Objective: The purpose of this study was to evaluate the influence of patient’s attitudes toward massage on pressure pain sensitivity and the immune effects of myofascial release in breast cancer survivors (BCS).

Methods: Twenty BCS participated. They presented to the laboratory at the same time of the day on 2 occasions separated by 2 weeks. At each session, they received either a myofascial release technique or control (special attention) intervention. Salivary flow rate, cortisol and immunoglobulin A (IgA) concentrations, and α-amylase activity were obtained before and immediately after intervention from saliva samples. Pressure pain thresholds (PPT) over the cervical spine and temporalis muscle were assessed bilaterally. The attitude toward massage (ATOM) scale was collected before the first session in all BCS.

Results: The analysis of covariance revealed a significant intervention × time interaction for salivary flow rate ($P = .010$), but not α-amylase ($P = .111$), IgA ($P = .655$), and cortisol ($P = .363$) in favor of the experimental group: BCS exhibited an increase of salivary flow rate after myofascial release intervention. When the ATOM scale was included in the analysis, significant influence on IgA ($P = .001$) was found: BCS with positive attitude had a significant increase in IgA ($P < .05$). The analysis of covariance did not find a significant intervention × time interaction for PPT over the cervical spine or temporalis muscle, with no effect of ATOM scales for PPT ($P > .05$).

Conclusion: The current study suggests that myofascial release may lead to an immediate increase in salivary flow rate in BCS with cancer-related fatigue. We also found that the effect of myofascial release on immune function was modulated by a positive patient’s attitude toward massage. (J Manipulative Physiol Ther 2012;35:94-100)

Key Indexing Terms: Attitudes; Manual Therapy; Breast Neoplasms; Immune System
recently postulated positive analgesic effects of massage in different oncology processes, whereas Sturgeon et al \(^8\) reported no effects. Discrepancies between reviews support the necessity for conducting more studies on this topic.

It has been recently reported that BCS also exhibit widespread pressure pain hypersensitivity. \(^9,10\) Some studies have demonstrated that the application of myofascial release exerts hypoalgesic effects in different conditions. \(^11-14\) In fact, patients feel that massage therapy produces relaxation and reduces muscle tension. \(^15\) It is possible that myofascial techniques may decrease pressure pain hypersensitivity in BCS, but no study has previously investigated this hypothesis.

In a cancer setting, massage has also shown effects within the immune system as an increase in the number of lymphocytes, \(^16\) and natural killer cells \(^17\) have been found after its application. However, a recent study has not confirmed the improvement of immune function induced by massage. \(^18\) Changes in immune function by analyzing salivary markers such as immunoglobulin A (IgA) or \(\alpha\)-amylase activity have been previously studied in other populations, \(^19,20\) but not in BCS. Cortisol concentration and \(\alpha\)-amylase activity are markers of stress response that are altered in BCS. \(^21\) It would be interesting to investigate changes in immune system in BCS after the application of myofascial release.

Finally, it seems that the experience of cancer symptoms as pain is a result of the complex processing of information relayed to the brain from the sensory periphery and other aspects such as cognitive and emotional processing. \(^22\) Interestingly, one of the more frequently postulated reasons for the use of different forms of complementary alternative medicine in BCS is to strengthen the immune system and improve the ability to relax muscles within the pain area. \(^23\) This type of belief and the patient’s attitude toward a therapeutic modality such as myofascial release could influence the effects of this therapeutic intervention.

We postulated that BCS who had a positive attitude to massage would be more likely to experience greater improvements than those with a negative attitude. To the best of the authors’ knowledge, no previous studies have investigated the modulating effect of a patient’s attitude toward massage on myofascial release in BCS. Therefore, the aim of the current study was to evaluate the influence of the patient’s attitude toward massage on pressure pain sensitivity and the immune effects of myofascial release in BCS.

