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Effects of Resistance Exercise & Dried Plum Consumption on Body Composition, Muscular Strength, & Physical Function in Breast Cancer Survivors

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EFFECTS OF RESISTANCE EXERCISE & DRIED PLUM CONSUMPTION ON BODY COMPOSITION, MUSCULAR STRENGTH, & PHYSICAL FUNCTION IN BREAST CANCER SURVIVORS

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Dedicated to all the men and women who have fought the battle against cancer. For those of you who remain, may you face each new day with a smile, and celebrate life. For those of you have gone, we will feel the love and comfort of your memories for all our remaining days.

“Momma” Vicki
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ABSTRACT

Breast cancer survivors (BCS) encounter side effects from cancer treatments that negatively affect body composition. Studies have shown that resistance training (RT) and dried plum (DP) consumption may elicit positive body composition changes. *PURPOSE*: to assess 27 BCS, (RT, n=14; RT+DP, n=13) pre-and post-intervention (6 months) on the following variables: total body and regional sites (lumbar spine, femur, and forearm) of bone mineral density (BMD) and body composition (by dual energy X-ray absorptiometry), biochemical markers of bone turnover [(bone-specific alkaline phosphatase (BAP) and tartrate resistant acid phosphatase (TRAP-5b)], muscular strength (chest press and leg extension 1-repetition maximums), and physical function (Continuous Scale Physical Functional Performance test). RT consisted of two days/week of ten exercises including two sets of 8-12 repetitions at ~60-80% of 1RM. RT+DP also consumed 90g of DP daily. *RESULTS*: A one-way analysis of variance (ANOVA) revealed no baseline differences between groups for any of the variables. A two-way group x time ANOVA revealed no interaction for any variables. Time effects were observed for BMD of the right forearm, with the RT+DP group losing significant (p<0.05) BMD from baseline to 6 months (0.476±0.059 to 0.464±0.054g/). No other BMD or body composition variables were changed over the course of the study. TRAP-5b was significantly (p<0.05) decreased for the RT group (4.55±1.57 to 4.03±1.81U/L) as well as for the RT+DP group (p=0.07) (5.10±2.75 to 3.77±1.80U/L). BAP did not change over the course of the study. BCS significantly (p<0.05) increased upper (RT:68±20 to 82±21kg; RT+DP:72±24 to 96±22kg) and lower (RT:72±19 to 88±28kg; RT+DP:77±17 to 99±19kg) body strength and total physical function (RT:67.2±10.2 to 73.5±10.1units; RT+DP:63.7±14.1to 73.6±14.5units). *CONCLUSIONS*: Results showed DP did not provide additional BMD or biochemical bone turnover benefits to RT for the variables assessed. RT could be an effective means to improve biochemical markers of bone turnover, muscular strength, and physical function in BCS. A longer intervention may be needed to elicit positive changes in body composition and BMD and to reveal the true effects of DP on modulating BMD and biochemical markers of bone turnover.

CHAPTER 1
INTRODUCTION

Approximately 1,479,350 new cases of cancer were diagnosed in the United States in 2009. Of these 1,479,350 new cancer diagnoses, it was estimated that approximately 194,280 were breast cancer (Jemal, Siegel, Ward, Hao, Xu, & Thun, 2009). While the prognosis of breast cancer is improving, with the death rate from breast cancer decreasing 37% from 1991 to 2005, breast cancer patients are often left to deal with the numerous adverse side effects caused by the cancer itself and the treatments of the cancer (Jemal et al., 2009). Typically, breast cancer treatment includes surgery, radiation, adjuvant chemotherapy, and/or hormone suppressant therapy, all of which present an extensive list of negative mental and physical side effects.

Among the long list of unfavorable side effects of cancer treatments are body composition changes, specifically decreased bone mineral density (BMD) and a decreased lean body mass to fat mass ratio, decreased muscular strength, decreased physical function, and decreased quality of life (QOL). A loss of BMD can lead to osteopenia and/or osteoporosis, ultimately, making bones more susceptible to fracture. This is of notable concern as a previous report showed significant increases in mortality following vertebral and hip fractures (Cauley, Thompson, Ensrud, Scott, & Black, 2000). Furthermore, osteoporosis is linked to decreased physical function as well as decreased QOL (Lips & van Schoor, 2005). In addition to the physical and psychological detriments that accompany osteoporosis, there is a significant financial burden for the diagnosed individual that is associated with the disease, with annual costs estimated to be approximately $6,259 in addition to the estimated annual costs of $13,925 associated with breast cancer (Sasser, Rousculp, Birnbaum, Oster, Lufkin, & Mallet, 2005). Twiss et al. (2001) state, “It is far from ideal to survive breast cancer, only to become a victim of osteoporosis” (p. 282). This quote speaks profound truth and addresses a growing concern within the breast cancer population.

The breast cancer population is vulnerable to BMD loss because of the direct and indirect effects of chemotherapy and a common hormone suppressant therapy

known as aromatase inhibitors (AIs). Chemotherapy has been reported to directly affect the number and size of bone cells (Friedlaender, Tross, Doganis, Kirkwood, & Baron, 1984); whereas both chemotherapy and AIs have been reported to indirectly affect BMD by decreasing the amount of estrogen produced in the body (Pfeilschifter & Diel, 2000; Ramaswamy & Shapiro, 2003). Specifically, during a 12-month chemotherapy regimen, women have been reported to experience a loss of approximately 7% in lumbar spine BMD (Shapiro, Manola, & Leboff, 2001). Similar detrimental effects can occur from one to five years usage of AIs, with a report of approximately 7.2% BMD loss during the treatment period (Brufsky, 2007).

Additional body compositional changes that cancer patients experience, such as a decreased lean body mass to fat mass ratio (decreased lean body mass and increased fat mass), are not clear in origin. It is possible that these negative body composition changes are due to decreased levels of physical activity. Specifically, it has been reported that physical activity levels significantly decrease during cancer treatment periods (Demark-Wahnefried et al., 2001). This decline in physical activity may extend into survivorship, as only 32% of breast cancer survivors engage in adequate physical activity (Irwin et al., 2004). Reductions in physical activity promote the disuse of skeletal muscles and may be a factor in the loss of lean body mass and increased fat mass that is experienced during the course of cancer treatment (Cheney, Mahloch, & Freeny, 1997; Freedman et al., 2004). These findings suggest that cancer-related treatments and the reduction in physical activity associated with treatments may account for the negative body composition that is commonly found in breast cancer survivors.

The negative body composition changes that breast cancer survivors experience are associated with decreased skeletal muscular strength and physical function. Skeletal muscle declines are notably linked to a decline in skeletal muscular strength, which is further tied to an increased morbidity and a decreased QOL (Argiles et al., 1999; Tisdale, 2002; Torodov et al., 1996). Specifically, declines in skeletal muscle strength are directly related to decreases in subjective measures of physical function and overall QOL in cancer patients (Crevenna, Maehr, Fialka-Moser, & Keilani, 2009).

While there are pharmacological options to combat some of the negative side effects associated with cancer treatments, prescription drugs carry the risk of causing even more side effects that are undesirable. Due to the possibility of adding to the list of undesirable side effects that cancer survivors battle, prescription drugs may not be the most appealing option to treat the issues associated with cancer treatment. Thus, non-pharmaceutical approaches play a vital therapeutic role in the cancer recovery process. Specifically, in healthy populations, exercise (resistance training) and dried plum consumption have shown to be promising therapies to attenuate many of the previously mentioned side effects that the breast cancer population encounters.

The successful effects of resistance exercise interventions on healthy post-menopausal women have been indicated by improvements in biochemical indices of bone formation and decreases in biochemical indices of bone resorption (Bemben, Fetters, Bemben, Nabavi, & Koh, 2000; Humphries et al., 1999; Kelntrou, Slack, Roy, & Lacouceur, 2007). Physical improvements of total and regional BMD are also well documented in post-menopausal women (Simkin, Ayalon, & Leichter, 1987; Vincent & Braith, 2002). Due to the lack of research investigating the efficacy of resistance training to improve biochemical markers of bone turnover and BMD in breast cancer survivors, more research is needed before similar conclusions can be made for the breast cancer population. Similarly, dried plum consumption has been shown to improve biochemical markers of bone turnover (Arjmandi et al., 2002) and may potentially be an effective means for improving BMD, as demonstrated in a recent clinical trial of post-menopausal women (Hooshmand et al., 2011).

In addition to producing positive changes in BMD, resistance training has also been shown to produce additional positive body compositional changes in cancer survivors, specifically increasing lean body mass and decreasing fat mass (Courneya et al., 2007; Schmitz, Ahmed, Hannan, & Yee, 2005). These positive body composition changes are likely linked with the significant skeletal muscular strength improvements (Courneya et al., 2007; Schneider, Hsieh, Sprod, Carter, & Hayward, 2007) and the improvements in physical function (Kolden et al., 2002; Stevinson, Lawlor, & Fox, 2004) elicited from resistance training interventions in cancer patient populations.

Previous studies suggest that breast cancer survivors encounter an array of detrimental physical changes resulting from the treatments for breast cancer. The studies have also shown that these physical changes have a negative impact on the QOL of the individual. Evidence from previous studies have indicated that resistance training and dried plum consumption have provided positive results in healthy post-menopausal women; however, there is very little research that has been conducted examining the effectiveness of resistance training to improve BMD, and no known research investigating the effectiveness of dried plum consumption to improve BMD in breast cancer survivors. Studies also indicate that resistance training improves other aspects of body composition (lean mass and fat mass), muscular strength, physical function, and QOL in breast cancer survivors. However, the majority of studies that have investigated the physical function of breast cancer survivors have done so utilizing subjective questionnaires. Objective physical function measures would be useful to assess the true physical function capacity as compared to the perceived physical function capacity of the breast cancer population. Studies reporting the negative physical and psychological changes that breast cancer survivors encounter, and the lack of studies investigating non-pharmacological approaches to combat these negative changes, warrant an investigation of non-pharmacological interventions to improve the conditions of this population.

PURPOSE

The purpose of the present investigation was to determine and compare the efficacy of resistance exercise training (RT) and a combination of RT and dried plum consumption (DP) on improving body composition (BMD, lean mass, and fat mass), muscular strength, physical function, and QOL in post-menopausal breast cancer survivors.

RESEARCH QUESTIONS

The present study was designed to answer the following research questions:

1. To what extent would a resistance exercise or combination resistance exercise and dried plum consumption intervention modulate total and regional (lumbar spine, femur, and forearm) BMD of post-menopausal breast cancer survivors?
2. To what extent would a resistance exercise or a combination resistance exercise and dried plum consumption intervention modulate the biochemical indices of bone formation and bone resorption of post-menopausal breast cancer survivors?
3. To what extent would a resistance exercise or a combination resistance exercise and dried plum consumption intervention modulate lean body mass, fat body mass, skeletal muscular strength, physical function, and QOL of post-menopausal breast cancer survivors?

RESEARCH HYPOTHESES

The hypotheses of the present study included the following:

1. Breast cancer survivors participating in both the resistance exercise intervention and the combination resistance exercise and dried plum consumption intervention would improve total and regional (lumbar spine, femur, and forearm) BMD.
2. Breast cancer survivors participating in both intervention groups would demonstrate increased levels of biochemical indices of bone formation and decreased levels of biochemical indices of bone resorption.
3. Breast cancer survivors participating in both intervention groups would demonstrate increases in lean body mass as well as decreases in fat body mass.
4. Breast cancer survivors participating in both intervention groups would demonstrate increased skeletal muscular strength.
5. Breast cancer survivors participating in both intervention groups would demonstrate improved physical function (both subjective and objective).
6. Breast cancer survivors participating in both intervention groups would experience improvements in QOL.

ASSUMPTIONS

Assumptions for the present study included the following:

1. All participants would accurately report their age, breast cancer medical history (diagnosis and treatment), menopausal status, current exercise status, and current dietary intake.
2. All participants would follow the instructions given to them regarding the maintenance of their current dietary habits and current daily physical activity outside of the prescribed intervention.
3. All participants would follow the instructions given to them regarding dried plum consumption and honestly and accurately report their adherence to the intervention when prompted to do so.
4. All laboratory equipment would yield accurate measurements over the course of repeated testing.

DELIMITATIONS

The delimitations of the present study included the following:

1. Only stage 0-III female breast cancer survivors would be allowed to participate in the present study. Therefore, male breast cancer patients, female survivors of stage four breast cancer, or females with active cancer, were not eligible to participate in the present study.
2. Individuals with uncontrolled hypertension, diabetes, or heart disease were not eligible to participate in the study.

LIMITATIONS

The limitations of the present study included the following:

1. Only female breast cancer patients were included in the present study, and therefore results obtained may not be generalized to male breast cancer patients or patients suffering from other forms of cancer.
2. Participants were recruited on a volunteer basis, and thus may have been more motivated than the general female breast cancer population. Therefore, the results obtained may not be generalized to the entire breast cancer population.

3. Participants were recruited from the Tallahassee, Florida and surrounding regions. Therefore, the results obtained may not be generalized to female breast cancer survivors in other geographical regions.

DEFINITION OF TERMS

- Adjuvant Chemotherapy—Chemotherapy that is used to destroy suspected undetectable residual tumor after surgery or radiation treatment has eradicated all detectable tumor; effective in the treatment of breast cancer (medical-dictionary.thefreedictionary.com).
- Aromatase Inhibitors—A class of drugs that suppress the synthesis of estrogen in the body by inhibiting the action of the aromatase enzyme and are used to treat breast cancer in postmenopausal women (www.cancer.gov/dictionary).
- Biochemical Markers of Bone Turnover—A blood or urine test to identify small changes in bone metabolism (medical-dictionary.thefreedictionary.com).
- Body Composition— the relative proportions of protein, fat, water, and mineral components in the body (medical-dictionary.thefreedictionary.com).
- Bone Mineral Density— A measurement of bone mass, expressed as the amount of mineral, in grams divided by the area scanned in (medical-dictionary.thefreedictionary.com).
- Breast Cancer—Cancer (a term for diseases in which abnormal cells divide without control and can invade nearby tissues) that forms in tissues of the breast, usually the ducts (tubes that carry milk to the nipple) and lobules (glands that make milk) (medical-dictionary.thefreedictionary.com).
- Dried Plums—The official name for prunes (dictionary.reference.com).
- Physical Function—The ability to perform mobility tasks, activities of daily living, and instrumental activities of daily living that are important for achieving and maintaining an independent living status (Spirduso, Francis, & Macrae, 2005).
- Progressive Resistance Training/Progressive Resistance Exercise—A training program in which the muscles must work against a gradually increasing resistance. An implementation of the overload principle (Powers et al., 2001).

- Quality of Life—An important consideration in medical care, quality of life refers to the individual's ability to enjoy normal life activities (www.medterms.com).
- Skeletal Muscular Strength—The maximal amount of force a muscle or muscle group can generate (Powers et al., 2001).

CHAPTER 2
REVIEW OF LITERATURE

Nearly 1.5 million new cases of cancer are diagnosed annually, and breast cancer is the most prevalent form of cancer that women develop (Jemal et al., 2009). Breast cancer survivors encounter numerous physical and psychological declines due to the cancer-related treatments that they endure. The following review explores the literature examining the physical and psychological detriments that breast cancer survivors experience during and after adjuvant chemotherapy and/or hormone suppressant therapies. Specifically, this review addresses several areas of body composition including bone mineral density (BMD), lean body mass, fat mass, and body fat percentage. Skeletal muscular strength, physical function, and quality of life (QOL) will also be addressed in this review. Further, this review is intended to report the effectiveness of two non-pharmacological approaches (resistance exercise and dried plum consumption) to combat the variables in which breast cancer survivors often experience declines, as well as to discuss the proposed mechanisms on how these interventions elicit positive changes.

The primary outcome variables that were investigated in this research project were total body and regional BMD. To understand the effects of chemotherapy and hormone suppressant therapy on BMD, and the beneficial effects of resistance exercise and dried plum consumption on BMD, understanding the basic components of the bone remodeling process is critical. The immediately following paragraphs provide a brief overview of the major components and the basic processes of bone remodeling, as well as the proposed mechanisms of how chemotherapy and hormone suppressant therapies alter BMD.

Effects of cancer treatments on BMD

Cancer treatments can directly affect bone through various physiologic actions and indirectly affect bone through reducing estrogen levels in the body. Specifically, some of the common adjuvant chemotherapy agents such as methotrexate,

cyclophosphamide, and doxorubicin, can act directly on the bone by interrupting the normal bone remodeling process (Michaud & Goodin, 2006).

Briefly, the bone remodeling process is comprised of many components and multiple processes. Bone is a highly dynamic network of metabolically active tissues. Normal bone remodeling is a coupled continuous process involving osteocytes (mechanoreceptors), osteoblasts (promote bone formation), and osteoclasts (promote bone resorption). These closely linked cells are formed from two origins: hematopoietic stem cells (osteoclast precursors) and stromal stem cells (osteoblast precursors). Osteoblast precursors contain a molecule known as RANKL or TRANCE, which can interact with a receptor known as RANK on osteoclast precursors. This interaction of RANKL and the receptor RANK allows osteoclast precursors to differentiate into mature osteoclasts (Horwood, Elliott, Martin, & Gillespie, 1998; Raisz, 1999; Yasuda et al., 1998). Osteoblasts also produce a molecule known as osteoprotegerin (OPG), which can interfere with the binding of RANKL to the RANK receptor, ultimately inhibiting mature osteoclast formation (Mizuno et al., 1998). Osteocytes are derived from osteoblasts that have stopped producing bone matrix. Osteocytes are buried in the bone matrix and are surrounded by an intricate network of tissues and spaces such as known as lacunae (cellular space), canaliculi (interconnections), and osteonals (vascular canals) (Zernicke, MacKay, & Lorincz, 2006). A number of environmental, biochemical, and mechanical factors can influence the bone remodeling process.

Of particular interest is the influence of estrogen on the bone remodeling process. Estrogen acts directly on bone by altering the ratio of osteoblast and osteoclast activity. Specifically, estrogen modulates osteoclast activity by increasing osteoclast apoptosis and decreasing differentiation and maturation of osteoclasts (Syed & Khosla, 2005). Estrogen is also believed to stimulate the release of OPG, which restrains osteoclast activity, ultimately preserving bone (Parfitt et al., 1984). The role of estrogen is important to consider as later hormone suppressant therapies will be discussed regarding their effects on BMD.

Detrimental effects of chemotherapy on bone have been studied in rodents for many years. Reports utilizing rodent models state that while the exact mechanisms are unknown, chemotherapy significantly decreases bone formation rates by nearly 60%.

Furthermore, osteoblasts showed a reduction in volume and thickness after exposure to chemotherapy (Friedlaender, Tross, Doganis, Kirkwood, & Baron, 1984), suggesting that chemotherapy also compromises the integrity of osteoblast cells. More recently, chemotherapy has been reported to have a dose-dependent toxicity to bone marrow stromal cells, which ultimately impairs new osteoblast formation (Banfi et al., 2001). Combined the direct effects of chemotherapy on osteoblasts are quite detrimental, and have been shown to cause negative effects on the bone remodeling process.

Chemotherapy agents further adversely affect bone by inducing ovarian failure. Between 50-85% of women treated with chemotherapy experience permanent ovarian failure (Bines, Oleske, & Cobleigh, 1996; Lower, Blau, Gazder, Tummala, 1999). Ovarian failure decreases the amount of estrogen produced, creating an imbalance in osteoblast and osteoclast activity, ultimately increasing the rate of bone turnover, with osteoclast activity occurring more readily than osteoblast activity (Pfeilschifter & Diel, 2000). Combined, the indirect and direct effects of adjuvant chemotherapy can greatly alter the bone remodeling process. During 12 months of chemotherapy treatment, Shapiro, Manola, and Leboff (2001) reported that women who experienced chemotherapy-induced ovarian failure exhibited a 4% decrease in spine BMD from baseline to six months and a further 3.7% decrease in spine BMD from six months to twelve months of the chemotherapy treatment period.

Similarly, Greep et al. (2003) reported post-menopausal breast cancer patients receiving adjuvant chemotherapy lost significantly more BMD at the spine and hip compared to breast cancer patients who did not have to take adjuvant chemotherapy treatment. Specifically, Robinson et al. (2005) reported that post-menopausal women receiving chemotherapy for six months or more experienced a 3.1% decrease in lumbar spine BMD (0.991 ± 0.5 vs. 0.965 ± 0.8 g/) and a 3.3% decrease in left hip BMD (0.864 ± 0.7 vs. 0.847 ± 0.9 g/) throughout a six-month chemotherapy treatment period.

Endocrine suppressant therapy also known as hormone suppressant therapy is another common form of treatment for breast cancer patients. Hormone suppressant therapy is typically prescribed after the primary cancer has been removed and/or treated with adjuvant chemotherapy or radiation. For post-menopausal women, Tamoxifen, a selective estrogen receptor modulator, had until recently been the most

common hormone suppressant therapy. Now, due to the superior efficacy of preventing breast cancer reoccurrences in post-menopausal women, the use of Tamoxifen alone has been replaced with a group of drugs known as aromatase inhibitors (AIs), or with a combination of Tamoxifen and AIs (Kudachadkar & O' Regan, 2005). Depending on the menopausal status of breast cancer patients, Tamoxifen has been shown to have either positive or negative effects on BMD.

In pre-menopausal women, two years of Tamoxifen treatment resulted in a 1.5% decrease in total body BMD (Sverrisdottir, Fornander, Jacobsson, von Schoultz, & Rutqvist, 2004). Conversely, post-menopausal breast cancer patients treated with five years of Tamoxifen had significantly higher BMD than breast cancer patients who did not receive Tamoxifen; however, within the first year of discontinuation of Tamoxifen BMD dropped a significant 4.8 ± 2.5% (Resch, Biber, Seifert, & Resch, 1998). This implies that for post-menopausal women, Tamoxifen can have temporary protective effects on bones during the course of treatment, but Tamoxifen does not provide long-lasting protective effects once its use is discontinued.

AIs prevent the conversion of androgens to estrogens in the peripheral tissues of the body; however, AIs do not inhibit estrogen synthesis in functioning ovaries. For this reason, AIs are only prescribed to post-menopausal breast cancer survivors (Osborne & Tripathy, 2005). AIs negatively affect bone due to the decreased circulating estrogen levels in the body, ultimately leading to less protective effects on bones (Pfeilschifter & Diel, 2000; Ramaswamy & Shapiro, 2003). The lack of estrogen protecting effects from taking AIs for one to five years can result in as much as a 7.2% BMD loss (Brufsky, 2007).

