Allegheny Health Network

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EXERT-BC: Prospective study of an **EXE**rcise **R**egimen designed to improve functional mobility, body composition, and strength after **T**reatment for **B**reast **C**ancer

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EXERT-BC: Prospective study of an **EXE**rcise **R**egimen designed to improve functional mobility, body composition, and strength after **T**reatment for **B**reast **C**ancer

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2. LIST OF ABBREVIATIONS

AE	Adverse event
BMI	Body mass index
CKC	Closed Kinetic Chain
CLIA	Clinical Laboratory Improvement Amendments
CMP	Comprehensive metabolic panel
CPC	Cancer Protocol Committee
CRF	Case report form
CSCS	Certified Strength and Conditioning Specialist
DEXA	Dual energy x-ray absorptiometry
DSMB	Data safety and monitoring board
eCRF	electronic case report form
EPOC	Excess post-exercise oxygen consumption
FDA	Food and Drug Administration
GCP	Good clinical practice
ICH	International Conference on Harmonization
FACT-B4	Functional Assessment of Cancer Therapy - Breast
FMS	Functional Mobility Screen
IRB	Institutional Review Board
MET	Metabolic equivalent of task
NSCA	National Strength and Conditioning Association
OARC	Office of Audit, Risk and Compliance
OKC	Open kinetic chain
PI	Primary investigator
QOL	Quality of Life
RDSP	Research Data Security Plan
SAE	Serious adverse event
SOC	Standard of Care
SOP	Standing operating procedures

3 PROTOCOL SYNOPSIS

3.1 Purpose:

This protocol seeks to analyze patient outcomes of the standard of care, monitored group exercise regimen of high-load resistance training and functional exercises with compound movements under close supervision on women who have been treated for breast cancer.

Primary Objective

1 Determine safety and feasibility measured by exercise compliance.

Exploratory Objectives

1 Determine changes in functional mobility testing changes at baseline, throughout, post-exercise assessment and 1 year after exercise assessment.
2 Determine quality of life at baseline, throughout, and post- exercise assessment
3 Determine changes in strength and load lifted at baseline, throughout, post-exercise assessment, and 1 year after exercise assessment.
4 Determine changes in resting metabolic rate at baseline, throughout, post-exercise assessment, and 1 year after exercise assessment.
5 Determine changes in body composition at baseline, throughout, post- exercise assessment and 1 year after exercise assessment, including body mass, fat mass, fat-free mass, % fat, and % fat-free mass.

Hypotheses

In this study, we hypothesize that an observed exercise regimen utilizing high-load resistance training initiated during or after cancer treatment is safe and feasible in women and may improve functional mobility, body composition, and resting metabolic rate.

3.2 Background and Significance:

Obesity is a risk factor for both breast cancer and disease recurrence after treatment.[1] Furthermore, weight gain during and after treatment for breast cancer is associated with a higher risk of recurrence, distant metastases, and death.[2] Yet, most women gain significant weight during and after breast cancer treatment, potentially compromising outcomes.

Contrary to these findings, activity levels have been repeatedly associated with a lower risk of breast cancer incidence, improved outcomes after breast cancer treatment, and improved breast cancer-specific and overall survival.[3] The majority of breast cancer survivors do not meet adequate daily activity level recommendations, potentially compounding issues with weight gain during and after breast cancer treatment.[4] As a result, attempts are underway to both quantify and increase activity levels during treatment and survivorship.[5] Furthermore, and based on these findings, several areas of

research have attempted to analyze both diet and exercise regimens in women with breast cancer to reduce weight. Beyond solely assessing weight gain, other data reveal a close association between several metabolic factors and poorer outcomes after breast cancer treatment, including elevated serum glucose, decreased insulin sensitivity, elevated serum insulin, increased inflammatory factors, and decreased muscle mass.[6–8] These factors can be generally improved through specific targeted exercise training, suggesting metabolic benefits of exercise beyond simple weight loss. Furthermore, as resistance training improves strength, muscle hypertrophy, and body composition, and leads to physical and cellular changes that appear to counter these metabolic perturbations – often unrelated to changes in overall weight – such training may be a prudent strategy to improve measurable variables associated with breast cancer specific and overall health benefit.[9–11] However, this approach differs from current exercise strategies that often aim to elicit cardiac benefits and calorie deficits through aerobic and extended activity that involves intermediate to low intensity exercises.[12]

