ABSTRACT

Title of Document:	DOES STRENGTH TRAINING IMPROVE MUSCULOSKELETAL HEALTH AND BODY COMPOSITION IN BLACK MEN WITH PROSTATE CANCER ON ANDROGEN DEPRIVATION THERAPY?
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Prostate cancer (PCa) is the most commonly diagnosed cancer in U.S. men and disproportionately affects black men more than any other racial or ethnic group. Despite this disparity, black men have been underrepresented in previous studies. PCa is commonly treated using androgen deprivation therapy (ADT). However, ADT induces numerous adverse side effects, including loss of muscle mass, strength, power, and physical function with concomitant increases in fat mass, fatigue, and bone fractures. Because strength training (ST) can reverse these factors in healthy older adults, it was hypothesized that ST would be effective in PCa patients on ADT but with an attenuated response. Therefore, the purpose of this study was 1) to examine the effects of ST on musculoskeletal and body composition side effects in black men on ADT, 2) to compare ST responses of black PCa patients on ADT to those of black healthy reference controls,

and 3) to determine if changes in musculoskeletal health and body composition with ST are associated with changes in fatigue, physical function, and quality of life (QoL).

PCa patients (N=17) completed a 12 week ST program, which produced many beneficial effects on factors adversely affected by ADT, including substantial gains in muscle power, size, strength, and endurance (all $P < 0.001$), resulting in a more favorable body composition ($P < 0.001$) and increased physical function (all $P < 0.05$). ST also improved fatigue perception and QoL (both $P < 0.05$). Compared with healthy reference controls (N=20), PCa patients responded to ST with similar gains in muscle power, strength, and mass, which was contrary to expectations. However, PCa patients had higher fat mass and lower muscle power and strength than controls at baseline (all $P < 0.05$). Finally, the changes in physical function, fatigue perception, and QoL were associated with some of the changes in muscle function with training. The findings in this study provide support for the hypothesis that ST improves musculoskeletal health and body composition in black men with PCa on ADT by demonstrating significant improvements in muscle power, mass, strength, and endurance, which can enhance physical function and QoL.

DOES STRENGTH TRAINING IMPROVE MUSCULOSKELETAL HEALTH AND BODY COMPOSITION IN BLACK MEN WITH PROSTATE CANCER ON ANDROGEN DEPRIVATION THERAPY?

By

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Dedication

To all those affected by cancer, including Russell Lindquist, Christine Bremmer, Carol Hanson, and Karen Schutte.

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Finally, I need to express gratitude to my family for their encouragement throughout my academic career. In particular, to my wife Ashley, I am eternally grateful for all of the patience, support, and love you so willing gave throughout our time in Maryland.

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List of Abbreviations

1RM	One repetition maximum
5RM	Five repetition maximum
ADT	Androgen Deprivation Therapy
BCAA	Branched Chain Amino Acids
BFI	Brief Fatigue Inventory
BMC	Bone Mineral Content
BMD	Bone Mineral Density
CT	Computed Tomography
CV	Coefficient of Variation
DEXA	Dual Energy X-ray Absorptiometry
FACT-P	Functional Assessment of Cancer Therapy-Prostate
FFM	Fat Free Mass
FSR	Fractional Synthesis Rate
GR	Glucocorticoid Receptor
IGF-1	Insulin-like Growth Factor One
IMF	Intermuscular Fat
LHRHa	Luteinizing Hormone Releasing Hormone agonists
mTOR	Mammalian Target of Rapamycin
MRI	Magnetic Resonance Imaging
MV	Muscle Volume
PCa	Prostate Cancer
PP	Peak Power
PT	Peak Torque
PV	Peak Velocity
RCT	Randomized Control Trial
SCF	Subcutaneous Fat
ST	Strength Training
QoL	Quality of Life

Introduction

Prostate cancer (PCa) is the most commonly diagnosed cancer in men. It is estimated that ~217,730 men in the U.S. will be diagnosed with PCa in 2010 alone and that ~32,050 will die by the end of the year (101). It is the most common type of hormone dependent tumor, the most commonly diagnosed non-dermatological malignancy in men, and the second leading cause of mortality due to cancer in the U.S. (101). While PCa incidence and mortality rates have improved in general, there is a large racial disparity that currently exists. Black men have the highest incidence of PCa than any other racial or ethnic group throughout the world, with 234.6 cases per 100,000 men compared with 150.4 per 100,000 for whites (101), and die of PCa at 2.4 times the rate of white men (2). This death rate increases to three times the rate of whites when examining men under the age of 65 (1).

Because PCa tumors have been shown to be hormone dependent (87), androgen deprivation therapy (ADT) is a classic form of treatment. Although this treatment is effective in slowing tumor growth, the suppression of endogenous testosterone reduces muscle strength (6, 65, 211), mass (20, 65, 186, 201), and bone mineral density (BMD) (33, 62, 65, 72) and increases fat mass (20, 62, 184, 201) and generalized fatigue perception (62, 103, 119, 190). The collective effect of ADT is a functional decline leading to reduced performance in activities of daily living (35, 65, 103, 125) and deteriorating quality of life (QoL) (6, 29, 40, 190). Although not directly assessed in previous cancer studies, it is quite likely that ADT increases fat infiltration in muscle, leading to the accumulation of intermuscular fat (IMF) and subcutaneous fat (SCF) (99). This has important health implications because of the relationship IMF has with insulin

resistance and type 2 diabetes (71), both co-morbidities with high prevalence in patients on ADT (7, 21). In addition, fat infiltration is associated with reduced strength (70), poorer leg function (202, 204), and greater incidence of mobility limitations in older adults (203).

These iatrogenic effects of ADT are similar to those associated with typical aging (sarcopenia) (75, 91), but occur at an accelerated rate (Figure 1). Strength training (ST) can reverse many of the factors associated with both the consequences of ADT and

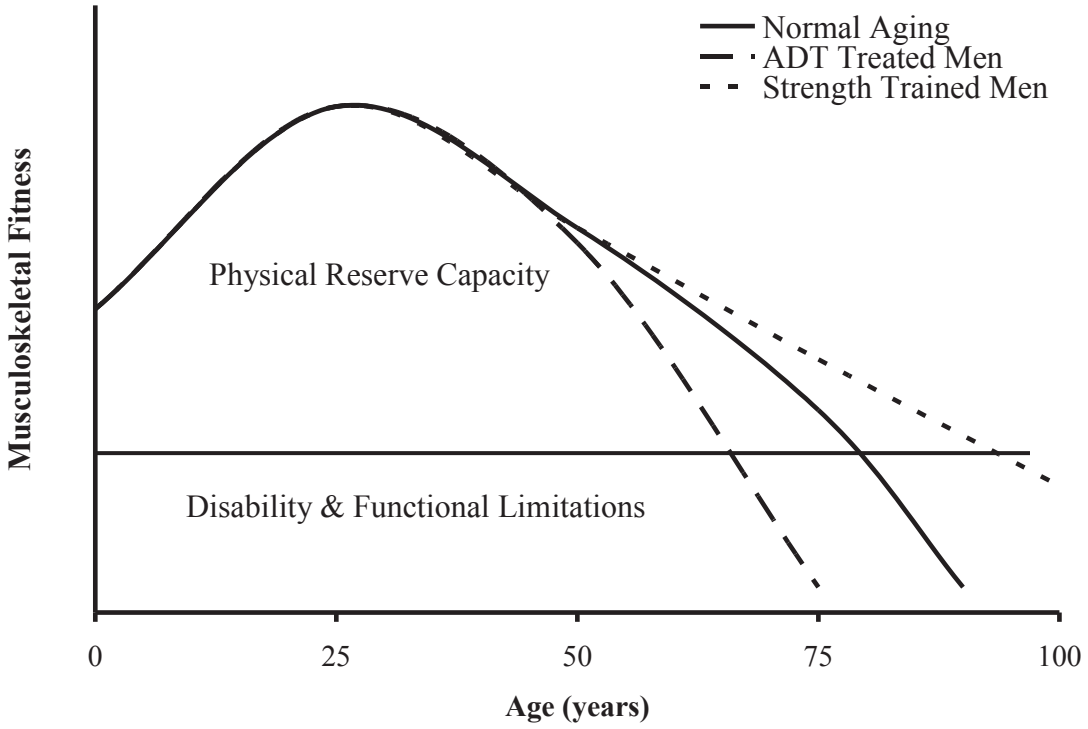

Figure 1. The reduction in musculoskeletal fitness with aging and ADT and the potential role of strength training to increase musculoskeletal fitness and maintain reserve capacity in ADT-treated men. Adapted from Galvao et al. (66).

sarcopenia (91, 92), including the reversal of the loss of muscle mass and strength (55,

90, 169), muscle power (42, 160), bone loss (138, 171, 172), regional fat deposition (198, 215), and functional declines (63, 76, 79).

Currently, there are only two published studies that address the independent effects of supervised ST in patients undergoing ADT (61, 176), though other relevant ADT investigations exist (115). Segal *et al.* (176) specifically examined basic aspects of muscle function in patients undergoing ADT before and after a 12 week ST program compared to a non-exercising control group. Men who underwent ST significantly improved their strength, muscle endurance, and QoL compared to the control group. No changes in body composition were observed. However, no direct assessment of muscle strength was performed, body composition was estimated using skinfolds, and muscle size, muscle power, bone mass, or physical function were not reported. Following up on this initial study, Galvao *et al.* (61) reported improvements in strength and functional abilities after 20 weeks of ST in a study of ten PCa patients. No change in total lean mass or BMD was observed, and the study did not include blacks. Kvorning *et al.* (115) observed that strength and muscle mass gains were attenuated in young men on ADT when compared to healthy controls. However, despite this finding, it is presently unclear whether the suppression of testosterone in those with PCa undergoing ADT would prevent or limit ST-induced improvements in muscle mass and power as few studies are available to support or reject such a hypothesis and none have examined this in black men on ADT.

Muscle power is of particular interest due to its strong relationship with activities of daily living performance (9, 80, 135). Our group has reported significant improvements in peak muscle power with ST in healthy older adults (42, 76) and we

observed a significant portion of the variability in physical functioning improvements with ST are accounted for by improvements in muscle power (76). Consequently, it was hypothesized that muscle power is an important contributor to QoL for men with PCa.

The ability of the muscle to undergo hypertrophy under castrate levels of testosterone is also unresolved, as a study in rats found no effect of an exercise-like stimulus on muscle mass in castrated vs. control animals (152) while another using electrical stimulation reports that muscle hypertrophy was suppressed in rats being administered androgen receptor antagonists (96). Reports in human populations are limited. We are aware of only one report that directly assessed changes in muscle size with ST in PCa patients on ADT (74). In this pilot study, five PCa patients on and five not on ADT completed 12 weeks of resistance exercise using recumbent, high force eccentric ergometry (74). The PCa patients who were on ADT showed no significant increase in muscle volume, whereas, those who were not on ADT experienced muscle hypertrophy. Although the differences between groups did not reach statistical significance with this sample size, it does raise the question about whether ADT might prevent or blunt the typical hypertrophic response to ST. It should not be assumed that the same changes that result from ST in normal healthy volunteers will necessarily occur in PCa patients on ADT.

Thus, the purpose of this study was 1) to examine the effects of ST on common musculoskeletal and body composition side effects of ADT in black men on ADT, 2) to compare ST responses of black PCa patients on ADT to those of black healthy reference controls, and 3) to determine if changes in musculoskeletal health and body composition with ST are associated with changes in fatigue perception, physical function, and QoL.

Methods

Recruitment

PCa patients were recruited by referrals from the Veteran Affairs Medical Centers in Washington, DC and Baltimore, MD and through advertisements sent to the general population and support groups in the communities that surround the University of Maryland campus. In addition, local urology physicians in the vicinity were targeted for referrals. An overview of the recruitment strategy is provided in Figure 2.

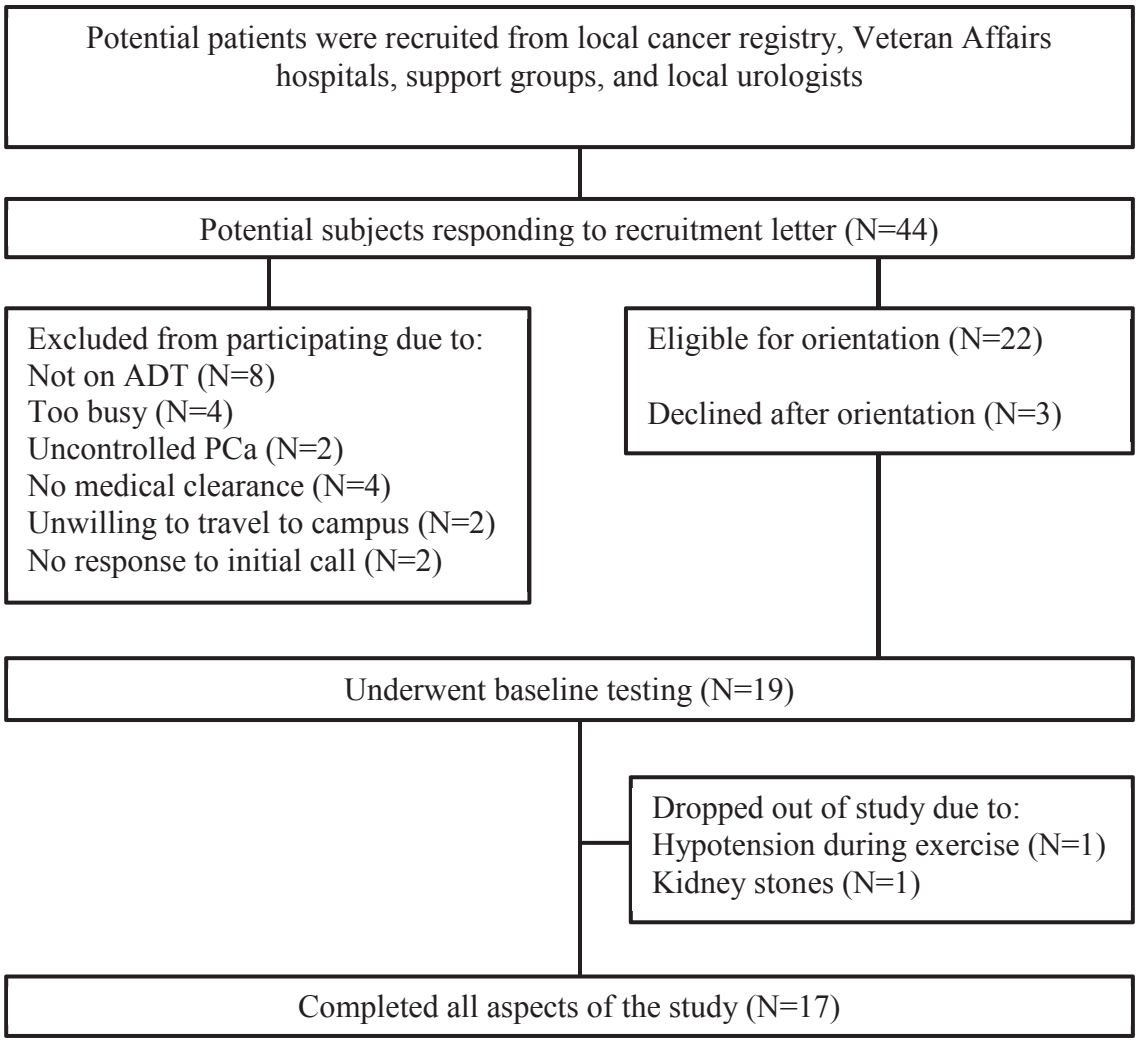

Figure 2. Flow chart of study recruitment and design.

To be eligible to participate, subjects needed to currently be on ADT and to remain on it throughout the duration of the study. Exclusionary criteria included severe cardiovascular disease, musculoskeletal diseases that cause severe joint pain at rest or upon exertion, having any condition that is likely to be aggravated by muscular exertion, Type I diabetes, history of bone fragility fractures, being unable to engage safely in mild to moderate exercise, such as independently walking up at least one flight of stairs or walking two blocks on level ground, unwilling to travel to campus for training, or lack of medical clearance from their primary care physician.

Subjects

Nineteen sedentary men ages 58 to 80 volunteered to participate in the study. Most subjects were sedentary in nature, defined as not having participated in a structured exercise program on a regular and consistent basis, with the exception of regular walking. Only one subject had participated in a ST program in the six months preceding enrollment in the study and analyses run with and without his data did not affect the results. Of the 19 subjects who completed baseline testing, 17 completed all follow-up testing.

All subjects underwent an initial phone screening interview, a detailed medical questionnaire, and also received medical clearance from their primary care physician. A PCa history questionnaire was also completed, which included diagnosis date, treatment types, and treatment duration. Subjects on medications in addition to ADT were requested to maintain the dosage throughout the study. All subjects maintained stable body weight, defined as within 5%, (monitored weekly) and were asked to maintain their regular physical activity levels and dietary habits throughout the study. This, along with

medication use, was verbally confirmed on a regular basis. After all methods and procedures were explained, subjects read and signed the informed consent which was approved by the University of Maryland Institutional Review Board.

A reference control group was obtained from a previous study in our laboratory. This group consisted of healthy, inactive black men who completed a 10 week unilateral ST program of the knee extensors designed to optimize gains in leg muscle hypertrophy. They were selected as a comparison group representing ideal responses to ST. The inclusion/exclusion criteria and screening processes used for subjects in the reference control group have been described previously (42).

Strength Testing

One repetition maximum (1RM) strength testing for the knee extension, chest press, and leg press were performed at baseline and after the ST program using Keiser air powered machines (Keiser Corporation Inc, Fresno, CA, USA) via standardized protocols (42, 76). The 1RM was achieved by gradually increasing the resistance after each successful repetition until the maximal load was obtained for each exercise, typically requiring eight to 12 trials to attain the 1RM. Prior to baseline testing, two sessions were performed with light resistance to familiarize the subjects with the equipment, to help control for the large 1RM strength gains that commonly result from skill acquisition during the initial stages of training, and to aid in injury prevention and reduce muscle soreness following the testing bout. The knee extension 1RM was assessed unilaterally while the chest and leg press were assessed bilaterally. The reference control subjects completed 1RM testing only for the knee extensors, but otherwise followed identical familiarization and testing protocols.

Muscle Endurance

Localized muscle fatigue was assessed using a repetition test on the chest and leg presses in the PCa patients. At the completion of the respective 1RM test, subjects rested for five minutes before performing as many consecutive repetitions as possible at 70% of baseline 1RM until failure occurred. Failure was defined by either pausing to rest at any point during the test or the inability to fully complete the final repetition. The same absolute load was replicated after the ST protocol. An increase in repetition number with ST constituted a decrease in localized fatigue and improved muscle endurance.

Power Testing

Peak power, peak velocity, and peak torque of the knee extensors were evaluated at baseline and after ST for all subjects on a Keiser A-430 air-powered machine designed specifically for muscle power assessment using methods described previously (42). After performing three familiarization trials, subjects completed three repetitions per leg at three different intensities, 50, 60 and 70% of their knee extension 1RM, in an alternating fashion for a total of nine repetitions. The rest period between each trial at a given load was one minute and two minutes of rest separated each increase in resistance. The peak power, velocity, and torque values were then selected for each relative intensity. An attempt was made to find an absolute load that could be replicated from baseline testing. If a relative load after ST was within 5% of a baseline load, then the same relative load was replicated from baseline testing. This typically occurred at 70% of 1RM at baseline and at 50 or 60% of 1RM after ST. If no such load could be found, an additional set of three trials was performed for the after ST test, using a replicated relative load from baseline.

Body Composition

Fat free mass (FFM), % fat, bone mineral content (BMC), and BMD for all subjects was estimated at baseline and after ST by dual-energy X-ray absorptiometry (DEXA) using fan-beam technology (model QDR 4500A, Hologic, Waltham, Massachusetts, USA) as described previously (42). Upper, lower, and appendicular body composition were determined in the PCa patients, in addition to overall body composition. The ischial crest of the pelvis was used as the boney landmark to differentiate between upper and lower body segments. Appendicular body composition was the sum of the lower body combined with the sum of the arms, defined using the medial aspect of the humeral head as the cutpoint to differentiate the arms from the trunk (62). Coefficients of variation (CV) for all DEXA measures of body composition were determined using scans from ten subjects, each who were scanned three consecutive times with body repositioning. The CV for FFM was <1.0% and 1.0% for % fat (42). The scanner was calibrated daily against a spine calibration block, a small step phantom, and an empty table background scan (Radiograph Uniformity Test).

To quantify leg muscle volume (MV) in the PCa patients, computed tomography (CT) (GE Lightspeed Qxi, General Electric, Milwaukee, Wisconsin, USA) imaging of the thighs was performed at baseline and after ST program using previously described methods (207) and was modified to include all leg musculature. Final MV was calculated using the truncated cone formula (197). Briefly, MV was calculated by manually outlining the cross-sectional area of the deep fascial plane outlined every 40 mm from the first section closest to the superior border of the patella to a point where the fascia was no longer reliably distinguishable from the subcutaneous adipose tissue, typically the most

superior cross-sectional slice. Care was taken to ensure that the same number of sections proximal from the patella was measured for a particular subject before and after ST to ensure within-subject measurement replication. Coefficients of variation were calculated using repeated measures of selected axial sections of one subject on two separate days. The within-investigator reliability average was <1.0% and the between investigator average was 2.6%. The MV values for the reference controls included only the quadriceps muscle groups and followed procedures described previously (207). All other procedures for assessing MV were identical to those described for the PCa patients.

Similar to thigh MV, SCF cross-sectional area was assessed in all subjects by additionally outlining the entire thigh and subtracting the area inside the deep fascial plane from the thigh area of a single CT slice at the midpoint of the thigh. The IMF cross-sectional area was distinguished by excluding the bone marrow fat from the deep fascial plane (71). The IMF was then segmented into a separate image, in which it was identified on the basis of Hounsfield units, where IMF ranged from -190 to -30, as previously described (71). The average within-investigator CV were both <1.0% and the between-investigator average was 2.8% for SCF and 4.3% for IMF, respectively. For all analyses, technicians were blinded to subject identification, date of scan, and training status for both baseline and post training scans.

Physical Function Testing

Physical function was assessed at baseline and after ST in PCa patients using six different functional tests: the 6m usual and rapid walks, a timed up and go test, the number of chairs stands that could be completed in 30 seconds, a stair climb, and a 400m walk. The walking tests, timed up and go, chair stands, and stair climb were completed as

described previously (76) with slight modification to the chair stand protocol. All trials were preceded by a practice trial and were performed in duplicate with the fastest time being recorded, with the exception of the 30 second chair stands and 400m walk.

6-m Walks. Habitual and maximal walking speed was assessed by measuring the time it took subjects to cover a 6-m course. To avoid bias from deceleration, subjects were instructed to walk to a mark 1.25 m beyond the 6-m line. The rest interval between trials was 30 seconds and one minute between tasks.

Timed Up and Go. The 43-cm chair used in the chair stands test was again used in the up and go test. In this task, subjects were required to rise from a seated position, walk 2.44 m (8 feet) around a cone, and return to the seated position. The rest interval between trials was one minute.

Chair Stands. A hard-seated, straight-backed, armless chair that was 43 cm in height was used to evaluate chair stand performance. Subject began the task in a seated position with arms folded across the chest. Over the course of 30 seconds, the number of successfully completed repetitions was measured. To be considered complete, the legs had to be fully extended before the 30 seconds had elapsed. To count as a complete repetition, subjects were required to stand fully and to sit completely and the final repetition needed to be completed prior to time expiring. This was monitored visually by the investigators. A single trial was performed and the rest interval following this task was five minutes.

Stair Climb. Stair climbing ability was assessed by timing subjects as they climbed a single flight of nine stairs. Each step was 19 cm in height. The standardized starting position for each subject was one foot length back from the first step. Subjects

were required to place at least one foot on each step, and no running or skipping of steps was permitted. The rest interval between trials was one minute.

400m Walk. 400m walk time was used as index of muscle endurance. Subjects completed 2.5 laps on an indoor synthetic surfaced track. A single trial was performed.

Blood Sampling and Biomarkers

Venous blood was sampled from PCa patients at baseline and after ST following an overnight fast. Samples were collected in K_2 EDTA coated and uncoated tubes for plasma and serum separation, respectively (Becton Dickinson, Franklin Lakes, NJ, USA). Hematocrit and hemoglobin (HemoCue Hb 201+ Analyzer, Lake Forrest, CA, USA) were measured in triplicate prior to all tubes being centrifuged at 3000g for 10 minutes at 4°C. The supernatant was removed and stored in 0.5 mL aliquots at -80°C until analysis. Prostate specific antigen (PSA) levels were determined in duplicate using a commercially available kit (R & D Systems Quantikine® Human Kallikrein 3/PSA ELISA, Minneapolis, MN, USA) and following the manufacturer's instructions. A set of low, medium, and high standards along with two negative controls were used to confirm that the assay worked correctly. The manufacturer reports an intra-assay CV of 5.2% and an inter-assay CV of 6.3% with a mean minimal detectable dose of 0.030 ng/mL. Free testosterone was measured in duplicate using a radioimmunoassay (Beckman Coulter, Brea, CA, USA) at the Baltimore Veterans Affairs Hospital following the manufacturer's instructions. The manufacturer reports an intra-assay CV of <6.2%, an inter-assay CV of <9.7%, and a sensitivity of 0.18 pg/mL. High and low standards and positive and negative controls were again included to confirm the assay.

Generalized Fatigue Perception and Quality of Life

The Brief Fatigue Inventory© (BFI) (University of Texas MD Anderson Cancer Center, Houston, TX, USA, used with permission) and the Functional Assessment of Cancer Therapy-Prostate (FACT-P) (FACIT.org, Elmhert, IL, USA, used with permission) were measured at baseline and after ST in PCa patients as indicators of generalized fatigue perception and QoL, respectively. The internal consistency and validity for the BFI has previously been reported, with a Cronbach α coefficient value of 0.96 (137). The BFI is highly correlated with other fatigue questionnaires (93, 137), including the Profile of Mood States (POMS) and FACT-Fatigue. The FACT-P is an extension of the 27 item FACT-General questionnaire, which consists of four primary QoL domains (Physical, Social, Emotional, and Functional Well-Being). An additional 12 questions specific to PCa symptoms and treatment designate this questionnaire as the FACT-P. The questionnaire demonstrates high internal consistency and validity with Cronbach α ranging from 0.60 – 0.83 for the four general QoL domains and 0.65 – 0.69 for the Prostate specific subsection from 0.65 – 0.69 (51). The clinically meaningful change for the overall FACT-P score is 6-10 units (31).

Near the end of the training period, one subject began iron supplementation therapy for anemia after complaining of fatigue. This violated the guidelines of the study protocol. Therefore, this subject was removed from the data analysis for BFI and FACT-P.

