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Proprioceptive neuromuscular facilitation in the functionality and lymphatic circulation of the upper limb of women undergoing breast cancer treatment

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ABSTRACT

Background: With the increase in survival of women treated for breast cancer, it is necessary to evaluate the effect of therapeutic resources on co-morbidities resulting from the surgical treatment of the disease. The aim of this study was to evaluate the effects of proprioceptive neuromuscular facilitation on the functionality and lymphatic circulation of the upper limb involved in the treatment of breast cancer.
Methods: The study was conducted according to randomized clinical trial design. Thirty-two women at a mean age of 52.20 (± 8.32) years, submitted to breast cancer treatment, divided into two groups, control - women submitted to standard breast cancer treatment, and treated group, composed of women who underwent breast cancer treatment and rehabilitation with the proprioceptive neuromuscular facilitation technique. Palmar grip strength with dynamometer and shoulder range of motion with goniometer were evaluated. Lymphatic circulation analysis was performed in a computerized scintillation chamber, before and after therapeutic intervention.
Findings: In the results obtained, a significant increase ($p < 0.05$) of palmar grip strength was observed, a significant increase in range of motion of flexion ($p < 0.001$), extension ($p < 0.0012$), abduction ($p < 0.0001$), external rotation ($p < 0.0001$), internal rotation ($p < 0.0001$), and not significant for lymphatic flow ($p > 0.05$).
Interpretation: The results obtained in this study allow us to conclude that proprioceptive neuromuscular facilitation favors an increase in muscle strength, range of motion, but not in lymphatic flow, in women undergoing surgical treatment for breast cancer.

1. Introduction

Currently, breast cancer is one of the most common types of cancer, frequently affecting women and presenting a high mortality rate in Brazil, due to advanced diagnosis (INCA, 2014). Early diagnosis is extremely important for determining survival and essential for the decision-making process in surgical and adjuvant treatment (Loh and Musa, 2015; Ding et al., 2016).

Among the consequences of breast cancer treatment are reported blood and lymphatic circulatory co-morbidities that predispose to lymphedema, in addition to musculoskeletal disorders such as fatigue, pain, limitation of movement, and range of motion of the homolateral upper limb to surgery, in addition to impaired motor skills. The consequences of surgical treatment, the main therapeutic procedure of this type of cancer, produce repercussions on work performance and daily living activities, directly influencing the functionality of women (Atalay et al., 2015; Nascinben Matheus and Guirro, 2011; Van Dijck et al., 2016).

Hypomobility of the shoulder joint can negatively influence proprioception, which is the neural information generated by the receptors of the joints, muscles, tendons, capsules, and ligaments, sent through the afferent pathways to the nervous system and thereby interfere with the quality of movement of this joint, especially during the execution of a functional shoulder activity (Dieli-Conwright and Breanna, 2015; Meneses-Echávez et al., 2015).

Allied to technological advances in the treatment of breast cancer, is

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observed the prospect of increased survival, however, this is inversely related to physical status and quality of life, since many treatments of the disease produce co-morbidities (Benton et al., 2013). Therefore, the evaluation of therapeutic procedures aimed at controlling and treating them is extremely important for the quality of life and socioeconomic impact of cancer treatment. Knowledge of the repercussion of the effects of these therapeutic procedures on co-morbidity may have repercussions on effective intervention strategies.

In order to find new alternatives for the rehabilitation of co-morbidities resulting from the treatment of breast cancer, such as proprioceptive neuromuscular facilitation (PNF), which can promote stretching and muscle strengthening, as well as increasing the amplitude of movement, it is necessary to devote more studies that can contribute to more effective clinical trials and thus promote better quality of life for women with breast cancer (Hindle et al., 2012; Hwang and Choi, 2013; Kyung-Jin et al., 2017; Byung, 2015).

