

## Effects of Qigong on Quality of Life, Fatigue, Stress, Neuropathy, and Sexual Function in Women with Metastatic Breast Cancer: A Feasibility Study

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### Abstract

**Background:** Women with metastatic breast cancer (MBC) suffer from psychological and physiological symptoms and side effects of therapy. When the treatment is non-curative, quality of life (QOL) is a major issue. This study aimed to examine the feasibility, safety, and effects of Medical Qigong (MQ: integration of gentle exercise and meditation) in improving QOL in women with MBC.

**Method:** Women with MBC were randomized to a MQ group (n=14) or meditation control group (n=13). QOL, fatigue, stress, neuropathy symptoms and sexual function were measured by the Functional Assessment of Cancer Therapy - Breast (FACT-B), Functional Assessment of Cancer Therapy-fatigue (FACT-F), Perceived Stress Scale (PSS), neurotoxicity subscale of the FACT/GOG-NTX, and Sexual Functioning Questionnaire (SFQ) subscales at pre-intervention and weeks 5 and 10.

**Results:** No serious adverse events were reported during or after MQ intervention. Sixty three percent of participants completed the study (MQ intervention (n=9) and meditation control (n=8)). There were no significant differences in overall QOL (p= 0.84), fatigue (p=0.71), perceived stress level (p=0.52), sexual satisfaction (p=0.55), sexual activities (p=0.95) and sexual relationship (p=0.79) between the groups, although difference in neuropathic symptoms (p=0.014) were significant.

**Conclusions:** A MQ trial in women with MBC is feasible and safe. MQ may have the potential to relieve symptoms experienced by women with MBC and prevent deterioration of neuropathy. A larger study with adequate power to confirm these results and detect clinically relevant effects is needed.

**Keywords:** Metastatic breast cancer; Quality of life; Fatigue; Stress; Peripheral neuropathy; Qigong

### Introduction

Breast cancer is the most common cancer affecting women and the second leading cause of cancer death among women in Australia and US [1,2]. Approximately 10% of newly diagnosed breast cancer patients present with locally advanced or metastatic breast cancer (MBC) [3] and 20% to 50% of patients first diagnosed with primary breast cancer will develop MBC [4,5].

Despite recent advances in research and clinical management, treatment of MBC is rarely curative. When treatment for MBC is non-curative, treatment is focused on improving quality of life (QOL) – ideally, without an undue burden of treatment related toxicity – as well as increasing survival [6]. MBC takes a serious toll on patients' QOL, yet many patients live for several years with the condition. Up to 90% of MBC patients experience chronic fatigue and anxiety [7,8]. Existing

treatment options for QOL and fatigue are limited and often ineffective in this population. Further, cumulative peripheral neuropathy becomes a symptomatic and dose limiting side effect for many women with MBC receiving chemotherapy [9].

Women with breast cancer are increasingly using complementary and alternative medicine (CAM) to improve their QOL during and after cancer treatment [10]. The main reasons given for using CAM are: to help alleviate the side effects caused by medical treatment; to satisfy needs unmet by conventional medicine and doctors, including provision of emotional support and humanistic care; to improve quality of life; as a last resort; and as way of finding hope [11]. Numerous studies have reported that mind-body practices (e.g. meditation, yoga, tai chi and Qigong) have positive effects on QOL, fatigue and other psychological symptoms of patients with cancer [12-15]. Yet, literature searches have not uncovered any prospective studies addressing the efficacy of Qigong for women with MBC.

Medical Qigong (MQ) is a form of Qigong specifically designed to improve the health of patients. It incorporates practice of coordinated

gentle exercise and relaxation through meditation and breathing. Recent studies have reported that MQ improved QOL, mood status, and reduced fatigue, depressive symptoms and cognitive function as well as reduced inflammatory biomarkers of cancer patients [12,16,17]. If the efficacy of MQ in women with MBC can be shown, it has the potential to significantly impact a large proportion of women with QOL issues. Thus, we conducted this study to evaluate the feasibility and safety of MQ in women with MBC. The secondary aim was to obtain preliminary information in regard to the potential efficacy of MQ in improving QOL, fatigue, stress, neuropathy and sexual functioning.