Strength Training Protocol

The training program for the PCa patients consisted of 12 weeks of ST, three days per week for approximately one hour using Keiser air powered equipment (Keiser

Corporation Inc., Fresno, CA, USA). Keiser equipment was selected for training due to its ease in changing the resistance without interrupting the cadence of the exercise. Exercises included unilateral knee extension, chest press, seated row, seated hamstring curl, abdominal crunch, and leg press. Upon arrival to the laboratory, subjects sat quietly for five minutes and had resting blood pressure measured prior to completing a brief cycling warm up. Subjects then performed two sets of each exercise. The first set was a warm-up at 50% of the training load on each particular day. A single training set of 15 repetitions was performed at each subject's five repetition maximum (5RM), which was continuously adjusted throughout the training program to reflect strength gains. To complete the training set, the first four to five repetitions were performed at the current 5RM value, then the resistance was lowered just enough to complete one or two more repetitions before reaching muscular fatigue. This process was repeated until all repetitions were completed. The resistance was adjusted accordingly for the following training session in order to ensure each repetition was performed using the proper resistance and form through the full range of motion. Upon completion of all training sets, subjects completed each session with a full body stretching routine. Training sessions were conducted individually or in small groups under direct supervision to provide motivation, to maintain intensity, and to ensure exercises were completed safely using a full range of motion. All sets and weights were recorded and the logs were checked weekly. The attendance compliance for all training sessions for the PCa patients was 94.6 ± 1.6%.

The ST program for the reference controls followed identical warm up procedures and is described in detail elsewhere (42). Briefly, the subjects trained only the knee

extensors of one leg (trained leg) three days per week for 10 weeks. This unilateral protocol was designed to combine heavy resistance with high volume while eliciting near-maximal effort on all repetitions and has been effective in increasing 1RM and MV of older adults (42, 98, 197, 207). All subjects completed a warm up set of five knee extension repetitions at 50% of the daily training load before completing training sets of five, 10, 15, and 20 repetitions at their 5RM, which was adjusted continuously throughout training. The rest intervals between the training sets were 90, 150, and 180 seconds, respectively. The attendance compliance for all training sessions for the PCa patients was 90.9 ± 1.8%.

Statistical Analyses

Data were analyzed using SPSS statistical software (SPSS Inc., Chicago IL, USA). To assess the role of ST on musculoskeletal and body composition side effects of ADT in PCa patients, paired t-tests were used to determine the change with ST for all variables. The t-tests were one-tailed, based on directional hypotheses. Next, mixed model repeated measures (group x training) ANOVAs were used to compare PCa patient responses to ST with those of the healthy reference controls using the trained leg of the reference control group for all comparisons. When significant interactions were observed, post hoc analyses were used to locate specific differences. If no interaction was observed, the between group differences (PCa vs. reference controls) were examined. Lastly, correlation and multiple regression analyses were performed to determine associations and predictive power of changes in physical function, fatigue, and QoL to those of muscle function and body composition. Variables with the highest correlations were used to construct multiple regression models to predict the changes with ST. The dependent

variables in the regression models were the change scores that were significantly different from baseline for physical function task times, BFI, and FACT-P. All data were expressed as means ± SEM. Statistical significance was accepted at $P < 0.05$ for all ANOVA and $P < 0.10$ for all regression models due to the lack of orthogonality of the independent regression variables and limited sample size.

Post-hoc power analyses were performed using G*Power 3.1 (53) based on effect sizes calculated using the original standard deviation, rather than the pooled standard deviation. This was done to avoid overestimation of the effect sizes due to smaller pooled standard deviations observed in repeated measures designs. The majority of the primary dependent variables were sufficiently powered, in excess of 0.90, including all measures of muscle strength and power and most of the physical function tasks. The statistical power for FFM, MV, BFI, and FACT-P scores were lower with values ranging from 0.22 to 0.50. A complete list of sample sizes, mean differences, standard deviations, effect sizes, and power calculations can be found in Appendix IV.

Results

Patient Characteristics

The characteristics for the 17 PCa patients and the 20 reference controls are described in Table 1. The PCa patients were borderline anemic, obese, and had variable

Table 1. Baseline and after ST physical characteristics of PCa patients and reference controls.

	PCa (N=17)		**Reference Controls** (N=20) ‡	
	Baseline	**After ST**	**Baseline**	**After ST**
Age (y) †	67 ± 2	-	61 ± 2	-
Height (cm)	172.8 ± 1.7	-	174.7 ± 2.0	-
Mass (kg) #	96.5 ± 4.7	97.9 ± 4.9 *	91.0 ± 3.2	91.2 ± 3.1
BMI (kg/m^2)	32.3 ± 1.2	32.7 ± 1.3	29.9 ± 1.0	30.0 ± 1.0
% Fat †	31.4 ± 1.4	30.7 ± 1.5 *	26.9 ± 0.9	26.3 ± 0.9 *
Fat Mass (kg) †	31.2 ± 3.0	31.1 ± 3.2	24.8 ± 1.6	24.3 ± 1.5
FFM (kg) #	62.4 ± 1.8	64.1 ± 1.8 ***	66.3 ± 1.9	66.9 ± 1.8 *
BMC (kg)	3.1 ± 0.2	3.0 ± 0.2	2.9 ± 0.1	2.9 ± 0.1
BMD (g/cm^2)	1.26 ± 0.05	1.24 ± 0.05	-	-
Free T (pg/mL) ¥	1.4 ± 0.5	2.9 ± 1.4	-	-
PSA (ng/mL)	0.58 ± 0.15	0.32 ± 0.15	-	-
Hemoglobin (g/dL)	12.9 ± 0.3	12.7 ± 0.3	-	-
Hematocrit (%)	38.3 ± 0.8	37.8 ± 0.9	-	-
PCa Diagnosis (d)	-	2958 ± 491	-	-
Length of ADT (d)	-	1449 ± 334	-	-
LHRHa (%)	93.8	-	-	-
Anti-A (%)	31.3	-	-	-
Radiation (%)	41.2	-	-	-
Prostatectomy (%)	29.4	-	-	-

‡ Healthy, older black men who underwent a unilateral knee extensor ST protocol and are provided as an example of optimal training conditions in subjects of similar age and race.

¥ Free T means and standard errors were calculated using nine PCa patients. The remaining eight patients had undetectable levels.

BMC = Bone Mineral Content; BMD = Bone Mineral Density; FFM= Fat Free Mass; Free T = Free Testosterone; PSA = Prostate Specific Antigen; LHRHa = Luteinizing Hormone Releasing Hormone agonist; Anti-A = Anti-Androgen treatment

Trend for interaction of group x training ($P < 0.10$)

† Significant effect of group ($P < 0.05$)

* $P < 0.05$

*** $P < 0.001$

lengths of ADT, ranging from less than one to 12.4 years. They experienced a significant increase in body mass (1.5 ± 0.5%, $P = 0.023$) and a trend for an increase in BMI (1.2 ± 0.5% $P = 0.057$) and a significant decline in % fat ($P = 0.013$) with ST. All PCa patients were on ADT throughout the study, as confirmed by assessing free testosterone levels both before and after ST. There was no change in free testosterone or PSA with ST. When the response to ST was compared to the reference control group, similar responses were observed for most variables. However, there was a trend for differences in body mass and FFM with ST ($P < 0.10$) favoring the PCa group. There were also significant between group differences for % fat and total fat mass (both $P < 0.05$), which were significantly lower in the reference controls.

Muscle Strength and Endurance

Figure 3 shows significant gains in unilateral 1 RM strength for the knee extensors (R leg: 27.8 ± 3.4%; L leg: 16.6 ± 3.3%, both $P < 0.001$), chest press (18.4 ± 3.3%, $P < 0.001$), and leg press (22.5 ± 3.3%, $P < 0.001$) with training in the PCa patients. Substantial improvements were also observed in chest press and leg press muscle endurance (64.5 ± 6.8% and 109.7 ± 40.2%, respectively both $P < 0.001$, Table 2). Reference controls also significantly improved their knee extensor 1 RM values ($P < 0.001$) and had a greater strength levels than PCa patients ($P < 0.001$), but the increases were not significantly different than those of the PCa group.

Muscle Power

Figure 4 displays significant increases in absolute (R leg: 15.1 ± 3.5%; L leg: 13.5 ± 3.6%, both $P < 0.001$) and relative muscle power of the knee extensors in PCa patients (R leg range: 10.3 – 17.1%, all $P < 0.01$; L leg range: 7.6 – 12.6%, all $P < 0.05$), whereas

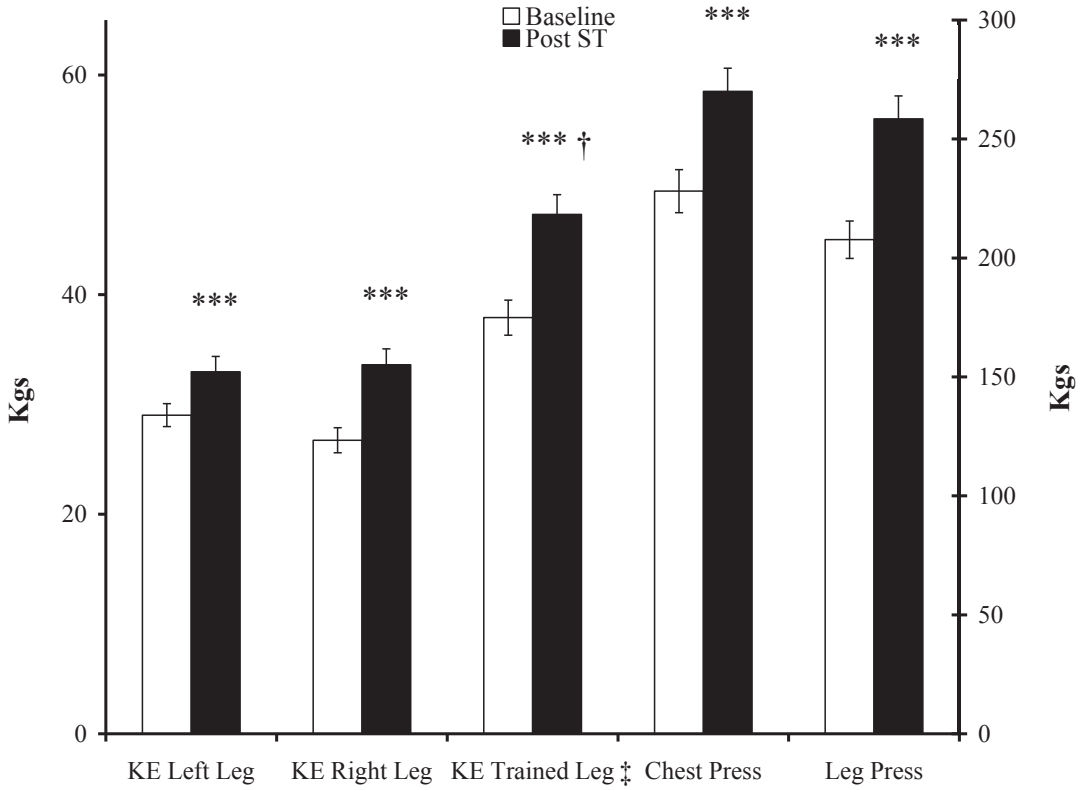

Figure 3. Baseline and after ST muscle strength (1RM) levels in PCa patients (N=14) and reference controls (N=15). The left Y axis is scaled in Kgs for the Knee Extension (KE) and Chest Press while the right Y axis is scaled in Kg for the Leg Press.
‡ Healthy, older black men who underwent a unilateral knee extensor ST protocol and are provided as an example of a reference control population of subjects of similar age and race
† Significant effect of group ($P < 0.05$)
*** Significantly different from baseline value ($P < 0.001$)

there were primarily only trends for increased power with ST in the reference controls. Nevertheless, there were no significant differences in the response to ST between the groups, though the reference controls showed greater power output at all loads (all $P < 0.01$). Training also significantly increased the peak torque achieved during power testing within all loads for PCa patients (all $P < 0.05$, Table 2). Absolute peak velocity significantly increased with ST (R leg: $P < 0.001$; L leg: $P = 0.018$) but remained

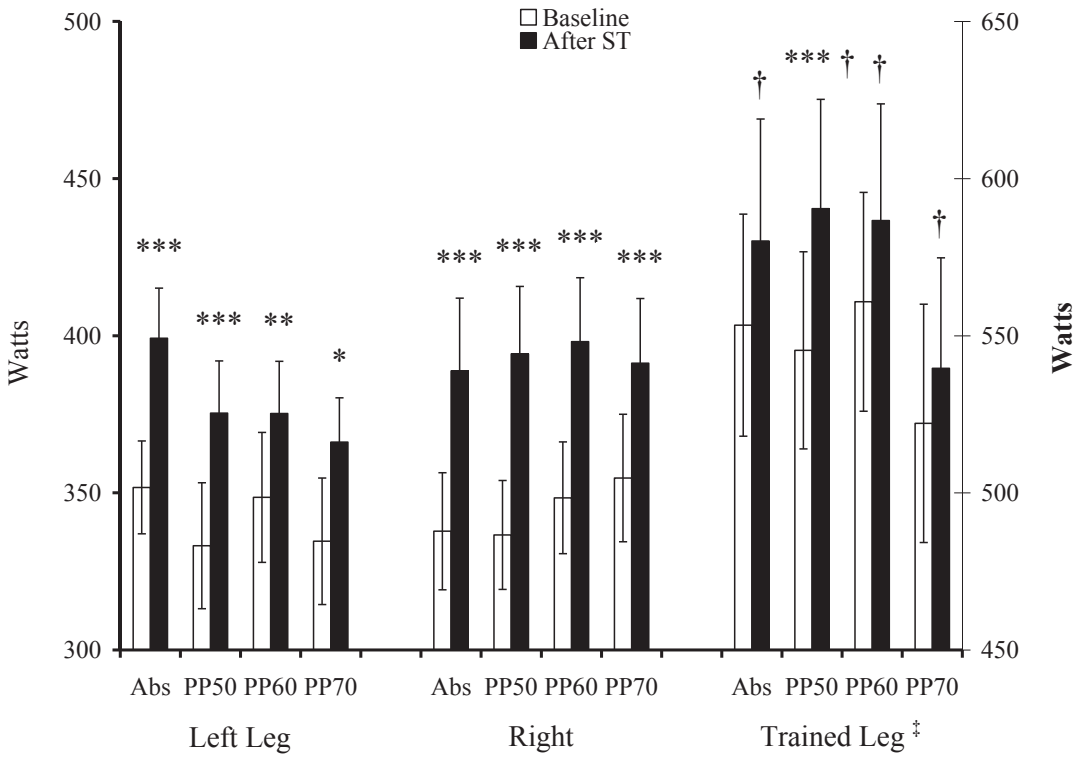

Figure 4. Baseline and after ST absolute and relative peak power output in PCa patients (N=15) and reference controls (N=14).
Abs = Absolute PP; PP = Peak Power at 50, 60, and 70% of 1RM
The left Y axis is scaled in Watts for the PCa patients while the right Y axis is scaled in Watts for the reference controls.
‡ Trained leg from the reference control group.
† Significant effect of group ($P < 0.05$)
* Significantly different from baseline value ($P < 0.05$)
** Significantly different from baseline value ($P < 0.01$)
*** Significantly different from baseline value ($P < 0.001$)

unchanged at the relative loads with one exception (R leg: 70% load), suggesting that both peak torque and movement velocity contributed to the gains in absolute power with training while increased peak torque appears to be the principle factor at relative loads. When compared to reference controls, there were no differences in the response to ST between groups for the increases in peak torque, whereas the increases in absolute peak velocity was greater in PCa patients ($P = 0.004$).

Table 2. Baseline and after ST muscle endurance, torque, velocity, and thigh fat values in PCa patients and reference controls.

	PCa (N=15-16)		**Reference Controls** (N=14) ‡	
	Baseline	**After ST**	**Baseline**	**After ST**
Chest Press End	12.1 ± 0.6	19.9 ± 1.3 ***	-	-
Leg Press End	17.6 ± 2.4	36.9 ± 3.7 ***	-	-
PT Abs (N)	188.3 ± 10.0	191.6 ± 10.3 **	148.4 ± 27.5	151.5 ± 27.7
PT 50 (N)	171.2 ± 5.3	200.7 ± 8.1 ***	136.9 ± 23.6	156.2 ± 25.5 ***
PT 60 (N)	200.4 ± 8.8	229.6 ± 10.0 *	162.0 ± 28.6	183.7 ± 30.3 ***
PT 70 (N)	229.8 ± 10.8	265.1 ± 11.9 **	176.3 ± 32.0	200.7 ± 34.6 ***
PV Abs (rads/sec) #	5.1 ± 0.2 a	5.7 ± 0.2 **	6.2 ± 0.2	6.2 ± 0.2
PV 50 (rads/sec) †	5.6 ± 0.2	5.5 ± 0.2	6.4 ± 0.2	5.8 ± 0.3 **
PV 60 (rads/sec)	5.0 ± 0.2	4.8 ± 0.2	5.6 ± 0.3	4.9 ± 0.2 **
PV 70 (rads/sec)	4.5 ± 0.2	4.1 ± 0.2 *	4.8 ± 0.2	4.2 ± 0.3 *
SCF (cm^2) †	116.6 ± 20.8	116.8 ± 21.0	57.0 ± 5.8	57.6 ± 5.5
IMF (cm^2)	7.9 ± 0.9	7.6 ± 1.0	6.3 ± 0.7	6.2 ± 0.6

‡ Healthy, older black men who underwent a unilateral knee extensor ST protocol and are provided as an example of optimal training conditions in subjects of similar age and race.
End = Endurance Repetition Test; PT Abs = Absolute Peak Torque of the knee extensors during power testing; PT = Peak Torque at 50, 60, and 70% of KE 1RM; PV = KE Peak Velocity; SCF = Subcutaneous Fat; IMF = Intermuscular Fat
# Significant interaction of group x training ($P < 0.05$)
a Significantly different between groups ($P < 0.001$)
† Significantly main effect of group ($P < 0.05$)
* $P < 0.05$
** $P < 0.01$
*** $P < 0.001$

Total and Regional Body Composition

Total body composition significantly improved with ST. Despite the ablation of endogenous testosterone from ADT, significant increases in FFM were observed in the upper body (2.2 ± 0.5%, $P = 0.0026$), lower body (3.8 ± 1.0%, $P = 0.0014$), appendicular (3.6 ± 0.9%, $P = 0.0011$), and in the total body (2.7 ± 0.4%, $P < 0.001$, Table 1). There were no significant changes in BMC, BMD or fat mass in any of the body regions. Total body % fat significantly decreased with ST (-2.2 ± 0.9%, $P = 0.012$), likely as a result of

the increased total body FFM. There was a trend for ST to increase FFM in reference controls (0.9 ± 0.6%, $P = 0.051$).

The changes in regional body composition are presented in Figure 5. Thigh MV increased significantly in both legs of the PCa patients and the trained leg of the reference controls (R leg: 6.4 ± 0.8%; L leg: 6.5 ± 0.9%; Trained Leg: 9.9 ± 1.1%, all $P < 0.001$), but there was no difference in the response to ST between groups. PCa patients displayed greater MV than reference controls ($P = 0.001$) which was primarily due to differences in

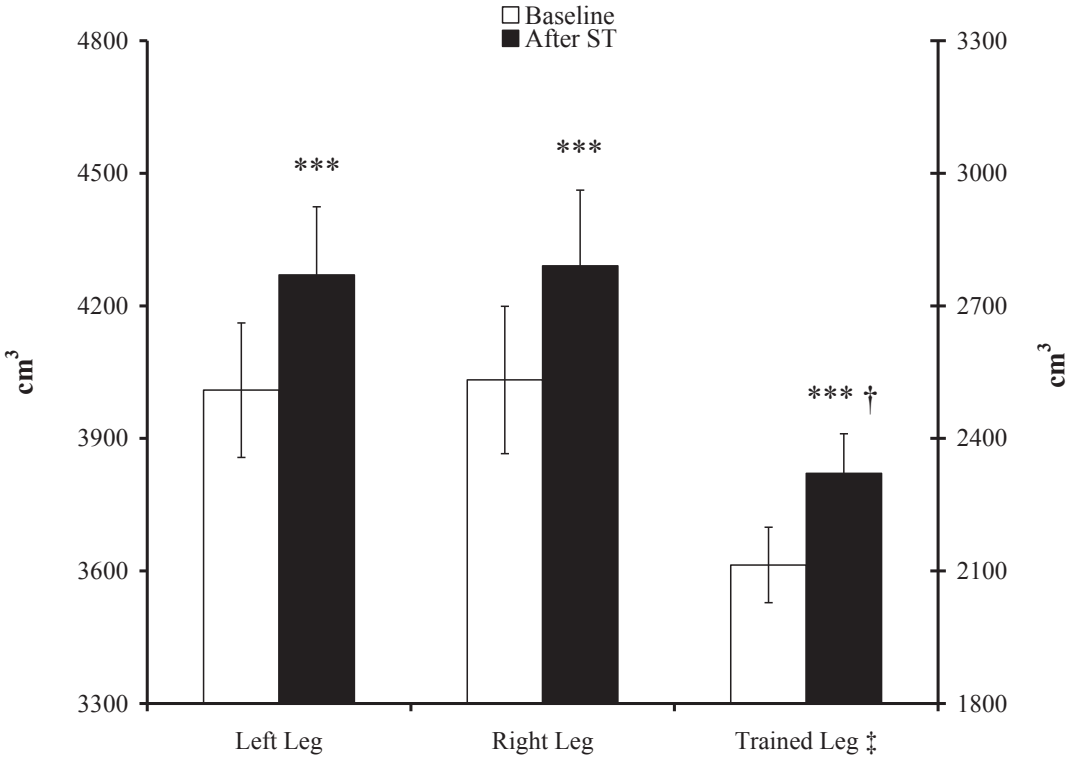

Figure 5. Baseline and after ST thigh MV in PCa patients (N=16) and reference controls (N=20). The left Y axis is scaled in cm^3 for the whole thigh MV for the PCa patients while the right Y axis is scaled in cm^3 for the MV of only the knee extensors of the reference controls.
‡ Trained leg from the reference control group provided as an example of optimal training conditions for muscle hypertrophy.
† Significant effect of group ($P < 0.05$)
*** Significantly different from baseline value ($P < 0.001$)

the measurement of MV. Finally, there was no significant change in SCF or IMF with ST in either group, but PCa patients had substantially greater SCF values (P = 0.005) than the reference controls (Table 2).

Physical Function

Figure 6 shows significant improvements in all indicators of physical function with ST. The largest gain in function was observed in the chair stands (20.3 ± 4.3%, P < 0.001), followed by the 6m rapid walk tests (12.0 ± 2.1%, P < 0.001). Smaller

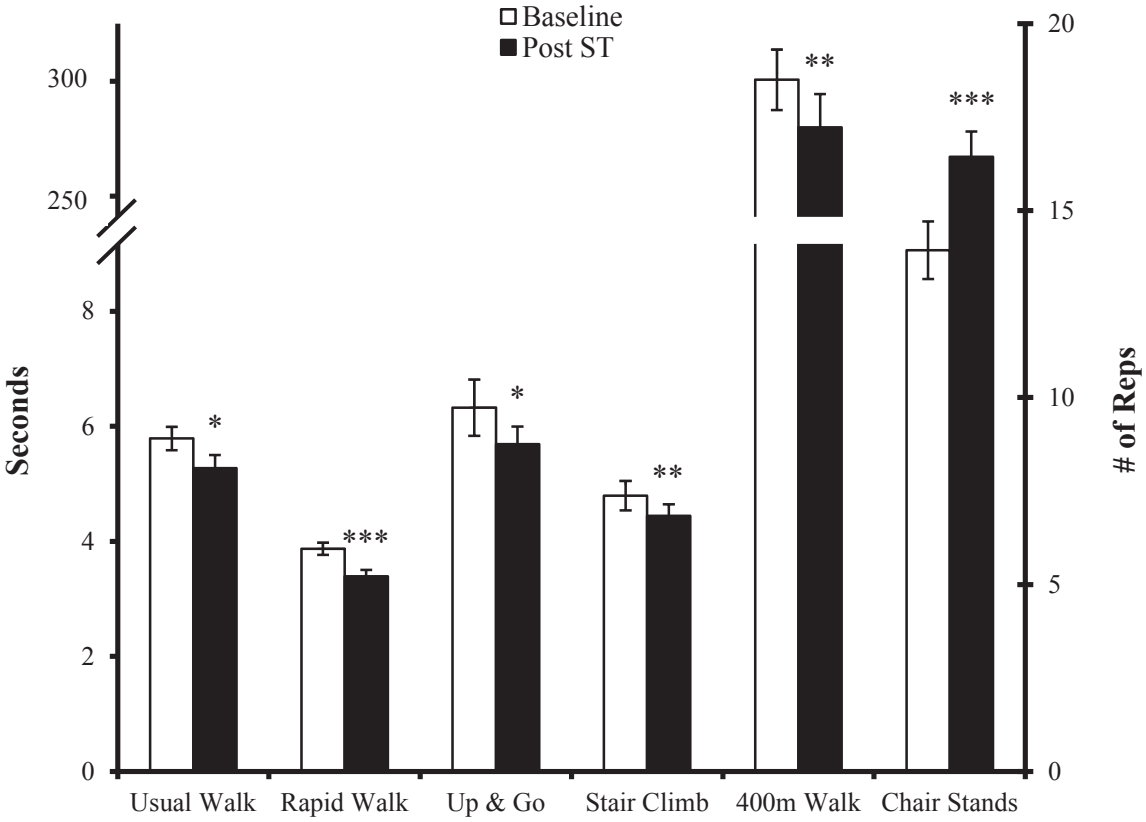

Figure 6. Physical function at baseline and after ST in PCa patients (N=17). The left Y axis is scaled in seconds for the Usual and Rapid walk, Up and Go, Stair Climb, and 400m walk tests while the right Y axis is scaled for the number of successful Chair Stands in 30 seconds.
* Significantly different from baseline value (P < 0.05)
** Significantly different from baseline value (P < 0.01)
*** Significantly different from baseline value (P < 0.001)

improvements were observed in the remaining functional tasks, but all remained significant (Range: 6.7 – 8.0%, all $P < 0.05$). The inclusion of length of ADT treatment as a covariate had no significant effect on all but two measures of physical function, i.e., 6m Rapid and 400m Walks, and did not change the overall interpretation of the results. Therefore, the raw values were reported.

