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Complementary Medicine for Fatigue and Cortisol Variability in Breast Cancer Survivors

A Randomized Controlled Trial

Shamini Jain, PhD^{1,2}; Desiree Pavlik, BA²; Janet Distefan, PhD²; Reverend Rosalyn L. Bruyere³; Julia Acer, MBA²; Rosalie Garcia, BA²; Ian Coulter, PhD⁴; John Ives, PhD¹; Scott C. Roesch, PhD⁴; Wayne Jonas, MD¹; and Paul J. Mills, PhD²

BACKGROUND: Fatigue is a chief complaint in cancer patients, and warrants effective treatment. Biofield therapies are complementary medicine approaches used by cancer populations. There is little information about their efficacy. **METHODS:** This blinded, randomized controlled trial examined the effects of 4 weeks (eight 1-hour sessions) of biofield healing compared with mock healing and a waitlist control group on fatigue in 76 fatigued breast cancer survivors (stages I-IIIa). Secondary outcomes were diurnal cortisol variability (via estimates of cortisol slope), depression, and quality of life (QOL). Treatment belief was assessed to explore whether belief predicted outcomes. Data were analyzed via hierarchical linear modeling. **RESULTS:** There were no significant differences between biofield healing and mock healing on belief; 75% thought they received biofield healing. Compared with controls, biofield healing significantly decreased total fatigue ($P < .0005$, Cohen's $d = 1.04$), as did mock healing ($P = .02$, Cohen's $d = 0.68$), with no significant differences between biofield healing and mock healing. Cortisol slope significantly decreased for biofield healing versus both mock healing and control ($P < .04$ in both cases; Cohen's $d = 0.58$). Belief predicted changes in QOL over and above group ($P = .004$, Cohen's $d = 0.84$). Belief did not impact fatigue or cortisol variability. **CONCLUSIONS:** Nonspecific factors are important in responses to biofield interventions for fatigue. Belief predicts QOL responses but not fatigue or cortisol variability. Biofield therapies increase cortisol variability independent of belief and other nonspecific factors. There is a need to further examine the effects of specific processes of biofield healing on outcomes for cancer populations. *Cancer* 2011;000:000-000. © 2011 American Cancer Society.

KEYWORDS: biofield, healing, complementary, cortisol, fatigue, cancer, breast, immune, complementary and alternative medicine, randomized controlled trial.

INTRODUCTION

Cancer-related fatigue (CRF) is among the most frequently reported and most troublesome side effects associated with cancer and cancer treatment, and continues to be a pervasive problem even during survivorship.¹ Approximately 1/3 of patients experience significant fatigue for 10+ years post-treatment.² CRF is also associated with decreased quality of life (QOL)³ and associated but not redundant with depression and mood disturbance.⁴ Although the etiology of CRF remains unclear, CRF in breast and ovarian populations is associated with dysregulation in the hypothalamic-pituitary-adrenal axis, as indexed by decreased diurnal cortisol variability (flattened diurnal cortisol slopes).^{5,6} Flatter cortisol slopes have also been found to distinguish metastatic disease^{7,8} and predict mortality in breast cancer patients.⁹ Although CRF remains a persistent and troublesome side effect, very little is understood on how best to treat it. Overall, pharmacological treatment for CRF has not been successful.¹⁰⁻¹⁴ The majority of exercise studies have yield mixed findings with respect to CRF in survivors, with noted small effect sizes and adherence issues.¹⁵⁻¹⁷ Findings for psychosocial interventions on CRF are also mixed.¹⁸⁻²⁰

Corresponding author: Shamini Jain, PhD, Senior Scientist, Samueli Institute, 2101 East Coast Highway, Suite 300, Corona Del Mar, CA 92625-1900; sjain@samueliinstitute.org

¹Samueli Institute, Alexandria, Virginia; ²Department of Psychiatry and Behavioral Medicine, University of California San Diego, San Diego, California; ³Healing Light Center Church, Sierra Madre, California; ⁴RAND Corporation, Santa Monica, California

We thank all the cancer survivors as well as the practitioners who participated in this study, and Patricia Ganz, MD for her helpful comments on the manuscript.

DOI: 10.1002/cncr.26345, **Received:** February 10, 2011; **Revised:** April 29, 2011; **Accepted:** May 16, 2011, **Published online** Month 00, 2011 in Wiley Online Library (wileyonlinelibrary.com)

Complementary and integrative medicine approaches are often sought out by breast cancer patients and survivors, with recent estimates of use across US states ranging from 28% to 73%.^{21,22} Biofield therapies are complementary and integrative medicine modalities often used by breast cancer patients,²³ and have been described as therapies that are intended to affect energy fields that purportedly surround and penetrate the human body for the purposes of healing.²⁴ These therapies include Reiki, Therapeutic Touch, Healing Touch, and others. Patients often report that they use these and other complementary and integrative medicine therapies to enhance physical, emotional, and spiritual QOL as well as to reduce stress and enhance the immune system.²³ However, there is a relative dearth of high-quality studies that have examined these approaches for the treatment of cancer-related symptoms.

The purpose of this study was to examine within a blinded randomized controlled trial (RCT) design whether a biofield therapy (hands-on-healing) would significantly reduce fatigue in survivors with persistent CRF, as compared with mock healing and a waitlist control group. Secondary outcomes included cortisol variability as well as depression and QOL. Finally, an exploratory aim was to examine whether belief itself predicted intervention responses.

