ELSEVIER

Journal of Psychosomatic Research 57 (2004) 45–52

Journal of Psychosomatic Research

Breast cancer patients have improved immune and neuroendocrine functions following massage therapy

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Received 22 August 2002; accepted 11 June 2003

Abstract

Objectives: Women with breast cancer are at risk for elevated depression, anxiety, and decreased natural killer (NK) cell number. Stress has been linked to increased tumor development by decreasing NK cell activity. The objectives of this study included examining massage therapy for women with breast cancer for (1) improving mood and biological measures associated with mood enhancement (serotonin, dopamine), (2) reducing stress and stress hormone levels, and (3) boosting immune measures. **Methods:** Thirty-four women (M age = 53) diagnosed with Stage 1 or 2 breast cancer were randomly assigned postsurgery to a massage therapy group (to receive 30-min massages three times per week for 5 weeks) or a control group. The massage consisted of stroking, squeezing, and stretching techniques to the head, arms, legs/feet, and back. On the first and last day of the study, the women were assessed on (1) immediate effects measures of anxiety, depressed mood, and vigor and (2) longer term effects on depression, anxiety and hostility, functioning, body image, and avoidant versus intrusive coping style, in addition to urinary catecholamines (norepinephrine, epinephrine, and dopamine) and serotonin levels. A subset of 27 women (n = 15 massage) had blood drawn to assay immune measures. **Results:** The immediate massage therapy effects included reduced anxiety, depressed mood, and anger. The longer term massage effects included reduced depression and hostility and increased urinary dopamine, serotonin values, NK cell number, and lymphocytes. **Conclusions:** Women with Stage 1 and 2 breast cancer may benefit from thrice-weekly massage therapy for reducing depressed mood, anxiety, and anger and for enhancing dopamine, serotonin, and NK cell number and lymphocytes.

Keywords: Massage therapy; Breast cancer; Natural killer cell number; Depression; Serotonin; Stress

Introduction

Breast cancer strikes one in every nine women in the United States [1] and is the leading cause of cancer death for women between the ages of 15 and 54 [2]. Psychological studies on women with breast cancer reveal that they are at risk for depression [3,4], elevated stress/anxiety levels [5,6], and anger [6].

Psychological stress has been correlated with lower natural killer (NK) cells and NK cell activity in women with breast cancer [7]. Reduced NK cells may present a significant problem inasmuch as these cells play an important role in anticancer defense by lysing tumor and virus-infected cells, as well as monitoring and combating neoplastic (new and abnormal) growth [8,9]. In one breast cancer study, higher NK cell activity predicted to lower cancer recurrence

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0022-3999/04/$ – see front matter
doi:10.1016/S0022-3999(03)00500-2

at a 5-year follow-up [10]. In another study, 30% of NK activity level variance could be accounted for by psychological stress [7].

Research also reveals that breast cancer patients have reduced NK cell number [8] and that stress increases tumor development by decreasing NK cell activity [8,11]. Because psychological stress has been shown to negatively impact immune response, reducing stress would be expected to positively impact the immune system (for a review, see Ref. [12]).

Studies on psychological interventions for boosting the immune response of cancer patients reveal positive effects from hypnosis [13], stress-management intervention [14–16], and cognitive behavioral therapies (for a review, see Ref. [17]). The positive effects from these interventions might relate to reduced cortisol stress hormone level, which would indicate healthier neuroendocrine functioning [18].

Massage therapy may provide another treatment for reducing psychological stress and enhancing immune function for the breast cancer patient in that massage has been shown to (1) increase NK cell number and NK cell activity in men [19] and adolescents with HIV [20] and (2) attenuate psychological stress and neuroendocrine (stress-related) levels in varying conditions (for a review, see Ref. [21]).

One mechanism underlying the enhanced immune function from massage may result from the relaxing effects of massage as evident by decreased stress hormone (cortisol) and catecholamine (norepinephrine, epinephrine) levels reported in other massage therapy studies [22,23]. Decreased cortisol levels would relate to increased NK cells, as cortisol is noted to destroy NK cells [24]. Massage therapy has also been associated with improved mood and increased serotonin (5-HIAA) and dopamine levels, which would also decrease cortisol levels and thereby increase NK cells [21].

