*Original article (short paper)*

# Exercise training improves mean arterial pressure in breast cancer survivors

Robert C. Mills
*University of North Carolina, Chapel Hill, USA*

Marcelo G. B. Nascimento
*University Center of Brasilia, Brazil*

Gislane F. de Melo
*Catholic University of Brasilia, Brazil*

Anthony C. Hackney
Claudio L. Battaglini
*University of North Carolina, Chapel Hill, USA*

**Abstract**—Currently, many breast cancer survivors worldwide live with treatment-related side effects, including cardiovascular health problems. This study examined effects of a 5-month exercise intervention on non-invasive markers of cardiovascular health in breast cancer survivors. Relationships between these markers and commonly used markers of overall health were also explored. Fifty-two survivors completed the exercise training at a rehabilitation center at the University of North Carolina at Chapel Hill between 2008-2011. A combined aerobic and resistance exercise intervention (3 times/week for 1h) at intensities progressing from low (40%) to moderate (65-70% of $VO_{2max}$) for aerobic and 8-12 repetitions max for the resistance exercise were implemented. Significant reduction in mean arterial pressure (MAP) was observed from baseline to final assessment. A significant correlation was found between MAP and Body Mass Index (BMI). In conclusion, 5-months combined aerobic and resistance exercise intervention positively improved MAP which was, in part, attributed to changes in BMI.

Keywords: exercise, breast cancer survivors, mean arterial pressure

**Resumo**—"O exercício físico melhora a pressão arterial média em sobreviventes de câncer de mama."Atualmente, muitos sobreviventes de câncer de mama em todo o mundo vivem com os efeitos secundários relacionados com o tratamento, incluindo problemas de saúde cardiovascular. Este estudo examinou os efeitos de uma intervenção de exercício de 5 meses com marcadores não-invasivos de saúde cardiovascular em sobreviventes de câncer de mama. As relações entre esses marcadores e os marcadores mais utilizados de saúde em geral também foram exploradas. Cinquenta e duas sobreviventes completaram o treinamento em um centro de reabilitação da Universidade da Carolina do Norte em Chapel Hill entre 2008-2011. Foram implementadas intervenção combinando exercício aeróbio e resistido (3 vezes / semana durante 1h) em intensidades progredindo de baixo (40%) a moderada (65-70% do $VO_{2max}$) para exercícios aeróbios, e 8-12 repetições máxima para o exercício de resistência. Redução significativa da pressão arterial média (PAM) foi observada a partir da linha de base para avaliação final. Foi encontrada uma correlação significativa entre o MAPA e Índice de Massa Corporal (IMC). Em conclusão, 5 meses de intervenção com exercícios combinados de resistência e aeróbio melhorou positivamente o MAP, que foi, em parte, atribuída a mudanças no IMC.

Palavras-chave: exercício, sobreviventes de câncer de mama, pressão arterial média

**Resumen**—"El ejercicio físico mejora la presión arterial media en los sobrevivientes de cáncer de mama."Actualmente, muchos de los sobrevivientes de cáncer de mama en todo el mundo viven con los efectos secundarios relacionados con el tratamiento, incluyendo problemas de salud cardiovascular. Este estudio examinó los efectos de una intervención de ejercicio durante cinco meses con marcadores no invasivos de la salud cardiovascular en sobrevivientes de cáncer de seno. También se exploraron las relaciones entre estos marcadores y los marcadores más utilizados de la salud general. Cincuenta y dos sobrevivientes completaron la formación en un centro de rehabilitación en la Universidad de Carolina del Norte en Chapel Hill de 2008 a 2011. Intervención se implementara la combinación de ejercicio aeróbico y de resistencia (3 veces / semana durante 1 h) a intensidades que van de la baja (40%) o moderada (65-70% $VO_{2max}$) para el ejercicio aeróbico, y 8-12 repeticiones máximas para el ejercicio de resistencia. Se observó una reducción significativa de la presión arterial media (MAP) desde el inicio hasta la evaluación final. Se encontró una correlación significativa entre el MAPA y el Índice de Masa Corporal (IMC). En conclusión, a cinco meses de intervención con ejercicio aeróbico y de resistencia combinado mejoraron positivamente el MAP, que se atribuye en parte a los cambios en el IMC.

Palabras clave: ejercicio, sobrevivientes de cáncer de mama, presión arterial media

## Introduction

Breast cancer is the most common cancer in women with an estimated 1.67 million new cases diagnosed in 2012 worldwide (IRAC, 2014). Today in the United States alone, there are more than 2.9 million breast cancer survivors (ACS, 2012). Due to early diagnosis and treatment improvements many more women are surviving longer than ever before. In addition, there have been advancements in modern technology, greater education, and a higher awareness of the importance of self-examination that have contributed to the increased survival rate of cancer patients. However, this means that an increasingly substantial number of women will be living with a multitude of cancer treatment-related side effects that can significantly reduce the quality of life in breast cancer survivors (Battaglini *et al.*, 2006).