MATERIALS AND METHODS

Recruitment, Eligibility, Screening, and Enrollment

Recruitment and enrollment took place between March 2006 and October 2009. Participants were recruited via brochure mailings from the University of California San Diego Moores Cancer Center, local brochure distributions, presentations to support groups, and a study website. Participants were screened by telephone for eligibility. Eligibility criteria follow: female breast cancer survivors between 18 and 70 years of age, ability to give informed consent, completion of adjuvant/neoadjuvant therapy for breast cancer (including surgery, radiation, and/or chemotherapy) 1 month to 10 years prior, and diagnosed stage I to IIIa. Patients were also screened for fatigue via the RAND SF-36 vigor-fatigue subscale.²⁵ We used the previously established cutoff score of <50 to screen for fatigue.²⁵ Exclusion criteria included current or planned radiation/chemotherapy/surgery, uncontrolled disease known to affect fatigue (eg, sleep apnea, thyroid disorder, diabetes, lupus, rheumatoid arthritis), history of

other cancers/stage IV cancer, male patients, or current use of another biofield-based intervention. All enrolled participants signed informed consent. The study was approved by University of California San Diego and San Diego State University institutional review boards.

Overview of Research Design

This was a phase 2, randomized, intention-to-treat clinical trial with fatigued breast cancer survivors randomized to either biofield healing, mock healing, or waitlist control. Survivors were informed that they would have a chance of being randomly assigned either to a group that received sessions (termed *hands-on healing* or *touch alone*) or to a waitlist control group. They were further informed that if assigned to receive sessions, these would be in silence, and they would not be told which group they were assigned to until the end of the intervention. After all data were collected and group assignment was disclosed, those in the mock healing and waitlist control groups were offered 5 hands-on healing sessions at no cost.

Participants were randomized using a computer-generated randomization table. A statistician not affiliated with the study generated this table, stratified by numbers needed per group (ie, $n = 30$ each for biofield healing and mock healing, and $n = 20$ for control). Group assignment for each participant was placed in opaque, sealed envelopes. Envelopes remained unopened until group assignment for a participant became necessary. Principal investigators were blinded to participant randomization both during the study process and in data analyses (group status was coded with random numbers until data analyses were completed, at which point the group assignment was revealed).

Intervention and Practitioners

The intervention period lasted 4 weeks, with 8 sessions (2 per week) given for both biofield healing and mock healing. Each session took place at the University of California San Diego General Clinical Research Center and was of 1 hour duration. Waitlist control participants provided questionnaire and salivary cortisol data during the 4-week intervention period. There were 8 total practitioners (4 biofield healing, 4 mock healing).

The specific technique used in the biofield healing group is termed *energy chelation*, and was selected by 1 of the authors (R.L.B.), whose healing techniques have been incorporated in modalities such as Healing Touch and Therapeutic Touch.^{26,27} During energy chelation, the practitioner practices hands-on healing with standard

hand positions, beginning with hands on the feet, then to the knees, hips, bladder area, stomach, hands, elbows, shoulders, heart, throat, head, and back to the heart. The practice of energy chelation is 45 to 60 minutes, with a practitioner generally focusing for 5 to 7 minutes on each position.

Mock healing practitioners were skeptical scientists who were trained to use the identical hand placements as biofield healing practitioners. Mock healing practitioners were asked not to intend to heal the patient when touching, but rather to disengage into “planning mind” by contemplating current and upcoming research-oriented studies and grants they were currently involved in. Given that biofield healing practitioners would have more familiarity with working with patients than mock healing practitioners, to preserve participant blinding mock healing practitioners practiced procedures with study personnel until the mock healing practitioner demonstrated mastery of the hand placements and confidence interacting with and fielding potential questions that a patient might ask the mock healing practitioner before or after the session. To maintain blinding of other General Clinical Research Center study personnel, all interviews for practitioner selection as well as training were conducted in a closed room, and practitioners were introduced to staff by name only.

Outcome Measures

Self-report questionnaires

Multidimensional Fatigue Symptom Inventory-short form

The Multidimensional Fatigue Symptom Inventory-short form is a 30-item questionnaire that provides a total fatigue score as well as subscales assessing vigor and general, emotional, mental, and physical aspects of fatigue. Mean Multidimensional Fatigue Symptom Inventory-short form total score values in a combined sample of breast cancer patients and survivors were reported as 8.12, whereas means in a female noncancer population were 0.85.²⁸ The Multidimensional Fatigue Symptom Inventory-short form has good reliability and validity, as well as sensitivity to change.²⁹

Center for Epidemiological Studies Depression Scale-revised

The Center for Epidemiological Studies Depression Scale-revised is a 20-item gold standard depression scale, showing excellent reliability and validity in several popu-

lations, including cancer patients.^{30,31} Scores >16 are indicative of major depression.

Functional Assessment of Cancer Therapy-Breast

The Functional Assessment of Cancer Therapy-Breast (FACT-B) is a 44-item scale specifically designed to measure QOL and functional outcome in breast cancer. We used the trial outcome index, which summates the physical well-being, functional well-being, and specific concerns subscales.³²

Demographics and disease

To track characteristics of participants in each group as well as to control for potential covariates, participants provided demographic and treatment information at their preintervention visit (see Table 1).

T1

Biofield Therapies Use and Expectancies Questionnaire

This questionnaire was administered at the beginning of the study, before group assignment. Participants noted any experience with giving or receiving any type of biofield/spiritual healing technique. They then rated on a 5-point Likert scale how much they believed that hands-on-healing would help to 1) reduce their fatigue, 2) improve their mood, and 3) improve their well-being.