The rates of cancer treatment-induced BMD loss shown in previous research are considerably accelerated compared to the normal progression of BMD loss. The American College of Obstetricians and Gynecologists (2004) indicates that the normal rate of BMD loss for healthy post-menopausal women is 2% per year for the first five to eight years after menopause; whereas, if recalled, as much as a 4% bone loss can result from only six months of chemotherapy (Shapiro et al., 2001). Despite the known adverse effects of cancer treatments on BMD in the clinical realm, breast cancer patients are often not aware of these risks. In a recent survey, 39% of patients thought

cancer treatments strengthened bones or did not know the effects of cancer treatments on bone (Mckean et al., 2008). Clearly, BMD loss in breast cancer patients is an immediate and serious concern that deserves investigative efforts to improve the overall health of this population.

Effects of cancer treatment on body composition and muscular strength

Other unfavorable body composition changes that occur because of cancer treatments are changes in total body weight, decreased lean body mass to fat mass ratio (decreased or maintenance of lean body accompanied by increased fat mass) and increased body fat percentage. These changes in body composition are not clear in origin, but may be partially explained by the increased levels of fatigue and decreased levels of physical activity that breast cancer survivors experience throughout treatment. Breast cancer patients receiving adjuvant chemotherapy have reportedly experienced a significant increase in fatigue from baseline to the completion of their first chemotherapy treatment; furthermore, 33% of the patients indicated that the heightened fatigue levels persisted past the completion of their adjuvant chemotherapy treatments (Byar, Berger, Bakken, & Cetak, 2006).

The previous study evaluated patients during and directly following adjuvant chemotherapy treatment and reported incidents of increased fatigue and decreased QOL. In contrast, Bower et al. (2000) assessed a sample of 1,957 breast cancer patients between one to five years post chemotherapy treatment and found that fatigue levels were comparable to healthy age-matched women. However, in agreement with Byar et al. (2006), Bower and colleagues reported that the breast cancer patients who indicated higher fatigue levels were more likely to have been treated with adjuvant chemotherapy. These results suggest that fatigue is a major adverse side effect of cancer treatment during the treatment period, and in some cases can persist past the completion of treatment.

The heightened levels of fatigue experienced during chemotherapy and sometimes after the completion of chemotherapy may account for the decreased levels of physical activity that breast cancer survivors demonstrate during and after chemotherapy. Specifically, it has been reported that physical activity levels

significantly decreased during cancer treatment periods (Demark-Wahnefried, 2001). This decline in physical activity may extend into survivorship, as only 32% of breast cancer survivors engage in adequate physical activity (Irwin, 2004). The increased fatigue levels of breast cancer survivors and the resulting decreases in physical activity may explain some of the negative body composition changes that breast cancer survivors encounter.

As previously mentioned, increased total body weight is a common side effect of chemotherapy. Specifically, 50-96% of women experience weight gain after breast cancer diagnosis (Demark-Wahnefried et al., 1997). The amount of weight gain has reportedly ranged from 5-50 pounds (Demark-Wahnefried et al, 1993). Several factors seem to influence how much weight is gained during a treatment period. The specific type of chemotherapeutic agent received has been shown to influence the amount of weight gained throughout the course of therapy. The commonly received cyclophosphamide, methotrexate, and 5-flourouracil (CMF) regimen induced significant weight gains (Del Rio et al., 2002; Lankester et al., 2002), whereas another commonly prescribed chemotherapy regimen of doxorubicin and adriamycin cyclophosphamide (AC), did not alter total body weight (Demark-Wahnefried et al., 1997; Goodwin et al., 1999; Kutynec et al., 1999). Aside from the type of chemotherapeutic agent received, menopausal status also seems to be associated with the likelihood to gain weight after treatment. Camoriano et al. (1990) reported that pre-menopausal women were significantly more likely to gain weight compared to post-menopausal women (18% versus 6%) over the course of chemotherapy.

Similar to body weight changes, different changes in lean body mass are also reported. Some authors report decreases in lean body mass, with losses ranging from approximately 1-2 kg over the course of chemotherapy (Freedman et al., 2004; Kutynec et al., 1999). Other studies have reported no significant change in lean body mass (Campbell et al., 2007), whereas there has also been a report of lean body mass gain after the completion of chemotherapy (Del Rio et al., 2002). It should be noted that in the latter study that reported gains in lean body mass, participants also experienced significant total body weight gains. The increase in total body weight may have induced

the reported increase in lean body mass, as the body may have adapted to accommodate the weight gain.

Fat mass is another variable of body composition that consistently increases because of chemotherapy. Over the course of treatment, despite what occurs in terms of total body weight or lean body mass, fat mass and body fat percentage increase throughout adjuvant chemotherapy. Increases in fat mass and body fat percentage have reportedly ranged from approximately 1-4 kg and 1-2.5%, respectively (Kutynec et al., 1999; Campbell et al., 2007; Freedman et al., 2004; Harvie et al., 2004). Follow up studies conducted six months after completion of chemotherapy have reported even further fat mass gains of approximately 2-3 kg (Harvie et al., 2004; Freedman et al., 2004). These findings indicate that breast cancer survivors suffer negative body composition changes over the course of treatment and that these changes may continue to worsen after the completion of chemotherapy.

Results of the reviewed studies indicate a tendency for breast cancer survivors to experience losses or maintenance of lean body mass accompanied with an increase in fat mass; thus, it is logical to consider that the lean body mass to fat mass ratio decreases during and after chemotherapy regimens. The lean body mass to fat mass ratio seems to be an important factor linked to physical performance and morbidity in healthy populations, and is likely to be an important factor in determining skeletal muscular function in the cancer population. While there have not been guidelines published that categorize lean body mass to fat mass ratios, a recent assessment of 947 women aged 56-84, reported an average lean mass-to-fat mass ratio of 1.45, with ranges from 0.98-2.45 (Haight, Tager, Sternfeld, Satariano, & van der Laan, 2005). The lean mass to fat mass ratio has been reported as more indicative of skeletal muscular function than lean body mass alone (Lebrun Van der Schow, De Jong, Grobbee, & Lamberts, 2006; Sternfeld, Ngo, Satariano, & Tager, 2002). Specifically, Sternfeld et al. (2002) reported that a higher lean mass-to-fat mass ratio was linked to better physical performance and less physical limitation. These findings indicate the serious consequences that the breast cancer population may encounter because of the changes in body composition that they experience.

Muscular strength is another variable that is negatively impacted in the breast cancer population. To date there has only been one known study that has specifically examined muscular strength declines that breast cancer survivors encounter immediately following treatment (less than six months after completion of treatment). This particular study examined the muscular strength of the affected shoulder (side of body affected by breast cancer) after women had completed treatment. The authors found that shoulder protractors (108.4 ± 32.5 vs. 115.0 ± 28.9 N), retractors (145.0 ± 39.7 vs. 152.1 ± 34.4 N), and extensors (113.2 ± 30.2 vs. 122.0 ± 27.4 N) were significantly weaker compared to the non-affected shoulder (Merchant, Chapman, Kilbreath, Refshauge, & Krupa, 2008). It is logical to infer that since the affected side was weaker than the non-affected side, that overall muscular strength for the examined area would also be lower compared to healthy-matched women. This inference is supported by recent evidence from our laboratory comparing the muscular strength of breast cancer survivors to healthy age and weight-matched women. While no difference was detected between groups for hand dynamometer strength (53 ± 11 vs. 50 ± 7 kg), the healthy age and weight-matched women were significantly stronger in both chest press (77 ± 20 vs. 61 ± 13 kg) and leg extension (91 ± 18 vs. 70 ± 13 kg) compared to the breast cancer survivors (Simonavice et al., 2011). Overall, the studies reviewed indicate that the treatments breast cancer patients complete in response to their diagnosis seem to have significant negative impacts on their body composition and strength, and these negative changes have been further been suggested to negatively affect physical performance.

Effects of cancer treatment on physical function & QOL

As previously mentioned the negative body composition changes that occur after cancer treatment have been associated with declines in muscular performance and physical function. The relationship between body composition, muscular declines, and physical function is significant, because physical function is strongly related to QOL. Many subjective measures of QOL are comprised of several sub-components, one of which is physical function. The relationship between physical function, QOL, and the time since the completion of cancer treatment is indefinite. It is typically reported that

women earlier in their survivorship (less than three years) have the most physical function limitations. Specifically, Broeckel, Jacobsen, Balducci, Horton, & Lyman (2000) found that women who were finished with adjuvant chemotherapy for less than three years had significantly lower subjective physical function and QOL scores compared to healthy age-matched women. Similarly, in a sample of 25,719 elderly female cancer survivors who had completed treatments less than two years prior, self-reported the most physical function limitations (Sweeney et al., 2006). The previous self-reported measures of physical function differ from recent results obtained from our laboratory comparing measures of objective physical function (via the Continuous Scale Physical Function Performance (CS-PFP) test) in recent breast cancer survivors (completed treatment no more than three years prior to the investigation) to healthy age and weight-matched women. Scores for the CS-PFP are based on a 0-100 scale. Results indicated that breast cancer survivors exhibited lower function in all components (upper body strength, upper body flexibility, lower body strength, balance/coordination, endurance, and total function) of the CS-PFP; however, no significant differences were detected between breast cancer survivors and healthy controls. It is noteworthy to report that the domains of lower body strength (69.8 ± 16.37 vs. 58.8 ± 16.4), endurance (77.91 ± 13.22 vs. 68.91 ± 13.47), and total function (75.13 ± 12.98 vs. 66.14 ± 13.83) were approaching significance with a $p = 0.08$ (Simonavice et al., 2011).

The controversy with physical function limitations and time since treatment exists with women who are long-term survivors (5-10 years). High scores for subjective physical function and QOL were reported in a sample of 817 breast cancer patients who had completed treatment 5-10 years earlier. However, within the sample, women having been treated with adjuvant chemotherapy scored lower on their physical function and QOL scores compared to women who had not been treated with adjuvant chemotherapy (Ganz et al. 2002). Conversely, Sweeney et al. (2006) found that long-term (over five years) elderly breast cancer survivors reported less physical function capacity than did healthy age-matched women for activities of daily living such as walking a half mile, walking up and down stairs, and performing heavy household work.

With the exception of the preliminary data performed in our laboratory (unpublished data), the literature investigating physical function is comprised mainly of

subjective measures. While subjective physical function measures are useful, there is a void of objective measures of physical function conducted within the breast cancer population. Objective measures would allow investigators to pinpoint specific detriments in the many domains of physical function and therefore implement interventions intended to improve the found detriments. Overall, the reviewed studies demonstrate the need to implement interventions with the goal of improving body composition, increasing muscular strength, increasing physical function, and increasing QOL among breast cancer patients going through cancer treatments and as survivors of breast cancer.

Problems with traditional pharmaceutical treatments

Clearly, the breast cancer population faces an extensive list of negative side effects during and after cancer treatments. While there are pharmacological options to combat some of the negative side effects associated with cancer treatments, prescription drugs carry the risk of causing even more side effects that are undesirable. Specifically, bisphosphonates, prescribed for reversing bone loss, may result in infection, back or abdominal pain, arthralgia, nausea, dysphagia, dyspsia, diarrhea, renal toxicity, and osteonecrosis of the jaw (Actonel prescribing information; Boniva tablets complete product information; Fosamax tablets prescribing information, 2005). Furthermore, patient adherence to bisphosphonates is less than optimal, with less than half of the patients adhering to the prescription regimen (Carr, Thompson, & Cooper, 2006; Siris et al., 2006). The lack of adherence to a bisphosphonate prescription leaves the patients' bones vulnerable.

Due to the possibility of adding to the long list of undesirable side effects that cancer survivors encounter, prescription drugs may not be the most appealing option to treat the issues associated with cancer treatment. Thus, non-pharmaceutical approaches play a vital therapeutic role in the cancer recovery process. Specifically, exercise has shown to be a promising therapy to attenuate many of the previously mentioned side effects that occurs within the breast cancer population.

Mechanisms of resistance training on bone remodeling modulation

Resistance exercise is an effective approach to counteract BMD loss. As stated, a number of factors influence the bone remodeling process. Resistance exercise has often been used to improve BMD; however, the precise physiologic actions that modulate bone remodeling in response to resistance exercise are not clearly understood. It is commonly reported that bone remodeling is stimulated in response to a load (such as resistance exercise) via mechanotransduction, defined as the process by which mechanical energy is converted to electrical or biochemical energy (Burger & Klein-Nulend, 1999).

Osteocytes are referred to as mechanosensors, which can essentially detect mechanical loads. The mechanical load, causing a deformation in the bone, is initially sensed by the flow of interstitial bone fluid through the canaliculi and osteonals surrounding the osteocytes. This fluid flow is perceived as shear stress force, which further activates many cellular processes in osteocytes such as growth factor production, hormonal and biochemical messenger secretion, and matrix synthesis (Burger & Klein-Nulend, 1999; Zernicke et al., 2006). Nitric oxide (NO) is one of the substances released as a result of mechanical loading. NO is a strong inhibitor of osteoclast activity by suppressing RANKL expression and increasing OPG expression (Fan et al., 2004; Kasten et al., 1994; MacIntyre et al., 1991).

Mechanical loading also stimulates the release of prostaglandins. The exact action of prostaglandins are not clearly understood, but are suspected to affect bone remodeling in the following ways: recruitment of new osteoblasts from marrow stromal cells, amplifying the release of more prostaglandins by stimulating the expression of prostaglandin synthase, decreased apoptosis of osteoblasts, and increased osteoblast expression of matrix proteins (Fan et al., 2004; Turner & Robling, 2004).

The effects of resistance exercise on bone remodeling are complex and poorly understood. However, numerous bone biomarkers help to clarify the actions and reactions that take place in response to the multitude of stimuli influencing the bone remodeling process. As previously mentioned bone remodeling is a coupled process; meaning resorption is linked with formation. Imbalances occur in the remodeling process when bone resorption and bone formation are not occurring at equal rates.

Biomarkers for bone resorption and formation are highly useful in determining the influence of stimuli on the bone remodeling process. Commonly used bone resorption markers include tartrate resistant acid phosphate (TRAP-5b) and products of bone breakdown (hydroxyproline, pyridinoline, deoxypyridinoline, N-telopeptides, and C-telopeptides). Bone formation biomarkers include bone specific alkaline phosphatase (BSAP), osteocalcin, and procollagen extension peptides (Watts, 1999).

While these biomarkers are helpful in understanding the bone remodeling process, numerous factors can alter the bone remodeling process and cause fluctuations in bone biomarkers. Day to day variation for bone formation biomarkers is approximately 10% and for bone resorption biomarkers approximately 20-25% (Eastell, Colwell, Hampton, & Reeve, 1997; Nielsen, Brixen, Bouillon, & Mosekilde, 1990). Menopause significantly increases bone turnover and consequently influences bone turnover biomarkers, with the onset of menopause causing a 37-52% and 79-97% increase in bone formation and bone resorption biomarker levels, respectively (Garnero, Sornay, Chapuy, & Delmas, 1996). Bone biomarkers and the factors that alter them are important to consider when examining the effects of stimuli on the bone remodeling process.

Resistance exercise effects on BMD in healthy post-menopausal women

Various types and modes of exercise each offer unique health benefits. While aerobic exercise, specifically walking (considered to be a low impact aerobic activity) is the most commonly preferred mode of exercise among breast cancer survivors (Rogers, Courneya, Shah, Dunnington, & Hopkins-Price, 2007), low impact activities are not the most beneficial form of exercise for improving BMD (Kohrt, Bloomfield, Little, Nelson, & Yingling, 2004). Most studies examining the effects of a walking program on the BMD of post-menopausal women have found that at best, specific sites of BMD can be maintained; however, there is evidence to suggest that a loss of BMD still may occur at various sites during a walking program (Ryan, 1998; Yamazaki, Ichimura, Iwamoto, Takeda, & Toyama, 2004). These findings reiterate that walking is not the ideal mode of exercise to combat BMD loss.

The successful effects of resistance exercise on BMD in healthy post-menopausal women are well documented; however, the effect of resistance exercise on BMD among the breast cancer population is still a very new avenue of research. It should be re-emphasized that since BMD loss is accelerated in breast cancer survivors compared to healthy post-menopausal women, maintaining, as opposed to improving BMD, is the more realistic and still desirable outcome. It is logical to predict that with the appropriate resistance exercise regimen, breast cancer survivors could also benefit from resistance exercise. In order to understand how resistance exercise may benefit breast cancer patients, it is important to recognize the major concepts that comprise a successful resistance exercise regimen in healthy post-menopausal women. Previous research indicates that the exercise intensities, site-specific exercises, and the duration of the resistance exercise program all are crucial components of a resistance exercise prescription.

Resistance exercise-induced changes in bone turnover biomarkers can be detected much sooner than the physical changes in BMD. Changes in bone biomarkers can be detected acutely following an exercise session. Whipple et al. (2004) reported that following a bout of moderate intensity resistance exercise, the ratio of bone formation biomarkers to bone resorption biomarkers was significantly increased. These results are similarly displayed after a chronic resistance exercise program of only 12 weeks at which point bone resorption was found to have decreased by 14%, ultimately increasing the bone formation to bone resorption biomarker ratio (Klentrou, Slack, Roy, & Ladouceur, 2007).

The minimum duration of a resistance exercise program needed to induce detectable physical changes in BMD remains equivocal. Resistance exercise programs enduring less than six months consistently fail to produce detectable changes in BMD in healthy post-menopausal women. Ryan, Treuth, Hunter, and Elahi (1998) performed a progressive resistance exercise program for 16 weeks with a group of 24 post-menopausal women. The participants were guided through a one-hour resistance training protocol three days a week, with the intensities individually adjusted every one to two weeks. Specific intensities at which the participants exercised were not accounted for. At the end of the study, the participants showed no significant changes

in total body (1.107 ± 0.018 vs. 1.101 ± 0.020 g/), lumbar spine (0.988 ± 0.029 vs. 0.988 ± 0.037 g/), femoral neck (0.750 ± 0.032 vs. 0.746 ± 0.032 g/), and 1/3 radius (0.555 ± 0.025 vs. 0.554 ± 0.016 g/).

In a 16-week study, Ryan et al. (1998) noted a positive correlation between baseline leg press strength and both lumbar spine BMD ($r = 0.72$, $p < 0.0001$) and femoral BMD ($r = 0.79$, $p < 0.0001$). Participants were able to increase their leg press strength by 98%, which suggests that had the study lasted longer, a direct positive relationship between strength and BMD may have developed. Nonetheless, the authors failed to show any significant improvements in BMD from the 16-week trial.

Resistance exercise interventions of approximately six months have produced conflicting BMD results (Bemben, Fetters, Bemben, Nabavi, & Koh, 2000; Simkin, Ayalon, & Leichter, 1987). Nonetheless, many six months studies provide encouraging results. Even in studies that have not found significant increases in BMD after six months of resistance exercise, a tendency for C-telopeptides to decrease has been noted (Humphries et al., 1999). These studies suggest that due to the tendency for bone resorption biomarkers to decrease, ultimately bone turnover decreases.

Unlike the previous studies that were unable to detect a significant change in total or regional BMD after six months of resistance exercise, several studies have been successful with improving BMD at various sites of the body. Simkin et al. (1987) reported significant increases (3.8%) in the distal radius of elderly osteoporotic women after only five months of three times weekly load bearing exercise to the forearm. Similarly, Jessup, Horne, Vishen, and Wheeler (2003) prescribed 18 healthy elderly women a combination weighted vest aerobic and strength training (8-10 repetitions at 50-75% 1-RM) intervention three times per week for 32 weeks. Following the intervention, Jessup and colleagues reported a significant increase in lumbar spine BMD (0.77 ± 0.07 vs. 0.88 ± 0.08 g/) and femoral neck BMD (0.67 ± 0.04 vs. 0.74 vs. 0.05 g/). Vincent and Braith (2002) examined the effects of three times weekly high intensity resistance exercise (1 set of 8 repetitions at 80% 1-RM) compared to low intensity resistance exercise (1 set of 13 repetitions at 50% 1-RM) on BMD in 62 healthy older adults. After six months, the femoral neck of the high intensity group had significantly improved by 1.96%. Both the low intensity and high intensity exercise

groups significantly increased levels of osteocalcin, with 25.1 ± 36.8% and 39 ± 44.6% changes, respectively (Low intensity: 10.7 ± 4.0 vs. 13.58 ± 7.2 ng/mL; High intensity: 11.94 ± 5.0 vs. 15.57 ± 7.4 ng/mL); whereas, only the high intensity resistance exercise group produced a significant BSAP increase of 7% (17.86 ± 6.6 vs. 19.15 ± 7.5 U/L). The authors reported that the high intensity intervention invoked a significant increase in the ratio of bone formation to bone resorption biomarkers compared to the low intensity resistance exercise. The change in the biomarker ratio signifies a change in bone turnover favorable to bone formation. Overall, these studies suggest that a resistance exercise program at least six months is needed to quantify the physical changes in BMD.

Resistance exercise studies that have lasted six months or more have consistently shown positive effects on BMD in healthy post-menopausal women. Pruitt, Jackson, Bartels, and Lehnhard (1992) implemented a nine-month weight training intervention in 17 post-menopausal women. The authors prescribed 11 resistance exercises three times per week for one set of 10-12 repetitions and one set of 10-15 repetitions for upper and lower body exercises, respectively. The exercises began at 50-60% of the participants' 1-RM, and progressively increased throughout the course of the study. Pruitt et al. (1992) reported that the lumbar spine had significantly increased at the half-way point (4.5 months) and remained elevated for the remaining duration of the nine-month study (1.128 ± 0.027 vs. 1.149 ± 0.023 g/) and (1.128 ± 0.027 vs. 1.140 ± 0.022 g/), respectively.

Bergstrom, Landgren, Brinck, and Freyschuss (2008) conducted a 12-month study on post-menopausal women with low baseline BMD and who had recently suffered a forearm fracture. The women were divided into a physical training group or a control group, while all participants received an unspecified supplement of calcium and vitamin D. The physical training component included both an aerobic and muscular strength component; however, details concerning intensities for the exercise program were not given. Bergstrom et al. (2008) showed that the physical training regimen had significant positive effects on total hip BMD (+0.005 ± 0.018 g/). These results indicate even post-menopausal women with low baseline BMD can benefit from a structured exercise regimen.

Kerr, Ackland, Maslen, Morton, and Prince (2001) performed a similar 24-month study combining resistance exercise and calcium supplementation on 126 post-menopausal women and measured the effects on BMD. The participants were divided into one of three groups: strength training, fitness training, or usual care. Both the fitness and the strength groups performed resistance exercises three times per week for 3 sets of 8 repetitions; however, the fitness group did not have a standard for intensity progression. The intensity for the strength-training group was adjusted periodically throughout the 24 months. All groups were given a calcium supplement of 600mg per day. Kerr et al. (2001) found that the strength-training group compared to the other groups demonstrated greater BMD benefits at the total hip (0.9 ± 2.6%) and intertrochanter (1.1 ± 3.0%). Specifically, the total hip was 3.2% higher in the strength group compared to the control and fitness groups. No significant differences were noted among the groups for BMD at the forearm or lumbar spine, indicating that the site-specific exercises used in the protocol may have been inadequate in terms of loading to these specific anatomical sites. The authors also reported that the majority of BMD gains from the strength group were made within the first 12 months. These results suggest that intentional and progressive increases in resistance training intensities are necessary to see BMD improvement. More specifically, the study also revealed that the specific exercise selection, in terms of anatomical loading, is also important.