The PNF technique in shoulder affected by the surgery to treat breast cancer induces functional joint movements and promotes increased flexibility, muscle strength and vascular blood flow, and can be effectively used in the prevention, treatment, and rehabilitation of shoulder disorders, and increase of the recruitment of motor units and of muscle strength (Feland and Marin, 2004; Sharman et al., 2006, Cho et al., 2016, Guirro et al., 2019).

In view of the above, this study aims to evaluate the effect of proprioceptive neuromuscular facilitation on the functionality of the upper limb involved in the treatment of breast cancer.

2. Methods

Randomized clinical study with women undergoing breast cancer treatment at the Pio XII Foundation - Barretos Cancer Hospital. A random draw made in closed and opaque envelopes with different groups (control / treated).

2.1. Subject

The study included 32 women, submitted to surgical treatment of breast cancer combined with axillary lymphadenectomy or sentinel lymph node biopsy, at a mean age of 52.20 (± 8.32) years, divided into two groups: control group (CG) - women submitted to standard breast cancer treatment, and treated group (TG), composed of women undergoing breast cancer treatment and rehabilitation with the technique of proprioceptive neuromuscular facilitation (Fig. 1).

The control group underwent conventional rehabilitation, considered the standard for surgical treatment of breast cancer involving active kinesiotherapy in active and active-assisted group, strengthening and stretching of the antero-internal shoulder chain. The treated group underwent conventional rehabilitation, associated with the proprioceptive neuromuscular facilitation technique with a periodicity of three days a week, totaling ten sessions, both groups being reassessed after the intervention period.

Exclusion criteria were muscle-tendinous lesions and/or joint injuries in the affected limb, skin disorders, diabetes, uncontrolled circulatory diseases, lymphedema, submitted to bilateral axillary emptying, diagnoses with metastasis in the upper limb during pregnancy, and women undergoing chemotherapy and/or radiotherapy.

All volunteers signed a formal informed consent form, and the research study was analyzed and approved by the Ethics and Research Committee on Human Beings of the Pio XII Foundation - Barretos Cancer Hospital, process n. 1277/2016, and by the Research Ethics Committee of the Clinical Hospital of the Ribeirão Preto Medical School of the University of São Paulo, protocol n. 2890/2017.

2.2. Dynamometry protocol

The evaluation of palmar grip of the homolateral upper limb surgery was measured by means of a Jamar® dynamometer (Plus + Hand Dynamometer, Patterson Medical® - UK) before and after treatment sessions, which allows visualizing the strength generated by a grip exercised in an isometric manner on the handles of the equipment. Isolated handgrip strength may be a predictor of muscle weakness related to other muscle groups (Rantanen et al., 2003).

The evaluations were performed in the sitting position with elbow flexed at 90°, forearm in a neutral position, with interval of 1 min performed between the measurements, performed three times in each upper limb, considering the average value obtained in kilogram (Cantarero-Villanueva et al., 2012; Leach et al., 2016).

2.3. Goniometry protocol

The goniometry of the homolateral shoulder surgery was performed in an orthostatic position using the Richmeters® digital goniometer, for analysis of flexion, extension, abduction, adduction movements. The movements of internal and external rotation of the shoulder were evaluated in a supine position with shoulder abduction at 90°, maintaining hip flexion at 30° (Stuiver et al., 2015).

2.4. Lymphoscintigraphy protocol

For the analysis of lymphatic circulation, directly influenced by muscle contraction, a computerized scintillation chamber was used, model Millenium VG - Hawkeye GE, equipped with two detectors, the collimator was low energy and high resolution. The volunteers were placed in a horizontal supine position, with a field of vision including the upper limb and axillary regions and the radiopharmaceutical used was the 99mTc phytate at the dose of 37 MBq (1 mCi), the volume of 0.5 mL, administered in syringe and insulin needle in the second interdigital space of the dorsum of both hands. The tests were performed in three stages: dynamic phase, static phase, and full-body scan (Sarri, 2009; Dylke et al., 2016).