Fatigue Perception and QoL

Fatigue perception and QoL data are presented in Figure 7. Fatigue perception decreased significantly with ST ($P = 0.011$). The overall FACT-P score significantly

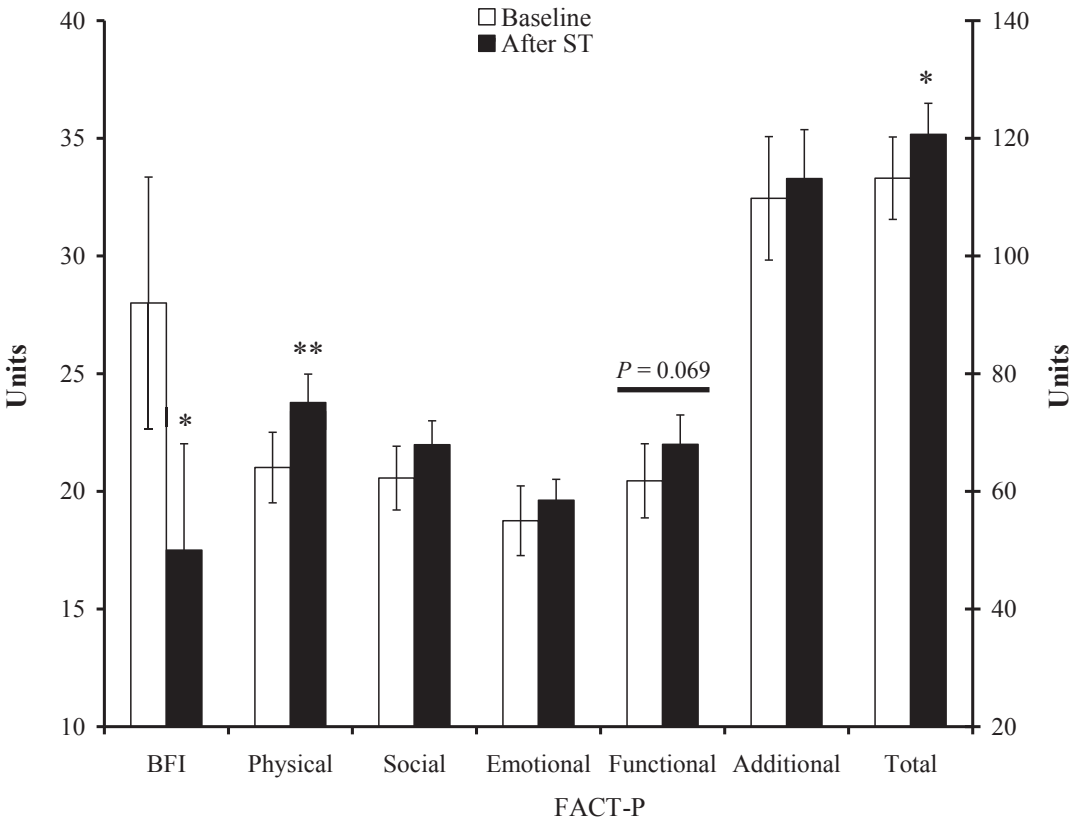

Figure 7. Fatigue perception and QoL at baseline and after ST in PCa patients (N=17). The left Y axis is scaled for the BFI score and each individual subsection of the FACT-P while the right Y axis is scaled for the composite FACT-P score.
* Significantly different from baseline value ($P < 0.05$)
** Significantly different from baseline value ($P < 0.01$)

increased as a result of ST ($P < 0.05$), as did the Physical Well-Being subsection ($P < 0.01$), while there was a trend for improvements in the Functional Well-Being subsections ($P = 0.069$).

Physiological Traits, Physical Function, and QoL Correlations

To establish the initial associations between baseline and ST-induced changes in muscle function, body composition, fatigue perception, physical function, and QoL, correlation matrices were established (Tables 3 - 5). At baseline, length of ADT treatment was significantly correlated with BFI and physical function, such that longer treatment resulted in greater fatigue and lower function. Higher baseline body mass, BMI, and total and regional fat masses were positively correlated with baseline BFI and physical function, while strength and power were negatively correlated with BFI and physical function (all $P < 0.05$, Table 3). Neither MV or FFM were consistently correlated with functional performance or fatigue perception at either baseline or with ST. The change scores for fatigue and physical function remained correlated with length of ADT treatment, in addition to changes in body mass and BMI (all $P < 0.05$, Table 4). The increases in absolute peak power and chest press 1RM were also consistently correlated with improved physical function ($P < 0.05$).

Overall FACT-P score, along with the Physical and Functional subsections, were significantly correlated with the BFI at baseline for the PCa patients (Pearson r values: -0.668, -0.676, and -0.693, all $P < 0.01$, Table 5). In addition, all estimates of physical function, except for 6m usual walk, were significantly correlated with QoL ($P < 0.05$). However, BFI change scores were not correlated with the Physical and Functional subsections of the FACT-P, but there was a trend for a relationship between BFI and

overall FACT-P score with ST. The correlations between changes in physical function and FACT-P were inconsistent as well, as only stair climb improvement was significantly correlated with changes in FACT-P scores (all $P < 0.05$).

Table 3. Correlations between BFI, Physical Function, Muscle Function, and Body Composition at baseline in PCa patients.

	BFI	Usual	Rapid	Up & Go	Chair	Stair	400m
ADT days	0.688**	0.018	0.353	0.522*	-0.634**	0.491*	0.533*
Mass	0.529*	0.087	0.488*	0.861**	-0.673**	0.762**	0.759**
BMI	0.403	0.069	0.525*	0.748**	-0.471*	0.699**	0.803**
% Fat	0.453*	-0.151	0.353	0.680**	-0.583**	0.679**	0.706**
Fat	0.571*	-0.005	0.481*	0.842**	-0.683**	0.770**	0.784**
FFM	0.362	0.231	0.387	0.743**	-0.558*	0.601**	0.585*
KE 1RM	-0.004	-0.074	0.054	-0.318	0.441*	0.001	-0.130
CP 1RM	-0.367	-0.272	-0.166	-0.555*	0.727**	-0.283	-0.418
LP 1RM	-0.270	-0.349	0.012	-0.138	0.351	-0.090	-0.030
CP End	-0.082	-0.093	0.208	-0.061	0.116	-0.099	-0.106
LP End	-0.114	-0.152	0.316	0.289	-0.332	0.462*	0.110
PP Abs	-0.604*	-0.064	-0.527*	-0.474*	0.567*	-0.454	-0.532*
MV	0.092	0.230	0.101	0.515*	-0.323	0.394	0.433
SCF	0.705**	0.297	0.484*	0.732**	-0.474*	0.528*	0.606**
IMF	0.468*	-0.043	0.330	0.694**	-0.664**	0.584**	0.615**

ADT days = length of ADT; BMI = Body Mass Index; FFM = Fat Free Mass; KE 1RM = Knee Extensor Maximal Strength; CP = Chest Press; LP = Leg Press; CP/LP End = Endurance Test; PP Abs = Knee Extensor; Absolute Peak Power; MV = Muscle Volume; SCF = Subcutaneous Fat; IMF = Intermuscular Fat; Usual = 6m Usual Walk; Rapid = 6m Rapid Walk; Up & Go = Timed Up and Go; Chair = Chair Stands Task; Stair = Stair Climb; 400m = 400m Walk

* $P < 0.05$

** $P < 0.01$

Regression Analysis

The results of the regression analysis are displayed in Table 6. The model for change in usual walk time was not significant, but all others were significant ($P < 0.10$) and had R^2 values ranging from 0.21 to 0.66. Based on sample size limitations, only two predictor variables could be used for each regression model, one of which was ADT

treatment length in nearly all models. The exclusion of ADT length in the physical function regression models resulted in a loss of statistical significance.

Table 4. Change score correlations between BFI, Physical Function, Muscle Function, and Body Composition.

	BFI	Usual	Rapid	Up & Go	Chair	Stair	400m
ADT days	-0.434*	-0.303	-0.563*	-0.402	0.261	-0.405	0.516*
Mass	0.022	0.005	-0.488*	-0.433*	0.168	-0.489*	0.623**
BMI	0.149	0.041	-0.495*	0.123	0.177	-0.126	0.509*
% Fat	-0.238	-0.005	-0.063	-0.244	-0.132	-0.058	0.423
FFM	0.277	0.127	-0.302	0.010	0.232	-0.253	0.164
KE 1RM	0.199	0.071	0.276	-0.094	-0.248	-0.102	-0.144
CP 1RM	-0.137	-0.416*	-0.494*	-0.667**	0.264	-0.640**	0.207
LP 1RM	-0.102	-0.103	-0.111	-0.433*	0.165	-0.526*	0.250
CP End	-0.131	-0.368	-0.382	-0.521*	0.382	-0.618**	0.252
LP End	-0.415	-0.160	0.224	0.167	-0.165	-0.113	0.079
PP Abs	-0.146	0.091	-0.736**	-0.358	0.276	-0.524*	0.156
MV	-0.459*	-0.061	-0.053	0.116	-0.006	-0.112	0.510*

ADT days = Length of ADT; BMI = Body Mass Index; FFM = Fat Free Mass; KE 1RM = Knee Extensor Maximal Strength; CP = Chest Press; LP = Leg Press; CP/LP End = Endurance Test; PP Abs = Knee Extensor Absolute Peak Power; MV = Muscle Volume; SCF = Subcutaneous Fat; IMF = Intermuscular Fat; Usual = 6m Usual Walk; Rapid = 6m Rapid Walk; Up & Go = Timed Up and Go; Chair = Chair Stands Task; Stair = Stair Climb; 400m = 400m Walk

* $P < 0.05$

** $P < 0.01$

Adverse Events

There were no adverse events during any of the testing sessions and only one instance of hypotension and dizziness during ST. After consulting with his personal physician, this patient elected to discontinue the study.

Table 5. Correlations between QoL, BFI, and Physical Function at baseline and after ST in PCa patients.

	Baseline			**Changes with ST**		
	Physical	Function	Total	Physical	Function	Total
BFI	-0.676**	-0.693**	-0.668**	-0.157	-0.295	-0.408
Usual	0.134	-0.074	-0.053	0.037	-0.232	-0.086
Rapid	-0.564*	-0.687**	-0.678**	-0.001	-0.152	-0.312
Up & Go	-0.548*	-0.577**	-0.623**	-0.332	-0.356	-0.281
Chair	0.616**	0.627**	0.617**	-0.057	0.119	0.023
Stair	-0.734**	-0.826**	-0.840**	-0.440*	-0.545*	-0.546*
400m	-0.647**	-0.686**	-0.692**	0.189	0.434	0.238

BFI = Brief Fatigue Inventory; Physical and Functional = Subsections of FACT-P; Total = Aggregate FACT-P score; Usual = 6m Usual Walk; Rapid = 6m Rapid Walk; Up & Go = Timed Up and Go; Chair = Chair Stands Task; Stair = Stair Climb; 400m = 400m Walk

* $P < 0.05$

** $P < 0.01$

Table 6. Regression models for the changes in Physical Function, Fatigue, and QoL with ST.

DV	IV	R^2	β coeff	P value
Δ Usual Walk		-		N/S
Δ Rapid Walk		0.66		0.002
	Δ Absolute PP		-0.004	0.030
	Δ Mass		-0.095	0.009
Δ Up & Go		0.36		0.083
	Δ KE 1RM		-0.028	0.139
	ADT days		-0.001	0.045
Δ Chair Stands		0.33		0.088
	Δ Absolute PP		0.007	0.441
	ADT days		0.001	0.052
Δ Stair Climb		0.63		0.002
	Δ Chest Press Endurance		-0.064	0.004
	ADT days		$1.47E^{-4}$	0.012
Δ 400m Walk		0.54		0.020
	Δ KE 1RM		0.146	0.570
	ADT days		0.011	0.006
Δ BFI		0.21		0.085
	Δ MV		-0.070	0.085
Δ FACT-P		0.45		0.022
	Δ BFI		-0.382	0.086
	Δ Stair Climb		-19.72	0.024

Δ = Change in; PP = Peak Power; KE 1RM = Knee Extensor 1RM; ADT = Androgen Deprivation Therapy; ADT days = Length of ADT; BFI = Brief Fatigue Inventory; MV = Muscle Volume; FACT-P = Functional Assessment of Cancer Therapy-Prostate

Discussion

The principal finding from this study is that ST can have highly beneficial effects on factors that are adversely affected by ADT in black men being treated for PCa. These benefits include substantial gains in muscle power, muscle size, a more favorable body composition, improved muscle strength, muscle endurance (fatigue resistance), physical function, and lower levels of fatigue perception. ST also had a positive impact on QoL. These results confirm previous reports in other racial groups, but also add new information to the existing literature by demonstrating for the first time significant improvements in muscle power and direct measures of muscle hypertrophy in black men on ADT, a previously understudied population.

Our unique finding of increases in muscle power with ST, both at the same absolute and relative loads, has important functional and health implications. Muscle power is a key predictor of physical function, to an even greater extent than strength (8, 9, 38). In support of this conclusion, improvements in power were more closely associated with activities of daily living, our surrogate measure of physical function, than strength improvements with training. To gain insight into which factors were likely most responsible for training-induced increases in muscle power, peak torque and peak velocity were examined. Both torque and velocity significantly increased at a given absolute power, whereas only torque production increased while velocity remained constant at each relative load. These data support the hypothesis that gains in strength are the major factor driving the increased power output as higher improvements in torque production were consistently observed across all relative loads. Furthermore, an increase

in strength reduces the relative effort required to move an absolute load, shifting the force/velocity relationship to faster movement velocities.

To provide a criterion reference for an effective ST program, we compared the subjects from the current study with healthy black reference controls from another study in our laboratory. Although the training protocol used for the reference controls was not designed to optimize muscle power, it was at least as specific for muscle power adaptations as the one used in the current investigation. While the reference controls displayed significantly higher power outputs at all loads, these data do not support our original hypothesis that men on ADT would have diminished gains in power with ST. To the contrary, our PCa patients appear to display a more consistent response across all power loads than the reference controls.

The earliest investigations of ST in men on ADT used skinfolds to assess body composition (176). Follow up studies have progressed to include more sophisticated techniques, such as ultrasound (61) and magnetic resonance imaging (74). The results of these studies are equivocal, with one reporting a significant increase in quadriceps thickness (61), whereas the other study did not detect gains in quadriceps MV (74) and neither study showed increases in total body FFM. While Hansen *et al.*, (74) did use direct measures of hypertrophy, it was unclear whether proper procedures were used to ensure replication of slice position, given that no description was provided for how this was accomplished. Failure to replicate slice position before and after training can lead to significant error. Moreover, these studies did not report the racial or ethnic composition of their subjects.

Contrary to our hypothesis, treatment with ADT does not appear to blunt the ability of the muscle to increase in response to overload as there was no difference in the response to ST between groups. However, due to differences in muscle group assessed (quadriceps only in reference controls vs. whole thigh muscles in PCa patients), a much smaller baseline value in the reference control group favors their larger % change in MV response to ST (9.9% vs. 6.4%). No analyses were performed on the % change values. Nonetheless, the results clearly show substantial ST-induced muscle hypertrophy in PCa patients in the absence of normal levels of testosterone. These findings dispute the long held belief that testosterone is necessary to induce muscle hypertrophy and to increase strength.

Another key finding of this study was the significant improvement in total body composition. Our study is the first to report increases in total body FFM along with direct measurements of local muscle hypertrophy in the same study. Both assessments were highly correlated, providing additional support for muscle hypertrophy in men being treated with ADT for PCa via two separate methods. These findings stand in contrast to most (61, 74, 176), but not all (64), of the previous ST and PCa studies. Using a combined training protocol with men on ADT, Galvao *et al.* (64) reported a 0.7 kg increase in total body FFM with exercise in men on ADT, 58% below the increase observed in the current study. A lower training frequency (two vs. three time per week) and the inclusion of aerobic exercise training in their study may contribute to these differences. Our FFM improvement is also similar to what has been reported in the literature for healthy older adults undergoing ST (63, 76).

In contrast, Kvorning *et al.* (115) reported the elimination of strength gains and reduced gains in lower body FFM with ST upon the suppression of testosterone in young men compared with eugonadal controls. However, the increase in FFM in the control group was slightly smaller than the increase in lower body FFM observed in the present study, which argues for a non-essential role of testosterone in muscle hypertrophy. This is supported by studies that compared the ST response of men vs. women. While investigations generally demonstrate a greater increase in MV in men, there are still significant gains in women (97, 196, 207). Thus, testosterone appears to enhance muscle hypertrophy, but it may not be of paramount importance, as previously suggested (115).

Although not essential for muscle hypertrophy, testosterone supplementation can increase protein synthesis and muscle mass (54, 200) whereas its suppression decreases both (136). Nevertheless, the mechanisms by which testosterone induces hypertrophy are currently unclear (15). Some (54, 200, 214), but not all (136) evidence suggests that testosterone may interact with insulin-like growth factor one, which can activate mammalian target of rapamycin (mTOR), p70S6K, and protein synthesis (69). Testosterone may also inhibit glucocorticoid receptor (GR) expression (106) and atrogin-1 gene expression (219). However, recent data suggest crosstalk between mTOR and the GR, as dexamethasone increases transcription of several muscle atrophy genes while inhibiting mTOR activity (182). Subsequent activation of mTOR with amino acids impeded GR induction of its target genes which were rescued when mTOR was inhibited by rapamycin (182). Thus, the loss of the testosterone with ADT and the declines in FFM could be explained by a shift in the dynamic balance between protein synthesis and breakdown. In this regard, ST may be able to reduce the deleterious effects of ADT on

muscle through activation of mTOR and thereby increasing protein synthesis, independent of sex (48). Inhibition of mTOR blocks protein synthesis increases with acute resistance exercise (49), implicating this as a plausible pathway to explain increases in FFM with ST in individuals with very low testosterone, e.g., in women or in men on ADT.

Beyond FFM and MV, body composition was unaltered in the current study. The finding of no significant change in fat mass, BMC, or BMD with ST confirms the results of previous studies (61, 64). The short duration of this study may have influenced the lack of change in bone given that bone remodeling requires a longer time frame than muscle hypertrophy (73). Overall, % fat significantly declined, but this is likely due to the increase in FFM, resulting in fat being a smaller portion of total body mass. A decrease in % fat was also observed in PCa patients undergoing combination training (64). The regional body composition measures of SCF and IMF did not change with ST, similar to observations from our laboratory in healthy older adults (207). However, SCF was significantly higher in men on ADT than in reference controls, but there were no between group differences in IMF. The increases in fat infiltration, along with lower muscle mass, are possible contributing factors for the reductions in 1RM and physical function which are associated with ADT (70, 204).

The gains in strength and fatigue resistance as assessed by 1RM and muscle endurance testing, respectively, in the current study are supported by previously published data (63, 74, 176). Galvao *et al.* (61) reported significant gains in chest and leg press 1RM and muscle endurance at both the midpoint and the end of a 20 week ST program. Interestingly, there are striking differences in baseline 1RM levels among the

studies. For example, our subjects had baseline values that were 38% and 61% higher for the chest and leg press, respectively, than those of Galvao *et al.* (61), but when chest press 1RM was normalized to FFM, the strength levels between the two studies were identical. These baseline differences likely account for the percent change differences between the studies (19.5% vs. 40.5%), given that the absolute gains in 1RM were nearly identical when similar training periods were compared. However, normalization to FFM did not rectify the strength discrepancy on the leg press at baseline. Other studies of PCa patients on ADT report improvements of 41% and 32% in muscle fitness on the chest and leg press exercises during the standard load test (176) and isometric knee extensor 1RM gains of 20% and 7% for the right and left leg, respectively (74). Within the current study, the improvement in 1RM across the different tests were consistent, with only the left leg knee extensor 1RM lagging slightly behind. The left leg was typically the non-dominant leg and patients reported greater and more frequent pain and discomfort in this limb during testing, both of which may explain the lower response.

Overall, the PCa patients in the current study had baseline physical function levels similar to other PCa patients on ADT (35, 61, 64, 74, 125) and lower than healthy controls (63, 65, 76) and non-ADT PCa patients (74). All functional tasks were improved with training in the current study. The extent of the improvements was greater than some studies (64), while similar to (74) and less than others (61). Generally, these differences were minor and may be related to variations in training duration, types of training, and the number of sets per exercise. In addition, the average change in physical function across studies was smaller than what was observed for muscle power, strength, or endurance, however, they exceeded the minimal meaningful and detectable changes for

the walking tests (117, 133). In addition, there may be a ceiling effect on the fitness levels necessary to successfully perform some functional tasks, limiting improvements. Because our subjects were willing and able to drive themselves to our training facility for every testing and training session, their initial fitness level may have been beyond the threshold for optimal improvements via increasing fitness level. Similar situations have been discussed previously with respect to healthy, well-functioning older adults (63, 76). Still, there is abundant evidence available that supports the use of ST to maintain and improve physical function in men with PCa on ADT.

The significant decline in fatigue with ST that we observed corresponds with and may even exceed changes reported by others, though comparing disparate fatigue scales makes direct comparisons difficult (64, 176, 177). Although most ST interventions report improvements in fatigue perception (176, 177), the changes within the intervention group alone rarely meet the benchmark for clinical significance (30). Only when the scores from the control group are factored in are consistent differences in fatigue observed with ST.

The overall FACT-P scores indicating QoL in the current study are nearly identical to previous investigations (74, 176, 177). After ST, the overall FACT-P score was 7.5 units higher, which falls within the range for representing clinically meaningful changes (31). This improvement is slightly larger than one study (176) while another study reported no statistical change in ADT patients, despite an increase of 8.2 units (74), though this was likely due to sample size constraints. Other studies using different exercise and PCa populations also observed improved QoL in the intervention group accompanied by no change or declines in the controls (64, 177). There is some

indications of a trend between ST intensity and QoL changes, as studies using moderate intensity training (60-70% of 1RM) report smaller changes (176, 177) than those using higher intensities (70-85% of 1RM) (64), including the current study.

Our finding that improvements in physical function could be at least partially predicted from improvements in muscle function with training and length of ADT treatment provides some support for our initial hypothesis. While ST can improve physical function, fatigue perception, and QoL in PCa patients, the factors that contribute to these gains are less clear. Knowledge of the physiological traits that best predict improvement could aid in tailoring exercise prescription to target specific attributes. While we, and others, have previously attempted to predict gains in function in older adults (26, 32, 76), we are not aware of any studies attempting this in PCa patients, though one study did examine the correlations between changes in muscle function and general health (64). Our findings confirm a previous study in healthy older adults where changes in strength were associated with improvements in function (32) but this relationship is not always observed (26). The lack of a relationship between body composition and physical function alterations with ST was contrary to our hypothesis, based on our earlier findings in healthy older adults (76). Unfortunately, the lack of a discernable pattern as to which variable(s) best predict physical function somewhat diminishes the impact of these findings.

The ability to predict changes in fatigue perception was limited whereas FACT-P scores could be predicted to a greater extent, supporting the idea that improvements in physical function and fatigue levels influence QoL. We are aware of only one other study that has also observed relationships with QoL, as Galvao and colleagues (64) reported a

correlation between the changes in lean mass and general health, but the strength of this relationship was not reported. Thus, valid comparisons between their findings and the current study are not possible. Although the regression analyses were only exploratory, it does appear to provide preliminary support for the hypothesis that physiological improvements with ST is linked to improvements in fatigue and function, and ultimately to QoL. This information may be useful in generating new hypotheses for future studies.

Despite racial differences in incidence and mortality rates of PCa (2, 101) and in baseline muscle and fat mass (70, 207), we found no indication that black men on ADT respond differently to ST than other racial or ethnic groups reported previously (61, 64, 74, 176, 177). Prior to the current study, there were no studies that compared racial influences on response to exercise training in PCa patients on ADT. Moreover, it was difficult to determine if black PCa patients were even included because information on the racial and ethnic backgrounds were not described (61, 64, 176, 177).

There were several limitations to this study. First, all subjects were volunteers and therefore may not reflect the typical PCa patient who chooses not to exercise as described in this study. Second, subjects were not randomized into exercise vs. no exercise groups. Difficulties in patient recruitment precluded recruitment of a separate non exercise control group. Although this may have prevented proper controls for methodological, biological, and seasonal variation, some of the variables, such as muscle mass, were not likely to be significantly influenced by these factors. In addition, any influences would likely be random and not systematic, making it unlikely to result in one direction of change. Also, subjects were familiarized twice with the ST equipment prior to undergoing baseline testing to help reduce variability and bias due to learning effects.

Finally, while all PCa patients were on ADT, the use of other treatment types (radiation therapy and/or radical prostatectomy) and the length of ADT varied between subjects. Although length of ADT was not a significant factor in most cases, we were only able to examine the effects of chronic ADT treatment (>1 year). The effects of ADT tend to be most prominent in the first six to 12 months, thus future ST interventions should be initiated during this time period.

Conclusion

Strength training is an effective intervention for counteracting the adverse musculoskeletal side effects of ADT in black PCa patients. The magnitude of improvements in muscle power, mass, and strength compare favorably to those improvements that occur in healthy black adults of similar age. The gains in muscle mass and power are particularly noteworthy, as they play key roles in maintaining functional independence and a high standard of living. Future studies should examine exercise intensities and training loads and the mechanisms responsible for gains in FFM in the absence of testosterone.

Appendix I:

Specific Aims

Research Hypotheses

Operational Definitions

Appendix I:

Specific Aims and Hypotheses

Specific Aim #1: To determine whether ST can improve musculoskeletal health and regional and total body composition in black men undergoing ADT for treatment of PCa.

Hypothesis #1: ST will induce significant gains in muscle strength, endurance, power, MV and total body FFM with no change in BMC, SCF, IMF, and total fat mass.

Specific Aim #2: To compare the musculoskeletal health and body composition response to ST of PCa patients on ADT with a healthy black reference control population.

Hypothesis #2: The absence of testosterone in PCa patients will blunt ST-induced gains in MV, strength, and power compared with a reference controls.

Specific Aim #3: To determine whether ST can improve physical function, fatigue, and QoL and are these improvements associated with the changes in muscle function and body composition in black men undergoing ADT for treatment of PCa.

Hypothesis #3a: ST will increase performance on simulated activities of daily living, decrease levels of generalized fatigue perception, and improve QoL.

Hypothesis #3b: ST induced improvements in muscle volume, strength, endurance (fatigue resistance), power, and FFM will be associated with significantly improved performance on simulated activities of daily living, reduced levels of generalized fatigue perception, and improved QoL.

Operational Definitions

1 RM: Refers to the maximal amount of resistance that an individual can successfully move throughout the complete range of motion only one time.

5 RM: Refers to the maximal amount of resistance that an individual can successfully move throughout the complete range of motion only five times.

Androgen Deprivation Therapy (ADT): The ablation of endogenous sources of testosterone as an adjuvant treatment of PCa. In this study, ADT was accomplished through the use of Luteinizing Hormone Releasing Hormone agonists and/or anti-androgen treatments that block testosterone from binding to the androgen receptor.

Appendicular Fat Free Mass: The sum of the lean tissue of the arms and legs, as determined by DEXA.

Brief Fatigue Inventory (BFI): A questionnaire used to quantify generalized fatigue perception and to distinguish it from localized muscle fatigue.

Computed tomography (CT): A technique for assessing regional muscle mass based on analysis of axial scans of the thigh. Visual images are created from the measurement of the intensity of x-rays and are analyzed to measure the cross-sectional area. The images are based on the attenuation of x-rays as they pass through the body. Attenuation scores are measured in Hounsfield units, which depend upon the level of absorption of emitted x-ray beams, -1000 in air to +1000 in bone. Skeletal muscle typically ranges from 0 to 100 Hounsfield units while adipose tissue is usually -190 to -30 Hounsfield units.

Dual-energy x-ray absorptiometry (DEXA): A technique used for assessing whole and regional body composition that considers the body to be composed primarily of three

compartments: bone mineral mass, soft tissue, and lean tissue. Tissue quantities are based on the attenuation of x-rays as they pass through the body.

Fatigue resistance: An increased number of successful repetitions on the muscle endurance repetition test.

Functional Assessment of Cancer Therapy-Prostate (FACT-P): A questionnaire that is a relevant, worldwide tool used for assessing the health-related quality of life in men with PCa. It is composed of physical, social, emotional, and functional well-being sections, along with a section of concerns specific to PCa.

