estimation using all available data. We will adapt an imputation technique if missing is not a completed random.

10. CLINICAL MONITORING

10.1 OHSU KNIGHT CANCER INSTITUTE DATA & SAFETY MONITORING PLAN

This study is under the oversight of the Knight Cancer Institute's DSMC as described in the Knight institutional DSMP. The Knight DSMP outlines the elements required to ensure the safety of clinical trial participants, the accuracy and integrity of the data and the appropriate modification of cancer-related clinical trials for which significant benefits or risks have been discovered or when the clinical trial cannot be successfully concluded. The Knight DSMP also describes the methods and procedures for ensuring adequate oversight of cancer-related research at OHSU.

As described in the Knight DSMP, regardless of a trial's risk level and any specific Knight oversight in place, the Investigator is singularly responsible for overseeing every aspect of the design, conduct, and final analysis of his/her investigation.

The Knight DSMC will review and monitor study progress, toxicity, safety and other data from this study. Information that raises any questions about participant safety or protocol performance will be addressed by the Investigator, statistician and study team. Should any major concerns arise, the Knight DSMC may recommend corrective action and determine whether or not to suspend the study.

The Knight DSMC will review each protocol every 6 months, but may occur more often, if required, to review toxicity and accrual data (please refer to Knight DSMP for additional details on audit frequency). The Knight DSMC will review accrual, toxicity, response and reporting information. Information to be provided to the DSMC may include: participant accrual; treatment regimen information; AEs and SAEs reported by category; summary of any deaths on study; audit results; and a summary provided by the study team. Other information (e.g. scans, laboratory values) will be provided upon request.

10.2 CLINICAL DATA & SAFETY MONITORING

The OHSU Investigator is ultimately, singularly responsible for overseeing every aspect of the investigation, including design, governing conduct at all participating sites, and final analysis of

study data.

In the absence of a formal monitoring plan, the Investigator may work with his/her study team to conduct and document internal monitoring of the study to verify protection of human participants, quality of data, and/or ongoing compliance with the protocol and applicable regulatory requirements.

If at any time Investigator noncompliance is discovered at OHSU, the Investigator shall promptly either secure compliance or halt the study.

Independent audits will be conducted by the Knight DSMC to verify that the rights and well-being of human participants are protected, that the reported trial data are accurate, that the conduct of the trial is in compliance with the protocol and applicable regulatory requirements, and that evidence of ongoing investigator oversight is present.

10.3 QUALITY ASSURANCE & QUALITY CONTROL

The investigational site will provide direct access to all trial related source data/documents, and reports for the purpose of monitoring by the monitor and/or sponsor, and auditing by the Knight DSMC and/or regulatory authorities.

Quality assurance (QA) auditing activities will occur as detailed in the Knight DSMP. All discrepancies, queries, deviations, observations, and findings will be compiled into a final audit report along with a Corrective and Preventative Action Plan.

The Sponsor-investigator, or study monitor, will verify that the clinical trial is conducted and data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirements (e.g., Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP)).

11. DATA HANDLING AND MANAGEMENT RESPONSIBILITIES

11.1 SOURCE DATA/DOCUMENTS

The Investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data. The Investigator will maintain adequate case histories of study participants, including accurate case report forms (CRFs), and source documentation.

11.2 PARTICIPANT & DATA CONFIDENTIALITY

The information obtained during the conduct of this clinical study is confidential, and unless otherwise noted, disclosure to third parties is prohibited. Information contained within this study will be maintained in accordance with applicable laws protecting participant privacy, including the provisions of the Health Insurance Portability and Accountability Act (HIPAA).

Participant confidentiality is strictly held in trust by the participating Investigator(s) and study team. This confidentiality is extended to cover testing of biological samples and genetic tests in addition to the clinical information relating to participants. Therefore, the study protocol,

documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

Authorized representatives of the sponsor, representatives of the IRB or manufacturer supplying study product may inspect all documents and records required to be maintained by the Investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by local IRB and institutional regulations. Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored within the Knight Cancer Institute per OHSU's Information Security Directives. Individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by clinical sites and by Knight Cancer Institute research staff will be secured and password protected per OHSU's Information Security Directives. At the end of the study, all study databases will be de-identified and archived within the Knight Cancer Institute.

