Assessing Changes in the Activity Levels of Breast Cancer Patients During Radiation Therapy

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Abstract

To our knowledge, this is the first study to assess changes in activity levels and sleep experienced by breast cancer patients during radiation therapy (RT) with continuous tracking. Activity varied between individuals, minimal changes occurred during and after treatment, and levels increased at completion. Because increased activity levels might improve outcomes, RT may be an opportune time to start implementing changes before survivorship.

Background: Radiation therapy (RT) is often delivered after lumpectomy for women with breast cancer. A common perceived side effect of RT is fatigue, yet its exact effect on activity levels and sleep is unknown. In this study we analyzed the change in activity levels and sleep using an activity tracking device before, during, and after RT for women with early stage breast cancer and ductal carcinoma in situ who underwent adjuvant RT. **Patients and Methods:** After institutional review board approval, activity levels were quantified before, during, and after RT with measurements of steps, miles walked, calories burned, and sleep metrics in 10 women fitted with activity trackers. All data were uploaded and tabulated on a secure database. Multivariable linear regressions were used to evaluate changes in these variables over time during the RT course. **Results:** Median step count was 5047 per day (range, 2741-15,508) and distance traveled was 1.6 miles per day (range, 0.9-5.3). Step count, distance, and calories decreased by an average of 54 steps per day, 0.02 miles per day, and 3 calories per day (median calories 1822; range, 1461-2712) during RT, respectively. These changes were statistically significant ($P < .001$), but not clinically relevant. There was no significant change in sleep (average 6.8 hours per night; range, 5.5-8.3). **Conclusion:** RT has a minimal effect on activity or sleep in women undergoing treatment for breast cancer. Activity levels varied greatly between patients in a population of women undergoing hypofractionated RT. Because increased activity levels correlate with improved outcomes, further studies evaluating attempts to increase physical activity during as well as after treatment with radiation are warranted.

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Introduction

Breast cancer remains the most common noncutaneous malignancy in women.[1] Breast conservation therapy with lumpectomy and adjuvant radiation therapy (RT) is commonly used as treatment for early stage breast cancer and ductal carcinoma in situ (DCIS). Side effects from treatment are minimal, with fatigue as one of the most common. Thus, it is generally believed that activity levels experienced by women decrease during treatment.[2] Decreased activity and exercise during RT and their effect on survivorship are concerning because increased activity levels after breast cancer treatment are associated with an improvement in survival.[3]

As little as 3 to 5 hours of walking per week can decrease a woman's risk of dying from breast cancer.[4] Additionally, an improvement in quality of life from exercise and increased activity levels is well known; an analysis of 14 studies has revealed that exercise significantly improves quality of life in breast cancer patients, including alleviating fatigue.[5]

Women who engage in aerobic as well as resistance exercise with weight training immediately after their breast cancer treatment

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experience significant health-related improvements,[6] and they experience these improvements more rapidly than women who wait to start exercising. Exercise programs that coincide with radiation treatment have also been shown to reduce fatigue, the most common perceived side effect treatment.[7]

The benefits of increased activity levels of breast cancer patients are encouraging, yet little is known about the quantitative effect of RT on patient energy and activity levels. To initiate potentially efficacious interventions, we need to quantify baseline changes during and after treatment. Personal activity tracking devices have recently been shown to provide an easy and more accurate method of measuring activity levels.[8] Multiple studies have shown their relative accuracy and reproducibility when measuring step counts and quantifying physical activity, along with high interdevice reliability when measuring steps, distance, energy expenditure, and sleep.[9] In this study we set out to quantitatively measure activity levels and sleep amount in patients before, during, and after RT for breast cancer using noninvasive activity tracking bracelets, worn by patients continuously.