The medical community has long used exercise as an intervention to address different health problems associated with chronic disease. Among many problems breast cancer survivors face during and after completion of cancer treatments are issues associated with cardiovascular health (Yeh & Bickford, 2009; Chen *et al.*, 2011). Regrettably, this is becoming increasingly more common. Abnormal lipid profiles and reduced cardiovascular efficiency are undesirable effects of cancer treatments that can influence disease prognosis and reduce the ability of survivors to perform simple tasks of daily living (Schmitz *et al.*, 2010). Cardiovascular-related problems may not appear until 10-15 years later, indicating that ongoing monitoring is essential as well as a need to attempt reduction of these treatment-related side effects (Jones, Stoner, Brown, Baldi, & McLaren, 2013).

Previous studies have shown that exercise can improve many physiological, psychological, and functional parameters including overall cardiovascular function in breast cancer survivors (Schmitz *et al.*, 2010). Such improvements in cardiovascular function have been associated with reduction in fatigue (Dimeo *et al.*, 1997), positive changes in body composition (Klika, Callahan, & Drum, 2009), and positive changes in overall quality of life (Courneya *et al.*, 2003).

Interestingly, non-invasive and relatively simple measurements of markers associated with cardiovascular efficiency/health such as resting heart rate (RHR) and resting blood pressure (RBP) have not been extensively reported in the research literature. Furthermore, associations between these non-invasive and simple markers of cardiovascular efficiency/health and more commonly reported measurements of overall health such as percent body fat (%BF), body mass index (BMI), and maximal oxygen uptake ($VO_{2max}$) may assist clinicians to monitor the patients' recovery from the negative health alterations associated with anti-cancer treatments to better health.

Therefore, the primary purpose of this study was to examine the effect of a 5-month exercise intervention on non-invasive markers of cardiovascular health (RHR and RBP) in breast cancer survivors. A secondary purpose was to explore the relationship between non-invasive markers of cardiovascular health and more commonly used markers of overall health (Percent Body Fat, BMI, estimated $VO_{2max}$).

## Methods

This retrospective study used data gathered from breast cancer survivors who participated in a randomized, controlled trial within a rehabilitation program at the University of North Carolina at Chapel Hill between the years 2008 to 2011. Participants were randomly assigned into a combined exercise and recreation therapy group (EXRT), an exercise only group (EX), a recreation therapy only group (RT), or to a no intervention control group (CO). For the purpose of this study, only the EXRT, EX, and CO groups (n = 52) were used in the statistical analyses. The reason these three groups were selected to make up the sample for this retrospective study was because all of the patients in these three groups participated in the standardized exercise intervention; The EX group underwent a 5-months exercise intervention only, the EXRT group underwent the same standardized intervention for five months and also participated in recreation therapy activities such as arts and crafts, received education on some stress management techniques, and engaged in non-physical leisure activities of their interest for 20-30 minutes 3 times per week. After evaluating all the physical fitness parameters between the EX and EXRT at the completion of the randomized controlled trial, no difference in changes were observed for any fitness parameters from baseline to completion of the intervention between the EX and EXRT group. As part of the randomized trial cancer rehabilitation program, the control group did not participate in the exercise program only during the initial 2-months of the randomized study. After the 2 initial months of the randomized trial was completed, the control group began to participate in the 5-months standardized exercise intervention. During the 5-months exercise intervention, MAP of the patients in the control group were assessed at the same time intervals as the patients who participated in the EX and EXRT groups.

Participation in the breast cancer rehabilitation program was completely voluntary, and participants consisted of breast cancer survivors (stages 0-III) between the ages of 34 and 71 years, who were within six months post-completion of their major cancer treatments (surgery, radiation, chemotherapy, or any combination of these). Some, but not all, participants were undergoing hormonal therapy throughout the duration of the 5-month study. Since the program inception in 2006, where the intervention lasted 6-months, a program evaluation of its efficacy showed similar benefits when patients underwent the intervention for 5 or 6 months. Because the program facility could only hold a certain number of patients, and to allow for a larger number of patients to participate in the breast cancer rehabilitation program, from 2008 to 2011, all patients underwent a 5-months intervention.

Before participating in the rehabilitation program, a signed informed consent form approved by the Lineberger Comprehensive Cancer Center Protocol Review Committee (LCCC PRC#: 0607) and the University Institutional Review Board (IRB #: 05-2785) as well as oncologist clearance was obtained from each participant. Following this, participants were then asked to complete a medical history questionnaire and the Physical Readiness Questionnaire (PAR-Q) to confirm their eligibility to participate in the program.

