Quantifying and predicting upper limb capability and dysfunction of breast cancer survivors

by

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Author's Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

Abstract

Breast cancer will affect one in every nine Canadian women during their lifetime. As diagnostic and treatment methods improve, survival rates are approaching 90%. However, an alarming 30-82% of survivors suffer from persistent upper limb morbidity as a result of their cancer treatments (Kwan, Jackson, Weir, Dingee, McGregor, & Olivotto, 2002; Lauridsen, Overgaard, Overgaard, Hessov, & Cristiansen, 2008; Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004). These persistent disabilities compromise function and quality of life, hindering survivors from returning to work and leading functional and independent lives. In order to prevent and rehabilitate upper limb morbidities, quantification of the physical capabilities of this population must occur.

This thesis quantified the upper limb physical capabilities and limitations of breast cancer survivors by producing the most comprehensive collection of 3-D kinematics, muscle activation patterns, muscle-specific strength, and quality of life and disability measures during a wide range of functional tasks. Compared to the contralateral limb, the affected side demonstrated reduced humeral elevation (-6.5°) and external rotation angles (-8.9°), increased humeral internal rotation (+13.1°), reduced scapular protraction (-3.9°) (although both sides demonstrated protraction), increased upward rotation (+2.8°) and increased posterior tilting (+4.1°) of the scapula. These relationships varied with the task being performed. Muscle activation patterns revealed increased total muscle effort on the affected side during work tasks ($p = 0.0258$), and reductions in pectoralis major sternal activation ($p<0.0001$ – $p = 0.0230$). Increased muscle effort, weakness and discomfort levels were evident in both primary and secondary muscles (muscles outside the field of surgery and radiation).

Humeral internal (IR) and external rotation (ER) co-activation was defined in both healthy (H) and breast cancer survivor populations (BCP) (H: $r^2 = 0.70$ (IR) and 0.35 (ER); BCP: $r^2 = 0.77$ (IR) and 0.77 (ER)). Humeral abduction angle and task intensity were important factors in the prediction of co-activation in both populations. Inclusion of physiological cross-sectional area

(PCSA) weightings did not sufficiently improve the representation of co-activation in the healthy population. Healthy co-activation relationships were successfully extrapolated to a novel set of IR exertions ($r^2 = 0.76$ IR exertions; $r^2 = 0.40$ ER exertions). Comparisons made between populations identified differing muscle strategies used by survivors to maintain glenohumeral joint stability. Compared to healthy population co-activation, the survivors demonstrated greater activation of IR and ER muscles during their respective rotation type. Survivors demonstrated increased (≤8.7%) activation of pectoralis major muscle activation compared to the healthy population.

An optimization-based muscle force prediction model was used to reflect specific muscle dysfunction of the pectoralis major muscles, and population-specific co-activation was enforced as a constraint. Empirically measured EMG was more closely associated to muscle force predictions of external rotator muscles ($r = 0.567$) than internal rotator muscles ($r = 0.347$). Model predictions were influenced by exertion type, co-activation constraint, hand force and pectoralis major capability constraints. The model predicted muscle forces more closely to empirical measurements of activation when the co-activation constraint was enforced, emphasizing the importance of consideration of antagonistic muscle activation in biomechanical modeling.

This comprehensive description of physical capabilities of the breast cancer population has never been performed in such detail. This body of work has furthered the knowledge available regarding the capacity and functional limitations of survivors and preliminary recommendations regarding therapeutic treatment and directions for future works have been suggested. The continued development of this research and future application of interventions designed to address these disabilities will promote the eventual return to function and work of survivors through targeted rehabilitation and treatment strategies. Development of effective rehabilitation and prevention strategies could potentially lower the social and economic burdens of survivor aftercare and dramatically enhance the quality of life of survivors, allowing them to lead highly functional and independent lives.

Acknowledgements

There is a common phrase that “it takes a village to raise a child”. I believe it. I also believe it is equally true that “it takes a village to complete a PhD”. This work would not have been possible without the support and guidance of many individuals.

I owe a huge amount of thanks to my supervisor Dr. Clark Dickerson. Upon entering my Master’s degree, I warned Dr. Dickerson that I had no interest in pursuing a PhD. He was fine with that decision, but somewhere along the path I saw the researcher in myself that Dr. Dickerson had seen in me years previous to that. I would like to thank Dr. Dickerson for his continued guidance, mentorship, support and patience. His insight into my work was always helpful with my best interest in mind, even though I didn’t always realize it.

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Saving the most important for last, I would like to express my most sincere and deepest thanks to my family. They all have been affected to no small degree during this degree. My husband Aaron has remained my steadfast companion whose love and support helped me continue through this challenging phase of our life. Thank you for all you have put up with. To my precious sons, Benjamin and Joshua, who daily bring me so much joy and love, and help me to grasp perspective of the most important matters of life. I love you more than words can express. From my parents, in-laws, grandparents and other loved ones – you have all helped out in so many different ways to make this possible. From child care to lawn cutting, gardening, meals, phone calls, prayers and so much more. Every bit helped and mattered. A very special thank you goes to my parents who put aside a lot of their own needs and responsibilities in business and life to support our little family. My mom, Sharon, daily sacrificed so much of her time, effort and life to watching the boys so I could work, and supported me in the many ups and downs of this long journey. Thank you seems so inadequate. Thank you to "my village", all of you mentioned and those unnamed - your presence and support in my life has not gone unnoticed, and has played a major factor in the completion of this PhD.

Above all, I must thank my Heavenly Father, from Whom comes all strength, knowledge, wisdom and ability.

Dedication

This work is dedicated to the breast cancer survivors that bravely and selflessly dedicated time and effort to perform this study. You each came with a story and experiences you were willing to share; it touched my life and gave me insight into yours. You worked hard, despite fear, fatigue and pain. You did all this in full realization that this research may not directly help you, but instead chose to devote yourself in the hopes that this work and future works would someday help others like you. I pray that this hope will soon be true.

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List of Abbreviations

ADL = activities of daily life

BCT = breast conserving therapy

BCP = breast cancer survivor population

CI = co-activation index

EMG = electromyography

ER = external rotation

FACT-B = Functional Assessment of Cancer Therapy Scale – Breast

iEMG = integrated electromyography

IR = internal rotation

LPF = low pass filter

LSM = least squared means

MRM = modified radical mastectomy

MVC = maximal voluntary contraction

MVF = maximal voluntary force

QoL = quality of life

ROM = range of motion

RPD = rating of perceived discomfort

TME = total muscle effort

Quick-DASH = Quick Disability of Arm, Shoulder and Hand Score

Chapter 1 Introduction

Breast cancer is a disease that often strikes women in their prime, compromising their ability to lead rich, productive lives as a result of persistent disability related to complications of the disease and its treatment. These persistent disabilities compromise quality of life, and arguably question successful survivorship status when resulting in such blatant and disruptive dysfunction. The first necessary step towards improving function and return to work of this valuable working population is comprehensive documentation of the physical capabilities of breast cancer survivors. This thesis seeks to do this with unprecedented quality and thoroughness, providing a strong basis for future rehabilitative and preventative ergonomics strategies to help improve the lives of those persons who have survived breast cancer. It is desired to make the post-cancer years count more for these affected women. Doing so will have the potential to generate profound social and economic benefits for Ontario and world-wide.