Treatment and Practitioner Rating Questionnaire

This questionnaire was administered at the end of each session (visits 2-9) for those in the biofield healing and mock healing groups. Participants were asked to guess which treatment (termed *hands-on-healing* or *touch alone*) they had just received and then rate (on a 5-point Likert scale) their feelings 1) of practitioner warmth and friendliness, 2) of connection with the practitioner, 3) that the treatment was helping with their fatigue, 4) that the treatment was helping their immune system, and 5) that the treatment was improving their well-being.

Cortisol measurement

Diurnal cortisol variability was determined via calculation of cortisol slope, by standard, previously described methods.^{6,33} Saliva was collected at 4 time points (awakening with time noted, 12 noon, 5 PM, and 9 PM) over 2 days at preintervention and postintervention (V1 and V9, respectively) for all groups. In addition, the mock and healing groups also provided saliva samples over a 2-day course at mid intervention (after visit 5, after the fourth session). Participants were instructed on the

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Table 1. Baseline Characteristics of 76 Female Breast Cancer Survivors: Means (Ranges) for Continuous Variables and Percentages for Categorical Variables

Characteristic	Healing, n=27	Mock, n=30	Control, n=19	P
Age, y	52 (36-75)	52 (31-69)	50 (29-69)	.62
Education, y	16 (12-20)	16 (11-20)	16 (12-20)	.74
BMI	26.8 (19.1-40.3)	28.5 (17.3-43.5)	27.9 (18.7-50.8)	.63
Menopausal status				.31
Premenopausal	18.5%	13.4%	26.3%	
Postmenopausal	81.5%	86.6%	73.6%	
Ethnicity				.034 [CA vs non-CA]
CA	88.9%	86.6%	52.9%	
Hispanic/Latino	3.7%	6.7%	21.0%	
African American	3.7%	6.7%	5.3%	
Native American	3.7%	0%	15.8%	
Cancer stage				.76
0/DCIS	3.7%	6.7%	10.5%	
I	44.4%	43.3%	26.3%	
II	33.3%	23.3%	36.8%	
IIIA	11.1%	23.3%	26.3%	
Unknown	7.4%	3.3%	0%	
Cancer grade				.49
1	44.4%	40.0%	15.8%	
2	25.9%	26.7%	26.3%	
3	22.2%	20.0%	31.6%	
Unknown	7.5%	13.3%	26.3%	
Time since diagnosis, mo	30 (7-82)	27 (6-80)	39 (3-117)	.25
Time since surgery, mo	27 (2-78)	22 (2-77)	33 (2-108)	.34
Received radiation	59.3%	66.7%	52.6%	.78
Time since radiation, mo	22 (2-72)	19 (2-78)	32 (4-96)	.39
Received chemotherapy	77.8%	66.7%	63.6%	.60
Time since chemotherapy, mo	25 (3-76)	16 (4-72)	35 (2-96)	.09
Current use tamoxifen	29.6%	26.7%	26.3%	.90
Current use aromatase inhibitors	37.0%	40.0%	15.8%	.24
Baseline (preintervention) questionnaire scores				
MFSI-sf total	29.7	30.6	26.1	.71
CESD	21.4	20.5	18.2	.63
FACT-B	59.2	58.5	58.2	.92

Abbreviations: BMI, body mass index; CA, Caucasian American; CESD, Center for Epidemiological Studies Depression Scale; DCIS, ductal carcinoma in situ; FACT-B, Functional Assessment of Cancer Therapy-Breast; MFSI-sf, Multidimensional Fatigue Symptom Inventory-short form.

proper use and storage of the salivettes, including refraining from eating, smoking, and consuming caffeine for 2 hours before use. Samples were collected from the participant and centrifuged, and supernatants were then frozen until assayed for cortisol, via enzyme-linked immunosorbent assay.³⁴

All cortisol processing was conducted by University of California San Diego General Clinical Research Center Core Laboratory personnel who were blinded to group assignment. Samples were assayed in 3 batches over the study period, with samples from each group represented in each batch. Cortisol assay performance characteristics were as follows: interassay coefficients (CVs) of variation,

1.1% to 11%; intra-assay CV, 6.1%. Sensitivity was 0.003 μ g/dL. All saliva samples from a single subject were assayed together to avoid effects of interassay variation. Slopes of change over time were calculated by regressing log-transformed cortisol values on the 4 times of day for each day of collection; these data were then averaged and entered as outcome measures in analyses.

Statistical Analysis Strategy

Power analyses

G-Power was used to conduct power analyses for sample size for 3 groups and 5 planned time points of Multidimensional Fatigue Symptom Inventory-short

form scores, and a small estimated effect size ($f^2 = .01$). A total of 65 participants were needed; to account for effects of ~20% attrition, we planned to study 80 participants. We elected to stratify our sample to recruit 30 participants in the mock healing and biofield healing groups, and 20 for a control group.

Data analyses for outcome variables

Group equivalence (t test and chi-square), distributions, and potential outliers (z scores >3) were tested using SPSS version 17 (SPSS Inc., Chicago, Ill). Demographic and disease variables were examined as covariates and were entered into the model if significantly associated ($|r| > 0.2$ and $P < .05$) with outcome variables. Data were analyzed via intention-to-treat analyses using hierarchical linear modeling (HLM 6; Scientific Software International, Lincolnwood, Ill) with previously described procedures.^{35,36} HLM is advantageous over other repeated measures approaches (ie, repeated measures analysis of variance), as it does not assume homogeneity of slopes, and more robustly accounts for missing data to enable more accurate intention-to-treat analyses.³⁷ Effect sizes were calculated using Cohen's d using the standard formula: $d_{IGPP} = (M_{post, E} - M_{pre, E}) / SD_{pre, E} - (M_{post, C} - M_{pre, C}) / SD_{pre, C}$.