2.5. Intervention

The muscle training protocol consisted of proprioceptive neuromuscular facilitation (PNF) exercises, in which the movement was manually resisted by the researcher on the upper limb of surgery side.

Proprioceptive neuromuscular facilitation was performed with the volunteer lying in a supine position, and hip joint in flexion of 30° with the lower limbs supported in semiflexion, the technique of proprioceptive neuromuscular facilitation was applied involving the diagonals of flexion-abduction-external rotation and extension-adduction-internal rotation maintaining extension of elbows, associated with a verbal command, aiming to stimulate mechanisms of contraction, muscle relaxation, and stretching in the upper limb of surgery side.

The therapeutic exercises of proprioceptive neuromuscular facilitation were applied with isolated or combined movements, with three sets of ten repetitions of each movement, finishing the sequence of movements with stretching (Hwang et al, 2015).

The intervention was applied three times a week, during four weeks, the exercises followed the proposal of Wicke et al. (2014), aiming at stretching the adjacent muscles of the shoulder, as well as training and muscle strength gain.

2.6. Statistical analysis

Initially, the quantitative variables were compared between the study groups, and the student *t*-test was applied to independent samples, the data show variance and normal distribution. Fisher's Exact Test was applied to compare the qualitative variables between the study groups, a test that aims to verify an association between two qualitative variables.

