# Journal of Bodywork & Movement Therapies The Reaching Movement in Breast Cancer Survivors: Attention to the Principles of Rehabilitation. --Manuscript Draft--

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Abstract:	Introduction: Breast-cancer is leading cause of morbidity and mortality in women. The prognosis and survival rate of women with breast-cancer have significantly improved worldwide; more attention needs to be paid to rehabilitative interventions after surgery. This paper describes use of reaching movement to assess upper limb motorcontrol and functional ability after breast-cancer surgery (BC). Material and Methods: We conducted a cross-sectional observational study consisting of biomechanical evaluation of upper limb limitations in women BC, versus a control-group (CG). Thirty breast-cancer survivors and thirty healthy women participated in this study. Both groups were subjected to clinical evaluation of the shoulder joint ROM on the operated side, as an assessment of the muscular-strength of the shoulder with the MRC-scale. The Functional-Assessment was evaluated by the DASH and Constant-Murley-Score. The EORTC QLQ-C30 and VAS were used to measure the quality of life assessment and pain respectively. A Biomechanical evaluation was performed, using Reaching-Task and Surface-EMG. Results: Normal Jerk for BC was higher than CG. Target approaching velocity and movement duration BC was lower than CG. Synergy Anterior Deltoid/Triceps Brachii muscles in CG was higher than BC.	

Conclusion: In BC, upper limb movement is less fluid. Upper limb movement analysis during reaching task is important to monitor rehabilitation. Further studies should verify condition before surgery.

## **INTRODUCTION**

Breast cancer (BC) is the most common malignancy and a leading cause of morbidity and mortality in women worldwide (Puliti et al 2017). Therapeutic advances and improved survival rates for women with BC have implications for its long-term impact on disability, psychological function, and quality of life (QoL), which may be amenable to rehabilitation (Amatya et al 2017; Michelotti et al 2019). The prognosis and survival rate of women with BC have significantly improved worldwide; thus, more attention needs to be paid to rehabilitative interventions after surgery. The rehabilitative aspect is paramount for breast cancer survivors: women who participate in exercise before, during, and after treatment for breast cancer are more likely to return to work where there are no complications that might negatively influence physical performance (i.e. severe lymphedema and web axillary syndrome) (Juvet et al 2017; Kraschnewski & Schmitz 2017; De Sire et al 2019). A woman's need to care for children, her perceived body image, and her existential well-being may also affect her return to work (Lee et al 2017).

The rehabilitative intervention must begin soon after surgery, regardless of the type of surgery (quadrantectomy or mastectomy), and should be aimed at recovering the range of motion (ROM) of the upper limb on the operated side, recovering strength, and controlling pain (De Groef et al 2015). At a later stage, it is also important to consider the recovery of a correct postural assessment. Multifactorial physical therapy and active exercises are effective in treating postoperative pain and impaired ROM after treatment for BC (Zengin Alpozgen et al 2017). Also, home-based, multidimensional survivorship programs are effective for BC survivors with regard to quality of life and functional

improvement (Mirandola et al 2017). Some groups have demonstrated the efficacy of exercises with adapted physical activity (APA), which might represent an effective countermeasure for reducing post-treatment upper limb disability and improving quality of life in BC survivors (Cheng et al 2017). Yet, no studies on exercise in women who have been treated for BC have attended to all principles of exercise training, have reported all components of the exercise prescription in their methods, or reported adherence to the prescription in their results (Neil-Sztramko et al 2017). Further, we cannot consider only the "quantity" of functional recovery after upper limb surgery in BC-the "quality" of recovery must also be measured (Brookham et al 2018).

In fact, some studies show how alterations in muscle activation - in reference to restricted shoulder mobility, which is common in BC patients - affect upper limb function. Moreover, alterations in muscle activity patterns differ by breast surgery and reconstruction type (Yang et al 2017). The reduction in grip strength appears to occur when surgery is performed on the non-dominant side, demonstrating the need to consider the affected side by surgery and dominance, too. Decreased grip strength and lower electromyographic activity of the upper limb are common after BC surgery. When the affected side is the non-dominant side, this loss is greater (Perez et al 2017).

Recent literature suggests that multi domain approaches that are related to not only clinical scales but also other domains, such as instrumental evaluations, might be useful for at least two reasons (Scano et al 2017). First, they might provide a deeper assessment, and second, they might suggest different groupings and, consequently, a disparate characterization of BC survivor populations, which could help physicians and physiotherapists choose the appropriate exercises to recover upper limb function. The coupling with instrumental evaluations should lead to a more detailed procedure that

helps orient therapies for neurological patients and those with other pathologies that involve a functional loss in the upper limbs (Caimmi et al 2015).

Gait analysis could help the rehabilitation physician to plan an adequate rehabilitative path since it would highlight the qualitative and quantitative criticalities of the articular biomechanics of the affected upper limb, as for example the speed of movement, the precision of the movement, the articular range and the fluidity of movement. In fact, this method is not subjective, and represents a valid support to make a datum objective and usable, guaranteeing an objective measure that can be followed over time during the follow-up, also thanks to the three-way evaluation, decidedly superior. Nowadays, in rehabilitation, only assessment scales are used which are lower for intra and inter operator reproducibility.

