A Cross-Sectional Study Comparing Body Composition, Bone Mineral Density, Strength, Power, Quality of Life Between Short-term and Long-term Breast Cancer Survivors

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A CROSS – SECTIONAL STUDY COMPARING BODY COMPOSITION, BONE MINERAL DENSITY, STRENGTH, POWER, QUALITY OF LIFE BETWEEN SHORT-TERM AND LONG-TERM BREAST CANCER SURVIVORS

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CHAPTER I: ABSTRACT

Abstract

The purpose of this study was to compare body composition, bone mineral density (BMD), strength, muscle power, and quality of life in short-term breast cancer survivors (ST-BCS) and long-term breast cancer survivors (LT-BCS). METHODS: Body composition and BMD measures were completed on 17 ST-BCS (57.2 ± 9.3 years) and 26 LT-BCS (62.0 ± 7.2 years) via dual energy X-ray absorptiometry (DXA). Upper body strength was measured by a 1 repetition maximum chest press and lower body strength was assessed using BIODEX isokinetic and isometric leg extension and flexion tests. Muscle power was measured by a Tendo unit and quality of life was assessed by the SF-36 questionnaire. RESULTS: Mean time since completion of primary treatment was 7.7 ± 7.1 years. Time since treatment completion for ST-BCS and LT-BCS was 1.8 ± 1.1 years and 11.5 ± 6.7 years, respectively. No significant differences were found between ST-BCS and LT-BCS in measures of body composition, BMD, strength, muscle power, or quality of life. A positive correlation was observed between time since completion of treatment and lumbar spine BMD (r=.38). CONCLUSION: Our findings show that ST-BCS and LT-BCS experience similar rates of changes in body composition, BMD, strength, power, and quality of life, regardless of time since the completion of treatment. This may be due to the similarity in menopausal age between the ST-BCS and LT-BCS in this study. Both may have experienced the same rate of age-related changes since the onset of menopause, as well as similar changes during the cancer treatment period. More research is needed to determine what factors influenced the changes specifically in the lumbar spine BMD over time. Furthermore, more research is needed comparing ST-BCS and LT-BCS to determine whether the effects of treatment persist over time and for how long.
CHAPTER II: INTRODUCTION

Introduction

Breast cancer affects 1 in 8 women throughout their lifetime. Both genders can develop breast cancer, however it is more common in women than men. Increases in life expectancy have resulted in a greater incidence of cancer, however advances in medicine has also increased the rate of survival for most cancers (“Breast Cancer,” 2015). Breast cancer survivors (BCS) experience lasting side effects from treatment that affect body composition, bone mineral density (BMD), strength, power, and quality of life (QOL).

Breast cancer is primarily ductal or lobular. Ductal breast cancer originates in the milk duct, whereas lobular breast cancer originates in the glands that produce milk. Breast cancer can metastasize and spread to other tissues through blood and lymph. Stages of breast cancer range from Stage 0 to Stage IV, with Stage IV being the most invasive cancer.

Diagnosis of breast cancer can only be made by testing a biopsy of the affected tissue. Mammograms, ultrasounds, and Magnetic Resonance Imaging (MRI) identify unusual masses in breast tissue that may be biopsied to prove cancerous. Once diagnosed, breast cancer is identified by stages determined by tumor size, node involvement, and the extent of spreading to other tissues (Peart, 2015).

Treatment of breast cancer includes surgical removal, chemotherapy, radiation, and hormone therapy. Surgical removal can be a lumpectomy that conserves breast tissue or a mastectomy that completely removes all breast tissue and affected lymph nodes. Most breast cancers are treated with this method along with another treatment. Chemotherapy is a drug or combination of drugs that slow or stop the growth of cancer by interfering with cellular replication processes (Peart, 2015). Similarly, radiation causes damage to the DNA within cells to prevent replication. Both chemotherapy and radiation affect healthy, non-cancerous cells as well as the cancer cells, but healthy cells are able to repair DNA. Hormone therapy is interference with the body’s normal production of a hormone or the cells’ ability to respond to a hormone. In the case of some breast cancers, cancerous cells respond to the hormone estrogen.
Medications like aromatase inhibitors and selective estrogen receptor modulators prevent the body from making estrogen to slow the growth of cancer.

Breast cancer treatments have side effects that cause changes in body composition, BMD, strength, power, and quality of life. Women who undergo breast cancer treatment lose muscle mass at a greater rate than healthy women (McDonald, Bauer, & Capra, 2011). Treatment also causes decreased BMD. A study by Conde et al. reported that BCS had a higher rate of osteoporosis, 27.2%, compared to postmenopausal women who have not had cancer, 19.4% (2012). Because BCS lose muscle mass, strength and power also decrease following treatment. Christenson et al. (2014) found that BCS have 20-30% lower strength in the performance of seven different measures of upper body strength compared to those who have not had breast cancer. Quality of life after breast cancer treatment has been shown to both increase and decrease depending on which treatment method is used, as well as each individual’s coping mechanisms. Chemotherapy is associated with a lower QOL, but some studies report that BCS can have comparable QOL to those who have not had breast cancer and greater QOL than those suffering from other chronic diseases (Bloom, Stewart, Chang, & Banks, 2004).

There is a lack of research comparing body composition, BMD, strength, power and QOL in short-term BCS and long-term BCS. More research is necessary to determine whether these changes due to treatment persist, improve, or worsen over time.

**Purpose**

The purpose of the study was to identify differences in body composition, BMD, strength, power, and QOL between short-term BCS (ST-BCS; within 5 years of primary treatment completion) and long-term BCS (LT-BCS; greater than 5 years since primary treatment completion).

**Specific Aims**

This study was designed to try and answer the following specific aims:

1. To compare body composition (lean mass, fat mass, body fat percentage) in ST-BCS and LT-BCS.

**Hypothesis:** The ST-BCS will have higher lean mass and lower fat mass and body fat percentage mass compared to LT-BCS.
2. To compare total and regional (lumbar spine, femur, and forearm) BMD in ST-BCS and LT-BCS.

   **Hypothesis:** The ST-BCS will have greater BMD measures compared to LT-BCS.

3. To compare upper body and lower body strength and power in ST-BCS and LT-BCS.

   **Hypothesis:** The ST-BCS will have higher strength and power compared to the LT-BCS.

4. To compare QOL measures assessed using the Rand Short-Form 36 (SF-36) in ST-BCS and LT-BCS.

   **Hypothesis:** The ST-BCS will have lower QOL scores compared to the LT-BCS.

**Assumptions**

1. All participants were truthful in their responses to medical history and QOL questionnaires.
2. All participants performed to the best of their abilities during strength and muscle power tests.
3. All equipment and testing procedures provided valid and reliable measurements during the course of the study.

**Delimitations**

1. BCS diagnosed with stage 0-III cancer who have completed primary treatment for breast cancer were eligible to participate in the study. Women diagnosed with stage IV breast cancer, BCS who have not undergone treatment or are currently undergoing treatment, and male BCS were ineligible to participate.

2. Women with chronic health conditions, such as hypothyroidism or hyperthyroidism, uncontrolled hypertension (>160/100 mmHg), uncontrolled diabetes, and uncontrolled heart disease were not eligible to participate in the study.

3. BCS who have completed treatment or had surgery less than 3 months prior to the study were ineligible to participate.

**Limitations**

1. All participants were recruited from the Tallahassee, FL area, so results of the study cannot be generalized to ST-BCS and LT-BCS living in other areas.
2. The results of the study cannot be generalized to BCS who have had stage IV breast cancer because BCS participants had stage 0-III breast cancer.

3. All BCS participants in the study are female. Results are not generalizable to male BCS.

**Definition of Terms**

1. **Adjuvant Chemotherapy** – medicine administered following the surgical removal of cancer to further prevent its recurrence (hopkinsmedicine.org)

2. **Aromatase Inhibitor** – a type of drug that indirectly suppresses the production of the hormone estrogen by blocking its enzyme, aromatase (breastcancer.org)

3. **Body Composition** – proportion of fat, muscle, and bone masses that make up an individual’s body (dictionary.com)

4. **Breast Cancer** – breast cancer is uncontrolled growth of cells in milk ducts (ductal cancers) or milk glands (lobular cancers); invasive breast cancer is the spread of cancerous cells from the initial source, either duct or glands, to other surrounding tissue (cancer.org)

5. **Estrogen** – a female hormone responsible for female secondary sex characteristics and regulation of menstrual cycle, as well as the maintenance of bones (medical-dictionary.thefreedictionary.com)

6. **Long-Term Breast Cancer Survivor (LT-BCS)** – a woman who has completed treatment for breast cancer greater than 5 years

7. **Menopause** – menopause is the period in a female’s life in which the menstrual cycle has ended, identified by 12 months without a menstrual period (mayoclinic.org)

8. **Osteoblast** – cell responsible for producing a matrix for the mineralization of bone during bone formation and remodeling (medicinenet.com)

9. **Osteoclast** – a multinucleated cell responsible for the resorption of bone (medicinenet.com)

10. **Osteoporosis** – a condition in which bones have become weakened and bone mass falls 2.5 standard deviations below the average bone mass of a young adult (endocrineweb.com)

11. **Physical Function** – the ability to accomplish everyday tasks, such as folding laundry, standing up from a seated position, or reaching items on a shelf, with ease (Zhang, Brown, and Schmitz, 2016)
12. **Quality of Life (QOL)** – a multifaceted assessment of one’s perception of physical, mental, and social well-being relevant to his or her cultural context and personal values (World Health Organization)

13. **Radiation Therapy** – a type of cancer treatment that kills cancer cells using X-rays, protons, or other types of energy (mayoclinic.org)

14. **Sarcopenia** – age-related loss in muscle mass (merriam-webster.com)

15. **Selective Estrogen Receptor Modulator** – a type of drug that binds to estrogen receptors and acts as an estrogen agonist or antagonist depending on the tissue (medical-dictionary.thefreedictionary.com)

16. **Short-Term Breast Cancer Survivor (ST-BCS)** – a woman who has completed treatment for breast cancer within the past 5 years
CHAPTER I: LITERATURE REVIEW

With current breast cancer trends, 1 in 8 women will develop invasive breast cancer at some time in their lifetime (“Breast Cancer,” 2015). Breast cancer affects both males and females, but it is significantly more prominent in the female population. Breast cancer is a slowly growing cancer, so it is not often identified until later in life. While 75% of breast cancer survivors (BCS) are 60 years old or older, it can affect women as early as their 20s (Desantis et al., 2014). Increases in life expectancy have resulted in a greater incidence of cancer, however advances in medicine has also increased the rate of survival for most cancers (“Breast Cancer,” 2015). Based on the population projection of 2024, nearly four million BCS will reside within the United States (Desantis et al., 2014). Many BCS live with ongoing symptoms from their treatments, which may include physical limitations and emotional instability that affect their participation in daily activities (“Breast Cancer,” 2015).

Cells within the tissues of the body regenerate and repair themselves following a cell cycle. The cell cycle involves multiple checkpoints to determine whether the cell is fit to divide by mitosis. Mitosis is a process in which the cell makes an exact copy of itself to replace damaged or aged cells, or develops new tissue. A normal cell stops division if a gene determines the cell is unfit to divide or if signals from nearby cells indicate it would invade adjacent tissues. Cells become cancerous when they lose the ability to control their rate of growth and spread. Cancer is caused by mutations in proto-oncogenes and tumor suppressor genes, genes which control the rate of cell division (Cooper, 2000). Proto-oncogenes signal a cell to divide and tumor suppressor genes signal a cell to stop dividing. These mutations are most often acquired mutations, but can be inherited (Cooper, 2000). Cells that undergo cellular division more frequently, such as those in the gastrointestinal tract or the skin are more likely to develop mutations. Uncontrolled cell division gives rise to tumors that may be benign or malignant. Benign tumors are not life threatening, but may increase risk of developing cancer in the future (Cooper, 2000). Tumors become malignant when they begin to spread into surrounding tissues.