Patients and Methods

As part of an institutional review board-approved pilot study, 10 women undergoing RT for early stage breast cancer after lumpectomy were fitted with activity trackers (Misfit Inc, Richardson, TX) on their wrist and instructed to wear them at all times, starting at the time of RT planning simulation and for a total of 10 weeks. Patients were not aware of their activity or sleep changes during the study to avoid any unwanted interactions or motivation to increase activity levels, and the trackers did not provide information to the study participants. Primary end points were activity levels quantified before, during, and after RT with measurements of steps, miles walked, and calories burned. Sleep was measured as total minutes asleep. The devices were worn approximately 2 weeks before the initiation of RT and removed approximately 4 weeks after completion of RT. The trial took place in the fall in Pittsburgh, Pennsylvania in an effort to avoid seasonal changes in sleep and activity. All data were uploaded and tabulated on a secure database (Koneksa Health Inc, New York, NY).

Inclusion Criteria

Women between the ages of 30 and 80 years who were diagnosed with DCIS or early stage (stage I), node-negative breast cancer suitable for hypofractionated RT were eligible for the clinical trial. Patients treated with chemotherapy or requiring RT to the regional lymph nodes were excluded. Patients requiring adjuvant hormonal therapy began this after completion of their RT course.

Patients must have had no physical impairment limiting exercise or mobility as deemed by the treating physician and able to walk 100 feet unaided. Patients with a history of cancer (excluding noncutaneous skin cancer) were excluded, as were patients with pregnancy, severe cardiac disease, uncontrolled hypertension, uncontrolled diabetes, bleeding disorders, and clinically active serious infection. Finally, all patients were required to have an Eastern Cooperative Oncology Group (ECOG) status of 0 to 1.

Radiation Therapy Details

All women received hypofractionated RT to a total dose of 42.56 Gy. The breast received an initial 16 fractions of 2.66 Gy to 42.56 Gy. A "boost" of 4 fractions at 2.5 Gy per fraction for a total dose of 10 Gy was given to the lumpectomy cavity plus a margin at the discretion of the treating physician. Patients were assessed for toxicity and examined by the treating physician at least once a week during treatment.

Activity Tracking Devices

Misfit Shine activity trackers were provided by Misfit Inc. The central device is constructed of aluminum, waterproof to 50 meters, and has an approximate 6-month battery life. The device contains a 3-axis accelerometer, which quantifies 3-dimensional movements and measures acceleration, movement frequency, patterns, intensity, and duration of movement. The Misfit Shine has been tested for accuracy, and approaches near 100% for step count accuracy, performing better than several similar tracking devices.[10] Participants were advised to wear the activity trackers at all times, as was confirmed during weekly treatment visits with the treating radiation oncologist. Data were uploaded via Bluetooth 4.0 to the Misfit Application during routine checkups and extracted to a secure central database at least every 30 days to minimize data loss. Devices were removed at first follow-up, 4 weeks after completion of RT. Anonymous data linked to a patient ID number was displayed graphically and available for physician review at a secure online Web site.

Activity levels were quantified before, during, and after RT with measurements of steps, miles walked, and calories burned. Calories were calculated within the Misfit application using patient height, weight, and activity metrics. Sleep metrics assessed were minutes asleep versus minutes awake and were captured on the basis of movement of the accelerometer. All final data were uploaded and tabulated on a secure database. Step counts, calories burned, miles walked, and hours slept were assessed only after completion of the study for each participant.

Statistical Analysis

Mean step counts were calculated for each subject in the time periods before, during, and after radiotherapy. Because the distribution of mean step counts across patients did not follow a normal distribution, median step count averages were reported. Multivariable linear regressions were used to evaluate changes in activity metrics and sleep over time during the RT course using Matlab (MathWorks Inc, Natick, MA).

Results

A total of 10 women participated in the study. Patient characteristics are listed in Table 1. All patients received their entire course of RT as planned, and 9 of 10 patients received a boost. No adverse events related to tracker usage occurred during the trial. Grade 1 skin erythema and Grade 1 fatigue were the most common side effects of RT. Confirmation of compliance was made by the treating radiation oncologist and all patients wore their trackers at all times. All devices recorded data points for the entirety of the trial period except for one patient's device, which did not include the final 20 days of the study. The patient's remaining data were included in the study calculations for comparison purposes.