A more recent study by Stengel et al. (2005) compared the effectiveness of power training to strength training for maintaining BMD in post-menopausal women. In this study, 42 osteopenic women who had recently been strength training were guided through 12 months of strength or power training. Additionally, both groups were given a calcium and vitamin D supplement of 1500 mg and 500 IU, respectively. The exercise regimen for both groups consisted of the same intensities (70-90% 1-RM, with intermittent 50% 1-RM periods) and volumes (unspecified); however, the difference between the groups was the concentric contraction speeds. The strength group was instructed to perform a four-second concentric contraction, while the power group was instructed to move explosively through the contraction (Stengel et al., 2005).

Stengel et al. (2005) reported that the power-training group demonstrated larger effects than the strength training group in BMD at the lumbar spine, total hip, and

intertrochanter; however, no significant differences in BMD were found at the total forearm or ultra-distal radius. Overall, the study revealed advantages of performing power training on BMD compared to strength training. While Stengel et al. (2005) reported no safety concerns or problems throughout the 12-month study; these recommendations should not yet be transferred to breast cancer patients and survivors until more research is conducted regarding the safety of such protocols for the breast cancer population.

The reviewed studies have demonstrated the positive effects on BMD that can be achieved in healthy post-menopausal women. Furthermore, the studies reveal the importance of details when prescribing a resistance exercise program. Studies performed on healthy post-menopausal women suggest that in order to see positive BMD effects, the duration of the resistance exercise program needs to be at least six months, the exercises need to be specific to the anatomical site of concern, and the intensities of the exercises need to be periodically adjusted to provide adequate loading to the bone. While several of the reviewed studies did not mention specific intensities at which exercise interventions were performed, a recent review (Zehnacker & Bemis-Dougherty, 2007) of resistance exercise in healthy post-menopausal women has proposed intensities at which BMD may improve. The recommendations state that in order to see positive BMD effects from resistance training, intensities and volumes should include two to three sets of 8-12 repetitions at 70-90% of 1-RM.

Overall, the past research provides encouraging results for breast cancer patients suffering from cancer treatment-related bone loss. While the safety and efficacy of prescribing breast cancer patients exercise regimens mimicking those prescribed for healthy post-menopausal women are still a concern, such ideas have provided direction for researchers attempting to implement resistance exercise programs among breast cancer patients and survivors.

As previously mentioned, in order to see positive bone benefits, resistance exercise intensity and progression must be thoughtfully prescribed and carefully monitored. The possibility that a resistance exercise program may exacerbate pre-existing conditions such as fatigue and/or lymphedema presents concerns that must be carefully addressed. However, recent studies have shown that exercise interventions

have been used to decrease fatigue in cancer patients (Cramp, 2008; Stricker, Drake, Hoyer, & Mock, 2004). Further, several studies and one recent review have noted that lymphedema is not likely developed or worsened (for patients currently with lymphedema) during a resistance exercise program (Ahmed, Thomas, Yee, & Schmitz, 2006; McKenzie & Kalda, 2003; Schmitz, 2009).

Resistance exercise effects on BMD in the breast cancer population

One of the first studies that implemented a resistance exercise program with breast cancer patients with BMD as a main outcome measure was conducted by Waltman et al. (2003). In this study, a multi-component intervention seeking to prevent osteoporosis in post-menopausal breast cancer survivors was implemented for 12 months. All participants were instructed to take 400 IU of vitamin D, 1500 mg of Calcium, and alendronate (a bisphosphonate drug). Participants were also instructed to engage in a progressive strength-training regimen two times per week. Waltman et al. (2003) reported the participants experienced significant increases in hip BMD (2.6 ± 3.0%) and spine BMD (2.4 ± 3.1%) while experiencing significant decreases in forearm BMD (-2.6 ± 2.6%). The authors explained that the loss of BMD at the forearm could have been a result of the lack of intensity in the exercises targeting the forearm area. Overall, Waltman et al. (2003) provided a useful protocol from which significant improvements were reported for BMD at the hip and spine. Despite the several positive outcomes of this study, the design of the study does not allow distinction as to whether the positive outcomes were a result of the combination of alendronate, calcium/vitamin D, and resistance exercise, or whether one of these treatments independently could have produced similar results.

Other studies have been less successful in terms of improving BMD in the breast cancer population. Ott et al. (2004) sought to determine the efficacy of a resistance exercise program on breast cancer patients who were at a risk for developing osteoporosis. During a six-month home-based resistance exercise intervention, the authors reported a steady progression of pounds that the participants lifted from baseline to six months. However, the heaviest weights lifted throughout the study were no more than 10 and 12 pounds for the upper body and lower body, respectively.

Hence, the authors suggested that even though the participants exhibited a steady progression of pounds lifted, the maximum amount lifted still might not have been heavy enough to create positive effects on the bone.

In a more recent study Schwartz, Winters-Stone, and Gallucci (2007) examined the preventative effects of exercise (resistance exercise or aerobic training) against BMD loss in 66 women during their adjuvant chemotherapy treatments. The interventions began simultaneously with the initiation of chemotherapy treatment. The aerobic exercise group performed 15-30 minutes of moderate aerobic activity (a mode of their choice) for four days per week, while the resistance exercise group performed a total body workout of two sets of 8-10 repetitions using Thera-bands™ for two days per week. A usual care group served as a control. Schwartz et al. (2007) found that all participants lost BMD. These results should not come as a surprise, recalling the significantly accelerated rates of bone loss during chemotherapy treatment. Specifically, the usual care group lost the greatest amount of BMD (6.23%), followed by the resistance exercise (4.92%) group, and aerobic group (0.76%).

Additionally, Schwartz et al. (2007) found that while none of the participants had osteopenia or osteoporosis at baseline, fifteen women (9% from the aerobic group, 19% from the resistance exercise group, and 39% from the usual care group) had osteopenia at the six-month mark, while 9% (from the usual care group), had osteoporosis. Even though all groups lost BMD, these results indicate that moderate-intensity aerobic exercise may help to reduce bone loss in breast cancer patients receiving chemotherapy. While, resistance exercise attenuated BMD loss compared to the usual care group, the protocol utilizing resistance Thera-bands™ may not have provided adequate loading, and thus may not provide a true indication of the protective effects of an adequate load bearing resistance exercise program against the BMD loss of breast cancer patients.

Exercise adherence among the breast cancer population

Another concern with implementing a resistance exercise program among the breast cancer population is adherence to the prescribed exercise. The benefits of exercise are well documented; however, in order to achieve these benefits, adherence

to the exercise prescription is critical. Ott et al. (2004) assessed the adherence rate to a home-based resistance exercise program in breast cancer survivors. A 94% adherence rate was reported and as previously mentioned a steady progression of pounds lifted from baseline to six months was achieved. However, as discussed the maximal amounts of weights lifted may not have been sufficient to elicit positive BMD effects.

While it is constructive to assess overall adherence rates to prescribed exercise, for examining the effects of resistance exercise on bone, adherence should be assessed for each of the crucial components of exercise (intensity, frequency, duration). Daley et al. (2007) emphasized that in order to obtain detailed information about an exercise sessions, adherence to each of these three components should be incorporated into the exercise intervention. In an exercise program for breast cancer survivors, Daley et al. (2007) reported that while adherence to attending exercise sessions was acceptable at 77%, only 52.9% were able to achieve the prescribed duration of exercise. These reports demonstrate how the phrase “adherence to exercise” can be deceptive and that adherence to each of the individual components of an exercise prescription is needed in order to achieve optimal benefits.

Courneya et al. (2007) reported somewhat different adherence encounters than the previous authors. In a resistance exercise program, breast cancer survivors’ adherence to attend exercise sessions was only 70%; however, adherence to the prescribed number of exercises, sets, and repetitions, were 96.8%, 96.9%, and 94.5%, respectively. These data imply that attending the exercise sessions was a bigger obstacle than adhering to the several components of the exercise session. To improve the adherence rates of exercise attendance and adherence to the prescribed components of exercise, an assessment of common barriers would be beneficial.

Courneya et al. (2008) reported that common barriers to exercise among the breast cancer population fell into one of three major categories: disease/treatment-related, life-related, or motivational-related. Disease/treatment-related (feeling sick, pain, fatigue, etc) accounted for 53% of the given reasons for missing an exercise session. These findings suggest that addressing the barriers to exercise and tailoring the exercise prescription to accommodate the noted barriers is needed in order to achieve maximal benefits from an exercise program.

In a sample of 75 breast cancer survivors, Irwin et al. (2008) reported an 80% adherence rate to prescribed exercise duration. The authors assessed what factors influenced the women to adhere to the exercise and found the most common responses to include the following: free health club membership, knowing a trainer was there to record the exercise session and check progress, and having supportive trainers. These reports support the concept of a supervised structured exercise setting for the breast cancer population.

The research reviewed provides encouraging information regarding the potential to implement a resistance exercise program among the breast cancer population to help combat many of the negative side effects caused by cancer treatments. The literature has shown that for positive BMD effects, a resistance exercise program must be thoughtfully prescribed and monitored. Furthermore, the literature has shown that adherence to each of the components of an exercise prescription is needed to provide maximal gains. To improve adherence rates, an assessment of barriers to exercise should be obtained. Knowing potential obstacles before beginning an exercise program will allow strategic planning to overcome the perceived barriers along the course of an exercise program and achieve the most benefits from the prescribed exercise as possible.

Dried plum effects on BMD

Similar to resistance exercise, the consumption of dried plums may also serve as a non-pharmacological approach to combat bone loss in breast cancer patients. Currently, there have not been any studies investigating the efficacy of the consumption of dried plums on bone loss within the breast cancer population; however, several rodent models and two clinical trials have shown promising results.

Several rodent models have been utilized in exploring the effects of dried plum consumption on BMD. Both male and female rodent models have displayed positive results. Researchers have shown that dried plum consumption can both prevent, and more importantly reverse orchidectomized-induced bone loss. Bu et al. (2007) performed orchidectomies on male rats and allowed bone loss to occur for 90 days. The rats were then fed a 25% dried plum diet for 90 days. The dried plum consumption

resulted in an 11% increase in vertebral and femoral BMD compared to the orchidectomized controls. Furthermore, Bu et al. (2007) reported that dried plum consumption tended to decrease urinary deoxypyridinoline and calcium, but did not alter BSAP or osteocalcin.

Franklin et al. (2006) examined the preventative effects of dried plum consumption on orchidectomized-induced bone loss in six-month-old male rats. The rats were fed a low dried plum (5%), medium dried plum (15%), or high dried plum (25%) diet for 90 days. The authors reported that both the medium and high dried plum diet groups completely prevented the orchidectomized-induced bone loss in the whole body, femur, and lumbar BMD sites. Similar to Bu et al. (2007), Franklin and colleagues reported a decrease in deoxypyridinoline excretion and no significant increase in osteocalcin or BSAP, but did note a significant increase in insulin like growth factor-I (IGF-I) in all groups consuming dried plums. Together these studies suggest that dried plum consumption both reverses and prevents bone loss via mechanisms of decreased bone resorption and possibly increased bone formation mediated by IGF-I. Bu et al. (2008) later reported evidence that the polyphenols (a group of chemical substances found in plants) found in dried plum reduced bone resorption by decreasing osteoclast activity. The authors observed that polyphenols downregulated osteoclast precursor expression, signifying that polyphenols primarily affect osteoclast differentiation as opposed to osteoclast activity.

Positive bone results have also been reported in female rodent models. Deyhim, Stoecker, Brusewitz, Devareddy, and Arjmandi (2005) used ovariectomized osteopenic rats that were fed a low dried plum (5%), medium dried plum (15%), or high dried plum (25%) diet. After consuming the diets for 60 days, the authors reported that all dried plum-consuming groups were successful in restoring tibia BMD. Only the high dried plum group was able to increase lumbar BMD. Johnson, Lucas, Hooshmand, Campbell, Akhter, and Arjmandi, (2008) also reported on the successful results of dried plum consumption on reversing ovariectomy-induced bone loss in female rats. The authors examined the effects of a soy-based diet (known to positively influence bone metabolism) compared to a combination soy and dried plum diet. Johnson et al. (2008)

found that the combination soy and dried plum diet was more effective in increasing BMD compared to the soy diet alone.

The positive bone results from dried plum consumption in the female rodent models are likely due to the modulation of bone resorption and formation, specifically, decreasing urinary deoxypyridinoline excretion and enhancing BSAP activity (Johnson et al., 2008). Arjmandi et al. (2001) found that dried plum consumption dose-dependently elevated circulation levels of IGF-I. As mentioned above, IGF-I is known to stimulate bone formation. Specifically, IGF-I is produced by bone cells at the local level, and acts to stimulate osteoblasts, increase collagen synthesis, and enhance matrix apposition (Pfeilschifter, Oechsner, Naumann, Gronwald, Minne, & Zielgler, 1990; Radcliff, Tang, Lim, Zhang, Abedin, Demer, Tintut, 2005). Therefore, the mechanism of action for decreasing bone loss through dried plum consumption in female rodents seem to rely more heavily on increased bone formation as opposed to the suppression of bone resorption.

The positive bone results demonstrated in the male and female rodent models are encouraging and raise the question as to whether similar results can be achieved in humans. To date there are only two known studies implementing a clinical dried plum intervention. Arjmandi et al. (2002) investigated the effects of three months of dried plum consumption on the bone turnover biomarkers of 58 post-menopausal women. The women were divided into two groups, one group consuming 75 g of dried apples, the other group consuming 100 g of dried plums daily. The authors found that only the dried plum group significantly increased serum IGF-I levels and BSAP activity. Neither group exhibited significant changes in bone resorption biomarkers. These findings suggest that with a longer intervention period dried plum consumption may result in detectable physical BMD changes in postmenopausal women due to the increased bone formation biomarkers. The second clinical trial extended the first trial and investigated the effects of 12 months of dried plum or dried apple consumption on BMD and bone turnover biomarkers in a group of 160 post-menopausal women. Again, the women were divided into two groups, one group consuming 100 g of dried apples, the other group consuming 100 g of dried plums daily. At the conclusion of the 12-month intervention, dried plum consumption produced significant improvements in forearm and

spine BMD compared to the dried apple group. Further, dried plum consumption significantly decreased levels of bone turnover biomarkers (Hooshmand et al., 2011). These findings are particularly encouraging as breast cancer survivors are especially prone to having lower forearm BMD compared to healthy age-matched women (Simonavice et al., 2011)

Resistance exercise effects on body composition and muscular strength

Excess fatigue during chemotherapy treatment may account for the decreases in physical activity and consequently, the negative body composition changes that the breast cancer population experiences during and after chemotherapy (Irwin et al., 2004). Ironically, moderate intensity aerobic activity during and after treatment has repeatedly been shown to decrease perceived fatigue levels in breast cancer patients (Cramp, 2008; Stricker et al., 2004). More recently, resistance exercise has also shown promising results in decreasing fatigue. Schneider, Hsieh, Sprod, Carter, and Hayward (2007) implemented a supervised exercise intervention consisting of both an aerobic component and a resistance exercise component in a group of breast cancer patients. The breast cancer patients were grouped according to whether the exercise intervention would take place during cancer treatment or whether it would begin after the completion of treatment. At the end of the six-month intervention, both groups indicated decreased total fatigue. Similar results were found by Milne, Wallman, Gordon, and Courneya (2008) who implemented a combined aerobic and resistance exercise intervention in early stage breast cancer patients who had recently completed treatment (less than two years prior). Milne et al. (2008) reported that at the end of the 12-week intervention, fatigue had significantly decreased. More importantly, the authors reported that 12 weeks after the completion of the exercise intervention, participants indicated a continued reduction in fatigue. These results are especially encouraging suggesting that the benefits of exercise may persist past the completion of a supervised exercise intervention.

Similarly, Headley, Ownby, and John (2004) found that advanced stage (metastatic) breast cancer patients benefited from a seated resistance exercise program. Participants were divided into an exercise or control group. The exercise

group was given an exercise video and instructed to perform the exercises three times per week for the duration of four cycles of chemotherapy. All participants demonstrated an increase in fatigue from baseline to the completion of the intervention; however, the exercise group indicated less of an increase in fatigue compared to the control group. Due to the few studies investigating the effects of exercise on advanced breast cancer patients, these finding are unique and encouraging.

The studies reviewed reveal that moderate intensity aerobic exercise and resistance exercise can attenuate the heightened fatigue that is associated with cancer treatments. These results suggest that breast cancer patients of all stages and at all points in their survivorship can benefit in terms of fatigue from both supervised and home-based exercise interventions. One may further infer that a reduction in fatigue accompanied by an increase in physical activity is likely to have a positive effect on body composition.

Just as resistance exercise has elicited improvements in BMD, other variables of body composition have also improved from resistance exercise. These improvements in body composition are often accompanied by increases in skeletal muscular strength. Resistance exercise prescribed for various time periods have consistently produced positive body composition and muscular strength results in the breast cancer population.

Even resistance exercise interventions that were initiated simultaneously with the onset of adjuvant chemotherapy, were able to produce significant increases in lean body mass as well as upper and lower body strength (Battaglini et al., 2007; Courneya et al., 2007). Courneya et al. (2007) implemented a resistance exercise intervention that began simultaneously with the prescribed chemotherapy regimen. Patients were asked to exercise three times per week performing two sets of 8-12 repetitions of nine different exercises at 60-70% of their 1-RM. This regimen was continued throughout the course of their chemotherapy, approximately 17 weeks. The resistance exercise intervention failed to produce changes in total body weight, body fat percent, or fat mass that were significantly different to the usual care group; however, lean body mass was significantly higher (41.3 ± 4.9 vs. 40.9 ± 5.6 kg) compared to the usual care group at the end of the intervention. From these data indicating no change in fat mass, but a

significant increase in lean body mass, it would be logical to anticipate an increase in lean body mass to fat mass ratio; however, when calculated, both baseline and post-resistance exercise intervention ratios were 1.54. This suggests that a further increase in lean body mass, while maintaining or decreasing fat mass, is needed in order to change the lean mass to fat mass ratio. While statistical analyses were not computed on lean mass to fat mass ratios, the resistance exercise group maintained their ratio, while the control group's ratio seemed to decrease over the course of the study (Resistance exercise: 1.54 vs. 1.54; Control: 1.43 vs. 1.39).

Body composition improvements have also been noted in breast cancer survivors with as little as eight weeks of resistance exercise. Cheema and Gaul (2006) prescribed a combination aerobic and resistance exercise intervention to breast cancer survivors (at least six months post treatment) twice weekly for eight weeks. The resistance exercise portion consisted of 10 different exercises for 1-3 sets of 8-12 repetitions (intensity not specified). The authors reported significant improvements in body composition in terms of hip and waist circumference compared to baseline measures (103.1 ± 9.4 vs. 105.6 ± 9.5 cm and 82.2 ± 12.2 vs. 85.0 ± 12.3 cm, respectively).

Even though short resistance exercise interventions have produced positive body composition results, interventions prescribed for longer periods have also produced positive body composition changes in breast cancer survivors. Schmitz et al. (2005) prescribed recent breast cancer survivors (completed cancer treatment no more than 36 months prior to baseline testing) a resistance exercise program consisting of nine different building up to 3 sets of 8-12 repetitions (intensity not specified) to be completed twice weekly. The entire program was designed to last 12 months, but at the six-month mark, breast cancer survivors already had shown significant improvements in lean body mass compared to baseline measures (38.78 ± 0.77 vs. 37.9 ± 0.77 kg) and body fat percentage (40.91 ± 1.31 vs. 42.05 ± 1.31%). Even further improvements were reported at the end of the 12-month period. These results suggest that body composition improvements are able to be detected within a short period, and continue to improve with longer interventions.

The improvements in body composition elicited from resistance exercise are often accompanied by improvements in muscular strength. Many of the studies reviewed regarding body composition improvements have also indicated improvements in muscular strength. Courneya et al. (2007) noted that their 17-week intervention during adjuvant chemotherapy yielded significantly increased chest press and leg press 1-RM values compared to baseline (31.9 ± 10.8 vs. 23.2 ± 7.2 kg and 32.8 ± 12.6 vs. 24.4 ± 11.2 kg, respectively). Similarly, Cheema and Gaul (2006) reported that their eight-week combination aerobic and resistance exercise intervention prescribed to breast cancer survivors elicited significant increases in both upper body and lower body strength compared to baseline measures (39.7 ± 16.4 vs. 29.8 ± 6.6 kg and 199.1 ± 46.6 vs. 134.8 ± 29.3 kg, respectively).

Longer resistance exercise interventions have also produced muscular strength improvements. Ahmed et al. (2006) implemented a resistance exercise program consisting of nine different exercises for 1-3 sets of 8-10 at an unspecified intensity twice weekly for six months in a group of cancer survivors (various types of cancer). The authors reported significant improvements in bench press and leg press 1-RM values compared to baseline (296.6 ± 10.2 vs. 214.8 ± 9.8 lbs and 83.0 ± 2.8 vs. 50.7 ± 2.7 lbs, respectively).

Combined, the studies reviewed provide encouraging results for cancer patients receiving chemotherapy as well as recent and long-term survivors. The results of the previous studies have shown that various lengths of resistance exercise interventions consisting of 2-3 times weekly for 1-3 sets of 8-12 repetitions at various exercise intensities can elicit both positive changes in body composition as well as improvements in upper and lower body muscular strength.

Resistance exercise effects on physical function and QOL

Just as moderate intensity resistance exercise has been shown to have positive effects on various components of body composition and muscular strength, it also has beneficial effects on subjective physical function and QOL. The use of resistance exercise to increase physical function and QOL has only begun to be researched in the past 10 years. Of the few existing studies investigating the effects of resistance

exercise on physical function and QOL, Ohira, Schmitz, Ahmed, and Yee (2006) reported positive results. The authors employed a resistance exercise program in a sample of 86 breast cancer patients who had completed cancer treatment no more than three years prior. Participants were trained twice a week under the supervision of a qualified trainer for 13 weeks and then were asked to carry out the exercise on their own, without the aid of a trainer, for an additional 13 weeks. Ohira et al. (2006) found that participants demonstrated increases in physical and psychological QOL from baseline to six months. These results suggest that a supervised resistance exercise program followed by a self-sustaining period can increase physical well-being and QOL. These results are similar to Wiggins and Simonavice (2009) who reported increased QOL scores among cancer survivors after a six-month supervised multi-component (aerobic and resistance) exercise intervention.