## Methods

### Patients

The participants in this study were recruited from two university teaching hospitals and one private hospital in Sydney, Australia. Patients considered by their medical oncologist to be eligible received a letter of invitation from their medical oncologist. Once patients expressed interest in study participation via a reply letter, a research assistant invited them to attend an information session about the study at which patients were further screened for eligibility. Eligibility criteria included: a confirmed diagnosis of MBC; age  $\geq 18$  years; an Eastern Cooperative Oncology Group (ECOG) performance status between 0-2; an expected survival of more than 6 months; an ability to complete all study questionnaires and provide informed consent. Patients were excluded from the study if they had a diagnosis of a major medical or psychiatric disorder (other than cancer), a history of epilepsy, brain metastasis, delirium or dementia, had medical contraindications for exercise (e.g., significant orthopaedic problem or cardiovascular disease) or were already practicing Qigong (once a week or more) in the last 6 months and/or had attended a meditation class (once a week or more) in the last 6 months. After giving written consent, patients completed the baseline QOL, fatigue, stress and sexual function measures and gave blood (reported elsewhere), and were randomly assigned into the intervention and control groups. The study was conducted between July 2009 and November 2011. The study received ethics approval from the participating hospitals.

### Intervention

This was a phase II randomized controlled trial (RCT) comparing the effect of a 10-week group MQ intervention to a meditation control group (controlling for attention and time) in women with MBC. Both the MQ intervention and meditation control treatments were delivered by the researcher (O.B.) to reduce therapist variability.

### Medical Qigong (MQ) program for the intervention group

Patients assigned to the intervention group received standard medical care and were invited to attend a MQ program held in the hospital where they were treated. The program was modified from traditional Qigong practice to specifically target the needs of cancer patients in order to control emotions and stress as well as to improve QOL. The program has been validated in previous studies [12,18], and was developed and delivered by an experienced MQ instructor with over 20 years experience and training in traditional Qigong in Korea, Daoist Qigong in China, Buddhist Qigong in Australia and mind-body medicine at the Harvard Medical School. The MQ program was a group class conducted over 10 weeks, with one supervised 60 minute

session per week. Each session consisted of: 10 minutes discussion of health issues; 30 minutes gentle stretching and body movement in standing postures to stimulate energy channels; and 20 minutes meditation and breathing exercises based on the energy channel theory in Chinese medicine, including natural breathing, chest breathing, abdominal breathing, breathing for energy regulation, and relaxation and visualization. Participants were also encouraged to undertake home practice every day for at least half an hour.

### Meditation program for the control group

Participants assigned to the meditation control group received standard medical care and were invited to attend a meditation program held in the hospital where they were treated. The meditation program was a group class conducted over 10 weeks, with a supervised 60 minute session per week. Participants were required to attend identical amounts of time and home practice as in the intervention group. The meditation program was led by the first author (O.B.), an experienced meditation and Qigong practitioner, using a compact disk (CD) developed by Dr Ann Webster, an experienced health psychologist. The CD has been previously piloted in breast cancer patients and was received very positively. The meditation program contained a 20 minute discussion of health issues and evidence based CAM, and two guided relaxations program that take approximately 20 minutes each: Gift of Relaxation, which encourages individuals to just "be" by using the power of their mind to calm their body and quiet their mind; and Garden of Your Mind, in which individuals are guided to becoming more present with what is meaningful and to plant seeds for goals, plans and dreams for their future. The CD for meditation was provided to the participants in the control group for home practice.

### Outcome measurements

**Feasibility and safety:** Participants were considered to have completed the MQ and meditation program if they attended a minimum of five out of ten weeks. To assess home practice, participants were asked how many days they practiced at home each week and duration of practice. Participants were also advised to report or discuss any adverse effects of MQ or meditation to their oncologist or instructor.