11.3 DATA COLLECTION & STORAGE: PRIVACY, CONFIDENTIALITY & SECURITY

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site Investigator. The Investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. Standard institutional practices will be followed as described in the OHSU's Information Security Directives to maintain the confidentiality and security of data collected in this study. Study staff will be trained with regard to these procedures.

Loss of participant confidentiality is a risk of participation. Efforts will be made to keep study participant identities confidential except as required by law. Participants' samples will be identified by code only. Specifically, each consenting participant will be assigned a unique coded identifier consisting of numbers. This identifier will be associated with the participant throughout the duration of their participation in the trial. The coded identifier will also be used to identify any participant specific samples.

Basic accrual tracking information (demographic, consent, visit information) will be captured in OHSU's electronic clinical information research system (eCRIS), hosted on OHSU secure servers and managed by OHSU's information technology group at their data center in downtown Portland, Oregon. Any additional printed documents containing participant identifiers, such as those from the medical record to confirm eligibility, will be filed in binders and kept in a locked, secure location.

Study outcome data will be captured in electronic case report forms (eCRFs) using an electronic data capture (EDC), REDCap, system on OHSU secure servers, which facilitates information being stored in a unified format and location. To further preserve confidentiality, PHI in the EDC system will be limited to just birth date and visit dates. The web-accessible EDC system is password protected and encrypted with role-based security, and administered by designated informatics staff within OHSU or Knight Cancer Institute. All users of the database are assigned

a unique ID, username, and password and must complete training appropriate to their role before they are authorized to enter, access, and store data in the database.

Survey responses and results of physical function assessments will be entered into the EDC system by study personnel at OHSU. All other electronic data extracts will be stored only on OHSU computers and restricted drives, limited only to study investigators and staff with authorization to access the data. Quality assurance will be conducted as outlined in Section 10.3, Quality Assurance & Quality Control.

Results of some physical function assessments may be shared with participants at the completion of the study.

11.4 MAINTENANCE OF RECORDS

Records and documents pertaining to the conduct of this study, source documents, consent forms, laboratory test results and medication inventory records, must be retained by the Investigator for a period of 2 years, after which all study databases will be de-identified and archived within the Knight Cancer Institute.

If the Investigator relocates or for any reason withdraws from the study, the study records must be transferred to an agreed upon designee, such as another institution or another investigator at OHSU. Records must be maintained according to institutional requirements.

11.5 PUBLICATION AND DATA SHARING POLICY

This study will adhere to the requirements set forth by the ICMJE and FDAAA that requires all clinical trials to be registered in a public trials registry (e.g., ClinicalTrials.gov) prior to participant enrollment.

12. ETHICS/PROTECTION OF HUMAN PARTICIPANTS

12.1 ETHICAL STANDARD

The Investigator will ensure that this study is conducted in full conformity with Regulations for the Protection of Human Participants of Research codified in 45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, and/or the ICH E6.

12.2 INSTITUTIONAL REVIEW BOARD

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form will be IRB approved; a determination will be made regarding whether previously consented participants need to be re-consented.

12.3 INFORMED CONSENT

Informed consent will be obtained from all participants, or the legally authorized representative of the participant, participating in this trial, as stated in the Informed Consent section of 21 CFR

Part 50. Documentation of the consent process and a copy of the signed consent shall be maintained in the participant's medical record.