Uniquely, Adamsen et al. (2006) conducted a multi-component exercise program consisting of high intensity aerobic and resistance exercise in a group of 86 cancer patients. This study is unique by the high intensity exercises that were prescribed to the participants. Adamsen et al. (2006) prescribed only three resistance exercises (leg press, chest press, and lat pull down) for 3-5 sets of 8 repetitions at 85-95% one-repetition maximum. The authors explained that the exercise prescription was designed to create a large impact in a short time. The authors reported no increases in injury or fatigue. Adamsen et al. (2006) were successful with their high intensity exercise intervention with the participants significantly increasing in physical capacity and QOL after only six weeks of the supervised exercise program; however, the study is limited by the lack of a full body program.

Of the few studies that have examined the effects of resistance exercise on physical functional and QOL, positive results have been conveyed. Other pertinent information to be learned from these studies is that both supervised and self-sustaining exercise programs may produce beneficial results. The intensities of the resistance exercise programs in the reviewed studies varied, demonstrating the need to identify at which resistance exercise intensity physical function and QOL are optimally enhanced. Lastly, all of the reviewed studies assessed physical function and physical well-being via subjective measures in the form of surveys/questionnaires. Objective assessments

of these variables would provide insight to the true changes occurring due to an exercise intervention.

Concluding remarks

Breast cancer is an extremely prevalent disease in the United States. Despite the improved five-year survival rate in the past several years, breast cancer survivors are left to struggle with numerous adverse side effects because of their cancer treatments. Cancer treatment-induced bone loss is far more aggressive compared to the normal bone loss that healthy post-menopausal women experience. Similarly, breast cancer survivors often experience heightened levels of fatigue that may cause decreased levels of physical activity, negative body composition changes, decreased muscular strength, decreased physical function, and lower QOL.

Due to the risk of additional side effects of prescription medications to treat the previously mentioned cancer treatment-induced side effects, non-pharmacological options such as resistance exercise and dried plum consumption serve as an alternative therapy to aid in the cancer recovery process. In the reviewed literature, resistance exercise has positively affected both bone turnover biomarkers and BMD levels of healthy post-menopausal women in as little as six months. Similarly after only three months of dried plum consumption (100 g daily), bone turnover biomarkers were positively modulated in healthy post-menopausal women. The reviewed studies have further shown resistance exercise has the potential to exhibit benefits for breast cancer survivors in the areas of fatigue, body composition, muscular strength, physical function, and QOL.

The inconclusive results examining the protective effects of resistance exercise against BMD loss in breast cancer survivors, and the complete absence of studies examining the effects of dried plum consumption on the BMD of breast cancer survivors, warrants further research in these areas. Therefore, purpose of the present study was to examine the effectiveness of a six-month intervention of resistance exercise or combination resistance exercise and dried plum consumption to produce positive changes in bone turnover biomarkers and BMD levels of post-menopausal breast cancer survivors. The present study also examined the effects of the six-month

intervention on body composition, muscular strength, physical function (both subjective and objective), and QOL.

CHAPTER 3
RESEARCH DESIGN AND METHODS

Study Overview

The present study was a randomized (by breast cancer stage, cancer treatment received, age, weight, baseline forearm BMD, and baseline chest press strength) controlled clinical trial designed to examine the effects of two non-pharmacological treatments on total body and regional BMD during a six-month period. Twenty-seven post-menopausal breast cancer survivors (stages 0-III) were recruited. The project included female breast cancer survivors who had completed all their treatments (with the exception of hormone suppressant therapy) prior to baseline of the study. Breast cancer survivors still receiving hormone suppressant therapies were eligible for the study because after initial treatments are completed, hormone suppressant therapies are prescribed for an additional period of three to five years. Excluding women still taking hormone suppressant therapies would have significantly decreased the number of women eligible for the study. A group by time interaction effect, with an effect size of 0.49, maintaining $\alpha=0.05$ and $1-\beta=0.80$, indicated that a sample size of 14 participants per experimental group was required to detect changes in spinal BMD based on a previous finding by Kohrt and colleagues (Kohrt, Ehsani, & Birge, 1997). Based on a predicted dropout rate of 34% (Oldervoll, Kaasa, Hjermstad, Lund, & Loge, 2004), approximately five additional participants were enrolled to both experimental groups, making the minimum sample size for each group 19. Though the recruitment goal was to achieve a total sample of 38 participants, 19 per experimental group, only 27 women were successfully recruited and analyzed for the study.

Inclusion Criteria

Post-menopausal female breast cancer survivors (stages 0-III), ages 40-80 years, having completed treatments prior to baseline of the study were eligible to participate. Women currently taking or who had completed hormone suppressant therapies were eligible to participate in this study.

Exclusion Criteria

Male breast cancer survivors were not eligible for this study. Women diagnosed with stage IV breast cancer or who were currently diagnosed with active cancer were excluded. Women with uncontrolled hypertension (≥160/100 mmHg), uncontrolled diabetes, or uncontrolled heart disease, were also excluded.

Data collection—laboratory visit 1

This study was approved by the University's Institutional Review Board (IRB Approval Letter—Appendix A). Participants were screened via the telephone (Telephone Interview—Appendix B) and invited to The Florida State University for an orientation to the study. During the orientation, the study coordinator reviewed the time commitment and explained the study protocol. Participants were given the opportunity to ask questions. If the participant was interested in taking part in the study, she completed an informed consent (Informed Consent Document—Appendix C) and filled out questionnaires regarding demographics and medical history (Demographic/Medical Questionnaire—Appendix D). Once eligibility was confirmed the participants were invited to the Clinical Exercise Physiology Laboratory at The Florida State University for their first of two baseline-testing visits. All visits were scheduled between the hours of 7:00 to 11:00 am in attempts to control variables being tested. Participants had their blood drawn and completed a questionnaire packet assessing the following measures: quality of life via SF-36 and physical activity status (Questionnaire Packet—Appendix E). Participants also had their BMD, body composition, and muscular strength measured.

During the first laboratory visit, fasted blood draws were taken in the amount of 20 mL under sterile conditions for the purposes of measuring serum biochemical markers of bone formation (BAP) and bone resorption (TRAP-5b). Serum was separated from whole blood by centrifugation (for 15 min @ 1000 X g) and aliquots were kept frozen at -. Biological samples were labeled and identified with participant ID, date, and time point they were obtained, with records kept on all biological samples. Biochemical assays and procedures included duplicate analysis of each sample; when test results did not meet the manufacturers' standards (or better) for control variables,

samples were re-run. Bone resorption and bone formation assays included high and low controls, as well as standards that were run with each assay. All blood samples were analyzed at the conclusion of the intervention at six months.

Height and weight were measured to calculate BMI as weight (kg)/height () via the use of a wall-mounted stadiometer and a digital scale, respectively (Seca Corporation; Hanover, MD). Body composition and BMD of the total body and regional areas of the lumbar spine, femur, and forearm were measured non-invasively via the use of the iDXA® scanner (GE Healthcare Inc.; Madison, WI). Before testing, participants were asked to change into clothing that was free of metal and/or hard plastic (buttons, zippers, snaps, etc.) and asked to remove all metal from the body (jewelry, eyeglasses, hair accessories, etc.). A total of four scans were performed on each participant: 1) anteroposterior (AP) view of the total body with the participant lying supine; 2) AP view of the lumbar (L1-L4) spine with the participant lying supine with hips and knees supported at a 90º angle; 3) AP view of the right and left femoral neck with the participant lying supine with thigh internally rotated; and 4) posteroanterior (PA) view of the right and left forearm with the participant lying supine. Testing was completed according to the manufacturer's instructions and specifications by a certified X-ray technician.

Following the body composition analyses, both upper and lower body strength were assessed using the chest press and leg extension exercises, respectively (MedX™; Orlando, FL). After a warm-up, participants were progressed towards the maximum weight that they could lift one time through a full range of motion to achieve a 1-RM. All measurements were recorded, with the goal of achieving a 1-RM within three to five maximal attempts.

Data collection—laboratory visit 2

On the second visit, participants had their resting blood pressure, resting heart rate, and hip and waist circumferences assessed. Participants also had their function measured objectively via the CS-PFP and their 1-RM strength measures repeated. Blood pressure and heart rate were measured in a quiet room on the brachial and radial artery respectively, after the participants had been seated for a period of five-minutes.

Blood pressure and heart rate were taken according to the standard guidelines outlined by the American College of Sports Medicine (Armstrong et al., 2009).

Waist circumference measures were taken at the narrowest part of the torso superior to the hip and inferior to the most distal rib. Hip circumference measures were taken at the greatest gluteal protuberance while the participant stood upright with feet together. Circumference measures were taken at least twice at both anatomical sites using a Gulick fiberglass measuring tape with a tension handle (Creative Health Products, Inc.; Ann Arbor, MI). If the readings were in excess of 5 mm of discrepancy, an additional measure was taken until the discrepancy between two readings was equal to or less than 5 mm (Armstrong et al., 2009). Waist circumference was divided by hip circumference to obtain the waist-to-hip ratio.

The CS-PFP test consists of tasks that simulate activities of daily living. In previously published research, this test has been shown to have convergent, construct, and face validity for 10 everyday household tasks. It has high reproducibility ($r = 0.97$; 21) and is sensitive to change, with an effect size of 0.8 (Cress et al., 1999). This test is able to measure higher levels of function without having ceiling effects as well as being able to test individuals that cannot perform a task, thus eliminating floor effects (Cress et al., 1996). The test was given under standard conditions that ultimately minimized variance and enhanced the ability to detect changes from intervention programs. The tasks included carrying a weighted pan, picking up scarves, putting on a jacket, reaching, floor sweeping, doing laundry, sitting and standing from the floor, stair climbing, getting on a bus, carrying groceries, and walking for six minutes. Measurements were taken according to the time it takes the participants to complete the individual tasks. Heart rate was monitored continuously during this test. After the conclusion of the CS-PFP test, 1-RM tests were verified by repeating the strength tests. The highest measurement for the upper and lower body from the two days of testing will be considered the 1-RM and used for calculating the resistance training exercise prescription.

Interventions

After the completion of baseline testing, each participant was randomly assigned to one of the two treatment groups (each treatment is described below): resistance exercise training (RT) or RT and dried plum consumption (RT + DP). With the exception of iDXA, measurements taken at baseline were repeated at three and six months. iDXA measures were only taken at baseline and six months in attempts to limit radiation exposure. At baseline, both groups were given a pedometer and physical activity journal to log physical activity (Pedometer log—Appendix F). For one randomly assigned week each of the six months, all participants were asked to record their steps daily. Since many of the participants were anticipated to be taking calcium and/or vitamin D supplements, participants were requested to replace their current supplements with one that we provided. The supplement replacement was meant to minimize heterogeneity of supplement use as a potential confounding factor. To ensure adequate intake of calcium and vitamin D, each participant, regardless of treatment, was instructed to consume twice daily a provided daily vitamin/mineral supplement containing approximately 450 mg calcium and 800 IU vitamin D. This low-dose supplementation also served to minimize potential skeletal effects due to anticipated individual differences in dietary intake. Participants were rationed the appropriate number of calcium/vitamin D pills to last for one month. At the end of each month, remaining pills were collected to calculate adherence for calcium/vitamin D. The participants were then rationed another month supply of supplements. This cycle continued for the remainder of the study.

For the duration of the study, both groups completed six months of supervised resistance exercise training. For the 24 weeks of the study, the groups completed all training sessions under the supervision of qualified instructors on two non-consecutive days each week. Participants performed two sets of 8-12 repetitions of 10 resistance exercises for the upper and lower body. All exercise sessions were carefully recorded by the exercise instructor. Exercise machines included the chest press, leg press, leg extension, biceps curl, triceps press down, overhead press, seated row, leg curl, abdominal crunch, and lower back hyperextensions. Training sessions began at approximately 60% of each participant's 1-RM and intensity was slowly progressed to

an intensity not exceeding 80% 1-RM throughout the six months. Once 12 repetitions could be completed with proper form, the weight was increased by approximately 10%. The instructions for the resistance exercise program are prescribed according to the American College of Sports Medicine recommendations (Feigenbaum & Pollock, 1999). During each resistance exercise session, participants performed five minutes of aerobic warm-up before, and concluded their session by performing stretches targeting all the major muscle groups. The duration of each resistance exercise session lasted approximately 45 minutes. Compliance to resistance exercise sessions was recorded by the exercise trainer scheduled to conduct the weekly exercise sessions. Participants that missed an exercise session were telephoned to remind them of their next appointment and to schedule a make-up session.

For the duration of the study, the RT+DP group was instructed to consume three packets of dried plums (see Figure 1), for a total of 90 ± 6 g of dried plums daily. The participants in the RT+DP group were advised to adjust their food intake accounting for macronutrients. Participants were rationed the appropriate number of dried plum packets to last for one month. At the end of each month, remaining packets of dried plum were collected to calculate adherence for dried plum consumption. The participants were then rationed another month supply of dried plums. This cycle continued for the remainder of the study.

Figure 1. Packaging of Dried Plums

Participant Recruitment, Retention, and Compliance

Breast cancer survivors (stages 0-III) with diverse ethnic backgrounds, including Caucasians, African Americans, and Hispanics who live in Tallahassee metropolitan and rural areas within reasonably commuting distances were recruited to participate in the study. Recruitment took place via newspaper advertisements, public service announcements, science articles in local newspapers, and flyers posted on campus, in health clinics and fitness centers, and in employment development centers. Recruitment also took place through Cooperative Extension nutrition and health specialists, local breast cancer support groups, local churches and hospitals, groups on campus, and community groups.

Anticipated Risks and Solutions

Participants engaging in resistance exercise testing and training had the risk of experiencing muscle soreness. Care was taken to minimize soreness by thoroughly stretching after resistance exercise testing and training sessions. Qualified exercise instructors supervised all exercise session in order to ensure proper exercise techniques and to monitor exercise intensity.

Lymphedema, swelling in one or more of the limbs, occurs when there is a blockage in the lymphatic system that prevents the lymph fluid in the arm or leg from draining adequately. Breast cancer patients and survivors are at risk for developing lymphedema if they have had surgery in which one or multiple lymph nodes have been removed. Lymphedema can also occur due to radiation treatment for cancer, causing scarring and inflammation of the lymph nodes or lymph vessels, ultimately restricting lymph flow. As the fluid accumulates, the swelling continues**.** No cure for lymphedema exists, but lymphedema can be controlled through appropriate exercise, therapeutic massage promoting manual lymph drainage, and compression garments. Doctors, for many years, instructed patients to abstain from exercise using the affected limbs, believing lymphedema would be exacerbated by the physical activity. Recent evidence has shown that moderate intensity exercise does not cause or exacerbate the condition (Ahmed et al., 2006; McKenzie & Kalda, 2003; Schmitz, 2009). Nonetheless, participants were monitored on a bi-weekly basis via limb circumference measurements.

Circumferences were measured every 3 cm beginning at the styloid process of the ulna and continuing 45 cm proximally, as well as at the metacarpals and midhand. Notable increases (>1.3 cm) at any landmark resulted in a reduction of the prescribed resistance exercise intensity. Participants noticing any of the following signs or symptoms of lymphedema were asked to notify the exercise instructor prior to an exercise appointment: Swelling in the arms, hands, fingers, shoulders, or chest; a "full" or heavy sensation in the arms, skin tightness, or decreased flexibility in the hand or wrist. Implications of any of these signs or symptoms resulted in an immediate reduction of the prescribed resistance exercise intensity. All participants were encouraged to wear their compression garments, if applicable, during the exercise session.

While consuming 90 ± 6 g of dried plums daily was not shown to cause any gastrointestinal distress in a group of post-menopausal women (Hooshmand et al., 2011), there was a risk of abnormal gastrointestinal function for the participants consuming dried plums. These risks were minimized by instructing the participants to incorporate additional water intake following dried plum consumption.

Statistical Analyses

Descriptive statistics (means, standard deviations, medians, minima and maxima) were calculated for all variables. Distributions of outcome variables were examined graphically for symmetry and for outliers. Extreme outliers were investigated for technical or clerical errors. If the size of the measurement could not be attributed to such an error, it was included in the analysis and the effect of deleting the observation was reported.

A one-way analysis of variance (ANOVA) was used to analyze baseline measures between the two groups. Dependent variables were analyzed by a two-way (group x time) repeated measures ANOVA with repeated measures performed on the last factor. When interactions were significant, ANOVAs were used to compare between group values. All significance was accepted at $p \leq 0.05$. In cases of sphericity violations, Greenhouse-Geisser adjustment was used to test the effects of experimental condition and time interactions on the dependent variables. All analyses were performed using the SPSS (version 15) statistical package. An intention-to-treat

analysis was used to evaluate pre, mid, and posttest scores to address the effects of the interventions on all randomized participants regardless of whether they completed the study or not. Using the principle of last observation carried forward, missing mid or post-test scores was filled using the test scores that were collected closest to the time of dropout.

CHAPTER 4

RESULTS

Participants

Fifty-one breast cancer survivors initially inquired about the study. Ten women declined participation after hearing the requirements/commitments of the study. Nine women were ineligible due to one of the following reasons: did not meet menopausal requirements, already participating in a vigorous resistance exercise training regimen, or were currently taking thyroid medication. Thus, of the initial 51 women, 32 were invited to the laboratory to participate in baseline testing. After the completion of baseline testing, 27 of the women committed to the study and were randomized into one of the two testing groups (resistance training=RT; or resistance training + dried plum consumption=RT+DP). Of the five women that completed baseline testing, but were not randomized into treatment groups, three had unexpected medical complications arise in the interim time between baseline testing and the beginning of the intervention. Two of the five women decided that the time commitment of the study was too great and opted not to participate. Fourteen women were assigned to the RT group, while only 12 women were able to complete the intervention. Two women were unable to complete the RT invention due to medical complications that surfaced during the course of the study and stopped all participation in the research project. One participant developed uncontrolled hypertension during the 18th week of the study and her physician would not grant clearance to remain in the study. The second participant, during the 8th week of the study was diagnosed with a reoccurrence of cancer that metastasized into her bones and was not allowed to continue with the study. Since an intention to treat analysis was implemented, all 14 women from the RT group were included in data analysis. Thirteen women were assigned and completed the RT+DP group, thus 13 women were used for data analysis. The overall dropout rate for the present study was calculated at 7%. A complete description of the participants' progression through the research study can be found in Figure 2.

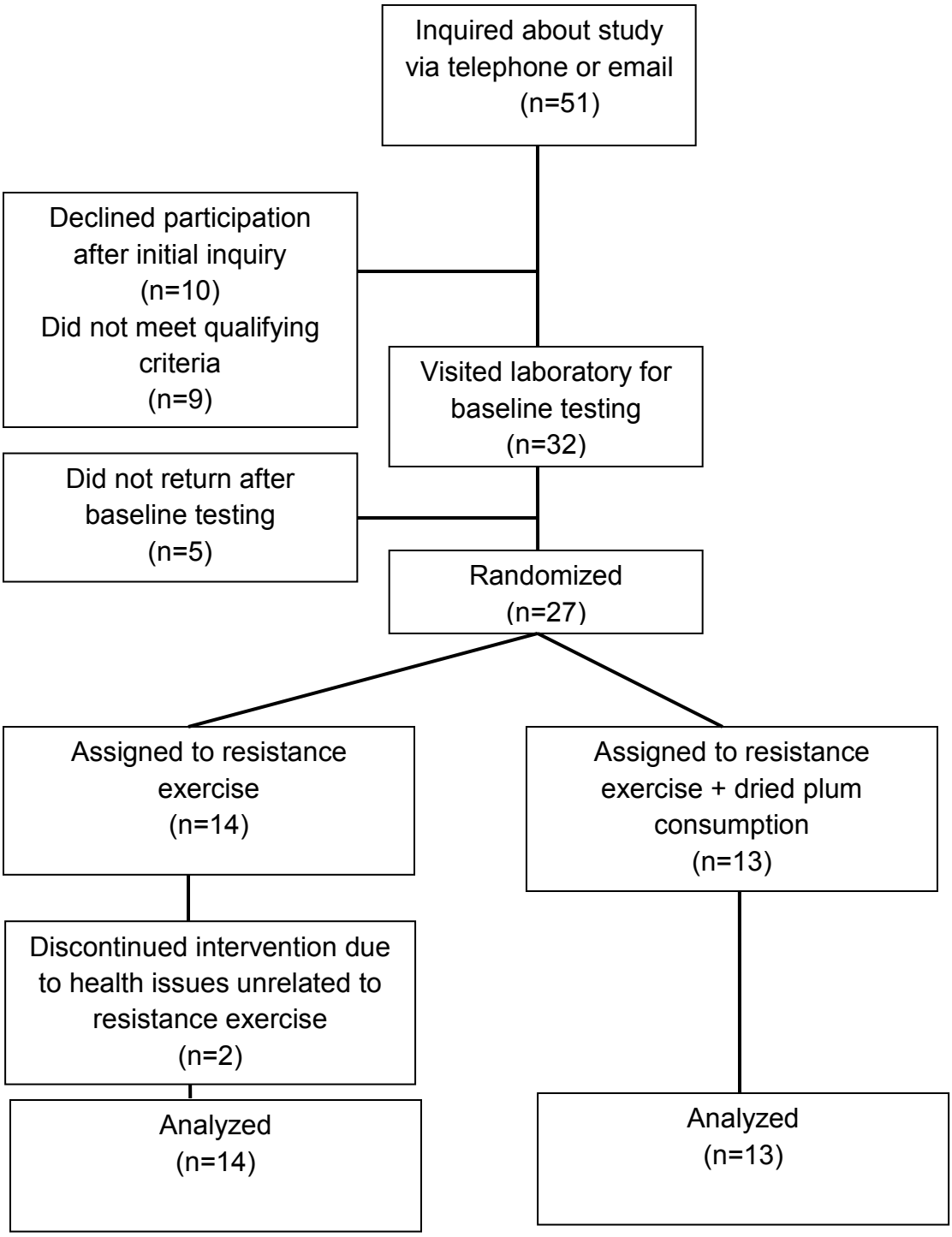

Figure 2. Flow chart of participants' progression through study

Women in the two treatment groups shared similar baseline characteristics in terms of age, height, weight, BMI, and body fat percent. Ages ranged from 51-74 years of age, with an overall average age of 64 ± 6 years. According to BMI, approximately 15% (n=4) of the participants were overweight, and 33% (n=9) of the participants were obese. The majority, 89% (n=24) of the participants were Caucasian, while the remaining 11% (n=3) were African American. Please see Table 1 for a complete description of baseline characteristics.