For comparison between the variables between the time periods of

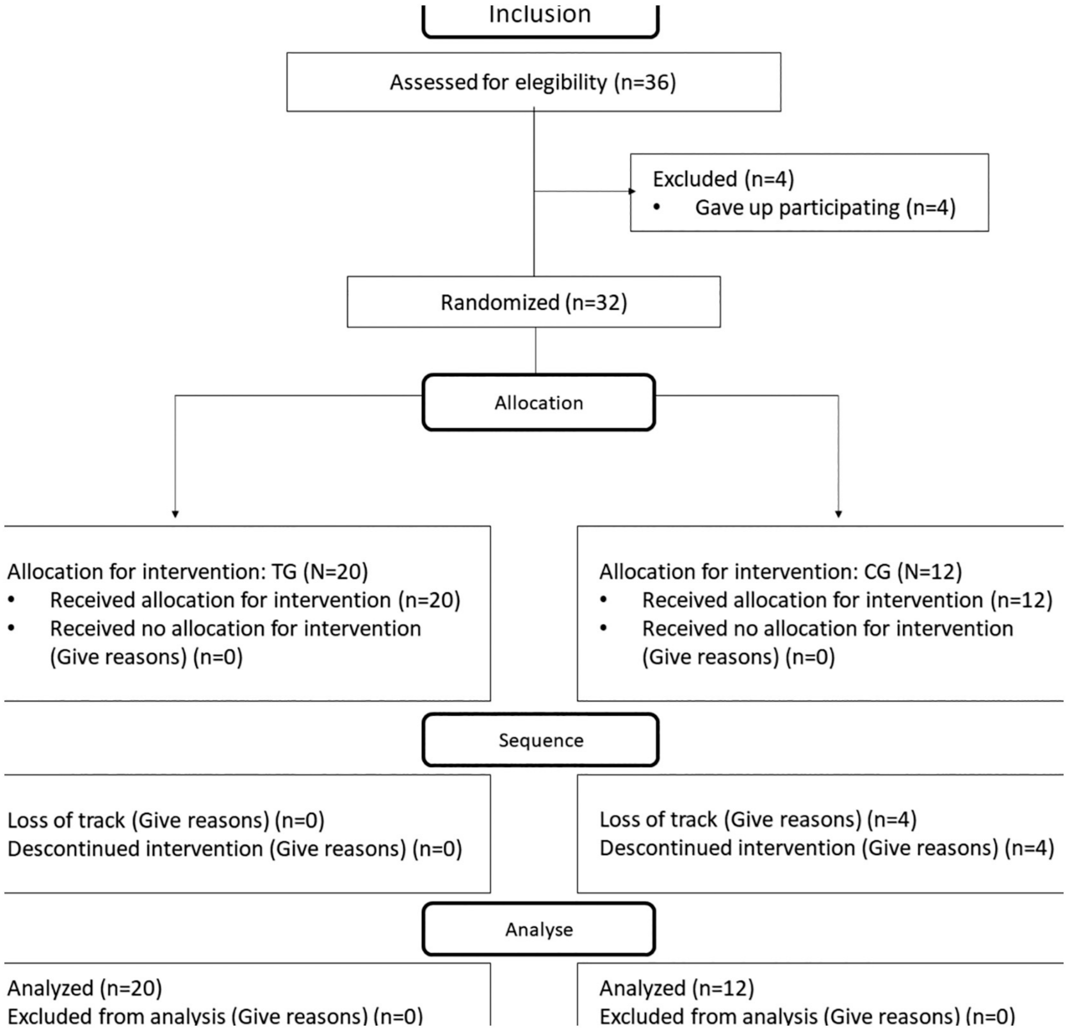

Fig. 1. Stratification flowchart for data collection.

each group and between the groups for each time, the linear model of mixed-effects (random and fixed effects) was used. The following covariates of the mixed model were considered as covariates: age, BMI (body mass index), type of surgery, and level of emptying. This methodology is used in data analysis, where the responses of the same individual are grouped, and the assumption of independence between observations in the same group is not adequate (Schall, 1991). The effects estimated by the mixed model showed that the factors that influenced most of the variables were time, surgical side and group, side and time interaction. The analyses were performed in the statistical software SAS 9.4, and the graphs were constructed in the statistical software R 3.6.1. The significance level $\alpha = 0.05$ was fixed for all analyses.

3. Results

Patients in the treated and control groups underwent modified radical mastectomy and simple mastectomy ($p < 0.34$), and axillary dissection at levels I, II and III ($p < 0.26$), with no difference between groups (Fisher's exact test). The characterization of the groups related to weight, body mass index and age are shown in Table 1.

Data regarding palmar grip strength showed that there is a significant difference between the control and treated groups for the non-surgical side and time related to pre-intervention and for the surgical side and post-intervention time ($p < 0.05$). For both cases, there was a higher mean for the treated group. The non-surgery side limb also showed a significant difference, suggesting movement overload to the detriment of the surgery side limb (Table 2).

Table 1
General characteristics of the sample.

Variable	Group	Mean	SD	Minimum	Medium	Maximum	*p*-value
Weight	Control	69.8	10.809	53	74	80	0.753
	Treated	71.333	13.135	52.5	70.275	100	
BMI	Control	27.189	4.942	18.27	28.08	33	0.624
	Treated	28.073	4.44	21.87	28.765	36.67	
Age	Control	48.417	7.128	40	49.5	62	0.200
	Treated	52.2	8.314	39	52.5	66	

Values presented in average (standard deviation, minimum and maximum).

Data regarding the evaluation of the difference of the joint angle in the pre and post treatment times, in the non-surgery side and surgery side limbs, surgery in the control and treated groups, showed significant results for flexion, abduction, internal rotation and external rotation, and not significant for extension and adduction (Table 3).

The results obtained in the comparison regarding the difference in the joint angle in the non-surgery side and surgery side members of the surgery, in the pre and post-treatment times, in the control and treatment groups (Table 4), showed a significant difference for the surgery side member for flexion, abduction, internal and external rotation, and there was no significant difference in extension and adduction for the non-surgery side and surgery side limbs, confirming the findings

Table 2
Mean values confidence interval of the difference in handgrip strength in the pre and post treatment times, in the non-surgery side and surgery side limbs during surgery in the control and treatment groups.