Thus, that massage therapy research reveals positive effects on the immune and the neuroendocrine systems and reduces psychological stress provided the rationale for this study to examine massage effects for women with breast cancer, and inasmuch as that massage therapy effects have not been studied for this group. Although no evidence exists suggesting that an increase in NK cells leads to clinical benefits that can be experienced by the patient, in that massage therapy has been associated with reduced stress and depressed mood would be of clinical importance to the cancer patient. Moreover, in that in our experience with different age groups and medical conditions, no adverse effects have been associated with massage, suggests the potential of massage therapy as a noninvasive, relaxing, and safe treatment for women with cancer.

The specific aim of this study was to assess, via a randomized control design, the effects of 5 weeks of massage therapy (15 massage sessions) on the immune, neuroendocrine, and perceived stress of women with early stages of breast cancer. The hypotheses included that the massage therapy group would report reduced stress and depression levels and show reduced urinary cortisol and increased serotonin, dopamine, and plasma NK cell number and NK activity compared to the control group.

Method

Participants

The HIV men's study demonstrated an effect of massage on NK cytotoxicity with a subset of 17 subjects. A power analysis indicated 80% power to detect a medium to large effect size (.70) for an alpha of .05, two tailed on the immune measure. To accommodate the large number of variables, we intended a sample size of 34 participants (or double the HIV men's sample size). The study was submitted to and approved by the University of Miami's Institutional Review Board.

The inclusion criteria included Stage 1 or 2 breast cancer diagnosis within the past 3 years and at least 3 months postsurgery, chemotherapy, and/or radiation therapy. Participants were not enrolled into the study until at least 3 months postcompletion of their radiation and/or chemotherapy treatments because radiation and chemotherapy affect immune measures. Moreover, because breast cancer patients have been shown to have impaired NK cell cytotoxicity (NKCC) after surgery [25], women were not enrolled into the study until at least 3 months after reconstructive surgery, if this was planned. Exclusion criteria included lymphoma, drug or alcohol abuse, smoking, psychiatric disorders (e.g., bipolar, schizophrenia), other medical condition (e.g., lupus), and use of beta blockers, as these also have been shown to alter immune response. Subjects on psychotropic medications, thyroid pills, or SSRIs who had been on these medications for at least 3 months were enrolled if they met the other inclusion/exclusion criteria and if they had no plans of starting or discontinuing their medication during the study period. Inclusion/exclusion criteria were determined based on a structured interview.

The women were screened for medications and whether they were taking herbs/vitamins/minerals during the study period. Chi-square analyses revealed no group differences on these. Overall, the participants reported taking the following during the study period: tamoxifen (53%), antidepressants (15%), synthroid (18%), and herbs/vitamins/minerals (9%). Additionally, two women (one assigned to massage) reported taking medication for anemia, one (massage group) reported taking postmenopausal medication, three were on diuretics (two from massage group), and two (one massage) were on anticholesterol medication.

Women responding to an announcement at a university cancer center or its support groups were screened for eligibility. In all, 40 women who met the eligibility criteria were randomized to massage or control groups. However, three participants were dropped due to scheduling conflicts that did not permit them to continue in the study or come in for the first or last day's assessments ($n=2$ massage); one woman

who had been screened and assigned to the control group developed lymphodema before starting the trial and had to be dropped, one woman became pregnant after the screening, and one woman assigned to the control group stated that she was not feeling well and did not want to return to complete the last day's assessments. The final sample was comprised of 34 women (M age = 53, S.D. = 10.4) who had been diagnosed with Stage 1 or 2 breast cancer and were ethnically distributed, 74% Caucasian and 26% Hispanic, and middle to upper middle socioeconomic status (M = 2.3 on the Hollingshead two-factor index). The women were randomly assigned to a massage therapy group (N = 18) or a standard treatment control group (n = 16) using a flip of a coin. The groups did not differ on stage of cancer, type of surgery, treatments received, or demographic variables (see Table 1). Because participants were assigned using a flip of a coin at time of screening, no method was used to conceal allocation. The women assigned to the control group were informed that they would receive complimentary massages at the completion of the study. No participant was changed from one to another group during the 5-week trial.

Of the 34 women comprising the final sample, 27 women (n = 15 massage and 12 control) provided immune measure data. Three women in the massage therapy group and four in the control group did not have their blood drawn due to missed appointments, phlebotomy scheduling conflicts, or request not to have blood drawn due to a recent blood draw. Analyses revealed that the seven women who did not contribute immune measures data did not differ from the rest of the women in the study on age, stage of cancer, SES, treatment, or surgery (all Ps > .10). Their self-report and urine data were included in the final analyses.