### *Assessments*

Prior to undergoing the exercise intervention, all participants in the EXRT, EX, and CO groups completed a baseline battery of assessments. These assessments were repeated again after the first 8-weeks of exercise training (mid-assessment – at the end of 8-weeks), and a third time at the completion of the 5-month intervention period (final assessment – assessment performed within a maximum of 1-week after the completion of the 5-months exercise intervention). Prior to participating in the study assessments, participants were instructed to adhere strictly to the following guidelines: 1) No eating 4 hours prior to reporting to the program for testing; 2) to void completely prior to testing; 3) maintenance of proper hydration prior to testing; 4) no caffeine consumption at least 2 hours prior to testing; 5) no alcohol consumption 48 hours prior to testing; and 6) to wear appropriate clothing for exercise testing.

When participants arrived for their assessments, resting vital signs including heart rate and blood pressure were recorded following a five-minute, quiet, seated rest period using a Pacer Polar heart rate monitor (Lake Success, NY) for heart rate and a Diagnostix 700 aneroid sphygmomanometer (Hauppauge, NY) and Litmann stethoscope (St. Paul, MN) for blood pressure. If blood pressure was over 150/100 participants were asked to continue to rest another 5 minutes and another measurement was taken to confirm the previous results. Once resting heart rate and blood pressures were evaluated, then height, weight, and body composition were assessed. Height and weight were taken using a balance beam physician scale with a height rod (Health-o-meter 402KL Rye, NY) and were used for the calculation of BMI. Since mean arterial pressure encompasses both systolic and diastolic pressures, mean arterial pressure (MAP) was used in this study to represent resting blood pressure. Mean arterial pressure was calculated using the following equation: 1/3(systolic pressure – diastolic pressure) + diastolic pressure.

Body composition was then assessed using ∑ 3 sites skinfold thickness technique with Lange C-130 Beta Technology calipers (Cambridge, MD). Skinfold thickness was assessed to the nearest 0.1 mm at three sites (Triceps, suprailiac, and abdomen), as described in the Anthropometric Standardization Manual (Heyward, 1998). To enhance the consistency of the measurements, all skinfolds were performed by the same research team member who was an experienced body composition technician. The results of two measurements that were within ± 1 mm of each other were used for the estimation of %BF using the ∑ 3 SKF population-specific equations proposed by Jackson and Pollock (Jackson & Pollock, 1985).

Following the body composition assessment, a cardiovascular endurance assessment was conducted using the modified Bruce submaximal treadmill protocol for the estimation of $VO_{2max}$ using a calibrated Quinton Q65 treadmill, Fitness Equipment (Bothell, WA) (Heyward, 2006). If a participant could not perform the treadmill test, the standardized YMCA cycle ergometer submaximal protocol was used to estimate $VO_{2max}$ (Tosti, Hackney, Battaglini, Evans, & Groff, 2011). The Modified Bruce protocol is a widely used test for the assessment of cardiovascular function in clinical populations. The criteria for test termination included: 1) When participants reached 75% of their estimated maximum heart rate calculated using the Karvonen formula, 2) Rate of Perceived Exertion (RPE) reached 15 on the Borg scale, or 3) the participant requested to terminate the test before these previously mentioned criteria were reached. Once the cardiovascular endurance test was concluded, participants completed a short cool down and stretched (5-10 minutes) while the estimated $VO_{2max}$ was calculated and recorded (ACSM, 2009).

### *Exercise intervention*

The exercise intervention consisted of individualized, prescriptive exercise training 3 times per week for 5-months in accordance with the guidelines set forth by the American College of Sports Medicine (ACSM, 2009). Participants exercised under the supervision of an exercise specialist. Each exercise session lasted approximately 60 minutes and was composed of 10-20 minutes cardiovascular exercise on a treadmill, cycle ergometer, or elliptical machine, followed by 20-30 minutes of resistance training and a 10-minute flexibility and cool-down period. All participants performed aerobic exercises with intensities varying between 40%-65% of estimated $VO_{2max}$. Depending on the physical state of participants prior to each exercise session, the intensity and volume of training was modified to accommodate each participant's needs.

For the resistance component of the exercise session, 8-12 different types of resistance exercises that use all major muscle groups were utilized. All exercises were performed using weight machines, free weights (hand dumbbells), elastic bands, or therapeutic balls (fit balls). For the development of a training effect, the increases in load during the study followed the ACSM guidelines for resistance exercise training methods (ACSM, 2009). Each exercise consisted of 1-3 sets of 8-12 repetitions max at an RPE between 3 and 7 on the Modified Borg Scale, with 30-60 seconds of rest in between subsequent exercises. When participants were able to perform 12 repetitions with a reported RPE of 3, the load was increased to create a training effect. During the first two weeks of the program, all participants performed only one set of each exercise and then progressed to 2 and 3 sets for the subsequent weeks. The movements for each exercise were performed at a moderate speed (three seconds of the concentric phase and three seconds of the eccentric phase of the movement during each repetition for each exercise).