Breast cancers are primarily carcinomas. Carcinoma is cancer that originates within epithelial cells. Epithelial cells are cells in the inner layer of tissues. More specifically, breast cancers are often
adenocarcinomas, cancer within epithelial cells of glands (“Breast Cancer,” 2015). Breast tissue is rich in glandular epithelial cells due to its function of milk production. Mammary glands produce milk that is delivered through milk ducts. These tissues are sources of frequent cell division, which increases the chance of developing a mutation. The majority of diagnosed breast cancers are ductal breast cancer and lobular breast cancer. Less common forms of breast cancer include inflammatory breast cancer, Paget disease of the nipple, phyllodes tumor, and angiosarcoma (“Breast Cancer,” 2015).

Ductal breast cancer is cancer originating in the milk duct. When cells that appear cancerous, but have not invaded other tissue are present in ductal tissue, it is called ductal carcinoma in situ (DCIS) (Simpson, Gale, Fulford, Reis-Filho, & Lakhani, 2003). Ductal carcinoma in situ is pre-cancerous and is the easiest to cure. When cells spread through the milk duct into bordering fatty tissue, it is called invasive ductal carcinoma (IDC). When cancerous cells have reached this severity, the cancer can metastasize by spreading through blood and lymph. This is the most common form of invasive cancer; 80% of invasive cancers are IDC (“Breast Cancer,” 2015). Invasive lobular breast cancer (ILC) originates in the lobules, glands that produce milk. It can spread to other tissues like IDC. Ten percent of invasive breast cancers are ILC (Simpson et al., 2003).

Although less common, other forms of breast cancer can be equally or more life threatening than ductal and lobular breast cancers. Inflammatory breast cancer (IBC) presents with no tumor, but skin may appear red, warm, thick, and pitted, similar to the appearance of an orange peel (“Breast Cancer,” 2015). Often mistaken for an infection, it is caused when cancer cells obstruct the flow of lymph at the skin’s surface (“Breast Cancer,” 2015). Pagets disease of the nipple is cancer associated with DCIS or IDC that spreads from the duct to the skin of the nipple and areola (“Breast Cancer,” 2015). Phyllodes tumor is a tumor within the stroma, or connective tissue, of the breast. Angiosarcoma is a quickly spreading cancer that originates in cells lining blood vessels and lymphatic vessels. Complications with previous radiation treatments or lymphedema can lead to angiosarcoma (“Breast Cancer,” 2015).

Genetic predispositions can increase the risk of developing breast cancer. Being a woman, aging, and having a family history of breast cancer can increase a person’s risk of developing breast cancer.
Breast cancer is often discovered during regularly scheduled mammograms, although false-positive and false-negative results are common. Patients with dense breasts are more likely to get an inaccurate result (Wang, 2007). A mammogram is an X-Ray targeted specifically on the breast. Manual breast exams can also identify suspicious masses in breast tissue. Ultrasound and MRI are other methods of imaging abnormalities. Ultrasound uses sound waves to identify solid masses in tissue. Sound waves will bounce off of breast tissue at different rates depending on the density of the tissue, producing a sonogram that may show possible abnormalities (Wang, 2007). MRI is used on women who have been identified as high risk for breast cancer because it is more sensitive, yet more expensive (Wang, 2007). MRI involves entering a machine, in the supine position, while it scans the body using radio waves and magnets to create an image of the soft tissue within the body (“Breast Cancer,” 2015). While these techniques may identify
irregularities, breast cancer is not confirmed until a biopsy of the tissue is positive for cancerous cells (“Breast Cancer,” 2015).

Once diagnosed, breast cancer severity is identified by stages, which are determined by cancer size and the extent of spread to other tissues (Peart, 2015). Stage 0 is when abnormal cells are present in breast tissue that may become cancer, but have not become cancerous yet (“Stages of Breast Cancer,” 2017a). Stage I is a tumor of less than 2 centimeters without spread to other tissues. Stage II is a tumor that is larger than 2 centimeters and may or may not have spread to other tissues. Stage III is a tumor of any size that has begun to spread into lymph nodes. Stage IV is the most advanced stage of breast cancer in which the cancerous cells have spread into distant tissue through lymph nodes (“Stages of Breast Cancer,” 2017b).

Another classification that helps doctors treat breast cancer is identifying hormone receptors on the cancer cells after taking a biopsy. Estrogen and progesterone are hormones that regulate the ovarian cycle, but can also increase the growth of breast cancer cells. Breast cancer cells that have estrogen receptors or progesterone receptors on their cell membranes are labeled ER-positive (ER+) or PR-positive (PR+), respectively (“Breast Cancer,” 2015). A biopsy will also show whether the cancer cells are producing too much of the HER2 protein, a protein that leads to more aggressive growth (“Breast Cancer,” 2015). Hormone information allows a physician to better target cancer cells during treatment.

**Breast Cancer Treatments**

The stage of cancer and severity determines the treatment plan. Treatment plans are likely to include a combination of techniques to ensure that all of the cancerous cells are removed or killed. Treatments include surgical methods, radiation, chemotherapy, and hormone therapy.

Surgical removal of cancerous cells in the breast can be a tissue conserving lumpectomy, in which only the cancerous mass and enough clearance of healthy tissue surrounding it are removed (“Breast Cancer,” 2015). Women under the age of 40 years and women who have more progressive tumors are more likely to choose to have a mastectomy, complete removal of the breast tissue and affected lymph nodes (Desantis et al., 2014). Along with the removal of the cancerous mass, some or all lymph nodes are
removed and biopsied to determine the extent of the spread (Zurrida & Veronesi, 2015). Fifty-nine percent of those who have been diagnosed with stage I or stage II elect to have a lumpectomies, whereas 59% of those who have been diagnosed with stage III or stage IV receive mastectomies (Desantis et al., 2014). For both types of surgeries, the patient will undergo general anesthesia for a procedure that may last two to three hours (“Breast Cancer,” 2015). A mastectomy requires an overnight stay while a lumpectomy is completed in an outpatient setting without an overnight stay (“Breast Cancer,” 2015). Prior to a surgical procedure, women must discuss with their doctor whether or not they will be pursuing breast reconstruction. Reconstructive surgery uses saline or silicone inserts, or autologous tissue to restore the breast area to its normal shape. It can be performed at the same time as a mastectomy or lumpectomy, or after the procedure (“Breast Cancer,” 2015).

Symptoms following surgery include soreness, stiffness, and lymphedema in the affected arm (“Breast Cancer,” 2015). Lymphedema is the result of lymph node damage or removal. Lymph nodes carry fluid throughout the body, without them fluid builds up causing uncomfortable or painful swelling (Lawenda, Mondry, & Johnstone, 2009). Twenty to thirty percent of women who elect to have surgical removal of their breast cancer experience post mastectomy pain syndrome, a chronic pain and tingling of the breast and armpit areas that does not improve over time (Gärtner R, Jensen MB, Nielsen J, Ewertz M, Kroman N, 2002).

Radiation can be a primary or adjuvant breast cancer treatment. Adjuvant treatment is a treatment that accompanies another form of treatment, such as following the surgical removal of breast cancer (Peart, 2015). Radiation as the primary or only form of treatment can be effective in the earliest stages of breast cancer. This form of treatment provides a specific and localized treatment to the breast and torso areas. Exposing tissue to radiation causes damage to DNA within cells. There is damage to both normal cells and cancerous cells, however normal cells have the ability to repair their DNA (Peart, 2015).

External radiation uses high energy electromagnetic radiation from gamma rays, x-rays, electrons, or neutrons in a beam specifically targeting breast tissue (Peart, 2015). An oncologist prescribes the dose of radiation and length of treatment. Treatment lengths are typically 5 days per week for 6 to 8 weeks.
Internal radiation uses a radioactive source close to the tumor, which increases the specificity of the treatment and prevents unintended damage to surrounding normal tissue (Peart, 2015). Internal radiation delivers a more intense dose of radiation and can be completed in 3 to 5 days (Peart, 2015). A balloon is inserted near the tumor bed after a lumpectomy. During treatments, radioactive material is inserted into the balloon through a catheter and directed to multiple points within the balloon. After each session, the radioactive material is removed, and after the treatment has been completed, the balloon is removed (Peart, 2015).

Radiation treatment does not cause immediate side effects, but women undergoing external radiation treatment may develop side effects 3-4 weeks into treatment or months to years later (Peart, 2015). These side effects include fatigue, swelling, heaviness in breast, and a sunburned appearance (Peart, 2015). Internal radiation can cause the same side effects as external radiation, as well as infection and breakdown of fat tissue within the breast. Both forms of radiation result in possible weakness and rib fracture (“Breast Cancer,” 2015).

Like radiation, chemotherapy treats cancer by damaging the DNA of cancer cells. It can be used as primary treatment, adjuvant treatment, or neoadjuvant treatment, which is treatment administered before the primary treatment. Although there is not a significant benefit to neoadjuvant chemotherapy over adjuvant chemotherapy in the likelihood that the cancer will return, neoadjuvant chemotherapy may shrink a cancerous mass, making an easier or less invasive surgical removal of the cancer (“Breast Cancer,” 2015). Treatment plans including chemotherapy were given to nearly 39% of women with early stage breast cancer and to nearly 74% of women with late stage breast cancer according to data from the National Cancer Database in 2011 (Desantis et al., 2014). Chemotherapy is a drug, or combination of drugs, that slow or stop the growth of cancer by interfering with cellular replication processes (Peart, 2015). Alkylating agents, anthracyclines, mitotic inhibitors, and antimetabolites are a few of more than 90 chemotherapy drugs that target cells at different stages of the cell cycle to halt the replication process (Peart, 2015; Zurrida & Veronesi, 2015).
Chemotherapy treatment lasts 3 to 6 months and is administered in cycles followed by rest periods so the body has time to heal between treatments. It can be administered in multiple ways. The drugs can be taken orally, administered intravenously, applied as a lotion, or injected within the muscle (Peart, 2015). A semi-permanent access device is inserted to administer chemotherapy intravenously to most breast cancer patients. These portals can be inserted non-surgically or surgically depending on the type and placement of the device required for treatment (Peart, 2015).

Chemotherapy is a systemic treatment and cannot target specific tissues, so its effects are detrimental to both cancerous and normal tissue. Bone marrow is largely affected by chemotherapy, decreasing the number of red blood cells, white blood cells, and platelets (Peart, 2015). Fewer white blood cells diminish the body’s ability to fight off infections, fewer red blood cells decrease the body’s ability to transport oxygen to tissues, and fewer platelets lead to increased bruising (Peart, 2015).

Symptoms of chemotherapy drugs are nausea, vomiting, diarrhea, constipation, mouth sores, decreased appetite, and temporary alopecia (Zurrida & Veronesi, 2015). A more severe side effect of chemotherapy is cardiomyopathy from anthracyclines and some other drugs (“Breast Cancer,” 2015). Another side effect of chemotherapy is the decline of mental abilities, referred to as “chemo brain”. Women who receive chemotherapy may struggle with concentration and memory for years following treatment (“Breast Cancer,” 2015).

Over 3 out of 4 breast cancers are ER+ (“Hormone Therapy for Breast Cancer,” 2017). A treatment option for breast cancer positive for estrogen or progesterone receptors is hormone therapy. Hormone therapy is the interference with the body’s production of a hormone or the cells’ ability to respond to a hormone (“Hormone Therapy for Breast Cancer,” 2017).