Table 1
Demographic data for the massage therapy and control group (number of participants in parentheses)

Variables	Massage	Control	χ^2 P value	t test P value
Stage of disease			.60	
I	56% (10)	56% (9)		
II	44% (8)	44% (7)		
Type of surgery			.92	
Lumpectomy	39% (7)	44% (9)		
Mastectomy	58% (11)	56% (7)		
Treatments received			.99	
Radiation	17% (3)	19% (3)		
Chemotherapy	22% (4)	19% (3)		
Radiation + Chemotherapy	28% (5)	31% (5)		
None	33% (6)	31% (5)		
Age (S.D.)	52.7 (9.5)	53.3 (11.7)		.86
Ethnicity			.58	
% Caucasian	72% (13)	75% (12)		
% Hispanic	28% (5)	25% (4)		
SES			.79	
% Upper middle	56% (10)	44% (7)		
% Middle	39% (7)	44% (7)		
% Lower middle	5% (1)	12% (2)		

Procedures

The women assigned to the massage therapy group received 15 massages during the study period (three massages each week for 5 weeks). Each massage was 30 min long and the massages were conducted in a quiet and private room on a massage table by a trained massage therapist.

The standard treatment control group received standard medical care alone. At the end of the 5-week study period, the women in the control group were offered massage therapy.

Massage therapy

The participant was asked to undress except for her undergarments and lie on the massage table, which had been covered with a soft cotton sheet. A second sheet was draped over the participant for warmth and security. As the massage proceeded, the therapist uncovered the body part to be massaged while keeping the rest of the woman's body covered with the top sheet. Female massage therapists were selected for the study as the women informed us that they felt better having a female therapist. The 30-min massage routine (designed by Iris Burman, LMT, of the Educating Hands School of Massage, Miami, FL) consisted of Swedish, trager, and acupressure techniques. The female massage therapists were trained on the protocol and delivered the massage on a rotating basis so that the participants had different massage therapists during the 5-week treatment period. Most massage therapists volunteered 1 day a week. The massage sessions followed a standardized protocol that was similar to the protocol that had been effective in reducing stress hormones and increasing NK cells in our HIV study [19].

With the participant covered in a supine position and the therapist standing at the head of the massage table, the following techniques were applied: head/neck—stretching of the neck; lateral stroking of the forehead; stroking and stretching of the muscles along the cheeks and jaw; depressing the shoulders with the flats of the palms; and pressing on trigger points at midshoulder (2 min). Arms—progressive intermittent compressions from the axillary region (armpit) to the chest (6 times); intermittent compression of the arm, beginning at the shoulder and increasing 4–6 in. of the arm and returning to shoulder each time before the addition of another section until the entire arm from the shoulder to the wrist has been included; broad circular movements with the flats of the hand to the chest from the sternum to the shoulder; long strokes (using oil) from the sternum to the shoulder and from the wrist to the shoulder; and slow range of motion of the arm including full arm flexion (overhead), abduction, horizontal adduction and abduction, and rotation of the humerus (4 min each arm). Standing at the foot of the massage table, the therapist delivered the following: legs/feet—pulling (or traction) of both legs and each leg separately; massage of the feet, including squeezing of the heel; long gliding strokes up the leg from ankle to knee; kneading of the thigh muscles; and

Table 2
Means (S.D.) and percentage change (%) for the massage therapy and standard treatment group for immediate effects (pre-/postsession) on first and last days

	Massage group				Control group			
	First day		Last day		First day		Last day	
Variables	Pre/post	%	Pre/post	%	Pre/post	%	Pre/post	%
Immediate effects								
Anxiety (STAI)	$37(14)_a/27(13)_b$**	27%↓	$35(10)_a/25(8)_b$**	29%↓	$32(9)_a/30(6)_a$	6%↓	$35(12)_a/32(9)_a$	6%↓
Mood (POMS)								
Depression	$12(11)_a/3(3)_b$**	75%↓	$7(7)_a/3(4)_b$	57%↓	$4(4)_a/3(3)_a$	25% ↓	$6(7)_a/5(7)_a$	17%↓
Anger	$10(8)_a/2(2)_b$**	80%↓	$3(3)_a/2(2)_a$	33%↓	$5(5)_a/5(4)_a$	0%	$3(4)_a/4(5)_a$	33% ↑
Vigor	$21(7)_a/21(5)_a$	0%	$19(6)_a/21(6)_a$	11% ↑	$18(5)_a/18(5)_a$	0%	$18(7)_a/19(6)_a$	6% ↑