Table 1. Baseline Participant Characteristics (N=27)

	RT Group (n=14)	RT+DP Group (n=13)
Age	63 ± 6	64 ± 7
Height (cm)	162.9 ± 5.5	163.4 ± 6.9
Weight (kg)	72.4 ± 16.3	74.8 ± 13.5
BMI (kg/)	27.4 ± 6.0	28.1 ± 5.2
Body fat (%)	43.2 ± 5.7	42.7 ± 4.8

RT=Resistance training; RT+DP=Resistance training + dried plum consumption
Data are presented as mean ± standard deviation

Women in the two treatment groups also shared similar characteristics in terms of breast cancer diagnosis history and treatment strategies. Thirty-six percent (n=5) of the women from the RT group and 39% (n=5) of the women from the RT+DP group were diagnosed with stage-one breast cancer. Fifty percent (n=7) of women from the RT group and 46% (n=6) of the women from the RT+DP group were diagnosed with stage-two breast cancer. Lastly, stage-three breast cancer diagnoses contributed to 14% (n=2) of the RT and 15% (n=2) of the RT+DP groups' overall diagnoses. Overall, 67% (n=18) of the women were diagnosed with primary breast cancer on the right side of the body. At the beginning of the study, both groups shared similar "time since diagnosis", with the RT group being diagnosed 89.5 ± 72.2 months, and the RT+DP group being diagnosed 86.1 ± 66.8 months prior to the start of the study.

In addition to similar diagnostic histories, both groups shared similar "time since treatment". The time since primary treatment (surgery, radiation, and/or chemotherapy) for the RT group and the RT+DP group were 72.4 ± 66.4 and 79.5 ± 67.2 months, respectively. Forty-three percent (n=6) of the women in the RT group and 39% (n=5) of the women in the RT+DP group were taking hormone suppressant therapies at the time of the study. The remaining women had completed hormone suppressant therapy, or

had never been prescribed this line of treatment. The time since completion of hormone suppressant therapy for the RT and the RT+DP groups were 48.7 ± 15.6 and 56 ± 53.4 months, respectively. During the course of the study, 21% (n=3) of the women in the RT group and 23% (n=3) of the women in the RT+DP group were receiving prescription bone medication. Table 2 provides a specific listing of the cancer diagnosis and treatment histories.

Table 2. Frequencies of Breast Cancer Diagnosis/Treatment Specifics (N=27)

(Frequency of diagnosis and treatment occurrences)	RT Group (n=14)	RT+DP Group (n=13)
Stage 1	5	5
Stage 2	7	6
Stage 3	2	2
Affected breast—left	5	4
Affected breast—right	9	9
Currently taking bone medication	3	3
Currently taking hormone therapy	6	5
Time since diagnosis (months)	89.5 ± 72.2	86.1 ± 66.8
Time since hormone therapy completed (months)	48.7 ± 15.6	56.0 ± 53.4
Time since *primary treatment completed (months)	72.4 ± 66.4	79.5 ± 67.2
Number of lymph nodes removed	7 ± 12	7 ± 11

RT=Resistance training; RT+DP=Resistance training + dried plum consumption
Data are presented as mean ± standard deviation
*Surgery, radiation, and/or chemotherapy

Adherence to vitamins, dried plums, and exercise sessions

In order to homogenize the study participants' calcium and vitamin D intake, all women were provided with a monthly ration of vitamin supplements. Adherence to vitamin supplements in the RT group and the RT+DP group were 89 ± 14% and 89 ± 24%, respectively. Participants similarly exhibited an acceptable level of adherence to resistance exercise attendance, as well as dried plum consumption (RT+DP group). The RT group attended 95 ± 9% of exercise sessions, while the RT+DP group attended 97 ± 5% of exercise sessions. Only the women who completed the entire intervention phase (n=25) were used to calculate adherence to vitamin supplementation and exercise attendance. In the RT+DP group, adherence to dried plum consumption was 87 ± 17%. Two women had adherence rates less than 50% for the consumption of dried plums. Excluding these two women, the adherence rate for dried plum

consumption was increased to 94 ± 5%. In order to monitor physical activity levels occurring outside of the study, all participants were given a pedometer for the duration of the study and asked to report seven consecutive days of step readings each month. There was no significant difference for physical activity between the groups at any of the time points, nor were there significant changes in physical activity within groups at any of the time points. See Table 3 for a complete description of physical activity level over the course of the study.

Table 3. Comparison of Physical Activity (N=27)

Pedometer (#Steps)	RT Group (n=14)	RT+DP Group (n=13)
Month 1	6233 ± 3370	6354 ± 3547
Month 2	6051 ± 2849	5829 ± 3207
Month 3	6003 ± 3056	6024 ± 2805
Month 4	6731 ± 2820	5774 ± 3095
Month 5	6283 ± 2574	6135 ± 3384
Month 6	6237 ± 2991	6024 ± 3091

RT=Resistance training; RT+DP=Resistance training + dried plum consumption
Data are presented as mean ± standard deviation

Muscular Strength Variables & Resistance Training Progression

Participants from both the RT and the RT+DP groups demonstrated similar baseline strength values for chest press, leg extension, and handgrip dynamometer strength measurements. No group time interactions were observed for any of the muscular strength variables over the course of the study. Similar to baseline values, there were no significant differences between groups at the 3-month or 6-month time points. There was a significant time effect observed for chest press ($F_{(1.363,25)}$=36.247, $p \leq 0.05$, ES=0.602) and leg extension ($F_{(1.308,25)}$=53.043, $p \leq 0.05$, ES=0.688). Mauchly's test of sphericity was violated for both chest press and leg extension strength, thus the Greenhouse-Geisser adjustments were used for the F statistics reported. Analyses revealed the RT and RT+DP groups both exhibited significant increases in the chest press and the leg extension over the course of the study. No significant time effect was observed for the handgrip dynamometer. The RT group experienced a significant 13% increase in chest press strength from baseline to the 3-month time point, and a further

significant 7% increase from month-3 to month-6. Overall, the RT group significantly improved their chest press strength by 21% from baseline to month-6. Similarly the RT+DP groups exhibited a significant 22% increase in chest press strength from baseline to the 3-month time point, as well as a further significant 9% increase from month-3 to month-6. Overall, the RT+DP group significantly improved their chest press strength by 33% from baseline to month-6. Though statistical analyses did not show significant differences between groups for increases in chest press strength, the RT+DP group demonstrated an insignificant strength gain of 12% more than the RT group from baseline to month-6. Removing the two dropout women from the RT group brings the overall chest press strength gains to 25%, thus slightly bridging the gap noted between the RT and the RT+DP group to an 8% difference.

The RT group experienced a significant 13% increase in leg extension strength from baseline to the 3-month time point, and a further significant 9% increase from month-3 to month-6. Overall, the RT group significantly improved their leg extension strength by 22% from baseline to month-6. The RT+DP group experienced a significant 16% increase in leg extension strength from baseline to the 3-month time point, and a further significant 11% increase from month-3 to month-6. Overall, the RT group significantly improved their leg extension strength by 29% from baseline to month-6. Similar to the insignificant overall differences between groups for upper body strength, the RT+DP group demonstrated an insignificant strength gain of 7% more than the RT group from baseline to month-6. Removing the two dropout women from the RT group brings the overall leg extension strength gains to 26%, thus bridging the gap noted between the RT and the RT+DP group to only a 3% difference. A detailed description of muscular strength changes over the course of the study can be found in Table 4.

Table 4. Comparison of Muscular Strength (N=27)

	RT Group (n=14)			RT+DP Group (n=13)		
	Baseline	**3-month**	**6-month**	**Baseline**	**3-month**	**6-month**
1-RM Chest Press (kg)	68 ± 20	77 ±	82 ± [,b]	72 ± 24	88 ±	96 ± [,b]
1-RM Leg Extension (kg)	72 ± 19	81 ±	88 ± [,b]	77 ± 17	89 ±	99 ± [,b]
Handgrip dynamometer (kg)	48 ± 8	49 ± 7	48 ± 8	48 ± 5	49 ± 6	48 ± 6

RT=Resistance training; RT+DP=Resistance training + dried plum consumption
Data are presented as mean ± standard deviation
1-RM=1 repetition maximum
different from baseline, within same group, $p \leq 0.05$
different from 3-month within same group, $p \leq 0.05$

Both intervention groups displayed similar progression for both upper body and lower body exercises throughout the 24-week intervention. No group time interactions were observed for kilograms lifted for any of the resistance training exercises. There were no significant differences between groups, at any time point, for kilograms lifted for any of the upper body exercises (chest press, seated row, triceps dip, biceps curl, and military press). There were significant time effects observed for chest press ($F_{(2.399,25)}$=125.135, $p \leq 0.05$, ES=0.850), seated row ($F_{(1.667,25)}$=166.744, $p \leq 0.05$, ES=0.883), triceps dip ($F_{(1.374,25)}$=142.222, $p \leq 0.05$, ES=0.866), biceps curl ($F_{(1.595,25)}$=120.350, $p \leq 0.05$, ES=0.845), and military press ($F_{(1.530,25)}$=177.203, $p \leq 0.05$, ES=0.890). Mauchly's test of sphericity was violated for chest press, seated row, triceps dip, and biceps curl, thus the Greenhouse-Geisser adjustments were used for the F statistics reported. For each of the upper body exercises performed, both groups demonstrated a significant increase in the amounts of kilograms lifted as they progressed through weeks 1-24. Exercise intensity for the chest press was calculated as a representation of upper body intensity. When assessing the intensity (percentage of 1-RM) for a particular 4-week period, the 1-RM test just prior to the 4-week period was used for calculating percentage of 1-RM lifted. For example, baseline 1-RM values were used when calculating the intensity at which the participants exercised during weeks 1-4. For weeks 1-4, both groups exercised at intensity less than the study design (60-80% 1-RM); with the RT group achieving an intensity of 53 ± 12% 1-RM and the RT+DP group achieving 52 ± 5% 1-RM. Beginning in weeks 5-8, both groups achieved an exercise intensity of $\geq$60%1-RM and continued to maintain compliance to

the study design of 60-80%1-RM for the remaining weeks of the intervention. A complete listing of kilograms lifted, repetitions performed, and exercise intensity (where applicable) for upper body exercises for the 24-week intervention can be found in Table 5.

Table 5. Upper Body Resistance Training (N=27)

	RT Group (n=14)			RT+DP Group (n=13)		
	Kilograms	Repetitions	Intensity (%1-RM)	Kilograms	Repetitions	Intensity (% 1-RM)
Upper Body (Chest Press)						
Weeks 1-4	36 ± 11	12 ± 1	53 ± 12	37 ± 12	12 ± 0	52 ± 5
Weeks 5-8	45 ±	11 ± 1	60 ±	47 ±	12 ± 2	60 ±
Weeks 9-12	48 ± [,b]	11 ± 1	66 ± [,b]	53 ± [,b]	11 ± 1	66 ± [,b]
Weeks 13-16	52 ± [,b,c]	11 ± 1	67 ± [,b,c]	57 ± [,b]	11 ± 1	65 ± [,b]
Weeks 17-20	54 ± [,b,c]	11 ± 1	69 ± [,b,c]	60 ± [,b,c]	11 ± 1	67 ± [,b,c]
Weeks 21-24	55 ± [,b,c]	12 ± 0	69 ± [,b,c]	61 ± [,b,c]	12 ± 0	67 ± [,b,c]
Seated Row						
Weeks 1-4	26 ± 6	12 ± 0	-	29 ± 8	12 ± 0	-
Weeks 5-8	32 ±	12 ± 1	-	35 ±	12 ± 1	-
Weeks 9-12	42 ± [,b]	12 ± 0	-	43 ± [,b]	12 ± 0	-
Weeks 13-16	52 ± [,b,c]	12 ± 1	-	54 ± [,b,c]	12 ± 0	-
Weeks 17-20	52 ± [,b,c]	12 ± 1	-	57 ± [,b,c,d]	12 ± 0	-
Weeks 21-24	52 ± [,b,c]	12 ± 1	-	57 ± [,b,c]	12 ± 0	-
Triceps Dip						
Weeks 1-4	35 ± 8	12 ± 0	-	37 ± 5	12 ± 1	-
Weeks 5-8	43 ±	12 ± 0	-	44 ±	12 ± 2	-
Weeks 9-12	54 ± [,b]	12 ± 0	-	55 ± [,b]	12 ± 1	-
Weeks 13-16	63 ± [,b,c]	12 ± 0	-	66 ± [,b,c]	13 ± 1	-
Weeks 17-20	65 ± [,b,c]	12 ± 1	-	69 ± [,b,c]	12 ± 1	-
Weeks 21-24	65 ± [,b,c]	12 ± 0	-	72 ± [,b,c,d]	13 ± 2	-
Biceps Curl						
Weeks 1-4	12 ± 2	12 ± 0	-	14 ± 2	12 ± 0	-
Weeks 5-8	15 ±	12 ± 1	-	16 ±	12 ± 1	-
Weeks 9-12	17 ±	12 ± 1	-	18 ± [,b]	12 ± 1	-
Weeks 13-16	19 ± [,b,c]	12 ± 1	-	22 ± [,b,c]	12 ± 0	-
Weeks 17-20	20 ± [,b,c]	12 ± 1	-	22 ± [,b,c]	12 ± 0	-
Weeks 21-24	20 ± [,b,c]	12 ± 1	-	23 ± [,b,c,d]	12 ± 1	-
Military Press						
Weeks 1-4	18 ± 6	12 ± 0	-	20 ± 6	12 ± 0	-
Weeks 5-8	23 ±	12 ± 1	-	26 ±	12 ± 1	-
Weeks 9-12	30 ± [,b]	12 ± 0	-	31 ± [,b]	12 ± 1	-
Weeks 13-16	39 ± [,b,c]	12 ± 1	-	40 ± [,b,c]	12 ± 1	-
Weeks 17-20	41 ± [,b,c]	12 ± 1	-	43 ± [,b,c]	12 ± 1	-
Weeks 21-24	42 ± [,b,c]	12 ± 0	-	44 ± [,b,c,d]	12 ± 1	-

RT=Resistance training; RT+DP=Resistance training + dried plum consumption

Data are presented as mean ± standard deviation

1-RM=1 repetition maximum

*Significantly different between groups at the same time point, $p \leq 0.05$

different from weeks1-4, within group, $p \leq 0.05$

different from weeks 5-8, within group, $p \leq 0.05$

different from weeks 9-12, within group, $p \leq 0.05$

different from weeks 13-16, within group, $p \leq 0.05$

For lower body exercises, there were significant time effects for leg extension ($F_{(1.358,25)}$=75.466, p≤0.05, ES=0.774), hamstring curl ($F_{(1.579,25)}$=97.686, p≤0.05, ES=0.816), leg press ($F_{(1.285,25)}$=84.799, p≤0.05, ES=0.794), abdominal crunch ($F_{(2.016,25)}$=37.412, p≤0.05, ES=0.630), and back extension ($F_{(2.132,25)}$=5415.088, p≤0.05, ES=0.407). Mauchly's test of sphericity was violated for leg extension, hamstring curl, leg press, abdominal crunch, and back extension, thus the Greenhouse-Geisser adjustments were used for the F statistics reported. With the exception of weeks 17-20 and weeks 21-24 for kilograms lifted on hamstring curl, there were no significant differences between groups, at any time point, for any of the lower body exercises. At the two significant time points for kilograms lifted on the hamstring curl exercise, the RT+DP group lifted significantly heavier weights than did the RT group, weeks 17-20 (RT: 46 ± 12kg; RT+DP: 57 ± 9kg) and weeks 21-24 (RT: 46 ± 11kg; RT+DP: 57 ± 9kg).

Within group analyses showed that both groups exhibited a significant steady progression of kilograms lifted throughout the 24-weeks on the remaining lower body exercises, with the exception of back extension. For the back extension exercise, both groups began using only their body weight, with no extra weight being added. The RT group did not significantly increase the weight being lifted for the back extension exercise at any time point throughout the intervention. Only at weeks 21-24 did the RT+DP group significantly increase kilograms lifted on the back extension exercise compared to baseline, concluding with 2 ± 2 kg. Exercise intensity for the leg extension was calculated as a representation of lower body intensity. When assessing the intensity (percentage of 1-RM) for a particular 4-week period, the 1-RM test just prior to the 4-week period was used for calculating percentage of 1-RM lifted. For example, baseline 1-RM values were used when calculating the intensity at which the participants exercised during weeks 1-4. For weeks 1-4, both groups exercised at an intensity less than the study design (60-80% 1-RM); with the RT group achieving an intensity of 52 ± 7%1-RM and the RT+DP group achieving 50 ± 2%1-RM. Beginning in weeks 5-8, the RT group achieved an exercise intensity of 61 ± 6%1-RM and continued maintain compliance to the study design of 60-80%1-RM for the remaining weeks of the intervention. The RT+DP group did not achieve an exercise intensity of ≥60%1-RM until weeks 9-12, but thereafter maintain compliance to the study design of 60-80%1-

RM for the remaining weeks of the intervention. A complete listing of kilograms lifted, repetitions performed, and exercise intensity (where applicable) for lower body exercises for the 24-week intervention can be found in Table 6.

Table 6. Lower Body Resistance Training (N=27)

	RT Group (n=14)			RT+DP Group (n=13)		
	Kilograms	Repetitions	Intensity (%1-RM)	Kilograms	Repetitions	Intensity (% 1-RM)
	Lower Body (Leg Extension)					
Weeks 1-4	38 ± 13	12 ± 1	52 ± 7	38 ± 10	12 ± 0	50 ± 2
Weeks 5-8	45 ±	11 ± 1	61 ±	48 ±	11 ± 1	59 ±
Weeks 9-12	50 ± ,b	11 ± 1	65 ± ,b	55 ± ,b	11 ± 1	65 ± ,b
Weeks 13-16	54 ±	11 ± 2	66 ±	59 ± ,b	11 ± 1	66 ± ,b
Weeks 17-20	56 ± ,b	11 ± 2	68 ±	61 ± ,b	11 ± 1	66 ± ,b
Weeks 21-24	56 ± ,b	12 ± 1	68 ± ,b	62 ± ,b	12 ± 0	67 ± ,b
	Hamstring Curl					
Weeks 1-4	29 ± 5	12 ± 0	-	32 ± 6	12 ± 0	-
Weeks 5-8	34 ± 7	12 ± 0	-	39 ±	12 ± 0	-
Weeks 9-12	40 ± ,b	12 ± 0	-	47 ± ,b	12 ± 0	-
Weeks 13-16	46 ± ,b	12 ± 1	-	55 ± ,b,c	12 ± 1	-
Weeks 17-20	46 ± 12*a,b	12 ± 1	-	57 ± ,b,c	12 ± 0	-
Weeks 21-24	46 ± 11*a,b	12 ± 1	-	57 ± ,b,c	12 ± 1	-
	Leg Press					
Weeks 1-4	52 ± 14	12 ± 1	-	58 ± 10	12 ± 1	-
Weeks 5-8	63 ±	12 ± 1	-	72 ±	13 ± 2	-
Weeks 9-12	77 ± ,b	13 ± 1	-	88 ± ,b	12 ± 1	-
Weeks 13-16	90 ± ,b	12 ± 2	-	105 ± ,b,c	12 ± 1	-
Weeks 17-20	94 ± ,b	12 ± 1	-	112 ± ,b,c,d	12 ± 1	-
Weeks 21-24	95 ± ,b	13 ± 2	-	113 ± ,b,c,d	12 ± 1	-
	Abdominal Crunch					
Weeks 1-4	11 ± 3	13 ± 2	-	12 ± 2	14 ± 6	-
Weeks 5-8	13 ±	13 ± 3	-	14 ± 3	15 ± 10	-
Weeks 9-12	15 ± ,b	14 ± 2	-	16 ±	16 ± 5	-
Weeks 13-16	15 ± ,b	16 ± 5	-	17 ± ,b	17 ± 7	-
Weeks 17-20	15 ± ,b	17 ± 4	-	17 ± ,b	20 ± 8	-
Weeks 21-24	15 ± ,b	21 ± 7	-	17 ± ,b	24 ± 10	-
	Back Extension					
Weeks 1-4	0 ± 0	12 ± 1	-	0 ± 0	12 ± 1	-
Weeks 5-8	0 ± 1	12 ± 1	-	0 ± 1	13 ± 2	-
Weeks 9-12	1 ± 1	13 ± 2	-	1 ± 1	13 ± 1	-
Weeks 13-16	1 ± 1	14 ± 3	-	1 ± 1	14 ± 1	-
Weeks 17-20	1 ± 1	13 ± 3	-	1 ± 2	14 ± 2	-
Weeks 21-24	1 ± 2	14 ± 3	-	2 ±	15 ± 3	-

RT=Resistance training; RT+DP=Resistance training + dried plum consumption

Data are presented as mean ± standard deviation

1-RM=1 repetition maximum

*Significantly different between groups at the same time point, $p \leq 0.05$

different from weeks1-4, within group, $p \leq 0.05$

different from weeks 5-8, within group, $p \leq 0.05$

different from weeks 9-12, within group, $p \leq 0.05$

different from weeks 13-16, within group, $p \leq 0.05$

Lymphedema Assessments

As a safety precaution, lymphedema screenings were conducted every two weeks for the duration of the study. Percent difference was calculated to compare bilaterally the total volumes of the upper extremities. A positive percent was representative of a greater volume in the extremity affected by breast cancer, whereas, a negative percent was representative of a greater volume in the extremity not affected by breast cancer. At baseline, three women had a pre-existing diagnosis of active lymphedema, while the remaining 24 women showed no clinical signs/symptoms of lymphedema. No group by time effect was discovered. There were no significant differences found between groups at any of the time points, nor were there any differences found within groups between any time points. Both groups stayed below the +10% bilateral difference, which is typically the point at which lymphedema may be developing. The three women having current a diagnosis of lymphedema at baseline of the study had a mean difference between extremities of (7 ± 14%). No signs of exacerbation to the condition were found, as the mean difference between extremities for these three women at the six-month mark of the study was (7 ± 17%). Figure 3 represents the percent differences between the upper extremities over the course of the intervention.