Halting estrogen production involves targeting either the ovaries that produce estrogen or an enzyme involved in the production of estrogen. Ovaries produce estrogen, increasing growth in ER+ cancer cells. A procedure called an ovarian ablation (OA) can be performed to stop the function of the ovaries. Ovarian ablation is performed on premenopausal BCS. The ovaries are either surgically removed or treated with radiation. Ovarian function can temporarily be stopped with gonadotropin-releasing
hormone agonist medication (“Hormone Therapy for Breast Cancer,” 2017). Gonadotropins, luteinizing hormone and follicle stimulating hormone signal the ovaries to produce estrogen. Interfering with gonadotropin function will inhibit estrogen from being produced.

Ovarian ablation initiates the onset of menopause early. Women who naturally reach menopause earlier have higher risk for cardiovascular disease, osteoporosis, and cognitive decline (Gold, 2011). Side effects from OA are early menopausal symptoms, such as osteoporosis, hot-flashes, night sweats, vaginal dryness, and mood swings (“Breast Cancer,” 2015). Early onset of osteoporosis in BCS who have had an OA is the result of decreased BMD (Nourmoussavi et al., 2017)

Another way to stop the production of estrogen is through aromatase inhibitors or selective estrogen receptor modulators (SERM) in the form of a pill after surgically removing cancerous tissue. Aromatase is an enzyme that converts androstenediones to estrogen in the adrenal glands and ovaries (“Hormone Therapy for Breast Cancer,” 2017). Aromatase inhibitors are the preferred adjuvant treatment for postmenopausal women with hormone positive breast cancer, because aromatase inhibitors can only inhibit aromatase in fat tissue, not in the ovaries. (“Breast Cancer,” 2015; Roberts, Rickett, Greer, & Woodward, 2017). SERMs act on estrogen receptors as an agonist or antagonist depending on the tissue (Jameera Begam, Jubie, & Nanjan, 2017). SERMs mimic estrogen on receptors in bone, liver, and cardiovascular tissue, but block receptors on breast and uterine tissue (Jameera Begam et al., 2017). A popular SERM is the drug tamoxifen. Tamoxifen is used as a preventative treatment in women who have a high risk of developing breast cancer, or as an adjuvant treatment to halt or reverse the growth of malignant tumors in the breast (“Breast Cancer,” 2015). It is prescribed for 5 to 10 years following surgery to prevent the cancer from returning. The National Cancer Institute discovered that the use of tamoxifen decreased the number of cases of invasive breast cancer by 50% when used for up to 5 years (Peart, 2015).

Women who are treated with tamoxifen can experience a variety of side effects, some of which can seriously impact health. Reported side effects include nausea, depression, hair thinning, headaches, and weight gain (Peart, 2015). The use of tamoxifen is also associated with an increase of endometrial cancer and uterine sarcoma in menopausal women, as well as deep vein thrombosis and pulmonary embolism
(Peart, 2015). Tamoxifen decreases BMD in premenopausal women but strengthens bones in postmenopausal women. Other SERMs have been marketed to have fewer side effects but have also shown to be less effective.

Compared to tamoxifen, aromatase inhibitors have fewer side effects. The primary side effect from aromatase inhibitor treatment is the weakening of bones. Consequently, many women who are prescribed aromatase inhibitors are also prescribed additional drugs to help counteract the effect aromatase inhibitors have on BMD (“Breast Cancer,” 2015). Other side effects include muscle pain and joint stiffness. Many BCS who have been treated with aromatase inhibitors experience myalgia, fibromyalgia, and arthralgia (Roberts et al., 2017). Some of these side effects may be lessened, by substituting a different aromatase inhibitor for the remainder of treatment.

**Cancer Treatment Effects on Body Composition and Bone**

Natural aging leads to changes in body composition and BMD. Breast cancer survivors experience more pronounced negative changes because of the effects of their treatments. The body undergoes many changes in response to aging. A prominent change is a decrease in muscle mass. An individual’s muscle mass peaks between the ages of 20 and 40 years (Lauretani et al., 2003). In a healthy adult, 40%-50% of the body is muscle (Christensen et al., 2014). After muscle mass peaks, it gradually declines with age. Muscle mass loss over the age of 50 years is typically 1-2% per year (Curtis, Litwic, Cooper, & Dennison, 2015). The occurrence of muscle loss related to aging is termed “sarcopenia”. An estimated 5-13% of people between the ages of 60 and 70 years are living with the effects of sarcopenia (von Haehling, Morley, & Anker, 2010). Weak muscles from sarcopenia can lead to falls, fractures, and disability.

Although men experience a more dramatic change in muscle mass, women are more susceptible to the effects of muscle loss because they begin to begin to lose muscle mass at an earlier age, have less muscle mass to begin with, and, on average, live longer than men (Horstman, Dillon, Urban, & Sheffield-Moore, 2012). Following menopause, a woman’s testosterone and estrogen levels are about 80% lower than her premenopausal state (Horstman et al., 2012). Testosterone, a precursor to estrogen, and estrogen itself play a role in protein synthesis and muscle repair.
Breast cancer treatments decrease levels of estrogen at a greater rate than the natural decline. A twin study using estrogen hormone therapy showed that the twin who received treatment had greater walking speed and muscle power than the twin who did not receive treatment (Horstman et al., 2012; Ronkainen et al., 2009). In healthy adults, sarcopenia can be minimized or prevented by regular participation in moderate physical exercise or hormone therapy (Perez, 2011).

Women who undergo breast cancer treatment lose muscle mass at a greater rate than healthy women. A study that followed body mass changes in BCS one year after chemotherapy treatment showed 0.4 kg to 1.7 kg in losses of lean body mass (McDonald et al., 2011). Doxorubicin and cyclophosphamide, two drugs used in some chemotherapy regimens, have shown to reduce muscle tissue (Visovsky, 2006). Chemotherapy may also cause nausea or loss of appetite, limiting the amount of protein taken in to sustain muscle mass.

Side effects from surgical procedures, radiation, chemotherapy, aromatase inhibitors, and SERMs may limit a woman’s participation in physical activity due to pain, discomfort, or lack of energy. Disuse of muscles leads to muscle atrophy, which can interfere with daily activities.

An increase in fat mass or body fat is a shift in body composition that accompanies the decrease in muscle mass with aging. As healthy adults age their body fat will increase. Increases in body fat can put strain on joints, make activity uncomfortable, and lead to a greater incidence of disability. Women treated for breast cancer can experience increases or decreases in body fat depending on their response to treatment. A study by Pederson et al. (2017) examined changes in weight in a population of women with recently diagnosed breast cancer. The population showed that the percent change of weight ranged from -12.7% to 20.5% (Delmar; Pederson, 2017).

In healthy adults, bones undergo constant modification: degrading and rebuilding based on the needs of the body. Sex hormones regulate the activity of osteoclasts, osteoblasts, and osteocytes, specifically through estrogen receptors located on their membranes (Hadji, 2015). Osteoclasts are cells that break bone down, while osteoblasts are cells that rebuild bone. Osteocytes are cells located within the bone matrix that respond to osteoclast or osteoblast activity. Increased osteoclast activity results in greater
bone resorption, making bones less dense. Estrogen’s role in bone remodeling is to interfere with the activity of osteoclasts and increase bone strength.

Typically, women have increased bone turnover rate following the onset of menopause because of the decreased amount of sex hormones in circulation. Studies that treat postmenopausal women with hormone therapy have found that treatment increases both muscle mass and BMD (Horstman et al., 2012). Within the first 5 years following menopause, BMD can decline by up to 3% annually (Hirbe, Morgan, Uluçkan, & Weilbaecher, 2006).

Bone mineral density is measured using dual energy x-ray absorptiometry (DXA). The machine takes images of the tissue within the body to determine the percentage of lean body mass, fat mass, and BMD. Low BMD leads to osteoporosis, a disorder in which bones become fragile and fracture easily (Hadji, 2015). Bone mineral density scans compare BMD to the average 30-year-old woman. If a woman’s BMD is lower than 2.5 standard deviations below the mean, she is considered osteoporotic. Those who are osteoporotic have weak bones and are at a higher risk of falling and sustaining a serious injury.

A study gathered data comparing BMD in postmenopausal women and BCS found that BCS had a higher rate of osteoporosis; 27.2% of BCS fell into the category of osteoporotic, compared to only 19.4% of postmenopausal women. (Chen et al., 2005) Breast cancer treatments can affect BMD directly or indirectly through hormonal changes. Chemotherapy can indirectly affect estrogen levels by causing ovarian failure. A study by Shapiro et al. (2001) showed that women who experienced ovarian failure from chemotherapy resulted in a 4% lower spine BMD compared to women who did not experience chemoinduced ovarian failure. Chemotherapy can also directly affect BMD. For example, a study on male rats showed that treatment with the chemotherapy drug methotrexate resulted in a decrease in cancellous bone (Hirbe et al., 2006).

Other breast cancer treatments indirectly affect BMD through induced hormonal treatments. Ovarian ablation, aromatase inhibitors, and SERM treat ER+ breast. The SERM tamoxifen has different effects on BMD depending on whether the BCS was premenopausal or postmenopausal. Tamoxifen causes bone loss in premenopausal women, but decreases bone loss in postmenopausal women (Hirbe et al.,
A double blind study following postmenopausal BCS who had previously been treated with tamoxifen for 5 years followed by treatment with letrozole, an aromatase inhibitor, showed to have an annual decrease in BMD of 2.72% compared to BCS receiving a placebo instead of letrozole (Hirbe et al., 2006).

Maintaining BMD is possible with diet and regular weight-bearing exercise such as resistance exercises and high impact activity. Long term calcium and vitamin D supplementation has been shown to decrease the risk of developing osteoporosis by up to 20% (Hadji, 2015).

**Cancer Treatment Effects on Strength and Power**

Reduced muscle strength due to aging is termed “dynapenia.” Originally, a decline in muscle strength was attributed primarily to age-related muscle loss. Studies have shown that the decline in strength occurs at a much greater rate than the decline in muscle mass, attributing the part of the decline in strength to be related to muscle quality rather than size only (Kalyani, Corriere, & Ferrucci, 2014).

For example, a study found that the rate of muscle mass decline in healthy older adults was 2% per year, while the decline of muscle strength declined at a rate three times as large (Reid & Fielding, 2012). Possible explanations for decline in muscle strength can be explained by changes in neuromuscular activation and contractile proteins. Neurons initiate muscle contractions through action potentials. A neuron and the muscles it communicates with make up a motor unit. Deficiency in motor neurons may slow the propagation of a signal, taking a longer period of time for a motor unit to reach peak force, consequently diminishing the power of the muscle (Reid & Fielding, 2012). Furthermore, muscle fibers are made of contractile proteins that control the rate of contraction. Fast twitch muscle fibers adopt more characteristics of slow twitch muscle fibers, decreasing the power of the muscle (von Haehling et al., 2010).

Breast cancer survivors experience a more severe decline in muscle strength after treatment because treatment causes changes in levels of regulatory hormones and decreases in physical activity. Decreases in strength usually occur near the affected site, such as the chest and shoulder muscles (Merchant, Chapman, Kilbreath, Refshauge, & Krupa, 2008). A review done by Christenson et al. (2014)
found that BCS have 20-30% lower strength in the performance of seven different measures of upper body strength compared to women who have not had breast cancer.