RESULTS

All self-report data were of normal distribution with no outliers. Cortisol data were log-transformed to obtain a normal distribution. There was 1 cortisol outlier with implausible values (z score = 7.5) that was excluded from analysis.

Enrollment and Attrition

F1 Figure 1 depicts the CONSORT flow diagram for participants through the study. Of the 125 inquires, 9 were ineligible. Forty chose not to participate, citing scheduling or commuting distance as factors, leaving a remaining 76 participants. Overall attrition was 9%, with no differential attrition between groups. No adverse events were reported.

Demographic and Disease Characteristics

Table 1 depicts demographic and disease characteristics for the 3 groups. Chi-square analysis revealed significant differences in ethnicity ($P = .034$), with fewer Caucasians in control versus other groups. There were no other significant baseline differences between groups for any other variable or outcome measure. Prior chemotherapy was sig-

nificantly associated with higher Multidimensional Fatigue Symptom Inventory-short form and Center for Epidemiological Studies Depression Scale, and lower FACT-B scores (respective r 's = .31, .28, and -.30). Chemotherapy was therefore entered as a covariate in all self-report outcome analyses. There were no covariates for cortisol measures. Mean baseline scores of the Multidimensional Fatigue Symptom Inventory-short form, Center for Epidemiological Studies Depression Scale, and FACT-B trial outcome index were 29.2, 20.1, and 58.7, respectively, indicating that these survivors had clinically significant and severe fatigue and depression, and low QOL.

Treatment Use, Expectancy, and Belief

Chi-square analyses revealed that nearly half (49%) of participants reported previous use of a biofield therapy, with no differences between groups. There were no differences on baseline (prerandomization) expectancy ratings.

During-session belief ratings revealed that 75% of women receiving sessions believed they were receiving healing, regardless of group assignment. There were no significant differences between biofield healing and mock healing groups in treatment belief, nor were there differences between groups in ratings of nonspecific factors (ie, friendliness of practitioner, feeling of connection with practitioner, feeling that treatment was helping them with fatigue, immunity, and/or well-being; $P > .2$ in all cases). By t tests it was revealed that survivors who believed they received healing did not differ from those who did not believe they received healing on nonspecific factors (ie, friendliness of practitioner, feeling of connection with practitioner; $P > .6$ in both cases).

HLM Results for Psychological Measures

Unconditional linear growth models

To examine time effects for each individual participant, we ran unconditional linear growth models (with repeated-measures scores for each participant entered as the dependent variable and time modeled as number of weeks as a level 1 predictor variable). Analyses suggested that time was significantly related to both Multidimensional Fatigue Symptom Inventory-short form total and FACT-B trial outcome index scores ($b = -2.15$, $P < .0005$ and $b = .98$, $P < .0005$, respectively), but not Center for Epidemiological Studies Depression Scale scores ($b = -17$, $P = .31$). This suggested that the passage of time predicted changes for the overall sample for fatigue and QOL, but not depression.