Moreover, studies in non-cancer populations reveal that exercise is generally minimally effective for weight loss, and specifically fat loss, when unaccompanied by other health changes.[13] Simply relying on aerobic exercise to induce caloric deficit for weight loss in the oncologic setting may be concerning in as it can lead to loss of lean mass and muscle tissue,[14] and the potential metabolic and functional benefits that accompany both. Studies reveal that resistance training requiring more intense effort may help support lean mass maintenance or even muscle gains during weight loss, which has been shown to simultaneously increase resting metabolic rate to increase fat oxidation and improve body composition.[11,15] Such changes may be more advantageous in the oncologic setting than previous exercise strategies.

For example a recent randomized trial of an unobserved home aerobic exercise regimen revealed no improvement in physical functioning in women with metastatic breast cancer, assessed via an array of physical tests.[16] Another recent study in overweight women with breast cancer utilizing a 52-week, home-based exercise program consisting of lightweight strength and resistance training twice per week and 180 minutes of walking per week revealed no weight loss.[17] Additionally, no improvement in aerobic fitness or strength tests was experienced by the women in the exercise group. Progression in resistance load during resistance training in the majority of studies has been slow with low loads to avoid exacerbating lymphedema.[18] Yet, multiple studies have now confirmed no increase, and potentially improvement, in lymphedema in women undergoing resistance training after breast cancer treatment.[17,19–21] For safety measures, many home exercise programs in breast cancer patients also utilize light-weight free-weights or open kinetic chain (OKC) movements where the body is fixed and the distal extremities are mobile (as in arm curls), both of which can often limit activation of core and accessory muscles, leading to a less intense regimen that may limit functional and mobility benefits and hypertrophy.[22,23] Closed kinetic chain (CKC) exercises involve fixation of the distal aspect of the extremity (as in the squat), as opposed to proximal isolation (with OKC), therefore requiring involvement of multiple joints and co-contraction of multiple

simultaneous muscles to stabilize the body during movement, also known as compound exercises. Such CKC exercises include lunges, squats, deadlifts, and power cleans; on the contrary, examples of OKC exercises are bench press, seated leg curls and extensions, and machine curls. CKC and compound exercises also mimic athletic movements, thus positively impacting mobility and function.

Studies in non-cancer patients reveal that resistance training routines that expose muscle tissue to extensive mechanical tension with subsequent muscle damage and metabolic stress promote training-induced muscle growth.[24] Additionally, more intense and heavier weight lifting regimens have been consistently shown to improve several factors associated with health, including: 1) Improved strength and fitness and decreased risk of injury, 2) Increased muscle mass and corresponding decrease in inflammation,[25] 3) Enhanced insulin sensitivity, elevated resting metabolic rate, and decreased risk of diabetes,[4] 4) Improved mobility and overall health,[26] and 5) Increased bone mineral density.[27] Furthermore, resting metabolic rate, which comprises the majority of daily total energy expenditure, is proportional to muscle mass.[28] Additionally, excess postexercise oxygen consumption (EPOC), or the continued enhanced metabolic effect after the completion of exercise, is enhanced via strenuous resistance training compared with aerobic training alone.[29]

While weight training has clear advantages over aerobic training for improving body composition and several measurable metabolic variables, there have been barriers to its implementation in exercise regimens for the breast cancer patient, including concerns of safety and lymphedema risk.[30] However, as stated above, these risks have been largely disproved by the current available research.[31] Adverse effects (AEs) reported in prior exercise studies include typical self-limiting musculoskeletal issues, including muscle strains, joint and back pain, shin splints, and tendinitis.[32] Overall, AEs are minimal. Furthermore, an observed environment with supervision by trained exercise personnel can further reduce the risk of injury,[33,34] as can adaption of a workout regimen that accounts for individuals' functional movement abilities, mobility, and function.[35]

3.3 Rationale:

To date, the majority of exercise intervention studies for women with breast cancer after treatment focus on aerobic exercise regimens and/or low to moderate-intensity resistance training. Additionally, the components of resistance training often rely on isolated and open kinetic chain exercises utilizing light weights and high repetition schemes that may not be optimal for hypertrophy and improvement of functional movements.[36] These regimens have generally been implemented with two major goals: 1) Provide weight reduction, 2) Increase energy expenditure measured via metabolic equivalent of task (MET). Such goals are based on significant literature revealing improved outcomes after breast cancer treatment in physically active women and worse outcomes in women who gain weight during and after treatment.[2] However,

mechanistically, it is unclear if these strategies are most prudent to improve health and breast cancer-specific outcomes.[37]