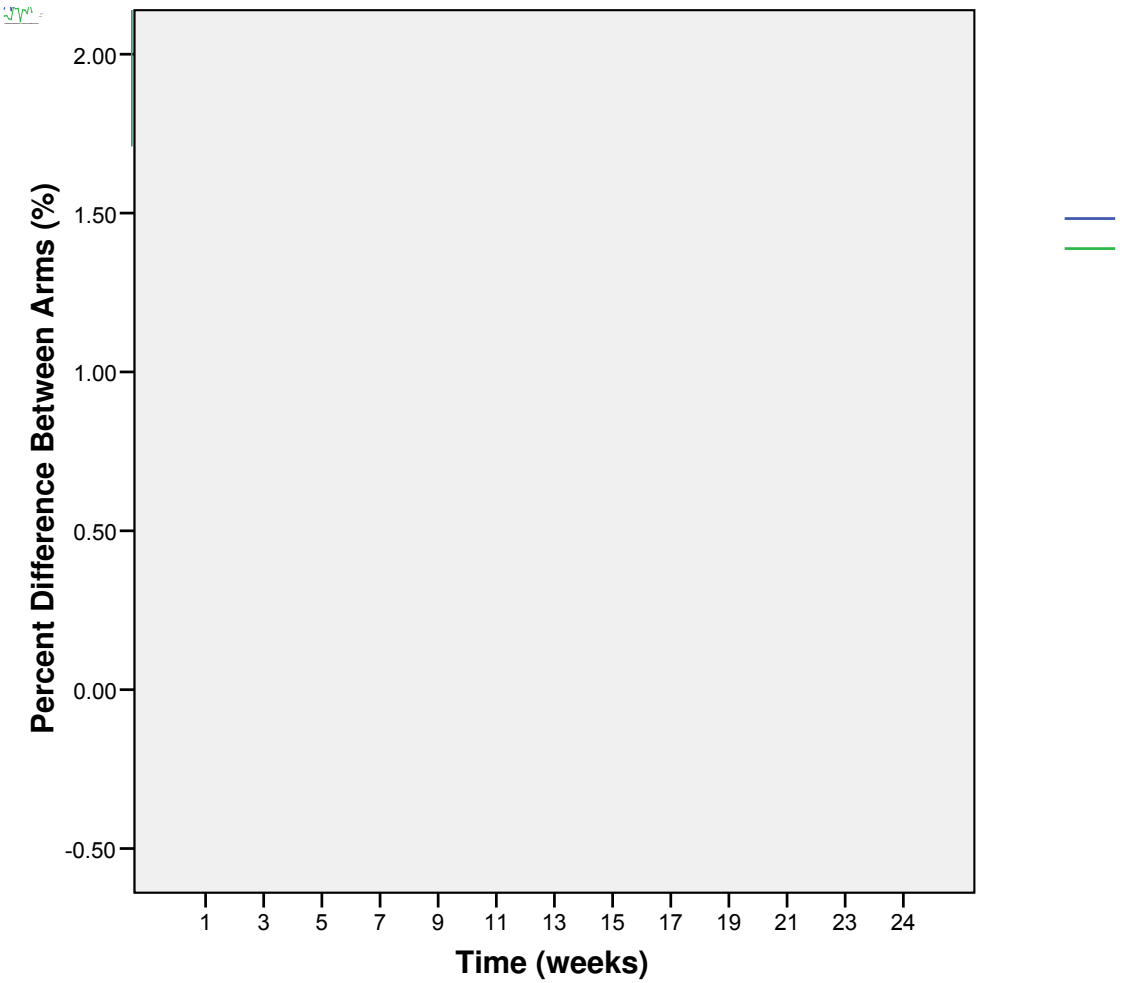

Figure 3. Lymphedema Monitoring: Percent Differences between Upper Extremities

Body Composition & Bone Mineral Density (BMD) Variables

Both the RT and the RT+DP group showed similar baseline characteristics in terms of body composition variables obtained via circumference measures and the iDXA bone densitometer. No group by time interactions were found for any of the body composition variables. Similarly, there were no significant differences calculated between groups between baseline and the 6-month time point, nor were there any significant differences found between time points within groups. A complete description of body composition variables can be found in Table 7.

Table 7. Comparison of Body Composition Variables (N=27)

	RT Group (n=14)		RT+DP Group (n=13)	
	Baseline	**6-month**	**Baseline**	**6-month**
Weight (kg)	72.4 ± 16.3	72.5 ± 16.2	74.8 ± 13.5	75.8 ± 13.7
BMI (kg/)	27.4 ± 6.0	27.4 ± 5.9	28.1 ± 5.2	28.4 ± 5.1
Waist girth (cm)	85.2 ± 12.4	83.6 ± 10.6	86.4 ± 14.1	87.3 ± 14.3
Hip girth (cm)	107.8 ± 10.9	107 ± 12.1	110 ± 9.2	110.2 ± 9.4
Lean mass (kg)	38.9 ± 6.8	39.2 ± 6.8	40.9 ± 6.0	41.4 ± 5.7
Fat mass (kg)	30.4 ± 10.2	30.2 ± 10.1	31.1 ± 8.5	31.6 ± 8.5
Lean/fat mass ratio	1.36 ± 0.34	1.38 ± 0.34	1.37 ± 0.29	1.36 ± 0.26
Android fat (%)	46.0 ± 7.7	45.3 ± 8.4	45.2 ± 8.3	45.6 ± 8.2
Gynoid fat (%)	47.6 ± 6.5	47.3 ± 6.3	47.2 ± 3.8	47.2 ± 3.5
Android/gynoid ratio	0.97 ± 0.11	0.96 ± 0.14	0.96 ± 0.15	0.96 ± 0.15
Total body fat (%)	43.2 ± 5.7	42.8 ± 5.8	42.7 ± 4.8	42.9 ± 4.5

RT=Resistance training; RT+DP=Resistance training + dried plum consumption
Data are presented as mean ± standard deviation

Both the RT and the RT+DP group showed similar baseline characteristics in BMD variables obtained via the iDXA bone densitometer. At baseline, 82% (n=22) of the women had at least one site (total body, lumbar spine, femur, or forearm) that was osteopenic. Of the remaining women, 11% (n=3) were considered osteoporotic at one or more sites, while 7% (n=2) were considered within normal range for BMD. Of all the BMD variables assessed, there was one significant group by time interaction over the course of the 24-week intervention. A significant interaction occurred for the right total ulna ($F_{(1,25)}$ = 4.307, $p \leq 0.05$, *ES*=0.147), indicating that the RT+DP group lost BMD at a higher rate than did the RT group at the regional site of the right total ulna. There were two participants within the RT+DP group that were <50% compliant with dried plum consumption. Secondary analyses revealed that when these two noncompliant women were removed from the RT+DP group, the group by time interaction was no longer present.

There were no significant differences found between groups for any of the BMD variables assessed at either baseline or 6-months. There were three significant time effects over the course of the study, occurring in the right total radius ($F_{(1,25)}$ = 11.385, $p \leq 0.05$, *ES*=0.313), the right total ulna ($F_{(1,25)}$ = 9.026, $p<0.05$, *ES*=0.265), and the right total forearm ($F_{(1,25)}$ = 12.301, $p \leq 0.05$, *ES*=0.330). Further analysis indicated that the three significant time effects were occurring within the RT+DP group. Over the course

of the study, the RT+DP group exhibited a significant 3% decrease in the right total radius (Baseline: 0.497 ± 0.064; 6-month: 0.483 ± 0.056g/), a 2% decrease in the right total ulna (Baseline: 0.448 ± 0.056; 6-month: 0.438 ± 0.053g/), and a 3% decrease in the right total forearm (Baseline: 0.476 ± 0.059; 6-month: 0.464 ± 0.054g/). A complete description of BMD variables can be found in Table 8.

Table 8. Comparison of Bone Mineral Density (N=27)

	RT Group (n=14)		RT+DP Group (n=13)	
Bone mineral density (g/)	**Baseline**	**6-month**	**Baseline**	**6-month**
Total body	1.152 ± 0.136	1.148 ± 0.134	1.138 ± 0.134	1.137 ± 0.137
Lumbar spine	1.129 ± 0.147	1.112 ± 0.161	1.101 ± 0.152	1.098 ± 0.153
Left femur neck	0.882 ± 0.130	0.882 ± 0.144	0.889 ± 0.136	0.893 ± 0.140
Left total femur	0.924 ± 0.136	0.933 ± 0.140	0.923 ± 0.114	0.927 ± 0.117
Right femur neck	0.900 ± 0.132	0.893 ± 0.132	0.892 ± 0.039	0.896 ± 0.135
Right total femur	0.937 ± 0.140	0.939 ± 0.141	0.939 ± 0.107	0.941 ± 0.105
Left radius 33%	0.656 ± 0.072	0.652 ± 0.072	0.637 ± 0.081	0.630 ± 0.065
Left total radius	0.510 ± 0.075	0.506 ± 0.072	0.488 ± 0.061	0.486 ± 0.056
Left total ulna	0.455 ± 0.074	0.456 ± 0.076	0.446 ± 0.059	0.444 ± 0.058
Left total forearm	0.487 ± 0.073	0.484 ± 0.072	0.470 ± 0.059	0.468 ± 0.055
Right radius 33%	0.670 ± 0.066	0.665 ± 0.062	0.660 ± 0.089	0.650 ± 0.082
Right total radius	0.511 ± 0.072	0.506 ± 0.069	0.497 ± 0.064	0.483 ± 0.
Right total ulna*	0.470 ± 0.070	0.468 ± 0.068	0.448 ± 0.056	0.438 ± 0.
Right total forearm	0.494 ± 0.070	0.490 ± 0.068	0.476 ± 0.059	0.464 ± 0.

RT=Resistance training; RT+DP=Resistance training + dried plum consumption

Data are presented as mean ± standard deviation

*Significant group by time effect, $p \leq 0.05$

different from baseline, within same group, $p \leq 0.05$

Biochemical Markers of Bone Turnover

Participants from the RT and the RT+DP groups demonstrated similar baseline values for both of the biochemical markers of bone turnover, bone-specific alkaline phosphatase (BAP) and tartrate resistant acid phosphatase (TRAP-5b). There were no significant group time interactions observed for either biochemical marker. Inter-assay coefficients of variation (CV) was determined from the individual sets of duplicates and ranged from 0 to 26% for the BAP assay and 0 to 33% for the TRAP-5b assay. Samples having a CV higher than >20% were deemed unacceptable, and were not analyzed (Kivlighan et al., 2004; Reed, Lynn, & Meade, 2002). This criterion made three samples ineligible for the BAP assay and five of the samples ineligible for analysis

of the TRAP-5b assay. Furthermore, the two women that dropped out of the study were excluded from both biochemical analyses. One of the participants dropped out due to a cancer re-diagnosis which indicated metastases to the liver and bone. This particular participant's baseline BAP sample was extremely high (90.486 U/L) in comparison to the overall mean (44.522 U/L) for the assays, thus she was excluded from analyses. Lastly, the two women from the RT+DP group that had less than 50% adherence to dried plum consumption were not included in the analyses. The total sample sizes for each of the biochemical assays can be found in Table 9.

No interaction effects were found for either marker of bone turnover, nor was there a significant time effect for BAP. Though statistically insignificant, the overall changes for BAP within the RT and the RT+DP groups were -3% and -19%, respectively. These BAP changes may have clinical relevance despite the lack of statistical representation. Despite the lack of changes found for BAP, there was a significant time effect ($F_{(1.137, 17)} = 8.728$, $p \leq 0.05$, $ES = 0.339$) observed for TRAP-5b. Mauchly's test of sphericity was violated for TRAP-5b, thus the Greenhouse-Geisser adjustments were used for the *F* statistics reported. Analyses of the main effects showed that the RT group demonstrated a significant 11% decline in TRAP-5b from baseline to 3 months, while the RT+DP group showed a similar decline of 16% from baseline to 3 months ($p = 0.07$). Though statistically insignificant, the overall change of TRAP-5b, from baseline to 6 months was -12% for the RT group and -26% for the RT+DP group. While these overall changes were deemed statistically insignificant, these changes may be clinically significant. Please refer to Table 9 for a complete description of the biochemical marker of bone turnover.

Table 9. Biochemical Markers of Bone Turnover

Biochemical markers of bone formation (N=21)						
	RT Group (n=11)			RT+DP Group (n=10)		
	Baseline	3-month	6-month	Baseline	3-month	6-month
BAP (U/L)	44.00 ± 14.00	45.80 ± 18.50	42.68 ± 17.08	45.10 ± 17.68	41.29 ± 13.98	36.53 ± 12.71
Biochemical markers of bone resorption (N=19)						
	RT Group (n=11)			RT+DP Group (n=8)		
	Baseline	3-month	6-month	Baseline	3-month	6-month
TRAP-5b (U/L)	4.55 ± 1.57	4.04 ± 1.	4.03 ± 1.81	5.10 ± 2.75	4.27 ± 2.	3.77 ± 1.80

RT=Resistance training; RT+DP=Resistance training + dried plum consumption
Data are presented as mean ± standard deviation
BAP=Bone-specific alkaline phosphatase
TRAP-5b=Tartrate resistant acid phosphatase
different from baseline, within same group, $p \leq 0.05$
different from baseline within same group, $p \leq 0.07$

Continuous Scale-Physical Function Performance (CS-PFP) Variables

Participants from both the RT and the RT+DP groups demonstrated similar baseline values for the five sub components of the CS-PFP (upper body strength, upper body flexibility, lower body strength, balance/coordination, and endurance), as well as total function. There were no significant group time interactions observed for any of the components of the CS-PFP test. Similar to baseline values, there were no significant differences between groups at the 3-month or 6-month time points for any of the CS-PFP variables. There were significant time effects observed for the upper body strength component ($F_{(2, 25)} = 12.848$, $p \leq 0.05$, $ES = 0.339$), lower body strength component ($F_{(2, 25)} = 26.380$, $p \leq 0.05$, $ES = 0.513$), balance and coordination component ($F_{(2, 25)} = 19.099$, $p \leq 0.05$, $ES = 0.433$), endurance component ($F_{(2, 25)} = 20.182$, $p \leq 0.05$, $ES = 0.447$), and total function ($F_{(2, 25)} = 24.831$, $p \leq 0.05$, $ES = 0.498$). Within group analysis showed that the RT group did not show any significant changes from baseline to month-3; however, they demonstrated a significant 7% increase in the lower body strength component from the 3-month to the 6-month time point. Overall, the RT group experienced a significant 14% increase in the lower body strength component over the duration of the intervention. From baseline to six months, the RT group also experienced significant improvements in the balance and coordination component (+9%), endurance component (+9%), and total function (+9%).

The RT+DP group demonstrated steady improvements in several of the components of the CS-PFP test over the course of the study. From baseline to month-3, the RT+DP group had significant improvements in the upper body strength (+12%), lower body strength (+14%), balance/coordination (+10%), and endurance components (+8%), as well as total function (+11%). The RT+DP group did not show any further significant improvements from month-3 to month-6; however, the group did exhibit significant time effects from baseline to 6 months. From baseline to month-6, the RT+DP group significantly increased the upper body strength (+16%), lower body strength (+21%), balance/coordination (+15%), and endurance components (+15%), as well as total function (+16%). Table 10 provides a complete description of the CS-PFP variables.

Table 10. Comparison of Continuous Scale-Physical Functional Performance* (N=27)

	RT Group (n=14)			RT+DP Group (n=13)		
	Baseline	**3-month**	**6-month**	**Baseline**	**3-month**	**6-month**
Upper body strength	65.3 ± 16.6	68.8 ± 16.6	70.8 ± 16.6	61.6 ± 16.4	69.0 ± 14.	71.6 ± 17.
Upper body flexibility	82.1 ± 7.0	83.0 ± 10.5	84.2 ± 5.8	80.0 ± 9.4	82.8 ± 8.2	83.8 ± 7.2
Lower body strength	60.6 ± 13.1	64.7 ± 13.	68.9 ± 13.[b]	56.2 ± 16.9	64.2 ± 17.	68.2 ± 19.
Balance & coordination	68.3 ± 9.4	71.8 ± 11.0	74.7 ± 9.	64.5 ± 14.8	71.8 ± 13.	74.4 ± 14.
Endurance	68.5 ± 9.2	71.9 ± 10.6	74.6 ± 9.	65.8 ± 14.8	72.8 ± 13.	75.4 ± 13.
Total function	67.2 ± 10.2	70.6 ± 11.4	73.5 ± 10.	63.7 ± 14.1	70.8 ± 13.	73.6 ± 14.

*Scores range from 0-100; 0=worst function; 100=best function
RT=Resistance training; RT+DP=Resistance training + dried plum consumption
Data are presented as mean ± standard deviation
[b] different from baseline, within same group, $p \leq 0.05$
different from 3-month within same group, $p \leq 0.05$

Short Form-36 (SF-36) Health Survey Variables

Participants from both the RT and the RT+DP groups demonstrated similar baseline values for the physical function, mental quality of life (QOL), and the physical QOL components of the SF-36 Health Survey. There were no significant group by time interactions observed for any of the components of the SF-36 Health Survey. Similar to baseline values, there were no significant differences between groups at the 3-month or

6-month time points for any of the SF-36 Health Survey components. Lastly, there were no significant time effects observed for any of the components of the SF-36 Health Survey at any of the time points. See Table 11 for a complete description of the components of the SF-36 Health Survey.

Table 11. Comparison of Short Form (36) Health Survey* (N=27)

	RT Group (n=14)			RT+DP Group (n=13)		
	Baseline	**3-month**	**6-month**	**Baseline**	**3-month**	**6-month**
Physical function	80.7 ± 13.7	80.0 ± 16.5	79.3 ± 20.0	84.6 ± 13.8	88.1 ± 11.8	90.4 ± 8.0
Mental QOL	54.2 ± 7.7	51.2 ± 12.5	52.7 ± 12.4	49.7 ± 12.5	50.4 ± 12.2	52.3 ± 9.4
Physical QOL	48.2 ± 7.4	46.9 ± 8.5	45.2 ± 11.5	50.0 ± 6.9	51.7 ± 7.3	51.7 ± 6.8

*Scores range from 0-100; 0=worst; 100=best
RT=Resistance training; RT+DP=Resistance training + dried plum consumption
Data are presented as mean ± standard deviation
QOL=Quality of life

CHAPTER 5
DISCUSSION

The present study was the first to investigate the efficacy of resistance exercise training (RT) or RT in addition to dried plum consumption (RT+DP) on modulating body composition, muscular strength, and physical function in a sample of breast cancer survivors. All of the women showed acceptable adherence to the RT sessions (96%) and dried plum consumption (87%). While there were no significant body composition changes, except for the significant decline in the right forearm components, the women experienced great improvements in both upper and lower body strength from baseline to the six-month time point. Similarly, the women demonstrated significant improvements in total function and all sub components of the CS-PFP, with the exception of the upper body flexibility component. Lastly, no changes were reported for subjective levels of physical or mental quality of life (QOL), measured via the Short Form-36 Health Survey. From the results of the present study, only two of the research hypotheses were supported. The first supported hypothesis was that all women participating in the research study would increase skeletal muscle strength. The second supported hypothesis was that all the women participating would increase objective physical functionality.

The present study failed to show any improvements in total body or the various regional sites of BMD assessed for either intervention group. Furthermore, a significant group time interaction was observed for the right total ulna, indicating that the RT+DP group lost BMD at the right ulna more rapidly than the RT group. However, when the two women that had adherence rates <50% to the dried plum consumption were removed, the interaction effect was negated. The present study was the first to implement a combination treatment group of RT+DP for examining the effects of this non-pharmalogical treatment on BMD. It was hypothesized that both the RT and the RT+DP group would experience positive BMD changes, but it was unknown as to whether the RT+DP group would experience additive benefits of DP compared to the RT group alone. Results revealed that the addition of DP to RT did not provide additional benefits regarding BMD improvements. A recent study implementing DP in a

group of health post-menopausal women showed that significant improvements in lumbar spine and ulna BMD were obtained over the course of 12 months (Hooshmand et al., 2011). These results leave speculation as to whether DP consumption alone would have elicited similar BMD results as the RT intervention. It is possible that in the RT+DP group, the benefits of DP were overshadowed by the positive effects of the RT.

Nonetheless, the significant time effect observed over the course of the study indicated that the RT+DP group demonstrated a significant decrease in several components of the right forearm. These results are not easily understood, nor explained. One possible explanation for the decreases in right forearm BMD may be that the women were unintentionally taking more precautions with their right arms when exercising. Nearly 70% of the women in the study were diagnosed with breast cancer on the right side of their body. This equates to all the surgeries and treatments being targeted toward the right arm area. Common procedures for breast cancer involve removing the sentinel lymph node for biopsy purposes. Even with a sentinel lymph node biopsy, there is an approximate 17% risk for the development of lymphedema (Francis et al., 2006). Lymphedema is an extremely common fear among breast cancer survivors. The present study took special precaution to monitor all participants every two weeks for signs of the development of lymphedema, and results showed that the exercise sessions did not cause any adverse lymphedema risks. Despite these precautions taken to avoid the development of lymphedema, some of the women may have avoided full exertion with their affected arms, and could account for the declines seen in right forearm BMD. Though this explanation may serve as a possible explanation as to why negative time effects were observed in the RT+DP group, the rationale does not account for the maintenance of forearm BMD seen in the RT group. This discrepancy is not easily understood, nor can it be explained.

The BMD results of the present study somewhat contradict the results found from studies conducted with healthy post-menopausal women, but actually coincide with the few existing studies that have implemented RT with breast cancer survivors. The few studies examining the effects of RT on BMD of breast cancer survivors have done so with far less intensive RT prescriptions, thus making comparisons between the present study and former studies difficult. Schwartz et al. (2007) implemented a RT intervention

with newly diagnosed breast cancer patients who had not yet initiated chemotherapy treatment. Schwartz and colleagues implemented a RT intervention that took place during the course of chemotherapy, for six months. Only lumbar spine was measured and it was found to significantly decrease (-4.92%) from baseline to the six-month time point. The RT prescription implemented with these patients differed from the present study in that the prescription was a home-based resistance band program; a seemingly far less intense RT exercise prescription than the current study.

A RT program that more closely mimicked the design of the present study was conducted by Waltman et al. (2003). In this study, Waltman and colleagues implemented a RT program in a group of breast cancer survivors (who had completed all forms of primary treatment). Waltman and colleagues also prescribed a similar frequency of training sessions as the present study, with a frequency of twice per week. Intensity and volume of RT were not accounted for in this study; however, the authors mentioned that free weights ranging from 3-20lbs for upper body and 2-20lbs for lower body were utilized. Unlike the present study, Waltman et al. prescribed prescription bisphosphonates in addition to the RT, and the study lasted 12 months, as opposed the present study design, lasting six months. Despite the addition of the bisphosphonates and the longer study design, Waltman et al. reported participants still lost a significant 2.6% in forearm BMD. These results closely mimic the 3% forearm BMD loss reported in the RT+DP group of the present study. Though the lack of significant BMD improvement from the current study coincide with the results of the few RT and breast cancer survivor studies in existence, it was hypothesized that the BMD changes of the present study would more closely mimic the BMD changes found for healthy post-menopausal women. This hypothesis was made based on the fact that the RT prescription of the current study more closely copied the prescriptions implemented with healthy post-menopausal women compared to the lesser stringent prescriptions seen in the few existing RT and breast cancer survivor studies.