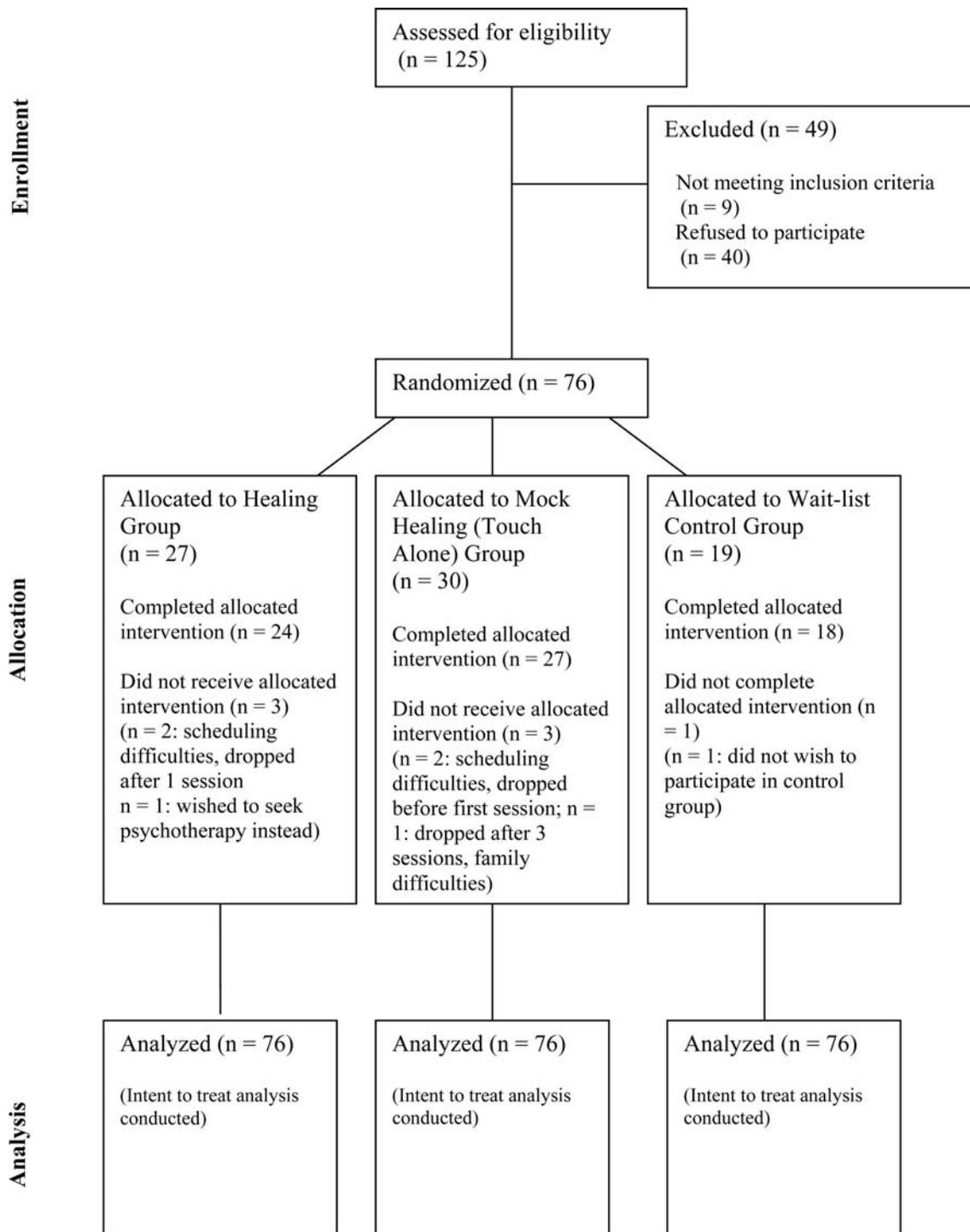


Figure 1. CONSORT flow diagram.

Conditional linear growth model with type of group as higher order predictors

To test for group × time effects on fatigue, a conditional linear growth model examined group status as a

level 2 predictor of level 1 Multidimensional Fatigue Symptom Inventory-short form time slope (with prior chemotherapy use as a level 2 covariate). A significant difference was found between control and biofield healing

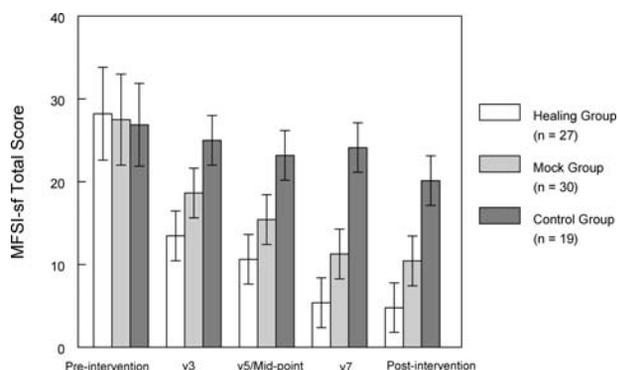


Figure 2. Depiction of group by time interaction for MFSI-sf Total Fatigue scores. Significant reductions were found for both the healing group ($P < .0005$, Cohen's $d = 1.04$) and the mock group ($P < .02$, Cohen's $d = .68$) compared to the wait-list control group. Belief did not affect outcomes.

($b = -2.0$, $P < .0005$), as well as between control and mock healing ($b = -1.3$, $P = .02$), with no difference between biofield healing and mock healing ($b = 0.70$, $P = .12$). Differences were characterized by a steep decrease in Multidimensional Fatigue Symptom Inventory-total fatigue over time for biofield healing versus control (Cohen's $d = 1.04$), a notable decrease in fatigue for mock healing versus control (Cohen's $d = 0.68$), and no significant change in fatigue for control. This is depicted in Figure 2.

F2

To better determine the effects of biofield healing and mock healing on specific dimensions of fatigue, we examined effects on Multidimensional Fatigue Symptom Inventory-short form subscales. For general fatigue, there were significant group \times time differences between biofield healing and control ($b = -0.9$, $P < .0005$), between mock healing and control ($b = -0.47$, $P = .04$), and between biofield healing and mock healing ($b = -0.43$, $P = .03$), with biofield healing showing significant decreases in general fatigue over time compared with both groups, and mock healing showing significant decreases in general fatigue compared with control. Biofield healing was also significantly decreased for mental ($P = .04$) and physical ($P = .016$) fatigue over time compared with control, with no differences between mock healing versus control nor biofield healing versus mock healing on these subscales. Biofield healing and mock healing both showed significant increases in vigor over time compared with control ($P < .04$ in both cases), but biofield healing and mock healing were not significantly different from each other. There were no differences between groups on the emotional fatigue subscale. Means and standard deviations for the Multidimensional Fatigue Symptom Inventory-short form are depicted in Table 2.

T2

For QOL, group status predicted changes in FACT-B over time, such that biofield healing scores increased over time, whereas control scores did not significantly change ($b = 1.22$, $P = .01$; Cohen's $d = 0.76$). There were no differences between biofield healing and mock healing ($b = 0.7$, $P = .10$), or mock healing and control ($b = 0.5$, $P = .3$). There were no interactions for the Center for Epidemiological Studies Depression Scale. Means and standard deviations for the FACT-B and Center for Epidemiological Studies Depression Scale are found in Table 3.

T3

Exploring Effects of Treatment Belief on Outcomes

A second conditional linear model was run for the mock healing and biofield healing groups with group status (biofield healing vs mock healing), belief status (believed hands-on healing vs believed touch alone), and a group \times belief interaction term as level 2 predictors and chemotherapy as a covariate. There were no significant effects of belief for Multidimensional Fatigue Symptom Inventory-short form or Center for Epidemiological Studies Depression Scale scores. However, belief predicted FACT-B changes over time, ($b = 1.6$, $P = .004$; Cohen's $d = 0.84$) over and above group status ($b = 0.3$, $P = .44$). This interaction, depicted in Figure 3, was characterized by increases in FACT-B scores for participants who believed they received healing, with participants who did not believe they received healing showing little change.