QOL, fatigue, perceived stress level, and sexual function were measured by self reported outcome questionnaires at baseline (prior to the MQ intervention) at week 5 and at the conclusion of the intervention 10 weeks later. Blood samples were collected to measure inflammatory biomarkers (C-reactive protein and cytokines (GM-CSF, TNF- $\alpha$ , IL-2, IL-4, IL-6, IL-8, IL-10, IL-12) (data will be reported elsewhere).

Quality of life (QOL) was measured by the FACT-B version 4 questionnaire. The FACT-B consists of the FACT-General (FACT-G) plus the Breast Cancer Subscale. FACT-G includes physical well-being, emotional well-being, functional well-being and social/family well-being. The FACT-B module was developed specifically for women with breast cancer. This yields a total score (range from 0 to 176) as well as individual subscale scores; higher scores reflect better QOL [19]. Fatigue was assessed by the FACT-Fatigue [20]. It consists of 13 items scored on a five Likert scale from 0 to 4. This instrument is scored that higher score indicate less fatigue. Stress level was measured by Perceived Stress Scale (PSS) [21]. It consists of 10 items scored on a five Likert scale from 0 to 4. The minimum score is 0, and the

maximum score is 40. Higher scores indicate a high level of stress. The PSS is commonly used to assess patient-reported stress [22]. Neuropathy symptoms were measured by the neurotoxicity (NTX) subscale of the FACT/GOG-NTX, version 4. The FACT/GOG-NTX, is 38-item self reporting questionnaire consists of two components, a general measure of QOL (FACT-G), and an 11 item NTX subscale. The NTX subscale has demonstrated sensitivity to meaningful clinical distinction and change over time [23]. Sexual function satisfaction, sexual function activities and sexual function relationship were measured with subscales of the sexual function questionnaire (SFQ), with higher scores reflecting more positive sexual functioning [24]. The SFQ is composed of two multi-item scales (sexual functioning and medical impact) and a few single items for sample description. Within the sexual functioning scale, there are nine multi-item subscales [24].

### Data analysis

Data analyses were conducted using SAS 9.3. Descriptive statistics (frequency, mean and standard deviation) were used to describe and summarize participants' demographic profiles. Participants who completed the intervention were evaluated at week 5 and week 10 assessments. Mixed analysis of variance, with group as the between-subjects variable and time as the within-subjects variable, was used to analyze each of the outcome variables separately. For all analyses, significance was set at the 0.05 alpha level. Intent-to-treat analyses were not conducted because the sample size was not big enough to use a multiple imputation method.

## Results

### Demographics

Twenty-seven women with MBC were enrolled in the study, and randomized into the MQ intervention group (n=14) and meditation control group (n=13). Demographic characteristics of participants are shown in Table 1. There were no significant differences between the MQ and meditation control groups in terms of the demographic variables and baseline QOL.

	Intervention (N=14)	Control (N=13)
Mean age (SD)	56.9 (12.1)	57.8 (10.8)
Marital status (%)		
Currently married or de facto relationship	10 (71.4)	10 (83.3)
Never married	1 (7.1)	1 (8.3)
Separated/divorced	2 (14.3)	1 (8.3)
Widowed	1 (7.1)	0 (0.0)
Ethnicity (%)		
Caucasian	11 (78.6)	12 (92.3)
Asian	2 (14.3)	1 (7.7)
Other	1 (7.1)	0 (0.0)
Educational level (%)		
> Secondary	6 (42.9)	4 (30.8)

< Tertiary	8 (57.1)	9 (69.2)
*ECOG Performance Status		
0	7 (50.0)	8 (61.5)
1	7 (50.0)	5 (38.5)