Lower numbers are optimal for all variables, except POMS vigor. Same letter subscripts (a,a) indicate that the two means were not significantly different, whereas different letter subscripts (a,b) indicate means that attained significance at $P<.05$ or $^{**}P<.01$. Percent sign indicates percent of increase or decrease for pre-/postmeasures in the two columns preceding the percent sign.

long strokes from the hip to the foot (4 min for each leg). With the participant in a prone position with a towel or small flat cushion under the breast area for comfort, the following steps were performed: legs—stretching of the achilles tendon; stroking and kneading of the calf muscles; long gliding strokes from the heel to the hip; rounding strokes to the hip area; and long strokes from the hip to the feet (3 min for each leg). Back—using both hands, slow pressing of the muscles of the lower back (10 times); long gliding stroking from the lower back to the shoulders and out to the arms; squeezing of the trapezius muscles; using the outer edge of each hand to perform short strokes along either side of the spine from the neck to the lower back; squeezing of the neck muscles; and long gliding strokes from the shoulders down to the lower back, to the legs and to the feet (5 min).

Assessments

Three standardized anxiety and mood scales were chosen to assess treatment effects: State Trait Anxiety Inventory (STAI), Profile of Mood States (POMS), and Symptom Checklist-90-R (SCL-90-R). These scales were selected because they had acceptable psychometric properties, had been used in breast cancer research [26,27] (Ahles et al., 1996), and were short and easy to complete. A Life Events Questionnaire that was used in our previous HIV study [18] was also given to the women to determine if any unusually stressful event might have impacted treatment effects over the course of the treatment.

Immediate/short-term effects (pre-/postsession measures)

On the first and last days of the 5-week session, pre- and post- the massage therapy or a 30-min control period, participants were asked to complete the STAI and POMS scales to assess anxiety, depression, anger, and vigor.

STAI [28] is a 20-item inventory on how the subject feels at the moment. The subject completes statements such as "I feel: very nervous, nervous, or not nervous." Research has shown that the STAI has adequate concurrent validity [28] and internal consistency ($r=.83$; [29]).

POMS [30] measures six different mood states. Only the subscales that measured depression, anger, and vigor were given because breast cancer survivors have shown fluctuations in these mood states [31,32]. Participants answered how they felt "right now" on a Likert scale ranging from 0=*not at all* to 4=*extremely*. Characteristic items include "sad," "blue," "discouraged," and "helpless" for the depressed scale; "angry," "annoyed," "bad-tempered," and "bitter" for the anger scale; and "lively," "vigorous," "full of life," and "energetic" for the vigor scale. The POMS has adequate concurrent validity and excellent internal consistency ($r=.95$; [33]) and has been shown to adequately measure intervention effectiveness in women with breast cancer [34,35].

Longer term effects (first/last day measures)

On the first and last days of the 5-week session, subjects were asked to complete scales to assess psychological well-being and stressful life events.

SCL-90-R [36] measures depression, anxiety, and hostility on a five-point scale ranging from 0=*not at all* to 4=*extremely*. Subjects respond to how distressed they felt over the past week on depression items (e.g., " crying easily," "loss of sexual interest or pleasure"), anxiety (e.g., "heart pounding or racing," "feeling tense or keyed up"), and hostility (e.g., "shouting or throwing things," "having urges to break or smash things"). This inventory has high internal consistency (*M* coefficient=.84) and test retest reliability (*M* coefficient=.84) and acceptable construct validity [37].

The Life Events Questionnaire asked participants to check whether any of the following events happened to them within the last 4 weeks: major financial difficulties, death of a significant other, family member or close friend, major difficulties in primary relationship or job, major personal event, or major life decision (retirement, child getting married, relocation). Participants were asked to rate the event checked on a Likert scale ranging from 0=*extremelypositive* to 6=*extremely negative*. This questionnaire was included as a possible confounding factor for treatment effects. Analyses revealed no differences between

the massage and control group on this questionnaire at the beginning or end of the 5-week study period.

Biochemical Measures

On the morning of the first and the last day of the 5-week study, the women were asked to refrain from eating or drinking and to provide a urine sample. This sample was logged, frozen, and sent to Duke University for assaying norepinephrine, epinephrine and cortisol (stress measures), dopamine (activating neurotransmitter), and urinary 5-HIAA (a metabolite of serotonin with lower levels suggestive of depression).