Section 1.1 Breast cancer statistics and impact on life

Breast cancer is the most common cancer among Canadian women (excluding non-melanoma skin cancer), and each year 24,400 women will be diagnosed with it and 5,000 will die from it (Canadian Cancer Society, 2014). Almost 9,000 of these new cases will be diagnosed in Ontario alone (Canadian Cancer Society's Steering Committee, 2010). The 5-year survival rate is 88% (Canadian Cancer Society, 2014) and amongst survivors there is a 30 - 82% prevalence of long term upper limb morbidity, most commonly including reduced range of motion (ROM), weakness, pain, swelling and numbness (Kwan, Jackson, Weir, Dingee, McGregor, & Olivotto, 2002; Lauridsen, Overgaard, Overgaard, Hessov, & Cristiansen, 2008; Maycock, Dillon, & Dixon, 1998; Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004). The prevalence of decreased ROM ranges from 2 to 51% with severe restrictions (greater than 50% reduction) in 2% of patients (Rietman, et al., 2003). Survivors also experience decreased functional capacity, meaning they exert more effort

relative to their maximal ability to perform usual activities, therefore leading to higher levels of fatigue (Mock, et al., 2005). Cancer treatment side effects can last days, months, and even years (Hsieh, Sprod, Hydock, Carter, Hayward, & Schneider, 2008). These impairments interfere with survivors' ability to perform activities of daily life (ADL) and return to work, and negatively affect quality of life (QoL) (Markes, Brockow, & Resch, 2006; Rietman, et al., 2003). Only 28% of new breast cancer cases are in women older than 69 years, indicating that the majority (72%) of diagnoses occur in the workforce-age population (Canadian Cancer Society's Steering Committee, 2010), effectively influencing the workforce across sectors and skill levels. As diagnostic and treatment techniques improve and survival rates increase, long-term adverse effects of adjuvant treatments are becoming more important as they may influence ADL and QoL (Nikander, Sievanen, Ojala, Oivanen, Kellokumpu-Lehtinen, & Saarto, 2007; Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004).

Chronic arm morbidity is relatively understudied and is one of the most troublesome long-term complications of breast cancer treatments (Kwan, Jackson, Weir, Dingee, McGregor, & Olivotto, 2002). As the survival rates increase, more research needs to focus on life after diagnosis and treatment (Sandel, Judge, Landry, Faria, Ouellette, & Majczak, 2005). Upper limb morbidity has rarely been accurately documented (Thompson, Air, Jack, Kerr, Rodger, & Chetty, 1995), and few have investigated the mechanisms of change associated with these morbidities (Courneya K. S., Mackey, Bell, Jones, Field, & Fairey, 2003). Late morbidity (symptoms appear some time after treatment is complete) interferes with ADL and QoL, but the relationships between impairments, disability, performance of tasks and QoL of breast cancer patients have only scarce documentation (Rietman, et al., 2003; Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004). Current quantitative measures of physical capacity of breast cancer populations (BCPs) consist of basic evaluations that thwart meaningful interpretations. Variability is high in assessments of impairments, and no uniform criteria exist for ROM, muscle strength, pain and arm volume measures

(Rietman, et al., 2003). Further, muscle coordination, muscle specific strength measures and 3-D kinematic assessments of this population during ADL and work tasks have not been assessed. This stark lack of description of upper limb disability requires immediate attention.

Section 1.2 Dissertation overview and context

Upper limb dysfunction within the BCP has not been systematically evaluated, which has limited development of specific and effective preventative and treatment strategies to promote healthy return to function and work. A prerequisite for creating these strategies is population physical capability description. This thesis will describe upper limb capacities and dysfunctions in a female BCP in terms of kinematics, muscle coordination and strength during ROM, ADL and work activities. These findings will be compared between unaffected (non-cancer) and affected (cancer-affected) sides. Further, a previously developed theoretical shoulder model will be adjusted to reflect proposed survivor changes in specific muscular capacity in attempt to improve predicted muscle forces. An accurate muscle force prediction model could assist in assessing return-to-work readiness.

This research will also act as a foundation for future research projects, which will ultimately improve the eventual return to work of the BCP through improved rehabilitation and treatment strategies. Future studies will also evolve follow-up assessments of capability to assess effective and sustainability of integration into the workspace, as well as general longitudinal recovery. Progression of these future studies is outlined in Figure 1. Development of effective rehabilitation and reduction of symptoms could potentially lower the social and economic burdens of survivor aftercare and dramatically enhance quality of life. Improving the health of this population will allow these survivors not just the ability to live – but to live highly functional and independent lives.

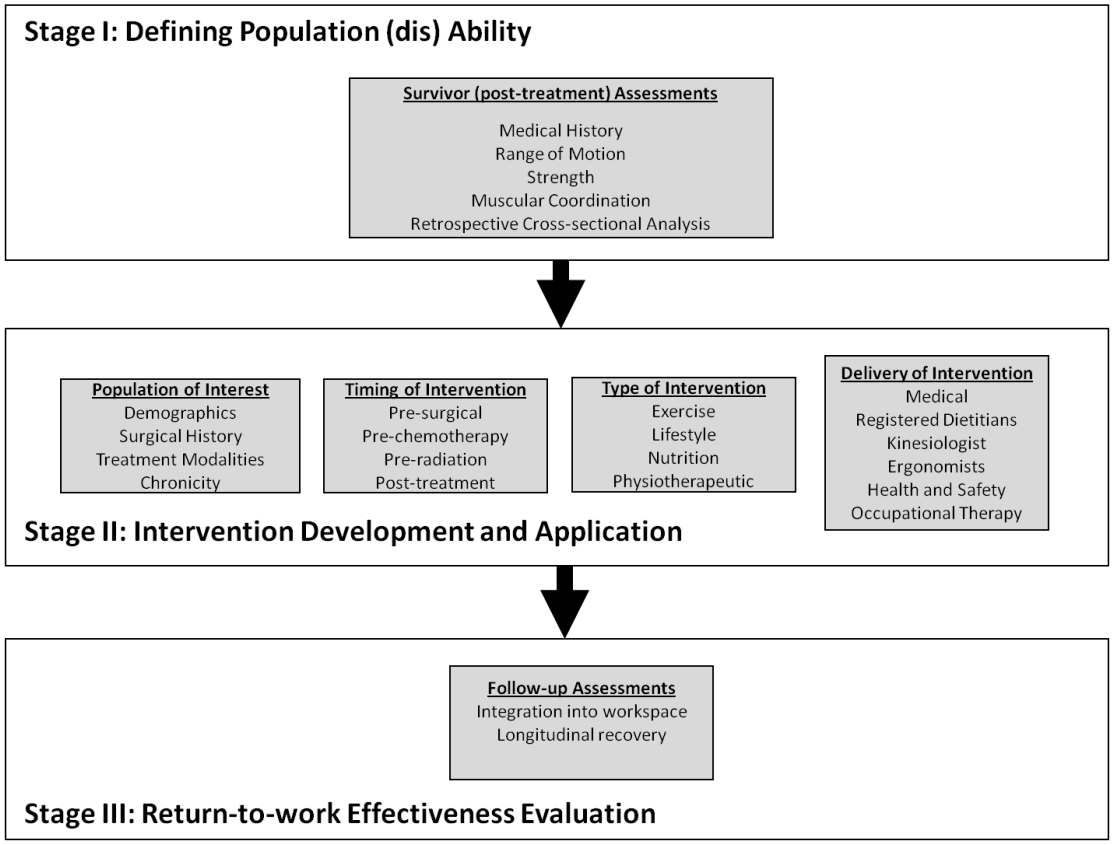

Figure 1 Flow chart depicting how future projects (Stage II and III) will extend from the findings of this thesis (Stage I).

