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THE EFFECT OF YOGA ON FATIGUE IN BREAST CANCER PATIENTS UNDERGOING RADIOTHERAPY

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Word count: 3795

ABSTRACT

Objective: Assess the effect of yoga on levels of fatigue among women with breast cancer currently undergoing radiotherapy. **Design:** Systematic literature review. **Methods:** Searches were done on PubMed, utilizing the terms “yoga,” “fatigue,” “breast cancer,” and “radiotherapy.” Limits that led to inclusion of studies included: published after 2008, studies researching breast cancer, and studies that were randomized controlled trials. **Results:** Randomized controlled trials studied were by Chandwani et al. (2010), Chandwani et al. (2014), and Vadiraga et al. (2009). **Conclusion:** Yoga can improve quality of life among women with breast cancer undergoing radiotherapy, specifically by decreasing levels of fatigue. We recommend that yoga be implemented into treatment plans for women undergoing radiotherapy for breast cancer. Yoga is a cost-effective, safe, and gentle intervention.

INTRODUCTION

More than 2000 years ago, Patanjali described yoga as a way of life in the treatise of *Yoga Sutras*¹. The practice has been utilized in India to treat diseases for millennia. Research has shown yoga to be beneficial as both a preventative and therapeutic tool in healthy and chronically ill populations¹. The positive impacts of yoga have previously been demonstrated in patients with hypertension, asthma, multiple sclerosis, tuberculosis, fibromyalgia, and neck and back pain².

Yoga has since spread to Western cultures, where mind-body practice primarily focuses on asana (postures), pranayama (breath control), and meditation³. Overall benefits of yoga include increased energy, strength, flexibility, and well-being⁴. As a result of increasing popularity in Western cultures, there has been an accumulation of studies conducted on the health impacts of yoga³. Research on the effects of the practice is now being conducted on the cancer population⁵.

According to the World Health Organization, breast cancer is the number one cancer afflicting women worldwide making up 25% of the cancers reported in women⁶. Currently, the most common treatment for breast cancer is surgery followed by adjuvant systemic therapy, including chemotherapy and radiotherapy.

For breast cancer patients, the diagnosis is associated with physiologic change, fear of death, changes in quality of life and social relationships, and an overall sense of loss of control¹. Additionally, breast cancer patients also experience depression, anxiety, fatigue, pain, lymphedema, skin changes, pulmonary symptoms, neuropathy, cardiotoxicity, and sleep and cognitive disturbances during treatment^{7,1}. It is reported that many clinicians underestimate the presence of emotional distress factors (anxiety, depression, fatigue) in this cancer population. The increasing incidence of breast cancer has directed research in evaluating the potential effects of yoga as a treatment to improve patients' quality of life and emotional distress symptoms. Furthermore, there is increasing literature available on the effects of yoga in improving fatigue as a surrogate outcome of quality of life.

We hypothesize that utilization of yoga in women with breast cancer undergoing radiotherapy can help to improve quality of life by decreasing fatigue.

Clinical Question: In females over the age of 18 with breast cancer, does yoga, as opposed to a control, decrease fatigue during radiotherapy treatment?

METHODS

The search engine PubMed was used to conduct an initial search in September 2018. The terms included were "yoga," "fatigue," "breast cancer," and "radiotherapy." Articles that were published prior to 2008 were excluded. This produced 9 articles, including randomized controlled trials and meta-analyses.

Meta analyses and articles that did not specifically look at fatigue or yoga and those that looked at other cancers besides breast cancer were eliminated from further assessment. This yielded 3 articles that were assessed in depth using a modified version of the Critical Appraisal Worksheet: Therapy Study from Dartmouth Library and Duke University Medical Center Library and Archives (Figure 1).