### Statistical analyses

Repeated-measures ANOVAs were used to assess changes in RHR and MAP at baseline (prior to begin exercise intervention), mid program (week 8), and at the completion of the 5-month intervention (final assessment). If a significant effect was observed, *post hoc* analyses using paired sample *t*-tests were employed to identify the time points at which RHR or MAP were statistically different. Simple regression analyses on delta scores were used to assess the relationship between changes in RHR and %BF, BMI, $VO_{2max}$ as well as the relationship between MAP and %BF, BMI, estimated $VO_{2max}$. All data was analyzed using SPSS 19.0 with an alpha-level set *a priori* at $p \leq .05$.

## Results

All participants had completed their major cancer treatments prior to enrolling in the rehabilitation program. The participant' treatment characteristics are presented in Table 1.

Participant characteristics as well as the mean and standard deviations for all parameters evaluated at baseline, mid assessment, and final assessment at the end of the intervention are presented in Table 2.

There was no significant difference in RHR throughout each of the assessment time periods (baseline, mid-assessment, and final assessment) ($p = .090$). There was, however, a significant reduction in MAP from baseline to mid-assessment ($p = .001$) as well as from baseline to final assessment ($p = .001$), but no significant difference in MAP between the mid and final assessments ($p = .897$).

No significant regression relationship was found between RHR and %BF, BMI, or $VO_{2max}$ ($p = .147$, $p = .364$, and $p = .207$, respectively). Also, no significant relationship was found between MAP and %BF or $VO_{2max}$ ($p = .790$ and $p = .667$, respectively). A significant relationship was however observed between MAP and BMI ($R^2 = .085$, $p = .036$) indicating that 8.5% of the changes in MAP were accounted for by changes in BMI.

Table 1. Treatment characteristics of participants enrolled in this study ($n = 52$).

| Treatment | Number of Participants | Percent of Sample |
|---|---|---|
| Chemotherapy, Radiation, and Adjunctive Therapy | 28 | 54% |
| Chemotherapy and Adjunctive Therapy | 2 | 4% |
| Chemotherapy and Radiation | 9 | 17% |
| Radiation and Adjunctive Therapy | 6 | 11% |
| Chemotherapy Only | 2 | 4% |
| Radiation Only | 0 | 0% |
| Adjunctive Therapy Only | 3 | 6% |
| No Treatment (Surgery Only) | 2 | 4% |

*Out of the sample of 52 patients, 24 underwent anthracycline type of chemotherapy (46% of the sample in the study).*

Table 2. Participant's characteristics and mean ± standard deviations of all parameters evaluated in the study ($n$=52).

| | Baseline (Mean ± SD) | Mid (Mean ± SD) | Final (Mean ± SD) |
|---|---|---|---|
| Age (yrs) | 52.3 ± 9.9 | N/A | N/A |
| Height (cm) | 164.8 ± 6.8 | N/A | N/A |
| Weight (kg) | $75.4 \pm 15.4^{*}$ | 75.6 ± 15.2 | $76.1 \pm 15.5^{*}$ |
| Systolic Blood Pressure (mmHg) | $119 \pm 15^{*+}$ | $114 \pm 15^{*\wedge}$ | $113 \pm 14^{+\wedge}$ |
| Diastolic Blood Pressure (mmHg) | $77 \pm 9^{*+}$ | $73 \pm 10^{*}$ | $73 \pm 9^{+}$ |
| Mean Arterial Pressure (mmHg) | $91 \pm 10^{*+}$ | $86 \pm 11^{*}$ | $86 \pm 10^{+}$ |
| Resting Heart Rate (bpm) | 77 ± 12 | 74 ± 11 | 74 ± 9 |
| Percent Body Fat (%BF) | $29.8 \pm 5.9^{+}$ | $29.0 \pm 5.0^{*}$ | $28.0 \pm 4.6^{*+}$ |
| Percent Fat Free Mass (%FFM) | $70.1 \pm 5.9^{+}$ | $70.9 \pm 5.0^{*}$ | $71.9 \pm 4.6^{*+}$ |
| Body Mass Index (BMI) | $27.7 \pm 5.7^{*}$ | 27.8 ± 5.7 | $28.0 \pm 5.7^{*}$ |
| $VO_{2max}$ (ml/kg/min) | $30.7 \pm 7.2^{*+}$ | $33.5 \pm 7.2^{*\wedge}$ | $36.3 \pm 6.7^{+\wedge}$ |

$^{*}p < .05$; $^{+}p < .05$; $^{\wedge}p < .05$

## Discussion

The purpose of this study was to examine the effect of a 5-month exercise intervention on non-invasive markers of cardiovascular health (Resting Heart Rate and Resting Blood Pressure) in breast cancer survivors. A secondary purpose was to explore the relationship between non-invasive markers of cardiovascular health and commonly used markers of overall health (%BF, BMI, estimated $VO_{2max}$).