There is a paucity of data utilizing and testing multiple-joint, closed kinetic chain, and compound exercises that rely on full body movements with the goal of improving strength, hypertrophy, and functional movement patterns in women after breast cancer treatment. This remains a concerning gap in the literature, as multiple studies in non-cancer populations have revealed body composition and metabolic improvements following such weight training regimens. Additionally, studies reveal that observed exercise programs lead to enhanced strength gains and hypertrophy,[38] and successful exercise interventions tend to be those that involve direct supervision.[39] Finally, many of the exercise regimens tested include prolonged exercise regimens like treadmill and aerobic sessions lasting 90 minutes or more. More intense weight training generally lasts a fraction of this and may therefore serve as a time-effective method of exercise.

Thus, this protocol will attempt to analyze patient outcomes of an observed exercise regimen utilizing high-load resistance training via compound CKC and functional resistance exercises with the goal of improving physical and metabolic function, mobility, muscle mass, and body composition in women previously treated for breast cancer utilizing guidelines from the National Strength and Conditioning Association (NSCA).

3.4 Design and Procedure:

Feasibility and safety single-arm registry study in subjects with newly diagnosed ductal carcinoma in situ (DCIS) or invasive carcinoma of the breast.

3.5 Selection of Subjects and Sample Size:

Women ages 20-89 treated for ductal carcinoma in situ or invasive carcinoma will be considered for this trial.

The accrual goal is 43 subjects to achieve a sample size of 40 subjects, allowing for enrolled subjects who are unable to be complete the exercise program. Estimated accrual and completion time is approximately 2 years.

3.6 Duration of Study:

Subjects will be on study for an approximate 15 months, with the exercise program encompassing 12 weeks and an assessment following 1 year after the exercise program. Thereafter subjects will continue to be followed by the treating medical oncologist and/or radiation oncologist per standard of care (SOC) for follow up care but utilizing the data for research purposes.

4. SUBJECT ELIGIBILITY

4.1 Inclusion Criteria:

1 Age 20-89 years
2 Women with a biopsy proven diagnosis of ductal carcinoma in situ or invasive carcinoma of the breast
3 Women must have undergone treatment for breast cancer, including one or more of the following: surgery, radiation therapy, chemotherapy, immunotherapy, or hormonal therapy. Women undergoing active chemotherapy or immunotherapy are not allowed on study.
4 Participants must have abstained from smoking for at least 12 months
5 Participants must be prescribed by their treating physician to engage in resistance training for 3 months (12 weeks).
6 Participants will be assessed 1 year following exercises as they were at baseline and post exercise as SOC.

4.2 Exclusion Criteria:

1 Any current treatment with chemotherapy for breast cancer
2 Inability to get and down off the ground or squat body weight
3 Inability to safely engage in group sessions
4 Severe arthritic, joint, cardiovascular, or musculoskeletal condition deemed by PI to be unsafe to engage in resistance training

4.3 Inclusion of Women and Minorities

Women of all races/ethnicities will be eligible for this study and accrual is expected to reflect the population of subjects seen within the Pittsburgh, PA area.

5. EXERCISE REGIMEN

5.1 Location:

The exercise facility participating in the study is located within AGH Suburban at the AHN Cancer Institute Exercise Oncology and Resiliency Center, 100 S Jackson Ave Pittsburgh, PA 15202.

5.2 Personnel:

As per SOC, the exercise regimens will be constructed and reviewed by the Exercise Oncology Consortium and monitored by Colin Champ, MD, CSCS, and associated Certified Strength and Conditioning Specialists and staff. Champ is a radiation oncologist trained in integrative medicine and is a Certified Strength and Conditioning Specialist. Resistance training classes will be directly observed by Champ or his team of CSCS, and

regimens will be continually adjusted for both exercise progression and safety as per SOC at the facility.