There was no significant weight change in any participant throughout the study, with maximum weight change of $< 2\%$ and a mean change of 1%. Furthermore, weighing errors might have accounted for this small change.

Table 1 Patient Characteristics

Patient	Age, y	Diagnosis	Stage	Receptor Status	Surgery	KPS	Weight, Pounds	BMI
1	72	DCIS	TisN0M0	ER/PR$^+$	Lump	90%	181	33
2	60	IDC	T1cN0M0, IA	ER/PR$^+$, HER2/*neu*$^-$	Lump and SLN	90%	144	28
3	52	IDC	T2N0M0, IIA	ER/PR$^+$, HER2/*neu*$^-$	Lump and SLN	90%	156	26
4	62	IDC	T1miN0M0, IA	ER/PR$^-$	Lump	90%	267	41
5	79	IDC	T1cN0M0, IA	ER$^+$, PR$^-$, HER2/*neu*$^-$	Lump and SLN	90%	147	27
6	57	IDC	T1cN0M0, IA	ER$^+$, PR-, HER2/*neu*$^-$	Lump and SLN	90%	186	31
7	72	DCIS	TisN0M0	ER/PR$^+$	Lump	90%	162	27
8	74	DCIS	TisN0M0	ER/PR$^-$	Lump	90%	220	40
9	79	IDC	T1cNxM0, IA	ER/PR$^+$, HER2/*neu*$^-$	Lump	90%	155	30
10	73	DCIS	TisN0M0	ER/PR$^+$	Lump	90%	143	25

Abbreviations: BMI = body mass index; DCIS = ductal carcinoma in situ; ER = estrogen receptor; IDC = invasive ductal carcinoma; KPS = Karnofsky performance status; Lump = lumpectomy; PR = progesterone receptor; SLN = sentinel lymph node excision.

Activity Levels and Sleep Metrics

Step counts varied significantly between individuals (Figure 1A). The median values of each patient's average step count before, during, and after RT were 5820, 5085, and 5088 steps per day, respectively (overall range, 2507-15,329 steps per day). Median overall step count for all participants was 5047 steps per day. However, after accounting for daily and interpatient variance, it was found that overall step counts decreased by an average of 54 steps per day from baseline during treatment ($P < .001$; Figure 1A).

Mean calories expended per day for all participants were 1910.5 calories per day (range, 1524-2712 calories per day) and the median was 1822 calories per day (Figure 1B). Linear regression revealed that energy expenditure decreased by 3 calories per day throughout the study period ($P < .001$). Median miles walked for each participant before, during, and after RT were 1.9, 1.6, and 1.7 miles, respectively. Daily distance walked decreased by 0.02 miles per day after adjusting for each patient ($P < .001$). The most active study participant walked 5.3 miles per day, whereas the least active walked 0.8 miles per day.

Differences in step count, calories expended, and miles walked throughout the course of RT, although minimal, were statistically significant because of the large number of events. Average time spent asleep for each participant before, during, and after RT was 6.9, 6.7, and 6.6 hours per night (Figure 1C). Although overall sleep duration minimally decreased throughout treatment and afterward, this was not statistically significant. Sleep amount did not appear to correlate with activity levels, which increased at week 7 and beyond, whereas sleep seemed to decrease slightly by the end of RT and then rose by the end of the study.

Because of the large number of variables, statistically significant changes were seen between the start and completion of the study. Median of average changes per week for all variables were assessed for description purposes only, and are shown in Figure 2. Although minimal and clinically insignificant changes occurred throughout the study, the largest visualized changes appeared to occur around weeks 6 to 7. This was at the completion of RT. After dipping, average steps increased significantly by the final 2 weeks of the study (which is 2 weeks after completing RT) and surpassed initial step counts before RT. Time asleep was also lowest at this point. Changes in steps and hours of sleep were compared with ECOG fatigue toxicity and body mass index (BMI) in Table 2. Forty percent of patients increased their activity levels during treatment, whereas 2 patients (1 and 9) had large decreases in their step counts. Treatment-induced fatigue was related to changes in activity levels, although the numbers were small. Age, BMI, and sleep changes did not correlate with changes in step counts.