In breast cancer patients, certain drugs (i.e., Antracycline-containing chemotherapy) have the potential to directly impact the cardiovascular system, a condition known as cardiotoxicity. Doxorubicin, an Antracycline-containing chemotherapy, is one type of anti-cancer drug, that depending on the dose administered, can progressively impact the heart by diminishing left ventricle ejection fraction and continued damage can even lead to heart failure. This potential problem can manifest acutely (after just a few bouts of chemotherapy and/or radiation therapy) or later on, months or even years post completion of cancer treatments (Jones *et al.*, 2013). Radiation treatments can also play a role in augmenting the negative effects on the cardiovascular system. Due to the potential impact that certain chemotherapeutic agents as well as radiation treatments can have on the cardiovascular system, the development of cardiomyopathies, including electromyography (EKG) abnormalities for example, are of great concern. To our knowledge, no study to date has looked into the exercise induced training adaptations of RHR as a potential marker of cardiovascular health, or most importantly, as a non-invasive, simple to measure, marker of cardiovascular function in breast cancer patients.

The results of the assessment of RHR throughout the intervention showed no significant changes in RHR from baseline to the completion of the exercise training intervention, even though there was a trend towards reduced RHR. The non-significant findings could probably be attributed to the already normal RHR ranges observed in more than half of all patients included in the analyses, but most likely due to the nature of the intensity used in the exercise training program, which ranged from low-to-moderate. It is possible that the exercise training was not conducted at a high enough intensity to induce meaningful cardiovascular adaptations associated with reduced RHR. Further, in a breast cancer population, 20 weeks of exercise training may not be sufficient enough to elicit physiological adaptations in RHR, which could be a potential explanation for the downwards trend in RHR, but a non-significant reduction. This is supported by the current literature in exercise oncology that describes only modest improvements in overall cardiovascular endurance after weeks of exercise training performed at moderate intensity (Courneya *et al.*, 2007; Jones *et al.*, 2011; Kim, Kang, Smith, & Landers, 2006; McNeely *et al.*, 2006).

In this study, %BF decreased between each assessment; from 29.84% at baseline to 29.07% at mid assessment, and finally to 28.02% at final assessment, which is consistent with the current literature (Herrero *et al.*, 2006; Battaglini *et al.*, 2007; Courneya *et al.*, 2007). If %BF in breast cancer patients can be maintained or slightly reduced with exercise training, this can be seen as a tremendous improvement from the normal trend of increasing %BF during and after cancer treatment (Battaglini *et al.*, 2007). Even though the nature of the current exercise program was not specifically designed for weight loss or reduction of %BF the low to moderate intensity exercise stimulus proved to be enough to promote loss of %BF.

Interestingly, BMI of participants in this study ended up increasing slightly from values obtained at baseline--from 27.78 kg/m$^2$ at baseline to 27.86 kg/m$^2$ at mid assessment, and finally to 28.06 kg/m$^2$ at final assessment. This slight increase in BMI is probably due to the increase in percent fat free mass (%FFM) the participants were gaining as a result of the resistance exercise training they were undergoing in the exercise intervention. Exploratory analyses showed that %FFB significantly increased from mid (70.9 ± 5.0) to final (71.9 ± 4.6, $p$ = .037) and from baseline (70.1 ± 5.9) to final assessment (71.9 ± 4.6, $p$ = .007), explaining the slight increase in BMI.

Changes in body composition in breast cancer survivors have controversial findings throughout the literature. Most studies have found no significant changes in weight following an exercise program, although body composition frequently improves (Herrero *et al.*, 2006; Battaglini *et al.*, 2007; Courneya *et al.*, 2007; Rogers *et al.*, 2009). Mixed results from studies observing changes in BMI are due to the many factors that can influence these findings. Factors such as the type of intervention, the short time period of certain studies, the lack of controlled diets along with the exercise program, and metabolic issues may all have an impact on the BMI changes found in different studies (Pinto, Frierson, Rabin, Trunzo, & Marcus, 2005; Daley *et al.*, 2007; De Backer *et al.*, 2008). Even the type of patients enrolled in the exercise program can influence different BMI changes across different programs and studies. Patients who undergo changes in increased %FFM may not experience significant changes in BMI due to the increased weight in the gain of muscle. This change might be of importance in maintaining a healthy weight in breast cancer patients and therefore, reducing the likelihood for the development of other co-morbidities associated with unhealthy weight as well as a possible cancer recurrence.