This paper describes the use of the reaching movement to assess upper limb motor control and functional ability after BC radical surgery, but before starting rehabilitation treatment, to plan the exercises that are offered to the patients. BC patients were compared with a population of healthy women. These two groups were compared based on kinematic and electromyographic data during reaching movement.

# MATERIALS AND METHODS

#### Study design and population

We conducted a cross-sectional observational study that consisted of a biomechanical evaluation of upper limb limitations in women after breast cancer radical surgery (BC), versus a control group of healthy women (CG).

Thirty (N=30) breast cancer survivors and 30 healthy women, matched and homogeneous by age, sex, body mass index (BMI) and handedness, participated in this study from January 1, 2018 to December 31, 2018 in the rehabilitation outpatient clinics of Policlinico Umberto I, Sapienza University of Rome (Italy) and the Don Carlo Gnocchi Foundation of Rome (Italy). The breast cancer survivors patients have been sent from the outpatient oncology present in our structure. Healthy women were enrolled for direct contact, looking for comparative control subjects. Between the 2 groups there were no differences between right and left handed people. The left-handed rate was comparable to that of the global population.

The inclusion criteria for the BC group were: total mastectomy with external breast prostheses or tissue expanders that was performed within 12 months prior to recruitment from waiting lists for rehabilitation treatment, age 18 to 60 years, BMI <30, and no cognitive dysfunction (MMSE>24) (Crum et al 1993). The exclusion criteria were: presence of lymphangitis or mastitis, surgical complications from the intervention, neurological deficits or complications, history of orthopedic problems in the upper limb prior to surgery, previously diagnosed postural problems (such as scoliosis >10° Cobb

angle), severe lymphedema or web axillary syndrome, and visual problems that were not corrected by lenses.

For the healthy group, who enrolled as volunteers at our rehabilitation center, the inclusion criteria were: age 18 to 60 years, BMI <30, and no cognitive dysfunction. The exclusion criteria were: postural problems, shoulder joint dysfunction, neurological or cognitive impairments, visual problems that were not corrected by lenses, oncological disease, rheumatologic disorders, and pregnancy.

All participants signed an informed consent form after receiving detailed information about the study aims and procedures per the Declaration of Helsinki. The rights of human subjects who were involved in the study were protected. The study protocol was approved by the Ethical Committee of the Don Gnocchi Foundation of Rome. This study protocol was developed in accordance with the STROBE guidelines (Von Elm et al 2014).

### **Measurements**

At the first evaluation, the patient's baseline age, height, weight, and BMI were measured by the physiatrist of the rehabilitation center. A clinical examination was performed to exclude participants with scoliosis or other postural disorders. If necessary, an X-ray of the spine was obtained.

A clinical evaluation of the shoulder joint range of motion (flexion, extension, adduction, abduction, and internal and external rotation) (Wingate et al 1989) on the operated side was performed with a goniometer by the physiatrist, as was an assessment of the muscular strength of the shoulder per the Medical Research Council Manual

Muscle Testing (MRC) scale (Ciesla et al 2011), also performed by a physician expert in the procedure. A grade of 5/5 on the MRC scale indicates that movement is possible against maximum resistance; 4/5indicates movement that is possible only against minimum resistance; 3/5 indicates movement that is possible only against gravity; 2/5 indicates movement that is possible only in the absence of gravity; 1/5 indicates evidence of movement; and 0/5 on the MRC scale indicates no movement.

#### Scales: Functional Assessment

The Disabilities of Arm, Shoulder, and Hand Questionnaire (DASH) (Hudak et al 1996) is a 30-item, self-reported questionnaire that measures physical function and symptoms in people with any of several musculoskeletal disorders of the upper limb. It quantifies general disabilities that are related to the upper extremity. The questions are related to the degree of difficulty in performing various functional activities due arm, shoulder, or hand impairments (21 items); the severity of pain, activity-related pain, tingling, weakness, and stiffness (5 items); and the effects on social activities, work, and sleep and their psychological impact (4 items). Each item has 5 options, ranging from 1 to 5. The responses to the 30 questions are summed to form a raw score that is then converted on a scale from 0 to 100. A higher score reflects greater disability. The use of the DASH has increased rapidly in clinical trials, and the instrument is available in several languages, including Italian (Padua et al 2003).

The Constant-Murley Score (CMS) is one of the most widely used, validated, and reliable outcome measures for assessing the shoulder (Bonaiuti 2011). This scoring system consists of subjective variables, such as pain (15 points), activities in daily living

(10 points), and arm positioning (10 points), and objective variables, such as range of motion (40 points) and strength (25 points).

# Quality of Life Assessment

The European Organisation for Research and Treatment of Cancer Quality of Life core questionnaire (EORTC QLQ-C30) (Aaronson et al 1993) is a global cancer-specific questionnaire that examines the health-related quality of life among patients with cancer. This is a 30-item core questionnaire that assesses physical and psychosocial functioning and symptom experiences. This scale has been validated and revised several times. The questionnaire is divided into five functional scales (physical, role, emotional, cognitive, and social functioning) and nine symptom scales and individual items (fatigue, nausea/vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties) (Fayers et al 1999). The acquired scores for each scale are added together, totaling 0–100. A higher score on the functional scales indicates better function, and on the symptom scales, it reflects a more extensive symptom; for the Italian population, its reliability and validity have been found to be adequate (Apolone et al 1998).