F3

HLM Results for Cortisol

A similar HLM setup as described above was conducted for cortisol slope. In the conditional growth model predicting group \times time interactions for cortisol slope, a significant difference was found for cortisol slope changes between biofield healing and control ($b = -0.07$, $P = .004$, Cohen's $d = 0.58$) and between biofield healing and mock healing ($b = -0.06$, $P = .039$, Cohen's $d = 0.36$), with no difference between mock healing and control ($b = -0.02$, $P = .39$). This interaction was characterized by a significant decrease in cortisol slope over time for the biofield healing versus both mock healing and control. Belief did not predict outcomes ($P > .5$). Means and standard deviations for cortisol slopes are shown in Table 3.

To explore what drove the decreased slope found for the biofield healing versus other groups, we ran a conditional HLM model with group as a predictor of pre-post intervention changes in cortisol levels for each collection time point (ie, awakening, 12 PM, 5 PM, 9 PM). A

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Table 2. Means (95% Confidence Intervals) for MFSI-sf Fatigue Total Score and Subscales

MFSI-sf Scale	Healing, n=27	Mock, n=30	Control, n=19
MFSIsf total preintervention	27.4 (20.1, 34.7)	28.1 (21.1, 35.1)	27.1 (18.3, 36.0)
MFSIsf total after session 2	12.9 (5.4, 20.5)	19.0 (11.8, 25.3)	25.1 (16.0, 34.4)
MFSIsf total midpoint	10.0 (2.1, 17.9)	15.9 (8.3, 23.4)	23.4 (13.8, 33.0)
MFSIsf total after session 6	4.8 (-2.4, 11.9)	11.7 (4.9, 18.5)	24.3 (15.6, 33.0)
MFSIsf total postintervention	4.2 (-3.9, 12.3)	10.9 (3.1, 18.6)	20.3 (10.4, 30.2)
MFSI-sf subscales			
General preintervention	15.9 (13.4, 18.0)	15.1 (13.1, 17.1)	15.3 (12.8, 17.9)
General after session 2	9.9 (7.2, 12.7)	11.3 (8.6, 13.9)	14.3 (11.0, 17.7)
General midpoint	8.1 (5.2, 11.0)	10.8 (8.0, 13.6)	13.9 (10.3, 17.5)
General after session 6	6.1 (3.4, 8.9)	9.2 (6.5, 11.8)	14.4 (11.1, 17.8)
General postintervention	6.3 (3.5, 9.2)	9.3 (6.6, 12.1)	13.5 (10, 16.9)
Physical preintervention	6.5 (4.5, 8.6)	7.3 (5.4, 9.3)	7.4 (4.9, 9.8)
Physical after session 2	4.3 (2.4, 6.2)	5.9 (4.1, 7.7)	6.6 (4.4, 8.9)
Physical midpoint	3.9 (1.9, 5.8)	5.5 (3.6, 7.4)	6.8 (4.4, 9.2)
Physical after session 6	2.8 (1.2, 4.5)	4.1 (2.5, 5.7)	5.9 (3.9, 7.9)
Physical postintervention	2.6 (0.8, 4.5)	4.2 (2.4, 5.9)	5.4 (3.1, 7.6)
Emotional preintervention	6.7 (4.7, 8.7)	6.0 (4.0, 8.0)	6.4 (3.9, 8.8)
Emotional after session 2	4.3 (2.3, 6.3)	4.6 (2.7, 6.5)	5.9 (3.4, 8.3)
Emotional midpoint	4.2 (2.2, 6.2)	4.0 (2.0, 5.5)	5.0 (2.5, 7.4)
Emotional after session 6	3.7 (1.9, 5.5)	3.8 (2.0, 5.4)	5.4 (3.2, 7.5)
Emotional postintervention	3.4 (1.5, 5.2)	3.2 (2.1, 5.7)	4.3 (2.0, 6.6)
Mental preintervention	8.2 (6.1, 10.2)	8.1 (6.1, 10.1)	8.2 (5.7, 10.7)
Mental after session 2	5.4 (3.5, 7.2)	6.7 (5.0, 8.6)	7.3 (5.0, 9.5)
Mental midpoint	5.1 (3.1, 7.1)	6.0 (4.1, 7.9)	6.3 (3.9, 8.8)
Mental after session 6	3.8 (2.1, 5.5)	5.2 (3.5, 6.7)	6.6 (4.5, 8.6)
Mental postintervention	3.7 (1.9, 5.6)	4.8 (3.0, 6.5)	5.9 (3.6, 8.0)
Vigor preintervention	9.9 (8.2, 11.6)	8.5 (6.8, 10.1)	10.2 (8.0, 12.3)
Vigor after session 2	11.0 (9.3, 12.5)	9.5 (8.0, 11.0)	8.9 (7.0, 10.8)
Vigor midpoint	11.3 (9.4, 13.2)	10.3 (8.5, 12.2)	8.6 (6.2, 10.9)
Vigor after session 6	11.7 (9.7, 13.6)	10.5 (8.6, 12.3)	8.0 (5.6, 10.3)
Vigor postintervention	11.3 (9.1, 13.5)	11.1 (9.0, 13.2)	8.7 (6.0, 11.3)

Abbreviation: MFSI-sf, Multidimensional Fatigue Symptom Inventory-short form.