Sex hormones play a role in mediating muscle strength. A study using female mice found that muscle power was significantly reduced 10-14 weeks after an ovariectomy. The authors considered the cause of lower force production to be attributed to a decreased number of cross bridges between the muscle fibers due to no significant change in muscle mass between the control mice and the treatment group (Lowe, Baltgalvis, & Greising, 2011). A human study compared postmenopausal women who were receiving hormone therapy with postmenopausal women who were not receiving hormone therapy. The study found a significant difference between the strength of the two groups, with those receiving hormone therapy having nearly 5% greater strength than those who did not receive hormone therapy (Lowe et al., 2011).

The aging population participates in increasingly less exercise, and disuse furthers the degradation of muscle and strength. A loss of muscle mass and strength can naturally lead to a loss in physical function. Ambulating, dressing oneself, reaching for an object on a shelf, preparing meals, and other everyday tasks become more physically tasking with age. Adults who maintain active lifestyles experience declines in physical function at a much slower rate. A study by Brach et al. (2004) found that older men and women who were moderately active (~400 kcal/d) scored higher on tests of physical function, including a timed 400 m walk, Health ABC performance battery, and Epidemiologic Studies of the Elderly battery.

Breast cancer survivors may have additional hindrances to physical function, such as lasting pain from a surgical procedure or lymphedema. Twenty to thirty percent of women experience post-mastectomy pain syndrome (PMPS), a syndrome linked to nerve damage as a result of surgery (“Breast Cancer,” 2015). Post-mastectomy pain syndrome can result in the loss of function in the affected arm over time (“Breast Cancer,” 2015). Furthermore, lymphedema greatly reduces range of motion in the arm of the affected side. Breast cancer survivors have also been shown to participate in less physical activity (Irwin et al., 2003).

Cancer Treatment Effects on Quality of Life
Quality of life is one’s satisfaction with life, which encompasses health, social fulfillment, and happiness. Chronic diseases, such as cardiovascular disease or obesity, and activity levels can be significant factors in QOL for the general population. The aging process typically includes a natural decline in cognitive and physical abilities and health. These declines can lead to decreased QOL.

Postmenopausal women characteristically report a lower QOL than premenopausal women. Symptoms of menopause can interfere with many aspects of life, including sexual satisfaction, sleep quality, and mood. Blumel at al. (2000) conducted a study on women who were premenopausal, perimenopausal, postmenopausal for less than 5 years, and postmenopausal for greater than 5 years and found that menopausal women consistently scored worse in vasomotor, psychosocial, physical, and sexual areas of the Specific Quality of Life Questionnaire for Menopause of Toronto University, although the study reported variable QOL experiences within cultural context and between different cultures (Blumel et al., 2000).

Breast cancer survivors experience additional stresses accompanying typical age-related declines. They may experience emotional struggles related to anxiety of the cancer returning, economic stress accumulated from treatment cost, and negative body image from the results of surgical removal of cancerous tissue. Some women may find coping methods to deal with the new set of cancer-related problems in their lives, such as social support, spirituality, and journaling (Shapiro et al., 2001). Women who do not use effective coping methods are likely to develop a lower QOL as a consequence of disease. Treatment type is also a major predictor of QOL in BCS. Those whose treatment included chemotherapy for a significant period of time are more likely to experience poorer QOL after treatment (Mols, Vingerhoets, Coebergh, & van de Poll-Franse, 2005).

Conversely, some studies support that BCS can have comparable QOL in women who have not had breast cancer and greater QOL in women suffering from other chronic diseases. For example, Dorval et al. (1998) conducted a study on 98 eight-year BCS compared to age-matched controls and found that there was no significant difference in functional abilities between both groups, except in movements specifically involving the BCS’s affected arm (Bloom et al., 2004). Furthermore, BCS may experience a renewed
perception of life that may be more positive than a woman who has not had cancer. Collins et al. (1990) found that cancer patients experienced more positive social interactions than those who have not had cancer (Collins, Taylor, & Skokan, 1990).

**Past Research on Short-Term Breast Cancer Survivors (ST-BCS) and Long-Term Breast Cancer Survivors (LT-BCS)**

Past breast cancer research has stratified survivors into ST-BCS and LT-BCS. Short-term breast cancer survivors are generally defined as women who have been diagnosed within the past 5 years and LT-BCS are women who are five or more years past initial diagnosis. The risk of cancer recurrence within the initial five-year period is considerably higher than after (Bloom et al., 2004).

**Body Composition and Bone**

There are few research studies directly comparing body composition and BMD in ST-BCS and LT-BCS. A study by Vagenas et al. (2015), showed that 57.8% of BCS gained weight between 6 and 18 months following surgery while 56.1% gained weight between 6 and 72 months following surgery. Of the BCS who gained weight between 6 and 72 months post-surgery, 79.7% gained more weight than age-matched non-cancer controls. Therefore, weight gain following breast cancer treatment may continue into long-term survivorship. Another study by Saquib et al. (2007) showed similar results with only 10% of BCS who gained significant weight after diagnosis returning to their pre-cancer weight four years after diagnosis. While not all studies have reported weight gain following treatment (Freedman et al., 2004; Kutyne, McCargar, Barr, & Hislop, 1999), changes in body composition have been observed regardless of change in weight. Irwin et al. (2005) found that 68% of BCS gained weight within three years of diagnosis with 74% gaining a mean of 3.6 ± 3.0% body fat. A higher disease stage, younger age, postmenopausal status, and lower physical activity levels were associated with greater increases in weight gain over three years (Irwin et al., 2005). Several studies have found decreases in lean mass following treatment, however, the farthest from diagnosis or treatment completion any study observed was one year post-treatment (Cheney, Mahloch, & Freeny, 1997; Demark-Wahnefried et al., 2001; Gordon, Hurwitz, Shapiro, & LeBoff, 2011; Kutyne, McCargar, Barr, & Hislop, 2016; Nissen, Shapiro, & Swenson, 2011). Therefore,
there is limited research observing long-term body composition changes in BCS beyond the first few years following treatment.

Bone can be affected both during and after the completion of breast cancer treatment. Shapiro et al. (2001) found a total of 7.7% loss of BMD within the first 12 months of since the start of chemotherapy treatment in women who experienced chemotherapy-induced ovarian failure. Vehmanen et al. (Vehmanen et al., 2001) observed significant long-term BMD losses within 2-5 years following treatment. The use of aromatase inhibitors is associated with higher incidences of fracture for up to 5 years after treatment (Body, 2012). However, further losses may not be observed after aromatase inhibitor use as Eastell et al. found that bone loss did not continue following the use of aromatase inhibitors or tamoxifen and 87.0% of participants on aromatase inhibitors and 44.4% on tamoxifen reported an increase in lumbar spine BMD two years (seven years-post primary treatment completion) after they finished use of the hormone treatment (Eastell et al., 2011). A study by Pawloski et al. (2013) found that LT-BCS were no more likely than matched ST-BCS to experience hip, wrist, or vertebrae fracture. Therefore, further losses in BMD due to cancer treatment may not occur following the treatment completion, and BCS may recover some losses as well.

**Strength and Power**

According to a study done by Iowa Women’s Health found that 32.7% of ST-BCS were unable to accomplish heavy household chores, compared to 20.5% of a non-cancer control (Schmitz, Cappola, Stricker, Sweeney, & Norman, 2007). Another study done by Sweeney et al. (2006) found that differences in function between LT-BCS was related more to the type of treatment rather than stage of breast cancer (Sweeney et al., 2006). Treatment with lumpectomy and radiation showed similar function to women who had never had cancer, whereas treatment with mastectomy resulted in more physical limitations. Shoulder strength and range of motion have been found to be maintained long-term following surgery (Merchant et al., 2008). These studies show decreases in strength and power in both ST-BCS and LT-BCS; however, they do not compare the two populations.

**Quality of Life**
A study by Weitzner et al. (1997) concluded that LT-BCS still experience emotional stress based on increased depression and lower QOL areas, based on a study of LT-BCS compared to low risk breast cancer screening patients. Yet, LT-BCS did show higher QOL in areas related to family functioning. A majority of research done on BCS focuses on all BCS as a whole, regardless of how far removed a woman is from treatment. There is a lack of research comparing body composition, BMD, strength, physical function, and QOL in ST-BCS and LT-BCS.
CHAPTER III: RESEARCH DESIGN AND METHODS

Overview

This study was a cross-sectional study identifying differences in body composition, BMD, strength, power, and QOL between ST-BCS and LT-BCS. Eligibility for participation in this study included BCS with stage 0-III breast cancer, who had completed treatment for at least three months or were three months post-surgery. Differences in body composition, BMD, strength, power, and QOL between the two populations were compared using independent t-tests.

Inclusion Criteria

Women between the ages of 40 and 75 years with stage 0-III breast cancer who completed breast cancer treatment for a minimum length of three months or completed surgery for a minimum of three months prior to participating in the study were eligible. Participants who were taking aromatase inhibitors or tamoxifen at the time of the study were eligible to participate because treatment regimens often last 5-10 years after primary treatment.

Exclusion Criteria

Participants who were diagnosed with stage IV breast cancer or who had active cancer were ineligible to participate in the study. Furthermore, women who were receiving breast cancer treatment or taking medication known to affect muscle or fat metabolism were also excluded from the study. Women who were living with other chronic health conditions such as uncontrolled hypertension (>160/100 mmHg), uncontrolled diabetes, and uncontrolled heart disease were excluded from the study. Women who participated in regular exercise were ineligible for participation in the study.

Data Collection

Laboratory Visit 1

The study was approved by the Institutional Review Board at Florida State University (Appendix A). Eligible participants met individually with the researchers at the Clinical Exercise Physiology Laboratory at Florida State University for the first of two visits. Visit 1 took approximately two hours and the second visit took approximately 1 hour. During the first visit, participants were briefed on the complete
details of the study and given the opportunity to ask questions and clarify information regarding the study.

If participants agreed to participate, they completed the informed consent (Appendix B). After completing the informed consent, participants completed a medical history questionnaire and the Rand SF-36 to measure QOL (Appendix C).

Body mass index (BMI) was calculated using height and weight measurements. The analysis of body composition (lean mass, fat mass, body fat percentage) total BMD, and regional (lumbar spine, femur, and forearm) BMD measures were completed using DXA (Lunar, GE Healthcare Inc., Madison, WI). The protocol for the DXA scan required the participant to lie on the DXA table for nearly 30 minutes during the different scans. Four DXA scans were completed for each participant: 1) anteroposterior view of the total body with the participant lying in a supine position; 2) anteroposterior view of the lumbar (L1-L4) spine with the participant lying in a supine position with hips and knees supported at a 90° angle; 3) anteroposterior view of both the right and left femoral neck with the participant lying in a supine position with internal rotation of the legs; and 4) posteroanterior view of the participant’s forearms with the participant lying in a supine position. The appendicular skeletal muscle index (ASMI) was calculated by dividing the sum of the upper and lower limb lean mass by the height in meters squared (kg/m^2).

Participants were classified as sarcopenic if their ASMI values were less than two standard deviations below healthy adult women (5.45 kg/m^2) (Baumgartner et al., 1998).

After measurements of body composition, strength was measured for the upper body using a one repetition maximum (1RM) chest press (MedX™; Orlando, FL) and lower body strength using the Biodex Medical System 3 (Biodex Medical Systems, Inc. NY, USA). Participants prepared for the 1RM chest press by completing a few repetitions at a low resistance. Resistance was increased gradually with 1-2 minutes between trials until the participant could no longer lift the resistance placed on the machine. The Biodex measured leg strength on the dominant leg. The participant was stabilized at the upper leg, waist, and shoulders by safety straps while seated in the upright position and the chair was positioned to line up the participant’s knee axis of rotation in line with the dynamometer shaft. Before beginning the test, the machine was calibrated to the participant’s extension and flexion range of motion. Isokinetic knee
extension and flexion was measured at a speed of 60, 120, and 180°/sec. The test began with three repetitions of concentric extension and flexion at 60°/sec, followed by 30 seconds of rest. After the rest period, the participant replicated the previous steps at 120°/sec and 180°/sec. Peak torque (N m) of extension and flexion from each repetition was recorded at all speeds. After the isokinetic tests, the participant completed an isometric leg strength test at 60° knee flexion by pushing against a stationary arm on the machine for 5 seconds in extension with 5 seconds of rest followed by 5 seconds of flexion followed by 5 seconds of rest. This was repeated two more times. Peak torque was recorded for extension and flexion. This was the final test of the first visit.