Section 1.3 Global thesis objectives & hypotheses

This thesis is made up of four studies that seek to investigate eight major objectives with associated hypotheses, as described below and illustrated in Figure 2.

Study 1 - Quantification of upper limb capabilities and dysfunction of breast cancer survivors, and relationship to quality of life (QoL) and performance of activities of daily living (ADL) and work tasks

Objectives:

1. Describe the upper limb capabilities and dysfunction of the BCP in terms of 3-D upper limb kinematics (specifically, motions of the humerus and scapula with respect to the thorax), muscle activation patterns (electromyography), and muscle-specific strength (force).
2. Determine relationships between total muscle effort (a physical muscle activation quantity of (dys)function) with subjective measures of function (QoL and disability scores) during ROM, ADL and work task performance.

The hypotheses of this study are as follows:

1. Three-dimensional kinematic description of the BCP will indicate reduced elevation angles and reduced external rotation range of motion, but increased scapular protraction range of motion on the affected side compared to the contralateral limb.

Past literature have reported reduced humeral abduction and flexion ROM (Hack, Cohen, Katz, Robson, & Goss, 1999; Isaksson & Feuk, 2000; Kuehn, et al., 2000; Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004; Swedborg & Wallgren, 1981), reduced external rotation ROM (Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004; Swedborg & Wallgren, 1981), and increased scapular winging (protraction) (Lauridsen, Torsleff, Husted, &

Erichsen, 2000) amongst the BCP. These measures have been recorded manually with goniometry and inclinometer tools or have been reported via clinicians' visual assessment. Two studies have recorded 3-D scapulothoracic kinematics with electromagnetic tracking, and have reported increase in scapular protraction on the affected side of survivors (Borstad & Szucs, 2012; Shamley, Srinaganathan, Oskrochi, Lascurain-Aguirrebena, & Sugden, 2009).

2. The BCP will demonstrate reduced strength and increased muscle activity (enhanced EMG amplitude) on the affected side when performing muscle specific strength tests, ROM, ADL and work tasks compared to their unaffected side.

Reductions in strength are commonly reported amongst the BCP (Isaksson & Feuk, 2000; Kuehn, et al., 2000; Rietman, et al., 2003), but often measures include subjective reports or quantitative measures of grip strength. Quantification of muscle-specific weakness is scarce amongst the BCP. Discrepancies exist even between the two groups that reported muscle activation in survivors. Shamley et al. (2007) reported decreased activation of the pectoralis minor, upper trapezius and rhomboid on the affected side during scaption; whereas increased activation of the upper trapezius was found in survivors performing a functional writing task by Galiano-Castillo et al. (2011). Later, Shamley et al. (2012) re-examined normalized muscle activity of pectoralis major, serratus anterior, rhomboids and upper trapezius during scaption of a BCP with mastectomy or wide local excision. With the exception of upper trapezius in the mastectomy group, the authors reported an increase in activity of all muscles on the left affected side of patients with either mastectomy or wide local excision compared to the left side of a healthy control group; and reported greater activation of the upper trapezius, rhomboids and serratus on the right affected side of patients with mastectomy compared to the right side of a healthy control, suggesting the BCP was working at a higher level of percent capability. Shamley et al. (2012) also reported a decrease in pectoralis major activity and an increase in serratus anterior activity on the affected side compared to the unaffected side.

3. As physical data indicates increased dysfunction (increased total muscle effort), there will be decreased QoL scores (FACT-B) and increased disability scores (QuickDASH).

The number of chronic symptoms of late morbidity of the BCP has been significantly correlated with anxiety and depression levels (Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004). Decreased muscular activity of the upper trapezius and rhomboid muscles have been associated with increased Shoulder Pain and Disability Index scores in the BCP (Shamley, et al., 2007). Box et al. (2002) reported a trend of decreased shoulder ROM associated with breast cancer patients' increased rating of performance difficulty while performing functional tasks.

Study 2 – Empirical quantification of internal and external rotation co-activation in healthy shoulders

Objective:

1. Quantification of the co-activation relationships of humeral internal and external rotators in young healthy adults using traditional (non-weighted) and PCSA-weighted co-activation index ratios.
2. Determine if the co-activation relationships defined from a subset of exertions can be extrapolated to other additional postures and intensities.

Hypotheses:

1. It was hypothesized that the PCSA-weighted co-activation prediction models would better represent empirically measured co-activation (with predictions yielding higher r^2 values) compared to the traditional non-weighted co-activation prediction models.
2. It was hypothesized that the co-activation relationship determined for a subset of postures (original data set) would be successfully extrapolated to a unique subset of exertions (extrapolated data set). Recent work has demonstrated that co-activation relationships

defined at the elbow for a subset of exertions can be extrapolated successfully to unique postural data sets (Brookham, Middlebrook, Grewal, & Dickerson, 2011; Middlebrook, Brookham, & Dickerson, 2013).

Study 3 – Comparison of humeral rotation co-activation of breast cancer survivors and healthy shoulders

Objectives:

1. Quantification of the co-activation relationships of humeral internal and external rotators in a BCP
2. Comparison of survivor co-activation relationships with those of a healthy population (defined in Study 2 of this thesis)

Hypothesis: It was hypothesized that muscle-activation patterns of the BCP will reveal survivors have a reduced internal/external humeral rotation co-activation ratio compared to healthy individuals during IR exertions (reflecting a decrease in pectoralis major activation).

The co-activation ratio provides a relative measure of internal rotation (IR) contribution to total activation (IR and external rotation (ER) activation) about the shoulder. Due to the location of the breast cancer treatment (surgery and radiation is typically directed to the anterior aspect of the chest), the pectoralis muscles are primarily in the field of disturbance. It is hypothesized that these anterior chest muscles (humeral internal rotators) will be unable to produce force, causing a reduction in total activation of the internal rotator muscles in relation to the posteriorly located humeral external rotators. It was hypothesized that this dysfunction would present as a reduction in magnitude of the numerator of the co-activation ratio, compared to the ratio of a healthy population.

Study 4 – Modelling changes in humeral internal and external rotation strength of breast cancer survivors to investigate employed muscle strategies

Objectives:

The purposes of this study were to modify an existing 3-D, inverse dynamic link-segment model of the right upper limb (specifically, the Shoulder Loading Analysis Modules (SLAM) (Dickerson, 2005; Dickerson, Chaffin, & Hughes, 2007)) in terms of survivor pectoralis major capability, co-activation (defined from Study 3 of this thesis) and population anthropometrics to determine the following:

1. Determine how muscle strategy is affected by specific muscle dysfunction (using an inverse dynamics approach). Specifically, compare how closely SLAM muscle force predictions represent empirically measured survivor EMG during IR and ER exertions with different pectoralis major force producing capabilities.
2. Determine if inclusion of BCP IR and ER exertion type co-activation constraints improve the physiological realism of the muscle force predictions (more closely represent the empirically recorded EMG).

It was hypothesized that:

1. SLAM muscle force predictions will be more closely associated with empirically measured EMG activation levels during states of reduced pectoralis major capability. Specifically, correlations between EMG and muscle force predictions will be highest when the pectoralis major capability is set to 0.25, 0.50 and 0.75; and correlations will be lowest when capability is set to 0.0 or 1.0.