Group	Surgical side	Time comparison	Difference	Confidence interval (95%)		p-value
Control	Non-surgery side	Pre - Post Treatment	-1	−3.35	1.35	0.40
	Surgery side	Pre - Post Treatment	−2.6	−4.95	−0.24	0.04
Treatment	Non-surgery side	Pre - Post Treatment	0.3	−1.36	1.96	0.72
	Surgery side	Pre - Post Treatment	−6.2	−7.86	−4.53	< 0.00

presented in Table 3.

Regarding the assessment related to the lymphatic flow in lymphoscintigraphy, it was observed that between the pre and post-intervention times of each group there was no significant reduction ($p > 0.05$) between the times for the treated group (Table 5).

Considering the lymphatic flow of the lymphoscintigraphy exam between the groups for each moment before and after the intervention, there is also no significant difference ($p > 0.05$) between the groups after the intervention, indicating that there was no significant change in the flow lymphatic system after intervention in the treated group (Table 6).

4. Discussion

The present study aimed to evaluate the effects of Proprioceptive Neuromuscular Facilitation (PNF) on muscle strength, range of motion, and lymphatic flow in women undergoing surgical treatment of breast cancer. The results obtained indicate that after intervention with PNF there was a significant increase in muscle strength and range of motion, but no in lymphatic flow.

There was a significant increase in palmar grip strength when we compared the control group with the treated group when related to the surgical side, indicating an increase in motor units and consequently, palmar grip strength on the surgical side of the post-intervention treated group with proprioceptive neuromuscular facilitation. The significant difference found in the control group in the second evaluation may have occurred because many women who underwent surgical intervention for breast cancer treatment reduced the movement of the upper limb homolateral to the surgery, saving it during their daily activities (Collins et al., 2014), naturally overloading the non-surgery side limb, a fact that may explain the finding.

Brookham et al. (2018) observed that primary and secondary muscles, not directly involved in surgical intervention for the treatment of breast cancer and adjuvant radiotherapy fields, are affected, and in general, this population works with higher levels of muscle effort to the surgery side to surgery, a fact that may explain the significant strength results found for the limb non-surgery side to surgery.

In the present study, significant differences were found for movements of flexion, abduction, internal and external rotation of the shoulder, and not significant for shoulder extension and adduction, both in the comparison between the treated and control groups, and confirmed by the results obtained in the comparison between the groups surgery side and control limbs. The results are important and expected, since the gain in joint amplitude, in addition to facilitating the performance of activities of daily living, facilitates proper positioning when adjuvant radiotherapy is necessary. Collins et al. (2014) points out that restrictions on the movement of the upper body continue to cause harm and distress for many women undergoing surgical treatment for breast cancer, who yearn to return to their normal daily activities.

The results of the study by Hwang et al. (2015) also agree with the findings of the present study regarding increased range of motion, however the study evaluated women undergoing treatment for breast cancer with lymphedema. The increased range of motion by PNF was observed in a study by Wicke et al. (2014), who found an increase in range of motion and stretching of the shoulder girdle muscles after intervention with the technician, providing greater recruitment of motor units and favoring functional performance in the rehabilitation

Table 3
Mean values confidence interval of the difference of the joint angle in the pre and post treatment times, in the non-surgery side and surgery side limbs, surgery in the control and treated groups, for the flexion, extension, abduction, adduction, internal and external rotation movements.