In this study, estimated $VO_{2max}$ increased between each assessment. Because $VO_{2max}$ was predicted using a submaximal aerobic protocol, it is possible that the increases in estimated $VO_{2max}$ from baseline to mid-program could be due to nervousness as a result of a lack of familiarization with the protocol at the baseline assessment. It is, therefore, recommended in future experiments that, instead of using one measurement at baseline, several measurements should be taken throughout the initial week. However, the 3 ml/kg/min increase from mid assessment to final assessment is consistent with findings reported in the literature (Kim *et al.*, 2006; Courneya *et al.*, 2007; Jones *et al.*, 2011).

The sharp decrease in RBP was somewhat unexpected, as most of the participants were already within the normal range at the beginning of the program. One possibility that should be mentioned in explaining the reduction in RBP from baseline to mid assessment could be the fact that participants were under the initial stress of participating in a battery of fitness assessments that they may have never participated in. Nevertheless, since RBP was represented in this study as mean arterial pressure (MAP), a reduction of 4 mmHg in MAP is clinically significant and could be attributed to the initial weeks of exercise training. The significant reduction in MAP during the initial 8-weeks of exercise training may have been enough to positively impact some of the negative alterations in both the physiology and psychology of these participants, thus potentially translating in a better overall cardiovascular response. However, more studies are needed to confirm or refute this possibility as well as to evaluate potential mechanisms influencing this response in this population.

The reduction in MAP observed in this study can also be in part explained by changes in BMI. The results of exploratory analyses revealed that even with the slight increase in BMI at the end of the study, BMI was significantly correlated to MAP. Changes in BMI accounted for 8.5% of the change in MAP. Mean arterial pressure could have also be influenced by the decrease in %BF along with the increase in %FFM, which explained the slight increase found in BMI at the end of the study. Participant muscle mass in kilograms increased from baseline (77.8 kg) to final assessment (78.7 kg). The increase in %FFM of (~1 kg) from baseline to the end of the exercise intervention confirms the efficacy of the exercise intervention and assists in part to explain the reduction in MAP. The reduction in MAP might be explained by the metabolic active nature of lean tissue. Metabolically active tissue can result in an increase in muscle capillary density that may help reduce total peripheral resistance, which may impact overall reduction in resting blood pressure (Brooks, Fahey, & Baldwin, 2005). This is speculation on our part. Future studies can help elucidate the benefits of exercise on cardiovascular health of breast cancer survivors by examining the effects of exercise on endothelium cells of the vasculature using non-invasive techniques such as flow-mediated dilation (FMD), which is considered the "gold standard" for assessing endothelial function (Jones *et al.*, 2013). In order to maintain a healthy body mass and to promote lean weight, the cardiovascular system plays a fundamental role in delivering $O_2$ and nutrients to the tissues, and in the removal of metabolic waste products from the body. This cycle promotes healthier vessel compliance and therefore less stress and lower systemic pressure (Powers & Howley, 2009). It is important to keep in mind that over 90% of the changes observed in MAP in the participants are attributed to other variables. BMI is a measurement that accounts for weight, while %BF is not a metabolic measurement and does not consider weight in its calculation. Therefore, the body weight component of metabolic tissue must be a key factor in the significant correlation between BMI and MAP.

Recent studies have been able to show positive changes in cardiovascular markers due to combined exercise and controlled diet interventions. Improvements in cardiovascular fitness including reductions on RHR and RBP, optimal decreases in %BF, and increases in estimated $VO_{2max}$ have been found as a result of these interventions that were approximately 24 weeks long. Although these studies are related, they are not applicable to the current study, since dietary interventions have been shown to influence RBP (Campbell *et al.*, 2012; Scott *et al.*, 2013).

The present study exhibits some limitations. Although no other studies have looked at simple markers, such as RHR and RBP, that can be good measurements of cardiovascular improvements in breast cancer patients, the measurement of RHR is variable and can fluctuate widely and easily based on diet, sleep, and other daily routines. Nevertheless, in this study, potential confounders that could interfere with the accuracy of the RHR measurement were carefully considered, and the procedure of obtaining accurate measurements followed recommended guidelines. The inclusion of pre-assessment guidelines to maximize reproducibly of the measurement throughout the study was implemented to ensure maximum reproducibility between measurements. Also, the majority of the breast cancer patients involved in this program was still undergoing hormonal therapy, which is possibly the leading factor in why greater decreases in %BF were not observed. Therefore, future experiments in breast cancer survivors should examine the effects of a longer and perhaps more specific exercise intervention designed to promote %BF loss.