Due to the nature of surgeries and adjuvant treatments received in the BCP, and the resultant evidence of dysfunctional changes prevalent in this population (as demonstrated by muscle activation and kinematic changes in Study 1 of this thesis), it is assumed that survivors will neither have total disability (pectoralis major capability of 0) nor total capability (100% capable of producing maximal

force) of the pectoralis major muscles. It is hypothesized that survivors maintain 0.25-0.75 ability of the pectoralis major capability, which will be reflected by higher correlations between EMG and model predictions during these conditions.

2. Inclusion of the co-activation constraint would result in the muscle force predictions more closely representing the empirically recorded muscle activation.

Previously, elbow flexor and extensor co-activation constraints were included in an optimization muscle force prediction model of the elbow, and results demonstrated that inclusion of these constraints improved the model predictions, bringing them closer to the empirically measured activation levels (Brookham, Middlebrook, Grewal, & Dickerson, 2011).

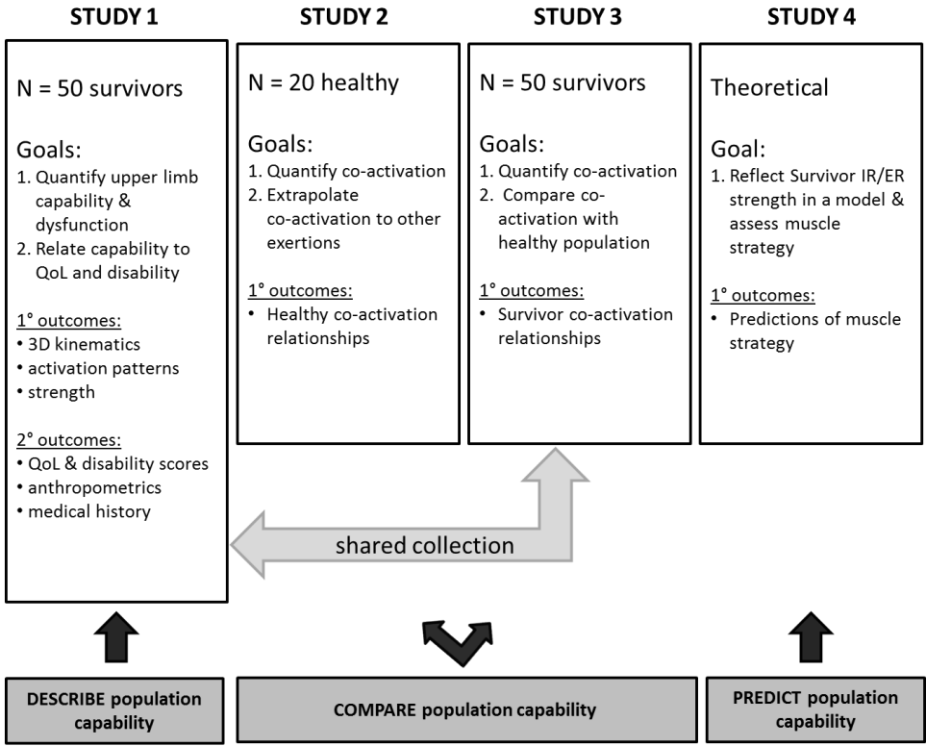

Figure 2 An outline of the specific goals and outcomes of the four studies which comprise this thesis. Shaded boxes indicate general study purposes. Studies 1 and 3 comprised of a shared data collection.

Chapter 2 General review of breast cancer research literature

This chapter introduces and describes the disease of breast cancer, its affected population, associated diagnostic and treatment regimens and the subsequent sequelae to these treatments. A review of literature investigating the effects of exercise treatment on these morbidities is presented, and is followed by identification of gaps in the current literature that relate to the proposed work.

Section 2.1 Breast cancer: disease stages, treatment and prognosis

Cancer is a class of diseases in which cells display abnormal and uncontrolled growth creating a mass of cells and in some cases metastasize to other areas of the body. Breast cancer is cancer originating in the breast tissue, which spans the region laterally from the sternum to the axilla and superiorly to the clavicle. Breast cancer can metastasize through the blood stream or the lymphatic system, spreading to other areas of the body. Breast cancer is the most frequently diagnosed cancer in females (Figure 3), and one in nine women will develop breast cancer in their lifetime. Approximately 23,200 cases of breast cancer were diagnosed in women in Canada in 2010, and 5,300 are expected to die from it (Canadian Cancer Society's Steering Committee, 2010) (Table 1). Almost 9,000 of these new cases were diagnosed in Ontario alone (Canadian Cancer Society's Steering Committee, 2010). Breast cancer occurs in males as well, and it was estimated that 150 males were diagnosed in Canada in 2010, with only 100 of these surviving (Canadian Cancer Society's Steering Committee, 2010).

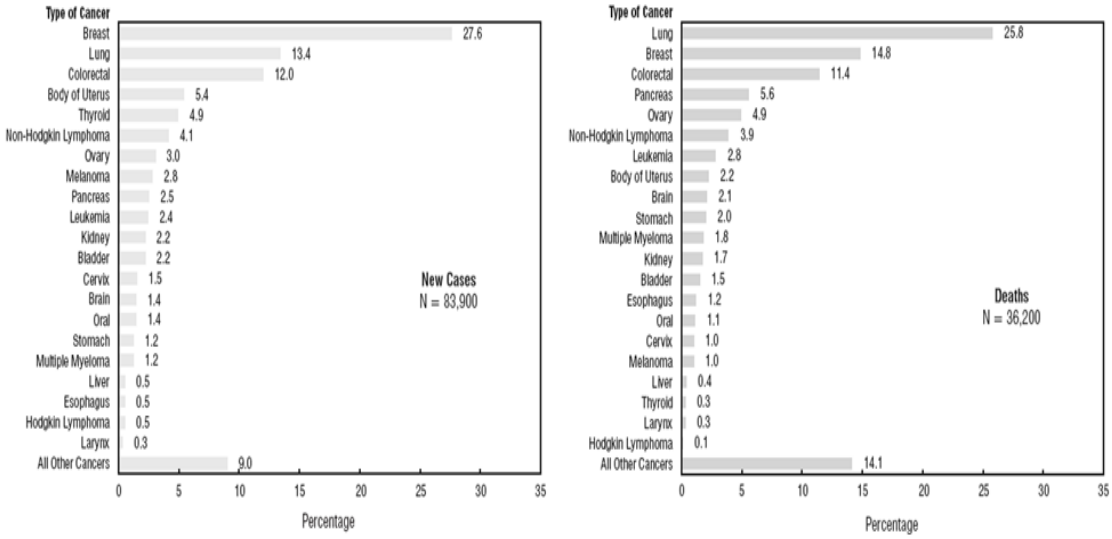

Figure 3 Percentage distribution of estimated new cases [left] and deaths [right] for selected cancers for females in Canada in 2010 (Canadian Cancer Society's Steering Committee, 2010). New cases exclude an estimated 34,300 non-melanoma skin cancer. Figure was taken from the Canadian Cancer Statistics 2010 (Canadian Cancer Society's Steering Committee, 2010).

Table 1 Estimated new cases and deaths for the most common cancers by age and sex in Canada in 2010. Dash lines (-) indicate fewer than three cases or deaths. Table was taken from the Canadian Cancer Statistics 2010 (Canadian Cancer Society's Steering Committee, 2010).