12.3.1 CONSENT PROCEDURES AND DOCUMENTATION

Informed consent is a process that is initiated prior to the individual's agreement to participate in the study and continues throughout the individual's study participation. Extensive discussion of risks and possible benefits of participation will be provided to the participants and their families as appropriate. Consent forms will be IRB-approved and provided to the participant in-person or via email, fax, mail or other modality. The participant will be asked to read and review the document. During the consent process, the subject will have access to a copy of the consent form and the consenting investigator or designee will discuss and review the entirety of the consent form with the subject. The Investigator will explain the research study to the participant and answer any questions that may arise. All participants will receive a verbal explanation in terms suited to their comprehension of the purposes, procedures, and potential risks/benefits of the study, alternatives to participation, and of their rights as research participants. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants should have the opportunity to discuss the study with their surrogates or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. The consent form will then be provided in-person, mailed, faxed, emailed, or returned to the site by other modality in its entirety. The consent process will be documented in the participant's health record. Upon receipt of the signed consent, the investigator or designee who performed the consent will sign and date the consent form and document the consent process in the participant's health record. The participants may withdraw consent at any time throughout the course of the trial. A copy of the informed consent document will be given to the participants or provided via email, fax mail or other modality for their records. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

12.4 PROTOCOL REVIEW

The protocol and informed consent form for this study must be reviewed and approved in writing by the OHSU Knight Cancer Institute's Clinical Research Review Committee (CRRC) and the appropriate IRB prior to any participant being consented on this study.

12.5 CHANGES TO PROTOCOL

Any modification of this protocol must be documented in the form of a protocol revision or amendment submitted by the Investigator and approved by the CRRC and IRB, before the revision or amendment may be implemented. The only circumstance in which the amendment may be initiated without regulatory approval is for a change necessary to eliminate an apparent and immediate hazard to the participant. In that event, the Investigator must notify the IRB (and sponsor/FDA if under an IND/IDE) within 5 business days after the implementation.

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OREGON HEALTH & SCIENCE UNIVERSITY

MED. REC. NO._____
NAME_____
BIRTHDATE_____

IRB#: 19942 NCT#: NCT04247425

CO1450

OHSU Knight Cancer Institute Consent and Authorization Form

TITLE: ***USE OF RESISTANCE TRAINING PROGRAM TO IMPROVE PHYSICAL FUNCTION IN SARCOMA SURVIVORS***

STUDY INVESTIGATOR: LARA DAVIS, MD

WHO IS PAYING FOR THE STUDY?: OHSU Knight Cancer Institute

WHO IS PROVIDING SUPPORT FOR THE STUDY: N/A

DO ANY OF THE RESEARCHERS HAVE A CONFLICT OF INTEREST WITH THIS STUDY?:
N/A

STUDY CONTACT INFORMATION

Purpose	Role	Contact Name	Contact Phone Number	Email
For medical questions about the study	Principal Investigator	Lara Davis, MD	503-494-6594	
	Co-Investigator	Christopher Ryan, MD	503-494-6594	
	Co-Investigator	Kerri Winters-Stone, PhD	503-494-6594	
	Co-Investigator	Katrina Winsnes, MD	503-494-6594	
For non-medical questions about the study	Study Coordinator			KnightSarcomaCRC@ohsu.edu
For questions about research in general	Ethics Committee	ORIO	503-494-7887	irb@ohsu.edu
For 24-hour medical emergencies	911	Emergency Dispatch	911	
	Oncologist On-Call	OHSU Operator	503-494-9000	

INTRODUCTION

WHAT IS THE USUAL APPROACH AFTER COMPLETING SARCOMA TREATMENT?

You are being asked to take part in this study because you have previously received treatment for a sarcoma.

Treatments for sarcoma can cause side effects such as fatigue, muscle loss, and weakness, which can negatively impact your ability to physically function and enjoy an independent lifestyle. People who do not take part in this study may receive recommendations such as encouragement to exercise, and/or ways to adjust their daily activities to help combat some of the physical side effects of cancer treatment.

WHAT ARE MY OTHER CHOICES IF I DO NOT TAKE PART IN THIS STUDY?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to continue your current care without change
- you may choose to take part in a different study, if one is available

PURPOSE

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to assess the feasibility of using a routine resistance training exercise regimen as a means to improve physical function in sarcoma cancer survivors. The study also aims to determine if a 3-month exercise program improves body composition and bone density in sarcoma survivors post-treatment.