5.3 Exercise Regimen:

The exercise regimen will utilize a mixture of compound movements utilizing both open and closed kinetic chain movements (CKC), focusing on exercises with the goal of improving body composition, strength, mobility, muscle mass, and several associated variables. CKC exercises are generally more intense as they require multi-joint movement patterns. Examples include lunges, squats, and deadlifts. Classes will be run by certified exercise and performance personnel and workouts will be directly observed and continually adjusted for both exercise progression and safety, as per SOC. It will follow a linear progression technique and guidelines from the National Strength and Conditioning Association (NSCA) will be followed. The observed classes will take place three times per week. Warm-up exercises focused on mobility, flexibility and core activation will be performed to increase mobility and reduce the risk of injury. Each individual exercise workout will generally progress from most intense, CKC, compound, and athletic movements to least intense throughout the workout to maximize safety. Additionally, each workout will provide full body resistance training to focus on functional exercises, intensity, and efficiency. Each workout will take approximately 45-60 minutes. When a participant has exceeded the goal number of repetitions by two for two consecutive weeks, the weight lifted will be increased via NSCA standards. The SOC total exercise regimen will last 3 months. The SOC follow up assessment will occur 1 year after exercise. Data from the SOC exercise and assessments will be used for research.

Exercise class attendance will be recorded. Workout regimens, including exercise type, sets, and repetitions will be recorded to aid in workout consistency and progression and to calculate load lifted. Initial strength assessment will occur during the initial two weeks of the workout regimen to help ascertain proper weight usage. Repetition schemes to mimic basic exercise principles for hypertrophy, strength, and power based on 1-repetition maximum (1RM) extrapolation and repetition range charts after assessing each exercise performed to near repetition fatigue/voluntary failure (i.e. when a repetition or safe lifting form can no longer be maintained while monitored by exercise physiologist).

Weight lifted, repetitions, sets, and notes will be recorded and utilized to estimate intensity via volume load calculations (volume load = weight lifted $\times$ repetitions $\times$ sets). An example of a workout is listed below.

Day One (anterior muscle closed-chain compound exercise focus):

A1: Split Squat 4X6 week 1-4, 4X4 weeks 5-8, 4X2 week 9-12

A2: Side plank 3X20 seconds each side week 1-6, 3X30 seconds each side week 7-12

B1: Bird dog row 3X10 week 1-6, 3x12 week 7-12

B2: Feet elevated glute bridge 3X10 week 1-6, 3x12 week 7-12

B3: Half Kneeling 1 arm overhead press 3X10 week 1-6, 3x12 week 7-12

Day Two (posterior muscle closed-chain compound exercise focus):

A1: Trap bar (or straight bar) Deadlift 4X6 week 1-4, 4X4 weeks 5-8, 4X2 week 9-12

A2: Band pull-aparts 3X10 week 1-6, 3x12 week 7-12

B1: Goblet squat 3X10 week 1-6, 3x12 week 7-12

B2: Incline bench press 3X10 week 1-6, 3x12 week 7-12

B3: Tall kneeling front raise 3X10 week 1-6, 3x12 week 7-12

Day Three (strength/hypertrophy focus):

A1: Bent over row 4X6 week 1-4, 4X4 weeks 5-8, 4X2 week 9-12

A2: Pushups (use bar to raise up height if needed) 3X10 week 1-6, 3x12 week 7-12

B1: Weighted hip bridge 3X10 week 1-6, 3x12 week 7-12

B2: Step ups 3X10 week 1-6, 3x12 week 7-12

B3: Farmers carries 3X10 steps each leg week 1-6, 3X12 steps each leg week 7-12

6. PATIENT ASSESSMENTS

Table 1: Participant Assessments

Assessment	Screening	Baseline Assessments (Prior to Program)	During Exercise Program	At Exercise Program Completion	1 Year After Exercise Program Completion
Consent	X				X[f]
History/Physical	X				
Weight, height, and BMI	X			X	X
Body Composition Assessment[a]		X		X	X
Resting Metabolic Rate Assessment		X		X	X

QOL and Exercise Forms[b]		X		X	X
Strength Assessment[c,d]		X	X	X	X
Mobility Assessment[c]		X		X	X
Compliance[e]			X		

a To calculate lean and fat mass and percentages, and total energy expenditure (kcal/day) SOC
b EQ-5D-5L, and Leisure-Time Exercise Questionnaire SOC
c Functional Mobility Survey and Y-balance test, includes grip strength SOC
d Will also occur periodically throughout program to adjust exercise regimen SOC
e Attendance collected at each workout
f Verbally reconsent to use SOC data for research purposes

6.1 Screening Assessments

An informed consent will be signed by the patient before any study enrollment and further workup ensues. Subject data to be collected from the medical record including retrospective care data, during the screening process including a complete history and outcome data from treatment and disease progression, all exercise information and questionnaires as well as assessments.