Age	Lung			Colorectal			Prostate	Breast
	Total	M	F	Total	M	F	M	F
New Cases								
All Ages	**24,200**	**12,900**	**11,200**	**22,500**	**12,400**	**10,100**	**24,600**	**23,200**
0–19	10	5	5	10	5	5	5	5
20–29	25	10	10	55	30	25	—	85
30–39	95	40	55	240	120	110	15	860
40–49	960	360	600	1,050	560	510	440	3,500
50–59	3,400	1,600	1,850	3,400	2,000	1,400	4,100	6,200
60–69	7,200	3,900	3,300	5,900	3,600	2,200	9,400	5,800
70–79	7,600	4,400	3,300	6,300	3,700	2,700	7,000	3,800
80+	4,800	2,700	2,100	5,400	2,400	3,100	3,600	2,800
Deaths								
All Ages	**20,600**	**11,200**	**9,400**	**9,100**	**5,000**	**4,100**	**4,300**	**5,300**
0–19	—	—	—	5	5	—	—	—
20–29	5	—	5	10	5	5	—	5
30–39	55	20	35	50	25	25	—	100
40–49	690	260	430	270	150	120	15	400
50–59	2,500	1,200	1,300	950	560	390	120	920
60–69	5,700	3,100	2,600	1,900	1,200	670	520	1,050
70–79	6,800	3,900	2,900	2,500	1,500	1,000	1,250	1,100
80+	4,900	2,700	2,200	3,500	1,550	1,950	2,400	1,750

Breast cancer occurs primarily in females between 50 and 69 years of age, with 28% of cases diagnosed in women older than 69 years, and 19% of cases being diagnosed in women younger than 50 years (Canadian Cancer Society's Steering Committee, 2010). Likely attributable to an increase in mammography screening, breast cancer incidence rates rose from 1980 through the early 1990s; and similarly perhaps due to increased mammography screening as well as the use of more effective adjuvant therapies following surgery, mortality rates have decreased since the mid-1980s (Figure 4). The 5 year survival rate is currently 88% for women with breast cancer (Canadian Cancer Society, 2014).

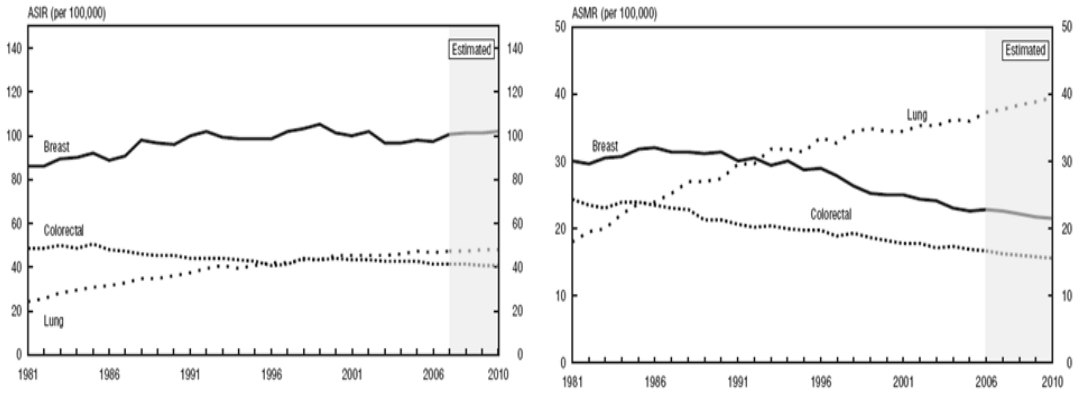

Figure 4 Age-standardized incidence rates (ASIR) and age-standardized mortality rates (ASMR) for selected cancers for females in Canada from the years 1981-2010. Rates were age-standardized to the 1991 Canadian population. Figure was taken from the Canadian Cancer Statistics 2010 (Canadian Cancer Society's Steering Committee, 2010).

The precise causes of breast cancer are unknown but it is believed to be a result of interactions between genetic and environmental risk factors. These include female gender, age, family history, breast density, early menstruation and late menopause, radiation exposure, hormone replacement therapy, oral contraceptives, increased body weight, and alcohol and tobacco use (Canadian Breast Cancer Foundation, 2010). The incidence of breast cancer is 2 - 4 times greater in women who have a family history of the disease (Fisher, Fisher, Sass, & Wickerham, 1984). The incidence of contralateral metastases from breast cancer is extremely rare (Fisher, Fisher, Sass, & Wickerham,

1984) and post-lumpectomy treatment, 85% of all local breast recurrences are noted within the first 4 years, and 95% are noted within 5 years (Fisher, Sass, Fisher, Gregorio, Brown, & Wickerham, 1986).

Section 2.1.1 Disease stages and prognosis

There are many types of breast cancer, with each type having dissimilar prognoses and treatment recommendations. The types are defined on the basis of what parts of the breast are infected (Figure 5), and how the cancer progresses. The Canadian Breast Cancer Foundation (2010) describes four main types of breast cancer as depicted in Table 2.

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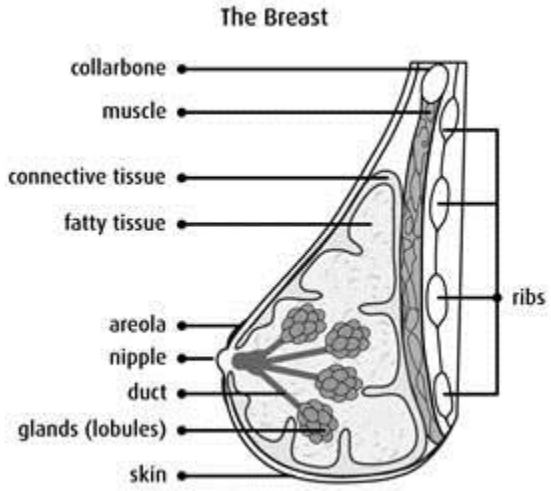


Figure 5 Anatomy of the breast from a lateral perspective. Figure taken from (Canadian Cancer Society, 2014).

Table 2 Four main types of breast cancer and associated description.

Breast Cancer Type	Description
Non-invasive (in situ) Breast Cancer i.e.) ductal carcinoma in situ or lobular carcinoma in situ	Cancer in which cells remain within the place of origin (within milk ducts or breast lobules) and have not spread to surrounding breast tissue.
Invasive Breast Cancer i.e.) invasive ductal, lobular, mucinous, tubular, medullary, micropapillary carcinomas	Cancer may grow and invade neighbouring tissue and spread to other body parts.
Inflammatory Breast Cancer	Indicated by redness and swelling of the breasts and is often misdiagnosed as a breast infection. Uncommon, occurring in only 1-4% of breast cancer cases.
Paget's disease	Affects the nipple (itchiness, scaling, weeping). Uncommon, occurring in only 1% of all breast cancer cases.

Breast cancer is staged according to the size of the tumor, the number of lymph nodes affected (if any), and the presence or absence of distant metastases (Segal, et al., 2001). The stages are indicated by levels 0 to IV, with a higher number indicating more advanced stages of cancer with poorer prognosis. The TNM Staging System was developed by the American Joint Committee on Cancer and the International Union Against Cancer, and is based on the extent of the tumor (T), the extent of spread to the lymph nodes (N), and the presence of metastasis (M) (AJCC, 2009).