**Methods**

This study used a randomized single-blind, placebo-controlled crossover design to accommodate for possible interindividual variability in the outcome measures.
pressure algometer (Somedic, Hörby, Sweden) consisting of a “pistol” handle and a rod with a pressure-sensitive gauge strain at the tip was used. Pressure pain threshold was assessed by a clinician blinded to group allocation. Pressure pain threshold measurements were taken over the articular pillar of C5-C6 zygapophyseal joint (cervical) and over the temporalis muscle. The cervical spine was selected because hypersensitivity has been previously found in BCS.\(^9\,10\) The temporalis muscle was selected because it is susceptible to increased contraction in response to stress.\(^27\,28\) The mean of 3 trials was calculated and used for the analysis. A 30sec resting period was allowed between each trial. The reliability of pressure algometry has been found to be high (intraclass correlation coefficient [ICC]: 0.91; 95% confidence interval [CI], 0.82-0.97).\(^29\)

### Attitudes Toward Massage Scale

A 9-item measure of overall patient attitudes toward massage (ATOM) that includes 2 distinct subscales assessing the attitudes of massage as healthful (ATOM-MH) and massage as pleasant (ATOM-MP) was used. Items were concerned with ATOM and consisted of a stem in the form of a sentence with 5 ordered category response options ranging from “strongly disagree” to “strongly agree” with a middle option of “neutral.” These subscales have shown adequate reliability (α = .70-.80).\(^30\)

### Saliva Sample

Saliva samples were collected from each participant for assessment of hypothalamic-pituitary-adrenal (HPA) axis, sympathetic nervous system, and immune system functions according to standardized procedures.\(^31\) Saliva was collected into a collection tube (passive drooling technique). Particular care was considered when collecting saliva to avoid collection immediately after mouth cleaning, meals, snacks, or medications.

The process was done for 3 minutes. All saliva sampling was performed between 10 to 12 AM and always 4 hours after waking to control for possible fluctuation associated with daily output and diurnal rhythms on cortisol and α-amylase secretions.\(^31\) It has been found that 4 hours after waking, α-amylase secretion reaches its highest level of the day. Participants were asked to refrain from eating, drinking, or chewing gum for 1 hour before sampling. They were also asked to refrain from brushing their teeth in the morning before saliva sampling. The volume of the sample was calculated (nearest 0.1 mL), and saliva flow rate (mL × min\(^{-1}\)) was determined by dividing the volume of saliva by the collection time. Immediately after collection, saliva samples were centrifuged at 3000 rpm for 15 minutes to remove any sediment and were stored at −70°C until analysis. Concentration of cortisol and IgA and α-amylase activity were assessed in thawed samples by an assessor blinded to group allocation.

Saliva was collected at preintervention and immediately after the intervention. Salivary cortisol and IgA concentrations, and α-amylase activity were calculated using a commercial luminescence immune assay (Salimetrics, State College, PA), reading the luminescence units with automatic luminometers (Sunrise; TECAN Group, Mannedorf, Switzerland). Saliva samples were analyzed in a single batch to eliminate interassay variance, and they were measured in duplicate. In fact, adequate intraassay accuracy was obtained with a coefficient of variance less than 8.5%.

### Statistical Analysis

Data were analyzed with SPSS version 19.0 (SPSS Inc, Chicago, Ill). Mean, standard deviations, and 95% CIs of the values were calculated for each variable. The Kolmogorov-Smirnov test showed a normal distribution (P > .05). Preintervention data before each session were compared using independent t tests. A 2-way repeated-measures analysis of covariance, with session (control, experimental) as between-subjects variable, time (pre-post) as within-subjects variable, and ATOM (ATOM-MH/ATOM-MP) as covariate, was used to examine the effects of interventions. Separate analyses of covariance were performed with each dependent variable. The hypothesis of interest was group × time interaction, with an ATOM subscale interaction. P < .05 was considered statistically significant.

### RESULTS

#### Demographic Data

Twenty BCS during their first year after treatment with a mean age of 49 ± 8 years were included. They had university-level education (40%), were married (80%), white, and from a metropolitan area. Eighteen (90%) participants had breast cancer stage I or II and had received both radiation and chemotherapy as adjuvant treatment after surgery (80%). Fourteen (70%) had received lumpectomy, whereas the remaining 6 (30%) had received mastectomy. In addition, 16 (80%) women were taking antagonist of estrogen receptors or aromatase inhibitors drugs, whereas 10% were taking monoclonal antibody HER2. None of the participants had received rehabilitation treatment. Three participants (15%) were taking analgesics (ibuprofen or acetaminophen).
Salivary marker for both sessions. Results may stimulate research focused on long-lasting effects of myofascial release in BCS, particularly in breast cancer survivor. We found a significant increase in salivary flow rate, not modulated by patient’s attitude, and an increased in IgA concentration, influenced by a positive patient’s attitude relative to the pleasant effects of massage. No changes in pressure pain sensitivity were found.