## Conclusion

Given the observed results of the study, it can be speculated that participant percent %FFM was the only parameter that had an influence on systemic blood pressure of the breast cancer survivors. Many breast cancer survivors are considered overweight as a result of treatment, and this excess weight is usually fat mass. It is also known that reduction in overall body mass is not easily attained while patients are undergoing hormonal therapies for protection against a potential cancer recurrence. Furthermore, the impact of some types of cancer treatment on the cardiovascular system appears to be more prominent than others, decreasing the functionality and overall health of the cardiovascular system of breast cancer survivors. In conclusion, a 5-months exercise program including aerobic and resistant modes of exercise reduces MAP in breast cancer survivors and changes in body composition (ê in %BF and é % FFM) appear to play a role in reducing MAP in breast cancer survivors. Future research needs to focus on implementing interventions that promote lean body mass along with reducing unhealthy weight in order to achieve a healthier cardiovascular system.

## References

American Cancer Society (2012). Breast cancer facts and figures, 2012. Atlanta, GA: American Cancer Society Publications. Available from *American Cancer Society*, http://www.cancer.org. Web site: http://www.cancer.org/downloads/STT/BCFF-Final.pdf. Accessed in 2012 (Aug 20).

American College of Sports Medicine (2009). ACSM's guidelines for exercise testing and prescription. 8th ed. Philadelphia, PA: Lippincott Williams and Wilkins.

Battaglini, C.L., Bottaro, M., Dennehy, C., Barfoot, D., Shields, E., Kirk, D., & Hackney, A.C. (2006). The effects of resistance training on muscular strength and fatigue levels in breast cancer patients. *Revista Brasileira de Medicina do Esporte*, *12*, 139e-144e.

Battaglini, C.L., Bottaro, M., Dennehy, C., Rae, L., Shields, E., Kirk, D., & Hackney, A. (2007). The effects of an individualized exercise intervention on body composition in breast cancer patients undergoing treatment. *Sao Paulo Medical Journal*, *125*, 22-28.

Brooks, G.A., Fahey, T.D., & Baldwin, K.M. (2005). *Exercise Physiology: Human Bioenergetics and its Applications* (Fourth ed.). Boston: McGraw Hill.

Campbell, K.L., Van Patten, C.L., Neil, S.E., Kirkham, A.A., Gotay, C.C., Gelmon, K.A., & McKenzie, D.C. (2012). Feasibility of a lifestyle intervention on body weight and serum biomarkers in breast cancer survivors with overweight and obesity. *Journal of the Academy of Nutrition and Dietetics*, *112*, 559-567.

Chen, T., Xu, T., Li, Y., Liang, C., Chen, J., Lu, Y., …Wu, S. (2011). Risk of cardiac dysfunction with trastuzumab in breast cancer patients: A meta-analysis. *Cancer Treatment Reviews*, *37*, 312-320.

Courneya, K.S., Friedenreich, C.M., Quinney, H.A., Fields, A.L., Jones, L.W., & Fairey, A.S. (2003). A randomized trial of exercise and quality of life in colorectal cancer survivors. *European Journal of Cancer Care*, *12*, 347-357.

Courneya, K.S., Segal, R.J., Mackey, J.R., Gelmon, K., Reid, R.D., Friedenreich, C.M., …McKenzie, D.C. (2007). Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: A multicenter randomized controlled trial. *Journal of Clinical Oncology*, *25*, 4396-4404.

Daley, A.J., Crank, H., Saxton, J.M., Mutrie, N., Coleman, R., & Roalfe, A. (2007). Randomized trial of exercise therapy in women treated for breast cancer. *Journal of Clinical Oncology*, *25*, 1713-1721.

De Backer, I.C., Vreugdenhil, G., Nijziel, M.R., Kester, A.D., van Breda, E., & Schep, G. (2008). Long-term follow-up after cancer rehabilitation using high-intensity resistance training: Persistent improvement of physical performance and quality of life. *British Journal of Cancer*, *99*, 30-36.

Dimeo, F.C., Tilmann, M., Bertz, H., Kanz, L., Mertersmann, R., & Keul, J. (1997). Aerobic exercise in the rehabilitation of cancer patients after high dose chemotherapy and autologous peripheral stem cell transplantation. *Cancer*, *79*, 1717-1722.

Herrero, F., San Juan, A.F., Fleck, S.J., Balmer, J., Perez, M., Canete, S., …Lucia, A. (2006). Combined aerobic and resistance training in breast cancer survivors: A randomized, controlled pilot trial. *International Journal of Sports Medicine*, *27*, 573-580.

Heyward, V.H. (1998). Practical body composition assessment for children, adults, and older adults. *International Journal of Sports Nutrition*, *8*, 285-307.

Heyward, V.H. (2006). *Advanced fitness assessment and exercise prescription,* 5th ed. Champaign, IL: Human Kinetics.