Individuals with breast cancer are usually termed as 'patients' or 'survivors' depending on their current state of treatment or completion thereof, however there is discrepancy in the literature concerning the definition of a cancer survivor. Some consider anyone who has been diagnosed with cancer, from the time of diagnosis throughout the rest of their life to be a survivor (Doyle, et al., 2006). Whereas, others consider survivorship to begin once cancer treatments are completed, and the individual continues to live with the memories of their treatment and the possibility of cancer recurrence (Pelusi, 1997; Thomas-MacLean, 2004). For the purposes of this dissertation, a cancer patient will be defined as an individual currently undergoing cancer treatment, whereas a cancer

survivor will be defined as an individual that has completed cancer treatment including surgery, chemotherapy and/or radiation treatment.

Although 5 year cancer survivor rates are approaching 90%, the associated physical and psychosocial prognoses are negative. Seventy nine percent of patients that had modified mastectomies and 83% of patients treated surgically with lumpectomies suffered from one or more late symptoms 1 – 4 years post-surgery (Husted, Lauridsen, Torsleff, & Erichsen, 1995). Late symptoms persist following treatments, and include pain around the scar and operative area, neck and shoulder pain, decreased ROM, weakness, swelling and sensation disturbances (Lauridsen, Torsleff, Husted, & Erichsen, 2000). The most common impairments of post breast cancer treatment are reported to be decreased shoulder ROM, numbness around the axilla and lateral chest wall, decreased grip strength, pain, and increased arm volume (Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004). Anemia is common in patients acquiring solid tumors, and it is associated with increased fatigue, decreased QoL and impaired exercise tolerance (Courneya, et al., 2008). More than 48% of Canadian breast cancer survivors are overweight or obese and 50% are inactive (Courneya, et al., 2008).

Section 2.1.2 Surgical treatment

The purpose of surgical treatment is to remove the cancerous tumor(s), and can involve various procedures depending on the cancer severity. Surgery is generally one of the first lines of treatment and is widely associated with causing fatigue (Cimprich, 1993).

Section 2.1.2.1 Mastectomy

In 1894 the radical mastectomy was introduced by William Steward Halsted, which involved breast ablation and removal of the overlying skin and pectoralis major muscle (Dalberg, Krawiec, & Sandelin, 2010). This procedure followed by radiation caused lymphedema and ROM restrictions in about 50% of patients (Sugden, Rezvani, Harrison, & Hughes, 1998). As imaging modalities and

adjuvant treatments improved, this procedure was considerably abandoned in the 1950s-1960s and replaced with a more limited surgery, the modified radical mastectomy (MRM) (Dalberg, Krawiec, & Sandelin, 2010).The MRM involves breast ablation and removal of the fascia overlying the pectoralis major muscle, but the muscle itself is preserved (Dalberg, Krawiec, & Sandelin, 2010). The change from radical to modified mastectomies reduced the incidence of lymphedema and restrictions in ROM (Sugden, Rezvani, Harrison, & Hughes, 1998). However, ROM restrictions, especially during shoulder abduction, flexion and external rotation, are still prevalent with this procedure because the subcutaneous tissues of skin flaps tend to adhere to the raw muscle, inhibiting the usual smooth gliding between the muscle and the subcutaneous tissue (Lauridsen, Overgaard, Overgaard, Hessov, & Cristiansen, 2008). Dalberg et al. (2010) evaluated the long term (11 year follow-up) benefits of fascia preservation in breast cancer patients undergoing modified radical mastectomies and found in cases of which the tumor did not involve the pectoralis fascia, preservation of the fascia did not have a significant impact on chest wall recurrence rate or survival, but there was a trend towards lower recurrence with those patients that had the fascia removed. Additional studies with larger sample sizes are required to examine these trends. Figure 6 depicts an anatomical perspective of changes occurring in a patient post radical or modified mastectomy.

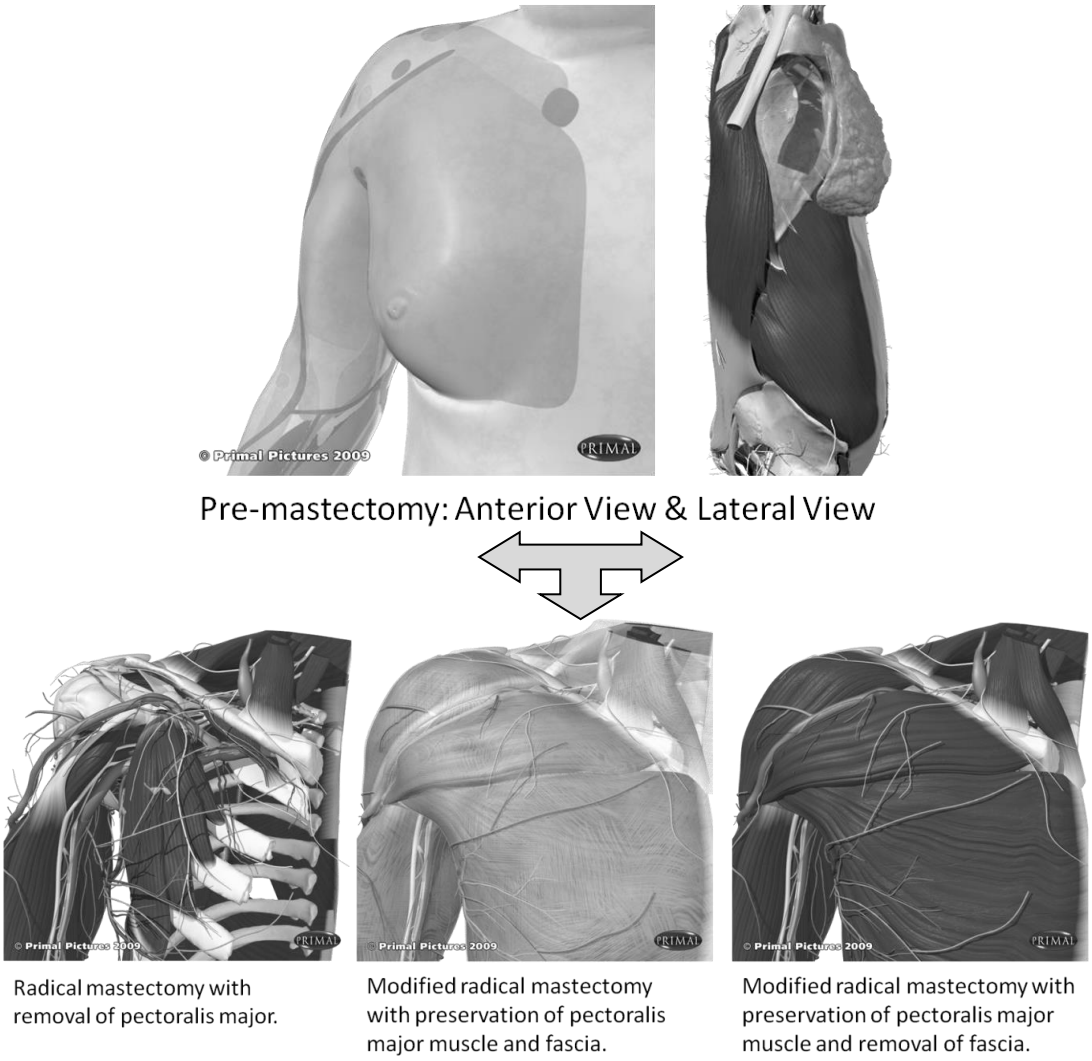


Figure 6 Depiction of radical and modified mastectomy. [Top row depicts surface anatomy prior to mastectomy; bottom row, left, depicts post radical mastectomy with pectoralis major removed; bottom row, centre and right, depict post modified mastectomy with and without fascia preservation, respectively.] Figures taken from (Primal Pictures, 2006).