Discussion

This is one of the first studies to assess activity changes during RT using activity trackers. Because of a large number of data points in this study, the decrease of 54 steps per day did reach statistical significance. However, because step counts ranged from 2507 to 15,329 steps per day, this small change was not clinically relevant. Sleep changes were minimal throughout the study and not significant. Several patients largely increased their activity levels during RT and in the last week of the study, activity levels increased significantly. These results are applicable for the design and implementation of future clinical trials.

Increased activity levels and daily walking in breast cancer survivors are associated with improved outcomes.[3,4] On the basis of these and other data, several clinical trials are currently enrolling participants with the goal of increasing activity levels in a population of breast cancer survivors, with activity trackers recording their activity levels. However, the effect of common treatments of breast cancer (like lumpectomy and RT) on activity levels and sleep is unknown. Indeed, this work represents a novel approach to investigating and reporting on the change in activity level during and after a course of RT and should prove valuable in aiding in the implementation and interpretation of ongoing as well as future clinical trials.

The exact mechanism by which increased activity levels improve outcomes in women with breast cancer is unknown, and is likely multifactorial. Exercise has been shown to improve global metabolic health, which might interact with cancer-specific outcomes.[11-19] These mechanisms are listed in Table 3.[11-19]

All women in this study were deemed physically fit and able to carry on normal levels of daily physical activity. Several women averaged less than a mile per day and half took less than 5,000 steps per day, a concerning finding because increased activity levels are associated with improved outcomes in these patient populations.[6,20]

Figure 1 Spaghetti Plots of: (A) Step Counts per Patient Versus Time After Radiotherapy Start; (B) Calories Burned per Patient Versus Time After Radiotherapy Start; (C) Sleep Duration per Patient Versus Time After Radiotherapy Start. Plots Smoothed Using a Moving Average. (D) Scatter Plot of Steps per Day for Each Patient