Localized Muscle Fatigue: The number of repetitions achieved throughout the full range of motion without pausing during the chest press and leg press when performed at 70% of baseline (pre training) 1RM.

Muscle volume (MV): Muscle volume with be determined from the cross-sectional axial CT scans using the MIPAV software and the equations of Tracy *et al.* (197). Briefly, this process entails an equation that utilizes the 8-10 thigh slices of each thigh to create an estimate for muscle volume.

Sarcopenia: A condition characterized by the loss of muscle size, quality, and function that occurs with aging. This typically leads to or exacerbates ailments such as osteoporosis and loss of functional independence.

Prostate Cancer (PCa): All physician diagnosed malignant tumors of the prostate gland, regardless of stage or Gleason score, were included as part of the inclusionary criteria for this study.

Appendix II: Forms

Initial Screening Form

Medical Clearance

Prostate Cancer History

Detailed Medical History

Institutional Review Board Letter of Approval

Consent to Participate

Venipuncture Record

DEXA Body Scan

Brief Fatigue Inventory

FACT-P

Knee Extension 1RM

Chest Press 1RM

Leg Press 1RM

Power Testing

Strength Training Log

Appendix II: Forms

Maryland CARES
Initial Screening Form

1. CONTACT INFORMATION:

   Name: _____

   Address:

   _____

   _____

   Home Phone number: _____

   Work Phone number: _____

   Cell Phone number: _____

   Email: _____

   Preferred method and time to reach you: _____

2. AGE and DATE OF BIRTH:

3. CURRENT HEIGHT and WEIGHT:

4. WOULD YOU CLASSIFY YOURSELF AS BLACK: YES / NO

5. PROXIMITY TO UMD COLLEGE PARK CAMPUS:
   -Distance from campus:

   -Willingness to travel to UMD campus 3 times per week for 12 weeks: YES / NO

   -Times available for training AM_____ PM_____ Other_____

6. MEDICAL HISTORY:
   -Have you been diagnosed by a physician as having prostate cancer? YES / NO

   -Currently being treated for PCa with Androgen Deprivation Therapy? YES / NO

-Current Androgen Deprivation Therapy medications you are taking:

GnRH Antagonists
1. Abarelix (Plenaxis)
2. Histrelin (Supprelin-LA)
3. Cetrorelix (Cetrotide)
4. Ganirelix (Antagon)
5. Other-please specify

GnRH Agonists
1. Leuprolide (Lupron, Eligard)
2. Buserelin (Suprefact)
3. Nafarelin (Synarel)
4. Histrelin (Supprelin)
5. Goserelin (Zoladex)
6. Deslorelin
7. Triptorelin
8. Other- please specify

-What is your current Prostrate-Specific Antigen (PSA) value?

-Do you have any medical conditions (other than PCa), surgeries or any other condition that you feel may prevent you from exercising vigorously? YES / NO If YES, please describe these conditions:

7. MEDICAL CONDITIONS:

-Please indicate YES / NO / DON'T KNOW if you currently have any of the medical conditions:

_____Severe cardiovascular disease, such as:
- _____unstable angina
- _____uncontrollable hypertension (high blood pressure)
- _____uncontrolled dysrhythmias (irregular heart rate)
- _____severe stenotic or regurgitant valvular disease
- _____hypertrophic cardiomyopathy
- _____symptomatic peripheral arterial disease

_____Severe COPD or other signs of significant pulmonary dysfunction
_____Intracranial aneurysm
_____Previous stroke
_____Musculoskeletal diseases that cause severe joint pain at rest or upon exertion
_____Diseases that promote muscle protein breakdown
_____Joint, vascular, abdominal or thoracic surgery in the past year
_____History of bone fragility fractures
_____Having any condition that is likely to be aggravated by muscular exertion
_____Being unable to engage safely in mild to moderate exercise, such as independently walking up at least one flight of stairs or walking two blocks on level ground
_____Diabetes
- _____Current use of Insulin

8. CORONARY ARTERY DISEASE RISK FACTORS

- Please indicate YES / NO / DON'T KNOW for the Coronary Artery Disease Risk

A. Family History as defined by:
_____Myocardial infarction (Heart attack)
_____Coronary revascularization
_____Sudden death before 55 years of age in father or other male first degree relative
_____Sudden death before 65 years of age in mother or other female first degree relative

B. Cigarette smoker as defined by:
_____Current smoker
_____Quit within the previous 6 months

C. Hypertension (High Blood pressure) as defined by:
_____Systolic blood pressure ≥ 140 mm Hg or Diastolic blood pressure ≥ 100mm Hg confirmed by measurements on at least 2 separate occasions.
_____On antihypertensive medications.

D. Dyslipidemia (High Cholesterol) as defined by:
_____Total cholesterol ≥ 200 mg/dl
_____High density lipoprotein (HDL) cholesterol < 40 mg/dl
_____Low density lipoprotein (LDL) cholesterol ≥ 130 mg/dl
_____On lipid lowering medications

E. Diabetes (High Blood Sugar)
_____Fasting Blood Glucose ≥ 126 mg/dl confirmed by measurements on 2 separate occasions

F. Obesity as defined by:
_____Body Mass Index (BMI) ≥ 30 kg/m^2
_____Waist Girth ≥ 102 cm for men
_____Waist hip ratio ≥ 0.95

9. CURRENT PHYSICAL ACTIVITY LEVEL:

- Do you participate in any type of regular physical activity or exercise? YES / NO

If YES, please describe what types of exercise you do:
How many days per week do you exercise? _____
How long does each exercise session typically last? _____
How difficult (on a scale of 1-10) is each session? _____
How long have you been on your current exercise program? _____

Medical Clearance to Participate in Research Project

It is my understanding that _____ (name of the volunteer), a patient under my care, has volunteered to participate in the study entitled, ***" Strength Training to Improve Muscle Function, Quality of Life, and Self Efficacy in Patients with Prostate Cancer."*** The volunteer must have the approval of his physician to participate in this study. Please record date and results of last exercise stress test, if known. _____

Exclusionary criteria for eligibility are listed below. If you believe that your patient named above has any of the medical conditions indicated below, please place a check in front of the condition(s) indicated:

____ Severe cardiovascular disease, such as ____unstable angina, ____uncontrollable hypertension, ____uncontrolled dysrhythmias, ____severe stenotic or regurgitant valvular disease, ____hypertrophic cardiomyopathy, and ____symptomatic peripheral arterial disease
____ Severe COPD or other signs of significant pulmonary dysfunction
____ Intracranial aneurysm
____ Previous stroke
____ Musculoskeletal diseases that cause severe joint pain at rest or upon exertion
____ Diseases that promote muscle protein breakdown
____ Joint, vascular, abdominal or thoracic surgery in the past year
____ History of bone fragility fractures
____ Having any condition that is likely to be aggravated by muscular exertion
____ Being unable to engage safely in mild to moderate exercise, such as independently walking up at least one flight of stairs or walking two blocks on level ground

There is evidence of non-fatal subarachnoid hemorrhage in patients with pre-existing intracranial aneurysms and aortic dissection in predisposed patients, associated with strength training. For this reason, any patient who has known, suspected, or at high risk for intracranial aneurysms, aortic dissection, connective tissue disease or uncontrolled hypertension should not participate in this study.

Please check one of the following:
____ Clearance granted
____ Clearance not granted
____ Send me the following information about the study

Volunteers in this study will participate in resistance exercise under the supervision of exercise specialists under the direction of the Principal Investigator, Ben Hurley Ph.D., Professor, Department of Kinesiology, College of Health and Human Performance, University of Maryland, College Park, Maryland 20742 (email: benhur@umail.umd.edu; tele: 301-405-2486). Please fax signed form: (301) 405-5578.

Physician's signature:_____ Date:_____

UNIVERSITY OF MARYLAND

Dept. of Kinesiology
School of Public Health
College Park, MD 20742
301.405.2569 Tel
301.405.5578 Fax

Re: Prostate Cancer History

4 November 2009

Dear Mr.

Thank you for your interest in our research study. In order to continue the screening process, we need to confirm information from you about your prostate cancer history. Please fill out the form below, being as specific as possible. If you do not know the answers to these questions, we ask that you speak with your urologist or oncologist to help obtain this information. Please bring the completed form with you to your orientation session. Thank you for your cooperation. If you have any questions, please feel free to contact us. We look forward to working with you.

1. Prostate Cancer Diagnosis Date (exact date):

_____

2. Androgen deprivation therapy (ADT) start date (exact date):

_____

3. Current ADT medications (please include all injections & oral medications):

_____

Frequency of ADT injections: _____

Will you remain on ADT medication for the next 3-4 months? ____ Yes ____ No

4. Once you started ADT therapy, have you been on it continuously? ____ Yes ____ No

Reason for stopping ADT (if applicable)? _____

_____

5. Radiation therapy start date and number of sessions (if applicable): _____

6. Have you ever had a prostatectomy? _____ Yes _____ No

Date of surgery: _____

7. Most recent PSA level & date: _____

Detailed Medical History for the Maryland CARES Study

Name:_____ Date:_____
Name of Interviewer: _____
Emergency contact:_____
_____
Have you ever been a patient at Washington Adventist Hospital?_____
DIRECTIONS:
Read the following questions out loud to each prospective volunteer and check "yes" or "no". Any answers that require qualification should be written in the space below the question or on the back of the sheet.

SECTION *A*
Musculoskeletal system: **YES NO**

Have you ever been told by your doctor that you have any of the following?

a. Osteoarthritis or degenerative arthritis ____ ____

b. Rheumatoid arthritis ____ ____

c. Unknown or other type of arthritis ____ ____

d. Osteoporosis ____ ____

e. Any other disease of joint or muscle: ____ ____

Comments:_____
_____

SECTION *B*
Cardiovascular system:

1. Has any family member had a heart attack prior to the age of 55? ____ ____

   If so, please describe the relationship:

2. Have you ever had frequent cramping in your legs? ____ ____

   If yes, is it a current problem? ____ ____

3. Have you ever had pain or cramping in your legs while walking? ____ ____

   If yes, is it a current problem? ____ ____

   If yes, is this pain relieved by rest? ____ ____

YES NO

4. Have you ever been told that you have high blood pressure? ____ ____

   If yes,

   a. What was the date of diagnosis? _____

   b. Were you given any medications? ____ ____

   (*Please list the medications with dose on the last page)*

   c. How long have you been on the medications? _____

   d. Has there been a recent change in the medications and if so, when?

   _____

5. Did a doctor ever tell you that you had a heart problem? ____ ____

   If yes,

   a. What was the date of onset?_____

   b. What did the doctor call it? (eg: Angina, Heart Failure, Heart Attack, Rhythm disturbances, heart murmurs, enlarged heart, diseases of heart valves, others). *Please circle relevant one(s). If others, please ask subject to explain.*

   c. Were you given any medications? (*Please list the medications with dose on the last page)*

   d. Was Echocardiography ever done? ____ ____

6. Have you ever had any chest pain due to a respiratory or digestive problem?

   ____ ____

   If yes,

   a. Month and year of the first occurrence? _____

   b. Month and year of the most recent occurrence? _____

   c. What was the frequency of occurrence? (eg: once a month, once a week, once a year etc.)

   _____

d. How would you describe the pain or discomfort? (Eg: Pressure, Burning, Squeezing, Piercing, Stabbing, Shooting or Sticking) *Circle appropriate one or if different, please describe:*

e.

How many minutes did it last?_____

f. Does the pain or discomfort move? If yes, to where?

g. Does the pain or discomfort tend to occur:	**YES**	**NO**
After meals?	____	____
At night?	____	____
When Exercising?	____	____
When walking in cold windy weather?	____	____
When upset, excited or nervous?	____	____
Other?		

h. Is this pain relieved by

A change in posture?	____	____
Rest?	____	____
Physical activity?	____	____
Bicarbonate of soda, Tums or antacids?	____	____
Prescribed medications?	____	____
Other?		

i. Did you ever consult a doctor for this pain or discomfort? ____ ____

If yes,

Do you know the diagnosis?_____

Were you given any medications and if so was there a recent change in the medication (within past one month)? (*List on last page*)

YES NO

7. Do you have any history of high cholesterol in your blood as evident by previous blood tests? ____ ____

Comments:_____
_____

SECTION *C*

Respiratory System:

1. Have you ever had persistent cough with sputum production for almost all days for 3 months? ____ ____

   If yes,

   a. How long did it last?

   b. Did your doctor prescribe any medications and has there been any recent change in the medications? (*Please list on last page, if any*)

2. Have you ever had attacks of wheezing? ____ ____

   If yes,

   a. Was it seasonal/ periodic? ____ ____

   b. Have you ever-required hospitalization to abort an acute attack?

   ____ ____

Comments:_____
_____

SECTION *D*

Endocrine system:

Has your doctor ever told you that you have any of the following problems?

a. Thyroid problems? ____ ____

b. Adrenal problems? ____ ____

c. Diabetes mellitus? ____ ____

If yes, which type?

Date of onset-_____

Were you on any medication or diet control? ____ ____

SECTION *E*

Neurological system:

	YES	NO
1.Do you have any problems with your memory?	____	____
If yes,		
a. When answering the telephone, do you recall what you were doing before it rang?	____	____
b. If someone calls you, can you give the directions to your house?	____	____
c. Can you keep appointments without a reminder?	____	____
d. Can you remember what clothes you wore yesterday?	____	____
If the subject answers "no" to any of the above questions		
Do a Mini Mental Status Examination of the subject.		
2. Any problems with vision other than corrective lens changes? If yes, which of the following conditions- Blindness, Temporary loss of vision, Double vision, Glaucoma, Cataract, Macular degeneration or others.	____	____
3. Ringing in your ears?	____	____
4. Vertigo (a feeling of spinning, or unsteadiness)?	____	____
5. Fainting Spells (black outs)?	____	____
6. Seizure or convulsions?	____	____
7. Migraine or severe headaches?	____	____
8. Paralysis of arm or leg?	____	____
9. A head injury with loss of consciousness?	____	____
10. Pain, numbness or tingling in your arm or hand?	____	____
11. Pain in your lower back?	____	____
12. Kidney stones	____	____

	YES	NO
13. Ruptured vertebral disc in neck or back?	____	____
14. Have you had pain in any part of body (including headache) while exercising?	____	____
15. Numbness or pain in your legs?	____	____
16. Have you been told that you have a peripheral neuropathy?	____	____
17. Tremors?	____	____
18. Problems with walking?	____	____
a. Do you fall frequently	____	____
b. Is your walking problem related to pain, weakness or loss of balance?	____	____
19. Stroke	____	____
20. Epilepsy	____	____
21. Operations on skull or brain?	____	____
22. Multiple sclerosis?	____	____
23. Meningitis or Brain fever?	____	____
24. Parkinson's disease?	____	____
25. Any history of neurological consultation?	____	____

Comments:_____

_____

SECTION *F*
Hematology/Immunology/Oncology:

1. Have you ever been told by your physician that you had a problem with anemia or any disease of the red blood cells or the white blood cells?	____	____
2. Any family history of this problem?	____	____

	YES	NO
3. Do you have any history of bleeding disorder?	____	____
4. Have you ever been diagnosed as having any type of cancer other than PCa?	____	____

If yes, which organ, date of onset?_____

6. Were you given any medications, radiation or undergone any surgery?	____	____

Comments:_____
_____

SECTION *G*
PCa History:

1. When were you first diagnosed with PCa?
2. When did you first start taking androgen deprivation therapy?
3. Which ADT medication(s) are you currently taking?

4. Have you had a stable PSA of <2ng/ml for 3 months?	____	____
5. Have you ever had a prostatectomy? If so, when?	____	____
6. Have you undergone radiation therapy? If so, when and how many sessions?	____	____

7. What is your Gleason score (2-10)?
8. What is the stage of your cancer progression?

SECTION *H*
Surgical History:

1. Have you undergone any surgeries? (Please include abdominal surgery).	____	____

If yes,
a. Where and for what purpose? _____
b. Date of Surgery? _____
c. Length of stay in hospital _____

d. Any complications of Surgery? _____

	YES	NO
2. Has a doctor ever told that you have been suffering from		
a) Cystic medial degeneration?	____	____
b) Any Connective tissue disorder?	____	____
3. Have any of your family members had an intracranial aneurysm or bleeding?	____	____
4. Have you ever been diagnosed with an abdominal aneurysm?	____	____
5. History of severe pain in the abdomen	____	____
If yes, Please specify_____		
6. Any history of severe headache?	____	____
If Yes, what was the date of onset?_____		
7. Was it associated with neurological signs like blurred vision, nausea/vomiting, seizures, drowsiness, memory impairment, sensory or motor loss(weakness)?	____	____
8. Was it a new or different type of headache other than tension, migraine etc?	____	____
9. Was it the worst ever experienced	____	____
10. Did it occur after exertion, coughing or straining?	____	____

Comments:_____
_____

SECTION *I*
Lifestyle:

1. Do you exercise regularly?	____	____
If yes,		
a. Do you perform aerobic exercise, strength training, both, or another form of exercise?		
b. How often do you exercise per week?		

c. How long are your training sessions? **YES** **NO**

d. How challenging would you say your training sessions are on a scale of 1-10, with 1 being easy and 10 being extremely challenging?

2. Do you smoke regularly? ____ ____
   If yes,
   a. How long have you been smoking?

   b. How many packs per day?

   If no,
   a. Have you ever smoked in the past? ____ ____

   b. How long ago did you quit smoking?

   c. How long did you smoke for?

3. How many alcoholic beverages do you consume per week (on average)?
   _____None
   _____Less than 3 per week
   _____3 to 5 per week
   _____6 to 8 per week
   _____9 to 11 per week
   _____12 to 14 per week
   _____More than 14 per week

4. Do you consume a particular diet? ____ ____
   If yes, please describe.

5. Do you avoid high fat foods? ____ ____

6. Do you avoid high carbohydrate foods? ____ ____

7. Are there any food groups or types that you avoid? ____ ____
   If so, which ones?

8. How many servings of fruits and vegetables do you consume per day?
   _____Less than 2 servings per day
   _____2 to 4 servings per day
   _____5 to 9 servings per day
   _____More than 9 servings per day

9. Do you consume any dietary supplements? ____ ____
   If so, which ones?

SECTION *J*
Demographics:

	YES	NO
1. Do you have children?	____	____
If so, how many?		
2. Have you ever been married?	____	____
3. Are you currently married?	____	____

4. What is the highest level of education that you completed?
   _____Some high school
   _____High school graduate or equivalent
   _____Vocational/Training school after High School
   _____Some College (no degree)
   _____Associates Degree
   _____College Graduate
   _____Some Graduate or Professional School after College Graduation
   _____Complete Graduate/Professional School

5. Are you currently employed?	____	____
If no,		
a. Are you retired?	____	____

If yes, what is your approximate income level?
_____Less than $10,000
_____$10,000-$19,999
_____$20,000-$34,999
_____$35,000-$49,999
_____$50,000-$74,000
_____$75,000-$99,999
_____$100,000 or more

6. What is your occupation?_____
   _____

7. How many hours per week do work on average?
   _____Less than 10 hours per week
   _____10 to 20 hours per week
   _____20 to 30 hours per week
   _____30 to 40 hours per week
   _____40 to 50 hours per week
   _____50 hours per week or more

8. Are you a homeowner?	____	____

Section *K*
Other:

YES NO

1. Do you have any other health problems not covered in this questionnaire?

   ____ ____

   If yes, please specify_____

   _____

2. Are you currently on any other medications not covered previously?

   ____ ____

3. How did you hear about this study?

Comments:_____
_____

Institutional Review Board Letter of Approval

UNIVERSITY OF MARYLAND
INSTITUTIONAL REVIEW BOARD

0101 Lee Building
College Park, Maryland 20742-5125
301.405.4212 TEL 301.314.1475 FAX
irb@deans.umd.edu
www.umresearch.umd.edu/IRB

May 26, 2010

MEMORANDUM

Application Approval Notification

To: Dr. Ben Hurley
Dr. Stephen Roth
Erik Daniel Hanson
Kinesiology

From: Joseph M. Smith, MA, CIM
IRB Manager
University of Maryland, College Park

Re: **IRB Application Number:** 06-0324

Project Title: "Strength Training to Improve Muscle Function, Quality of Life, and Self Efficacy in Patients with Prostrate Cancer"

Approval Date: May 26, 2010

Expiration Date: May 26, 2011

Type of Application: Renewal

Type of Research: Non-Exempt

Type of Review for Application: Expedited

The University of Maryland, College Park Institutional Review Board (IRB) approved your IRB application. The research was approved in accordance with the University IRB policies and procedures and 45 CFR 46, the Federal

Policy for the Protection of Human Subjects. Please include the above-cited IRB application number in any future communications with our office regarding this research.

Recruitment/Consent: For research requiring written informed consent, the IRB-approved and stamped informed consent document is enclosed. The expiration date for IRB approval has been stamped on the informed consent document. Please keep copies of the consent forms used for this research for three years after the completion of the research.

Continuing Review: If you intend to continue to collect data from human subjects or to analyze private, identifiable data collected from human subjects, after the expiration date for this approval (indicated above), you must submit a renewal application to the IRB Office at least 45 days before the approval expiration date. If IRB approval of your project expires, all human subject research activities including the enrollment of new subjects, data collection, and analysis of identifiable private information must stop until the renewal application is approved by the IRB.

Modifications: Any changes to the approved protocol must be approved by the IRB before the change is implemented, except when a change is necessary to eliminate apparent immediate hazards to the subjects. If you would like to modify the approved protocol, please submit an addendum request to the IRB Office. The instructions for submitting a request are posted on the IRB web site at : http://www.umresearch.umd.edu/IRB/addendum app.htm

Unanticipated Problems Involving Risks: You must promptly report any unanticipated problems involving risks to subjects or others to the IRB Manager at 301-405-0678 or jsmith@umresearch.umd.edu.

Student Researchers: Unless otherwise requested, this IRB approval document was sent to the Principal Investigator (PI). The PI should pass on the approval document or a copy to the student researchers. This IRB approval document may be a requirement for student researchers applying for graduation. The IRB may not be able to provide copies of the approval documents if several years have passed since the date of the original approval.

Additional Information: Please contact the IRB Office at 301-405-4212 if you have any IRB-related questions or concerns or email at irb@umd.edu.

May 03, 2010

To: **Investigator:** Ben F. Hurley
Co-Investigator(s): Stephen M. Roth
Student Investigator: Erik Daniel Hanson
Department: KNES - Kinesiology

From: Joseph M. Smith, MA, CIM
Manager
University of Maryland, College Park

Re: **IRB Application Number:** 08-0412 (PAS# 2102.2)
Project Title: "Effects of Gene Variations on Age- and Strength Training-Induced Changes in Muscular Strength, Body composiiton, Glucose Metabolism, & Lipoprotein-lipid Profiles"

Approval Date: 05-03-2010

Expiration Date: 05-03-2011

Type of Application: Renewal

Type of Research: Non-Exempt

Type of Review: Expedited

The University of Maryland, College Park Institutional Review Board (IRB) approved your IRB application. The research was approved in accordance with the University's IRB policies and procedures and 45 CFR 46, the Federal Policy for the Protection of Human Subjects. Please reference the above-cited IRB application number in any future communications with our office regarding this research.

Recruitment/Consent: For research requiring written informed consent, the IRB-approved and stamped informed consent document is enclosed. The IRB approval expiration date has been stamped on the informed consent document. Please keep copies of the consent forms used for this research for three years after the completion of the research.

Continuing Review: If you want to continue to collect data from human subjects or analyze data from human subjects after the expiration date for this approval, you must submit a renewal application to the IRB Office at least 30 days before the approval expiration date.

Modifications: Any changes to the approved protocol must be approved by the IRB before the change is implemented except when a change is necessary to eliminate apparent immediate hazards to the subjects. If you want to modify the approved protocol, please submit an IRB addendum application to the IRB Office.

Unanticipated Problems Involving Risks: You must promptly report any unanticipated problems involving risks to subjects or others to the IRB Manager at 301-405-0678 or jsmith@umresearch.umd.edu.

Student Researchers: Unless otherwise requested, this IRB approval document was sent to the Principal Investigator (PI). The PI should pass on the approval document or a copy to the student researchers. This IRB approval document may be a requirement for student researchers applying for graduation. The IRB may not be able to provide copies of the approval documents if several years have passed since the date of the original approval.

Additional Information: Please contact the IRB Office at 301-405-4212 if you have any IRB-related questions or concerns.

Consent to Participate in a Research Study

Project Title: **Strength training to improve muscle function, quality of life, and self efficacy in patients with prostate cancer**

Why is this research being done? This is a research project being conducted by Drs. Ben Hurley and Stephen Roth at the University of Maryland, College Park. We are inviting you to participate in this study designed to determine the effectiveness of regular resistance type exercise (strength training). We will test the effects of strength training on muscle mass, muscle function, body composition, quality of life, performance of common physical tasks and desire to continue to exercise regularly in men with prostate cancer who are taking androgen deprivation therapy. We are seeking this information to determine if strength training can serve as an appropriate adjunct therapy for prostate cancer patients who are on androgen deprivation therapy.

What will I be asked to do? The study will take place in the Department of Kinesiology at the University of Maryland in College Park and the procedures will involve three phases. During the first phase, you will undergo baseline testing, which will include a blood draw to analyze blood proteins and DNA (genetic material) related to prostate cancer, assessments of blood pressure, body composition, bone mineral density, leg muscle mass, fat surrounding leg muscles, muscle strength, muscle power, muscle fatigue, quality of life, desire to exercise regularly, and ability to complete selected tasks designed to mimic common physical activities of daily living. This first phase of baseline testing will require approximately 4 hours. The second phase of the study involves your participation in a strength training program three times a week for approximately six months. The strength training program will involve training all the major muscle groups (full body training) for approximately 12 weeks. Each training session will require approximately 30 minutes, with an additional 10 minutes required for blood pressure measurements, warm-up and stretching at each session. The third and final phase will be a repeat of all baseline testing. Leg muscle mass, fat surrounding leg muscles, muscle strength, muscle power and muscle fatigue assessments will be repeated after the training program. The blood draw will require providing approximately 2 to 3 tablespoons of blood at baseline and this amount will be required again after the training program, for a total of 4 to 6 tablespoons of blood. This blood will be separated and stored at the University of Maryland for later analysis of blood proteins thought to be important for prostate cancer. A portion of this sample may also be used for potential future studies, but only as such studies apply to a better understanding of exercise and prostate cancer. However, you may contact the principal investigator at any future point in time to request that any stored blood sample be destroyed immediately. Another portion of the blood sample will also be used for extracting your DNA to assess the variation of some of your genes related to prostate cancer risk. This information will be used only to determine if specific DNA variants influence your response to the exercise training program. It will not be used for diagnostic, prognostic, or treatment purposes. You will be asked to make your DNA sample available for future studies, but only for a period of no longer than 10 years and for

Project Title: Strength training to improve muscle function, quality of life, and self efficacy in patients with prostate cancer

the purpose of identifying new genes and gene sequence variants that relate to exercise and prostate cancer. Because this part of the study is exploratory, we will not provide your genetic information to you. If you choose not to provide a DNA sample, it will not make you ineligible to participate in the study.