The resistance training exercise regimen we are studying is experimental. We do not know if it is better than the usual approach for improving physical function in people that have been treated for sarcoma.

This is a clinical trial, a type of research study. Medical personnel who carry out research studies are called "investigators." The investigator will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You can discuss your decision with your friends and family. You can also discuss it with your health care team or another doctor. If you have any questions, ask the investigator.

WHAT DATA WILL BE COLLECTED?

We are asking you to provide information for a data bank, also called a repository. This information will be stored indefinitely and may be used and disclosed in the future for research. We will ask you to provide the following information:

- Your demographics – your current age and your sex, race, ethnicity, and the zip code where you currently live.

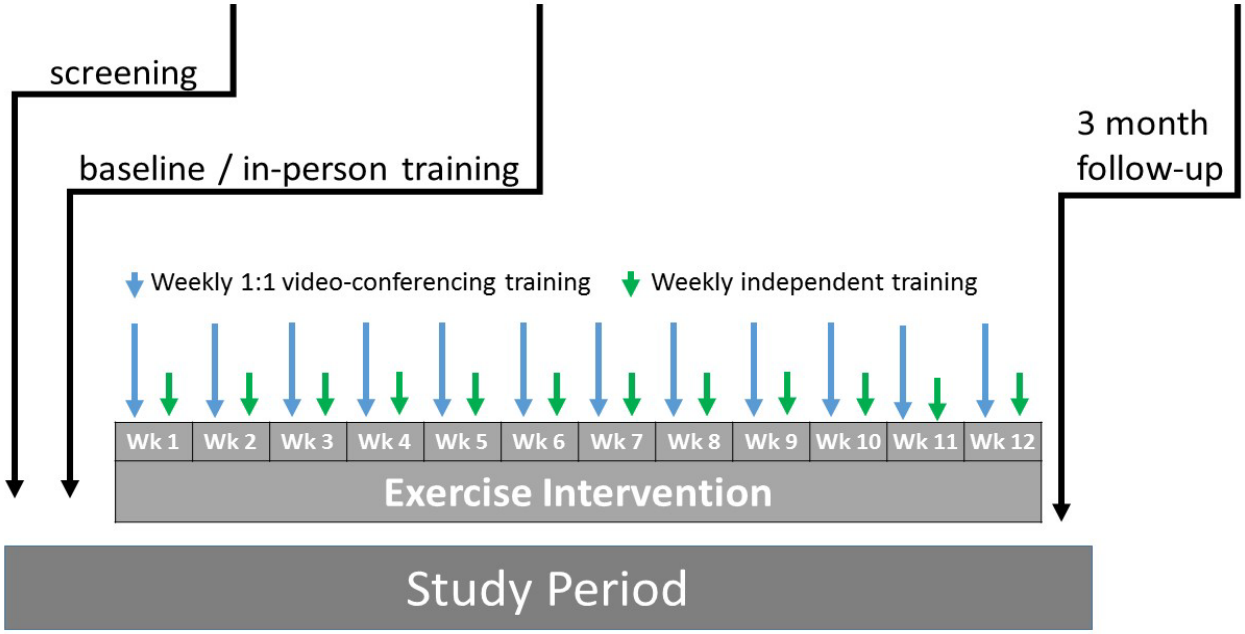
- Your sarcoma history – the age at which you were diagnosed, your specific diagnosis (for example, rhabdomyosarcoma or osteosarcoma), and what you remember about the treatment you received (which might have included chemotherapy, surgery, and/or radiation).
- Your medical history – other cancers you may have also been diagnosed with, any chronic illnesses you might have, and any surgeries you've had that weren't related to your sarcoma.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

As many as 10 people will take part in this study, which will be conducted at Oregon Health & Science University (OHSU).

PROCEDURES

STUDY DESIGN OVERVIEW



HOW LONG WILL I BE IN THIS STUDY?

You will receive an individualized therapeutic resistance exercise plan to complete over a 12-week period. After you finish the resistance exercise regimen, your doctor will see you for a 3-month follow up visit to assess side effects. The total length of your participation is about 3-months.