Section 2.1.2.2 Breast conserving therapy

Breast conserving therapy (BCT) (or lumpectomy) was introduced in the 1960s and further developed in the 1970s and 1980s and is a less invasive surgery requiring tumor excision which is generally followed by radiation (Rietman, et al., 2003). It often involves excision of a tumor with cancer free margins (distance between the tumor and edge of surrounding tissue that is removed along with it) greater than 3 mm (Nesvold, Dahl, Lokkevik, Mengshoel, & Fossa, 2008). In most

Western countries this type of surgery is predominately performed (except in the case of large and/or multi-centric tumors), but in the world, mastectomies are still the dominating surgical option (Dalberg, Krawiec, & Sandelin, 2010). Figure 7 depicts a local region excised during BCT. Gerber et al., (1992) compared morbidities from patients who had received modified radical mastectomies versus breast conserving therapies and found that mastectomy patients were slower to achieve pre-surgical ROM measures, but that patients receiving breast conserving therapies (followed by axillary dissection and radiation) had more chest wall tenderness at 1-2 years post-surgery.

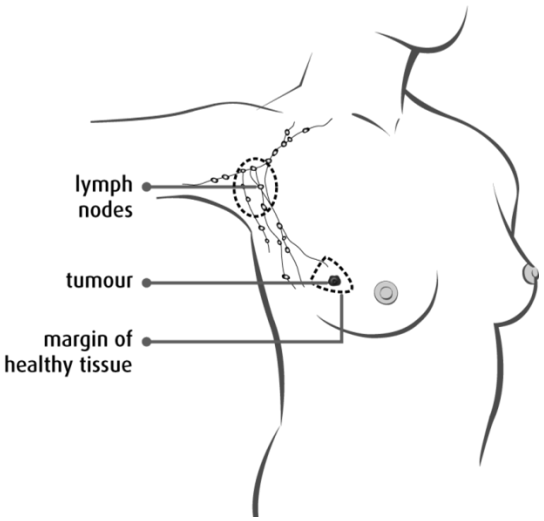


Figure 7 Breast conserving therapy (lumpectomy). The tumor and a small portion of surrounding breast tissue [area surrounding by dashed triangular shape] are removed. Figure taken from (Canadian Cancer Society, 2011).

Section 2.1.2.3 Axillary node dissection

The lymphatic system is an extensive drainage system which functions to return interstitial fluid to the blood, absorb fats and fat-soluble vitamins from the digestive system and transport them to venous circulation and aid the immune system in defending against invading microorganisms and disease. The lymphatic system is made up of a series of lymphatic channels and lymph nodes throughout the body (Figure 8). The axillary lymph nodes (Figure 9) are an essential prognosis factor

for breast cancer recurrence and survival, along with the size of the tumor (Carter, Allen, & Henseon, 1989; Hack, Cohen, Katz, Robson, & Goss, 1999; Maycock, Dillon, & Dixon, 1998). Axillary lymph nodes are the most common site of tumor metastases from breast cancer (Maycock, Dillon, & Dixon, 1998) and the presence of cancer cells in the axilla indicates that cancer has spread from the breast, suggesting a poorer patient prognosis (Hack, Cohen, Katz, Robson, & Goss, 1999). It is recommended that about 10 lymph nodes be removed during axillary dissections to minimize the risk of erroneous classification (Mathiesen, Carl, Bonderup, & Panduro, 1990). However, axillary dissections lead to several morbidities including decreased shoulder and arm ROM, decreased strength, pain, seroma, lymphedema and numbness (Bendz & Olsen, 2002; Haid, et al., 2002; Ivens, Hoe, Podd, Hamilton, Taylor, & Royle, 1992; Kuehn, et al., 2000; Polinsky, 1994; Sugden, Rezvani, Harrison, & Hughes, 1998).

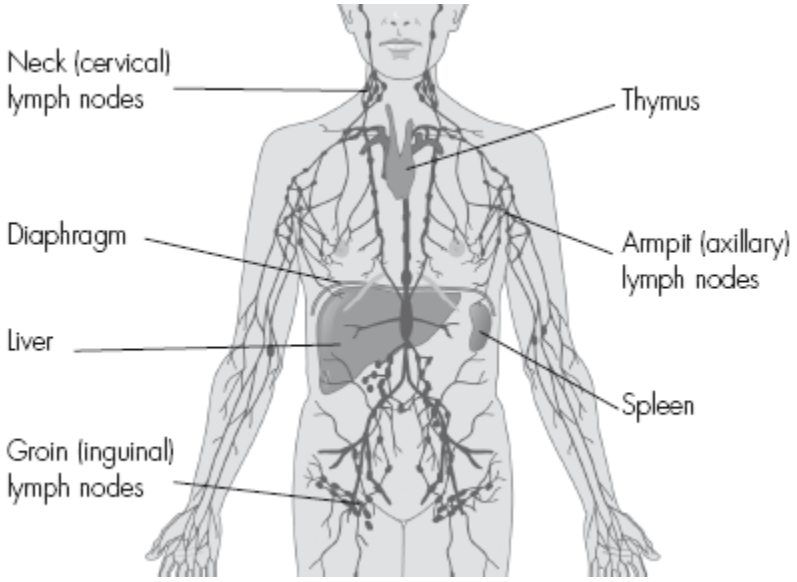


Figure 8 Depiction of the lymphatic system. Figure taken from (The-Human-Body.Net, 2011).

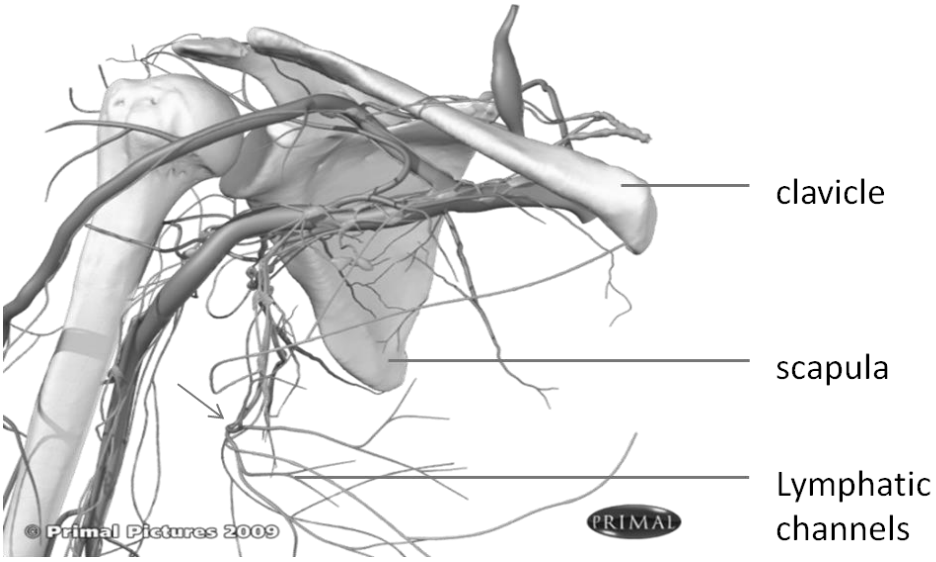


Figure 9 Axillary lymph nodes. Anterior view of the scapula: thin axillary lymph channels and small nodes [an example directed by the arrow] within the area of the axilla. Figure modified from (Primal Pictures, 2006).