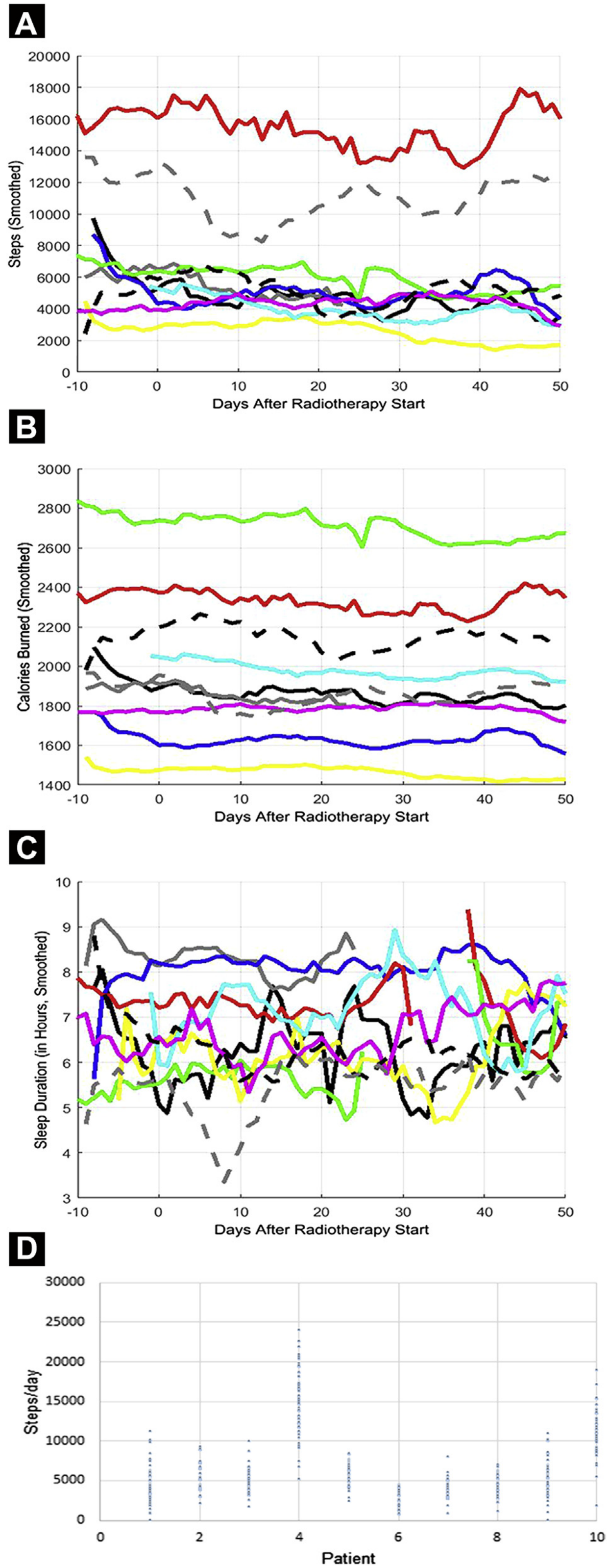
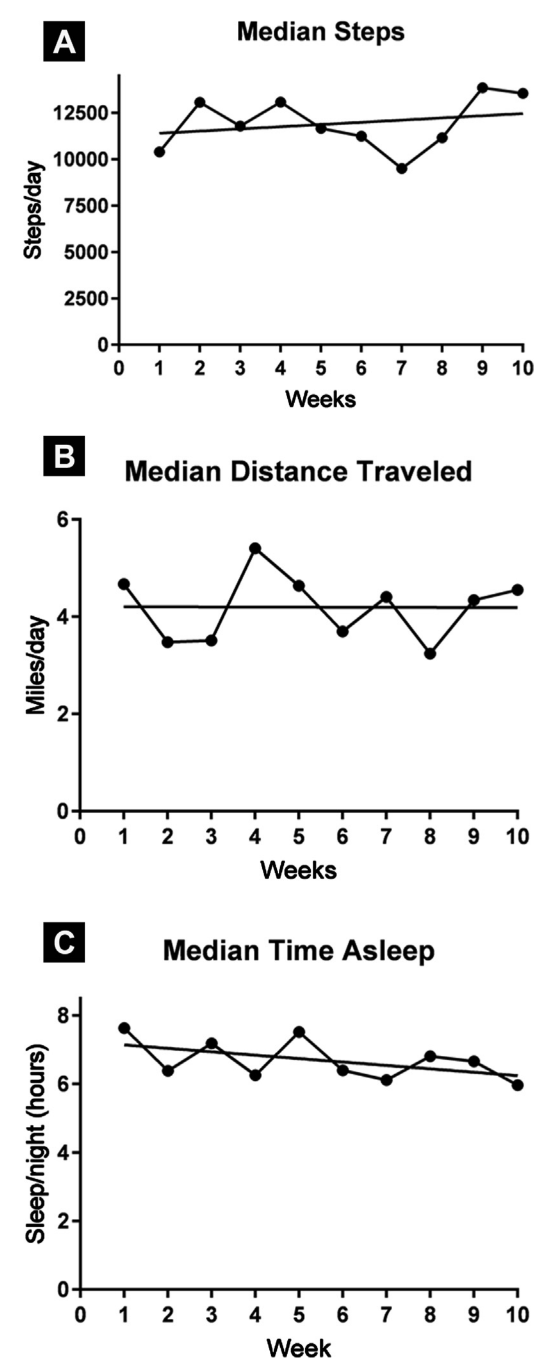


Figure 2 (A) Median Number of Steps per Day per Week. (B) Median Number of Miles Walked per Day per Week. (C) Average Minutes Slept Per Day Per Week



Furthermore, although the American College of Sports Medicine recommends at least 150 minutes of moderate-intensity exercise each week, they also suggest that approximately 10,000 steps might serve as a benchmark for activity trackers.[21] However, the minimal change seen in activity levels during RT for breast cancer is encouraging because treatment planning to completion and initial follow-up elapses a 10-week period, which might be sufficient time to engage women in a diet, exercise, and lifestyle program to incorporate healthy changes as they enter the period of survivorship. Also, as women are followed closely during RT, they can receive feedback and guidance to provide reinforcement, which might be more difficult in other outpatient scenarios.