6.2 Study-Specific Assessment

a. Baseline Examinations

If not already collected during screening, baseline complete history and physical, weight, height, and BMI will be collected as SOC. In addition, baseline QoL forms, and the Leisure-Time Exercise Questionnaire that are SOC, will be administered. It will take 15-20 minutes to complete both questionnaires. All baseline assessments will be performed at the Exercise Oncology Center as per SOC, and must be collected within the 3 months prior to starting the exercise regimen. No laboratory draws for this protocol are required.

b. Baseline Metabolic, Body Composition, Strength, and Mobility Testing

Prior to initiation of the exercise regimen, each participant will undergo body composition analysis via an InBody 970. InBody testing is noninvasive and requires no ionizing radiation. The individual simply stands on the machine while holding handles. An ultrasound will also be used to measure muscle and adipose tissue thickness to provide additional metrics for body composition. This will be performed via a traditional ultrasound and software (BodyMetrix) will calculate

muscle mass, fat mass, and body composition metrics. More information is supplied in Appendix VI. Both also supply resting metablic rate calculations. Functional movement assessments will be performed at this visit as well, and takes approximately 10 minutes.

Resting metabolic rate may also be assessed per SOC at this session via a VO2 Master device (VO2 Master Health Sensors Inc., British Columbia, Canada),where the individual will breathe into the device for several minutes at a time. The total test takes less than 15 minutes. The test is noninvasive and measures respiratory airflow and oxygen consumption in order to calculate resting metabolic rate. Alternatively, the InBody machine and ultrasound can be utilized to measure metabolic rate as well. Additional testing with this device is at the discretion of the staff as per SOC. Grip strength will be assessed via a Jamar Hand Dynamometer Grip Strength Measurement Meter bilaterally at the neutral position and with the arm of the head.

These tests are part of the SOC exercise regimen and workup and no additional costs will be associated with these procedures.

6.3 Exercise Period:

The exercise program will last three months. The initial exercise schema was developed by the PI and exercise personnel. Throughout the exercise program, participants will continuously be assessed via load lifted calculations and observations of exercise mechanics, both of which will impact increases in load and exercise difficulty during the program, as per SOC.

6.4 Follow-up Period:

There will be no follow-up once an individual completes the study.

6.5 Early Withdrawal of Subject(s):

If at any time the constraints of this protocol are detrimental to the patient's health and/or the patient no longer wishes to continue in the study, the patient will be removed from the protocol follow-up. In this event the reason(s) for discontinuation of study participation will be noted by the PI in the record. Data acquired up until that point will be retained for analyses.

There will be a SOC follow up assessment 1 year after the completion of the exercise program. The data from the SOC assessment will be used for research purposes.

6.5.1 Criteria for Early Withdrawal

Subjects may voluntarily withdraw from the study at any time. The PI may also discontinue a subject from the study at any time based on certain criteria. Reasons for PI-initiated discontinuation include:

- Pregnancy
- Inability to continue the exercise program

- Potential for harm to the participant

6.5.2 Follow-up Requirements for Early Discontinuation

There will be no follow-up once an individual completes or withdraws from the study. Data that was already collected from participants who discontinue will be used in analyses up to the point of discontinuation, and attempts will be made to collect data from participants at appropriate time points even after discontinuation of the exercise program.

6.5.3 Replacement of Early Withdrawal(s)

Subjects who prematurely withdraw will not be replaced unless withdrawal occurs prior to initiation of the exercise regimen.

7. STATISTICAL METHODS AND DATA ANALYSIS

7.1. Analysis of Safety

Safety will be continually assessed during each workout regimen by the exercise physiologist, and adjustments will be made to exercise performance during the workout to increase safety as per standard of care.

The AEs will be reviewed and assessed by the PI and reported per AHN IRB reporting requirements. Accidental disclosure of confidentiality is the only adverse event that would occur.