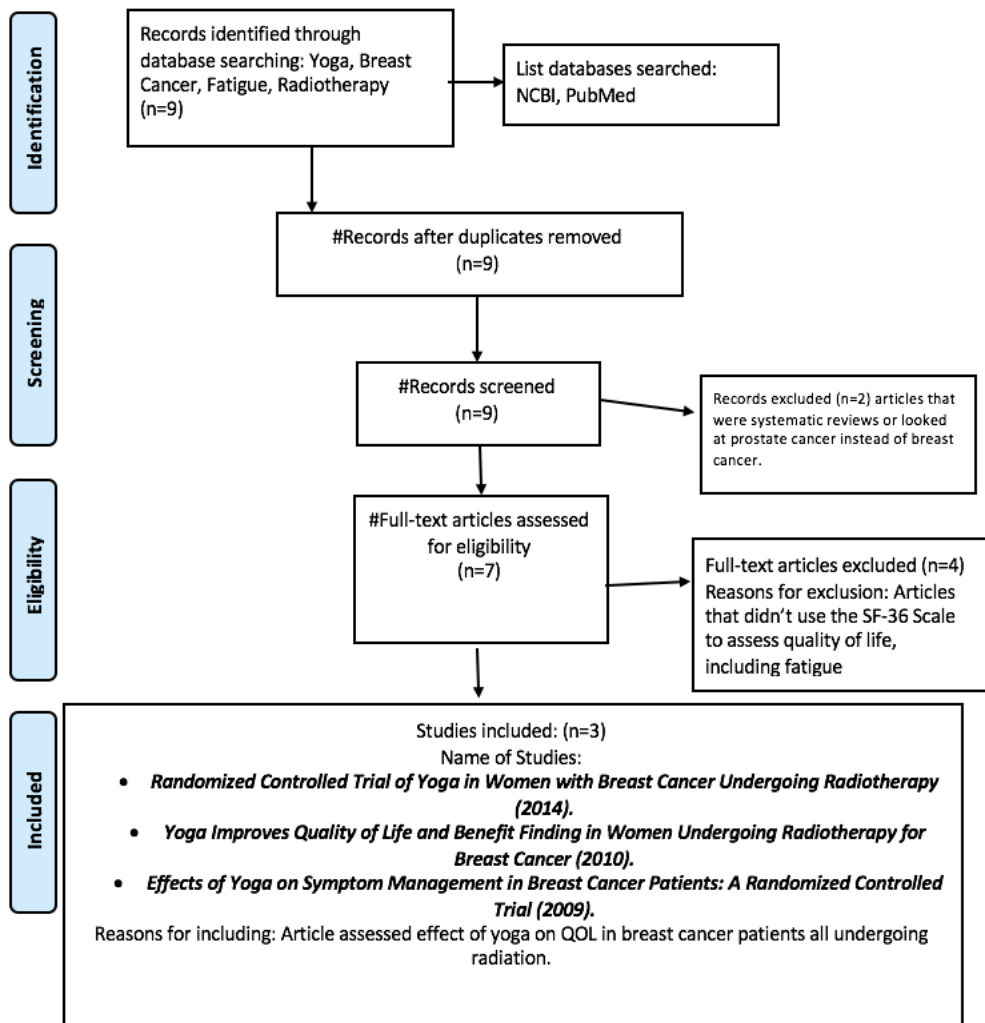


Figure 1: This flowchart shows the research process that resulted in the three selected articles in this review.

RESULTS

Study #1

Yoga improves quality of life and benefit finding in women undergoing radiotherapy for breast cancer. Chandwani et al. (2010)¹.

Study Objective

To evaluate the effect of yoga on quality of life, including fatigue, in women with breast cancer currently undergoing radiotherapy.

Study Design

This was a randomized controlled trial that took place at the University of Texas M.D. Anderson Cancer Center. Sixty-one women scheduled to undergo radiotherapy for stages 0-III breast cancer, who were older than 18 and could read, write, and speak English were included in this study. Patients who could not participate in a yoga class due to physical limitations and those who had any previously diagnosed psychiatric problems were excluded.

Participants underwent an initial baseline assessment before starting radiation and then were randomly assigned to either the Yoga Group (YG) (n=30) or the Waitlist Group (WL) (n=31). The WL acted as the control group, but participants were given the opportunity to undergo the yoga therapy after the study was completed. Women in the YG took up to 2, 60-minute yoga classes each week taught by a trained

yoga instructor at M.D. Anderson, during their 6 weeks of radiotherapy. Only participants in this study were present for the yoga classes, and some classes were one-on-one with the instructor due to scheduling issues. If a class was missed, a make-up class was scheduled for the patient. Participants were also asked to do yoga at home using a CD and pictures to guide them.

After the completion of radiotherapy, each participant (in both groups) underwent assessments after 1 week, 1 month, and 3 months. The Medical Outcomes Study is a 36-item short form survey (SF-36) used to assess different aspects of quality of life. This survey specifically observes how health effects daily activities, emotions, pain, and energy. Fatigue specifically was assessed using the Brief Fatigue Inventory questionnaire consisting of 9 questions regarding the patients' fatigue and how it affected their day-to-day life. The scoring ranged from 0-10 with higher numbers correlating with worse fatigue.