WHAT TESTS AND PROCEDURES WILL I HAVE IF I TAKE PART IN THIS STUDY?

Before you begin the study:
If you are interested in participating, you will be asked a few questions regarding your cancer history, current physical activity, and quality of life. Your doctor will assess you for medical clearance for you to participate in exercise training before your exercise plan starts. Physician clearance is required to participate in the study because it will help ensure your safety to perform moderate level intensity exercise. We will collect information about your cancer diagnosis and treatment from your medical records. You will next be scheduled to complete a series of baseline assessments (see below) with a Research Assistant. You will need to have the following tests and procedures to find out if you can be in the study:

Baseline assessment visit:

- Record height and weight
- DXA scan to evaluate your bone density and body composition. A urine pregnancy test for women who can become pregnant is required prior to DXA scan.
- Questionnaires, which will take roughly 1 hour to complete.
- A series of physical tests to measure a baseline for strength, balance, and function. A Research Assistant will guide you through a series of activities. These activities include rising and sitting from a chair five times as quickly as you can and rising from a chair, walking about 10 feet, turning around, walking about 10 feet back to the chair, and sitting down.

If in-person assessments are not feasible, the study visits may be omitted, delayed, or modified to best suit your needs.

During the study:
If the exams, tests, and procedures show that you can take part in the study, and you choose to take part, then you will be asked to complete a one-hour exercise training session two times per week for the next 3 months. For the first two weeks, participants will perform one weekly training under the supervision of a trainer via 1:1 web-based videoconferencing, and the second training session will be completed on your own. An Exercise Physiologist (EP) trainer will create an individualized training program for you. After two weeks, you may decide to join a group video conference with 1-2 other participants, or continue 1:1 with the EP. At the baseline visit, participants will be provided with the necessary equipment (i.e., resistance bands, weights, weighted vest as appropriate) and receive in-person verbal and written instruction from a trainer on how to use the equipment and perform each assigned exercise.

Participants will perform all exercise sessions remotely (e.g., at home). One exercise session per week will be conducted under the supervision of an EP trainer using videoconferencing software. During these web-based video conferences, the EP trainer will observe the participant and provide feedback on technique, as well as implement progressive resistance (e.g., increase number of repetitions or increase weight). Each participant will also complete one-hour of prescribed resistance exercise independently each week and record in a provided training log.

The exercise intervention will be conducted for a total of 12 weeks, but participants will be encouraged to continue resistance training after completing the study. At the end of your 3-month participation, you will be asked to return for a follow up visit.

A study schedule that shows how often these tests and exercises will be done is attached.

RISKS

WHAT POSSIBLE RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?

DXA Scans: In this study you will be exposed to radiation during the DXA scans. While no radiation dose has been determined to be entirely safe, the amount to which you will be exposed is not known to cause health problems. For women of childbearing potential, a urine pregnancy test will be checked prior to the DXAscan.

Physical Tests: There are some discomforts and risks from the physical tests. In order to try to minimize risks, all testing will be conducted by trained personnel. You may feel sore after the physical tests. Muscle soreness usually goes away after two or three days. You may sustain an injury during the physical testing. The risk of this is low and the researchers are trained to show you the best ways to avoid injury during the tests.

Questionnaires: As part of this study, you will be asked to complete questionnaires. Some of these questions may seem very personal or embarrassing. They may upset you. You may refuse to answer any of the questions that you do not wish to answer. If the questions make you very upset, we will help you to find a counselor.

As with any form of regular exercise training, the risk of injury is increased. We have taken precautions to make the exercises as safe as possible. The exercises will be led by a certified exercise professional. The study exercises have been performed before in cancer survivors who have reported no significant injuries as a result of the study.

Here are important points about how you and the investigator can make these risks less of a problem:

- Tell the investigator if you are unable to complete a test or a survey. The investigator can allow for a longer rest period during the test or reschedule it for a different day.
- Tell the investigator if you are unwilling to complete a test or survey. You do not have to complete some or all tests and surveys.