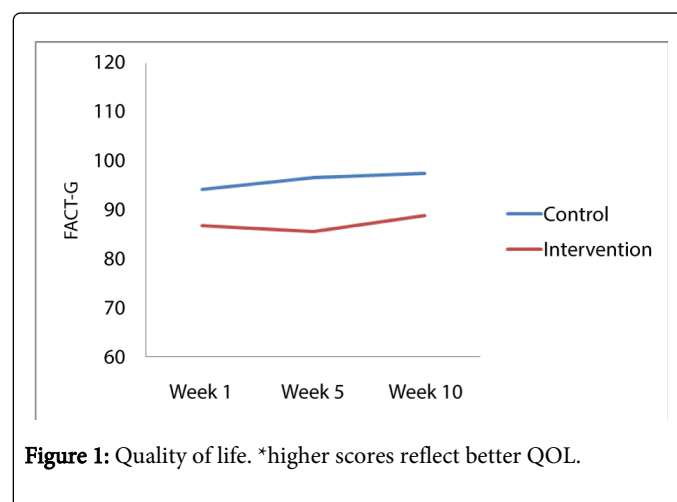
**Table 1:** Demographic characteristics of participants. Note: N's vary due to missing data. \*ECOG 0: Fully active, able to carry on all pre-disease performance without restriction, \*ECOG 1: Somewhat limited with slightly symptoms.

### MQ feasibility

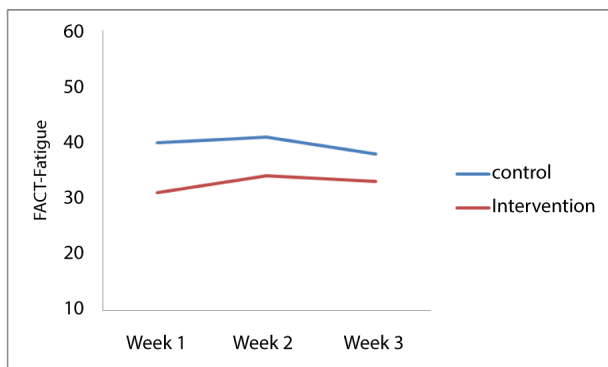
Of the 27 women participating, 63% of participants completed the full 10 weeks of the study (MQ intervention (n=9) and meditation control (n=8)). The main reasons for dropping out were medical treatment and holiday. The adherence rate for the MQ intervention was 80% and for the control group was 75%. Participants reported practicing MQ at home 3-4 days a week for 15-30 minutes a day. No serious adverse events were reported during or after the MQ intervention.

### Effect of MQ on QOL, fatigue, stress, neuropathy and sexual function

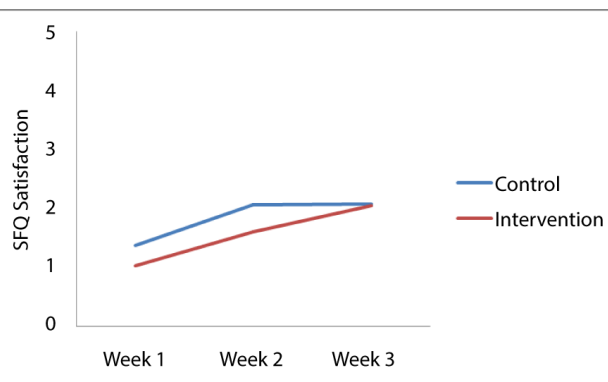
There were no statistically significant differences between the groups in scores of overall QOL (p=0.84), fatigue (p=0.71), perceived stress level (p=0.52) and sexual satisfaction (p=0.55) sexual activities (p=0.95) and sexual relationship (p=0.79). However, there was a significant group difference in neuropathy symptoms (P=0.014); neuropathy symptoms in the MQ group improved marginally while those in the control group deteriorated moderately. There were also, in pre and post data analysis, positive trends observed in the overall QOL fatigue, stress and sexual function (satisfaction and activities) scores, in both the mind body MQ and meditation intervention groups (Figures 1-7).



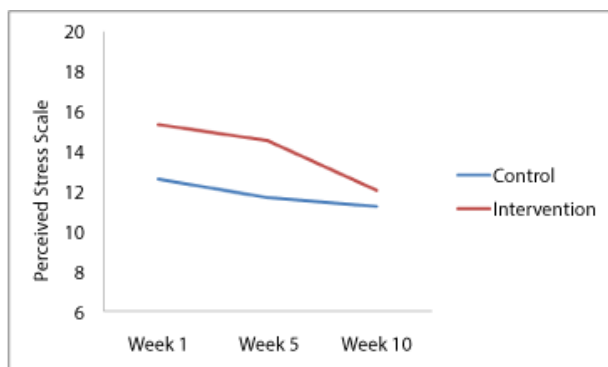
**Figure 1:** Quality of life. \*higher scores reflect better QOL.