While you are lying on a padded table, your leg muscle and fat mass will be measured by computed tomography (CT). The CT scan will be performed at Washington Adventist Hospital. Your percent body fat and bone mineral density measurements will be performed at the United States Department of Agriculture in Beltsville, Maryland by dual-energy x-ray absorptiometry (DXA). This will require lying still on a padded exam table wearing metal-free clothing for about 10 minutes at a time, totaling less than 30 minutes for the entire procedure for each test. The DXA and CT testing will be performed before and after both strength training program.

Muscle strength, power and fatigue assessment*s* will be performed on machines that measure how much force, how fast, and how long you can continue to exert force through a typical range of knee extension motion. Strength testing will also be performed by measuring the maximal force that you can move through the full range of an exercise on the same machine. During each strength training session you will be asked to exercise on machines that offer resistance against extending and flexing your legs, arms, and trunk region three times a week for up to *4* months. You will be asked to complete some tasks to measure your ability to carry out normal daily activities. These tasks include rising from a chair, short brisk walks and climbing stairs. You will be asked to fill out questionnaires before and after the strength training programs, which present questions related to your perception of fatigue, health related quality of life, and attitude toward participating in strength training exercises on a regular basis. The questions will ask you to identify specific feelings and consequences elicited from your fatigue and your overall well being. Questions will also deal with your concerns specific to prostate cancer and its treatment, as well as your attitude concerning adopting strength training as a life style habit (self-efficacy). Additional questions will be administered to determine whether self-efficacy is related to quality of life indicators or side effects from medications.

If you are taking other medications in addition to androgen deprivation therapy prior to the study, you will be permitted to participate as long as you have been on these mediations for at least 4 weeks prior to the study and do not stop taking them prior to the end of the study.

To be eligible to participate, your physician must sign a medical clearance form. It is possible that you could go through baseline evaluations and be determined to be ineligible to participate. Upon completing all aspects of the study, you will also receive *$300* for your participation.

What are the risks of this research? There is a risk of bruising, pain and, in rare cases, infection or fainting as a result of blood sampling. However, these risks will be minimized by allowing only qualified people to draw your blood. The body composition

Project Title: **Strength training to improve muscle function, quality of life, and self efficacy in patients with prostate cancer**

and bone density testing completed by CT and DXA involves radiation exposure, which increases the risk of passing genetic mutations to offspring, but this risk is a concern primarily among women of childbearing age. There will be a total radiation dose of no more than 1 Rem (1000 millirems) to the whole body from each CT scan. This amount is well below the maximal annual radiation dose (5000 millirems) allowed for exposure in the workplace. The radiation exposure from DXA is equal to an exposure of less than 50 millirems to the whole body. Naturally occurring radiation (cosmic radiation, radon, etc.) produces whole body radiation of about 300 millirems per year. Therefore, the total dose of radiation exposure due to the combined dose of DXA and CT is considered low. However, x-ray exposure is cumulative and there is no known lower limit below which x-ray exposure is known to be safe for men or women. You may experience some temporary muscle fatigue and soreness as a result of the testing sessions.

There is also a risk of muscle or skeletal injury from strength, power, and fatigue testing, as well as from strength training. The investigators of this study will use procedures designed to minimize this risk. It is also possible that heart or blood vessel problems could arise during your participation in the testing or training involved in this study. Although unusual, it is even possible that these problems could lead to a heart attack or stroke. For this reason, prior medical evaluation and clearance from your physician at your expense will be required to participate in this study. It is possible that these risks will not be eliminated completely, even with a medical evaluation prior to participation in the study. There is a risk of injury from falling, but any risk of injury during the completion of these tasks will be minimized by having all sessions supervised by an exercise physiologist qualified to direct this type of testing. Also, we will require those who are at risk of falling, based on their walking ability and performance on other functional tests, to wear a safety harness during the short brisk walks and climbing a flight of stairs.

What are the benefits of this research? This study is not designed to help you personally, but rather to help the investigators of this study and eventually to society in general to better understand the utility of using strength training as an adjunct therapy for prostate cancer patients who are taking androgen deprivation therapy. However, previous research has demonstrated that you will likely benefit in many ways as a result of your participation in the strength training program. This includes, but is not limited to, improvements in strength, muscle tone, resistance to fatigue, body composition, resting metabolic rate, muscle function, gastrointestinal transit, and sugar (glucose) metabolism. For your participation in the study, after completing the study, you will receive your results that are available at the time, upon your request.

Project Title: **Strength training to improve muscle function, quality of life, and self efficacy in patients with prostate cancer**

Do I have to be in this research? Your decision to participate in this study is voluntary and you are free to ask any questions about this study before you decide whether or not to participate.

May I stop participating at any time? If you consent to participate, you are free to withdraw from participation at any time without penalty or coercion, or without any requirement to provide an explanation to anyone about your decision to withdraw. In addition, your refusal to participate will not involve a penalty or loss of benefit to which a volunteer would otherwise qualify.

What about confidentiality? We will do our best to keep your personal information confidential. To help protect your confidentiality, we will keep your confidential records in secure and private storage areas, use password protected computer files for all collected data, and use identification codes instead of your name on data files, whenever possible. If we write a report or article about this research project, your identity will be protected to the maximum extent possible. Your information may be shared with representatives of the University of Maryland, College Park or governmental authorities if you or someone else is in danger or if we are required to do so by law.

Is any medical treatment available if I am injured? The University of Maryland does not provide any medical, hospitalization or other insurance for participants in this research study, nor will the University of Maryland provide any medical treatment or compensation for any injury sustained as a result of participation in this research study, except as required by law.

What if I volunteer as a control? A subgroup of volunteers will serve as a no exercise control group. If you are identified as a control for this study, you will undergo the identical testing as the other volunteers in the study and repeat testing at approximately the same time points as those who will participate in the strength training program, but you will not participate in any part of the strength training program. However, as compensation for your time for undergoing the testing procedures, controls will be permitted to have 6 weeks of supervised use of our exercise machines after all testing is complete, but will receive no financial compensation.

What if I have questions? This research is being conducted by Drs. Ben Hurley and Stephen Roth in the Department of Kinesiology at the University of Maryland, College Park. If you have any questions about the research study itself, please contact Dr. Ben Hurley at 301-405-2486. If you have questions about your rights as a research subject or wish to report a research-related injury, please contact: **Institutional Review Board Office, University of Maryland, College Park, Maryland, 20742; (e-mail) irb@deans.umd.edu; (telephone) 301-405-0678.** This

Project Title: **Strength training to improve muscle function, quality of life, and self efficacy in patients with prostate cancer**

research has been reviewed according to the University of Maryland, College Park IRB procedures for research involving human subjects.

Statement of Age of Subject and Consent. Your signature indicates that you are at least 18 years of age, the research has been explained to you, your questions have been fully answered, and you freely and voluntarily choose to participate in this research project.

Principal investigator: Ben Hurley, Ph.D., Dept of Kinesiology, HLHP Building, University of Maryland, College Park, MD 20742-2611, Ph: (301) 405-2486.

Printed Name of Subject_____

Signature of Subject_____ **Date**_____

CONSENT TO PARTICIPATE IN A RESEARCH PROJECT

Project Title: Effects of Gene Variations on Age- and Strength Training-Induced Changes in Muscular Strength, Body Composition, Blood Pressure, Glucose Metabolism, and Lipoprotein lipid Profiles

I state that I am over 18 years of age, in good physical health, and have elected to participate in a program of research being conducted by Dr. Ben Hurley in the Department of Kinesiology at the University of Maryland, College Park, MD 20742.

I understand that the primary purpose of this study is to assess the role that genetics may play in causing losses of muscular strength and muscle mass with age and gains in strength and muscle mass as a result of strength training. I understand that another purpose of the study will be to assess the influence of genes on changes in body composition, blood pressure, blood sugar metabolism, blood fats muscle power, and performance of common physical tasks with age and strength training.

I understand that the procedures involve three phases. During the first phase, I will undergo testing, which will include a blood draw to analyze my DNA (genetic material), blood sugar and fats, and other blood proteins. My blood pressure, body composition, bone mineral density, leg muscle volume, muscle strength, muscle power, and ability to complete selected tasks similar to common activities of daily living will also be assessed during this first phase. The second phase of the study involves my participation in a strength training program three times a week for approximately six months. The third and final phase will be a repeat of all previously taken measures, except analysis of my DNA, which will not need to be repeated. Some of the tests will be repeated both after~ 10 weeks of training and again after the entire training program. These repeat tests will include blood pressure, strength, power, muscle volume and body composition. Other tests will be repeated only after the entire training program.

I understand that the blood draw will require providing about 2 to 3 tablespoons of blood. I understand that there is a risk of bruising, pain and, in rare cases, infection or fainting as a result of blood sampling. However, these risks to me will be minimized by allowing only qualified people to draw my blood. A portion of this blood sample will be sent to the University of Pittsburgh to analyze my DNA. I understand that the remainder will be stored at the University of Maryland for later analysis of my blood sugar, the hormone that regulates my blood sugar (insulin), blood fats, and other blood proteins. I understand that a portion of this sample may also be used for potential future studies, but only as such studies examine strength, body composition (i.e., fat, muscle & bone), metabolism of blood sugar, and blood pressure. I understand that I may contact the principal investigator at any future point in time to request that any stored blood sample be destroyed immediately.

I understand that while I am lying on a padded table, my leg muscle and fat mass will be measured by computed tomography (CT). The CT scan will be performed at Washington Adventist Hospital. My percent body fat and bone mineral density measurements will be performed at the United States Department of Agriculture in Beltsville, Maryland by dual-energy x-ray absorptiometry (DXA). This will require my lying still on a padded exam table wearing metal-free clothing for about 10 minutes at a time, totaling less than 30 total minutes for the entire procedure.

I understand that there will be a total radiation dose of no more than 1 Rem to the whole body (effective dose equivalent) from each CT scan. This amount is well below the maximal annual radiation dose (5 Rems) allowed for exposure in the workplace. The body composition and bone density testing completed by DXA involves a small radiation exposure. The radiation exposure I will receive from DXA is equal t to an exposure of less than 50 millirems to the whole body. Naturally occurring radiation (cosmic radiation, radon, etc.) produces whole body radiation of about 300 millirems per year. Therefore, the total dose of radiation exposure due to the DXA measurement is minimal and the combined dose of DXA and CT is considered low.

I understand that strength and power assessments will be performed on machines that measure how much force and how fast I can exert force through a typical range of knee extension motion. Strength testing will also be performed on the same exercise machines used for training by measuring the maximal amount of force that I can move through the full range of an exercise. During each strength training session I will be asked to exercise on machines which offer resistance against extending and flexing my arms, legs, and trunk region for approximately 40 minutes or less a day, three times a week for up to six months. I understand that I may experience some temporary muscle soreness as a result of the testing sessions. There is also a risk of muscle or skeletal injury from strength and power testing, as well as from strength training. The investigators of this study will use procedures designed to minimize this risk.

I understand that I will be asked to complete some tasks to measure my ability to carry out normal daily activities. These tasks include rising from a chair, short brisk walks and climbing a flight of stairs. Any risk of injury during the completion of these tasks will be minimized by having all sessions supervised by an exercise physiologist qualified to direct this type of testing and wearing a safety harness during the short brisk walks and climbing a flight of stairs.

I understand that it is also possible that heart or blood vessel problems could arise during my participation in the testing or training involved in this study. Although unusual, it is possible that these problems could lead to a heart attack or even death. Therefore, prior evaluation and permission from my physician at my expense will be required to participate in this study. I also understand that it is possible that these risks will not be eliminated completely, even with a medical evaluation prior to participation in the study.

I understand that this study is not designed to help me personally, but may help the investigators better understand who is likely to be most and least susceptible to losing strength, power, and muscle mass with advanced age and who is most and least likely to benefit from strength training.

I understand that my decision of whether or not to participate in this study is voluntary. I understand that I am free to ask questions about this study before I decide whether or not to participate in the study. I understand that if I consent to participate in the study I am free to withdraw from participation at any time without penalty or coercion, or without any requirement that I provide an explanation to anyone of my decision to withdraw. In addition,

I understand that refusal to participate will not involve a penalty or loss of benefit to which a volunteer would ordinarily be entitled to at that time. If I am on hormone replacement therapy (HRT) prior to the study, I must remain on them and if I am not on

HRT prior to the study, I must remain off them throughout the study to qualify for continued participation. If I am taking other medications prior to the study, I will be permitted to participate as long as I had been on these mediations for at least 4 weeks prior to the study and do not stop taking them prior to the end of the study. I understand that all information collected in this study is confidential. For my participation in the study I will receive information after the study is completed about my blood pressure, blood test results, bone mineral density, body composition, and functional ability upon request, free of charge. However, I understand that I will not receive any financial compensation in exchange for my participation in this study.

In the event of physical injury resulting from participation in this study, upon my consent, emergency treatment will be available at the medical center of Washington Adventist Hospital with the understanding that any injury that requires medical attention becomes my financial responsibility. I understand that the University of Maryland at College Park will not provide any medical or hospitalization insurance coverage for participants in this research study, nor will they provide compensation for any injury sustained as a result of this research study, except as required by law.

I understand that I can discuss this research study at any time with the principal investigator, Dr. Ben Hurley at (301) 405-2457 or with the study coordinator of this project at (301) 405-2569.

I have read and understand the above information and have been given an adequate opportunity to ask the investigators any questions I have about the study. My questions, if any, have been answered by the investigators to my satisfaction. By my signature I am indicating my decision to consent to participate voluntarily in this study.

Principal investigator: Ben Hurley, Ph.D., Dept of Kinesiology, HLHP Building, University of Maryland, College Park, MD 20742-2611, Ph: (301) 405-2486.

Printed Name of Subject_____

Signature of Subject_____ Date_____

Contact information of Institutional Review Board: If you have questions about your rights as a research subject or wish to report a research-related injury, please contact: Institutional Review Board Office, University of Maryland, College Park, MD 20742; e-mail, irb@deans.umd.edu; telephone, 301-405-4212.

Maryland CARES
Venipuncture Record

Subject Name_____ ID_____ Date_____

Tech Initials_____ Time_____ **Baseline / After ST**

1. Are you allergic to latex? Yes / No
2. Have you fasted overnight? Yes / No
3. Did you have a cold, flu, dental infection or other infection in the last 2 weeks? Yes / No

   If yes, ( ) within one week? ( ) within 48 hours?
4. Do you have any seasonal allergies? Yes / No

   If yes, please describe any symptoms in the last 48 hours

   _____
5. Did you seek medical attention for a cold, flu, or infection in the past month? Yes / No

   If yes, what was the diagnosis_____
6. Have you taken any pain medications within the last 48 hours? Yes / No
7. Do you require us to use a specific arm for all blood draws? Yes / No

   If yes, please specify which arm you need us to use_____
8. Have you ever fainted or felt dizzy/nauseous during a blood draw? Yes / No

Tech: Please note arm & vein used, needle type & gauge, success or failure to obtain sample

_____

_____

_____

Tube Type: Purple Top / Tiger Top / Red Top

Hemoglobin #1_____ Hemoglobin #2_____

Hemoglobin #2_____ Hematocrit #2_____

Hemoglobin #3_____ Hematocrit #3_____

Data Entry #1_____Date_____Initials

Data Entry #2_____Date_____Initials

Maryland CARES

DEXA Body Scan-**USDA**

Name:_____ Subject Number:_____

Date:_____ Time:_____ am/pm Gender: M / F

Date of Birth:_____

Height:_____ inches _____ cm

Weight:_____ lbs. _____ kg

Dominant Leg: R / L

Time and composition of last meal (or snack):

_____
_____
_____
_____
_____

Comments:_____
_____

Initials of DXA technician:_____

Data entry #1_____Initials_____Date
Data entry #2_____Initials_____Date

Brief Fatigue Inventory

STUDY ID# _____ HOSPITAL # _____

Date: _____/_____/_____ Time: _____

Name _____ _____ _____

Last First Middle Initial

Throughout our lives, most of us have times when we feel very tired or fatigued. Have you felt unusually tired or fatigued in the last week? Yes ☐ No ☐

1. Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your fatigue right NOW.

0 1 2 3 4 5 6 7 8 9 10

No Fatigue — As bad as you can imagine

2. Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your USUAL level of fatigue during past 24 hours.

0 1 2 3 4 5 6 7 8 9 10

No Fatigue — As bad as you can imagine

3. Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your WORST level of fatigue during past 24 hours.

0 1 2 3 4 5 6 7 8 9 10

No Fatigue — As bad as you can imagine

4. Circle the one number that describes how, during the past 24 hours, fatigue has interfered with your:

A. General activity

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — Completely Interferes

B. Mood

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — Completely Interferes

C. Walking ability

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — Completely Interferes

D. Normal work (includes both work outside the home and daily chores)

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — Completely Interferes

E. Relations with other people

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — Completely Interferes

F. Enjoyment of life

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — Completely Interferes

FACT-P (Version 4)

Below is a list of statements that other people with your illness have said are important. **By circling one (1) number per line, please indicate how true each statement has been for you during the past 7 days.**

	PHYSICAL WELL-BEING	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
GP1	I have a lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
GP4	I have pain	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4

	SOCIAL/FAMILY WELL-BEING	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
GS1	I feel close to my friends	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4
GS3	I get support from my friends	0	1	2	3	4
GS4	My family has accepted my illness	0	1	2	3	4
GS5	I am satisfied with family communication about my illness	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my main support)	0	1	2	3	4
Q1	*Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please check this box* ☐ *and go to the next section.*					
GS7	I am satisfied with my sex life	0	1	2	3	4

FACT-P (Version 4)

By circling one (1) number per line, please indicate how true each statement has been for you during the past 7 days.

	EMOTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GE1	I feel sad	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness	0	1	2	3	4
GE3	I am losing hope in the fight against my illness	0	1	2	3	4
GE4	I feel nervous	0	1	2	3	4
GE5	I worry about dying	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4

	FUNCTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GF1	I am able to work (include work at home)	0	1	2	3	4
GF2	My work (include work at home) is fulfilling	0	1	2	3	4
GF3	I am able to enjoy life	0	1	2	3	4
GF4	I have accepted my illness	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4
GF7	I am content with the quality of my life right now	0	1	2	3	4

FACT-P (Version 4)

By circling one (1) number per line, please indicate how true each statement has been for you during the past 7 days.

	ADDITIONAL CONCERNS	Not at all	A little bit	Some-what	Quite a bit	Very much
C2	I am losing weight	0	1	2	3	4
C6	I have a good appetite	0	1	2	3	4
P1	I have aches and pains that bother me	0	1	2	3	4
P2	I have certain parts of my body where I experience significant pain	0	1	2	3	4
P3	My pain keeps me from doing things I want to do	0	1	2	3	4
P4	I am satisfied with my present comfort level	0	1	2	3	4
P5	I am able to feel like a man	0	1	2	3	4
P6	I have trouble moving my bowels	0	1	2	3	4
P7	I have difficulty urinating	0	1	2	3	4
BL2	I urinate more frequently than usual	0	1	2	3	4
P8	My problems with urinating limit my activities	0	1	2	3	4
BL5	I am able to have and maintain an erection	0	1	2	3	4

Maryland CARES

Knee Extensor 1RM

Baseline / Posttest

Subject ID _____ Date_____ Seat_____

Examiners Initials_____ Body weight_____ Age_____ Resting BP_____

Participant's initials indicating that the P/D and RPE scale is understood and that he/she has the right to stop the test at anytime _____

Right leg / Left leg

	Resistance	P/D scale	RPE scale
	__0__	_____	_____
Set 1	_____	_____	_____
Set 2	_____	_____	_____
Set 3	_____	_____	_____
Set 4	_____	_____	_____
Set 5	_____	_____	_____
Set 6	_____	_____	_____
Set 7	_____	_____	_____
Set 8	_____	_____	_____
Set 9	_____	_____	_____
Set 10	_____	_____	_____
Set 11	_____	_____	_____
Set 12	_____	_____	_____

Most severe P/D: _____ Subject's initials: _____ **Valid** **Invalid**

If invalid, please explain: _____

_____

_____

Data entry #1:_____initials _____date

Data entry #2:_____initials _____date

Maryland CARES

Chest Press 1RM

Baseline / Posttest

Subject ID _____ Date_____ Seat_____

Examiners Initials_____ Body weight_____ Age_____ Resting BP_____

Participant's initials indicating that the P/D and RPE scale is understood and that he/she has the right to stop the test at anytime _____

	Resistance	P/D scale	RPE scale
	__0__	_____	_____
Set 1	_____	_____	_____
Set 2	_____	_____	_____
Set 3	_____	_____	_____
Set 4	_____	_____	_____
Set 5	_____	_____	_____
Set 6	_____	_____	_____
Set 7	_____	_____	_____
Set 8	_____	_____	_____
Set 9	_____	_____	_____
Set 10	_____	_____	_____
Set 11	_____	_____	_____
Set 12	_____	_____	_____

Most severe P/D: _____ Subject's initials: _____

Post BP_____ **Valid** **Invalid**

If invalid, please explain: _____

_____

Muscle Endurance Test

70% 1 RM _____ **Valid** **Invalid**

Number of Reps_____

Data entry #1:_____initials_____Date

Data entry #2:_____initials_____Date

Maryland CARES

Leg Press 1RM

Baseline / Posttest

Subject ID _____ Date_____ Seat_____

Examiners Initials_____ Body weight_____ Age_____ Resting BP_____

Participant's initials indicating that the P/D and RPE scale is understood and that he/she has the right to stop the test at anytime _____

	Resistance	P/D scale	RPE scale
	__0__	_____	_____
Set 1	_____	_____	_____
Set 2	_____	_____	_____
Set 3	_____	_____	_____
Set 4	_____	_____	_____
Set 5	_____	_____	_____
Set 6	_____	_____	_____
Set 7	_____	_____	_____
Set 8	_____	_____	_____
Set 9	_____	_____	_____
Set 10	_____	_____	_____
Set 11	_____	_____	_____
Set 12	_____	_____	_____

Most severe P/D: _____ Subject's initials: _____

Post BP_____ **Valid** **Invalid**

If invalid, please explain: _____

_____

Muscle Endurance Test

70% 1 RM _____ **Valid** **Invalid**

Number of Reps_____

Data entry #1:_____initials_____Date

Data entry #2:_____initials_____Date

Maryland CARES

Power Testing

Baseline / Posttest

Subject ID _____ Date _____
Tester _____ Time _____

Resting BP: ___/___mmHg
Seat Position:____ 1-RM R:_____ Converted 1-RM : R: _____
1-RM L :_____ Converted 1-RM : L: _____
30% 1-RM R____Practice P/D:_____ 30% 1-RM L____ Practice P/D:_____

% 1-RM	**Right Resistance**	Test #	P/D & Location (0-6)	Immed dissip (Y/N)	**Left Resistance**	Test #	P/D & Location (0-6)	Immed dissip (Y/N)	File Name Initials number P1 %1-RM.txt
50									**ex. EDH_001_P1**
50									
50									
60									
60									
60									
70									
70									
70									

Constant Reminders: Back against seat
Look straight ahead
Breathe Normally

General Comments: _____
_____

Test Comment

Most Severe P/D _____ Subject's Initials _____

Data entry #1:_____initials_____Date

Data entry #2:_____initials_____Date

Maryland CARES

Physical Function Testing

Baseline / After Training

Subject Name_____ ID_____ Date_____

Examiner_____ Resting BP_____ Initial P/D_____

6m usual walk

Trial #1_____ P/D_____

30 sec rest

Trial #2_____ P/D_____

1 min rest

Comments_____

6m Rapid walk

Trial #1_____ P/D_____

30 sec rest

Trial #2_____ P/D_____

2 min rest

Comments_____

8 foot Get up and Go

Trial #1_____ P/D_____

1 min rest

Trial #2_____ P/D_____

2 min rest

Comments_____

30 second chair stands

Trial #1_____ P/D_____

5 min rest

Comments_____

Stair Climb

Trial #1_____ P/D_____

1 min rest

Trial #2_____ P/D_____

5 min rest

Comments_____

400m Walk

Trial #1_____ P/D_____

Comments_____

Post BP_____ P/D_____

Data Entry #1_____Date_____Initials

Data Entry #2_____Date_____Initials

University of Maryland CARES-Full Body Strength Training Log

Name_____ **ID#**_____

		Seat #										
		1RM										
Date	BP #1	P/D Pre	Knee Ext	Chest Press	Seated Row	Leg Curl	Ab Crunch	Leg Press	BP #2	P/D Post	BP #3	Weight (Fri)

Pain / Discomfort Rating Scale

0 No significant pain or discomfort
1 Slight or minimal pain
2 Moderate or bothersome pain
3 More than moderate but less than severe pain
4 Somewhat severe pain
5 Severe pain
6 Very severe pain

Comments:

Date	Pain	Joint(s) Affected? Which exercises? Treatment Plan

Appendix III: Raw Data

Raw Data

Appendix III: Raw Data

ID	Age	Height	Pre Weight	Post Weight	Pre BMI	Post BMI	Pre % Fat	Post % Fat	Pre Fat	Post Fat
RefCon1	71	180.0	89.9	89.9	27.76	27.74	24.94	25.21	22.4	22.7
RefCon2	53	161.5	77.2	78.8	29.61	30.21	30.88	30.06	23.8	23.7
RefCon3	59	161.8	83.0	81.5	31.70	31.15	23.41	22.21	19.4	18.1
RefCon4	70	184.9	89.5	91.0	26.18	26.63	28.23	26.27	25.3	23.9
RefCon5	64	173.2	81.1	82.8	27.02	27.59	20.06	19.21	16.3	15.9
RefCon6	71	162.0	74.6	75.5	28.41	28.77	32.51	29.61	24.2	22.4
RefCon7	68	171.5	84.1	84.4	28.58	28.70	25.03	25.26	21.0	21.3
RefCon8	55	175.3	125.3	122.3	40.81	39.81	34.71	34.40	43.5	42.1
RefCon9	56	170.2	99.7	100.2	34.42	34.61	29.64	27.69	29.6	27.8
RefCon10	56	167.6	88.6	89.5	31.52	31.86	23.14	21.64	20.5	19.4
RefCon11	61	172.7	76.5	75.0	25.63	25.12	26.47	25.83	20.2	19.4
RefCon12	52	178.9	66.7	68.5	20.83	21.39	22.29	20.73	14.9	14.2
RefCon13	74	182.8	78.9	80.3	23.62	24.04	18.84	20.95	14.9	16.8
RefCon14	61	177.8	90.3	89.1	28.56	28.20	28.24	28.50	25.5	25.4
RefCon15	62	169.4	99.0	98.7	34.48	34.39	25.84	23.42	25.6	23.1
RefCon16	51	188.9	96.6	97.3	27.07	27.26	25.93	28.08	25.0	27.3
RefCon17	67	183.9	113.7	111.1	33.63	32.85	28.56	28.89	32.5	32.1
RefCon18	54	191.0	106.2	107.7	29.12	29.53	31.08	31.40	33.0	33.8
RefCon19	57	168.2	92.6	92.7	32.75	32.77	26.42	27.35	24.5	25.4
RefCon20	56	171.7	106.6	108.3	36.16	36.72	30.83	29.05	32.9	31.4
PCa 10	67	182.4	117	118.8	35.37	35.86	38.0	38.6	44.7	46.1
PCa 11	77	167.2	76.9	79.2	27.72	28.63	29.9	29.4	23.2	23.5
PCa 12	62	185.1	154.3	159.7	44.66	45.92	44.9	45.4	68.7	71.4
PCa 13	58	183.5	104.9	108.6	31.20	32.50	32.4	32.4	34.1	35.4
PCa 14	60	164.6	102.5	106.2	37.74	39.14	39.4	38.5	40.3	40.8
PCa 15	74	167.1	75.3	76.3	27.22	27.54	30.3	28.6	23.0	22.0
PCa 16	66	184.1	89.1	89.2	26.67	26.51	29.5	27.8	26.6	24.9
PCa 17	62	167.6	80.4	83	28.82	29.69	23.4	24.2	18.9	20.2
PCa 18	77	169.2	95.7	96.1	33.71	33.86	26.3	25.1	25.4	24.4
PCa 20	72	174.7	97.1	97.9	32.03	32.17	33.2	32.4	32.5	31.8
PCa 21	64	167.7	81.1	82.1	28.83	29.18	30.6	30.0	24.8	24.6
PCa 22	61	174.3	101.6	101.6	33.72	33.47	30.6	28.8	31.3	29.3
PCa 23	62	166.4	81.4	84.5	29.57	30.59	26.6	24.5	21.8	20.8
PCa 24	67	166	109.4	109.7	39.62	39.80	36.8	36.1	40.2	39.6
PCa 25	73	171.4	102.4	101.2	35.17	34.78	31.5	30.2	32.5	30.8
PCa 26	80	177.1	80.8	83	25.98	25.38	20.2	21.5	16.4	18.0
PCa 28	64	169.9	91.1	86.8	31.56	30.54	30.2	28.6	26.7	25.4