## Pain

The Visual Analog Scale (VAS) is a simple, robust, sensitive, and reproducible instrument that enables patients to express their pain intensity as numerical values from 0 to 10 cm (Davidson et al 2002). Patients associated the severity of their upper limb pain on the side of the surgery with a 10-cm continuous line, marked "no pain" on one end and "worst pain" on the other (Strong et al 1991).

# **Biomechanical evaluation**

## Reaching Task

For the Reaching Task, the side that was chosen for the patient evaluation was the side of surgical intervention (regardless of whether it was the dominant limb). For healthy subjects, one of the two sides was analyzed, chosen randomly.

The evaluations were carried out in the same manner between healthy volunteers and BC patients. According to Caimmi et al (2008), we performed one task: frontal reaching, during which patients were asked to reach a target that was placed in front of them. The biomechanical evaluation was conducted using the Smart D500 stereo-photogrammetric system (BTS, Italy), placing 7 markers on anatomical landmarks (Postacchini et al 2015). The subject sat on a chair, adjustable for height, with the feet resting on the floor and knees and hips bent at 90 degrees. In the rest position, both hands were lying on the thighs, and the arms were positioned with flexed elbows and slightly extended shoulders. Each subject, starting from the rest position, was asked to carry out two prescribed movements without moving her back away from the backrest.

First, the subject was asked to move one hand toward a target in front of her at shoulder height, at a distance that was slightly longer than that of the fully extended upper limb. The movements were performed at a speed that was freely chosen by the subject. At the "go" command, each subject repeatedly performed the movements, without pausing, until the test operator issued a "stop" command. At least five repetitions were acquired for the movement. The trial was repeated immediately if the subject did not complete every single movement (i.e., reaching the target and returning to the starting position) or if she did not respect the instruction keep her trunk and head still. Each healthy volunteer was specifically asked to perform the movements, starting with the dominant or non-dominant hand, whereas BC patients were asked to carry out the task on the operated side. The biomechanical outcomes that were measured were: kinematics, kinetics, velocity, and fluidity of movement (jerk) parameters. In particular, we considered: the movement duration (MD); the angle of arm flexion at end of movement (AAF) (AAF is conventionally assigned a value of 0 when the arm is along the side - positive values represent flexion, and negative values represent extension); the angle of the elbow at end of movement (AE) (AE is measured in degrees; the value is assigned 0 when the elbow is extended completely - positive values correspond to flexion, and negative values correspond to hyperextension); the mean targetapproaching velocity (TAV) (normalized for the sum of the lengths of the arm); forearm coefficient of periodicity, calculated for the target approaching acceleration (ACP); and normalized jerk (NJ), calculated for the wrist-target marker distance.

# Surface EMG

We recorded surface EMG signals using a multi-channel Pocket Free EMG system (BTS) at a sampling rate of 1000 Hz and band pass-filtered at 10–500 Hz. EMG activity was recorded through pairs of Ag-AgCl surface electrodes that were precoated with electroconductive gel (diameter 1 cm, distance between electrodes 2 cm). After the skin was carefully shaved and cleansed with alcohol, the electrodes were placed per the SENIAM project (Hermens et al 1999): over the biceps brachialis (BB), anterior deltoid muscle (DA), triceps muscles (TB), and major pectoral muscle (PM), according to standard anatomical landmarks. Five trials were acquired for each subject (Don et al 2007). The EMG signal was elaborated using Myolab software (BTS, Milano, Italy).

We acquired surface myoelectric signals at a sampling rate of 1000 Hz using a 16channel telemetric transmission surface electromyography (pocket EMG System; BTS, Milan, Italy). The lower and upper cutoff frequencies of the Hamming filter were 10 and 400 Hz, respectively, whereas the common mode reaction ratio was 100 dB. To record surface EMGs, we used a pair of Ag-AgCl electrodes, with an interelectrode space of 2 cm, placed on the skin over the muscle belly of the anterior deltoid (DA), biceps brachii (BB), triceps brachii (TB), and major pectoral muscle (PM). We rectified, low-pass-filtered with an upper cutoff frequency of 5 Hz, and integrated the raw signal using a mobile window of 125 ms to obtain the envelope. The co-activity level was determined sample by sample using a formula for these muscles that has been modified from that proposed by Rudolph et al. (Rudolph et al 2000):

1. SynDA/TB (agonist muscles)

2. CoCoBB/TB (antagonist muscles)

Co-activity=  $[(EMG_L + EMG_H)/2 \chi (EMG_L/EMG_H)]$ 

 $EMG_L$  and  $EMG_H$  represent the EMG amplitudes of the less and more active muscles, respectively, normalized to the highest value that was recorded during the movements. A co-activity index was then obtained by calculating the mean values of the co-activity level in the corresponding time windows of the entire movement. Data from the five trials were averaged to obtain each subject's mean values.

The major pectoral was calculated only for the peak of activation (PPM).