Table 3. Means (95% Confidence Intervals) for Cortisol Indices, FACT-B, and CESD by Group

Cortisol Index/Test	Healing, n = 27	Mock, n = 30	Control, n = 19
Cortisol slope preintervention	-1.4 (-1.8, -.98)	-1.4 (-1.8, -.93)	-1.3 (-1.8, -.89)
Cortisol slope total midpoint	-1.6 (-1.9, -1.2)	-1.5 (-1.8, -1.1)	n/a
Cortisol slope total postintervention	-1.8 (-2.2, -1.4)	-1.3 (-1.7, -.81)	-1.1 (-1.5, -.67)
FACT-B TOI preintervention	59.2 (55.3, 63.0)	58.5 (53.7, 63.1)	58.2 (50.9, 65.5)
FACT-B TOI total midpoint	66.5 (61.9, 71.2)	64.2 (60.4, 67.9)	61.1 (53.7, 68.5)
FACT-B TOI total postintervention	68.8 (64.8, 72.8)	66.2 (61.4, 71.12)	63.0 (55.3, 70.7)
CESD preintervention	19.6 (15.2, 24.0)	20.2 (16.0, 24.4)	18.4 (13.3, 23.4)
CESD midpoint	18.3 (13.6, 23.0)	20.2 (15.7, 24.6)	17.3 (23.0, 22.6)
CESD postintervention	17.0 (12.3, 21.7)	20.4 (16.0, 24.9)	16.4 (11.0, 21.7)

Abbreviations: CESD, Center for Epidemiological Studies Depression Scale; FACT-B, Functional Assessment of Cancer Therapy-Breast; n/a, not applicable; TOI, total outcome index.

significant difference was found between biofield healing and controls ($b = 0.05, P = .037$), such that biofield healing showed increased awakening cortisol levels from pre to post-intervention, compared with controls. A similar,

although nonsignificant, effect was found for biofield healing versus mock healing. Mean cortisol slopes at pre-intervention and postintervention for the 3 groups are depicted in Figure 4.

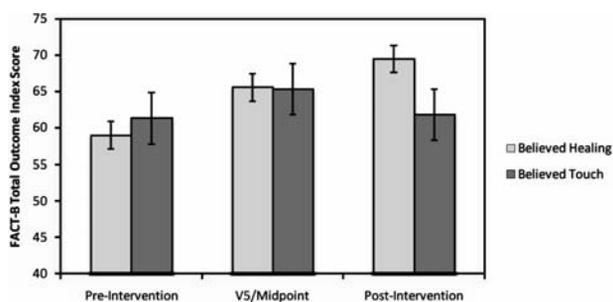


Figure 3. Depiction of group by time interaction of belief on quality of life scores. Survivors who believed they received healing showed significant increases in quality of life from pre to post-intervention, compared to survivors who did not believe they received healing ($P = .004$, Cohen's $d = .84$). Results were independent of group status.

DISCUSSION

This RCT examined whether biofield healing, compared with both active (mock healing) and waitlist control groups, positively affected fatigue as well as cortisol slope, depression, and QOL in breast cancer survivors with persistent fatigue. In addition, this study explored the role of belief in receiving healing as a potential predictor of responses. Findings indicate that both touch-based interventions reduce fatigue in fatigued breast cancer survivors, with considerable effect sizes. Previous research by our group on a separate sample of breast cancer patients indicated that the mean Multidimensional Fatigue Symptom Inventory-short form total scores was 5.99 immediately before the start of anthracycline-based chemotherapy, and rose to 19.9 immediately before the fourth cycle.³⁸ Our fatigued survivors in the mock healing group (mean post-intervention score = 10.9) dropped to fatigue scores lower than those found for breast cancer patients toward the end of chemotherapy, and the biofield healing group (mean postintervention score = 4.2) fell to fatigue scores that were below prechemotherapy scores, as well as below previously published means noted for breast cancer patients overall.²⁸ This drop in fatigue appears to have clinical as well as statistical significance. Given that both active groups showed significant fatigue reductions but that belief did not predict fatigue ratings, results suggest that biofield healing effects on reducing fatigue may be partially because of nonspecific factors (eg, scheduled rest, touch, clinical interaction) but not belief. However, besides the notably larger effect size found for biofield healing on total fatigue, the significant differences between biofield healing and mock healing on general fatigue (the most reliable and valid subscale of the Multidimensional Fatigue Symptom Inventory-short form²⁸) and the significant impact of biofield healing on physical and mental fatigue suggest that biofield healing may be more effective in reducing fatigue than mock healing. This finding warrants further study for replication and examination of specific processes that may underlie biofield healing effects on fatigue. The notable effects of mock healing on fatigue also suggest that utilization of nonspecific factors