Pre = Baseline; Post = After ST; RefCon = Reference Control Subject; PCa = Prostate Cancer Patient

ID	Pre BMC	Post BMC	Pre FFM	Post FFM	Pre KE 1RM ‡	Post KE 1RM ‡	Pre MV ‡	Post MV ‡
RefCon1	3.0	3.0	67.5	67.2	36.3	56.2	1985.4	2148.6
RefCon2	2.2	2.2	53.4	55.1	37.5	42.3	1580.8	1755.5
RefCon3	2.3	2.4	63.6	63.4	22.4	28.8	1815.3	1908.7
RefCon4	3.0	3.0	64.2	67.1			2245.2	2372.1
RefCon5	3.2	3.2	64.8	66.9	37.5	47.5	1996.7	2309.7
RefCon6	2.3	2.3	50.3	53.1	30.5	39.2	1572.3	1765.5
RefCon7	2.7	2.7	63.0	63.1	25.9	36.1	1651.7	1846.6
RefCon8	3.0	3.0	81.8	80.2	51.7	56.5	2689.3	2706.0
RefCon9	3.1	3.1	70.1	72.5	39.8	65.2	2535.8	2997.1
RefCon10	2.7	2.7	68.1	70.2	38.2	60.2	2151.0	2477.5
RefCon11	2.7	2.6	56.2	55.6	26.7	38.0	1877.3	1922.2
RefCon12	2.0	2.0	51.8	54.3	28.8	37.1	1568.0	1843.9
RefCon13	3.1	3.1	64.1	63.5	34.0	40.2	1754.2	1983.4
RefCon14	2.7	2.7	64.8	63.7	48.6	48.6	2020.2	2290.9
RefCon15	2.7	2.7	73.4	75.6	31.9	35.0	2032.1	2191.8
RefCon16	3.4	3.5	71.6	70.0	35.9	53.8	2391.1	2645.5
RefCon17	3.7	3.7	81.3	79.0	51.7	56.9	2562.8	2744.1
RefCon18	3.5	3.6	73.2	73.9	53.8	58.9	2599.8	2839.2
RefCon19	2.6	2.6	68.2	67.4	41.3	47.5	2206.3	2477.0
RefCon20	3.3	3.3	73.7	76.8	45.4	50.6	2680.0	2848.8
PCa 10	3.5	3.5	69.5	69.7	26.7	34.2	5089.3	5432.0
PCa 11	2.2	2.1	52.1	54.4	23.6	24.2	3467.5	3844.1
PCa 12	3.6	3.1	80.7	82.9	27.8	36.1	5009.8	5298.8
PCa 13	3.6	3.6	67.4	70.4			4016.0	4454.6
PCa 14	3.1	3.1	58.8	62.1	20.5	35.0	3932.0	4261.8
PCa 15	2.1	2.1	50.8	52.8			2408.6	2658.0
PCa 16	2.9	2.9	60.8	62.0	28.4	38.2	4103.0	4489.2
PCa 17	3.2	3.1	58.8	60.1	38.2	45.9	3754.3	4119.4
PCa 18	3.4	3.4	67.7	69.1	23.6	30.5	3908.5	4004.3
PCa 20	2.4	2.3	62.9	64.0	28.8	37.1	4339.1	4460.7
PCa 21	2.8	2.7	53.5	54.7	28.8	36.7	3479.9	3613.9
PCa 22	3.1	3.1	68.0	69.2	27.8	39.2	4536.7	4810.3
PCa 23	1.8	1.8	58.2	62.1	30.5	40.7	4124.8	4440.4
PCa 24	3.8	3.8	65.1	66.3	30.9	33.4	4263.5	4389.3
PCa 25	3.2	3.3	67.6	68.1	27.8	35.0	4677.3	4844.4
PCa 26	3.4	3.3	61.7	62.2	31.1	34.2	3406.1	3524.8
PCa 28	4.0	4	57.7	59.6	20.5	29.9		

BMC = Bone Mineral Content; FFM = Fat Free Mass; KE 1RM = Knee Extension Maximal Strength; MV = Muscle Volume; ‡ = Trained Leg for Reference Controls and R Leg for PCa Patients

ID	Pre PPAbs ‡	Post PPAbs ‡	Pre PP50 ‡	Post PP50 ‡	Pre PP60 ‡	Pre PP60 ‡	Pre PP70 ‡	Post PP70 ‡
RefCon1								
RefCon2								
RefCon3							394.4	529.7
RefCon4								
RefCon5	544.5	506.3	544.5	567.5	596.5	560.7		
RefCon6	510.5	519.2	476.5	519.2	510.5	555.1	479.6	558.5
RefCon7							371.4	370.2
RefCon8	720.9	761.2	720.9	699.7	724.7	695.8	730.4	599.9
RefCon9								
RefCon10	684.2	801.7	633.6	801.7	684.2	775.1	679.5	622.0
RefCon11	411.4	434.4	428.4	434.4	411.4	422.0	463.5	390.1
RefCon12	318.7	437.3	360.8	437.3	318.7	450.5	269.3	430.2
RefCon13	437.0	462.8	429.9	462.8	437.0	397.6	423.3	364.2
RefCon14	685.3	684.1	685.3	684.1	658.7	653.3	622.0	607.9
RefCon15	448.1	396.4	448.1	462.6	515.7	471.0	517.7	475.2
RefCon16								
RefCon17	526.7	494.9	526.7	531.3	518.0	499.3	453.6	460.4
RefCon18	664.9	656.9	664.9	715.4	699.0	769.4	717.5	778.9
RefCon19	684.6	729.6	614.0	692.7	681.0	729.6	672.9	722.3
RefCon20	569.7	670.0	568.6	679.7	547.7	659.7	528.7	659.1
PCa 10			395.7	402.1	410.6	412.1	408.9	415.5
PCa 11	310.7	327.2	310.7	327.2	338.3	357.6	342.3	389.3
PCa 12	303.6	423.2	291.8	423.2	303.6	403.7	401.5	400.1
PCa 13								
PCa 14	344.2	378.5	344.2	416.3	362.6	390.2	365.1	407.2
PCa 15	240.4	290.2	240.4	290.2	234.1	329.1	226.9	313.8
PCa 16	412.3	435.8	381.6	469.9	412.3	451.7	411.3	418.5
PCa 17	454.8	544.6	481.1	544.6	454.8	538.8	409.2	491.1
PCa 18	290.8	326.4	301.1	326.4	290.8	355.5	315.0	390.4
PCa 20	312.2	366.1	287.0	366.1	312.2	378.9	317.6	377.8
PCa 21	415.3	479.5	421.6	479.5	415.3	495.0	430.8	507.7
PCa 22	383.4	411.4	363.7	411.4	411.8	429.0	383.4	384.1
PCa 23	417.2	550.4	379.3	538.9	417.2	529.1	515.5	539.6
PCa 24	278.1	257.3	278.1	268.8	286.0	267.9	265.6	254.0
PCa 25	361.2	408.1	351.9	408.1	361.2	411.9	370.6	407.4
PCa 26	348.6	358.9	348.6	360.2	353.8	369.6	317.6	332.1
PCa 28	194.0	274.0	209.0	274.0	210.0	250.0	194.0	231.0

PPAbs = Absolute Peak Power; PP50, 60, 70 L = Peak power at 50,60, and 70% of KE 1RM; ‡ = Trained Leg for Reference Controls and R Leg for PCa Patients

ID	Pre PTAbs ‡	Post PTAbs ‡	Pre PT50 ‡	Post PT50 ‡	Pre PT60 ‡	Post PT60 ‡	Pre PT70 ‡	Post PT70 ‡
RefCon1			111.9	146.1	136.8	175.0	160.6	203.4
RefCon2								
RefCon3							75.1	86.6
RefCon4								
RefCon5	84.3	82.4	84.3	96.9	97.2	112.4		
RefCon6	83.3	82.8	72.6	82.8	83.3	101.9	94.2	117.9
RefCon7							76.2	102.4
RefCon8	108.9	111.4	108.9	129.5	128.4	138.7	146.3	158.6
RefCon9								
RefCon10	93.8	117.5	81.0	117.5	93.8	138.6	107.1	154.9
RefCon11	73.1	83.6	65.5	83.6	73.1	94.1	84.4	107.9
RefCon12	64.2	64.1	64.2	73.6	73.9	90.5	84.2	104.7
RefCon13	85.0	85.4	72.7	85.4	85.0	98.4	97.8	112.4
RefCon14	104.8	100.8	104.8	100.8	122.3	119.1	140.1	117.2
RefCon15	77.1	72.2	77.1	80.0	90.4	95.0	101.3	109.7
RefCon16								
RefCon17	283.2	286.0	283.2	303.1	334.6	362.4	385.7	429.0
RefCon18	290.3	296.1	290.3	326.1	346.0	382.2	403.2	445.7
RefCon19	323.5	330.6	241.9	275.1	278.9	330.6	323.5	374.6
RefCon20	258.1	256.6	258.1	285.9	324.2	332.7	364.3	385.4
PCa 10			169.5	198.4	192.6	232.0	218.9	272.0
PCa 11	154.6	155.6	154.6	155.6	175.2	176.2	194.5	197.8
PCa 12	191.5	198.7	168.9	198.7	191.5	245.2	220.7	276.5
PCa 13								
PCa 14	145.1	149.8	145.1	210.2	163.4	237.5	181.4	274.8
PCa 15	128.6	133.2	128.6	133.2	141.8	154.4	157.5	168.7
PCa 16	202.2	203.1	179.1	221.0	202.2	258.2	233.0	296.1
PCa 17	255.6	265.7	216.2	265.7	255.6	306.6	299.0	353.5
PCa 18	173.2	176.6	154.1	176.6	173.2	198.2	195.0	233.4
PCa 20	195.7	199.1	172.5	199.1	195.7	247.7	228.8	291.6
PCa 21	204.2	208.4	181.2	208.4	204.2	252.6	236.5	291.5
PCa 22	224.6	225.3	172.2	225.3	195.4	266.7	224.6	310.3
PCa 23			184.8	234.1	277.3	193.6	319.1	228.8
PCa 24			181.5	189.2	220.7	198.5	255.6	235.9
PCa 25	197.0	200.4	172.6	200.4	197.0	241.0	228.0	279.6
PCa 26	186.8	183.0	186.8	195.3	219.6	235.2	253.7	266.0
PCa 28								

PTAbs = Absolute Peak Torque; PT50, 60, 70 = Peak Torque at 50, 60, & 70% of KE 1RM; ‡ = Trained Leg for Reference Controls and R Leg for PCa Patients

ID	Pre PVAbs ‡	Post PVAbs ‡	Pre PV50 ‡	Post PV50 ‡	Pre PV60 ‡	Post PV60 ‡	Pre PV70 ‡	Post PV70 ‡
RefCon1			5.3	3.2	4.3	2.4	2.9	1.9
RefCon2								
RefCon3							5.4	6.2
RefCon4								
RefCon5	6.9	6.1	6.9	5.9	6.4	5.1		
RefCon6	6.3	6.4	6.9	6.4	6.3	5.5	5.3	4.9
RefCon7							5.0	3.7
RefCon8	6.7	7.0	6.7	5.4	5.8	5.1	5.1	3.8
RefCon9								
RefCon10	7.5	7.1	8.0	7.1	7.5	5.6	6.4	4.2
RefCon11	5.7	6.0	6.5	5.4	5.7	4.7	5.5	3.8
RefCon12	6.0	5.7	6.0	5.9	4.7	5.0	3.5	4.2
RefCon13	5.2	5.4	6.0	5.4	5.2	4.2	4.4	3.4
RefCon14	6.5	6.8	6.5	6.8	5.5	5.6	4.5	5.2
RefCon15	5.8	5.5	5.8	5.8	5.7	5.0	5.1	4.4
RefCon16								
RefCon17	5.1	4.9	5.1	4.9	4.2	3.9	3.4	3.2
RefCon18	6.4	6.1	6.4	6.1	5.6	5.5	4.8	4.8
RefCon19	5.8	6.0	7.2	6.9	6.9	6.0	5.8	5.3
RefCon20	6.2	7.2	6.2	6.6	5.0	5.5	4.3	4.6
PCa 10			6.4	5.6	5.8	4.9	5.1	4.2
PCa 11	5.5	5.8	5.5	5.8	5.3	5.6	4.8	5.4
PCa 12	4.3	5.8	4.7	5.8	4.3	4.5	5.0	4.0
PCa 13								
PCa 14	6.5	6.9	6.5	5.5	6.1	4.5	5.5	4.0
PCa 15	5.1	6.0	5.1	6.0	4.7	5.8	4.1	5.1
PCa 16	5.6	5.9	5.9	5.8	5.6	4.8	4.8	3.9
PCa 17	4.9	5.6	6.4	5.6	4.9	4.9	3.9	3.9
PCa 18	4.6	5.1	5.4	5.1	4.6	4.9	4.4	4.6
PCa 20	4.4	5.0	4.6	5.0	4.4	4.2	3.8	3.5
PCa 21	5.7	6.3	6.4	6.3	5.7	5.4	5.0	4.8
PCa 22	4.7	5.0	5.9	5.0	5.8	4.4	4.7	3.4
PCa 23	5.3	6.9	5.7	6.3	5.3	5.3	5.7	4.7
PCa 24	4.2	3.9	4.2	4.0	3.7	3.3	3.0	2.8
PCa 25	5.0	5.6	5.6	5.6	5.0	4.7	4.5	4.1
PCa 26	5.1	5.3	5.1	5.1	4.5	4.4	3.5	3.5
PCa 28								

PVAbs = Absolute Peak Velocity; PV50, 60, 70 = Peak Velocity at 50, 60, & 70% of KE 1RM; ‡ = Trained Leg for Reference Controls and R Leg for PCa Patients

ID	Pre SCF ‡	Post SCF ‡	Pre IMF ‡	Post IMF ‡
RefCon1	36.3	36.9	4.1	5.4
RefCon2	58.8	67.0	5.0	4.8
RefCon3	38.1	34.9	3.0	3.5
RefCon4	39.8	39.4	2.3	2.5
RefCon5	30.2	33.8	4.5	4.4
RefCon6	44.1	45.8	7.2	7.2
RefCon7	53.8	52.2	4.8	4.4
RefCon8	118.1	117.0	14.4	13.7
RefCon9	91.2	81.4	11.6	10.8
RefCon10	36.5	39.7	4.8	5.4
RefCon11	41.0	39.5	3.6	3.2
RefCon12	40.2	40.1	4.4	3.1
RefCon13	34.0	35.2	2.4	3.8
RefCon14	53.5	56.0	10.4	7.5
RefCon15	32.2	34.3	7.1	7.0
RefCon16	53.6	58.5	6.5	6.8
RefCon17	103.1	99.3	6.7	6.5
RefCon18	69.0	72.9	9.0	8.5
RefCon19	83.5	83.0	9.3	8.7
RefCon20	82.0	85.4	5.8	6.1
PCa 10	153.0	156.4	11.8	11.0
PCa 11	61.4	64.9	7.6	6.9
PCa 12	307.9	287.8	14.9	17.0
PCa 13	112.2	109.8	7.6	7.8
PCa 14	97.7	100.0	10.1	9.4
PCa 15	54.1	54.1	3.1	3.3
PCa 16	72.4	68.5	6.3	6.1
PCa 17	43.9	47.1	2.5	2.6
PCa 18	60.4	52.1	9.1	7.3
PCa 20	101.4	108.5	8.6	8.5
PCa 21	67.3	73.2	6.1	6.0
PCa 22	104.9	100.9	5.7	3.9
PCa 23	65.3	62.0	5.5	4.7
PCa 24	162.4	162.9	13.0	12.3
PCa 25	84.8	82.8	11.6	11.2
PCa 26	316.9	337.0	3.5	3.7
PCa 28				

SCF = Subcutaneous Fat; IMF = Intermuscular Fat; ‡ = Trained Leg for Reference Controls and R Leg for PCa Patients

ID	PCa Diagnosis	ADT days	LHRHa	Anti-A	Rad	Prost
PCa 10	4002	4002	Y	N	Y	N
PCa 11	2574	2392	Y	N	Y	N
PCa 12	4639	4548	Y	N	N	N
PCa 13	3581	296	N	Y	Y	N
PCa 14	2826	514	Y	Y	N	Y
PCa 15	6989	3181	Y	N	Y	N
PCa 16	2081	1008	Y	N	Y	Y
PCa 17	3350	501	Y	N	N	Y
PCa 18	886	802			Y	N
PCa 20	6665	1282	Y	N	N	Y
PCa 21	375	254	Y	N	Y	N
PCa 22	1550	728	Y	Y	N	Y
PCa 23	972	900	Y	N	Y	N
PCa 24	4543	1957	Y	Y	N	N
PCa 25	989	559	Y	N	Y	N
PCa 26	1302	256	Y	N	N	N
PCa 28	768	514	Y	N	N	N

PCa Diagnosis = Days Since Diagnosis; ADT days = Length of ADT treatment; LHRHa = Luteinizing Hormone Releasing Hormone agonist; Anti-A = Anti-Androgen; Rad = Radiotherapy; Prost = Prostatectomy

ID	Pre Free T	Post Free T	Pre PSA	Post PSA	Pre Hb	Post Hb	Pre Hct	Post Hct
PCa 10	0.91	1.00	U/D	U/D	13.3	14.0	35.0	35.0
PCa 11	0.99	1.40	U/D	U/D	12.2	14.1	36.3	37.7
PCa 12	0.28	U/D	U/D	U/D	11.7	12.5	37.7	32.7
PCa 13	1.14	0.95	U/D	0.14	15.2	14.0	40.0	43.0
PCa 14	0.85	0.70	U/D	U/D	12.0	10.8	33.0	37.0
PCa 15	0.83	0.51	0.28	0.33	15.8	13.5	46.0	41.0
PCa 16	0.73	1.11	U/D	0.06	13.6	12.5	37.7	41.3
PCa 17	2.29	13.60	U/D	U/D	12.3	12.0	38.3	30.3
PCa 18	5.83	5.47	U/D	U/D	12.1	11.8	34.0	39.3
PCa 20								
PCa 21	1.52	1.21	0.80	0.14	13.2	11.9	39.8	36.3
PCa 22	U/D	U/D	U/D	U/D	13.1	12.7	42.0	40.7
PCa 23	0.30	U/D	U/D	U/D	12.4	13.0	37.3	38.7
PCa 24	U/D	U/D	0.65	0.91	11.7	11.6	38.3	39.7
PCa 25	U/D	U/D	U/D	U/D	11.4	13.0	38.7	36.3
PCa 26	U/D	U/D	U/D	U/D	12.8	13.7	40.7	38.0
PCa 28								

Free T = Free Testosterone; PSA = Prostate Specific Antigen; Hb = Hemoglobin; Hct = Hematocrit

ID	Pre KE L 1RM	Post KE L 1RM	Pre CP 1RM	Post CP 1RM	Pre LP 1RM	Post LP 1RM	Pre CP End	Post CP End	Pre LP End	Post LP End
PCa 10	34.0	30.9	52.2	53.1	213.2	238.1	8	8	16	30
PCa 11	21.5	20.5	40.8	49.9	217.7	222.3	12	20	15	25
PCa 12	27.8	29.9	38.6	65.8	208.7	303.9	15	33	20	39
PCa 13	19.5	26.7	51.3	59.0	149.7	206.4	11	21	50	72
PCa 14	23.6	27.8	52.2	59.0	265.4	288.0	13	20	14	30
PCa 15	23.0	29.6	47.6	52.2	149.7	220.0	10	16	9	55
PCa 16	30.9	35.7	40.8	44.0	203.2	272.2	10	20	15	35
PCa 17	34.0	44.4	70.3	79.4	267.6	303.9	16	24	14	32
PCa 18	20.1	27.8	56.7	68.0	240.4	288.0	17	23	23	40
PCa 20	29.9	35.9	54.4	59.9	186.0	240.4	10	15	11	20
PCa 21	26.3	30.5	47.6	59.0	190.5	267.6	15	23	25	30
PCa 22	31.9	44.4	56.7	68.0	222.3	281.2	11	20	15	30
PCa 23			49.0	59.0	220.0	256.3	12	21	14	30
PCa 24	29.9	30.9	49.9	54.4	242.7	249.5	10	15	20	25
PCa 25	38.2	41.3	50.3	63.5	213.2	272.2	10	20	9	67
PCa 26	34.8	37.1	45.4	50.8	183.7	199.6	13	20	12	30
PCa 28	17.4	23.6	36.3	49.9	204.1	272.2				

KE = Knee Extension; CP = Chest Press; LP = Leg Press; End = Endurance Repetitions Test

ID	Pre PPAbs L	Post PPAbs L	Pre PP50 L	Post PP50 L	Pre PP60 L	Post PP60 L	Pre PP70 L	Post PP70 L	Pre MV L	Post MV L
PCa 10			463.5	435.4	467.7	437.6	439.8	449.4	4910.2	5191.4
PCa 11	267.9	323.7	267.9	323.7	297.9	348.5	301.4	374.4	3225.9	3667.0
PCa 12	270.0	381.3	270.0	381.3	296.2	382.1	215.2	390.1	4995.0	5301.3
PCa 13			251.5	280.4	261.9	309.2	264.6	320.5	4169.3	4667.3
PCa 14	309.1	349.1	301.3	349.1	309.1	335.5	312.9	325.0	3664.9	4087.9
PCa 15	322.6	369.7	328.9	369.7	322.6	361.1	319.7	347.0	2816.3	3050.4
PCa 16	407.5	414.5	391.5	414.5	407.5	419.4	412.0	414.5	4004.1	4193.8
PCa 17	411.1	487.9	419.8	483.0	411.1	461.4	381.5	404.4	3799.0	4089.1
PCa 18	303.2	314.5	290.3	314.5	303.2	311.2	324.9	364.9	3821.5	4084.0
PCa 20	375.6	376.4	288.4	376.4	375.6	385.7	344.6	370.9	4136.5	4191.1
PCa 21	385.3	400.3	379.7	378.2	380.8	400.3	385.3	366.1	3621.4	3736.7
PCa 22	354.5	416.6	351.8	416.6	423.3	395.6	354.5	312.1	4773.0	5061.2
PCa 23	355.4	485.5							3863.9	4176.1
PCa 24									4116.9	4289.8
PCa 25	430.1	480.6	430.1	466.2	440.7	474.7	458.1	451.3	4712.0	4878.6
PCa 26	380.1	389.7	380.1	388.3	368.5	382.0	332.6	361.4	3516.2	3658.3
PCa 28			183.0	253.0	162.0	224.0	172.0	240.0		

PPAbs L = Absolute Peak Power for the L Leg; PP50, 60, 70 L = Peak power at 50,60, and 70% of KE 1RM for the L Leg

ID	Pre Upper BMD	Pre Lower BMD	Pre BMD	Post Upper	Post Lower	Post BMD
PCa 10	1.249	1.343	1.275	1.259	1.407	1.299
PCa 11	0.916	1.132	1.012	0.923	1.088	0.995
PCa 12	1.521	1.344	1.477	1.054	1.258	1.289
PCa 13	1.337	1.425	1.381	1.312	1.385	1.348
PCa 14	1.314	1.360	1.340	1.308	1.350	1.312
PCa 15	1.005	1.008	1.024	0.998	1.029	1.028
PCa 16	1.051	1.227	1.139	1.079	1.263	1.171
PCa 17	1.272	1.455	1.363	1.248	1.388	1.318
PCa 18	1.269	1.600	1.435	1.299	1.600	1.449
PCa 20	0.955	1.095	1.037	0.926	1.105	1.028
PCa 21	1.207	1.206	1.185	1.198	1.189	1.181
PCa 22	1.184	1.489	1.296	1.213	1.523	1.313
PCa 23	0.855	0.983	0.928	0.817	0.992	0.910
PCa 24	1.428	1.484	1.430	1.472	1.455	1.445
PCa 26						
PCa 27						
PCa 28	1.272	1.647	1.540	1.253	1.629	1.525

BMD = Bone Mineral Density

ADLs ID	Pre Usual	Post Usual	Pre Rapid	Post Rapid	Pre Up & Go	Post Up & Go
PCa 10	4.4	3.7	3.4	2.8	6.1	5.2
PCa 11	5.7	5.2	3.9	3.3	4.8	5.3
PCa 12	6.4	4.0	4.9	3.4	10.4	6.2
PCa 13	5.6	5.0	4.3	4.4	7.4	8.2
PCa 14	4.4	4.8	3.7	3.2	6.1	5.2
PCa 15	5.7	6.5	3.9	3.5	5.6	5.8
PCa 16	6.4	5.1	3.4	3.0	5.0	4.7
PCa 17	4.5	4.6	3.8	3.2	4.3	4.5
PCa 18	6.4	4.1	3.9	3.2	5.0	4.9
PCa 20	5.3	5.1	3.6	3.2	5.5	4.7
PCa 21	5.0	6.5	3.5	3.1	4.4	4.4
PCa 22	6.2	5.4	3.5	3.6	5.9	5.4
PCa 23	6.7	6.5	4.1	3.0	5.8	5.4
PCa 24	7.1	6.2	4.8	4.4	7.3	7.0
PCa 25	5.7	4.4	3.6	3.2	5.9	5.4
PCa 26	6.5	6.4	3.9	3.7	6.1	5.4
PCa 28	6.4	6.1	3.6	3.5	11.9	9.0