We have evaluated the reaching movement only on the outward and not on the return, which is a very simple movement that takes place on a linear trajectory. We have carried out this type of evaluation in order to evaluate the movement as a whole. Our outcome was to evaluate the fluidity that is assessed globally, since it is an index of functionality during daily life activities.

# Sample size calculation

The sample size was evaluated by considering the *jerk parameter*, which measures the fluidity of the upper limb movement, as the primary outcome. According to Caimmi et al (2008), we used one-tailed student t-test for independent samples, considering a power of 85%,  $\alpha$  equal to 0.05, for BC mean value of 30±9 and for control group 25±5. With these parameters, the required sample was 30 subjects per group. The sample was calculated using the G \* Power Version 3.1.9.2.

# **Data analysis**

The mean and standard deviations were computed for all data. We verified the normal distribution of all variables in both groups by D'Agostino-Pearson test, and we applied parametric or nonparametric tests, as appropriate, to compare means.

Mann-Whitney U-test was used to compare data between groups (BC and CG), applying Bonferroni correction to reduce type I errors. The critical alpha level was set to 0.05 for all analyses. All statistical analyses were performed using MedCalc 12.2.1.0 (MedCalc Software).

## **RESULTS**

Table 1 lists the kinematic task data for both groups (breast cancer group and control group) in terms of median and range values. The clinical and biomechanical parameters are summarized in Tables 2, 3 and 4.

**Jerk parameter:** the normalized jerk for the breast cancer group (BC) was significantly higher than for the control group (CG) (p<0.0001).

All the kinematic and EMG variables did not present a normal parametric distribution and therefore in the comparisons between BC and CG we used the U Mann-Whitney Tests for comparison between the groups.

The target-approaching velocity for BC was significantly lower versus CG (p=0.001).

The movement duration for BC was significantly lower compared with CG (p=0.008).

The angle of arm flexion at end of movement for BC and CG was not significant (p=0.983).

The angle of the elbow at end of movement for BC and CG was not significant (p=0.735) (Hidding et al 2014).

For EMG: Syn Anterior Deltoid / Triceps Brachii (SynDA/TB) for CG was significantly higher than for BC (p = 0.036).

The peak of activation of pectoral major muscle for BC was significantly higher than for CG (p = 0.05).

CoCo Biceps Brachii / Triceps Brachii (CoCoBB/TB) for BC and CG was not significant (p =0.983).

No adverse events were detected during the recording of the data.

# **DISCUSSION**

As a result of breast cancer radical treatment, many patients suffer from serious complaints in their arm and shoulder, leading to limitations in activities of daily living and participation.

The standard currents in the literature are that, during a mastectomy, the muscles are usually spared. Only the pectoralis major, rarely, is raised for easier access. For breast reconstruction, if the device is positioned under the muscle, into the submuscular pocket behind the pectoral major, the surgeon must perform an elevation of the pectoralis major and serratus anterior muscles. In the case, instead, of a pre-pectoralis reconstruction, all the muscles are saved (Marcasciano M et al 2018).

The literature and various studies emphasize the importance of obtaining a complete overview of a patient's medical treatment and analyzing outcomes in relation to the treatment; consequently, the use of uniform validated measurement instruments has to be encouraged (Liao & Kirsch 2014). Upper limb movements should be analyzed to objectively monitor rehabilitation interventions, contributing to improving the overall treatment outcomes. Every shoulder movement and upper limb action can use multiple degrees of freedom; thus, various strategies can be implemented to perform the same goal-directed movement.

Our study, between the 2 groups, there were no differences between right and left handed people and the left-handed rate was comparable to that of the global population. The choice of the evaluation through gait analysis performing a reaching movement is due not only to the objectivity of the data obtained but also precisely because it is a simple movement, selected so as to exclude influences of limb dominance. This study is the first attempt to study the reaching movement of upper limb after breast cancer. It investigates the quantitative aspect of the movement of the upper limb and its qualitative aspects through the analysis of jerk parameters. In this regard, our data are notable: BC patients demonstrated a reaching movement that was less fluid, slower, and longer lasting than the control group, with a median for normalized jerk of 14.71 in the BC group, compared with 7.95 in the latter - a difference that was significant.

There were no differences between groups regarding the angle of arm flexion at the end of movement of the shoulder or the angle of the elbow at end of movement, because our BC sample had slight to moderate limitations in shoulder range of motion, and all of them had a shoulder flexion of at least 90 degrees. After breast cancer, arm reaches can be represented through linear testing for qualitative and quantitative analysis of the upper limb. Arm reaches can also be used to decide the best rehabilitative program. In fact, the exercises should consider not only the joint recovery of the shoulder but, most importantly, the overall recovery of the movement of the upper limb, seeking to achieve fluidity of the motor action (Wininger et al 2009). The reaching tasks are considered well executed if they appear "smooth," a quality that is typically quantified by its opposite movement - jerk - and the change in acceleration (Nakano et al 1999). As the brain plans and learns to plan, the optimal trajectory intrinsically coordinates arm and muscle dynamics and uses representations for motor commands that control muscle tensions; thus, it is desirable in rehabilitation to use exercises with a neurocognitive approach that contain elements of work on the "position sense" and "proprioceptive sense" of the shoulder and upper limb (Paolucci et al 2016) (Todorov & Jordan 1998). Further, our results agree with what has been reported - that the speed profiles of arm movements have a number of regularities, including bell-shaped speed profiles in straight reaching movements and an inverse relationship between speed and curvature in extemporaneous movements (Flanders & Herrmann 1992).