Though RT interventions of six months or less have produced inconclusive reports as to whether BMD can be favorably changed, it was anticipated that the breast cancer survivors of the present study could experience gains in BMD as reported by several studies involving health post-menopausal women. Simkin et al. (1987) reported

significant (+3.8%) BMD changes in the distal radius of a group of osteoporotic elderly women, while Jessup et al. (2003) reported significant increases in lumbar spine, and Vincent and Braith (2002) reported significant (+1.96%) increases in femur neck after six months of RT. The present study design differed from aforementioned studies by way of frequency of RT session per week and intensity of exercise sessions. All three of the studies that found significant BMD improvements in six months or less prescribed RT session three days per week, unlike the present study, which prescribed RT session twice per week. Another discrepancy between the training programs of the present study and the three successful studies is the different RT intensities that were carried out over the course of the intervention. Jessup and colleagues progressed from 50-75% 1-RM, whereas Vincent and Braith performed 80% 1-RM. The present study was intended to have women lift 60-80% 1-RM; however, the two training groups did not reach 60% 1-RM until 5-12 weeks into the study, and even then, the highest %1-RM attained was 69%1-RM for upper body and 67% 1-RM for lower body.

Given the differences between the study designs of the present study and those that have had successful BMD improvements, it could be speculated that the frequency of RT session and intensities of RT sessions could account for the lack of BMD improvement found in the present study. However, there are several six-month studies involving healthy post-menopausal women that prescribe RT sessions three times per week and intensities ranging from 60-90% 1-RM that report no significant improvement in any of the BMD variables assessed (Humpheries, 2000; Bemben, 2000; Chuin, 2009). Thus, it can be inferred that the RT intensity prescribed and the weekly frequency of RT session cannot solely be responsible for the lack of BMD improvements found in the present study.

A more likely contributor to the lack of BMD improvements is the length of the intervention. Studies implementing RT with healthy post-menopausal women that lasted at least nine months have consistently reported significant improvements in BMD. The prescription components of these successful RT studies typically involved two to three sessions per week with intensities ranging from 60-90% 1-RM (Zenacker, 2007; Stengel, 2005; Kerr, 2001; Bergstrom, 2008).

Even though the women from the present study showed no significant improvements in BMD, it is noteworthy that all sites except the right forearm were maintained over the course of the six months. Maintaining BMD should be considered a desirable outcome for post-menopausal women, and even more so for breast cancer survivors, given the vulnerability of their bone health. Though the present study lacked a true control group, it can be expected that without the interventions, the women in the study may have experienced a significant decline in one or more BMD sites over the course of the six months. Pruitt et al. (1992) reported that while the women in the RT group of their study maintained BMD over the course of the nine month study, their control group lost a significant 3.6% in the lumbar spine. Similarly, Jessup and colleagues reported significant losses of the femur neck in their control group over the course of their 32-week intervention. Simonavice et al. (2011) followed a group of breast cancer survivors and healthy controls over the course of 15 months and noted that both groups lost a significant 2% for the lumbar spine, total femur, and total forearm. Thus, the results from several previous studies indicate that it likely that the women from the present study may have experienced a significant decrease in BMD had they not been participating in the intervention.

The findings from the aforementioned studies provide insight into the experimental design downfalls that may explain why the women from the present study did not experience significant improvements in any of the BMD sites assessed. From the information gathered, it can be inferred that a RT program lasting nine months or more may elicit positive changes as compared to interventions lasting only six months. On the contrary, the literature reviewed gives merit to the present study for the efficacy to maintain total body and most of the regional BMD sites assessed. The studies reviewed confirmed that it is likely that post-menopausal women will lose BMD if no active measures are taken to prevent loss.

The success in maintaining BMD, with the exception of the right forearm, seen in the present study is reflective of the positive changes demonstrated in the biomarkers representing bone turnover. Though there were no group time interactions observed for either of the biochemical markers of bone metabolism, there was a significant time effect observed for the biomarker of bone resorption over the course of the study.

Results showed that over the course of the study bone resorption, by measurement of TRAP-5b was significantly decreased by 11% for the RT group and by 16% for the RT+DP group. These findings are especially encouraging given the fact that breast cancer patients that have been treated with hormone suppressant therapies (aromatase inhibitors) have significantly higher levels of bone resorption as compared with healthy post-menopausal women (Heshmati et al., 2002). Eastell et al. (2006) reported that two years of aromatase inhibitor treatment elicited a 15% increase in bone resorption indicies and a 20% increase in bone formation indicies. This increase in bone turnover, was associated with a loss of BMD ranging from 1-4%, depending upon the site measured (Eastell et al., 2006). Given the increase in bone turnover elicited by hormone suppressant therapies, the ability of the present study to decrease bone resorption and maintain bone formation provides a viable option for breast cancer patients to decrease bone turnover.

The initial hypothesis that TRAP-5b would decrease was accepted but the hypothesis that BAP would increase was rejected. From reviewing the literature, it became clear that increased bone formation markers were not always indicative of positive bone status, which was the initial thinking when forming hypotheses for the present study. Garnero et al. (1996) found that with the onset of menopause both bone resorption and bone formation dramatically increase by 37-52% and 79-97%, respectively. Furthermore, Garnero and colleagues showed that the rate of bone turnover accounts for nearly 52% of the BMD variance seen in elderly healthy women. These findings indicate that high levels of bone formation are not always associated with positive bone metabolism. In fact, high levels of bone formation biomarkers have even been used to detect the presence of malignant bone disease (Chao, Ho, Lee, Chen, Janckila, & Yam, 2003). This turned out to be the case for the one participant that dropped out of the study due to a cancer reoccurrence that involved bone metastasis. This participant had noticeably higher levels of BAP as compared to the remaining women. It is now clear that the bone remodeling process is a complex series of events involving bone resorption and bone formation. These two remodeling components are closely coupled, and the patterns of bone resorption, will foreshadow the patterns of bone formation. In an example of where anti-resorptive medications are given to

individuals, typically within the first three months of treatment bone resorption markers will decline, and shortly following, bone formation markers will also begin to decline (Barginear, Clotfelter & Van Poznak, 2009). This trend gives explanation to the results of the present study since a significant decline in TRAP-5b was noted; however, there was no significant change in BAP observed. Given the trend for formation markers to follow the pattern of resorption markers, it can be speculated that had the study been of longer duration, bone formation markers would have also declined.

The results from the present study are somewhat similar to the results of studies that have implemented a form of anti-resorptive medication among post-menopausal women. Common results of anti-resorption medication are declines in both TRAP-5b and BAP. Garnero et al. (1996) showed that after one year of treatment with Tamoxifen (a sister drug to raloxifene), bone resorption and bone formation rates decreased by 52% and 16%, respectively (Garnero, et al., 1996). Another study administered ibandronate (a bisphosphonate), for one-year, to breast cancer survivors who were being adjuvantly treated with hormone suppressant therapies and found a 26% decline in bone resorption and a 23% decline in bone formation (Lester et al., 2008). Thus it appears that the intervention groups from the present study benefited in terms of bone resorption, on a similar principle as individuals who are receiving anti-resorption bone medications. It can further be speculated that similar to these studies implementing anti-resorptive medications, the women from the present study may have seen declines in bone formation markers, in addition to the declines in bone resorption, if the study had lasted 12 months as opposed to six months.

Studies implementing non-pharmacological interventions have also shown promising results in terms of decreasing bone turnover. Hooshmand and colleagues reported significant declines (-7%) in the bone resorption marker, TRAP-5b, after only three months of consuming a similar amount of dried plums as the present study. Furthermore, Hooshmand and colleagues reported that after 12 months, biomarkers of bone formation, BAP, were significantly reduced by -11% (Hooshmand et al., 2011). These percent changes are somewhat lower compared to the results of the present study where the RT+DP group, although statistically insignificant, experienced -19% and -26% change for BAP and TRAP-5b, respectively. The higher percent changes

seen in the present study compared to Hooshmand and colleagues could be due to the much higher baseline values reported for the present study. From the present study, the RT+DP group had baseline values of 45.013 ± 17.682 U/L for BAP and baseline values of 5.103 ± 2.753U/L for TRAP-5b. Hooshmand et al. (2001) reported baseline BAP values of 17.26 ± 10.70 U/L and baseline values of 3.73 ± 0.10 U/L for TRAP-5b.

Nonetheless, the trends reported by Hooshmand et al. (2011) reiterate the pattern that bone formation markers closely follow the patterns of bone resorption, but do so on a delayed timeline. Again, with a longer study intervention it is likely that the women from the present study would have shown significant declines in BAP. The results of the present study indicated that DP consumption does not provide added benefit to bone turnover in addition to RT. However, the design of the present study does not allow for clear distinction of the benefit of DP consumption on breast cancer survivors, but it is highly speculated that DP consumption alone could have elicited similar changes in bone turnover in breast cancer survivors, as seen with the data from the previously reviewed study (Hooshmand et al., 2011).

Similar to the article examining the effects of dried plum consumption on bone turnover, RT interventions have also shown that biochemical markers of bone turnover can be modulated through resistance exercise. The results from the present study showed decreased bone resorption with no statistically significant change in bone formation markers. These results are in agreement with past studies implementing RT interventions with healthy post-menopausal women. Klentrou and colleagues (2007) reported a 14% decline in bone resorption after 12 weeks of RT, but showed no changes in bone formation markers (Klentrou et al., 2007). Another study trained post-menopausal women for 24 weeks and did not show any changes in bone formation or bone resorption, but did report the control group significantly increased (+22%) bone turnover markers (Humpheries et al, 1999). The physical changes of BMD from these studies also mimicked the results of the present studies, in that when there was a decrease or maintenance of bone turnover, BMD was also maintained. These results are in accordance to the results found in the present study. To date there are very few RT studies involving breast cancer survivors, and even fewer studies that examine bone turnover biochemical markers in breast cancer survivors after a RT intervention.

Recently, Winters-Stone et al. (2011) completed a 12-month RT intervention with breast cancer survivors and reported bone resorption markers were decreased by 38%, while bone formation markers remained constant. These results are representative of the results found in the present study (Winters-Stone, Dobek, Nail, Bennet, Leo, Naik, & Schwatz, 2011).

From the studies reviewed it appears that the RT modulates bone turnover primarily by means of decreasing bone resorption. The exact mechanisms by which RT can decrease bone resorption are somewhat unclear, but past research has provided several compelling possibilities. When a mechanical load (such as RT) produces sheer stress of interstitial fluid flow throughout the canaliculi and osteonals, the osteocytes activate a number of processes including growth factor production, hormonal and biochemical messenger secretion, and matrix synthesis (Burger & Klein-Nulend, 1999; Zernicke et al., 2006). Nitric oxide (NO) is one of the substances released as a result of mechanical loading. NO is a strong inhibitor of osteoclast activity by suppressing RANKL expression and increasing OPG expression (Fan et al., 2004; Kasten et al., 1994; MacIntyre et al., 1991). Essentially these events lessen the ability of osteoclast differentiation into mature osteoclasts, which will ultimately decrease the number of osteoclast recruitment to the bone surface, resulting in a lowered bone resorption rate. Thus, it is likely that the participants of the present study experienced a decline in osteoclast maturation, thus accounting for the significant declines observed for TRAP-5b. In conclusion, since there was a significant decline in bone resorption and no change noted for bone formation, most BMD sites were maintained throughout the study.

Similar to the BMD results of the study, the women participating in the present study exhibited no changes in body composition over the course of the six months. Thus, our hypothesis that the participants would improve body composition by means of increasing lean mass, decreasing fat mass, and decreasing body fat percent, was rejected. These results only add to the ambiguity of whether or not RT can effectively alter body composition in breast cancer survivors. The initial thought, according to past studies, was that breast cancer survivors could acquire positive body composition changes as a result of a RT intervention. These thoughts were based upon studies

such as Schmitz et al. (2005) that stated breast cancer survivors gained 2% of lean mass while decreasing their body fat percent by 3% over the course of a twice weekly, six month RT intervention. Other studies have reported significant improvement in girth measurements, such as Cheema and Gaul (2006) who reported that eight weeks of RT elicited a 2% improvement in hip circumference and a 3% improvement in waist circumference. One difference between the present study participants and those in the study conducted by Schmitz et al. (2005) was that the lean mass baseline values for the women in the current study (RT: 38.9 ± 6.8kg; RT+DP: 40.9 ± 6.0kg) were higher than the six month lean mass values (38.78 ± 0.77kg) reported for Schmitz and colleagues. This discrepancy provokes questions as to whether women starting at a lower baseline level for lean mass can achieve gains more easily than women beginning with higher baseline values.

Supporting this idea, as well as the results from the present study is a recent study conducted by Winters-Stone et al. (2011). Winters-Stone and colleagues implemented a 12-month thrice weekly RT plus weight vest plyometric intervention with a group of breast cancer survivors. At the completion of the intervention, Winters-Stone reported no changes for lean mass, fat mass, or body fat percent. The baseline variables from the Winters-Stone study for lean mass (43.4 ± 6.5kg), fat mass (30.4 ± 9.4kg), and body fat percent (40.5 ± 5.7%) closely mirrored the baseline results from the present study for lean mass (RT: 38.9 ± 6.8kg; RT+DP: 40.9 ± 6.0kg), fat mass (RT: 30.4 ± 10.2; RT+DP: 31.1 ± 8.5kg), and body fat percent (RT: 43.2 ± 5.7%; RT+DP: 42.7 ± 4.8%). The results from Winters-Stone et al. (2005) and from the present study may seem undesirable; however, maintaining lean mass, fat mass, and body fat percent should be given some merit considering that the normal aging process yields unfavorable body composition changes. In a longitudinal study following a sample of breast cancer survivors and healthy post-menopausal women, results showed that over the course of approximately 15 months, all women in the study exhibited a significant 3% increase in body fat percent as well as a significant 7% decline in their lean to fat mass ratio (Simonavice, Liu, Ilich, Kim, & Panton, 2011, ACSM abstract).

Despite having to reject the initial hypothesis that women in the current study would improve various aspects of their body composition, the literature supports the

conclusion that body composition changes of breast cancer survivors participating in RT are not always predictable. Furthermore, merit to the present study can be given for maintaining lean mass, fat mass, and body fat percent, since it seems likely that these variables may have changed unfavorably without the intervention.

The lack of improvement in lean mass did not hinder the women's ability to make significant strength gains in both upper and lower body muscular groups. Overall the women in the RT group experienced a significant increase in upper body strength (+21%) and lower body strength (+22%). The RT+DP group experienced a significant increase in upper body strength (+33%) and lower body strength (+29%). These results coincide with the strong support of previous literature indicating the abilities for breast cancer survivors to make improvements in skeletal muscle strength. Courneya et al. (2007) showed that even while breast cancer patients were in the course of their chemotherapy regimen, a RT program elicited a 31% increase in upper body strength and a 32% increase in lower body strength. Other studies implementing a RT program after the completion of cancer treatments (as did the present study) have reported gains of 33% for upper body strength and 48% increase in lower body strength (Cheema & Gaul, 2006). Both of the studies reviewed implemented similar RT exercise prescriptions with training occurring 2-3 times per week for 1-3 sets of 8-12 weeks at various intensities.

The ability for breast cancer survivors to gain skeletal muscular strength is especially encouraging given the fact that typically after cancer treatments, breast cancer survivors are significantly weaker compared to healthy age-matched controls (HC). Simonavice et al. (2011) found that breast cancer survivors were significantly weaker for upper body (BC: 61 ± 13; HC: 77 ± 20kg) and lower body (BC: 70 ± 13; HC: 91 ± 18kg) strength compared to healthy post-menopausal women. Comparing the six-month strength values for upper body (RT: 82 ± 20; RT+DP: 96 ± 22kg) and lower body (RT: 88 ± 28; RT+DP: 99 ± 18kg) from the present study to the baseline values of the healthy controls in Simonavice et al. (2011) indicates that the RT intervention increased strength up the levels of healthy post-menopausal women. The results from the present study in combination with the reviewed studies confirm the idea that breast cancer survivors are very capable of making both upper and lower body strength gains.

Women participating in the study showed excellent capabilities to improve objective physical function; however, the same cannot be said for the subjective levels of physical function or for quality of life (QOL). Thus, the hypothesis that women participating in the study would increase QOL was rejected. To date the present study was the first to implement the CS-PFP test among breast cancer survivors for an assessment of objective physical function. Results showed that the RT group increased total function by 9%, while the RT+DP group increased total function by 16%. While there are no studies examining breast cancer survivors that the results of the present study can be compared, there are similar RT studies that have been measured objective physical function, with a slightly different populations or methods of functional assessment. Janowski et al. (2008) implemented the CS-PFP in a group of older cancer survivors (cancer type not specified) and found that after four months of RT, both upper body and lower body strength components of the CS-PFP were significantly higher as compared to the control group. Total physical function was not accounted for. The baseline values for the women from the present study were seemingly higher for the upper body strength component (RT: 65.3 ± 16.6; RT+DP: 61.6 ± 16.4 units) as compared to the baseline values from Janowski and colleagues (59 ± 29 units). Similarly, for the lower body strength component, the women from the present study had higher baseline values (RT: 60.6 ± 13.1; RT+DP: 56.2 ± 16.9 units) compared to Janowski and colleagues (45 ± 16 units). These discrepancies are likely due to the older population (71 ± 5 years) with which Janowski and colleagues studied, as compared to the present study where the sample population was seemingly younger (RT: 63 ± 6; RT+DP: 64 ± 7 years).

Though time effects were not reported by Janowski et al. (2008), pre-to-post differences were calculated to be +20% for the upper body strength component and +11% for the lower body strength component. These improvements are in accordance with the results from the present study. Another study reported that a RT intervention significantly improved six-minute walking distance in a sample of breast cancer survivors (Yeun & Sword, 2007). The six-minute walk test is essentially the “endurance” components of the CS-PFP. Thus, these results are in accordance to the significant 9%

and 15% improvements in the endurance component of the CS-PFP test as seen respectively for the RT and RT+DP groups of the present study.

The ability for breast cancer survivors to increase physical function is especially important given the fact that after the completion of cancer treatments, breast cancer survivors have significantly (p=0.08) lower physical function scores as compared to healthy age-matched post-menopausal women (Simonavice et al., 2011). It should also be noted that while the baseline values from the present study for total function (RT: 67.2 ± 10.2; RT+DP: 63.7 ± 14.1units) mimicked those of the baseline values for total function (66.1 + 13.8 units) from Simonavice and colleagues, the six-month values from the present study for total function (RT: 73.5 ± 10.1; RT+DP: 73.6 ± 14.5 units) more closely mirrored the results from the healthy controls (75.1 + 13.0 units) from Simonavice and colleagues. These results imply that RT is an effective way to improve the physical functional status of breast cancer survivors to that of healthy post-menopausal women.

The lack of QOL improvement for the women in the present study was inconsistent with most previous literature. Many studies have reported that following RT interventions of various durations, intensities, and volumes have produced significant improvements in QOL in breast cancer survivors (Adamsen et al., 2006; Ohira et al., 2006; Simonavice & Wiggins, 2009). The difference between these previous studies and the present study is the type of subjective questionnaire implemented. The Functional Assessment of Cancer Therapy-General (FACT-G) or the Functional Assessment of Cancer Therapy-Breast (FACT-B) were the most commonly used survey tools assessing QOL among the studies reviewed. The present study implemented the Short Form-36 Health Survey (SF-36). The lack of significant improvement for QOL in the present study suggests that the FACT-B and FACT-G may address more specific questions regarding the impact that cancer and cancer-related treatments may have on QOL and thus may be more sensitive to detecting QOL changes within breast cancer survivors. Despite the fact that neither the physical or mental QOL scores were changed over the course of the 6-month intervention, the fact remains that all the women from the present study significantly improved physical function, as measured

objectively via the CS-PFP. These results emphasize the importance of objective measures of physical function in the breast cancer population.

The present study had several limitations that may have hindered the ability to accurately interpret the results. The present study was unable to acquire an adequate number of participants to achieve a power of 80%, maintaining an $\alpha=0.05$. This may have hindered the obtainment of statistical significance for many of the variables assessed. Additionally, due to the two non-compliant women in the RT+DP group and the two women that had to drop out of the study, the results obtained may not have provided an accurate portrayal of the efficacy of RT or a combination RT+DP intervention on modulating the many variables assessed. Furthermore, for the biochemical markers of bone turnover assays, several samples had to be excluded due to the high coefficient of variance (>20%) detected within duplicate samples. This criterion, in addition to the non-compliant women from the RT+DP group and the two dropouts, lowered our sample size to n=21 for the bone formation markers and n=19 for the resorption marker.

Another limitation of the current study was a lack of a true control group, which may have lessened the magnitude of the results reported; however, reviewing past literature with similar study designs that did include control groups was able to provide pertinent information on what may have happened to the women of the present study had they not be involved with the study. The current study also lacked a DP only group. The combination RT+DP group implemented in the present study indicated that DP did not provide any added benefit to RT; however, the question as to whether DP could elicit similar BMD and biochemical markers of bone turnover results as RT among breast cancer survivors remain unanswered.

Conclusions

Our findings indicate that a RT or combination RT+DP intervention was very well tolerated among breast cancer survivors. All women displayed high levels of adherence to the attendance of exercise sessions as well as to the calcium/Vitamin D supplements. With the exception of two women from the RT+DP group, adherence to DP consumption was also very good. One of the research questions of the study was to

determine whether the addition of DP to a RT intervention would elicit added BMD or biochemical markers of bone turnover benefits. Results indicated that there was no additive effect of DP to RT observed over the course of the study for any of the variables assessed, with the exception of the right ulna BMD; however, this effect was negated after accounting for the non-compliant women within the RT+DP group. Thus, it was concluded that the addition of DP to a RT intervention does not provided added BMD or biochemical markers of bone turnover benefits among breast cancer survivors.

Results further showed that the maintenance of all BMD sites, except for the right forearm, was the physical manifestation of the observed changes of bone turnover markers. These biochemical changes indicated maintenance of bone formation, with a decline in bone resorption. Thus, the intervention was successful for favorably modulating bone turnover, resulting in a maintenance of most BMD sites of breast cancer survivors. A review of the literature provided some rationale that had the intervention lasted of longer duration (>9 months), further changes in biochemical markers of bone turnover as well as BMD may have been attained. Like most sites of BMD, the intervention maintained all body composition variables assessed (lean mass, fat mass, body fat percent, and girth measurements). Though this outcome was not what was hoped for when designing this study, literature suggests that had the women not been participating in the study, they may have experienced unfavorable age-related body composition changes.

The participants exhibited large capabilities for improving both upper and lower body muscular strength over the course of the study. It is likely that the significant improvements in skeletal muscle strength played a role in the advancements of physical functional abilities demonstrated by the women participating in the study. With the exception of upper body flexibility, the women drastically improved all sub components as well as total function, measured via the CS-PFP. It is also noteworthy that at the end of the six-month intervention, upper and lower body strength as well as objective physical function measures were boosted to levels that mimicked those achieved by healthy post-menopausal women. This implies that a RT intervention is capable of helping breast cancer survivors achieve similar levels of strength and function that they may have had prior to their diagnosis and treatment of breast cancer. The present

study was unable to detect any changes in QOL among the participants; however, from the literature reviewed, the QOL assessment tool may have not been the best choice for the breast cancer survivor population. Furthermore, the significant gains in objective levels of physical function that the participants achieved should be more heavily considered as opposed to the subjective assessment of QOL, as it provides a more accurate depiction of their true physical capacities and physical well-being.