7.2 Analysis of Adherence

The primary feasibility endpoint will be session attendance and will be calculated as the proportion of participants completing at least 75% of the planned exercise sessions. Dropout rate, defined as individuals who quit the workout regimen altogether, is 20%. It is assumed that the rate of attendance will be similar in this pilot study. The 90% lower confidence bound (LCB) for the proportion of patients completing at least 75% of exercise sessions will be constructed. A 90% LCB ≥ .56 will be considered a success (that is, the proportion of patients successfully completing the exercise regimen is at least 0.56 with 90% confidence). With 40 patients studied, a 90% LCB of 0.56 is associated with a completion rate of 0.7. Data from all participants will be analyzed for anthropometric, metabolic, fitness and QOL regardless of attendance level but a subgroup analysis will be performed using data from participants with ≥75% attendance.

7.3 Analysis of Anthropometric, Metabolic, Fitness and QOL Measurements

All of the anthropometric, metabolic, fitness and QOL measurements are continuous variables. After assessing for normality, changes from baseline will be made using a paired t-test if the distribution is normal or by the Wilcoxon signed-rank test if the distribution is non-normal.

8. SAFETY MONITORING AND REPORTING

8.1 Adverse Events and Serious Adverse Events:

Adverse events (AE) and serious adverse events (SAE) as a result of participating in the study are not expected because EXERT-BC is an observational study, including quality of life questionnaires.

From the time the subject signs the informed consent form through the exercise program completion visit, data will be collected for all AEs and SAEs recorded in the subject's medical record and adverse events case report form for summary reporting of the study's objective.

9. QUALITY CONTROL AND QUALITY ASSURANCE

9.1 Monitoring:

This clinical research study will be monitored continuously by the PI for study conduct and data to ensure that:

Risk/benefit ratio is not altered to the detriment of the subjects;

Over-accrual does not occur;

Under-accrual is addressed with appropriate amendments or actions;

Data are being appropriately collected in a reasonably timely manner.

10. ADMINISTRATIVE AND ETHICAL CONSIDERATIONS

10.1 Regulatory and Ethical Compliance:

This protocol was designed and will be conducted and reported in accordance with the International Conference on Harmonization (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice, the Declaration of Helsinki, and applicable federal, state, and local regulations.

10.2 Informed Consent:

The informed consent form is written in a manner that is understandable to the subject population. Prior to its use, the informed consent form must be approved by the IRB. The Principal Investigator or authorized key personnel will discuss with the potential subject the purpose of the research, methods, potential risks and benefits, subject concerns, and other study-related matters. This discussion will occur in a location that ensures subject privacy and in a manner that minimizes the possibility of coercion.

Appropriate accommodations will be made available for potential subjects who cannot read or understand English or are visually impaired that are first approved by the IRB. Potential subjects will have the opportunity to contact the Principal investigator or authorized key personnel with questions and will be given as much time as needed to make an informed decision about participation in the study.

Before conducting any study-specific procedures, the Principal Investigator or authorized key personnel must obtain written informed consent from the subject or a legally acceptable representative. The original informed consent form will be stored with the subject's study records, and a copy of the informed consent form will be provided to the subject. The Principal Investigator is responsible for asking the subject whether the subject wishes to notify his/her primary care physician about participation in the study. If the subject agrees to such notification, the Principal Investigator will inform the subject's primary care physician about the subject's participation in the clinical study.

Reconsenting of the subjects will be conducted at the time of SOC assessments. PI and/or study staff will inform the subjects that their 1 year follow up assessment data will also be used for research purposes. A note of this consenting with the subjects will be placed in the research record and EPIC. If subject does not consent, their follow up assessment data will not be used for research.

10.3 Study Documentation:

Study documentation includes but is not limited to source documents, case report forms (CRFs), monitoring logs, appointment schedules, study team correspondence with sponsors or regulatory bodies/committees, and regulatory documents that can be found in the AHN electronic "regulatory binder."

Source documents are original records that contain source data, which is all information in original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source documents include but are not limited to hospital records, clinical and office charts, laboratory notes, memoranda, evaluation checklists, and subject files. When possible, the original record should be retained as the source document. However, a photocopy is acceptable provided that it is a clear, legible, and an exact duplication of the original document.

10.4 Privacy, Confidentiality, and Data Storage:

The Principal Investigator will ensure that subject privacy and confidentiality of the subject's data will be maintained.

To protect privacy, every reasonable effort will be made to prevent undue access to subjects during the course of the study. Prospective participants will be consented in an exam room where it is just the research staff, the patient and her family, if desired. For all future visits, interactions with research staff (study doctor and study

coordinators) regarding research activities will take place in a private exam room. All research related interactions with the participant will be conducted by qualified research staff who are directly involved in the conduct of the research study.