The results of the muscle activities for the muscle groups that were analyzed showed a similar trend, with less activation of the major pectoral in BC relative to CG and major synergy between the anterior deltoid and triceps brachii during the reaching task in BC. To correctly interpret these data, we must consider that the disability of our patients with respect to upper limb function is moderate (CMS  $62 \pm 10.7$ ; DASH  $65 \pm 15.4$ ), based on improvements in the surgical technique and the immediate implantology of expanders or direct reconstruction.

The activity of muscles during upper limb movements is considered to consist of tonic and phasic components that account for arm-weight compensation and movement dynamics, respectively (D'Avella et al 2006) (D'Avella et al 2008) (Kong 2014).

Muscle coordination has been studied recently by many groups using muscle synergies (Sabatini 2002) (Bizzi & Cheung 2013) (Coscia et al 2014). The study of muscle synergies is based on the assumption that muscles are synergistically co-activated via discrete motor modules of neural origin, aimed at fulfilling an elementary biomechanical demand: a modular organization has been viewed as a strategy that is used by the central nervous system (CNS) to reduce the complexity of the control of motion. However, the relationship between the tonic and phasic components of muscle activity and how their activation is coordinated during movement are not fully understood. Muscle synergy is considered a vector that specifies a pattern of relative muscle activation (Tang et al 2014) (Shamley et al 2012) (Brookham & Dickerson 2016). The significant differences in scapular kinematics between the affected and

unaffected sides of women who report shoulder pain following treatment for breast cancer are notable: scapula kinematic and muscle EMG parameters in both arms are altered in breast cancer survivors compared with healthy participants.

In other studies, the BC experiences increased (8.7%) activation of the pectoralis major: our study has provided insights into how biceps brachii muscles compensate during dysfunction. Compared with healthy co-activation, the BC demonstrated greater activation of internal (IR) and external rotator (ER)-type muscles during their respective rotation type. Comparing muscle co-activation strategies between biceps brachii and healthy populations may help identify muscle dysfunction and facilitate clinical interpretation of the dysfunction, which can guide preventative and therapeutic interventions. In general, BC patients expend greater muscle effort on the affected side but demonstrate weakness in strength testing, which might reflect tissue damage.

Gait analysis has proved to be a valid tool for an adequate biomechanical evaluation of the movement in patients after breast cancer and certainly represents a good starting point for an adequate personalized rehabilitation process, since it can show all the critical aspects that they must be considered for a comprehensive approach to this kind of patient.

#### **Strengths, Weaknesses and Limitation**

Strengths: Our study is the first attempt to investigate the reaching function of upper limb in women after surgery for BC. Examining reaching in common clinical practice during rehabilitation would allow clinicians to evaluate the extent of recovery and the quality of recovery of upper limb function. Weaknesses of this study: nowadays in literature there is a lack concerning the subject, which attracts more interest. We have to consider that lacked the evaluation of function of the upper limb before surgery. Thus, future studies with a larger sample of patients are desirable. Also, to render the data homogeneous, the findings should consider the upper limb on the operated side, without considering the side of the dominant hand. Study limitation: no pre-evaluation was performed before breast cancer surgery. We have no information on the type of cancer operated, although we have included women with the same surgery. The number of the size is reduced and a greater follow-up is necessary in order to better quantify the differences between the groups and better quantify the rehabilitation intervention over time.

#### **CONCLUSIONS**

In the BC, even if a patient appears to perform the movement of reaching correctly, the movement of the upper limb is qualitatively less fluid (jerk test). These results must be taken into account when suggesting the rehabilitation exercise. Also, upper limb movement analysis during a reaching task is important to objectively monitor rehabilitation interventions, contributing to improvements in the overall treatments for BC. Further studies are warranted to verify the patient's condition before surgery and include pre-surgical data, in order to better follow and quantify the rehabilitation intervention over time.

#### **REFERENCES**

Aaronson NK, Ahinedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, Filiberti A, Flechtner H, Fleishman SB, De Haes JCJM, Kaasa S, Klee M, Osoba D, Razavi D, Rofe PB, Schraub S, Sneemv K, Sullivan M, Takeda F 1993 The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. Journal of the National Cancer Institute 85(5):365–376

Amatya B, Khan F, Galea MP 2017 Optimizing post-acute care in breast cancer survivors: a rehabilitation perspective. Journal of Multidisciplinary Healthcare 30; 10:347-357

Apolone G, Filiberti A, Cifani S, Ruggiata R, Mosconi P 1998 Evaluation of the EORTC QLQ-C30 questionnaire: a comparison with SF-36 Health Survey in a cohort of Italian long-survival cancer patients. Annals of Oncology 9(5):549–557

Bizzi E, Cheung VC 2013 The neural origin of muscle synergies. Frontiers in Computational Neuroscience 7:51

Bonaiuti D 2011 Scale di Misura in Riabilitazione. 3rd. Societa Editrice Universo, Rome - Italy