Study Results

This study used general linear model (GLM) analyses to compare different assessments among the two groups. SAS software was used to perform data analyses. No significant differences in demographics, medical, and baseline scores for outcome measures were found among the 2 groups. Only 50% of participants in the YG attended all 12 yoga classes. 3% of participants in the YG stated that they did not practice yoga outside of class during the study.

The only significant decrease in fatigue found in the YG compared to the WL group was 3 months after the end of radiotherapy ($P=0.01$). No significant differences in fatigue were found after 1 week ($P=0.18$) or 1 month ($P=0.26$). Results of the study are summarized in Table 1.

Study Critique

This study has many strengths, including being a randomized controlled trial, studying a specific population of breast cancer patients, which includes those currently undergoing radiotherapy, and giving many opportunities to participants in the YG to keep up with the yoga even if they missed a class.

However, one weakness with the number of yoga classes is participants in the YG group may have practiced yoga at home more or less than other participants. This difference may have affected the significance of changes in fatigue.

There are other weaknesses of this study, as well. One weakness is the sample size. With only 61 women that completed the study, this causes concern for a type II error. It would be a stronger study if it had a more significant sample size, which may in turn produce more significant results. The study also lacks a third group, which should include another form of activity to compare to yoga. The researches do offer data on exercise, specifically yoga, and its effect on fatigue compared to no exercise. However, it would be a stronger study if yoga was compared to another form of exercise to find if it is truly superior in the treatment of fatigue in breast cancer patients.

Table 1. Results of yoga's effect on fatigue among breast cancer patients in Study 1.

BFI	Baseline T1			1 wk (T2)			1 mo (T3)			3mo (T4)		
	YG	WL	P value	YG	WL	P value	YG	WL	P value	YG	WL	P value
	2.3 (0.3)	2.3 (0.4)	0.97	1.9 (0.7)	2.5 (0.8)	0.32	1.5 (0.5)	1.4 (0.4)	0.93	1.6 (0.6)	2.0 (0.6)	0.55

Study #2

*Randomized controlled trial of yoga in women with breast cancer undergoing radiotherapy. Chandwani et al. (2014)*⁷.

Study Objective

To evaluate the effect of yoga compared to stretching and no exercise on quality of life, including on fatigue, in women with breast cancer currently undergoing radiotherapy.

Study Design

This was a randomized controlled trial that took place at the University of Texas M.D. Anderson Cancer Center. One hundred and sixty-three women scheduled to undergo radiotherapy with diagnosed breast cancer stages 0-III, who were older than 18, and who could read, write, and speak English were included in this study. Patients that had lymphedema, metastatic bone disease, deep vein thrombosis, documented diagnosis of a formal thought disorder, extreme mobility problems, or who had practiced yoga in the previous year were excluded from this study.

Participants underwent an initial baseline assessment before starting their 6 weeks of radiotherapy and then were randomly assigned to 1 of 3 groups: Yoga Group (YG) (n=53), Stretching Group (ST) (n=56), and Waitlist Group (WL) (n=54). The WL acted as the control group, but participants were given the opportunity to practice yoga and stretching therapy after the study was completed. Women in the yoga and stretching groups performed their assigned exercise in 60-minute-long classes, 3 days a week during their 6 weeks of radiotherapy. The yoga class was taught by a Vinyasa-trained teacher while the stretching class was taught by physiotherapists from the Rehabilitative and Physical Therapy at M.D. Anderson and included stretches recommended specifically for women undergoing or recovering from breast cancer treatment. Some classes were one-on-one with the instructor due to scheduling issues. If a class was missed, a make-up class was scheduled for the patient. Participants were also asked to do yoga at home using a CD and pictures to guide them.

After the completion of radiotherapy, each participant underwent assessments during the last week of radiotherapy and 1, 3, and 6 months later. The Medical Outcomes Study 36-item short form survey (SF-36) was used to assess different aspects of quality of life. Fatigue specifically was assessed using the Brief Fatigue Inventory questionnaire consisting of 9 questions regarding the patients' fatigue and how it affected their day-to-day life. The scoring ranged from 0-10 with higher numbers correlating with worse fatigue.