Salivary flow rate is a marker of vegetative influence in stress situations. Our results support a parasympathetic effect of the myofascial release intervention when applied on BCS, which agree with previous studies related to physical stress situations and pain conditions. Physiologic mechanisms implied by these results are not currently understood. It is possible that the parasympathetic response may be mediated by the stimulation of type 3 and 4 mechanoreceptors during myofascial release interventions. These mechanoreceptors exhibit a relationship with the autonomic nervous system, which is able to trigger the response of salivary glands. These results may stimulate research focused on long-lasting effects of myofascial release in BCS, particularly in subgroups of patients having Sjögren syndrome associated with adjuvant hormone therapy or xerostomy after cancer treatment.

### Discussion

This is the first study investigating the influence of a patient’s attitude toward massage on pressure sensitivity and immune system function after myofascial release in breast cancer survivor. We found a significant increase in salivary flow rate, not modulated by patient’s attitude, and an increased in IgA concentration, influenced by a positive patient’s attitude relative to the pleasant effects of massage. No changes in pressure pain sensitivity were found.

### Effects of Myofascial Release on Salivary Markers

The analysis of variance revealed a significant intervention × time interaction for salivary flow rate (F = 8.587; P = .010) but not for α-amylase activity (F = 2.960; P = .111), IgA concentration (F = 0.210; P = .655), and cortisol concentration (F = 0.892, P = .363). Pairwise comparisons revealed that BCS exhibited significant increases in salivary flow rate (P = .005) after the myofascial release intervention, with no changes after the control intervention (P = .244). When the ATOM-MP subscale was included in the analysis, a significant influence for IgA (F = 20.001, P = .001) was found: BCS with a positive attitude toward massage experienced greater increases in IgA. The attitude scale did not influence cortisol concentration (ATOM-MP: P = .744; ATOM-MH: P = .711) or α-amylase activity (ATOM-MP: P = .676; ATOM-MH: P = .983). Table 1 summarizes pre- and postintervention scores of each salivary marker for both sessions.

### Table 1. Preintervention, postintervention and change scores of salivary flow rate, α-amylase activity, cortisol, and IgA concentrations

<table>
<thead>
<tr>
<th></th>
<th>Control session</th>
<th>Myofascial release session</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salivary flow rate (mL × min⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before intervention</td>
<td>1.3 ± 0.5 (95% CI, 1.0-1.6)</td>
<td>1.2 ± 0.5 (95% CI 1.0-1.4)</td>
</tr>
<tr>
<td>After intervention</td>
<td>1.3 ± 0.5 (95% CI, 1.0-1.5)</td>
<td>1.5 ± 0.5 (95% CI 1.2-1.7)</td>
</tr>
<tr>
<td>Pre-post differences</td>
<td>0.0 (95% CI, 0.1-0.1)</td>
<td>0.3 (95% CI 0.2-0.4)</td>
</tr>
<tr>
<td>α-Amylase activity (U × min⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before intervention</td>
<td>159.9 ± 85.1 (95% CI, 118.9-200.9)</td>
<td>162.1 ± 79.0 (95% CI, 123.9-200.1)</td>
</tr>
<tr>
<td>After intervention</td>
<td>225.3 ± 106.3 (95% CI, 174.0-276.5)</td>
<td>287.7 ± 162.2 (95% CI, 209.5-365.9)</td>
</tr>
<tr>
<td>Pre-post differences</td>
<td>65.4 (95% CI, 35.9/94.7)</td>
<td>125.6 (95% CI, 57.7/193.6)</td>
</tr>
<tr>
<td>Cortisol concentration (µg × min⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before intervention</td>
<td>0.3 ± 0.2 (95% CI, 0.2-0.4)</td>
<td>0.3 ± 0.1 (95% CI, 0.2-0.4)</td>
</tr>
<tr>
<td>After intervention</td>
<td>0.2 ± 0.1 (95% CI, 0.1-0.3)</td>
<td>0.2 ± 0.2 (95% CI, 0.1-0.3)</td>
</tr>
<tr>
<td>Pre-post differences</td>
<td>−0.1 (95% CI, −0.2/0.1)</td>
<td>−0.1 (95% CI, −0.2/0.1)</td>
</tr>
<tr>
<td>IgA concentration (mg × min⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before intervention</td>
<td>16.5 ± 7.5 (95% CI, 12.7-20.4)</td>
<td>15.5 ± 7.2 (95% CI, 11.8-19.2)</td>
</tr>
<tr>
<td>After intervention</td>
<td>19.1 ± 10.2 (95% CI, 13.9-24.4)</td>
<td>21.8 ± 12.8 (95% CI, 15.2-28.4)</td>
</tr>
<tr>
<td>Pre-post differences</td>
<td>2.6 (95% CI, −1.4/6.7)</td>
<td>6.3 (95% CI, 1.3/11.2)</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD for pre- and postintervention data and as mean (95% CI) for within- and between-group change scores.