Brookham RL, Dickerson CR 2016 Comparison of humeral rotation co-activation of breast cancer population and healthy shoulders. Journal of Electromyography and Kinesiology 29:100-6 Brookham RL, Cudlip AC, Dickerson CR 2018 Examining upper limb kinematics and dysfunction of breast cancer survivors in functional dynamic tasks. Clinical biomechanics (Bristol, Avon) 55:86-93

Caimmi M, Guanziroli E, Malosio M, Pedrocchi N, Vicentini F, Molinari, Tosatti L, Molteni F 2015 Normative Data for an Instrumental Assessment of the Upper-Limb Functionality. BioMed Research International 2015:484131

Caimmi M, Carda S, Giovanzana C, Maini ES, Sabatini AM, Smania N, Molteni F 2008 Using kinematic analysis to evaluate constraint-induced movement therapy in chronic stroke patients. Neurorehabil Neural Repair. 22(1):31-9

Cheng KKF, Lim YTE, Koh ZM, Tam WWS 2017 Home-based multidimensional survivorship programmes for breast cancer survivors. Cochrane Database of Systematic Reviews 24; 8:CD011152

Ciesla N, Dinglas V, Fan E, Kho M, Kuramoto J, Needham D 2011 Manual muscle testing: a method of measuring extremity muscle strength applied to critically ill patients. Journal of Visualized Experiments 12; (50)

Coscia M, Cheung VC, Tropea P, Koenig A, Monaco V, Bennis C, Micera S, Bonato P 2014 The effect of arm weight support on upper limb muscle synergies during reaching movements. Journal of NeuroEngineering and Rehabilitation 11:22

Crum RM, Anthony JC, Bassett SS, Folstein MF 1993 Population- based norms for the Mini-Mental State Examination by age and educational level. The Journal of the American Medical Association 269:2386-91 D'Avella A, Portone A, Fernandez L, Lacquaniti F 2006 Control of fast-reaching movements by muscle synergy combinations. Journal of Neuroscience 26: 7791–7810

D'Avella A, Fernandez L, Portone A, Lacquaniti F 2008 Modulation of phasic and tonic muscle synergies with reaching direction and speed. Journal of Neurophysiology 100:1433–1454

Davidson M, Keating JL 2002 A comparison of five low back disability questionnaires:reliability and responsiveness. Physical Therapy 82:8-24

De Groef A, Van Kampen M, Dieltjens E, Christiaens MR, Neven P, Geraerts I, Devoogdt N 2015 Effectiveness of postoperative physical therapy for upper-limb impairments after breast cancer treatment: a systematic review. Archives of Physical Medicine and Rehabilitation 96(6):1140-53

De Sire A, Invernizzi M, Lippi L, Cisari C, Özçakar L, Franchignoni F 2019 Blurred lines between axillary web syndrome and Mondor's disease after breast cancer surgery: A case report. Ann Phys Rehabil Med. 2019 May 20

Dinneen LC, Blakesley BC 1973 Algorithm AS 62: a generator for the sampling distribution of the Mann– whitney U statistic. Journal of Applied Statistics 22(2):269–273

Don R, Ranavolo A, Cacchio A, Serrao M, Costabile F, Iachelli M, Camerota F, Frascarelli M, Santilli V 2007 Relationship between recovery of calf-muscle biomechanical properties and gait pattern following surgery for achilles tendon rupture. Clinical biomechanics (Bristol, Avon) 22(2):211-20

Fayers P, Aaronson NK, Bjordal K, Curran D, Groenveld M 1999 EORTC QLQ-C30 Scoring Manual. 2nd. EORTC, Brussels - Belgium

Flanders M, Herrmann U 1992 Two components of muscle activation: scaling with the speed of arm movement. Journal of Neurophysiology

Hermens HJ, Freriks B, Merletti R, Hagg G, Stegeman D, Block J 1999 SENIAM: European Recommendations for Surface Electromyography. Roessingh Research and Development, The Netherlands

Hidding JT, Beurskens CH, van der Wees PJ, van Laarhoven HW, Nijhuis-van der Sanden MW 2014 Treatment related impairments in arm and shoulder in patients with breast cancer: a systematic review. PLoS One 9(5):e96748

Hudak PL, Amadio PC, Bombardier C 1996 Development of an upper extremity outcome measure: the DASH (disabilities of the arm, shoulder and hand. The Upper Extremity Collaborative Group (UECG) American Journal of Industrial Medicine 29(6):602–608

Juvet LK, Thune I, Elvsaas IKØ, Fors EA, Lundgren S, Bertheussen G, Leivseth G, Oldervoll LM 2017 The effect of exercise on fatigue and physical functioning in breast cancer patients during and after treatment and at 6 months follow-up: A meta-analysis. Breast. Jun;33:166-177

Kong YK 2014 The effects of co-ordinating postures with shoulder and elbow flexion angles on maximum grip strength and upper-limb muscle activity in standing and sitting postures. International Journal of Occupational Safety and Ergonomics 20(4):595-606) Kraschnewski JL, Schmitz KH 2017 Exercise in the Prevention and Treatment of Breast Cancer: What Clinicians Need to Tell Their Patients. Curr Sports Med Rep. Jul/Aug;16(4):263-267