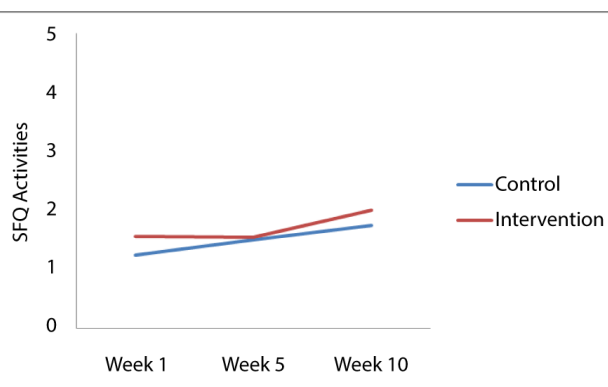
**Figure 2:** Fatigue. \*higher scores reflect less fatigue. \*higher scores reflect better QOL.



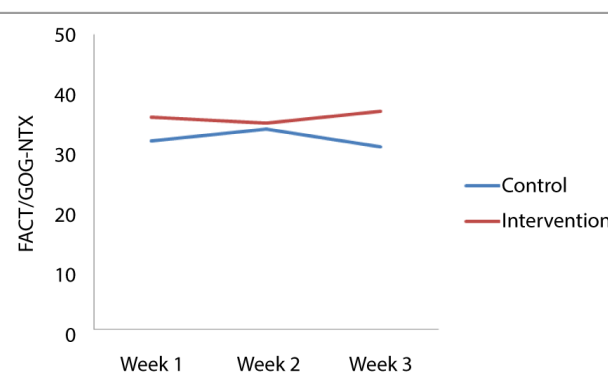
**Figure 5:** Sexual function satisfaction. \*Higher scores reflect better sexual function satisfaction.



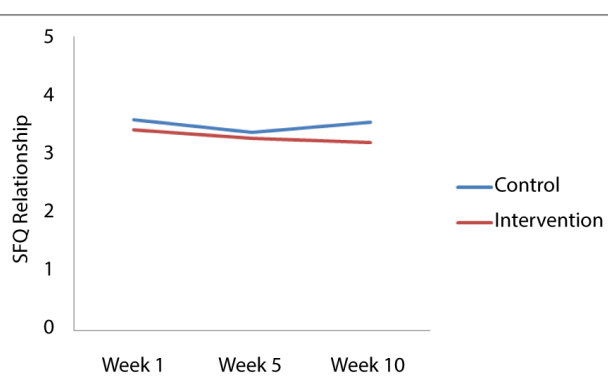
**Figure 3:** Perceived Stress Scale. \*lower scores reflect less stress level.



**Figure 6:** Sexual function activity. \*Higher scores reflect better sexual function activity.



**Figure 4:** Peripheral neuropathy symptoms. \*Higher scores reflect less peripheral neuropathy symptoms.



**Figure 7:** Sexual function relationship. \*Higher scores reflect better sexual function relationship.

## Discussion

This feasibility study provides preliminary information on the safety and potential effect of MQ on women with MBC. To the best of



our knowledge, this is the first randomized controlled phase II feasibility study evaluating the effects of MQ in women with MBC. The results of this study suggest that a RCT of MQ in women with MBC is safe, feasible and has the potential to reduce treatment related symptoms.

During the MQ study intervention, participants did not report any adverse effects in relation to MQ practice at home 3 to 4 days a week in addition to attending the MQ program once a week for 10 weeks. This is consistent with findings from previous studies [12,18]. It also demonstrated the sustainability of MQ with women with MBC, although the dropout rate was higher (37%) than in a non-metastatic cancer population (7-32%) [12,25]. This high dropout rate factor should be considered when designing future Qigong studies in advanced cancer populations.