Moviment	Group	Surgical side	Time comparison	Difference angles	Confidence interval (95%)		p-value
Flexion	Control	Non-surgery side	Pre - Post Treatment	−1.7	−16.13	12.73	0.81
		Surgery side	Pre - Post Treatment	−5.4	−19.83	9.03	0.45
	Treated	Non-surgery side	Pre - Post Treatment	−0.8	−11.01	9.41	0.87
		Surgery side	Pre - Post Treatment	−29.75	−39.96	−19.53	< 0.00
Extension	Control	Non-surgery side	Pre - Post Treatment	−2.3	−6.98	2.38	0.33
		Surgery side	Pre - Post Treatment	0.2	−4.48	4.88	0.93
	Treated	Non-surgery side	Pre - Pos Treatment	−1.35	−4.66	1.96	0.42
		Surgery side	Pre - Post Treatment	−1.3	−4.61	2.01	0.43
Abduction	Control	Non-surgery side	Pre - Post Treatment	−1.6	−16.55	13.35	0.83
		Surgery side	Pre - Post Treatment	−10.4	−25.35	4.55	0.17
	Treated	Non-surgery side	Pre - Post Treatment	−6.15	−16.72	4.42	0.25
		Surgery side	Pre - Post Treatment	−38.85	−49.42	−28.27	< 0.00
Adduction	Control	Non-surgery side	Pre - Post Treatment	−1.9	−7.75	3.95	0.52
		Surgery side	Pre - Post Treatment	−4	−9.85	1.85	0.17
	Treated	Non-surgery side	Pre - Post Treatment	−0.65	−4.79	3.49	0.75
		Surgery side	Pre - Post Treatment	−2.05	−6.19	2.09	0.32
Internal rotation	Control	Non-surgery side	Pre - Post Treatment	−0.9	−11.34	9.54	0.86
		Surgery side	Pre - Post Treatment	−6.5	−16.94	3.94	0.21
	Treated	Non-surgery side	Pre - Post Treatment	−2.35	−9.73	5.03	0.52
		Surgery side	Pre - Post Treatment	−15.35	−22.73	−7.96	< 0.00
External rotation	Control	Non-surgery side	Pre - Post Treatment	−3.4	−11.84	5.04	0.42
		Surgery side	Pre - Post Treatment	−5.2	−13.64	3.24	0.22
	Treated	Non-surgery side	Pre - Post Treatment	−1.1	−7.07	4.87	0.71
		Surgery side	Pre - Post Treatment	−15.35	−21.32	−9.37	< 0.00

Table 4
Mean values confidence interval of the difference of the joint angle in the non-surgery side and surgery side limbs of the surgery, in the pre and post treatment times, in the control and treatment groups, for the flexion, extension, abduction, adduction, internal and external rotation movements.

Moviment	Group	Time	Surgical side comparison	Difference angles	Confidence interval (95%)		p-value
Flexion	Control	Pre Treatment	Non-surgery side - Surgery side	12.26	41.13	< 0.00	12.26
		Post Treatment	Non-surgery side – Surgery side	8.56	37.43	< 0.00	8.56
	Treated	Pre Treatment	Non-surgery side – Surgery side	25.93	46.36	< 0.00	25.93
		Post Treatment	Non-surgery side – Surgery side	−3.01	17.41	0.16	−3.01
Extension	Control	Pre Treatment	Non-surgery side – Surgery side	2.3	−2.38	6.98	0.33
		Post Treatment	Non-surgery side – Surgery side	4.8	0.11	9.48	0.40
	Treated	Pre Treatment	Non-surgery side – Surgery side	5.55	2.23	8.86	< 0.00
		Post Treatment	Non-surgery side – Surgery side	5.6	2.28	8.91	< 0.00
Abduction	Control	Pre Treatment	Non-surgery side – Surgery side	34	19.04	48.95	< 0.00
		Post Treatment	Non-surgery side – Surgery side	25.2	10.24	40.15	< 0.00
	Treated	Pre Treatment	Non-surgery side – Surgery side	41.15	30.57	51.72	< 0.00
		Post Treatment	Non-surgery side – Surgery side	8.45	−2.12	19.02	0.11
Adduction	Control	Pre Treatment	Non-surgery side – Surgery side	9	3.14	14.85	< 0.00
		Post Treatment	Non-surgery side – Surgery side	6.9	1.04	12.75	0.02
	Treated	Pre Treatment	Non-surgery side – Surgery side	2.5	−1.64	6.64	0.23
		Post Treatment	Non-surgery side – Surgery side	1.1	−3.04	5.24	0.59
Internal rotation	Control	Pre Treatment	Non-surgery side – Surgery side	16.1	5.65	26.54	< 0.00
		Post Treatment	Non-surgery side – Surgery side	10.5	0.05	20.94	0.04
	Treated	Pre Treatment	Non-surgery side – Surgery side	17.2	9.81	24.58	< 0.00
		Post Treatment	Non-surgery side – Surgery side	4.2	−3.18	11.58	0.26
External rotation	Control	Pre Treatment	Non-surgery side – Surgery side	8.5	0.05	16.94	0.04
		Post Treatment	Non-surgery side – Surgery side	6.7	−1.74	15.14	0.11
	Treated	Pre Treatment	Non-surgery side – Surgery side	13.1	7.12	19.07	< 0.00
		Post Treatment	Non-surgery side - Surgery side	−1.15	−7.12	4.82	0.70