- **Statistical significant differences between sessions without ATOM influence (P < .05).**
- **Statistical significant differences between sessions with ATOM-MP influence (P < .05).**

Preintervention data for each variable were not significantly different between each treatment session: PPT cervical affected side (P = .130), cervical nonaffected side (P = .306), temporalis affected side (P = .167), temporalis nonaffected side (P = .089), salivary flow rate (P = .225), α-amylase activity (P = .859), cortisol (P = .750), and IgA (P = .533) concentrations.

Effects of Myofascial Release on PPTs

The analysis of variance did not find an intervention × time interaction for PPT over the cervical spine (affected side: F = 0.003, P = .957; nonaffected side: F = 0.931, P = .351) or the temporalis muscle (affected side: F = 0.160, P = .694; nonaffected side: F = 0.016, P = .990). There were also no significant attitude scale–influenced changes in PPT levels over temporalis muscle (P = .245) and over cervical spine (P = .441). Table 2 details pre- and postintervention scores of PPT for both the temporalis muscle and the cervical spine. No adverse effects associated with the myofascial release were reported.

**DISCUSSION**

This is the first study investigating the influence of a patient’s attitude toward massage on pressure sensitivity and immune system function after myofascial release in breast cancer survivor. We found a significant increase in salivary flow rate, not modulated by patient’s attitude, and an increased in IgA concentration, influenced by a positive patient’s attitude relative to the pleasant effects of massage. No changes in pressure pain sensitivity were found.

Salivary flow rate is a marker of vegetative influence in stress situations. Our results support a parasympathetic effect of the myofascial release intervention when applied on BCS, which agree with previous studies related to physical stress situations and pain conditions. Physiologic mechanisms implied by these results are not currently understood. It is possible that the parasympathetic response may be mediated by the stimulation of type 3 and 4 mechanoreceptors during myofascial release interventions. These mechanoreceptors exhibit a relationship with the autonomic nervous system, which is able to trigger the response of salivary glands. These results may stimulate research focused on long-lasting effects of myofascial release in BCS, particularly in subgroups of patients having Sjögren syndrome associated with adjuvant hormone therapy or xerostomy after cancer treatment.
Our results did not support the ability of myofascial release to improve immune function or improve cortisol and α-amylase activity in BCS having cancer-related fatigue. These findings agree with a recent meta-analysis that did not find effects for different forms of massage on cortisol concentrations. Nevertheless, the results of our study are contrary to those reported for reflexology where changes in α-amylase-activity were found, but in line with a previous study on healthy people where changes in α-amylase-activity were not reported. However, one of the more relevant findings of our study is the influence of the patient’s attitude toward massage on the ability of myofascial release to improve IgA concentrations in BCS. In fact, 50% to 75% of BCS during first year after treatment use different forms of alternative medicine because they believe that this can boost their immune system. It is possible that BCS with a positive attitude toward the immune boosting effects of massage may be more susceptible to the relaxation effects of myofascial release. A relaxation response has been previously associated with increases in IgA after different therapeutic modalities.

These findings are extremely helpful for clinicians who apply specific manual therapies adapted to their patient’s attitudes, especially by inexperienced recipients. Current findings warrant future studies for identifying long-term effects of myofascial release in immune function in different attitude subgroups of BCS.

An interesting finding was that we did not observe any change in pressure hypersensitivity after myofascial release in our sample of BCS. Furthermore, attitude did not appear to exert any significant effect on pressure pain sensitivity. It is possible that one treatment session may not be enough to activate pain inhibitory mechanisms in BCS. Future studies investigating the cumulative effects of consecutive sessions of myofascial release applied on BCS on pressure sensitivity are needed.