Let your investigator know of any questions you have about possible side effects. You can ask the investigator questions about side effects at any time.

BENEFITS

WHAT POSSIBLE BENEFITS CAN I EXPECT FROM TAKING PART IN THIS STUDY?

Participants may not benefit from participating in this study; however, their participation may contribute to knowledge used for future studies that address patients with cancer. Additionally, an exercise regimen may improve your physical function.

No compensation will be provided to you for your involvement in this study. After successful completion, you will be allowed to keep all study-related exercise equipment provided (e.g., resistance bands, dumbbells, weighted vests). Participants will be required to return the webcam if one was provided.

PRIVACY

ACCESS TO YOUR TEST RESULTS

We will give you the results of your DXA bone scans during the study. The results will be placed in your medical record. We plan to share the results of the physical tests with you at the end of the study.

WHO WILL SEE MY MEDICAL INFORMATION?

We will take steps to keep your personal information confidential, but we cannot guarantee total privacy.

We will create and collect health information about you as described in the WHY IS THIS STUDY BEING DONE and the WHAT TESTS AND PROCEDURES WILL I HAVE IF I TAKE PART IN THIS STUDY?

sections of this form. Health information is private and is protected under federal law and Oregon law. By agreeing to be in this study, you are giving permission (also called authorization) for us to use and disclose your health information as described in this form.

The investigators, study staff and others at OHSU may use the information we collect and create about you in order to conduct and oversee this research study and conduct future research.

We may release this information to others outside of OHSU who are involved in conducting or overseeing this research, including:

- The Food and Drug Administration (FDA)
- The Office of Human Research Protections (OHRP), a federal agency that oversees research in humans
- The National Cancer Institute (NCI)

Those listed above may also be permitted to review and copy your records, including your medical records.

We may also share your information with other researchers, who may use it for future research studies.

We will not release information about you to others not listed above, unless required or permitted by law. We will not use your name or your identity for publication or publicity purposes, unless we have your special permission.

When we send information outside of OHSU, it may no longer be protected under federal or Oregon law. In this case, your information could be used and re-released without your permission.

You may be asked to give us health information about your relatives. Any information you give us will be kept confidential as described in this consent. You may be asked to provide emergency contact information. We will not contact your relatives without their permission. We may discuss with you the possibility of including your relatives in the study in the future.

After all of the analyses are completed using your collected data, some participant data, including your contact information, will be stored in a private locked-repository managed by Dr. Lara Davis, the Principal Investigator of this study. A code number will be assigned to your data, as well as information about you. Only the investigators named on this consent form will be authorized to link the code number to you. Other investigators who may receive your data for research will be given only the code number which will not identify you.

We may continue to use and disclose your information as described above indefinitely. Some of the information collected and created in this study may be placed in your OHSU medical record. While the research is in progress, you may or may not have access to this information. After the study is complete, you will be able to access any study information that was added to your OHSU medical record. Ask the investigator if you have questions about what study information you will be able to access, and when it will be available.

PARTICIPATION

CAN I STOP TAKING PART IN THIS STUDY?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the investigator know as soon as possible so you can stop safely. Another reason to tell the investigator that you

are thinking about stopping is to discuss what testing, follow-up, or additional treatment could be most helpful for you. If you stop, you can decide whether or not to let the investigator continue to provide your medical information to the organization running the study.

Once your participation has ended, your cancer doctor will help you choose the next step in your cancer care.

The investigator will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study. The investigator may take you out of the study if:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the IRB or FDA.

WHAT ARE MY RIGHTS IN THIS STUDY?

Your participation in this study is voluntary. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights. If you have any questions, concerns, or complaints regarding this study now or in the future, contact the principal investigator listed at the beginning of the form.

This research has been approved and is overseen by an Institutional Review Board ("IRB"), a committee that protects the rights and welfare of research participants. You may talk to the IRB at (503) 494-7887 or irb@ohsu.edu if:

- Your questions, concerns, or complaints are not being answered by the research team
- You want to talk to someone besides the research team
- You have questions about your rights as a research participant
- You want to get more information or provide input about this research.