Table 5
Comparison of lymphatic flow between times for each group.

Group	Comparison between times	Difference	Standard error	Confidence interval (95%)		p-value
Control	Pre - Post Treatment	0.00063	0.001802	−0.00307	0.004334	0.72
Treated	Pre - Post Treatment	0.001192	0.00114	−0.00115	0.003534	0.30

Table 6
Comparison of lymphatic flow between groups for each time.

Time	Comparison between groups	Difference	Standard error	Confidence interval (95%)		p-value
Pré Treatment	Control - Treated	−0.00149	0.001814	−0.00522	0.002238	0.41
Post Treatment	Control - Treated	−0.00093	0.001814	−0.00466	0.0028	0.61

of the shoulder, as observed in the findings of the present study, in which we observed muscle strength and range of motion in the affected upper limb.

The activation of muscle fibers promotes an increase in the recruitment of motor units, effectively favoring muscle strength, the range of motion related to the shoulder joint and increasing blood and lymphatic circulation, favoring functional autonomy, since it is essential to implement new oncological rehabilitation techniques that favor physical health functionality during breast cancer treatment (Brookham and Dickerson, 2016). The present study also aimed to assess the possible effect of PNF on lymphatic circulation, directly affected by surgical intervention. Although the results of the present study showed an increase in the strength of the treated limb, it does not seem to have been sufficient to promote an increase in lymphatic circulation, as a non-significant result observed by lymphoscintigraphy.

Valinote et al. (2013) points out the importance of assessing lymphatic circulation through lymphoscintigraphy in patients undergoing surgical treatment for breast cancer, which can be used to assess the predisposition for upper limb lymphedema related to the treatment of the disease. A study (Vaz et al., 2017) observed that pre-existing functional and anatomical changes in the lymphatic system can promote predisposition to lymphedema after dissection of axillary lymph nodes.

Gashev and Zawieja (2001) observed that regular exercise can stimulate lymphangiogenesis, thus reducing the damage caused by surgical resection associated with axillary emptying. For Tartaglione et al. (2010), exercise can increase lymphatic circulation. However, this increase was not observed in the present study, probably due to the fact that the increase in strength, although significant, was not enough to increase the lymphatic circulation.

The results of the present study are limited to women undergoing breast cancer treatment without lymphedema, new studies on the subject should be carried out, since the effects of proprioceptive neuromuscular facilitation in this population, seems to produce interesting effects in the rehabilitation process.

5. Conclusion

The results obtained in this study allow us to conclude that proprioceptive neuromuscular facilitation favors an increase in muscle strength, range of motion, but not significant for lymphatic flow in women undergoing surgical treatment for breast cancer.

Ethics approval

The research was analyzed and approved by the Ethics and Research

Committee on Human Beings of the Pio XII Foundation - Barretos Cancer Hospital, process n. 1277/2016, and by the Research Ethics Committee of the Clinical Hospital of the Ribeirão Preto Medical School of the University of São Paulo, under protocol n. 2890/2017.

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Declaration of Competing Interest

The authors have no relevant conflict of interest to declare.

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