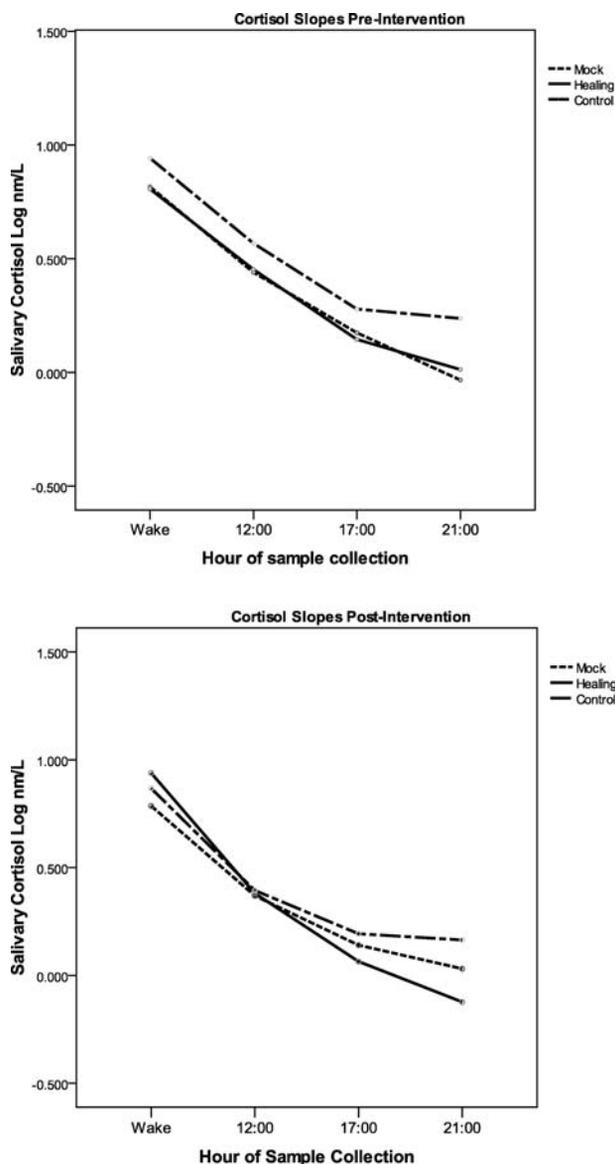


Figure 4. Graphical depiction of group by time interactions of diurnal salivary cortisol slopes at pre-intervention and post-intervention. The biofield healing group showed significantly decreased cortisol slope (increased variability) compared to both mock and control groups ($P < .04$ in both cases). Belief did not impact results.

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(touch, rest, and therapeutic interaction) may be of value and could be incorporated within other modalities (eg, massage) for these patients.

The significant decrease in cortisol slope for the biofield healing versus mock healing and control groups suggests that the impact of biofield healing on cortisol variability is not simply because of nonspecific effects such as rest, clinical interaction, and touch. Moreover, belief did not impact outcomes on this variable. Increases in variability found for the biofield healing group appeared to be driven by increased rising cortisol levels. This is particularly interesting given previous reports of decreased morning cortisol levels in fatigued versus non-fatigued breast cancer survivors.³⁹ If replicated with follow-up, our preliminary results on the significant impact of biofield healing on increasing cortisol variability suggest positive endocrine benefits that may improve symptomatology in this population. The heterogeneity in our sample of fatigued breast cancer survivors in terms of stages, time since diagnosis, and previous treatment suggest that these results may be generalizable to a large distribution of fatigued breast cancer survivors.

Our results on the large predictive impact of belief on QOL are particularly interesting in the context of evidence linking QOL ratings with survival and recurrence in breast and other populations,^{40,41} and the numerous studies demonstrating the positive impact of numerous placebo-controlled approaches on QOL in cancer. Our study suggests the need to directly assess patients' belief in treatment efficacy when assessing the impact of interventions on QOL.

Interestingly, we found no evidence for efficacy of biofield healing or mock healing on depression for our sample. Our findings are in contrast to those reported by Lutgendorf et al,⁴² who reported significant reductions in depression (but not fatigue) for cervical cancer patients receiving Healing Touch while undergoing chemoradiation. It should be noted that the interventions of these 2 studies were different by population, timing of intervention, biofield modality, and method of practice (Lutgendorf et al's study allowed for dialogue between practitioner and patient, whereas our interventions were conducted in silence).

There are noted limitations to this study, including lack of follow-up assessment, a relatively modest sample size, and lack of generalizability to other cancer populations. Some of this study's strengths include the inclusion of an active control group to assess nonspecific factors as well as a waitlist control group, explicit analysis of the

effect of belief factors on outcomes, a dose-response design, and clinically relevant biological endpoints. Finally, we note that our overall attrition in this study was relatively low (9.3%), suggesting that further intervention studies in this area may be well received.

Overall, our results suggest that biofield healing may be a promising intervention for ameliorating cancer-related fatigue, and that it warrants further study. Effects of biofield healing on fatigue may in part to be because of nonspecific factors such as touch and rest, but not belief. Biofield healing's effects on increasing cortisol variability appear to be independent of nonspecific factors such as rest and touch as well as belief. Potential mechanisms remain to be elucidated. Finally, belief factors appear to play a major role in quality of life responses to both biofield healing and touch. Further investigation of specific and nonspecific factors in the study of biofield healing for cancer-related fatigue is warranted.

FUNDING SOURCES

This research was funded by National Institutes of Health/National Center for Complementary and Alternative Medicine F31AT003021, National Institutes of Health/National Center for Research Resources MO1RR-00,827, and the Samuelli Institute.

CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

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Complementary Medicine for Fatigue and Cortisol Variability in Breast Cancer Survivors: A Randomized Controlled Trial

Shamini Jain, Desiree Pavlik, Janet Distefan, Reverend Rosalyn L. Bruyere, Julia Acer, Rosalie Garcia, Ian Coulter, John Ives, Scott C. Roesch, Wayne Jonas, and Paul J. Mills

Results from this study suggest that biofield and mock healing reduce fatigue, and that biofield healing alone increases cortisol variability in fatigued breast cancer survivors. Belief in receiving healing significantly predicts improvements in quality of life (but not fatigue or cortisol variability) in response to touch-based interventions.