International Agency for Research on Cancer (2014). Cancer Fact Sheets: GLOBOCAN, 2012. France: IRAC, 2014. Available from *International Agency on Cancer Research,* http://www.iarc.fr. Web site: http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx. Accessed in 2014 (Apr 20).

Jackson, A.S., & Pollock, M.L. (1985). Practical assessment of body composition. *Physician and Sports Medicine*, *13*, 76-90.

Jones, L.M., Stoner, L., Brown, C., Baldi, C., & McLaren, B. (2013). Cardiovascular disease among breast cancer survivors: the call for a clinical vascular health toolbox. *Breast Cancer Research and Treatment*, 142, 645-653.

Jones, L.W., Liang, Y., Pituskin, E.N., Battaglini, C.L., Scott, J.M., Hornsby, W.E., & Haykowsky, M. (2011). Effect of exercise training on peak oxygen consumption in patients with cancer: A meta-analysis. *The Oncologist*, *16*, 112-120.

Kim, C., Kang, D., Smith, B.A., & Landers, K.A. (2006). Cardiopulmonary responses and adherence to exercise in women newly diagnosed with breast cancer undergoing adjuvant therapy. *Cancer Nursing*, *29*, 156-165.

Klika, R.J., Callahan, K.E., & Drum, S.N. (2009). Individualized 12-week exercise training programs enhance aerobic capacity of cancer survivors. *The Physician and Sports Medicine*, *37*, 68-77.

McNeely, M.L., Campbell, K.L., Rowe, B.H., Klassen, T.P., Mackey, J.R., & Courneya, K.S. (2006). Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis. *Canadian Medical Association Journal*, *175*, 34-41.

Pinto, B.M., Frierson, G.M., Rabin, C., Trunzo, J.J., & Marcus, B.H. (2005). Home-based physical activity intervention for breast cancer patients. *Journal of Clinical Oncology*, *23*, 3577-3587.

Powers, S.K. & Howley, E.T. (2009). Exercise Physiology: theory and application to fitness and performance. 7th ed. New York, NY: McGraw-Hill.

Rogers, L.Q., Hopkins-Price, P., Vicari, S., Pamenter, R., Courneya, K.S., Markwell, S., …Lowy, M. (2009). A randomized trial to increase physical activity in breast cancer survivors. *Medicine and Science in Sports and Exercise*, *41*, 935-946.

Schmitz, K.H., Courneya, K.S., Matthews, C., Demark-Wahnefried, W., Galvao, D.A., Pinto, B.M., …Schwartz, A.L. (2010). American college of sports medicine roundtable on exercise guidelines for cancer survivors. *Medicine and Science in Sports and Exercise*, *42*, 1409-1426.

Scott, E., Daley, A.J., Doll, H., Woodroofe, N., Coleman, R.E., Mutrie, N., …Saxton, J.M. (2013). Effects of an exercise and hypocaloric healthy eating program on biomarkers associated with long-term prognosis after early-stage breast cancer: a randomized controlled trial. *Cancer Causes and Control*, *24*, 181-191.

Tosti, K.P., Hackney, A.C., Battaglini, C.L., Evans, E.S., & Groff, D. (2011). Exercise in patients with breast cancer and healthy controls: Energy substrate oxidation and blood lactate responses. *Integrative Cancer Therapies*, *10*, 6-15.

Yeh, E.T., & Bickford, C.L. (2009). Cardiovascular complications of cancer therapy: incidence, pathogenesis, diagnosis, and management. *Journal of the American College of Cardiology*, *53*, 2231-2247.

## Authors' note

Robert C. Mills is affiliated with the Department of Exercise and Sport Science, Exercise Oncology Research Laboratory, University of North Carolina at Chapel Hill, USA

Marcelo G. B. Nascimento is affiliated with University Center of Brasilia (UniCeub)

Gislane F. de Melo, PhD., is affiliated with the Catholic University of Brasilia, Brazil.

Anthony C. Hackney, Ph.D., DSc. is affiliated with the Department of Exercise and Sport Science, Exercise Oncology Research Laboratory, and Department of Nutrition, University of North Carolina at Chapel Hill, USA

Claudio L. Battaglini, Ph.D, is affiliated with the Department of Exercise and Sport Science, Exercise Oncology Research Laboratory, Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, USA

### *Corresponding author*

Claudio L. Battaglini
125 Fetzer Hall
CB# 8700
University of North Carolina
Chapel Hill, NC 27599, USA
Fax Number: 1-(919) 962-0489
Phone Number: 1-(919) 843-6045
Email: claudio@email.unc.edu

### *Acknowlegments*

The author(s) declare no potential conflicts of interest. This study was part of an undergraduate honors thesis. This study was presented as an abstract at the 2013 American College of Sports Medicine Southeast Chapter meeting in Greenville, South Carolina.

*Manuscript received on June 5, 2014*
*Manuscript accepted on July 17, 2014*