Usual = Usual Walk; Rapid = Rapid Walk

ID	Pre Chair	Post Chair	Pre Stair	Post Stair	Pre 400m	Post 400m
PCa 10	14	14	5.0	4.7	284.5	288.4
PCa 11	13	18	4.1	4.3	266.0	256.6
PCa 12	7	12	7.4	5.8	426.5	450.1
PCa 13	12	13	6.4	6.1	299.2	310.2
PCa 14	17	19	4.9	4.5	294.4	269.2
PCa 15	14	17	4.8	4.6	297.8	273.5
PCa 16	13	18	4.5	4.0	241.1	226.5
PCa 17	20	23	4.0	3.8	242.3	219.2
PCa 18	14	17	4.2	4.0	257.6	253.5
PCa 20	16	20	3.7	3.5	301.0	279.6
PCa 21	17	19	3.9	3.8	270.0	229.9
PCa 22	17	16	4.1	4.1		
PCa 23	18	21	4.4	3.9	287.2	249.9
PCa 24	14	17	6.7	6.2	403.3	356.5
PCa 25	14	16	4.7	4.4	303.3	245.4
PCa 26	16	17	4.2	4.3	279.4	256.7
PCa 28	10	13	4.5	3.5	356.4	315.3

Chair = # of Chair Stands in 30 seconds; Stair = Stair Climb; 400m = 400m Walk

BFI ID	Pre Q1	Pre Q2	Pre Q3	Pre Q4a	Pre Q4b	Pre Q4c	Pre Q4d	Pre Q4e	Pre Q4f	Pre Total
PCa 10	4	4	6	3	2	6	1	1	4	31
PCa 11	4	5	3	5	2	5	4	1	1	30
PCa 12	9	9	9	10	9	10	9	9	10	84
PCa 13	3	4	6	2	1	4	2	1	3	26
PCa 14										
PCa 15	6	5	5	5	6	9	4	8	8	56
PCa 16	1	3	3	1		1	1	0	0	10
PCa 17	0	4	4	5	2	1	2	1	3	22
PCa18	0	0	0	0	0	0	0	0	0	0
PCa 20	2	6	5	2	2	3	1	1	1	23
PCa 21	3	0	0	1	1	0	1	0	1	7
PCa 22	5	6	7	3	0	4	3	0	2	30
PCa 23	0	0	0	0	0	0	0	0	0	0
PCa 24	3	5	6	3	3	4	5	2	7	38
PCa 25	0	6	6	2	0	2	1	0	0	17
PCa 26	4	7	8	5	7	4	4	5	2	46
PCa 28	3	5	8	0	3	0	7	0	2	28

BFI = Brief Fatigue Inventory; Q = Question #1, 2, 3, etc

BFI ID	Post Q1	Post Q2	Post Q3	Post Q4a	Post Q4b	Post Q4c	Post Q4d	Post Q4e	Post Q4f	Post Total
PCa 10	0	0	0	0	0	1	1	0	1	3
PCa 11	1	1	1	1	1	1	2	2	2	12
PCa 12	7	6	8	8	5	8	8	5	6	61
PCa 13	0	2	4	0	0	2	2	0	1	11
PCa 14										
PCa 15	2	3	3	3	2	2	2	1	3	21
PCa 16	7	2	2	0	0	0	0	0	0	11
PCa 17	2	2	2	0	0	0	0	0	0	6
PCa 18	1	1	1	1	1	1	1	1	1	9
PCa 20	2	6	5	6	5	5	7	8	10	54
PCa 21	1	1	2	1	1	1	1	1	0	9
PCa 22	0	0	2	0	0	1	1	0	1	5
PCa 23	0	0	0	0	0	0	0	0	0	0
PCa 24	2	5	7	1	0	6	7	0	3	31
PCa 25	0	0	0	0	0	0	0	0	0	0
PCa 26	3	4	6	4	3	2	2	2	2	28
PCa 28	2	2	6	2	1	2	2	0	2	19

BFI = Brief Fatigue Inventory; Q = Question #1, 2, 3, etc

FACT-P ID	Pre PWB	Post PWB	Pre SWB	Post SWB	Pre EWB	Post EWB
PCa 10	18	24	24	24	17	19
PCa 11	22	23	21	19	24	20
PCa 12	2	8	9	13	2	11
PCa 13	18	24	18	19	16	19
PCa 14						
PCa 15	23	21	21	20	13	22
PCa 16	24	27	17	22	17	14
PCa 17	17	25	22	26	16	21
PCa 18	25	24	25	28	24	24
PCa 20	23	23	26	24	24	16
PCa 21	22	28	13	23	24	20
PCa 22	25	27	25	20	17	20
PCa 23	28	28	12	28	16	20
PCa 24	19	20	21	19	20	19
PCa 25	23	25	24	18	24	24
PCa 26	27	25	28	26	24	24
PCa 28	20	28	23	23	22	21

FACT-P = Functional Assessment of Cancer Therapy-Prostate; PWB = Physical Well-Being subsection; SWB = Social Well-Being; EWB = Emotional Well-Being

FACT-P ID	Pre FWB	Post FWB	Pre Add	Post Add	Pre Total	Post Total
PCa 10	23	23	35	39	117	129
PCa 11	20	22	38	38	125	122
PCa 12	5	13	16	18	34	63
PCa 13	13	22	17	21	82	105
PCa 14						
PCa 15	15	14	34	32	106	109
PCa 16	24	25	37	37	119	125
PCa 17	18	24	23	35	96	131
PCa 18	28	27	43	42	145	145
PCa 20	28	25	38	22	139	110
PCa 21	24	22	43	38	126	131
PCa 22	25	26	40	39	132	132
PCa 23	25	28	48	48	129	152
PCa 24	15	12	18	25	93	95
PCa 25	19	19	34	36	124	122
PCa 26	27	25	37	35	143	135
PCa 28	18	25	18	28	101	125

FWB = Functional Well-Being; Add = Additional Concerns

Appendix IV: Power Analysis Tables

Table 7. Post hoc effect size and power estimates for multiple regression.

Table 8. Post hoc effect size and power estimates for differences between two dependent means (paired t-test).

Appendix IV: Power Analysis Tables

Table 7. Post hoc effect size and power estimates for multiple regression.

	N	R^2	IV #	Power	*P* value
Usual Walk	-	-	0	-	-
Rapid Walk	15	0.66	2	0.99	0.002
Up & Go	15	0.36	2	0.63	0.083
Chair Stands	15	0.33	2	0.57	0.088
Stair Climb	16	0.63	2	0.98	0.002
400m Walk	16	0.54	2	0.92	0.020
BFI	16	0.21	1	0.49	0.085
FACT-P Total	16	0.45	2	0.94	0.022

Table 8. Post hoc effect size and power estimates for differences between two dependent means.

	N	Mean Difference	Original SD	Cohen's *d*	Power	*P* value
FFM	17	1.7	7.5	0.22	0.22	<0.001
Fat	17	0.1	12.8	0.01	0.05	0.68
% Fat	17	0.6	6.2	0.10	0.10	0.012
BMC	17	0.04	0.6	0.07	0.08	0.197
FACT-P Total	16	7.4	28.0	0.27	0.27	0.043
FACT-P Physical	16	2.8	6.0	0.46	0.54	0.003
FACT-P Function	16	1.6	6.3	0.25	0.25	0.069
BFI	16	10.5	21.4	0.49	0.59	0.011
KE 1RM R	15	37.0	21.5	1.72	0.99	<0.001
KE 1RM L	16	22.3	30.1	0.74	0.88	<0.001
Chest Press 1RM	17	20.1	17.8	1.12	0.99	<0.001
Leg Press 1RM	17	104.2	73.3	1.42	0.99	<0.001
CP Endurance	16	7.8	2.6	3.00	0.99	<0.001
LP Endurance	16	19.3	9.8	1.97	0.99	<0.001
PP Abs R	15	51.0	34.7	1.47	0.99	<0.001
PP 50 R	16	57.6	20.3	2.83	0.99	<0.001
PP 60 R	16	49.7	27.5	1.81	0.99	<0.001
PP 70 R	16	36.5	34.9	1.05	0.99	<0.001
PP Abs L	13	47.5	32.8	1.45	0.99	<0.001
PP 50 L	15	42.2	23.0	1.84	0.99	<0.001
PP 60 L	15	26.7	31.0	0.86	0.91	0.003
PP 70 L	15	31.5	38.8	0.81	0.91	0.015
MV R	16	258.1	666.3	0.39	0.44	<0.001
MV L	16	261.1	609.0	0.43	0.50	<0.001
SCF	16	0.1	83.4	0.00	0.05	0.950
IMF	16	0.4	4.0	0.10	0.10	0.154
Usual Walk	17	0.5	0.8	0.65	0.82	0.020
Rapid Walk	17	0.5	0.4	1.19	0.99	<0.001
Up & Go	17	0.6	2.0	0.32	0.35	0.024
Chair Stands	17	2.6	3.1	0.83	0.95	<0.001
Stair Climb	17	0.4	1.1	0.32	0.35	0.002
400m Walk	16	20.6	52.5	0.39	0.44	<0.001

FFM = Fat Free Mass; Fat = Fat Mass; BMC = Bone Mineral Content; BFI = Brief Fatigue Inventory; KE 1RM = Knee Extensor Maximal Strength; CP/LP Endurance = Chest and Leg Press Endurance Tests; PP Abs, 50, 60, 70 = Peak Power at Absolute, 50, 60, and 70% of KE 1RM ; MV = Muscle Volume; SCF = Subcutaneous Fat; IMF = Intermuscular Fat

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Appendix V: Review of Literature

1. Introduction

The incidence of PCa has risen dramatically over the years, with more than 217,000 new cases estimated to be diagnosed in 2010. It is also estimated that ~32,000 men will die from PCa in 2010, making it the second leading cause of cancer-related death in the U.S. Black men have incidence rates almost 60% higher than white men and are twice as likely to die from PCa. The factors directly responsible for these differences are currently unknown, although diet, family history, screening frequency, and nationality all may contribute. To combat the rising prevalence of PCa, effective treatment strategies have been developed to halt or slow tumor growth. Unfortunately, some of these strategies are associated with many undesirable side effects which compromise body composition, functional independence, and QoL. Recently, exercise interventions, ST in particular, have gained in popularity as a means of reducing or even reversing many of the treatment related side effects. Therefore, the following review of the literature will address the history and prevalence of PCa, racial disparities, treatments and the associated side effects of PCa, as well as the role of ST in mitigating these side effects.

2. PCa History and Background

PCa is metastatic tumor that forms in the glandular cells (adenocarcinoma) of the prostate (109). It is a slow growing cancer and often remains undetected for years. The first description of PCa was in the early 1800's and was referred to as fungus hematodes, a term used at this time to describe all metastatic tumors (123). Over the next century, a clearer description of PCa was slow to be established as incidences of PCa were rare and were often confused with bladder dysfunction (132). Data of PCa incidence rates first

became available in the 1970's and a slow yet steady rise from 1975 through 1988 was observed (101). After the U.S. Food and Drug Administration approved PSA testing in 1986 and it became widely used for PCa screening in 1988, the PCa incidence increased sharply and had more than doubled by 1993 (101). The incidence rates fell in 1995 and have fluctuated around current levels for the past decade. PCa mortality rates have existed for much longer than incidence rates, dating back to 1930. Mortality rates doubled over the next 65 years, before experiencing a rapid decline in 1995 and are currently comparable to the levels in 1940s (101). Current mortality rates are greatly exceeded by the incidence rates, as PCa mortality is 25 men per 100,000 and incidence is 170 per 100,000 and is the basis for the supposition that men are more likely to die with PCa rather than from it. Also in support of this conclusion is that five year survival rates of PCa patients are among the highest of all cancers, independent of stage at diagnosis (101). Localized and distant stage PCa survival rates are both nearly 100%, but drop to 31% when the cancer metastasizes (101).

3. PCa Risk Factors

There are many risk factors that contribute to PCa, including age, family history, race or ethnicity, nationality, and diet (18, 104, 109).

3.1 Age. Age is one of the most significant risk factors, as the mortality rate for U.S. men who are 65 years of age is approximately three times greater than men who are 55 years of age, and 22.5 times greater than men who are 45 years of age (1). Similar findings were observed for men in the United Kingdom, as the cumulative percentage of PCa cases were negligible prior to age 60 (163).

3.2 Family History. Family history is another factor that influences PCa incidence rates. Men who have a brother or father with PCa have a relative risk of developing PCa that is 2.5 times greater than those without a family history (102) and the greater the number of first degree relatives that were affected, the greater the risk (22). A positive family history for PCa is a risk factor that is higher in younger individuals and slow declines with age (22, 102).

3.3 Race and Ethnicity. Race and ethnicity are also related to PCa incidences, as U.S. black men have the highest incidence and mortality rates throughout the world (2, 101). Nationality also plays a role, as incidence rates vary by more than 25 fold across the globe (100). For example, U.S. born men have rates twice that of those in Australia and Sweden, three times the rate observed in the United Kingdom, and more than ten times higher than what is observed in Central and South America and Asia (163). Despite the highest incidence rates, the U.S. mortality rate was not different than other developed countries but was still higher than those from Asia (163). Interestingly, when Japanese men immigrated to the U.S., the mortality ratios were higher than those who had remained in Japan (129), which implicates environmental factors, such as diet and lifestyles that are related to the particular country. However, immigrants still had lower relative mortality risks than U.S. born men for PCa (183), which suggests that genetic factors still play an important role.

3.3 Diet. Diet has also been linked to PCa, although the nutrients responsible for impacting PCa risk are less clear. The consumption of dietary fat and red meat increased the odds ratios for being diagnosed with PCa (18, 113, 174) while eating foods rich in lycopene may decreased it (67, 174), although not all studies support this (113, 159).

Alcohol consumption elevated PCa risk in moderate (22-56 drinks per week) and heavy drinkers (>56 drinks per week) and this risk was similar between black and white men (78). Supplementation of micronutrients such as selenium and zinc have also been implicated as possible mediators of PCa risk, but the data are inconclusive (18).

4. Screening for PCa

As the relevant risk factors for PCa became known, screening techniques to detect PCa early became more common, particularly in high-risk populations. The most widely used screening techniques are the digital rectal exam (DRE) and the PSA blood test (109), which may be more effective when used together (127) and it appears that more men are now taking this approach (166).

Human tissue kallikrein 3, more commonly known as PSA, is a serine protease of the human tissue kallikrein family (208) and is produced primarily by the epithelial cells lining the prostate gland. PSA is released in its inactive form, which is then activated by cleaving seven amino acids from the N-terminus and displays chymotrypsin-like enzymatic activity (131). The major physiological function of PSA is to cleave the seminal vesicle proteins seminogelin I and II (126). PSA has also been identified in breast, lung, colon, ovary, liver, kidney, adrenal tumors and biological fluids, such as breast and saliva, however, the expression levels are much lower than in the prostate and its biological roles in these tissues remains unknown (43). Much of the circulating PSA in serum (70 - 90%) complexes with α1-antichymotrypsin with the remaining fraction exists as unbound inactive enzyme (free PSA) (191). The sum of the free and bound PSA is total PSA, which is used as a biomarker of prostatic tissue damage that can occur with PCa, benign prostate hyperplasia, and infection (109). PSA leaks into the circulation and

produces elevated serum levels which can then be detected. Total and free PSA levels, PSA velocity, and PSA density are all used to screen for early detection of PCa (127). Total PSA values less than 4.0 ng/mL are considered normal.

The DRE is performed as part of a routine exam in men over the age of 50 and in high risk patients beginning at age 40 (109, 187). During the exam, an urologist will palpate the prostate for abnormalities. If suspicious areas are detected and/or the patient has an elevated PSA level, a biopsy can be used to check for PCa histologically (109). Unfortunately, with both PSA and the DRE, there are several shortcomings. In particular, false positives can lead to psychological distress and additional healthcare expenses while false negatives may give PCa patients a false sense of security and the potential inability to treat PCa in its earliest stages (4). The lead time for PCa diagnosis has improved by several years as a result of DRE and PSA screening procedures (46), although it can vary based on the aggressiveness of the tumor. While lead time is crucial for those who have aggressive PCa, concerns with overdiagnosis and overtreatment are now being raised (4, 46). Presently, there is an extensive catalog of research available discussing the screening tools and their ability to detect PCa and to reduce mortality, but there is insufficient evidence available to provide specific recommendations to the general public regarding screening with the PSA or DRE (4, 127, 187). However, those topics are beyond the scope of this review.

5. Racial Disparities

While the incidence and mortality rates for PCa have declined in recent years, there is a striking racial disparity that exists. U.S. black men have the highest incidence of PCa, with 234.6 cases per 100,000 men compared with 150.4 per 100,000 for white men,

than any other racial or ethnic group throughout the world and die of PCa at 2.4 times the rate of white men (2, 101). This death rate increases to three times the rate of whites when examining men under the age of 65 (1). PCa accounts for ~42% of all cancers diagnosed among black men (1). While five year survival rates are similar across race, black men have a lower survival if the cancer has metastasized (101).

A specific reason for this health disparity in PCa mortality has not been determined, but several aspects are thought to be involved. One possible physiological explanation may be race differences in androgen hormone signaling to the prostate (68, 146, 156). For example, androgen receptor expression is higher in black vs. white men, which may predispose them to higher rates of PCa and related morbidity (68, 156). In addition, black men may have higher circulating androgen levels (50, 167, 213), although evidence for this is not conclusive (114, 128, 165). Increased androgen receptor expression and binding with its primary ligand, testosterone, enhances tumor progression in the prostate (193). In support of the hypothesis of increased androgen activity in the prostate, healthy black men across the age range had higher total PSA and a trend for higher free PSA than white or Hispanic men (120). Alternatively, men with no history of PCa had similar PSA levels across black, white, and Asian men, but the percentage of individuals with PSA values in excess of 4.0 ng/mL is highest in black men (34). Black men with metastatic PCa also had higher PSA levels, more advanced PCa, and were diagnosed younger than their white counterparts (194), although it is possible that the higher PSA levels and more advanced cancer could be the result of longer intervals between screenings in black men (27).

Racial differences in socioeconomic status, stage at diagnosis, and health insurance coverage are additional factors that influence long-term prognosis (104). Of all PCa patients, black men routinely had a higher percentage of advanced PCa and were poorer, less educated, younger, and had fewer previous screenings than white men (27, 28, 85, 86, 218). Because income and access to healthcare have be suggested to affect survival rates, patients from Veteran Affairs hospitals were studies as this eliminates differences in the access to and costs attributable to PCa. Early studies concluded that race was not affecting PCa mortality across all ages, but in patients under the age of 65, black men had higher mortality (162). Similar findings were observed in another investigation using patients from the Veterans Affairs hospital system (57), suggesting that when equal access to health care is provided, morality rates may not differ. However, both studies reported more advanced PCa in black men, as did others (23, 56). When black and white men received treatment from private sector healthcare providers, the more advanced PCa still persisted but the probability of survival was lower in black men (57). A recent meta-analysis demonstrated that unadjusted all-cause and PCa specific mortality rates were higher in black men and the PCa specific mortality rates remained elevated after adjusting for age and socio-economic status (52). Because income and access to health care do not completely account for differences in tumor progression and survival rates, this supports the notion that biological dissimilarities could exist between races. This, however, remains controversial as other evidence suggests that after correcting for the effect of lower quality treatment and higher mortality due to additional illnesses, cancer biology differences between races was unlikely (3, 23, 162). Regardless of the reasons for these racial disparities, many professional organizations and

investigators are working to reduce, if not eliminate, the racial differences in PCa incidence and mortality rates.

6. Treatment of PCa

The overall goal of any cancer treatment is suppress the growth and to prevent the spread of the tumor. The currently available treatments for PCa can be divided into two basic types, primary and adjuvant treatments. Primary treatments are designed to remove or kill the PCa cells and adjuvant treatments are administered to reduce the risk of recurrence. Because prostate tumors were discovered before modern pharmacology, surgery was initially the only option and still remains a primary method of treatment (109, 132). The first prostatectomy procedures were performed in 1905 (216). This surgical procedure formed the basis from which many of the current techniques were derived (144, 206). Other primary treatments include external beam radiotherapy or internal bradytherapy to shrink the tumor (109). Radiotherapy (also referred to as radiation therapy or XRT) can also be used in conjunction with a prostatectomy, either in the neoadjuvant (before primary treatment) or adjuvant setting. In the early to mid-portion of the 20th century, it was discovered that PCa tumors were androgen dependent (87, 132). This led to the implementation of ADT, initially in the form of surgical (132) and later chemical castration (195). Luteinizing hormone releasing hormone agonists (LHRHa) and anti-androgen treatment are commonly used adjuvant ADT treatments for PCa (109, 179). The abundance of LHRHa causes down-regulation of the gonadotropin releasing hormone receptor via negative feedback mechanisms and less production of luteinizing hormone in the anterior pituitary and ultimately less testosterone production in the Leydig cells (211). The final method of treatment is watchful waiting where no active

treatment occurs and tumor progression is closely monitored. This treatment is usually reserved for older patients, those with low risk tumors, or in situations where the PCa has likely metastasized. Older patients are more likely to use watchful waiting when life expectancy is less than ten years and the patient will probably die with PCa, not from it (175). The second case when watchful waiting is used is when a patient is diagnosed with an advanced stage tumor. If the Gleason score is above eight (scaled from two – ten based on tumor cell differentiation) and the tumor grade is T2c or higher (scaled from T1 – T4 based on tumor size, lymph node, and metastatic progress), these are cases when the tumor is advanced and has likely spread. Treatment will not likely significantly extend life and the adverse consequences of the side effects may outweigh any potential benefits.

Racial factors may influence the treatment options. For example, using the Surveillance Epidemiology and End Results-Medicare (SEER) database, black men were less like to receive ADT than white men following PCa diagnosis and those that did had longer wait times until the onset of ADT (28, 86). Aggressive PCa treatment (surgery or radiotherapy) was 26% less likely in black men (218) and they were more likely to be treated with watchful waiting, even after adjusting for income, marital status, and education levels (181). Using a different dataset, white men were again more likely to receive aggressive treatment compared with black and Hispanic men with education and income levels also adversely affected treatment types (175). The discrepancies regarding race may be yet another contributing factor (along with biological and screening inconsistencies) to the observed differences between PCa incidence and mortality rates in black men.

The effect of each treatment on survival outcomes is an area of contentious debate among researchers. Randomized control trials (RCT) using ADT as an adjuvant therapy with either radiation or surgery in both local and metastatic PCa patients demonstrate significant decreases in mortality compared to patients treated only with a primary therapy (16, 140). However, the use of ADT alone does not appear improve prostate-specific or overall survival in men with localized PCa (44, 130), as in both studies the majority of men died from causes other than PCa. Finally, a review of the effectiveness and harms of treatments for localized PCa exhibited similar survival rates at five and ten years between radiotherapy, brachytherapy, radical prostatectomy, and watchful waiting (212). It was not until after 15 or 20 years that watchful waiting and brachytherapy showed lower survival. However, very limited numbers of randomized trials comparing treatments are available, so this information should be interpreted cautiously (212). Much like the debate surrounding screening recommendations, the conflicting reports with respect to survival outcomes make establishing guidelines difficult, particularly because treatment is influenced by many different factors. However, despite the lack of definitive evidence on mortality rates, ADT remains a common treatment option for both local and metastatic PCa.

The effect of androgen suppression in PCa patients was first established in a classic study by Huggins and Hodges who examined the effects castration, estrogen, and testosterone on serum phosphatases in PCa patients (87). Bilateral orchiectomy resulted in a large decline in acid phosphatase levels (an enzyme produced by the prostate that is elevated during PCa, similar to PSA) while the addition of testosterone increased acid phosphatase to more than twice the pre-castration values, providing the initial evidence of

the androgen dependence of PCa tumors. This discovery, along with additional work in this area, resulted in the 1966 Nobel Prize in physiology and medicine for Huggins (132). ADT was originally permanent, as surgical castration was the sole option. However, in 1982, LHRHa were given to ten non-metastatic PCa patients. Declines in total testosterone and acid phosphatase were observed, along with a decrease in prostate size and bone lesions (195) and provided an alternative option to surgical castration. The number men electing to undergo surgical castration dropped from 50% to 10% in the decade following LHRHa therapies, during which the number of patients on this therapy rose to 60% while the remaining 30% did not undergo any form of ADT (28).

The use of ADT has continued to increase, yet there are still several issues that remain controversial with this treatment, such as the appropriate level of testosterone suppression and how frequently testosterone levels should be monitored throughout treatment. Historically, castrate levels of total testosterone were considered to be <50 ng/dL (154), based on sensitivity limitations of the assays used to measure sex hormones (24). The development of commercially available radioimmunoassay kits capable of accurately measuring total and free testosterone allowed direct measures to replace estimates such the free androgen index and calculated free testosterone (210). Using the newer methods, Oefelein and colleagues measured testosterone levels in both surgically (153) and chemical castrated PCa patients (154). It was rare (5% of patients) that surgical patients had total testosterone levels exceeding 20 ng/dL (153) whereas LHRHa patients had a greater percentage (13%) who exceeded the 20 ng/dL threshold (154). While this is a relatively small difference, the authors suggest that monitoring of testosterone levels with LHRHa therapy is important and testosterone levels exceeded in 20 ng/dlL may

impact long-term survival. Morote *et al.* (148) examined the impact of this newer castration definition on survival and observed that the lowest testosterone levels that had a significant impact on survival was 32 ng/dL as the mean survival dropped from 137 to 88 months. Another study examined LHRHa administration on a monthly basis vs. the standard three month dose and found no differences in patterns of testosterone suppression as both groups had mean testosterone levels that were below 20 ng/dL (180). Chemical castration compared with surgical castration is likely to remain the preferred method ADT because it is reversible and can be administered intermittently, but considerations should be given to adopting newer cutoff values, as higher testosterone levels may decrease survival. More frequent monitoring may be required to ensure that testosterone levels remain suppressed.

7. Adverse Side Effects

Although ADT treatment slows the growth of existing tumors, the suppression of testosterone leads to numerous physiological and psychological side effects which negatively influence the patient's ability to live an independent, meaningful life. These side effects are well documented in the literature and include significant loss of muscle strength (6, 65, 211), muscle mass (20, 62, 65, 184-186, 201), a decline in resting energy expenditure (136), and BMD (6, 33, 62, 65, 72, 108, 157, 178, 217). PCa patients also experience increased fat mass (6, 20, 33, 40, 62, 65, 184-186, 201), fatigue (62, 82, 103, 119, 190), and anemia (10, 11, 62, 185) with ADT. Men on ADT also have an increased number of co-morbidities (40), including insulin resistance (7, 186), glycoslyated hemoglobin (186), negative lipoprotein profiles triglycerides (21, 185), and prevalence rate of metabolic syndrome (21). The collective effect is a functional decline leading to

reduced performance in activities of daily living (35, 62, 65, 103, 125) and poorer QoL (6, 40, 82, 103, 151, 190).

7.1 Muscle Mass and Strength. Significant loss of muscle mass is routinely observed in the first six to 12 months of ADT in PCa patients (6, 20, 62, 184-186, 201) and the longer the treatment period, the greater the loss (125). The decline of total FFM during the various length treatments averaged ~2.5% with no change being reported in controls (20, 65, 125, 201). The loss of lean mass is likely contributing to lower resting energy expenditure after ADT treatment (136). Cross-sectional investigations using healthy controls and PCa patients on ADT also revealed substantial group differences in upper body (9.6 – 28.4%) and lower body muscle strength (23.7 – 27.9%) (6, 65). Ultimately, the loss of muscle mass and strength may be linked to survival as greater levels of muscular strength are inversely associated with cancer mortality, independent of other risk factors (170).