To protect confidentiality, subject files in paper format will be stored in secure cabinets under lock and key accessible only by the research staff. Subjects will be identified only by a unique study number and subject initials. Electronic records of subject data will be maintained using a secure password-protected database. Access to the database will be limited to essential study personnel. Subject data may be stored temporarily on encrypted and password-protected portable memory devices such as flash drives and external hard drives, but only when absolutely necessary. Data stored on portable memory devices will be de-identified. Subject data will be deleted from the portable memory device at the earliest opportunity.

Upon completion of the study, research records will be archived and handled securely.

Subject names or identifiers will not be used in reports, presentations at scientific meetings, or publications in scientific journals.

Data Collection:
The following data will be stored in the secure database:
- Age
- Diagnosis
- Weight, height, and BMI
- Comorbid medical conditions
- Surgical procedure for breast cancer or orthopedic procedures
- Type of hormonal therapy
- Body composition at start/completion (body fat percentage, % fat-free mass, fat mass, fat-free mass, body mass)
- Resting metabolic rate at start/completion
- Exercise details (specific exercise, repetitions, weight, load lifted)
- FMS and Y-balance test
- Grip strength at start/completion
- QOL forms (EQ-5D-5L)
- Godin Leisure-Time Exercise Questionnaire
- Adherence rates (percentage classes)
- Assessments that are SOC

10.5 Protocol Amendments:

All protocol amendments must be initiated by the Principal Investigator and approved by the IRB prior to implementation. IRB approval is not required for protocol changes that occur to protect the safety of a subject from an immediate hazard. However, the Principal Investigator must inform the IRB and all other applicable regulatory agencies of such action immediately.

10.6 Records Retention:

The Principal Investigator will maintain study-related records for the longer of a period of at least six years after study completion, or per AHN policy, whichever is more strict.

APPENDICES

APPENDIX I: References

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APPENDIX II: Quality of Life – EQ-5D-5L

Under each heading, please check the ONE box that best describes your health TODAY.

MOBILITY

I have no problems walking ❑
I have slight problems walking ❑
I have moderate problems walking ❑
I have severe problems walking ❑
I am unable to walk ❑

SELF-CARE

I have no problems washing or dressing myself ❑
I have slight problems washing or dressing myself ❑
I have moderate problems washing or dressing myself ❑
I have severe problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

I have no problems doing my usual activities ❑
I have slight problems doing my usual activities ❑
I have moderate problems doing my usual activities ❑
I have severe problems doing my usual activities ❑
I am unable to do my usual activities ❑

PAIN / DISCOMFORT

I have no pain or discomfort ❑
I have slight pain or discomfort ❑
I have moderate pain or discomfort ❑
I have severe pain or discomfort ❑
I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION

I am not anxious or depressed ❑
I am slightly anxious or depressed ❑
I am moderately anxious or depressed ❑
I am severely anxious or depressed ❑
I am extremely anxious or depressed ❑

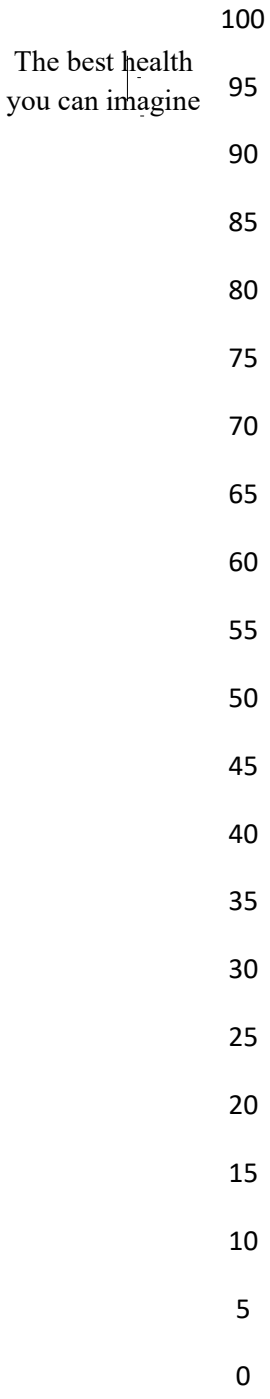
1 We would like to know how good or bad your health is TODAY.

