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]

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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.

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.

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.

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

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.

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.

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.

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.

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,