7.2 Muscle Power. Muscle power is derived from both the force and speed generated during muscular contractions. It is a strong predictor of physical function which is necessary for maintaining a high QoL in older adults (80), to an even greater extent than muscle strength (8, 9). For this reason, power has the potential to be an important QoL indicator for cancer patients. Muscle power declines with advancing age (141), even in master's athletes undergoing ST (155), and is associated with all-cause mortality (142). However, the effects of ADT on muscle power have not yet been reported in PCa patients. It is hypothesized that muscle power would decline with ADT due to muscle strength loss. In addition, supraphysiological doses of LHRHa may also

reduce muscle power by adversely affecting the neuromuscular junction and thereby interfering with muscle action potentials (211).

7.3 Bone Mineral Density. Similar to muscle mass and strength, there are significant declines in BMD with ADT. Healthy controls and men on ADT have total body BMD differences of between 4.5 – 7% (6, 33, 65, 72). Longitudinal examinations lasting up to a year revealed smaller losses in BMD (62, 72). These dissimilarities could be due to differences in the length of ADT treatment between study designs, as BMD has been shown to be inversely related to length of ADT treatment (6, 108). However, BMD values may stabilize with time, as chronic ADT users (mean duration 33 months) showed no change in BMD over 12 months (72), whereas other reports show continuous declines in BMD over ten years, but used very small sample sizes (108).

7.4 Fat Mass. The treatment of PCa is consistently associated with a significant increase in fat deposition (5, 20, 62, 125, 177, 184, 185). In studies with a variety of treatment lengths, there were significant percent increases in % fat (4.3 – 11%) which was greater with longer treatment (20, 62, 184-186). The absolute changes in % fat were typically between 2-3%. In a combined cross-sectional and longitudinal investigation, Levy *et al.* (125) reported only a trend for group differences increased fat mass, although there were group differences in % fat with healthy controls. A two year follow-up also revealed small but significant changes in % fat in both the acute and chronic PCa patients but there were no differences in the change between groups.

The consistent increase in fat can lead to obesity, as well as diabetes, and metabolic syndrome. Treatment of PCa with ADT likely increases fat infiltration within the muscle, leading to the accumulation of IMF (99), although this has not been directly

assessed in PCa patients. Elevated levels of IMF are associated with insulin resistance and type 2 diabetes (71). In addition, fat infiltration is associated with reduced strength (70), poorer leg function (204), and greater incidence of mobility limitations in older adults (203).

7.5 Fatigue. Fatigue may be the most prevalent and distressing side effect during and after cancer treatment and high numbers of patients report suffering from chronic fatigue during ADT (62, 103, 119, 176, 177). Forty percent of patients who remained on ADT reported chronic fatigue compared with only 25% in those who had ceased treatment (119). Aging and hormone therapy both likely contribute to fatigue by eliciting physiological events that promote loss in fatigue resistance and the ability or willingness to engage in physical activity. PCa patients have reduced physical activity levels after the onset of ADT (62) and similar declines in activity are also seen in animal studies (94, 95). The changes in body composition along with anemia are likely candidates affecting physical activity levels. These reduced levels, in part, result in overall reductions in fitness levels, leading to declines in physical function and ultimately to loss in QoL.

7.6 Anemia. There is a connection between testosterone and hemoglobin levels, as prepubertal boys and girls have similar hemoglobin values that then increased in boys while remaining constant in girls after puberty (110). Moreover, testosterone administration in boys with constitutional delay of puberty led to increases in hemoglobin of 1.6 g/dL, bringing them to similar levels of that in normal adolescent boys (81). Thus, it is not surprising that the ablation of testosterone can lead to anemia (39, 192), which is linked to fatigue, QoL, and survival (139). Declines in hemoglobin of 6.5 – 10.5% are reported in ADT patients over time (62, 184, 185). Furthermore, declines in hemoglobin

over three months of ADT are associated with shorter overall survival (10, 11). When anemia was examined as a dichotomous variable (hemoglobin greater vs. less than 12 g/dL), black men were significantly more likely to be anemic than whites (11).

7.7 Co-morbidities. PCa treatment is associated with a number of additional co-morbidities, including insulin resistance (7, 186), cardiovascular disease (173, 199), and the metabolic syndrome (5, 21). Basaria *et al.* (7) observed a substantially higher prevalence of insulin resistance in PCa patients on ADT vs. PCa patients not on ADT and healthy aged-matched men, independent of age and obesity. Similar declines in insulin sensitivity were found after a 12-week prospective study at the onset of ADT (186). These findings are supported by two review articles that show a connection between ADT administration and insulin resistance (5, 107) and that this association becomes evident within the first few months of treatment. Cardiovascular morbidity is also elevated with ADT, as one group showed cardiovascular death rates of 5.5% for ADT patients and 2.0% in non-ADT patients (199) and another estimated that ADT increased cardiovascular mortality by 20% (173). Along these lines, several studies show elevated triglycerides and a trend for higher LDL cholesterol levels with androgen suppression (21, 185, 186). Finally, the use of ADT for 12 months revealed a higher prevalence of diabetes and metabolic syndrome (5), and 55% of the men in an ADT group met the criteria for metabolic syndrome compared with only 20% in the non-ADT and healthy control groups (21).

The number of co-morbidities in PCa patients is affected by race, as black men have higher numbers of co-morbidities (27, 40, 85, 218) and a higher co-morbidity index

(calculated using Medicare claims through diagnoses or procedures made from one year prior to one month following PCa diagnosis) (86).

7.8 Physical Function. A decrease in physical function during ADT treatment is a common side effect (35, 65, 125) and is likely related to the loss of muscle mass and lower physical activity levels coupled with increases in fat mass and fatigue. Using cross-sectional investigations, physical function assessed using common daily tasks and the short physical performance battery composite score were lower in chronic vs. acute ADT and non-ADT controls (Clay 2007, Levy 2008). Galvao *et al.* (65) consistently observed large differences between ADT patients and controls across a number of walking tasks, which exceeded the smallest meaningful clinical differences of 0.05 m/s (117, 133, 158). There was a study which found no differences between controls and men on ADT therapy (103), but it is not clear why this may have happened, considering that the functional tasks were identical to those used in studies reporting differences. One limitation of all these studies is that the PCa patients were high functioning, and in several cases those with severe impairments were either not recruited or dropped out. It is largely unknown if the effects of ADT are different in patients with limited function. An emphasis to recruit or retain these individuals should be considered for future studies.

7.9 Quality of Life. QoL is perhaps the most egregious side effect of ADT and is intertwined with strength, body composition, fatigue, and physical function. Changes in the above traits that are well documented with ADT are likely to affect QoL. Thus, it is not surprising that men undergoing hormone therapy for PCa report reduced QoL (6, 40, 103, 176). Several different QoL questionnaires are available, so direct comparisons are not always possible, but there were several apparent trends. The physical function and

health perceptions sections but not the mental health sections were depressed in ADT patients compared to non-ADT patients (6, 40). Conflicting findings were reported by Joly et al (103), as these authors saw only trends for physical and functional differences compared to healthy controls when using a general QoL questionnaire but reported large differences when examining PCa-specific symptoms. Segal *et al.* (176) reported a small decline in QoL (3.3 units) over 12 weeks in men who had been on ADT, but this was not significant and was below the 6-10 unit clinically meaningful change for overall FACT-P score (31).

In summary, ADT impacts on most of the body systems and the effects are most severe in the early stages of treatment. The long term consequences of ADT have been less studied, but the available evidence suggests that continuous declines in musculoskeletal health, physical function, and body composition can occur throughout treatment.

8. Aging and ADT

Many of the iatrogenic effects of ADT mimic the natural aging process but at an accelerated rate (25, 75, 91, 92). ST is considered the intervention of choice to offset the consequences of sarcopenia, aging, and chronic diseases (91, 92). In healthy older adults, ST can reverse the loss of muscle mass and strength (55, 90, 169), muscle power (42, 160), bone (138, 171, 172), declines in resting metabolic rate (124), functional declines (63, 76, 79), and the reversal of increased regional fat deposition (198, 215), which can all lead to a deterioration in the QoL. It is, therefore, logical to postulate that the use of ST would be ideal in alleviating the adverse effects of ADT during the treatment of PCa. Recent reviews of this topic support this hypothesis (66, 75), and while it is well

established that ST increases muscle mass and power in older adults (91, 92), it is unclear whether androgen ablation would blunt ST-induced muscle hypertrophy as limited investigations are available to support or reject such a hypothesis and none have examined this in black men on ADT (75).

9. Exercise Training in PCa patients on ADT

Exercise training has only recently been used as a means of reducing the side effects of cancer treatment. Across many different cancer types, training is well tolerated by both patients undergoing treatment and in cancer survivors, conferring an array of physical and psychological benefits (59). However, the data were from primarily breast cancer patients using aerobic training, were plagued by small sample sizes, lacked randomization, and rarely examined ST. More recently, studies have addressed some of these limitations by including significant numbers of PCa patients and ST, and these individuals experienced gains in strength, endurance, and cardiopulmonary function but no effect on body composition (41). Very recently, the independent effects of ST in hormone dependent cancer treatment was reviewed (75) and, contrary to previous findings, changes in body composition in PCa patients were reported for the first time in two studies using high intensity ST.

Because the scope of this review of the literature is primarily focused on ST in PCa patients on ADT, only exercise interventions that meet these criteria will be included. In a few instances, the only data available regarding a particular side effect of ADT and the response to exercise is from animal studies. Information on additional types of cancer and various exercise interventions are outside the scope of this review but have been discussed elsewhere (41, 59).

9.1 ST and ADT. To the best of our knowledge, the first investigation of ST in PCa patients on ADT was a multi-site, RCT to examine the effects of 12 weeks of moderate intensity ST (60-70% of 1RM) on muscle endurance, fatigue and QoL (176). Compared to a waitlist control group (N = 73), men in the intervention group (N = 82) experienced significant gains in upper and lower body muscle endurance and had less interference from fatigue and enhanced QoL. There was no effect of ST on weight, BMI, waist circumference, or body composition, but the body composition analysis was limited to skinfolds. ST did not lead to increases in testosterone or PSA, which had been the reason why ST had not been previously recommended in ADT patients.

In a follow up study, a two phase ST intervention lasting 20 weeks was used in ten men on ADT (61). Like previous studies (176), gains in muscle endurance were reported, along with increased upper and lower body strength, physical function, and balance with no change in testosterone or PSA (61). Neither FFM, fat mass, or BMD, assessed using DEXA, were altered with ST, although ultrasound imaging reported increased quadriceps muscle thickness but no changes at in the hamstrings, biceps, or triceps. The progressive ST protocol used higher intensities, ranging from 70-85% of 1RM, based on the American College of Sports Medicine recommendations for ST in healthy adults (111), providing additional evidence that PCa patients on ADT respond well to ST.

To investigate the importance of testosterone for increasing muscle mass and strength, healthy young men with limited ST experience were injected with an LHRHa or placebo for four weeks before completing an eight week ST program (115). The ADT treatment effectively suppressed testosterone to castrate levels. Ablation of testosterone

resulted in a diminished response to ST, as gains in muscle strength were completely abolished and the gains in leg mass were attenuated compared with the placebo group, despite similar total training volumes. There were, however, no differences in the mRNA response between groups for the myogenic regulatory factors, myostatin, and IGF-1 (116). Thus, testosterone does not appear to have any influence on these genes within the muscle hypertrophy pathway and the blunted increase in FFM appears to be the result of factors.

One possible reason that increases in FFM are inconsistently observed in ADT patients could be influenced by the lack of direct measurements of muscle mass. Previous studies in PCa used either skinfolds (176) or DEXA (61, 115), each having several limitations. The most accurate methods of assessing muscle mass are CT and magnetic resonance imaging (MRI) (99). Cross-sectional area measurements at the mid-thigh and mid-arm derived from direct imaging techniques of skeletal muscle mass produced values that were nearly identical to actual measurements made in cadavers, and the correlations between CT, MRI, and cadaver were all 0.97 (145). Although CT and MRI imaging are accurate, non-invasive, and reliable, they are also expensive and time consuming as images must be manually outlined by a technician. There are also the inherent dangers due to radiation exposure with serial CT measurements (168).

Direct measures of muscle mass in PCa patients was recently completed by Hansen and colleagues (74). In a small pilot study, ten PCa patients performed 12 weeks of eccentric resistance exercise using a recumbent leg cycle ergometer. The patients trained three times per week for 12 to 15 minutes per session at an intensity described as "somewhat hard." MRI was used to evaluate quadriceps MV before and after exercise

training in five men on ADT and five men who were not. The resistance exercise produced a significant gain of 2.9% in left leg MV of non-ADT patients. The right leg and neither leg in the ADT patients did not undergo any change in MV. Regrettably, the authors do not describe the methodology used to calculate MV in sufficient detail, nor do they specify whether boney landmarks were used to ensure adequate replication between baseline and post testing.

There are two additional studies that investigated PCa patients and the response to training. Despite being well-controlled RCTs, neither study allows for the independent effects of ST on ADT to be examined. However, these studies do provide additional insight onto the training response in men with PCa. Segal et al (177) randomized 120 PCa patients receiving radiation therapy into ST, aerobic training, or usual care groups for 24 weeks. Approximately 60% of the patients were on ADT, but the analyses did not adjust for this. Compared with usual care, ST participants had lower fatigue levels and improved QoL, aerobic fitness, upper and lower body strength, and triglyceride levels. ST also prevented an increase in % fat, which was observed in the usual care group. In a second RCT, 57 patients on ADT were assigned to a combined ST and aerobic program or usual care for 12 weeks (64). The authors report significant increases in FFM, similar in magnitude to that of Kvorning et al (115), but this is the first instance of muscle hypertrophy in PCa patients on ADT. Because aerobic training is not typically associated with gains in FFM, it is reasonable to assume that these gains were likely induced by the ST portion of the training program. In addition, the PCa patients increased their strength, physical function, and QoL with a decrease in fatigue. The changes in strength, muscle endurance, and physical function with the combined exercise protocol were substantially

less than what the authors report in an earlier study (61) and could be the result of a shorter training program (12 vs. 20 weeks), the inclusion of aerobic training, or both. Combined ST and aerobic training has been shown to attenuate strength but not aerobic capacity gains in healthy individuals (12, 83).

Over the past decade, a number of studies have been conducted evaluating the effectiveness of ST to reduce the negative side effects of ADT. One of the most striking and consistent observations that many research groups report are the high compliance and subsequent low dropout rates in this patient population. Only one investigation reported a high dropout rate as a study limitation (74). Moreover, the ST programs are well-tolerated with few adverse events being reported. Although studies are only beginning to uncover the potential of complementary therapies, such as exercise training, to attenuate the side effects of PCa treatment, the existing data provide a strong basis for moving this area forward.

9.2 Additional exercise training and ADT. To fully examine the widespread effects of ADT and exercise, there are measurements that cannot be completed using human subjects. For example, the effects of ADT on cardiac function and bone strength and composition (rather than just BMD) have been studied in rats. In addition, direct measures of muscle mass are very limited in PCa patients, but there are several relevant rodent studies that model ADT. While not the ideal model of ADT for humans, animal investigations provide additional insight and allow information to be obtained in situations where it might not be possible otherwise.

Similar to humans, animal studies also present conflicting reports on hypertrophy. One example of this is a study in which rat gastrocnemius muscles were trained with

needle type electrical stimulation for two weeks with and without administration of the androgen receptor antagonist, oxendolone (96). The increase in muscle mass induced by electrical stimulation was effectively suppressed by the androgen receptor blockade as muscle hypertrophy was significantly lower than the control group. To the contrary, orchiectomized rats engaged in climbing a 200 cm tower to reach their drinking water had hindlimb muscle weights that were not significantly different compared to non-climbing sham and orchiectomized rats (152). However, climbing exercise did reduced body fat mass in the castrated animals and preserved femur and vertebrae bone mass at four but not eight weeks. Access to voluntary wheel running in rats on ADT and control animals revealed no differences between groups for the cortical (compact) bone volumes, however, cancellous (spongy) bone volume was significantly reduced with ADT and running slightly improved it, although the volumes were still significantly lower than both control groups (94). These findings provide a better understanding of specific effects of ADT treatment on bone mass. The data are consistent with others (61), as exercise stimuli failed to induce changes in BMD. Bone loss with ADT remains an issue to be addressed in PCa patients (84). A phase III clinical trial has been proposed that will focus on, along with other ADT-related endpoints, bone health in PCa patients over 12 months, but the results have not yet been published (150).

The other set of relevant studies in men on ADT are the home-based exercise and lifestyle modification programs (19, 36, 37). In a pilot study, 31 men on ADT completed a 12 week intervention composed of walking, stretching, and light resistance exercise (36). The patients also attended a group booster session at a cancer center every two weeks. After training, more frequent bouts of higher intensity physical activity were

reported, six minute walk distance and QoL were increased, and less fatigue was reported. Four months after the intervention concluded, there were trends for declining physical activity levels and QoL, indicating that importance of continued exercise during PCa treatment. In a more comprehensive study by the same research group, men randomized to the 16 week intervention failed to replicate their earlier findings as most of the primary outcomes did not undergo significant changes (37). This study had a high dropout rate, 34%, which included 11 patients from the intervention and 23 from the wait-list control group, and may have left the study underpowered to detect between and within group differences. Bourke et al (19) performed a randomized 12 week combined exercise intervention with a six month follow up. Men in the intervention group performed supervised ST and aerobic training sessions with additional walking sessions at home. Post testing revealed a decrease in fatigue and improved physical function, strength, and aerobic exercise tolerance in trained men compared to controls. There was no change in QoL with this intervention. Six months following the intervention, all of the above changes were maintained. The attendance for the supervised training sessions was 95% and 87% for the home based portions.

The home-based investigations highlight three particular issues with exercise intervention studies in PCa patients. First, when training sessions are scheduled at a university or cancer center, the exercise adherence rates are usually at or in excess of 90% (19, 61, 64, 74, 177) whereas home based rates are lower (19, 37). Second, the intensity of home based exercises may be limited because the patients are training using Thera-Bands®, light weights, or body weight exercises (36, 37). The lower adherence rate and the intensity and choice of exercise may be affecting the response to exercise.

However, studies of this nature are likely next steps for applying the findings of controlled laboratory investigations into more practical training interventions capable of reaching large numbers of patients. Finally, RCTs are considered the gold standard. However, subjects randomized to control groups are more likely to drop out (37, 176) or indicated they would not have participated in the study if they were allocated into the control group (61). Moreover, because exercise has been demonstrated to be beneficial, it calls into question whether it is ethical to assign individuals to a treatment that may inevitably receive a lower level of care. Studies have addressed this situation by assigning patients to a waiting control group (37, 64, 176). However, it is not clear if PCa patients in the control groups completed the training after the waiting period, what the exercise adherence rates were, or whether or not they experienced similar gains in the above cited studies.

10. Potential Mechanisms of ST-Induced Hypertrophy during ADT

The final section of this literature review will examine the evidence for potential mechanisms to explain the gains in MV and FFM with ST in ADT patients. The number of studies on this topic is small, as only one study performed muscle biopsies (116) and no information on muscle proteins or cell signaling was presented in this study. Thus, most of the studies reviewed provided indirect evidence in healthy controls or blood biomarkers that are associated will protein synthesis and muscle mass gains.

10.1 Anabolic and Catabolic Hormone Responses to ST. The normal hormone response to acute resistance exercise and to ST in both young and older men and women have been well cataloged (112). Briefly, the typical profile shows a large surge in the anabolic hormones immediately following acute exercise with few changes with ST. The

increase in the androgens can activate transcription and translational events leading to increased protein synthesis and accretion of muscle mass. While ADT chronically suppresses testosterone, the acute and training hormonal responses with ST have not been extensively studied. There appear to only be two reports on this topic (60, 116). Galvao *et al.* (60) examined the acute and chronic hormone response to ST. Testosterone, as expected was highly suppressed and did not change in either instance. Growth hormone and IGF-1 showed small but not significant increases with an acute exercise bout and no changes with ST. Cortisol and C-reactive protein levels were unchanged in all instances while tumor necrosis factor alpha increased significantly with acute ST. Kvorning et al (116) observed that both free and total testosterone significantly decreased in the ADT group with a bout of resistance exercise, albeit the declines were rather small, and the placebo group underwent a large increase. Growth hormone increased significantly in both groups immediately after the training session and was no longer significantly elevated 15 minutes after cessation of exercise. No between group differences were noted. However, the growth hormone response with training was altered between groups, as men on LHRHa had a different response before training. The authors conclude that testosterone is of paramount importance for developing and maintaining muscle mass and strength with ST. This may conflict with data from Galvao et al (64) as the gains in FFM they report with combined training are similar to what is reported in the placebo group. Because Galvao and colleagues have only a non-exercise control (and no non-ADT + ST group), more definitive conclusions cannot be drawn without further study.

10.2 Cell Signaling and Protein Synthesis with ST. There is little doubt that testosterone administration can produced gains in muscle mass and strength. This was

elegantly demonstrated when 40 men were randomly allocated into one of four groups, no exercise, testosterone with no exercise, placebo plus exercise, and testosterone plus exercise for ten weeks. Supraphysiological doses of testosterone (600 mg/week) were associated with gains in strength, FFM, and muscle cross-sectional area and these gains are compounded when undergoing ST (14). Furthermore, testosterone plays a role in protein synthesis, as the addition of exogenous testosterone increases fractional synthesis rates (FSR) (54, 200) and its suppression leads to declines (136).

Presently, the signaling mechanisms that may be responsible for the accretion of muscle mass in men on ADT is unclear (15). Some (54, 200, 214), but not all (136) evidence suggests that testosterone may interact with IGF-1, via the PI3K-AKT-mTOR pathway, to activate p70S6K and protein synthesis (17, 69). However, the role of AKT as a signaling marker of increased protein synthesis in humans has recently been called into question as AKT phosphorylation has been observed with no changes in protein synthesis (134). Moreover, because a functional IGF-1 receptor is not necessary for muscle hypertrophy to occur (188), testosterone and its potential effects on IGF-1 may be beneficial rather than essential for increases in protein synthesis in response to mechanical overload. While there is ambiguity surrounding the exact signaling pathways associated with increased FSR, the literature strongly implicates a centralized role for mTOR (17, 69). For example, an increase in mTOR phosphorylation and FSR were observed following acute resistance exercise (47, 48) while rapamycin treatment to inhibit mTOR blocked the increase in FSR (49). Similarly, inhibition of the stretch activated channels during muscle contraction decreased activation of p70S6K (189). Protein supplementation can also stimulate the muscle hypertrophy mechanisms, as

branched chain amino acids (BCAA) alone or combined with resistance exercise in both young and older adults led to increases in FSR and p70S6K phosphorylation, respectively (77, 105, 205). Persistent daily supplementation of BCAA over three months also increased FSR and FFM in older women (45).

Testosterone may also inhibit the catabolic effects of the GR (106) and atrogin-1 gene expression (219). Recent data indicates that there may be crosstalk between mTOR and the GR. In rat gastrocnemius and soleus muscle, dexamethasone treatment was used to activate the GR and increased transcription of REDD1, atrogin-1, MuRF1, FoxO1, FoxO3, myostatin, and KLF15, and inhibition of mTOR activity was observed (182). The effects were more prominent in the fast-twitch gastrocnemius fibers. Activation of mTOR with amino acid supplementation blocked GR induction of its target genes which were rescued when mTOR was inhibited by rapamycin (182). Thus, the loss of the testosterone with ADT and the declines in FFM could be explained by a shift in the dynamic balance between protein synthesis and breakdown. In this regard, ST may be able to reduce the deleterious effects of ADT on muscle through activation of mTOR and thereby increasing protein synthesis (48). The inhibition of mTOR completed ablated the increase in FSR with acute resistance exercise (49), implicating this as a plausible pathway to explain increases in FFM with ST in individuals with very low testosterone, e.g., in women or in men on ADT.

11. Summary

There appears to be a racial disparity regarding the prevalence and mortality rates of PCa. The exact cause of these differences remains elusive. Some studies implicate biological differences between the races, whereas others that control for income and

access to health care suggest otherwise. Race may also affect the prescribed treatment options, as black men are less likely to receive aggressive treatment, including ADT.

ADT has been associated with a number of adverse effects, notably the loss of musculoskeletal health and physical function along with altered body composition (Table 9). Minimizing the side effects of PCa treatment is crucial in order to enhance QoL, as simply living longer is not an acceptable outcome.

One of the most effective complementary therapies to offset ADT treatment is ST. Most exercise intervention studies are well tolerated by the patients and have demonstrated significant improvements in muscle strength and function, physical function, and QoL, and a few also reported of increases in FFM. Many of the improvements are on par with changes observed in healthy older adults with ST. Future investigations should focus on the ability of ST to reverse ADT-induced muscle atrophy and the potential mechanisms by which the increase in muscle mass is occurring. Additional areas of study could also in include interventions to reversed ADT-induced BMD loss and the high incidences of insulin resistance and metabolic syndrome in PCa patients. This additional information will help guide clinicians in exercise prescription designed specifically to reduce comorbidities and particular side effects to enhance QoL in men undergoing ADT for PCa.

Table 9. Effects of Aging, ADT, and Strength Training on Select Physiological Traits.

Trait:	**Effect of Aging**	Refs	**Effect of ADT¶**	Refs	**Effect of ST on ADT**	Refs	**Research hypothesis**
Strength	▼	(58, 122, 141, 161)	▼▼	(6, 65, 177, 211)	↑	(61, 74, 176, 177)	↑
Muscle Mass	▼	(58, 118, 122)	▼▼	(20, 62, 65, 184-186, 201)	↔, ??	(61, 74)	↑
Power	▼	(122, 141, 161)	??		??		↑
Endurance	▼,▲	(89, 161, 164)	↔	(65, 176, 177)	↑	(61, 176)	↑
Fat	▲	(13, 88, 118)	▲▲	(6, 20, 33, 40, 62, 65, 177, 184-186, 201)	↔	(61, 176, 177)	↔
IMF	▲	(143, 220)	??		??		↔
SCF	▼	(88, 143)	??		??		↔
BMD	▼	(121)	▼▼	(6, 33, 62, 65, 72, 108, 157, 178, 217)	↔	(61)	↔
Fatigue	▲	(147)	▲▲	(62, 82, 103, 119, 177, 190)	↓	(176, 177)	↓
ADL	▼	(122, 147)	▼▼	(35, 62, 65, 103, 125)	↑	(61, 74)	↑
QoL	▼	(149, 209)	▼▼	(6, 40, 82, 103, 151, 190)	↑	(74, 176, 177)	↑

¶ Effect of ADT compared with the Effect of Aging

ADT = Androgen Deprivation Therapy; IMF = Intermuscular Fat; SCF = Subcutaneous Fat; BMD = Bone Mineral Density; ADL = Activities of Daily Living simulations; QoL = Quality of Life

▲, Increase with age/ADT; ▼, Decrease with age/ADT; ↑, Increase with ST, ↓, Decrease with ST, ↔, No change with ST; ??, unknown

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