2 This scale is numbered from 0 to 100.

3 100 means the <u>best</u> health you can imagine.
0 means the <u>worst</u> health you can imagine.

4 Mark an X on the scale to indicate how your health is TODAY.

5 Now, please write the number you marked on the scale in the box below.



YOUR HEALTH TODAY = ☐

APPENDIX III: Strength Assessment

Strength assessment will be performed and recorded for each exercise during the initial two weeks of the exercise program, known as the “run-in” period, as is SOC. These numbers will be recorded for each participant. Loads will be calculated at three weeks and then recalculated every

4 weeks until completion of the protocol. Load lifted will be calculated by multiplying the number or repetitions, weight per workout, and number of sets.

APPENDIX IV: GODIN LEISURE-TIME EXERCISE QUESTIONNAIRE

a) STRENUOUS EXERCISE (HEART BEATS RAPIDLY) (e.g., running, jogging, hockey, football, soccer, squash, basketball, cross country skiing, judo, roller skating, vigorous swimming, vigorous long distance bicycling)		**X9**	
b) MODERATE EXERCISE (NOT EXHAUSTING) (e.g., fast walking, baseball, tennis, easy bicycling, volleyball, badminton, easy swimming, alpine skiing, popular and folk dancing)		**X5**	
c) MILD/LIGHT EXERCISE (MINIMAL EFFORT) (e.g., yoga, archery, fishing from river bank, bowling, horseshoes, golf, snow-mobiling, easy walking)		**X3**	
WEEKLY LEISURE-TIME ACTIVITY SCORE			

EXAMPLE
Strenuous = **3** times/wk
Moderate = **6** times/wk
Light = **14** times/wk
Total leisure activity score = (9 × **3**) + (5 × **6**) + (3 × **14**) = 27 + 30 + 42 = 99

Godin Scale Score	Interpretation
24 units or more	Active
14 – 23 units	Moderately Active
Less than 14 units	Insufficiently Active/Sedentary

Adapted from: Godin, G. (2011). The Godin-Shephard leisure-time physical activity questionnaire. Health & Fitness Journal of Canada, 4(1), 18-22.

APPENDIX V: Functional Movement Screen and Y-Balance Test

The Functional Mobility Screen is a tool used prior to the initiation of an exercise protocol to assess individual mobility and movement patterns. These patterns are general accompanied by compensatory mechanisms that may predispose participants to injury, but can be improved through specific exercises which can reduce the risk of chronic injury.

During the test, 7 movement patterns are assessed and each one is rated between 0 and 3 by an examiner. These movements include the deep squat, hurdle step, inline lunge, shoulder mobility test, active straight leg raise, trunk stability push up, and rotary stability test. A score of zero is given if any pain is felt during the movement, 1 if the subject is unable to perform the movement, 2 if the subject performs the movement through compensatory movements, and 3 if the movement is performed correctly.[40] Each movement score is summed and a final score out of 21 is calculated. A score below 14 is felt to identify individuals at risk of injury. Normal values in the general population range from a score of 12.56 in individuals over the age of 65 to 14.79 in individuals aged 20-39, and women generally have a slightly higher score.[41]

The FMS has an acceptable degree of inter-rater reliability and is currently the most well-researched movement screen available.

The Y-balance test has the participant stand on one leg while reaching out in 3 different directions with the other lower extremity. They are anterior, posteromedial and posterolateral. When using the Y-Balance test kit, the 3 reaches yield a “composite reach distance” or composite score used to predict injury.

APPENDIX VI: Body Composition Testing

All participants will undergo body composition testing via the InBody 970 model.

InBody testing will take place at Exercise Oncology Center during initial assessment. The InBody test takes about 3 minutes. Participants are required to abstain from food, drink or exercise prior to the test and will be fasted overnight. During the exam, they merely stand quietly on the machine

The InBody 970 is a bioimpedance analysis device, which utilizes electric currents to calculate a phase angle and resulting body composition metrics. Users stand barefoot on a device that is similar to a traditional scale, and they hold one handle for each hand, with the feet and hands touching metal electrodes. The device sends a low-dose electrical current and measures the change in phase angle. There is no risk to the user.

An ultrasound will also be used to measure muscle and adipose tissue thickness to provide additional metrics for body composition. This will be performed via a traditional ultrasound and software (BodyMetrix) will calculate muscle mass, fat mass, and body composition metrics.