Immune measures

The women had their blood drawn to be assayed for immune cells that fight off tumors and viruses [8,37]. The blood samples were collected between 9:00 and 11:00 in the morning to reduce diurnal variability and because the immunology laboratory conducted their assays at noon. The selected measures were NK cell numbers and NKCC. These were assayed using the whole blood chromium release assay as described by Fletcher et al. [38]. The NK-sensitive erythroleukemia K562 cell line was used as the target cell line. The assays were done in triplicate at four target to effector cell ratios with a 4-h incubation. The whole blood was also prepared and assayed for lymphocyte phenotypic markers as described by Fletcher et al. [38]. Lymphocytes appear to play a role in augmenting the cytotoxicity of NK cells and when stimulated may become active cytotoxic cells [39].

Statistical evaluation

Separate MANOVAs, ANOVAs, and *t* test analyses were planned and conducted for the self-report, biochemical, and immune measures. The data were first examined for group means, skew, kurtosis, and the equivalence of sample variance on each variable. The inspection of the self-report data revealed no violations of the assumptions underling the *F* statistics. Hence, parametric statistics were used. However, because the biochemical and immune measures data are typically variable, baseline differences were likely to occur. Baseline measures were also examined for equality of means, and in the cases where means differed, the variable was entered as a covariate and an analysis of covariance (ANCOVA) was performed. Wilcoxon tests were conducted for data that did not conform to assumptions underlying the *F* distribution.

Results

Immediate effects (pre-/postsession measures)

Self-report anxiety and mood measures

The analyses revealed for the massage group the following: (1) reduced anxiety on the STAI, $F(1,32)=4.49$, $P<.05$, after the first and the last session; (2) reduced depression on the POMS depression score, $F(1,32)=6.36$, $P<.05$, after the first and last session and from the first to the last day of the study; and (3) reduced anger on the POMS anger scale, $F(1,32)=3.93$, $P<.05$. Means and percent change on the within-groups differences are reported in Table 2.

Table 3
Means (S.D.) and percentage change (%) for the longer term (first–last days) measures for the massage therapy and control groups

	Massage group			Control group		
Variables	First day	Last day	%	First day	Last day	%
Symptom checklist (SCL-90-R)						
Depression	13(11)$_a$	7(6)$_b$	46%↓	9(8)$_a$	11(12)$_a$	22%↑
Anxiety	4(4)$_a$	3(3)$_a$	25%↓	4(5)$_a$	4(5)$_a$	0%
Hostility	4(4)$_a$	2(2)$_b$	50%↓	3(3)$_a$	3(3)$_a$	0%
Urinary biochemistry						
Creatinine (mg/ml)	0.48(.7)$_a$	0.67(.5)$_a$	40%↑	1.34(1.0)$_a$	0.58(.85)$_b$	57%↓
Cortisol (ng/mg)	156(47)$_a$	173(77)$_a$	11%↑	185(74)$_a$	179(72)$_a$	3%↓
Norepinephrine (ng/mg)	44(32)$_a$	54(16)$_a$	23%↑	42(25)$_a$	73(33)$_b$	74%↑
Epinephrine (ng/mg)	7(3)$_a$	8(4)$_a$	14%↑	6(4)$_a$	7(3)$_a$	17%↑
Dopamine[a] (ng/mg)	258(110)$_a$	325(80)$_b$	26%↑	224(150)$_a$	281(77)$_a$	25%↑
Serotonin[a] (ng/mg)	2114(1369)$_a$	3391(2064)$_b$	60%↑	3395(2004)$_b$	3456(1775)$_b$	2%↑
Immune measures						
NK cell numbers	235(129)$_a$	263(95)$_b$	12%↑	254(90)$_a$	236(67)$_a$	7%↓
NKCC	27(13)$_a$	29(13)$_a$	7%↑	29(13)$_a$	29(16)$_a$	0%
Lymphocytes	29(4)$_a$	32(7)$_b$	10%↑	30(8)$_a$	30(7)$_a$	0%

Different letter subscripts (a,b) indicate differences between first and last day's measures within or between groups at $P<.05$. Same letter subscripts (a,a) indicate that the first and last day's means for that measure did not differ within groups. Percent sign indicates percent of increase or decrease.

[a] Higher score is optimal.