Future studies among breast cancer survivors may benefit from implementing a RT intervention of longer duration in hopes of seeing more favorable biochemical bone turnover and BMD changes. Additionally, the role of DP consumption in affecting bone health in breast cancer survivors remains unclear, thus future research would benefit from designing a study that would more clearly reveal the role of DP in modulating biochemical markers of bone turnover and BMD. Lastly, the present study discouraged any changes in diet and in physical activity levels, outside of the study, for the participants. Future studies may benefit from implementing a multi-component intervention (aerobic + resistance exercise + nutrition) in attempts to favorably modulate body composition among breast cancer survivors.

APPENDIX A—IRB APPROVAL LETTER

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: 1/14/2011
To: Emily Simonavice

Address: [redacted]
Dept.: NUTRITION FOOD AND MOVEMENT SCIENCES

From: Thomas L. Jacobson, Chair

Re: Re-approval of Use of Human subjects in Research
Dried plums and resistance training effects on bone 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 1/11/2012, you must request a renewal of approval for continuation of the project. As a courtesy, a renewal notice will be sent to you prior to your expiration date; however, it is your responsibility as the Principal Investigator to timely request renewal of your approval from 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
HSC No. 2010.5521

APPENDIX B—Telephone Interview

Hello, my name is (state your name) calling from The Florida State University regarding the breast cancer research project that you called about. We are currently looking for breast cancer survivors, ages 40-80 years, having completed chemotherapy treatment at least three years prior and/or who have completed at least one year of hormone suppressant therapies. We expect the study to last approximately 30 weeks. The 30 weeks will consist of 2 weeks of initial testing, 2 weeks of mid-point testing, and 2 weeks of post testing. The intervention period will last 24 weeks. With the exception of DEXA, which will only be conducted at baseline and at the conclusion of the intervention, the pre/mid/post testing periods will consist of the following assessments: blood markers of bone turnover and C-reactive protein, muscular strength by one-repetition maximal tests, physical function by the Continuous Scale Physical Functional Performance test, and quality of life measured via the short form-36 health survey.

The women in the study will be randomly assigned to one of the two following treatment groups for a period of six months: 1) resistance exercise training, 2) resistance exercise + dried plum. Both groups will be given a pedometer to wear for one randomly assigned week per month and be instructed to record the number of steps obtained daily. The resistance exercise group will consist of meeting twice a week with an exercise instructor for a guided exercise session lasting approximately 45 minutes at The Florida State University. The dried plum group will be provided with dried plums and be instructed to consume 90 ± 6 g of dried plums per day. Additionally, all participants will be asked to replace their current supplementations with a multivitamin containing 450 mg of calcium and 800 IU of vitamin D.

Do you have any questions? If not, and you are interested, I would like to ask you some questions regarding your present state to determine your eligibility. If you have any of the following conditions or are taking any of the medicines listed below, you may not participate in the study.

1. Were you diagnosed with stage IV breast cancer or are currently diagnosed with active cancer?
2. Do you have uncontrolled hypertension (>160/100 mmHg), uncontrolled diabetes, or uncontrolled heart disease?

Since you do not have any of the exclusion criteria, would you to schedule with me a time for you get started with the study?

APPENDIX C—Informed Consent Document

INFORMED CONSENT DOCUMENT

1. I voluntarily consent to be a participant in the research project entitled "The effects of dried plum consumption and resistance exercise on bone mineral density, physical functionality, and quality of life in breast cancer survivors." conducted by Lynn Panton, Ph.D., Bahram Arjmandi, Ph.D., Jeong-su Kim, Ph.D., Jasminka Ilich-Ernst, and Emily Simonavice, M.S., of the department of Nutrition, Food & Exercises Sciences at Florida State University.

2. The purpose of the proposed study is to examine the effects of a six-month intervention consisting of dried plum consumption and resistance exercise training on bone mineral density, physical function, quality of life, body composition, and muscular strength in breast cancer survivors who have completed chemotherapy at least three years prior and/or who have completed at least one year of hormone suppressant therapy. Forty-eight post-menopausal breast cancer survivors, ages 40-70, will be recruited for this study.

3. My participation in this project will involve coming to the Clinical Exercise Physiology Laboratory at Florida State University for testing on six occasions to undergo the assessments described below I will undergo testing on two separate visits at each of the following time points of the study: baseline, three months, and six months.

   During my first visit, I will be given an informed consent document to sign and a medical history form to complete before I can participate in the study. I cannot participate in this study if I was diagnosed with stage IV breast cancer, am currently diagnosed with active cancer, am receiving endocrine (e.g., prednisone, other glucocorticoids) or neuroactive (e.g., dilantin, phenobarbital) drugs or any other prescription drugs known to influence bone and calcium metabolism, have had a history of hypo or hyperthyroidism or any other disease known to alter bone metabolism, have uncontrolled hypertension (>160/100 mmHg), uncontrolled diabetes, uncontrolled heart disease, or am participating in a vigorous exercise program, or have been treated with pharmacologic doses of vitamin D, calcitonin, bisphosphonate, sodium fluoride, or anabolic steroids within six months prior to the start of the study.

   During this visit, I will complete a questionnaire packet assessing the following measures: quality of life, nutritional status, and physical activity status. I will also have my blood drawn and my bone density, body composition, and muscular strength measured. Blood will be drawn under sterile conditions in the amount of 20 milliliters. The blood samples will not be used for any other research or testing purposes other than those specified in the research proposal. My body composition and bone mineral density at the forearm, hip, and spine will be measured via the use of a dual-energy X-ray absorptiometry (DEXA) scanner. Very low doses of radiation are used; however, this test is non-invasive. I will lie on a padded table for approximately 15 minutes while the scan is being completed. Testing will be completed according to the manufacturer's instructions and specifications by a certified X-ray technician. Both upper and lower body strength will be assessed using the chest press and leg extension exercises, respectively. After a warm-up, I will be progressed towards the maximum weight that I can lift one time through a full range of motion, also called a one-repetition maximum (1-RM). All measurements will be recorded within three to five attempts. This visit will take approximately two hours.

On the second visit (occurring at least 72 hours following the first visit), I will have my resting blood pressure, resting heart rate, height and weight, hip and waist circumferences assessed. I will also have my 1-RM strength measures repeated and my physical functionality measured objectively. Blood pressure and heart rate will be measured in a quiet room on my forearm and radial artery respectively, after I have been seated for a period of five minutes. Height and weight will be assessed using a standardized scale. Waist and hip circumference measures will be taken a minimum of two times at the smallest part of the torso and the largest part of the buttock, respectively. My 1-RMs will be verified by repeating the strength tests. The highest measurement for the upper and lower body from the two days of testing will be considered the 1-RM. The Continuous Scale–Physical Functional Performance (CS-PFP) test, will measure physical functionality. This test consists of tasks that simulate activities of daily living. The tasks will include carrying a weighted pan, 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 six minutes. Measurements will be taken on the time it takes to complete the individual tasks. I may stop and rest at any time during the test. I may also choose not to do any portion of this test if I feel uncomfortable about an activity. My heart rate will be monitored continuously during this test. The second visit will take approximately one and a half hours. Combined visits one and two will last approximately three and a half hours. Visits one and two will be replicated at the end of the third and six month of the intervention.

After finishing baseline testing, I will be randomly assigned to one of three intervention groups for the duration of the six-month intervention: 1) resistance exercise (RE), 2) dried plum consumption (DP), 3) resistance exercise and dried plum consumption (RE+DP). Participants in all groups will be given a pedometer to wear daily for the duration of the six-month intervention. I will record the number of steps I achieve daily in a provided physical activity log. Participants in all groups will also be asked to replace their personal multivitamin and calcium supplements with one multivitamin supplement containing 450mg calcium and 800IU of vitamin D. For the length of the six months, the DP and RE+DP groups will be instructed to consume approximately 90±6g of dried plums daily. Additionally, the RE and RE+DP groups will complete six months of a supervised resistance exercise-training program. The RE and RE+DP groups will complete all training sessions under the supervision of qualified instructors on two non-consecutive days each week for six months. Each exercise session will last approximately 45 minutes.

4. I understand there is a minimal level of risk involved if I agree to participate in this study. I will not be able to participate in this study if I was diagnosed with stage IV breast cancer, am currently diagnosed with active cancer, am receiving endocrine (e.g., prednisone, other glucocorticoids) or neuroactive (e.g., dilantin, phenobarbital) drugs or any other prescription drugs known to influence bone and calcium metabolism, have had a history of hypo or hyperthyroidism or any other disease known to alter bone metabolism, have uncontrolled hypertension (>160/100 mmHg), uncontrolled diabetes, uncontrolled heart disease, or am participating in a vigorous exercise program, or have been treated with pharmacologic doses of vitamin D, calcitonin, bisphosphonate, sodium fluoride, or anabolic steroids within six months prior to the start of the study.

There is the possibility that the groups engaging in resistance exercise testing and training will experience muscle soreness. Care will be taken to try to minimize soreness by thoroughly stretching after exercise sessions. There is also the possibility that participants may pull muscles and/or cause damage to ligaments and joints during an exercise session. Qualified exercise instructors will oversee all exercise sessions in order to ensure proper exercise techniques and to monitor exercise intensity, and to reduce the risk of any musculoskeletal injuries. The risk of a cardiovascular event during testing and training will be minimized by careful review of my medical history and monitoring of my exercise sessions.

Breast cancer survivors are at risk for developing lymphedema if they have had surgery in which one or multiple lymph nodes have been removed. Lymphedema can also occur due to radiation treatment for cancer, causing scarring and inflammation of the lymph nodes or lymph vessels, ultimately restricting lymph flow. Recent evidence has shown that exercise can aid in lymph circulation and causes no exacerbation to the condition. Nonetheless, participants in the resistance exercise training groups will be monitored on a bi-weekly basis via limb circumference measurements. Subjects noticing any of the following signs or symptoms of lymphedema will be asked to notify the exercise instructor prior to an exercise appointment: 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. Implications of any of these signs or symptoms will result in an immediate reduction of the prescribed resistance exercise intensity. All participants in the resistance exercise groups will be encouraged to wear their compression garments, if applicable, during the exercise session.

Bone density will be evaluated by Dual-Energy X-ray Absorptiometry (DXA). This involves some radiation of approximately 12 mREM per spine or hip scan and .5 mREM per total body scan, or a total of about 25 mREM for the three scans. This is comparable to the radiation a person receives from a chest X-ray (20-50 mREM), but substantially less than a full dental X-ray (300 mREM) or an abdominal X-ray (250 mREM). The measurement of bone mineral using the DEXA 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.

If I am randomly assigned to one of the two dried plum consumption intervention groups, I may experience some gastrointestinal distress. This risk will be minimized by the investigators by instructing me to increase my water intake following dried plum consumption.

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 the enclosed questionnaires. I may choose not to complete the questionnaires and will still be able to participate in the study.

5. The possible benefits of my participation in this research project include learning about my bone mineral density, physical functionality, body composition, resting vital measures, waist and hip circumferences, and muscular strength levels. Participants in all groups have the potential to increase their bone mineral density. The potential benefits for the resistance exercise and the combination resistance exercise and dried plum consumption groups include improved physical functionality, quality of life, body composition, and muscular strength.

6. 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 each subject a code number and recording all data by code number. The only record with the subject's name and code number will be kept by the principal investigator, Emily Simonavice, in a locked office. Data will be kept for 10 years and then destroyed.

7. 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.

8. I will not be paid for my participation in this research project.

9. Any questions I have concerning this research study or any aspect of my participation, before or after my consent, will be answered by the investigators or they will refer me to a knowledgeable source. I understand that I may contact Emily Simonavice or via email at or Dr. Lynn Panton at for answers to questions about this research project or my rights. Group results will be sent to me upon my request.

10. 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.

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

12. 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.

_____ _____

(Subject) (Date)

APPENDIX D—Demographic/Medical Questionnaire

DEMOGRAPHIC INFORMATION

Home phone _____
Office phone _____

Emergency Information

Individual to be contacted in the event of an emergency:

Name: _____

Relationship to you: _____

Home phone_____

Office phone_____

Personal Information

Age _____ Date of birth _____/_____/_____
Month Day Year

Race ____ White
____ Black
____ Asian
____ Hispanic
____ Other: _____

Are you currently involved in an exercise program? N____ Y____ If yes, please describe (Include days/week, intensity, types of exercise)

_____

_____

MEDICAL HISTORY FORM

Primary oncologist: Name:_____

Address and City:_____

Phone:_____

Primary Care Physician: Name:_____

Address and City:_____

Phone:_____

Do you: **Smoke?** _____ **Packs per day** _____ **# Years smoked** _____

Drink Alcohol? _____ **Drinks per day** _____

List any allergies you have to drugs, food or other items:

_____

_____

List medications you are taking below:

Name of Drug	Dosage	Times/day	Duration of drug use
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____

Cancer History

- Diagnosis: _____
  _____
- Date of diagnoses:_____
- Types of TX: (surgery, radiation, chemotherapy, hormone therapy)
  _____
  _____
  _____
- Beginning and ending dates of each treatment:
  _____
  _____
  _____
  _____
- Menopausal Age: (Natural or Treatment induced) _____
- Additional Concerns/Information:
  _____
  _____
  _____

OTHER MEDICAL PROBLEMS: Indicate if you have had any of the following medical problems:

Past	Now	
____	____	Alcoholism
____	____	Anemia
____	____	Arthritis
____	____	Asthma
____	____	Back injury or problem
____	____	Blood clots
____	____	Bronchitis
____	____	Chest pain
____	____	Cirrhosis
____	____	Claudication
____	____	Diabetes
____	____	Elbow or shoulder problems
____	____	Emotional disorder
____	____	Eye problems
____	____	Gall bladder disease
____	____	Glaucoma
____	____	Gout
____	____	Headaches
____	____	Heart Attack
____	____	Heart Disease
____	____	Hemorrhoids
____	____	Hernia
____	____	Hip, knee, or ankle problems
____	____	Hypertension
____	____	Intestinal disorders
____	____	Kidney disease
____	____	Liver disease
____	____	Lung disease
____	____	Mental illness
____	____	Neck injury or problem
____	____	Neuralgic disorder
____	____	OB/GYN problems
____	____	Obesity/overweight
____	____	Osteoporosis
____	____	Parkinson's disease
____	____	Phlebitis
____	____	Prostate trouble
____	____	Rheumatic fever
____	____	Seizure disorder
____	____	Stomach disease
____	____	Stroke
____	____	Thyroid disease
____	____	Ulcers
____	____	Other - specify: _____

APPENDIX E—QUESTIONNAIRE PACKET

The SF-36 Health Survey

(Courtesy of Kaplan & Bush, 1982)

Instructions for Completing the Questionnaire

Please answer every question. Some questions may look like others, but each one is different. Please take the time to read and answer each question carefully by filling in the bubble that best represents your response.

1. In general, would you say your health is:

Excellent	Very good	Good	Fair	Poor
O	O	O	O	O

2. Compared to one year ago, how would you rate your health in general <u>now</u>?

Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than year ago	Much worse now than one year ago
O	O	O	O	O

3. The following items are about activities you might do during a typical day. Does your health <u>now</u> limit you in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited
a. Vigorous Activities: such as running, lifting heavy objects, participating in strenuous sports	O	O	O
b. Moderate Activities: such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	O	O	O
c. Lifting or carrying groceries	O	O	O
d. Climbing several flights of stairs	O	O	O
e. Climbing one flight of stairs	O	O	O
f. Bending, kneeling, or stooping	O	O	O
g. Walking more than a mile	O	O	O
h. Walking several blocks	O	O	O
i. Walking one block	O	O	O

j. Bathing or dressing yourself	O	O	O

4. 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?

	Yes	No
a. Cut down on the amount of time you spent on work or other activities	O	O
b. Accomplished less than you would like	O	O
c. Were limited in the kind of work or other activities	O	O
d. Had difficulty performing the work or other activities (for example, it took extra time)	O	O

5. 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)?

	Yes	No
a. Cut down on the amount of time you spent on work or other activities	O	O
b. Accomplished less than you would like	O	O
c. Didn't do work or other activities as carefully as usual	O	O

6. 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?

Not at all	Slightly	Moderately	Quite a bit	Extremely
O	O	O	O	O

7. How much bodily pain have you had during the past 4 weeks?

None	Very mild	Mild	Moderate	Severe	Very Severe
O	O	O	O	O	O

8. During the past 4 weeks, how much did <u>pain</u> interfere with your normal work (including both work outside the home and housework)?

Not at all	Slightly	Moderately	Quite a bit	Extremely
O	O	O	O	O

9. 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…

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
a. Did you feel full of pep?	O	O	O	O	O	O
b. Have you been a very nervous person?	O	O	O	O	O	O
c. Have you felt so down in the dumps nothing could cheer you up?	O	O	O	O	O	O
d. Have you felt calm and peaceful?	O	O	O	O	O	O
e. Did you have a lot of energy?	O	O	O	O	O	O
f. Have you felt downhearted and blue?	O	O	O	O	O	O
g. Did you feel worn out?	O	O	O	O	O	O
h. Have you been a happy person?	O	O	O	O	O	O
i. Did you feel tired?	O	O	O	O	O	O

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

All of the time	Most of the time	Some of the time	A little of the time	None of the time
O	O	O	O	O

11. How TRUE or FALSE is each of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a. I seem to get sick a little easier than other people	O	O	O	O	O
b. I am as healthy as anybody I know	O	O	O	O	O
c. I expect my health to get worse	O	O	O	O	O
d. My health is excellent	O	O	O	O	O

Physical Activity Assessment

Section I.

1. **Moderate physical activities** are of moderate intensity, such as fast walking 3-4 miles per hour. Which of the following moderate activities did you do for **at least 10 minutes at a time without stopping** during the last 7 days? (*Circle all that apply*)

▪ Walking fast (3-4 mph)	▪ Walking downstairs	▪ Aerobics (low impact)
▪ Bicycling (Less than 12 mph; <150W)	▪ Bowling	▪ Calisthenics (light)
▪ Carpentry	▪ Dancing	▪ Fishing (while standing)
▪ Gardening (planting, raking, weeding)	▪ Frisbee	▪ Golf
▪ Housework (mopping, sweeping, vacuuming)	▪ Gymnastics	▪ Horseback riding
▪ Lifting, turning, carrying less than 50 pounds	▪ Mowing lawn (power mower)	▪ Ping pong
▪ Playing with children (walking, kneeling, lifting)	▪ Rowing, Sailing	▪ Skateboarding
▪ Tai Chi, Qi gong	▪ Volleyball	▪ Yoga, vigorous stretching
▪ Water Aerobics	▪ Washing or working on car	▪ Weight lifting

2. During the last 7 days, on how many days did you do a moderate physical activity for **at least 10 minutes at a time** without stopping? _____ **days**

3. On those days that you did moderate physical activities, how much time did you spend **on average** doing the activities? _____**minutes per day**

Section II.

4. **Vigorous physical activities** are of more vigorous intensity, such as jogging or running. Which of the following vigorous activities did you do for **at least 10 minutes at a time without stopping** during the last 7 days? (*Circle all that apply*)

▪ Jogging, Running	▪ Walking upstairs	▪ Aerobics (high impact)
▪ Carrying loads more than 50 pounds	▪ Basketball	▪ Calisthenics (vigorous)
▪ Bicycling fast (more than 12mph; >150W)	▪ Judo, Karate, Kick Boxing	▪ Jumping rope
▪ Roller skating, roller blading	▪ Stair Climbing/Stairmaster	▪ Soccer
▪ Ski machine (Nordic Track)	▪ Swimming laps	▪ Tennis, Racquetball

5. During the last 7 days, on how many days did you do a vigorous physical activity for **at least 10 minutes at a time** without stopping? _____ **days**

6. On those days that you did vigorous physical activities, how much time did you spend **on average** doing the activities? _____ **minutes per day**

7. Compared to how physically active you have been over the last 3 months, how would you describe the last 7 days: (*Check one*)

_____**More active**
_____**Less active**
_____**About the same**

APPENDIX F—Pedometer Log

Week ____ Subject ID _____

Day One Date:_____

Time pedometer was put on: _____ Time pedometer was taken off:_____

Was the pedometer worn today if yes how many steps?_____

Was pedometer removed during the day (e.g. while swimming, showering)?How long___

What general activities did you do today?_____

Day Two Date_____

Time pedometer was put on: _____ Time pedometer was taken off:_____

Was the pedometer worn today if yes how many steps?_____

Was pedometer removed during the day (e.g. while swimming, showering)?How long___

What general activities did you do today?_____

Day Three Date_____

Time pedometer was put on: _____ Time pedometer was taken off:_____

Was the pedometer worn today if yes how many steps?_____

Was pedometer removed during the day (e.g. while swimming, showering)?How long___

What general activities did you do today?_____

Day Four Date_____

Time pedometer was put on: _____ Time pedometer was taken off:_____

Was the pedometer worn today if yes how many steps?_____

Was pedometer removed during the day (e.g. while swimming, showering)?How long___

What general activities did you do today?_____

Day Five Date_____

Time pedometer was put on: _____ Time pedometer was taken off:_____

Was the pedometer worn today if yes how many steps?_____

Was pedometer removed during the day (e.g. while swimming, showering)?How long___

What general activities did you do today?_____

Day Six Date _____

Time pedometer was put on: _____ Time pedometer was taken off:_____

Was the pedometer worn today if yes how many steps?_____

Was pedometer removed during the day (e.g. while swimming, showering)?How long___

What general activities did you do today?_____

Day Seven Date_____

Time pedometer was put on: _____ Time pedometer was taken off:_____

Was the pedometer worn today if yes how many steps?_____

Was pedometer removed during the day (e.g. while swimming, showering)?How long___

What general activities did you do today?_____

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BIOGRAPHICAL SKETCH

Emily Meghan Simonavice is a native of Liberty, Kentucky. Emily received both her Bachelor of Science degree in Exercise Science and her Master of Science in Exercise & Leisure Studies from Murray State University (Murray, Kentucky). After completion of her Master of Science degree, she gained employment at the Exercise & Cancer Recovery (ECR) establishment at Murray State University, serving as the Exercise Coordinator. She is now pursuing a Doctorate of Philosophy degree in Movement Science, with a concentration in Exercise Physiology, at Florida State University in Tallahassee, FL. Emily served as a Graduate Teaching/Research Assistant while completing her graduate degrees, and was awarded the Legacy Fellowship, several scholarships, and honors throughout her academic career. She will receive her Doctor of Philosophy degree in December, 2011.