Table 2 Changes in Sleep and Steps Compared With Fatigue and BMI

Patient	Changes in Steps[a]	Changes in Sleep, min[a]	ECOG Fatigue Score		BMI
			Before Tx	During Tx	
1	−1584	4	0	0	33
2	−629	−16	0	0	28
3	−986	13	0	1	26
4	−559	−14	0	1	41
5	228	7	0	0	27
6	472	−70	1	1	31
7	577	−24	0	0	27
8	1055	−61	1	1	40
9	−1302	−20	1	1	30
10	−139	76	0	1	25

Abbreviations: BMI = body mass index; ECOG = Eastern Cooperative Oncology Group; Tx = treatment.
[a]From pretreatment to treatment.

Finally, several studies have revealed that increased sleep quantity is associated with improved survival after breast cancer diagnosis.[22,23] The short sleep duration (< 8 hours per night) by most women in this study is concerning and methods to increase this should be addressed in future clinical trials. Although patients report sleep dysfunction from RT, studies have yet to quantify this dysfunction, and it is unclear if amount of sleep is actually affected.[24] Sleep was minimally affected in this study, and future clinical trials are needed in this domain.

Limitations of this study include the small sample size and lack of a randomized cohort. Thus, the potential for observation bias exists and it is difficult to parse out potentially causative factors that influence activity level. Still, the prospective nature of the investigation and the novel approach to examining and quantifying the patterns of sleep and activity in women undergoing one of the most common radiotherapeutic interventions led to practical, actionable, and noteworthy findings. Future clinical trials should build off these data in attempts to increase activity levels in similar patient groups.

Conclusion

Women experience a small, clinically insignificant decrease in their activity levels during RT for breast cancer. These levels appear to rebound shortly after completion of RT. Sleep is unaffected by treatment. In many patients, activity levels and amount of sleep was inadequate. Because increased activity levels are associated with better survival and less toxicity after breast cancer treatment, future studies in women should focus on assessing methods to increase patients' activity levels and improve patients' sleep habits during the course of radiation treatment.

Table 3 Mechanisms of Interaction Between Exercise and Improved Cancer-Specific Outcomes

Mechanism	Physiologic Impact	Cancer-Specific Interaction	Citation
1. Improvement in Insulin Sensitivity	Lower levels of circulating insulin and serum glucose	Insulin and glucose correlated with worse outcomes after treatment	11
2. Reduction of Several Inflammatory Factors	Decreased inflammation	Inflammatory factors shown to promote cancer recurrence and progression	12
3. Reduction in Estrone and an Increase in the 2-Hydroxyestrone to 16α-Hydroxyestrone Ratio	Lower levels of circulating estrogenic hormones	Might decrease risk of recurrence of hormonally-sensitive breast cancers	13
4. Decrease in Adipose Tissue	Adipose tissue secretes inflammatory hormones, causes metabolic dysregulation, and increases circulating estrogen	Inflammation, metabolic dysfunction, and estrogen correlated with worse outcomes	14-16
5. Activation and Gain of Lean Muscle Mass	Increase anti-inflammatory mediators, reduced adipose tissue, and improve immune function	Reduced factors that might fuel tumor cells	17
6. Reduction in Mental Stress During Treatment	Increases cortisol, blood glucose, and insulin	Stress-derived metabolic changes might worsen outcome	18,19

Clinical Practice Points

- While fatigue is one of the most common side effects of radiation therapy for early stage breast cancer patients, this is the first study to prospectively quantify activity level and sleep changes during treatment with activity trackers.
- The study provided the following novel findings: Activity levels are minimally affected by radiation therapy during the treatment of early stage breast cancer.
- Sleep amount is minimally affected by radiation therapy during the treatment of early stage breast cancer.
- Many women are getting inadequate amounts of activity and sleep during breast cancer treatment and afterwards.

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Disclosure

The authors have stated that they have no conflicts of interest.

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