You may also submit a report to the OHSU Integrity Hotline online at https://secure.ethicspoint.com/domain/media/en/gui/18915/index.html or by calling toll-free (877) 733-8313 (anonymous and available 24 hours a day, seven days a week).

You do not have to join this or any research study. You do not have to allow the use and disclosure of your health information in the study, but if you do not, you cannot be in the study. Some parts of the study are optional. You can choose not to participate in some or all of the optional parts but still participate in the rest of the study

If you do join the study and later change your mind, you have the right to quit at any time. This includes the right to withdraw your authorization to use and disclose your health information. You can choose to withdraw from some or all of the optional parts of this study without withdrawing from the whole study. If you choose not to join any or all parts of this study, or if you withdraw early from any or all parts of the study, there will be no penalty or loss of benefits to which you are otherwise entitled, including being able to receive health care services or insurance coverage for services. Talk to the investigator if you want to withdraw from the study or change which parts of the study you are participating in.

If you no longer want your health information to be used and disclosed as described in this form, you must send a written request or email stating that you are revoking your authorization to:

Knight Cancer Institute Clinical Trials
Attn: CRQA Assistant Director
Mail Code: KR-CRQA
3181 SW Sam Jackson Park Road
Portland, OR 97239
Email: trials@ohsu.edu

Your request will be effective as of the date we receive it. However, health information collected before your request is received may continue to be used and disclosed to the extent that we have already taken action based on your authorization.

Your health care provider may be one of the investigators of this research study and, as an investigator, is interested in both your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may ask for a second opinion about your care from another doctor who is in no way involved in this project. You do not have to be in any research study offered by your physician.

You will be told of any new information that might make you want to change your mind about continuing to be in the study.

WHAT TRAVEL REIMBURSEMENTS ARE AVAILABLE IN THIS STUDY?

There is no travel reimbursement available for this study.

WHAT HAPPENS IF I AM INJURED OR HURT BECAUSE I TOOK PART IN THIS STUDY?

In an emergency, dial 911 or your local emergency number immediately. If you believe you have been injured or harmed as a result of participating in this research and require treatment, contact Dr. Lara Davis at 503-494-6594.

If you are injured or harmed by the study procedures, you will be treated. OHSU and the funder, do not offer any financial compensation or payment for the cost of treatment if you are injured or harmed as a result of participating in this research. Therefore, any medical treatment you need may be billed to you or your insurance. However, you are not prevented from seeking to collect compensation for injury related to negligence on the part of those involved in the research. Oregon law (Oregon Tort Claims Act (ORS 30.260 through 30.300)) may limit the dollar amount that you may recover from OHSU or its caregivers and researchers for a claim relating to care or research at OHSU, and the time you have to bring a claim.

If you have questions on this subject, please call the OHSU Research Integrity Office at (503) 494-7887.

WHAT IS COMMERCIAL DEVELOPMENT AND HOW DOES IT AFFECT ME?

Information about you or obtained from you in this research may be used for commercial purposes, such as making a discovery that could, in the future, be patented or licensed to a company, which could result in a possible financial benefit to that company, OHSU, and its researchers. There are no plans to pay you if this happens. You will not have any property rights or ownership or financial interest in or arising from products or data that may result from your participation in this study. Further, you will have no responsibility or liability for any use that may be made of your samples or information.

ADDITIONAL INFORMATION

WHERE CAN I GET MORE INFORMATION?

You may visit the NCI website at https://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

If you want more information about this study, ask the investigator.

OPTIONAL

This part of the consent form is about optional portion of the study that you can choose to take part in. You may or may not personally benefit from being in this study. However, by serving as a participant, you may help us learn how to benefit patients in the future.

In the main portion of this study, an Exercise Physiologist (EP) will create an individualized training program for you using 1:1 videoconferencing. After two weeks, you may decide to join 1-2 other participants in optional group videoconferencing. If you do not wish to participate in the group videoconferencing, you will continue 1:1 videoconferencing with the EP.