Lee MK, Kang HS, Lee KS, Lee ES 2017 Three-Year Prospective Cohort Study of Factors Associated with Return to Work After Breast Cancer Diagnosis. Journal of Occupational Rehabilitation 27(4):547-558

Liao JY, Kirsch RF 2014 Characterizing and predicting submovements during human three-dimensional arm reaches. PLoS One 9(7):e103387

Marcasciano M, Kaciulyte J, Gentilucci M, Barellini L, Ribuffo D, Casella D 2018 Skin-reduction breast reconstructions with prepectoral implant covered by a combined dermal flap and titanium-coated polypropylene mesh. J Plast Reconstr Aesthet Surg. 71(8):1123-1128

Michelotti A, Invernizzi M, Lopez G, Lorenzini D, Nesa F, De Sire A, Fusco N 2019 Tackling the diversity of breast cancer related lymphedema: Perspectives on diagnosis, risk assessment, and clinical management. Breast. Apr;44:15-23

Mirandola D, Miccinesi G, Muraca MG, Belardi S, Giuggioli R, Sgambati E, Manetti M, Monaci M, Marini M 2017 Longitudinal assessment of the impact of adapted physical activity on upper limb disability and quality of life in breast cancer survivors from an Italian cohort. Supportive Care in Cancer

Nakano E, Imamizu H, Osu R, Uno Y, Gomi H, Yoshioka T, Kawato M 1999 Quantitative examinations of internal representations for arm trajectory planning: minimum commanded torque change model. Journal of Neurophysiology 81(5):2140-55 Neil-Sztramko SE, Winters-Stone KM, Bland KA, Campbell KL 2017 Updated systematic review of exercise studies in breast cancer survivors: attention to the principles of exercise training. British Journal of Sports Medicine pii: bjsports-2017-098389

Padua R, Padua L, Ceccarelli E, Romanini E, Zanoli G, Amadio PC, Campi A 2003 Italian version of the disability of the arm, shoulder and hand (DASH) questionnaire: cross-cultural adaptation and validation. The Journal of Hand Surgery 28(2):179–186

Paolucci T, Zangrando F, Piccinini G, Sciarra F, Pallotta R, Mannocci A, la Torre G, Bini F, Marinozzi F, Gumina S, Padua L, Saraceni VM 2016 A New Neurocognitive Interpretation of Shoulder Position Sense during Reaching: Unexpected Competence in the Measurement of Extracorporeal Space BioMed Research International 2016:9065495

Perez CS, das Neves LMS, Vacari AL, de Cássia Registro Fonseca M, de Jesus Guirro RR, de Oliveira Guirro EC 2017 Reduction in handgrip strength and electromyographic activity in women with breast cancer. Journal of Back and Musculoskeletal Rehabilitation

Postacchini R, Paoloni M, Carbone S, Fini M, Santilli V, Postacchini F, Mangone M 2015 Kinematic analysis of reaching movements of the upper limb after total or reverse shoulder arthroplasty. Journal of Biomechanics 48(12):3192-8

Puliti D, Bucchi L, Mancini S, Paci E, Baracco S, Campari C, Canuti D, Cirilli C, Collina N, Conti GM, Di Felice E, Falcini F, Michiara M, Negri R, Ravaioli A, Sassoli De' Bianchi P, Serafini M, Zorzi M, Caldarella A, Cataliotti L, Zappa M 2017 IMPACT COHORT Working Group. Advanced breast cancer rates in the epoch of service screening: The 400,000 women cohort study from Italy. European Journal of Cancer 75:109-116

Rudolph KS, Axe MJ, Snyder-Mackler L 2000 Dynamic stability after ACL injury: who can hop? Knee Surgery, Sports Traumatology, Arthroscopy 8 262–269

Sabatini AM 2002 Identification of neuromuscular synergies in natural upper-arm movements. Biological Cybernetics 86:253–262

Scano A, Chiavenna A, Malosio M, Molinari Tosatti L, Molteni F 2017 Muscle Synergies-Based Characterization and Clustering of Poststroke Patients in Reaching Movements. Frontiers in Bioengineering and Biotechnology 13; 5:62

Shamley D, Lascurain-Aguirrebeña I, Oskrochi R, Srinaganathan R 2012 Shoulder morbidity after treatment for breast cancer is bilateral and greater after mastectomy. Acta Oncologica 51(8):1045-53

Strong J, Ashton R, Chant D 1991 Pain intensity measurement in chronic low back pain. The Clinical Journal of Pain 7:209-18

Tang L, Li F, Cao S, Zhang X, Chen X 2014 Muscle synergy analysis for similar upper limb motion tasks. 36th Annual International Conference of the IEEE Engineering in Medicine and Biology Society 2014:3590-3

Todorov E, Jordan MI 1998 Smoothness maximization along a predefined path accurately predicts the speed profiles of complex arm movements. Journal of Neurophysiology 80(2):696-714

Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP 2014 STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. International Journal of Surgery 12(12):1495-9

Wingate L, Croghan I, Natarajan N, Michalek AM, Jordan C 1989 Rehabilitation of the mastectomy patient: a randomized, blind, prospective study. Archives of Physical Medicine and Rehabilitation 70(1):21-4