**Laboratory Visit 2**

The participant completed a second 1RM test for upper body strength and the greatest measurement of the two laboratory visits was used as the criterion measure. Then, a test for muscle power was completed using the Tendo Power Analyzer Unit. The participant stood up as quickly as possible from a seated position in a chair while attached to the Tendo Unit at the hip. This was repeated 5 times. Measurements included average and peak power and velocity.

**Participant Recruitment, Retention, and Compliance**

All participants were recruited from Tallahassee, FL and surrounding areas. All races and ethnic background were equally targeted as ideal participants in the study. Flyers were placed in public areas such as school campuses and community buildings. Advertisements were placed in local newspapers. BCS (stages 0-III) were further recruited at local breast cancer support groups, as well as from Tallahassee Memorial Hospital (TMH) Cancer Center and Capital Region Cancer Center.

**Anticipated Risks and Solutions**

There were minimal anticipated risks associated with participating in this study. The exclusion criteria limited the possible risks to participation. Due to the risk that breast cancer survivors may experience mobility limitations due to lymphedema, participants completed a warm-up prior to completing strength tests to prevent injury. Following the completion of strength tests, participants may have felt slight soreness but warm-ups and cool downs were completed to help alleviate some of the soreness. It was
made clear to participants that if they wished to opt out of answering any question in the questionnaires or refrain from completing any test, they may have done so.

**Statistical Analysis**

Descriptive statistics were calculated for each variable and included means and standard deviations for normally distributed continuous variables and medians, minima and maxima for non-normally distributed continuous variables. Differences between groups were analyzed using a One-way analysis of variance (ANOVA). All significance was accepted at $p \leq 0.05$. Pearson product-moment correlations were used to determine the relationship between time since menopause and time since treatment completion with body composition, BMD, strength, power, and QOL. Analyses were performed using the SPSS (version 23) statistical package.
CHAPTER IV: RESULTS

Forty-three BCS participated in this study. The age of BCS participants ranged from 41 to 77 years with an average age of 60.1 ± 8.3 years. The average weight of BCS participants was 78.1 ± 19.5 kg. The BCS participants had an average BMI of 29.3 ± 7.1 kg/m², classifying them as overweight. The participants had previously been diagnosed with stage 0 (n=4), stage 1 (n=16), stage 2 (n=14), and stage 3 (n=9) breast cancer. Treatments for BCS included surgery (n=43), chemotherapy (n=25), radiation (n=22), and hormone therapy (n=21). Mean time since diagnosis was 8.2 ± 7.1 years while time since completion of primary treatment (surgery, chemotherapy, and radiation) was 7.7 ± 7.1 years. Mean time since the onset of menopause was 12.3 ± 8.3 years.

The BCS participants were further separated into two groups: ST-BCS (n=17) or LT-BCS (n=26). Short-term survivorship was defined as having completed breast cancer treatment within the past 5 years, and LT-BCS was defined as having completed treatment for greater than 5 years. The average weight and BMI for ST-BCS was 74.0 ± 19.1 kg and 27.5 ± 6.5 kg/m², respectively. Short-term BCS were between the ages of 41 and 74 years, with an average age of 57.2 ± 9.3 years. Short-term BCS had stage 0 (n=2), stage 1 (n=8), stage 2 (n=4), and stage 3 (n=3) breast cancer, as well as surgical (n=17), chemotherapy (n=9), radiation (n=11), and hormone therapy (n=10) treatments. Average time since breast cancer diagnosis was 2.3 ± 1.0 years and average time since treatment completion was 1.8 ± 1.1 years. Long-term BCS were between the ages of 46 and 77 years, with an average age of 62.0 ± 7.2 years. The average weight and BMI of LT-BCS were 80.7 ± 19.8 kg and 30.5 ± 7.4 kg/m², respectively. Long-term BCS also received treatments of surgery (n=26), chemotherapy (n=16), radiation (n=11), and hormone therapy (n=11).

There was no significant difference in age (p = 0.065), weight, (p= 0.278), or BMI (p= 0.178) in ST-BCS compared to LT-BCS although age was approaching significance. There was a significant difference between the time since diagnosis (p<0.001) as well as time since treatment completion (p<0.001). There was no difference in time since the onset of menopause between the groups (p=0.253) with a mean of 10.5 ± 8.8 years and 13.6 ± 7.8 years in ST-BCS and LT-BCS, respectively.
No differences were observed in body composition including total lean mass, fat mass, body fat percentage, and ASMI (Table 2). Total lean mass was $40.5 \pm 7.3$ kg for ST-BCS and $42.2 \pm 7.2$ kg for LT-BCS. Total fat mass for ST-BCS was $34.0 \pm 10.2$ kg and $35.5 \pm 13.2$ kg for LT-BCS. Short-term BCS had a total body fat percentage of $44.5 \pm 5.4\%$ and LT-BCS had a total body fat percentage of $44.8 \pm 7.9\%$. Mean ASMI value was $7.0 \pm 1.4$ kg/m$^2$. Only two participants, both ST-BCS, were classified as sarcopenic using the ASMI sarcopenic cut-off value of $5.45$ kg/m$^2$ (Baumgartner et al., 1998).

Furthermore, there were no differences between ST-BCS and LT-BCS in total BMD (ST-BCS: $1.050 \pm 0.122$ g/cm$^2$; LT-BCS: $1.109 \pm 0.121$ g/cm$^2$), lumbar spine, right and left femurs, and right and left forearm measurements (Table 2). Lumbar BMD averaged $1.057 \pm 0.155$ g/cm$^2$ and $1.146 \pm 0.199$ g/cm$^2$ for ST-BCS and LT-BCS, respectively. Mean right and left combined femur BMD for ST-BCS was $0.895 \pm 0.151$ g/cm$^2$. Mean right and left femur BMD in LT-BCS was $0.932 \pm 0.138$ g/cm$^2$. Total forearm BMD in short- and LT-BCS was $0.470 \pm 0.087$ g/cm$^2$ and $0.466 \pm 0.071$ g/cm$^2$, respectively.

No differences between ST-BCS and LT-BCS were observed in strength and power measurements. Short-term BCS had an average 1RM chest press of $62.6 \pm 16.8$ kg, with a relative ratio of $0.82 \pm 0.15$ when divided by body weight in kg. The 1RM chest press mean for LT-BCS was $68.4 \pm 16.7$ kg, with a relative body weight ratio of $0.88 \pm 0.25$. Strength measurements on all Biodex tests were not different between the groups (Table 3). Short-term BCS showed an average of $119.0 \pm 39.5$ Nm and LT-BCS showed an average of $120.0 \pm 36.2$ Nm on measures of quadriceps isokinetic extension at $60^\circ$/sec. On measures of isokinetic flexion at $60^\circ$/sec, ST-BCS averaged $59.7 \pm 14.3$ Nm and LT-BCS averaged $60.0 \pm 22.4$ Nm. At $120^\circ$/sec, ST-BCS averaged $97.0 \pm 29.4$ Nm and $54.0 \pm 14.3$ Nm for extension and flexion, respectively. Likewise, LT-BCS averaged $97.8 \pm 30.5$ Nm and $51.7 \pm 18.7$ Nm for extension and flexion at $120^\circ$/sec, respectively. Short-term BCS had mean torque of $83.7 \pm 22.8$ Nm and $53.9 \pm 18.7$ Nm for extension and flexion, respectively, at $180^\circ$/sec, and LT-BCS had mean torque of $83.9 \pm 22.8$ Nm and $50.1 \pm 19.6$, respectively, at $180^\circ$/sec. The mean isometric peak torque for extension was $111.2 \pm 39.3$ Nm for ST-BCS and $116.4 \pm 32.7$ Nm for LT-BCS. Mean isometric peak torque flexion was $65.3 \pm 9.8$ Nm for
ST-BCS and 69.3 ± 18.7 Nm for LT-BCS. Average power on the Tendo sit-to-stand measurement was 401.8 ± 123.7 watts for ST-BCS and 440.6 ± 101.0 watts for LT-BCS. Peak power was 633.9 ± 181.5 watts for ST-BCS, and 737.6 ± 215.9 watts for LT-BCS.

No difference was observed in the eight domains of QOL in the SF-36 between ST-BCS and LT-BCS (Table 4). The average scores for ST-BCS and LT-BCS in the domain of physical function were 78.5 ± 17.7 and 72.9 ± 25.2, respectively. Short-term BCS had a mean score of 69.1 ± 38.1 and LT-BCS had a mean score of 64.4 ± 40.7 in the domain of role limitations due to physical health. In the domain of role limitations due to emotional problems, ST-BCS had a score of 78.4 ± 37.2 and LT-BCS had a score of 70.5 ± 40.4. Short-term BCS had a mean score of 56.5 ± 22.7 and LT-BCS had a mean score of 55.0 ± 24.0 in the domain of energy/vitality. Short-term BCS had mean scores of 73.2 ± 16.7, 80.1 ± 26.2, 69.0 ± 24.1, and 66.2 ± 16.3 in domains of emotional health, social functioning, bodily pain, and general health perceptions. Long-term BCS had mean scores of 76.0 ± 16.5, 82.2 ± 21.0, 70.1 ± 27.6, 65.0 ± 18.2 in domains of emotional health, social functioning, bodily pain, and general health perceptions, respectively.

Correlations were run to assess the relationship between time since treatment completion and time since the onset of menopause with all body composition and BMD measurements, strength, power and QOL measurements. The only significant relationship that was observed was a positive correlation ($r=0.38$, $p=0.015$) between time since treatment completion and lumbar spine BMD.
Table 1: Descriptive values for ST-BCS and LT-BCS (N=43).

<table>
<thead>
<tr>
<th>Variable</th>
<th>ST-BCS (n=17)</th>
<th>LT-BCS (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>57.2 ± 9.3</td>
<td>62.0 ± 7.2</td>
</tr>
<tr>
<td>Min-Max</td>
<td>41 – 74</td>
<td>46 – 77</td>
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<tr>
<td>Menopausal Age (yrs)</td>
<td>46.7 ± 5.2</td>
<td>49.2 ± 4.7</td>
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<tr>
<td>Min-Max</td>
<td>37 – 55</td>
<td>36 – 56</td>
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<tr>
<td>Weight (kg)</td>
<td>74.0 ± 19.1</td>
<td>80.7 ± 19.8</td>
</tr>
<tr>
<td>Min-Max</td>
<td>38.3 – 110.3</td>
<td>49.8 – 152.6</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.5 ± 6.5</td>
<td>30.50 ± 7.4</td>
</tr>
<tr>
<td>Min-Max</td>
<td>12.46 – 36.7</td>
<td>17.8 – 58.7</td>
</tr>
<tr>
<td>Time Since Diagnosis (years)</td>
<td>2.3 ± 1.0</td>
<td>12.0 ± 6.8*</td>
</tr>
<tr>
<td>Min-Max</td>
<td>0.4 – 3.7</td>
<td>5.3 – 30.3</td>
</tr>
<tr>
<td>Time Since Treatment Completion (years)</td>
<td>1.8 ± 1.1</td>
<td>11.5 ± 6.7*</td>
</tr>
<tr>
<td>Min-Max</td>
<td>0.1 – 3.2</td>
<td>4.7 – 30.3</td>
</tr>
<tr>
<td>Cancer Stage</td>
<td>Frequency</td>
<td>Percentage</td>
</tr>
<tr>
<td>Stage 0</td>
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<tr>
<td>Types of Treatment</td>
<td>Frequency</td>
<td>Percentage</td>
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<td>Radiation</td>
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<td>64.7</td>
</tr>
<tr>
<td>Hormone Therapy</td>
<td>10</td>
<td>58.8</td>
</tr>
</tbody>
</table>

ST-BCS: short-term breast cancer survivors; LT-BCS: long-term breast cancer survivors; BMI: body mass index
* p≤0.05, significant difference between ST-BCS and LT-BCS
Table 2: Body composition and BMD in ST-BCS and LT-BCS (N=43).