A highly important finding of this study was that MQ might have the potential to provide a positive impact on neuropathic symptoms in women with cancer. Significant group differences in the self-reported FACT-NTX between the MQ group and meditation control group at 10 weeks were observed. This may be a statistical artifact due to multiple testing and a small sample size, but if replicated in a larger sample, would have clinical significance. Chemotherapy-induced peripheral neuropathy (CIPN) is a prominent dose-limiting toxicity of commonly used chemotherapy agents [9]. Many women after breast cancer treatment experience peripheral neuropathy symptoms that impair daily activities as well as QOL. Although CIPN symptoms, generally, resolve after completion of treatment, they are often partially reversible and can persist for years. Current recommended treatments for CIPN include gabapentin [26], Acetyl-L-carnitine [27], pregabalin [28], venlafaxine [29], and duloxetine [30]. However, the efficacy of these treatment options is under debate and needs to be evaluated in well designed RCTs. Considering the treatment of CIPN is difficult, it would be worthwhile to examine the effect of MQ on CIPN within a phase III RCT to confirm the current result.

Recent Qigong RCT studies have compared a Qigong intervention with a usual care or wait-list control group [12,17,18]. The main criticism of these studies was that the effect of Qigong may have been due to the additional care offered in the intervention group, in addition to standard care. In the current study, to control for this additional care effect, we used meditation delivered identically in terms of time and homework to the Qigong intervention for the control group.

Notably, both mind-body medicine MQ and meditation showed the potential to improve general QOL, fatigue, stress and satisfaction with sexual function in women with MBC. We observed a positive trend (non-significant) from pre to post intervention scores, but no statistically significant difference between groups. These results are consistent with our previous MQ studies [12,18], demonstrating that MQ improved QOL and fatigue, as well as Carlson et al. [13] study that suggested meditation [13] has the potential to improve QOL and reduces fatigue and stress. Thus, it may be that meditation alone is sufficient to engender positive changes, although this needs to be established in a larger phase III RCT.

Sexuality is recognized as an important factor in QOL for patients with cancer. Current cancer treatments such as surgery, chemotherapy, hormone therapy and radiation therapy all have consequences on sexuality in cancer patients [31], but this issue is generally unaddressed unless specifically raised by patients. Furthermore, treatment of female sexual dysfunction with medication

has limitations and frequent contraindications in this population (e.g. lubricants, estrogen therapy and selective serotonin reuptake inhibitor (SNRIs) [32]. Thus, mind-body medicine (MQ and meditation) may be a safe alternative for management of sexual dysfunction in women with breast cancer.

Although our results have shown that MQ is feasible and safe in women with MBC, several limitations of the current study should be noted. Firstly, peripheral neuropathy symptoms was not the primary endpoint of this study. When we recruited subjects for this study, we did not screen for neuropathic symptoms at baseline. Thus, interpretation of this result should be cautious. A further limitation was that blinding of participants to their treatment allocation was not possible due to the nature of the intervention. The inclusion of a control group was nonetheless important to compare changes between those who did and did not receive a MQ intervention, and to control for changes in self-reported outcome instruments that may occur over time without an intervention. We acknowledge that it is possible that some of the benefits reported for both the MQ intervention and the meditation control group may be due to experimental bias and confounding factors (e.g. extra care, participants' expectancy (placebo effects) and social interactions due to being a member of a group). To control for this in a future study, a third group, incorporating a non-mind-body intervention (e.g. an education group) with the same amount of contact time could be offered, although this would present logistical issues. It would also be interesting to investigate any relationship between the MQ dosage level (including home practice) and efficacy in a future study.

## Conclusion

Improving QOL of women with MBC is important for patients as well as clinicians. The results from this study suggest that a randomized controlled trial of MQ in women with MBC is feasible and safe. It also appears that MQ has the potential to relieve cancer treatment related neuropathy symptoms experienced by women with MBC, and that both mind-body MQ and meditation have a positive impact on QOL, fatigue, stress, and sexual functioning. A further study with a larger sample size and including an objective biomarker is needed to validate results and identify the mechanisms by which components of MQ achieve positive results.

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