Study Results

This study used general linear model analyses to compare different assessments among the 2 groups. SAS software was used to perform data analyses. 87% of YG participants and 85% of ST participants attended more than 12 yoga or stretching classes throughout the study. Though some participants practiced yoga and stretching outside of class, this number decreased as the study and post-study analysis progressed.

Significant decreases in fatigue were found by the end of the study between the YG and ST groups compared to the WL group (*YG P=0.04, ST P=0.02*). Less of a significant decrease in fatigue was found for the YG group compared to the WL group at 1 month (*P=0.09*) as well as for the ST group compared to the WL group at 3 months (*P=0.07*). All other comparisons at 1 week, 1, 3, and 6 months showed no significant changes in fatigue levels among the 3 groups. Study results are summarized in Table 2.

Study Critique

This study's advantages included having a larger sample size than its previously completed sister study as well as comparing yoga to another form of exercise in addition to no exercise.¹ Both of these strengths were weaknesses in the previous study.

The drawbacks of this study included still having a relatively small sample size. Like the previous study, there was no control over how often participants practiced yoga or stretching outside of the scheduled classes, which may affect the significance of fatigue changes. In the future, expanding the practice of yoga to treat fatigue in other cancers besides breast cancer may be of interest.

Table 2. Results of yoga's effect on fatigue among breast cancer patients in Study 2.

BFI	Baseline				Last wk of tx				1 mo post tx				3 mo post tx				6 mo post tx			
	YG	ST	WL	P value	YG	ST	WL	P value	YG	ST	WL	P value	YG	ST	WL	P value	YG	ST	WL	P value
	3.2	3	2.6	0.3	2.9	2.5	3.2	0.03	2.7	2.7	2.7	0.22	2.6	2.3	3	0.15	2.8	2.5	2.6	0.56

Study #3

*Effects of yoga on symptom management in breast cancer patients: A randomized controlled trial. Vadiraga et al.*⁸.

Study Objective

To evaluate the effects of yoga on quality of life (QOL), and symptom control with a focus on the effects of yoga in managing distressful symptoms in early breast cancer patients receiving adjuvant radiotherapy.

Study Design

Eighty-eight women recently diagnosed with stage II and III breast cancer who had already undergone primary treatment of surgery and were receiving radiotherapy consented to participate in a randomized controlled study. Subjects were recruited between January 2004 and June 2006 from 2 different urban cancer centers. Inclusion and exclusion criteria are shown in Table 3. All subjects were prescribed adjuvant radiotherapy with a cumulative dose of 50.4 Gy with fractionation spread over 6 weeks.

Prior to randomization, demographic information, medical history, and clinical data were collected from all subjects. Randomization was performed using computer generated numbers in a concealed allocation protocol into 2 study groups: Receive Yoga (n=44) or Supportive Therapy (acted as control group) (n=44) prior to intervention with adjuvant radiotherapy by personnel who had no part in the trial.

Of the 88 participants, 74 completed the prescribed radiation therapy and follow-up assessments resulting in 14 dropouts of the study (yoga n=40; control n=34). Reasons for dropout included migration to other hospitals (n=4), refusal to continue study (n=2), time constraints (n=4), and diagnoses of infection that delayed radiotherapy and intervention (n=1). Yoga intervention was based on principles of attention diversion, mindful awareness, and relaxation to cope with day-to-day stressful experiences, which consisted of a set of asanas, breathing exercises, pranayama, meditation, and yogic relaxation techniques with imagery.

The intervention subjects were required to attend at least 3 in-person one-hour sessions a week for 6 weeks throughout their adjuvant radiotherapy treatment in the hospital. On the remaining days of the week, subjects were encouraged to self-practice. Sessions taught by a trained yoga therapist included the preparatory practice (asana, breathing exercises, pranayama, savasana) for 20 minutes followed by 30 minutes of guided meditation practices (Table 4). Control intervention consisted of brief supportive therapy incorporating education, which is a component that is routinely offered to patients as a part of care in the cancer center. Control counseling occurred with subjects and caretakers by a trained social worker once a week for 15 minutes.

The European Organization for the Research and Treatment of Cancer— Quality of Life (EORTC QoL C30 questionnaire, version 1) was used to assess treatment-related symptoms, including fatigue. Assessments were completed prior to and after radiotherapy treatment.

Table 3. Inclusion and exclusion criteria for participation in Study 3.