### LIMITATIONS

Some methodological limitations of the current study should be acknowledged. First, the same therapist performed all manual therapy interventions that may limit the generalizability of the results. It would be expected that other clinicians may be able to provide similar treatments with similar results. Second, we investigated the short-term effects of myofascial release, which may have limited clinical relevance at this moment. It is possible that subsequent sessions may induce longer-lasting effects. Third, alterations of stress response, that is, a flattened diurnal cortisol slope present in BCS having cancer-related fatigue could reduce the ability of myofascial release in changing salivary cortisol concentrations and α-amylase activity. Future studies including cortisol slope changes and other HPA-axis biomarkers altered during breast cancer treatment, such as serotonin, should be conducted to investigate the ability of myofascial release to affect endocrine function in this population. Fourth, we cannot exclude the placebo effect associated with hands-on techniques. Future studies should compare different manual techniques to placebo interventions including manual contact on the patient. Finally, we should recognize that blinding patients may be not effective because the placebo intervention was different from the treatment. Therefore, the placebo effect associated with hands-on technique should not be ignored in studies testing the influence of patients’ attitudes in relation to myofascial release.

### CONCLUSIONS

The current study suggests that myofascial release may lead to an immediate increase in salivary flow rate in BCS. In addition, myofascial release induces an effect on immune function by increasing IgA, but this effect is modulated by a patient’s positive attitude toward massage.

#### Table 2. Preintervention, postintervention, and change scores of PPTs (kPa) in temporal and cervical muscles

<table>
<thead>
<tr>
<th></th>
<th>Control session</th>
<th>Myofascial release session</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temporals muscle affected side</td>
<td>Before intervention 214.9 ± 56.9 (95% CI, 188.2-241.5)</td>
<td>194.9 ± 56.0 (95% CI, 168.7-221.2)</td>
</tr>
<tr>
<td></td>
<td>After intervention 216.5 ± 59.5 (95% CI, 184.8-244.1)</td>
<td>196.5 ± 63.4 (95% CI, 166.8-226.2)</td>
</tr>
<tr>
<td></td>
<td>Pre-post differences 1.6 (95% CI, –27.5/24.8)</td>
<td>1.6 (95% CI, –10.9/13.1)</td>
</tr>
<tr>
<td>Temporals muscle unaffected side</td>
<td>Before intervention 213.4 ± 64.8 (95% CI, 183.0-243.7)</td>
<td>192.3 ± 59.7 (95% CI, 164.3-220.4)</td>
</tr>
<tr>
<td></td>
<td>After intervention 215.3 ± 49.9 (95% CI, 192.0-238.7)</td>
<td>203.3 ± 61.9 (95% CI, 174.3-232.3)</td>
</tr>
<tr>
<td></td>
<td>Pre-post differences 1.9 (95% CI, –18.5/22.1)</td>
<td>11.0 (95% CI, 1.46/23.5)</td>
</tr>
<tr>
<td>Cervical spine affected side</td>
<td>Before intervention 188.7 ± 58.4 (95% CI, 161.4-216.0)</td>
<td>204.5 ± 73.3 (95% CI, 170.1-238.8)</td>
</tr>
<tr>
<td></td>
<td>After intervention 193.7 ± 56.3 (95% CI, 167.4-220.1)</td>
<td>215.3 ± 63.8 (95% CI, 185.5-245.1)</td>
</tr>
<tr>
<td></td>
<td>Pre-post differences 5.0 (95% CI, –9.4/19.6)</td>
<td>10.8 (95% CI, –13.9/35.6)</td>
</tr>
<tr>
<td>Cervical spine unaffected side</td>
<td>Before intervention 204.5 ± 81.6 (95% CI, 166.3/242.6)</td>
<td>184.4 ± 68.8 (95% CI, 152.2-216.6)</td>
</tr>
<tr>
<td></td>
<td>After intervention 210.7 ± 55.5 (95% CI, 184.7-236.7)</td>
<td>193.1 ± 76.9 (95% CI, 157.0-229.1)</td>
</tr>
<tr>
<td></td>
<td>Pre-post differences 6.2 (95% CI, –24.9/38.0)</td>
<td>8.7 (95% CI, –9.6/27.0)</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD for pre- and postintervention data and as mean (95% CI) for within- and between-group change scores.
Clinicians should be aware of the interaction between effects of different manual therapies used for the management of BCS and the personal attitudes of the patients to the technique itself.

Practical Applications

- This study showed that myofascial release leads to an immediate increase of salivary flow rate in BCS, suggesting a parasympathetic effect of the intervention.
- Myofascial release induced an effect in immune function by increasing the concentrations of immunoglobulin A, but this effect was modulated by a positive attitude toward massage from the patients.
- For this study, a session of myofascial release was not able to decrease pressure pain sensitivity in BCS.

Funding Sources and Potential Conflicts of Interest

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