Wininger M, Kim NH, Craelius W 2009 Spatial resolution of spontaneous accelerations in reaching tasks. Journal of Biomechanics 42(1):29-34

Yang EJ, Kwon Y 2017 Changes in shoulder muscle activity pattern on surface electromyography after breast cancer surgery. Journal of Surgical Oncology

Zengin Alpozgen A, Razak Ozdincler A, Karanlik H, Yaman Agaoglu F, Narin AN 2017 Effectiveness of Pilates-based exercises on upper extremity disorders related with breast cancer treatment. European Journal of Cancer Care (Engl) 26(6)

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Reaching kinematics	BC	CG	р
Normalized Jerk	14.718 (9.05- 40.64)	7.958 (6.77- 20.10)	<0.0001*
Median Value Of Target-Approaching Velocity	0.521 (0.29- 0.811)	0.693 (0.55-1.07)	0.001*
Movement Duration	0.850 (0.47-1.37)	0.55 (0.49-0.76)	0.0008*
Angle Of Arm Flexion At End Of Movement	66.640 (51.67- 76.40)	67.111 (61.65- 72.23)	0.983
Angle At Elbow At End Of Movement	132.113 (64.24- 161.97)	132.897 (115.41- 158.40)	0.735
			* significant at the p<0.05 level

Table 1. Reaching kinematic task data for both groups of women (median andrange value).Legenda: BC: Breast cancer group; CG: Control Group.

**Table 2 Demographic and clinical characteristics of women included in the sample**. Cases (and percentages) or mean ± standard deviation of demographic and clinical characteristics of the sample. BMI: Body Mass Index; QoL: quality of life; DASH: Disabilities of the Arm, Shoulder, and Hand Questionnaire; CMS: Constant-Murley Score; EORTC QLQ-C30: Quality of Life core questionnaire (GH: global health; FS: function scale; SS: symptom scale).

Womens' Clinical	Control Group (N=30)	Breast	
Parameters		Cancer Group (N=30)	
Age (mean ± SD)	50 ± 5.80	52 ± 6.49	
BMI (mean ± SD)	24 ± 0.5	23 ± 0.7	
Married/common-law wife	75%	84%	
Working	Working 85%	Working 73 %	
not employed	not employed 10%	not employed 20%	
or retired from work	retired 5%	retired 7%	
At least a high school education	30%	28%	
Regular exercise	63.3%	43.3	
Left Handedness	10%	20%	
Womens' Clinical characteristics			
Chemotherapy	-	47.5%	
Radiotherapy	-	67.5%	

Mild Lymphedema	-	13%
Time from surgery [months]	-	$5.56 \pm 4.03$
Womens' Scale-scores		
EORTC QLQ-30 GH	-	63 ± 5.4
EORTC QLQ-30 FS	-	$72 \pm 8.3$
EORTC QLQ-30 SS	-	28 ± 3.5
DASH	-	65 ± 15.4
CMS	-	$62 \pm 10.7$
VAS	-	2.30 ± 1.64

EMG	BC	CG	р
Syn Anterior Deltoid / Triceps Brachii	1.03 (0.55-3.52)	1.27 (1.72-2.11)	0.036*
(SynDA/TB)			
CoCo Biceps Brachii / Triceps Brachii	1.28 (0.50-4.20)	1.42 (0.83-2.37)	0.063
(СоСоВВ/ТВ)			
Major Pectoral Muscle	5.81 (2.02-17.40)	4.70 (2.07-12.20)	0.050*
(PPM)			
		*	significant at
			<mark>the p&lt;0.05</mark>
			level

# Table 3 EMG parameters of women included in the sample.Legenda: EMG:Electromyography; BC: Breast cancer group; CG: Control Group.

# Table 4. Mann-Whitney U-test to compare data between groups, using an exact sampling

# distribution for U.

	<b>Breast Cancer Group</b>	<mark>Contro Group (mean</mark>	
	<mark>(mean rank)</mark>	rank)	
Normalized Jerk	<mark>20.57</mark>	<mark>8.73</mark>	U=30; z=-3.393;
			p<0.0001*
Target-approching	<mark>12.74</mark>	<mark>23.68</mark>	U=194.500; z=3.135;
velocity (m/s)			p=0.001*
<b>Movement duration</b>	<mark>19.62</mark>	10.55	U=50; z=-2.601;
<mark>(m/s)</mark>			p=0.008*
Angle of arm flexion at	15.53	15.45	U=104; z=-0.022;
<mark>end of movement (deg)</mark>			<mark>p=0.983</mark>
Angle of the elbow at	15.42	14.20	U=87; z=-0.367;
<mark>end of movement (deg)</mark>			p=0.735
Syn Anterior Deltoid /	<mark>40.61</mark>	52.29	U=1293; z=2;102;
Triceps Brachii			p=0.036*
Peak of activation of	<mark>47.41</mark>	<mark>44.36</mark>	<mark>U=960; z=-0.549;</mark>
<mark>pectoral major muscle</mark>			<mark>p=0.05*</mark>
CoCo Biceps Brachii /	<mark>15.53</mark>	15.45	U=104; z=-0.022;
Triceps Brachii			<mark>p=0.983</mark>

\* significant at the p<0.05 level

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# **CRediT** author statement

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