Inclusion Criteria	
	Women recently diagnosed with operable breast cancer
	Ages between 30-70 years
	Zubrod's performance status 0-2 (Ambulatory >50% of time)
	High school education
	Written consent to participate
Exclusion Criteria	
	Concurrent medical condition likely to interfered with treatment
	Major psychiatric, neurological illness or autoimmune disorders
	Known metastases

Table 4. Options of 30-minute meditation practices utilized in Study 3.

Meditation
Focused awareness on sounds and Chang's from Vedic texts
Breath awareness and impulses of touch from palms and fingers while practice yogic mudras
Dynamic form of meditation with eyes closed practicing four yoga postures interspersed with relaxation while supine

Study Results

A GLM repeated-measures ANOVA was done with the within-subjects factor being time/assessment at 2 levels and between-subjects factor being groups at 2 levels — yoga vs. supportive therapy. The study utilized Bonferroni's correction for changes at different time points between groups. Intention to treat analysis was completed with baseline and postradiotherapy measures (post-RT) for all participants. Baseline values were utilized for post-RT measures for study dropouts. Pearson's correlation analyses studied the bivariate relationship between QOL domains and treatment-related symptoms.

Symptom scores of fatigue assessed by EORTC QoL C30 completed a repeated-measure analysis of variance. There was a significant group-by-time interaction effect on the symptoms of fatigue [F (1,72)= 7.74, P=0.007]. Using Bonferroni's correction for post hoc tests comparing yoga and control groups in post-RT measures, statistically significant differences in fatigue symptoms were demonstrated with a (mean difference +/- SE, -20.72 +/- 5.36; P=0.001). The study found there was a significant decrease in fatigue (mean difference +/- SE, 13.39 +/- 3.61; P<0.001; 95% CI 6.2-20.5). Intention to treat (ITT) analysis on the eighty-eight randomized sample showed statistically significant improvement of fatigue (-17.26 +/- 4.89, P=0.001, -26.99 to -7.53) between groups following intervention (Table 5).

Bivariate relationships between outcome measures were completed on physical distress, psychological distress and activity with comparison to fatigue. Pearson's correlation (r-values) were reported with p-values at <0.01. There was a significant positive correlation between physical and psychological distress and fatigue with r-values reported at 0.68 and 0.62 respectively. There was a significant negative correlation of activity levels with fatigue with a revalue of -0.40.

The study reports that the level of adherence to intervention did not seem to affect symptom scores. Adherence was overall reported well with 29.7% attending 10-20 supervised sessions, 56.7% attending 20-25 supervised sessions and 13.7% attending greater than 25 supervised sessions over the 6-week period.

Table 5. Results of yoga’s effects on fatigue among breast cancer patients in Study 3.

Per Protocol (PP)	Yoga (y) (n=42)		Control (C) (n=33)	
	Pre	Post	Pre	Post
	44.76	31.37	50.46	52.09
	(22.98)	(21.79)**	22.41	24.24
PP Adjusted Mean (95% CI)	-20.72 (-31.40 to -10.04)			
PP Effect Size	0.33			
Intention To Treat (ITT)	Pre	Post	Pre	Post
	45.48	33.26	49.32	50.52
	(24.08)	(23.82)**	(20.72)	(22.31)
<i>P values <0.01 for post-hoc tests comparing groups at different time points using Bonferroni’s correction</i>				

Study Critique

A strength of this study is that it is a randomized controlled trial with randomization assigned by nonaffiliated personnel. Along with this, the study chose a control intervention to control for nonspecific effects of the yoga program that could be associated with factors such as attention, support, and a sense of control over the effects of the disease process and adjuvant radiotherapy treatment. Finally, all subjects had similar sociodemographic and medical characteristics.

Study weaknesses include the reporting of 2 different numbers of participants that completed prescribed radiotherapy (75 and 74). There was also variation in the treatment of patients prior to adjuvant therapy in that 16 of the patients had mastectomies alone and 57 patients had mastectomies along with 3 rounds of completed chemotherapy. Differences in goals of yoga intervention and supportive therapy could also be a confounding factor of the study in that yoga was aimed at stress reduction and appraisal changes, whereas therapy was aimed at education, reinforcing social support and coping preparation. A large discrepancy between the number of sessions between yoga and control over the duration of 6 weeks at 18-24 sessions as compared to 3-4 respectively was also found. There was variation within the yoga intervention in that the 30-minute meditation had 3 different meditation practices of which the study did not report specifics on how they were assigned. Other limitations of the study include being unmasked and subjective results.