Longer term effects (first/last day)

Self-Reports on mood

The analyses on the SCL-90-R scale confirmed for the massage group a reduction in (1) depression, $F(1,32)=7.43$, $P<.01$, and (2) hostility, $F(1,32)=3.98$, $P<.05$, from the first to the last day (see Table 3).

Biochemical and immune measures

Biochemistry

Wilcoxon's matched pairs signed ranks tests revealed for the massage therapy group an increase in (1) dopamine, $Z=2.98$, $P<.05$, and (2) serotonin levels, $Z=2.29$, $P<.05$, from the first to the last day (see Table 3). The control group showed a significant increase in norepinephrine, $Z=2.45$, $P<.05$.

Immune measures

An ANCOVA on computed change scores (last day's scores minus first day's scores) was expected to show increased NK cell number and cytotoxicity if the massage effects from the HIV men and adolescents generalized to enhancing immune function in women with breast cancer. The ANCOVA revealed a significant group effect, $F(1,26)=4.22$, $P<.05$, and reflected a positive change score for the massage therapy group (actual $M=27.6$, S.D. = 16.8; covariate estimated $M=24.4$, S.D. = 12.6) and a negative change score for the control group (actual $M=-17.80$, S.D. = 18.2; covariate estimated $M=-13.9$, S.D. = 13.6) on NK cell number (see Fig. 1). NKCC did not attain significance. Paired sample t tests, conducted separately for each group, revealed a significant increase for the massage therapy group in NK cell numbers, $t(14)=1.73$, $P<.05$ (one tailed), and lymphocytes, $t(14)=1.85$, $P<.05$ (one tailed), see Table 3.

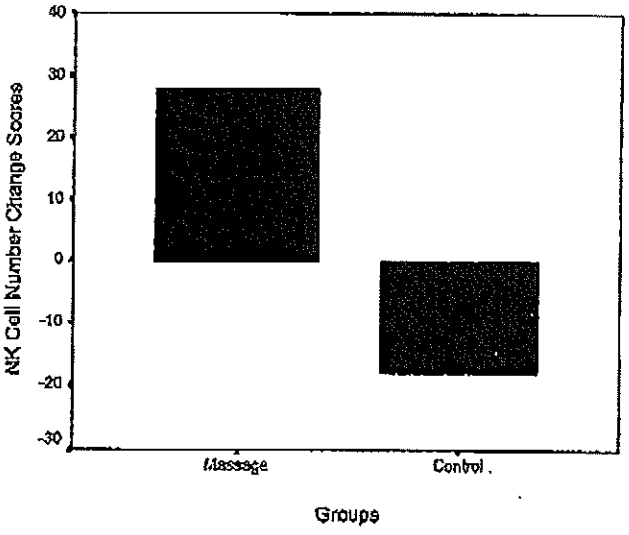

Fig. 1. Change scores from first to last day's measures for NK cell number for the massage and control groups.

Discussion

In the present breast cancer study, women who received 15 massage treatments over a 5-week period showed an increase in NK cell number and lymphocytes. NK cells spontaneously destroy a wide variety of cancer and virus-infected cells and are involved in eliminating metastases [40]. A boost in NK cell number would be beneficial given that some cancer patients have reduced NK cell numbers [41]. Lymphocytes are precursor cells of immunological function as well as regulators and effectors of immunity [39]. Hence, an increase in lymphocytes also benefits the cancer patient.

The increase in NK cell number supports a previous HIV men's massage therapy study [19] and a recent HIV adolescent massage therapy study [20]. Although the massage effects on immune responses are encouraging, the increase in NKCC reported in the HIV men's [19] and HIV adolescents' [20] studies was not replicated in the current breast cancer group. Perhaps for breast cancer, more frequent massages or massage of longer duration would be necessary to achieve a change in NK cytotoxicity. In the HIV men's study, the participants received daily 1-h massages for 1-month, and in the HIV adolescents' study, they received 20-min twice-weekly massages for 12 weeks compared to 30-min thrice-weekly massages for 5 weeks for the current breast cancer study.

Surprisingly, cortisol stress hormone, norepinephrine, and epinephrine levels did not decrease following massage therapy in the breast cancer study as reported in other massage therapy studies [19,23,42]. Again, this might relate to the need for more frequent and/or longer massage treatments for cancer patients to achieve changes in these measures. Another explanation is that in relation to the HIV men's study data, the breast cancer participants in the present study had higher catecholamine and cortisol values, suggesting that they might have been more stressed. Perhaps women with breast cancer have higher stress hormone levels, as they have been reported to have lower NK cell number [8]. Higher cortisol levels might also explain why NKCC did not change in that cortisol is known to negatively impact NK cell activity [43].