HOW WILL INFORMATION ABOUT ME BE KEPT PRIVATE?

There will be no information collected from this optional portion of the study.

ARE THERE ANY COSTS OR PAYMENTS?

There are no costs to you or your insurance. You will not be paid for taking part.

WHAT IF I CHANGE MY MIND?

If in the future you decide you no longer want to participate, we will stop inviting you to the optional group videoconferencing. During the videoconferencing, none of your private information will be obtained. If you wish to no longer participate, you can call the investigator listed at the beginning of this consent form.

WHAT IF I HAVE MORE QUESTIONS?

If you have questions about the videoconferencing, contact the investigator listed at the beginning of this consent form.

PARTICIPANT OPTIONS:

Please initial to show whether or not you would like to take part in the optional study. You can still participate in the main part of the study even if you choose not to participate in the optional portion.

	Yes, I agree	*No, I decline*
I choose to take part in the optional study and will participate in the optional group videoconferencing.	_____ *Participant initials*	_____ *Participant initials*

This is the end of the section about optional studies.

SIGNATURE

MY SIGNATURE AGREEING TO TAKE PART IN THE STUDY

Your signature below indicates that you have read this entire form and that you agree to be in this study. We will give you a copy of this signed form.

Participant Printed Name	Participant Signature	Date

Person(s) Obtaining Consent Printed Name	Person(s) Obtaining Consent Signature	Date

Use of an Interpreter: Complete if the participant is not fluent in English and an interpreter was used to obtain consent. Participants who do not read or understand English must not sign this full consent form, but instead sign the short form translated into their native language. This form should be signed by the investigator and interpreter only. If the interpreter is affiliated with the study team, the signature of an impartial witness is also required.

Print name of interpreter: _____

Signature of interpreter: _____ Date:_____

An oral translation of this document was administered to the participant in _____ (state language) by an individual proficient in English and _____ (state language).

If applicable:
Print name of impartial witness: _____
Signature of impartial witness: _____ Date: _____

See the attached short form for documentation.

STUDY SCHEDULE

This schedule lists study procedures so you can see all of the things that will happen during the study in one place.

Procedures	Screening	Baseline†/W1	Intervention Period (12 weeks [W])											Follow Up*
			W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12	
Eligibility review	X													
Treating physician evaluation	X													
Informed Consent	X													
Questionnaires														
Physical Function: PROMIS-PF/Cancer		X												X
Quality of Life: SF-36		X												X
Exercise: GLTEQ		X												X
Fatigue: FACT-F		X												X
Baseline demographics		X												
Self-reported limitations		X												
Adverse Events		X	X		X		X		X		X		X	
Physical Tests														
BMI — height + weight		X												X
Strength – 1RM		X												X
Strength – grip														
Lower extremity function – short PPB		X												X
Gait – iTUG		X												X
Balance – ISway		X												X
Gait/Balance – i6MWT		X												X
DXA		X												X***
Urine Pregnancy test**		X												X
In-Person Training****		X												
Videoconferenced PRT‡			X	X	X	X	X	X	X	X	X	X	X	
Independent PRT‡			X	X	X	X	X	X	X	X	X	X	X	
ESTIMATED TIME (hours)	**0.5**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**

† Baseline assessments should occur within 14 days before initiating the exercise intervention; however, these assessments may be performed during Week 1 prior to initiating exercise intervention or may be omitted, delayed, or modified to be performed virtually.

‡ The PRT regimen will consist of 2 one-hour training sessions per week (1 videoconference, 1 independent) for a total of 12 weeks (i.e., a total of 24 training sessions).

*12-week assessments may occur ±14 days before or after completing the exercise intervention, however; these assessments may be omitted, delayed, or modified to be performed virtually.

** Prior to DXA, for women of whom can become pregnant only.

*** DXA at follow-up will omit bone mineral density.

**** In-person training may be omitted, delayed, or modified to be performed virtually.