DISCUSSION

Breast cancer is currently the leading cause of death of women worldwide and is associated with many mental manifestations including anxiety and depression, which affect quality of life and perception of fatigue⁸. Of the 3 treatment options for breast cancer, radiotherapy is associated with varying levels of fatigue during and post treatment⁷.

Historically, yoga is a mind and body practice that improves psychological, physical, and spiritual aspects of quality of life⁵. Yoga is a gentle practice, more recently used to increase focus, relaxation, flexibility, and strength in cancer patients⁹. Due to the high prevalence of cancer-related fatigue among breast cancer patients, yoga is a safe practice for even severely fatigued patients. It offers both physical and mental rewards, allowing patients to better cope with their diagnosis and associated symptoms of the disease and treatments. The purpose of this review was to determine if yoga can significantly improve cancer-related fatigue among breast cancer patients undergoing radiotherapy.

An overview of the 3 studies assessed in this review is provided in Table 6. Both Chandwani et al. articles are extensions of one another. The earlier study (2010) compared yoga to a control group to assess the effect of yoga on quality of life, but this review specifically assessed levels of fatigue. The later article

(2014) expanded upon this first study with a larger sample size and compared yoga's effects on fatigue to a control group as well as a stretching group^{1,7}. Therefore, this later study showed several advantages over its sister study in 2010 and study 3, Vadiraja et al.^{7,8}. Though the second Chandwani et al. study (2014) had a larger sample size than the first study (2010), all 3 studies had relatively small sample sizes^{1,7,8}. These 3 studies also assessed different yoga techniques. All 3 studies assessed yoga's effect on quality of life, specifically fatigue, among only women with breast cancer undergoing 6 weeks of radiotherapy.

All 3 studies showed an improvement in fatigue after practicing yoga throughout radiotherapy and after treatment. However, each study found improvement in fatigue at different times during and after treatment. Chandwani et al. (2014) also found stretching to improve fatigue, but at different assessment times than yoga⁷. No side effects or negative outcomes were found in any of the 3 studies; therefore, it was concluded that yoga is a safe and gentle practice that all breast cancer patients should participate in during and after treatment. The benefits of yoga, including improvement in fatigue and possibly other quality of life measures, outweigh the risk of participating in this practice.

Future studies should assess the effects of yoga on other aspects of quality of life, as well as study women and men undergoing other treatments for breast cancer including chemotherapy and surgery alone. Larger sample sizes may also produce more significant results. We suggest assessing 1 specific type of yoga to better compare its effect on fatigue. We also support the idea of studying more objective outcomes of fatigue, possibly including cortisol levels and markers of inflammation. If future studies also find improvements in fatigue after radiation or chemotherapy, it may be recommended for breast cancer patients to practice yoga regularly, whether it is in a support group for breast cancer patients or at home. The CD of yoga practices offered to patients in the Chandwani et al. studies (2010, 2014) should be provided to all breast cancer patients to safely practice yoga on their own^{1,7}. Each patient would need clearance from her provider before participating in yoga practices.

Table 6. Table comparing the 3 studies reviewed in this article.

Study	Chandawani et al. 2010	Chandawani et al. 2014	Vadiraja et al. 2009
Patients	61	109	74
Population	Stage 0 to III breast cancer	Stage 0 to III breast cancer	Stage II, III breast cancer with completed surgical treatment
Gender	Females	Females	Females
Study type	RCT	RCT	RCT
Control	Waitlist control group	Active stretching for women undergoing or recovering from breast cancer treatment	Supportive therapy 1X week for 15 minutes
Intervention	Biweekly 60 minute yoga classes	Up to three 60 minute yoga classes per week	Yoga and Meditation guided sessions 3X a week for 50 mins
Interest	QOL: Fatigue	QOL: Fatigue	QOL: Fatigue
Measurement Scales	BFI	BFI	EORTC QoL C30 questionnaire version 1
Length of XRT exposure	6 weeks	6 weeks	6 weeks

CONCLUSION

Yoga is a safe, gentle practice shown to improve aspects of quality of life, including fatigue, among cancer patients. Due to the inability to blind these studies, there are some concerns about if yoga is directly improving fatigue or if it is a placebo outcome. The variability among the yoga classes themselves is also a concern among these studies. There is also the question about the logistics about having yoga practices covered under insurance for breast cancer patients, as stretching currently is with physical therapy.

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