<table>
<thead>
<tr>
<th>Body Composition</th>
<th>ST-BCS (n=17)</th>
<th>Mean ± SD</th>
<th>LT-BCS (n=26)</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Lean Mass (kg)</td>
<td>40.5 ± 7.3</td>
<td>42.2 ± 7.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Body Fat (%)</td>
<td>44.5 ± 5.4</td>
<td>44.8 ± 7.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Fat Mass (kg)</td>
<td>34.0 ± 10.2</td>
<td>35.5 ± 13.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASMI (kg/m²)</td>
<td>6.6 ± 1.2</td>
<td>7.2 ± 1.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone Mineral Density (g/cm²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1.050 ± 0.122</td>
<td>1.109 ± 0.121</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lumbar</td>
<td>1.057 ±0.155</td>
<td>1.146 ±0.199</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right Femoral Neck</td>
<td>0.856 ± 0.136</td>
<td>0.896 ± 0.139</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left Femoral Neck</td>
<td>0.875 ± 0.137</td>
<td>0.887 ± 0.143</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right Femur Total</td>
<td>0.887 ± 0.156</td>
<td>0.928 ± 0.139</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left Femur Total</td>
<td>0.902 ± 0.146</td>
<td>0.936 ± 0.136</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right Forearm Radius</td>
<td>0.487 ± 0.094</td>
<td>0.476 ± 0.064</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left Forearm Radius</td>
<td>0.478 ± 0.092</td>
<td>0.477 ± 0.070</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right Forearm Ulna</td>
<td>0.459 ± 0.086</td>
<td>0.455 ± 0.073</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left Forearm Ulna</td>
<td>0.446 ± 0.076</td>
<td>0.445 ± 0.084</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right Forearm Total</td>
<td>0.475 ± 0.089</td>
<td>0.467 ± 0.067</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left Forearm Total</td>
<td>0.465 ± 0.084</td>
<td>0.464 ± 0.075</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ST-BCS: short-term breast cancer survivors; LT-BCS: long-term breast cancer survivors; ASMI: appendicular skeletal muscle index
Table 3: Strength and Power in ST-BCS and LT-BCS (N=43).

<table>
<thead>
<tr>
<th></th>
<th>ST-BCS (n=17)</th>
<th>LT-BCS (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biodex (Nm)</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>60°/sec Extension</td>
<td>119.0 ± 39.5</td>
<td>120.0 ± 36.2</td>
</tr>
<tr>
<td>60°/sec Flexion</td>
<td>59.7 ± 14.3</td>
<td>60.0 ± 22.4</td>
</tr>
<tr>
<td>120°/sec Extension</td>
<td>97.0 ± 29.4</td>
<td>97.8 ± 30.5</td>
</tr>
<tr>
<td>120°/sec Flexion</td>
<td>54.0 ± 14.3</td>
<td>51.7 ± 18.7</td>
</tr>
<tr>
<td>180°/sec Extension</td>
<td>83.7 ± 22.8</td>
<td>83.9 ± 22.8</td>
</tr>
<tr>
<td>180°/sec Flexion</td>
<td>53.9 ± 18.7</td>
<td>50.1 ± 19.6</td>
</tr>
<tr>
<td>Isometric Peak Torque</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extension</td>
<td>111.2 ± 39.3</td>
<td>116.4 ± 32.7</td>
</tr>
<tr>
<td>Flexion</td>
<td>65.3 ± 9.8</td>
<td>69.3 ± 18.7</td>
</tr>
<tr>
<td>1 RM Chest Press</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absolute 1RM (kg)</td>
<td>62.6 ± 16.8</td>
<td>68.4 ± 16.7</td>
</tr>
<tr>
<td>Relative 1RM ratio (kg/kg)</td>
<td>0.82 ± 0.15</td>
<td>0.88 ± 0.25</td>
</tr>
<tr>
<td>Sit-to-stand (Tendo)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Power (W)</td>
<td>401.8 ± 123.7</td>
<td>440.6 ± 101.0</td>
</tr>
<tr>
<td>Average Velocity (m/s)</td>
<td>0.5 ± 0.2</td>
<td>0.6 ± 0.1</td>
</tr>
<tr>
<td>Peak Power (W)</td>
<td>633.9 ± 181.5</td>
<td>737.6 ± 215.9</td>
</tr>
<tr>
<td>Peak Velocity (m/s)</td>
<td>0.9 ± 0.2</td>
<td>0.9 ± 0.2</td>
</tr>
</tbody>
</table>

ST-BCS: short-term breast cancer survivors; LT-BCS: long-term breast cancer survivors; 1RM: one repetition maximum
Table 4: Quality of life in ST-BCS and LT-BCS measured by the eight domains of the SF-36 (N=43).

<table>
<thead>
<tr>
<th></th>
<th>ST-BCS (n=17)</th>
<th>LT-BCS (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF-36</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Physical Function</td>
<td>78.5 ± 17.7</td>
<td>72.9 ± 25.2</td>
</tr>
<tr>
<td>Role Limitations Due to Physical Health</td>
<td>69.1 ± 38.1</td>
<td>64.4 ±40.7</td>
</tr>
<tr>
<td>Role Limitations Due to Emotional Problems</td>
<td>78.4 ± 37.2</td>
<td>70.5 ± 40.4</td>
</tr>
<tr>
<td>Energy/Vitality</td>
<td>56.5 ± 22.7</td>
<td>55.0 ± 24.0</td>
</tr>
<tr>
<td>Emotional Health</td>
<td>73.2 ± 16.7</td>
<td>76.0 ± 16.6</td>
</tr>
<tr>
<td>Social Functioning</td>
<td>80.1 ± 26.2</td>
<td>82.2 ± 22.0</td>
</tr>
<tr>
<td>Bodily Pain</td>
<td>69.0 ± 24.1</td>
<td>70.1 ± 27.6</td>
</tr>
<tr>
<td>General Health Perceptions</td>
<td>66.2 ± 16.3</td>
<td>65.0 ± 18.2</td>
</tr>
</tbody>
</table>

ST-BCS: short-term breast cancer survivors; LT-BCS: long-term breast cancer survivors
CHAPTER V: DISCUSSION

There were no differences observed between ST-BCS and LT-BCS in body composition and total and regional BMD measurements. This does not support the hypothesis that LT-BCS would have lower lean mass, greater fat mass and body fat percentage, and lower BMD. All participants may have experienced similar changes during treatment, but further treatment-related changes in lean mass, body fat, and BMD may not have occurred following the completion of treatment. Simonavice et al. (2011) found that BCS had significantly lower total body BMD and regional BMD than a healthy, non-cancer control population, which supports that treatment does have a negative effect on BMD in BCS. The results of this study showed that such detriments are not different in ST-BCS compared to LT-BCS. Therefore, after the completion of treatment, the rate of change in body composition and BMD may be similar to the normal age-related changes experienced by postmenopausal women who have not had cancer. This is supported by Artese et al. (2018) who compared BMD and body composition changes in BCS who had completed treatment and a non-cancer control over the course of 12-15 months. They found that the rate of change in BMD and body composition was similar between BCS and the non-cancer control, concluding that changes in body composition and losses in BMD following treatment occur at a similar rate as postmenopausal women who have not had cancer. Furthermore, findings from this study are congruent with a study done by Makari-Judson, Judson, & Mertens (2007) who found that weight gain is significant in the year following treatment, and then plateaus in the following two years. The plateau of weight gain may persist longer than 5 years after the completion of treatment, which could explain why both groups had no difference in body composition measures. We did find a significant relationship between time since treatment completion and lumbar spine BMD. This suggests that lumbar spine BMD may recover with greater time following treatment completion. This is supported by Eastell et al. (2011) who found that lumbar spine BMD increased over the course of two years post-hormone therapy completion. While our analysis measured time since primary treatment completion (surgery, chemotherapy, and radiation), our findings support the idea that BMD can recover over time.
A reason why there were no differences between the groups for BMD and body composition may have been due to the menopausal age. There was no difference in menopausal age between the two BCS groups. Chemotherapy treatments and other BCS treatments induce menopause due to treatment-induced ovarian failure, causing accelerated changes in BMD and body composition in BCS. At the onset of menopause, the body stops the natural production of estrogen, a hormone that prevents bone loss by decreasing resorption activity of osteoclasts (Kameda et al., 1997). Since there were no group differences in the participants’ ages and time since the onset of menopause, both the ST-BCS and LT-BCS may have experienced similar changes in body composition and decreases in BMD since the onset of menopause and then similar changes during the cancer treatment period, regardless of when the treatment period occurred. Toth et al. (2000) observed significant increases in fat mass and body fat percentage in postmenopausal women compared to premenopausal women. Since all BCS participants were postmenopausal, they may have had similar changes in body composition after treatment-induced or naturally occurring menopause.

No difference was observed in upper and lower body strength and power between the groups. Muscle mass is an important contributor of muscle strength and power. Rate of strength in BCS declines at a rate three times the rate of muscle mass decline in healthy older adults (Reid & Fielding, 2012). Since there were no differences seen in muscle mass between the groups, it follows that there would be no observable differences in strength and power. However, this does not support the hypothesis that LT-BCS would have lower strength and power than that of ST-BCS. Because there was no difference in age and all participants were sedentary, all may have had similar changes in strength and power due to effects of treatment. Multiple studies support that breast cancer treatment leads to significant losses in strength in BCS (Dieli-Conwright & Orozco, 2015; Simonavice, Liu, Ilich, Kim, & Panton, 2011). For example, a study by Simonavice et al. (2011) found that BCS have 21% lower upper body strength as measured by chest press compared to a non-cancer control. A review article by Dieli-Conwright and Orozco (2015) concluded that BCS decrease their physical activity on average by 11%, which leads to significant losses in strength, as well as other negative changes in body composition. Because there was no difference observed between ST-BCS and LT-BCS in measures of strength and power in this study, it is likely that strength and...
power changes occurred at similar rates to women who have not had cancer outside of any accelerated changes that may have occurred during treatment.

Participants in both groups experienced similar treatments of surgery, chemotherapy, radiation, hormone therapy, or a combination of treatments. Every BCS underwent a surgical procedure to remove cancerous tissue. The similarity in treatments may account for similarities in body composition, BMD, strength, and power in all BCS participants. Participants were excluded from the study if they were taking any medications that could affect muscle or fat metabolism or BMD, such as antiresorptive or bisphosphate medication, so body composition and BMD changes in either group should not have been affected by medication.