Although in the present study stress hormone levels were not reduced following massage therapy, neither did these levels increase for the massage group, suggesting that massage therapy several times a week may be sufficient for keeping stress hormone levels from rising. In contrast, the women in the control group showed an increase in norepinephrine from the first to the last day of the study. In that the control group's responses on the Life Events Questionnaire did not differ from those of the massage group suggests that both groups were comparable on stressful events by the end

of the study. Thus, it is unclear why the control group's norepinephrine levels were higher than their baseline.

In the present study, as expected, massage therapy was associated with reduced psychological distress. On the self-report measures, the breast cancer patients who received massage reported a decrease in anxiety, depressed mood, anger, and hostility. Similar massage therapy effects have been reported for other chronic illnesses including HIV [19], multiple sclerosis [44,45], fibromylagia [46], and chronic fatigue syndrome [22]. Decreased depression and anxiety have also been reported for breast cancer patients from cognitive behavioral therapy [17], mind–body–spirit therapy (meditation, imagery, affirmation, and ritual) [47], and from aromatherapy [48].

An improvement in mood is often associated with a change in biochemical levels, and as expected, the breast cancer patients who received massage therapy showed an increase in dopamine and serotonin levels from the first to the last day of the study. These increases complement the massage group's self-reports of improved mood and decreased depression, as both serotonin and dopamine have been noted to increase in depressed individuals following massage therapy (see Ref. [21]). These and other massage findings support that massage therapy is effective in reducing psychological distress, enhancing mood biochemicals, and boosting the immune system.

One caveat, however, is that although the massage therapy findings in the current study are provocative, the study needs to be replicated with a larger sample size. Also, participants were assigned with a "flip of the coin," which might produce biased results. The replication study should employ a more adequate method for assigning participants, such as a random-number table or a computerized random-number generator. Perhaps future studies could also examine whether massages of longer duration or greater frequency result in increased NKCC for breast cancer patients as it has for men and adolescents with HIV. Future studies might also examine massage therapy effects in combination with psychosocial interventions, such as group therapy, and for different types of cancer, such as prostate or ovarian cancer. The addition of massage therapy may reveal additive effects, which may enhance the psychological intervention.

An increase in complimentary and alternative medicine (CAM) use among cancer patients [49,50] and among breast cancer patients in particular [51,52] suggests that there is a need for these therapies. In a survey study that encompassed recruiting breast cancer participants during a 3-year period across three different universities, CAM therapies reportedly used by 60% of the sample included massage, acupuncture, homeopathy, meditation, and imagery. Because of its wide use and the potential for interaction effects especially from herbal medicine, CAM research is necessary (and has been mandated by the National Institutes of Health) to demonstrate the safety and efficacy of CAM use [53]. In the current study, massage therapy was found to be a safe treatment, as no adverse effects were reported, and massage was found to positively impact the psychology, immunology, and biochemistry of women with breast cancer. Future issues that need addressing include covering the cost of massage therapy for cancer patients, examining the generalizability of massage therapy for varying cancers, and perhaps exploring the effects of long-term use of massage therapy on morbidity and mortality rates.

In summary, the self-reports of reduced stress, anxiety, anger/hostility, and improved mood, and the corroborating findings of increased dopamine and serotonin levels and increased NK cell number (the primary outcome measure) and lymphocytes suggest that massage therapy has positive applications for breast cancer survivors. That women with breast cancer have lower NK cell number [8] and that they might have higher stress hormone levels, which have been associated with tumor growth and metastases [8,11], suggest the need for further research on interventions like massage therapy that impact the neuroendocrine and immune systems while attenuating psychological stress symptoms.

Acknowledgments

We thank the women who participated in this study, Iris Burnam, LMT, for designing the massage therapy procedure, our lead therapists Susan D'Arienzo, LMT, and Carmen Figueroa, LMT, and all of the massage therapists who provided the massage therapy sessions, Patricia Marzol who helped with data collection and Chris Sanders for his assistance with data analyses. This research was supported by USAMRMC DAMD Grant 17-99-1-9292 to Gail Ironson, an award from the Sylvester Comprehensive Cancer Center in Miami, FL, and funds from Johnson & Johnson.

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