When analyzing the questionnaire for QOL, it showed that there were no differences between ST-BCS and LT-BCS in any of the eight domains of the SF-36. This also does not support the hypothesis that ST-BCS would score lower than LT-BCS on QOL. Simonavice et al. (2011) reported that BCS score significantly lower than a healthy non-cancer control in the domain of physical function on the SF-36, with a lowest scoring domain for BCS being bodily pain. In the domain of bodily pain in this study, ST-BCS and LT-BCS scored much greater than the BCS collected in the study by Simonavice et al., 69.0 and 70.1 compared to 24.2. Additionally, the population used in this study may have had an overall greater sense of well-being considering they scored higher in every domain than the study done by Simonavice et al. The average time since treatment for BCS in the study by Simonavice et al. was 17 months, whereas the average time since treatment completion for this study for ST-BCS was 2.3 years, so there may be a difference in QOL if ST-BCS were defined as having completed breast cancer treatment less than 2 years prior to this study. A study by Bloom et al. (2004) that compared QOL in BCS from baseline, after treatment, and a follow-up of 5 years. The 5-year follow-up scores yielded QOL results from the SF-36 that were similar to the results of this study. Although the follow-up scores of the SF-36 were closer to the scores of participants in this study, they were higher in all domains. This could be because the participants in Bloom et al. (2004) ranged from age 22-51 years, whereas the minimum age in this study was 41 years with a range of 41 to 77 years.
A strength of the present study was the similarity in average age between the groups. This allowed differences or similarities to be attributed to effects of the cancer treatments rather than differences in age-related changes. Another strength of the study was the use of the DXA to determine body composition and BMD values. The DXA scan is considered the most accurate BMD measurement tool available, while also being relatively low in cost, minimally invasive, and quick (Lustgarten & Fielding, 2011).

A weakness of the study is the cross-sectional design. Baseline tests before treatment and after treatment would be more helpful in determining true treatment-related changes in body composition, BMD, strength, power, and QOL measures. Since participants recruited had already completed treatment, we do not know what their initial body composition, BMD, strength, power, and QOL scores were before diagnosis and treatment to measure changes before, during, and after treatment. Another weakness of the study is the small sample size. Gathering data from a larger sample would improve the strength and generalizability of the study results. Participants all had different treatments and with a larger sample size, participants’ data could have been analyzed based on treatments. Additionally, there may have been differences between the groups that were unable to be controlled. Differences in diets of the participants, as well as the degree to which their activity before, during, and after treatment, may have affected their body composition, BMD, strength, power, and QOL over time.

Conclusion

In conclusion, the study found no significant differences between body composition, BMD, strength, power, and QOL between ST-BCS and LT-BCS. This may be due to the similarity in menopausal age between the groups, so both may have experienced the same rate of age-related changes, as well as changes due to treatment. While we did find a positive relationship between time since treatment completion and lumbar spine BMD, more research is needed to determine what factors may have influenced changes specifically in the lumbar spine BMD over time. Because no improvements were seen in body composition, BMD, strength, power, and QOL in LT-BCS compared to ST-BCS, this supports a need for the implementation of exercise interventions to improve these variables after breast cancer treatment. There has been little research done comparing ST-BCS and LT-BCS; therefore, more research is
needed to determine whether the effects of treatment persist over time and for how long. A long-term longitudinal study on BCS would better compare changes over time.
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https://doi.org/10.1097/JES.0b013e3181d496bc.Mechanisms


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https://doi.org/10.1186/bcr624


https://doi.org/10.1177/1534735406291962


https://doi.org/10.3390/s17071572

Weitzner, M. a, Meyers, C. a, Stuebing, K. K., & Saleeba, a K. (1997). Relationship between quality of


**Appendix A**

The Florida State University  
Office of the Vice President For Research  
Human Subjects Committee  
Tallahassee, Florida 32306-2742  
(850) 644-8673, FAX (850) 644-4392

RE-APPROVAL MEMORANDUM Date:  
8/10/2017

To: Ashley Artese [ala13b@my.fsu.edu]

Address: 120 Convocation Way  
Dept.: NUTRITION FOOD AND EXERCISE SCIENCES

From: Thomas L. Jacobson, Chair
Re: Re-approval of Use of Human subjects in Research

The Effects of Functional Impact Training and Yin Yoga on Body Composition in Breast Cancer Survivors

Your request to continue the research project listed above involving human subjects has been approved by the Human Subjects Committee. If your project has not been completed by 8/8/2018, you must request renewed approval by the Committee.

If you submitted a proposed consent form with your renewal request, the approved stamped consent form is attached to this re-approval notice. Only the stamped version of the consent form may be used in recruiting of research subjects. You are reminded that any change in protocol for this project must be reviewed and approved by the Committee prior to implementation of the proposed change in the protocol. A protocol change/amendment form is required to be submitted for approval by the Committee. In addition, federal regulations require that the Principal Investigator promptly report in writing, any unanticipated problems or adverse events involving risks to research subjects or others.

By copy of this memorandum, the Chair of your department and/or your major professor are reminded of their responsibility for being informed concerning research projects involving human subjects in their department. They are advised to review the protocols as often as necessary to insure that the project is being conducted in compliance with our institution and with DHHS regulations.

Cc: Lynn Panton, Advisor [lpanton@admin.fsu.edu] HSC No. 2017.21640

Appendix B

Consent Form

The effect of functional impact training and yin yoga on body composition in breast cancer survivors

You are invited to participate in this research study entitled “The effects of functional impact training and yin yoga on body composition and bone mineral density in breast cancer survivors.” This study is being conducted by Lynn Panton, PhD and Ashley Artese, M.S. from the Department of Nutrition, Food & Exercise Sciences at Florida State University.

Study Purpose:
The purpose of this study is to examine the effects of 6 months of functional impact training or yin yoga on body composition, bone mineral density, muscular strength, physical function, quality of life, affect, and fatigue in breast cancer survivors who have completed primary treatment. In addition, this study will evaluate baseline body composition, BMD, strength, physical function, and quality of life measures in
women without cancer to compare body composition and functional outcomes in BCS and women who have not had cancer.

**Procedure:**
Following the initial orientation visit I will learn about the details of the project, my participation in this study will involve five visits to the Clinical Exercise Physiology Laboratory at Florida State University. Two visits will take place before the 6-month intervention for baseline testing. The third visit will occur after 3 months of training for mid term testing. The last two visits will take place after the intervention for post-testing. During these visits, I will complete several questionnaires about health and quality of life. I will also complete several strength tests, perform the continuous scale physical functional performance test (CS-PFP), have body composition measured via dual energy x-ray absorptiometry (iDXA) and bioelectrical impedance, and have bloodwork done. I will also be asked to replace any current supplementation with a multivitamin that contains 600 mg of calcium and 400 IU of vitamin D (twice per day) at the start of the intervention. This will be provided by the researchers.

During my orientation visit, I will complete an informed consent document as well as a medical history questionnaire. I cannot participate in this study if I have been diagnosed with stage IV breast cancer, am currently diagnosed with active cancer, or am receiving endocrine (e.g., prednisone, other glucocorticoids) or neuroactive (e.g., dilantin, phenobarbital) drugs or any other prescription drugs known to influence muscle and fat metabolism. I am also ineligible to participate if I have hypo or hyperthyroidism, uncontrolled hypertension (>160/100 mmHg), uncontrolled diabetes, uncontrolled heart disease, or am participating in a vigorous exercise program, being treated with pharmacologic doses of vitamin D, and/or anabolic steroids less than 6 months prior to the start of the study. If I have had surgery, it must be at least three months.
prior to beginning this study. I will be given a physician’s consent form to take to my oncologist or primary care physician to make sure he or she does not have any concerns for me to participate in the study. I will also be given a 3-day food diary to fill-out and bring back for my first visit.

After the physician’s form has been returned to the laboratory, I will be scheduled for my first visit. My orientation visit will take approximately 1 hour to complete.

During the first baseline visit, I will complete several questionnaires that assess exercise barriers and benefits, quality of life, health, and fatigue. Blood will be drawn under sterile conditions in the amount of 20 milliliters. Waist and hip measurements will be assessed along with body composition via bioelectrical impedance and the iDXA. For the bioelectrical impedance, a non-invasive technique, two electrodes will be placed on my hand and foot and a low electrical current will travel through my body to measure body composition. For the iDXA, I will lie on the iDXA table for approximately five minutes until the scan is complete. Very low doses of radiation are used during the scan. Five total scans will be completed: 1) anteroposterior view of the total body with the participant lying in a supine position; 2) anteroposterior view of the lumbar (L1-L4) spine with the participant lying in a supine position with hips and knees supported at a 90° angle; 3) anteroposterior view of both the right and left femoral neck with the participant lying in a supine position with internal rotation of the legs; 4) posteranterior view of the participant’s forearms with the participant lying in a supine position; and 5) lateral view of the spine (T8-L4) with the participant lying on her left side. The test will be completed according to the manufacturer’s instructions and specifications by a certified X-ray technician. Following the body composition measures, I will complete several upper and lower body strength tests including a one-repetition maximum (1RM) test on the bench press and leg press machines. For these tests, I will warm-up by completing several repetitions with a light weight. We will then progressively increase the weight until I have reached a weight at which I can only complete one repetition. Then I will complete an isokinetic knee flexion and extension strength test on the Biodex where I will perform three repetitions for leg extension and flexion at 60°, 120°, and 180° per second with 30 seconds of rest in between. I will then perform an isometric quadriceps and hamstring contraction for three repetitions with 10 seconds rest in between. Following these tests, I will be given an activity monitor to wear for one week. I will return the activity monitor when I come in for the second visit. This first visit will take approximately two hours to complete.

The second visit will consist of baseline blood pressure, heart rate, height, and weight measurements. Before assessing these baseline measurements, I will sit quietly in a room for five minutes and then my blood pressure will be measured at the brachial artery and pulse at the radial artery. Two measurements of each will be completed. The 1RM tests will also be completed again and the higher of the two values will be recorded as my 1RM test value. I will also complete the CS-PFP, a test designed to evaluate physical function with tasks that include picking up scarves, putting on a jacket, reaching, floor sweeping, transferring laundry from washer to dryer and dryer to basket, sitting and standing from the floor, stair climbing, getting on a simulated bus while carrying groceries, and walking for 6 minutes. The time it takes to complete each task, the amount of weight carried, and distance walked will be recorded. I will then
perform a sit-to-stand test for five repetitions with a one-minute rest in between with a Tendo gage attached to my hip to measure muscle power. This second visit will take approximately an hour and a half. The 1RM tests, bioelectrical impedance, CS-PFP, and blood work will all be completed again after the first three months of the intervention for the third visit. All procedures will be repeated during the two post-testing visits 4 and 5.

Once the two baseline visits are completed, I will be randomized to one of two groups, stratified by age, lean mass, stage of cancer, and type of cancer treatment for the duration of the 6-month intervention. The two groups are the functional impact training group (FIT) and the yin yoga group (yoga). Participants assigned to the FIT group will be instructed to complete 6 months of supervised exercise training sessions consisting of exercises that are performed using body weight and some equipment including dumbbells. These exercises will be high impact exercises that may include jumping and hopping. Each exercise session will last approximately 45 minutes and will be completed twice per week. The intensity of the exercise program will start out low to prevent injury and introduce me to the exercises and will gradually increase over the course of the 6 months. All sessions will be monitored and led by a certified fitness professional and all exercise sets and repetition numbers will be recorded. Participants assigned to the yin yoga group will be instructed to complete 6 months of supervised yin yoga training sessions, which consist of exercises that focus on stretching and relaxation. Exercises will be lying or seated and will be performed on a yoga mat using equipment such as yoga mats, yoga blocks, and bolsters. Each yoga session will last approximately 45 minutes and will be completed twice per week. The yoga sessions will be led by a Yoga Alliance registered yoga teacher (RYT 200).

During one session in the 23rd week of exercise training, I will be asked to complete a series of questionnaires to assess affective responses to one exercise session. I will complete these questionnaires immediately before, during, immediately after, and 10 minutes after the exercise session.

Following the completion of the FIT or yoga intervention and the final testing visits (visits 5 and 6), I will be invited back to complete a one-hour interview to assess my experience as a participant in the study. The interview will be recorded on an audio recording device.

Possible Risks and Benefits:
There is minimal risk to me in this study. There is a possibility that I may experience muscle soreness and risk for injury related to engaging in strength and flexibility exercises. The instructors will facilitate a safe class that is designed to minimize soreness or risk for injury by leading me through a thorough warm-up, providing thorough explanations and appropriate safety cues for each exercise, and guiding me through an appropriate cooldown period. In addition to the certified instructors that will be leading the exercise session, there will also be additional trained individuals present that will assist me with each exercise to ensure that I am completing the exercise with proper technique and to monitor exercise intensity. The risk of a cardiovascular event during testing and training will be minimized by careful review of my medical
history, physician’s consent, and monitoring of exercise sessions.

In addition, breast cancer survivors are also at risk for developing lymphedema if lymph nodes were removed during surgery or if lymph nodes were damaged during radiation treatment. While exercise has not been shown to exacerbate symptoms of lymphedema, symptoms will be monitored on a monthly basis via arm circumference measurements. I will notify the exercise instructor and researchers if I experience any of the following conditions: Swelling in the arms, hands, fingers, shoulders, or chest; a "full" or heavy sensation in the arms; skin tightness; decreased flexibility in the hand or wrist. If these symptoms do arise, the exercise intensity will be reduced. I will be encouraged to wear my compression garments, if applicable, during the exercise sessions.

Body composition will be evaluated by iDXA. This involves some radiation of approximately 0.5 mREM per total body scan. This is much less than the radiation a person receives from a chest X-ray (20-50 mREM) and substantially less than a full dental X-ray (300 mREM) or an abdominal X-ray (250 mREM). The measurement is non-invasive.

The CS-PFP test is safe and no adverse conditions have been reported in our laboratory. I will be instructed to perform each task at maximal effort within the bounds of safety and comfort. Heart rate monitors will be worn during the duration of the test and blood pressure will be measured before testing is initiated and once again when testing is completed. I may stop the test at any time to rest or get drinks of water. Juice will also be made available in case I need to have a drink with sugar in it. I may choose not to complete a task if I feel uncomfortable. I will wear a transfer belt during the CS-PFP test that will allow the technician to support me when I do some of the different tasks such as moving from the floor to a standing position. My heart rate will be monitored throughout this test.

The risks of drawing blood are small; there may be some discomfort at the site of needle placement with possible bruising or swelling. The risk will be minimized by the use of skilled technicians using sterile techniques and equipment.

There are minimal risks or discomforts with answering questionnaires. I may choose not to complete the questionnaires or the recorded interview and will still be able to participate in the study.

In case of an injury, first aid will be provided to me by the laboratory personnel working on the research project. Any other necessary treatment or care will be provided at my expense.

The possible benefits of participation in this research project include gaining information about my blood pressure, waist and hip circumferences, and muscular strength levels. I will also be given a breakdown of my body composition values including body fat percentage, muscle mass, and bone mineral density. In addition, both exercise groups have the potential to improve quality of life and physical function. Participants in the FIT group have a greater opportunity for improvements in body composition and...
Confidentiality:
The information that we will collect will be kept confidential. My name will not be kept with my survey responses. Research personnel will keep all surveys and contact information in separate files in a locked filing cabinet in a locked office within the Department of Nutrition, Food and Exercise Sciences. Only the study’s researchers will have access to the study files. My name will not be mentioned during the recorded interview. Only my ID number will be identified.

The results of this research study may be published but my name or identity will not be revealed. Information obtained during the course of the study will remain confidential, to the extent allowed by law. My name will not appear on any of the results. No individual responses will be reported. Only group findings will be reported in publications. Confidentiality will be maintained by assigning me a code number and recording all data by code numbers.

Voluntary Nature of the Study:
My participation in this study is voluntary. If I decide to participate, I can choose to skip any questions on the surveys that I would prefer not to answer and I can choose to skip any of the physical assessments that I do not feel comfortable completing.

Contacts and Questions:
If you have any comments, questions, or concerns, you can contact the researchers listed below.

Dr. Lynn Panton
Department of Nutrition, Food and Exercise Sciences
120 Convocation Way
100C Sandels Building
Tallahassee, FL 32306
(851) 644-4685
lpanton@fsu.edu

Ashley Artese
Department of Nutrition, Food and Exercise Sciences
120 Convocation Way
100K Sandels Building
Tallahassee, FL 32306
(856) 534-8926
ala13b@my.fsu.edu

In case of injury, or if I have questions about my rights as a subject/participant in this research, or if I feel I have been placed at risk, I can contact the chair of the Human Subjects committee, Institutional Review Board, through the Office of the Vice President for Research, at (850) 644-8633.
Consent Statement:

The nature, demands, benefits and risks of the project have been explained to me. I knowingly assume any risks involved.

I have read the above informed consent document. I understand that I may withdraw my consent and discontinue participation at any time without penalty or loss of benefits to which I may otherwise be entitled. In signing this consent form, I am not waiving my legal claims, rights or remedies. A copy of this consent form will be given to me.

_________________________________________________  __________________________
Signature of Participant   Date

_________________________________________________  __________________________
Printed Name   Date

**Person Explaining the Research:** My signature below means that I have explained the research and have answered any questions the participant had about the research project.

_________________________________________________
Signature of personal explaining research

_________________________________________________
Printed Name

Page 6 of 7
FSU Human Subjects Committee approved on 08/25/2017, void after 08/08/2018. HSC #2017.21883
Future Studies:
If the researchers of this study want to contact you for future follow-up studies, which will all be approved by the appropriate Institutional Review Boards for Human Subjects Research. Are you willing to be contacted by these researchers regarding any future studies?

Yes
No

If yes, please provide your mailing address and telephone number below.

Please Print:

Mailing Address: _________________________________________________________
_________________________________________________________

Telephone Number: ________________________________________________

Email Address: _____________________________________________________

Preferred Mode of Contact: _____Telephone _____Email _____Mailing Address
Appendix C

36-Item Short Form Survey Instrument (SF-36)

RAND 36-Item Health Survey 1.0 Questionnaire Items

Choose one option for each questionnaire item.

1. In general, would you say your health is:
   - 1 - Excellent
   - 2 – Very good
   - 3 - Good
   - 4 - Fair
   - 5 - Poor

2. Compared to one year ago, how would you rate your health in general now?
   - 1 - Much better now than one year ago
   - 2 - Somewhat better now than one year ago
   - 3 - About the same
   - 4 - Somewhat worse now than one year ago
   - 5 - Much worse now than one year ago
The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

<table>
<thead>
<tr>
<th>Activity</th>
<th>Yes, limited a lot</th>
<th>Yes, limited a little</th>
<th>No, not limited at all</th>
</tr>
</thead>
<tbody>
<tr>
<td>3. Vigorous activities, such as running, lifting heavy objects,</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
</tr>
<tr>
<td>participating in strenuous sports</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
</tr>
<tr>
<td>5. Lifting or carrying groceries</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
</tr>
<tr>
<td>6. Climbing several flights of stairs</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
</tr>
<tr>
<td>7. Climbing one flight of stairs</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
</tr>
<tr>
<td>8. Bending, kneeling, or stooping</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
</tr>
<tr>
<td>9. Walking more than a mile</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
</tr>
<tr>
<td>10. Walking several blocks</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
</tr>
<tr>
<td>11. Walking one block</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
</tr>
<tr>
<td>12. Bathing or dressing yourself</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
</tr>
</tbody>
</table>
During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**?

13. Cut down the **amount of time** you spent on work or other activities

14. **Accomplished less** than you would like

15. Were limited in the **kind** of work or other activities

16. Had **difficulty** performing the work or other activities (for example, it took extra effort)

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

17. Cut down the **amount of time** you spent on work or other activities

18. **Accomplished less** than you would like

19. Didn’t do work or other activities as **carefully** as usual

20. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

   - 1 - Not at all
   - 2 - Slightly
   - 3 - Moderately
   - 4 - Quite a bit
   - 5 - Extremely
21. How much **bodily** pain have you had during the **past 4 weeks**?

- 1 - None
- 2 - Very mild
- 3 - Mild
- 4 - Moderate
- 5 - Severe
- 6 - Very severe

22. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home and housework)?

- 1 - Not at all
- 2 - A little bit
- 3 - Moderately
- 4 - Quite a bit
- 5 - Extremely
These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the past 4 weeks...

<table>
<thead>
<tr>
<th>Question</th>
<th>All of the time</th>
<th>Most of the time</th>
<th>A good bit of the time</th>
<th>Some of the time</th>
<th>A little of the time</th>
<th>None of the time</th>
</tr>
</thead>
<tbody>
<tr>
<td>23. Did you feel full of pep?</td>
<td>○ 1</td>
<td>○ 2</td>
<td>○ 3</td>
<td>○ 4</td>
<td>○ 5</td>
<td>○ 6</td>
</tr>
<tr>
<td>24. Have you been a very nervous person?</td>
<td>○ 1</td>
<td>○ 2</td>
<td>○ 3</td>
<td>○ 4</td>
<td>○ 5</td>
<td>○ 6</td>
</tr>
<tr>
<td>25. Have you felt so down in the dumps that nothing could cheer you up?</td>
<td>○ 1</td>
<td>○ 2</td>
<td>○ 3</td>
<td>○ 4</td>
<td>○ 5</td>
<td>○ 6</td>
</tr>
<tr>
<td>26. Have you felt calm and peaceful?</td>
<td>○ 1</td>
<td>○ 2</td>
<td>○ 3</td>
<td>○ 4</td>
<td>○ 5</td>
<td>○ 6</td>
</tr>
<tr>
<td>27. Did you have a lot of energy?</td>
<td>○ 1</td>
<td>○ 2</td>
<td>○ 3</td>
<td>○ 4</td>
<td>○ 5</td>
<td>○ 6</td>
</tr>
<tr>
<td>28. Have you felt downhearted and blue?</td>
<td>○ 1</td>
<td>○ 2</td>
<td>○ 3</td>
<td>○ 4</td>
<td>○ 5</td>
<td>○ 6</td>
</tr>
<tr>
<td>29. Did you feel worn out?</td>
<td>○ 1</td>
<td>○ 2</td>
<td>○ 3</td>
<td>○ 4</td>
<td>○ 5</td>
<td>○ 6</td>
</tr>
<tr>
<td>30. Have you been a happy person?</td>
<td>○ 1</td>
<td>○ 2</td>
<td>○ 3</td>
<td>○ 4</td>
<td>○ 5</td>
<td>○ 6</td>
</tr>
<tr>
<td>31. Did you feel tired?</td>
<td>○ 1</td>
<td>○ 2</td>
<td>○ 3</td>
<td>○ 4</td>
<td>○ 5</td>
<td>○ 6</td>
</tr>
</tbody>
</table>

32. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

○ 1 - All of the time
○ 2 - Most of the time
○ 3 - Some of the time
○ 4 - A little of the time
○ 5 - None of the time
How TRUE or FALSE is each of the following statements for you.

<table>
<thead>
<tr>
<th>Statement</th>
<th>Definitely true</th>
<th>Mostly true</th>
<th>Don't know</th>
<th>Mostly false</th>
<th>Definitely false</th>
</tr>
</thead>
<tbody>
<tr>
<td>33. I seem to get sick a little easier than other people</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>34. I am as healthy as anybody I know</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>35. I expect my health to get worse</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>36. My health is excellent</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>