Several nerves are exposed and susceptible to damage during axillary dissections (Figure 10). Numbness and altered sensation have been attributed to disruptions or division of the intercostobrachial nerve (Sugden, Rezvani, Harrison, & Hughes, 1998). Damage to other nerves can affect muscles and movements including: serratus anterior resulting in winged scapula (long thoracic nerve), latissimus dorsi affecting shoulder internal rotation and abduction (thoracodorsal nerve), and the pectoralis major affecting shoulder flexion, adduction and internal rotation (pectoral nerve) (Lauridsen, Torsleff, Husted, & Erichsen, 2000). The intercostobrachial nerve is commonly sacrificed or damaged during axillary dissections (Chiverton & Perry, 1987), and the preservation of such is considered difficult and time-consuming, leading to only modest improvements in sensory deficits (Abdullah, Iddon, Barr, Baildam, & Bundred, 1998; Salmon, Ansquer, & Asselain, 1998).

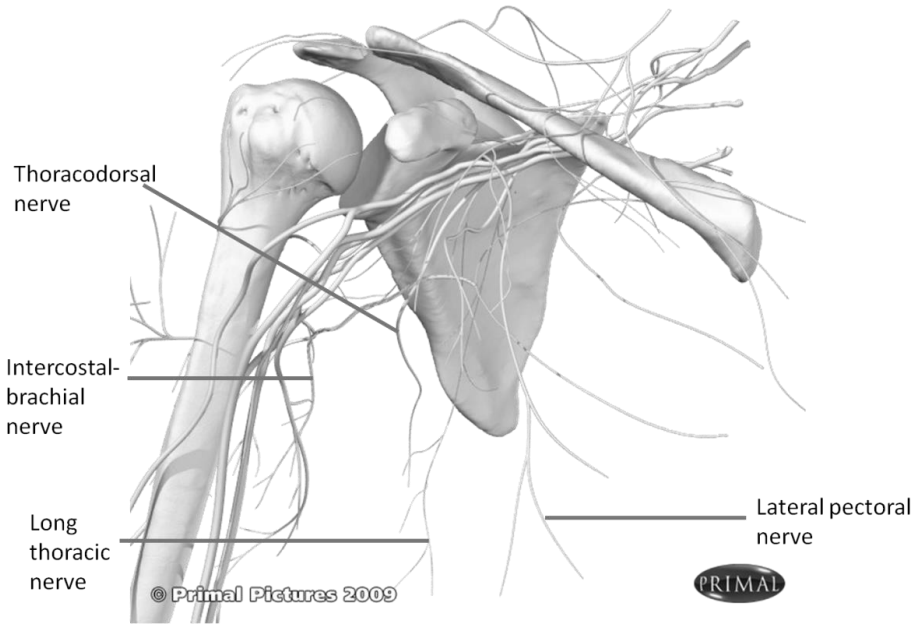


Figure 10 Nerves within the axilla. [Anterior view of the scapula] Intercostalbrachial nerve is commonly sacrificed during axillary dissections. Other nerves within this area may also be affected. Figure modified from (Primal Pictures, 2006).

Sentinel lymph node biopsies are a newer procedure which involve sampling (dissecting) only one or a few sentinel lymph nodes. The sentinel lymph node is the first node in a cluster of nodes that receives lymph fluid from the area around the tumor, and is the first node the cancer cells will likely spread to (Canadian Cancer Society, 2011). If cancerous cells are not found in these sentinel nodes, it is unlikely (less than 5% chance) that the cancer has spread to other nodes (Canadian Cancer Society, 2011). Sentinel node biopsies have become the standard procedure in managing the axilla (Lauridsen, Overgaard, Overgaard, Hessov, & Cristiansen, 2008) and were developed to reduce the number of unnecessary axillary lymph node dissections and reduce morbidity rates associated with these dissections (Rietman, et al., 2003). Maycock et al. (1998) examined long term problems associated with axillary sampling compared to clearance and concluded that patients who received axillary sampling reported less post-operative numbness than patients who received axillary clearance. However, despite improvements in tumor detection techniques and resultant decreases in

the total number of mastectomies and sentinel node dissections, there are still a significant number of women that require mastectomies and axillary dissections (Kilgour, Jones, & Keyserlingk, 2008). Imaging techniques such as ultrasound or positron emission tomography are insufficiently sensitive and specific for the detection of positive axillary lymph nodes (Avril, et al., 1996; De Freitas, Costa, Schneider, Nicolau, & Mrussi, 1991; Tate, Lewis, Archer, Guyer, Royle, & Taylor, 1998), so histological evaluation of axillary status through surgery seem indispensable at present.

Section 2.1.3 Chemotherapy treatment

Adjuvant therapies are defined as a type of treatment that is used once the primary tumor has been removed surgically and may include chemotherapy, radiation, hormonal therapy or any combination thereof (Segal, et al., 2001). Adjuvant therapies are administered if the risk of metastatic disease may be favourably influenced by the adjuvant therapy and the form of therapy depends on the tumor prognostic factors, cancer stage, surgical approach, patient menopausal status and any pre-existing co-morbidities (Segal, et al., 2001).

Chemotherapy is a form of cancer treatment that uses medication to control suspected micro metastases. It is a systemic treatment, meaning that it affects the whole body by going through the blood stream. It is administered intravenously or orally and works to destroy cancer cells that may have spread from the breast, but this treatment affects healthy cells as well. Chemotherapy is generally administered in cycles, given for about 4-8 cycles over approximately 9-21 weeks (Courneya, Mackey, & McKenzie, 2002). It is well established that chemotherapy causes fatigue (Courneya, Mackey, & McKenzie, 2002; de Jong, Kester, Schouten, Abu-Saad, & Courtens, 2006; Markes, Brockow, & Resch, 2006). Chemotherapy also causes impaired exercise tolerance (Pihkala, et al., 1995), nausea, vomiting, mood disturbances and weight gain (Markes, Brockow, & Resch, 2006) and has been found to increase the fat to lean body mass ratio (Demark-Wahnfried, et al., 2001). Chemotherapy has been reported to interfere with performance of ADL and return to work (Markes, Brockow, & Resch, 2006).

Section 2.1.4 Radiation treatment

Radiation is a local method of cancer treatment during which high energy x-rays are used to destroy cancer cells. Radiation has been reported the most effective adjuvant treatment for prevention of loco-regional recurrences after mastectomies or breast conserving surgeries (Early Breast Cancer Trialists' Collaborative Group, 1995; Overgaard, et al., 1997; Overgaard, et al., 1999). Radiation usually occurs in short sessions only lasting a few minutes for 5 days a week, for approximately 3-6 weeks (Canadian Breast Cancer Foundation, 2010). Since the early 1970s the standard treatment of radiation includes moderate doses (50 Gr) to the breast and local regions of lymphatic drainage including the axilla and supraclavicular areas (Rietman, et al., 2003). Radiation can also affect healthy cells, resulting in irreversible lung fibrosis (Courneya, Mackey, & McKenzie, 2002), coronary and carotid artery arteriosclerosis (Rubin, Finkelstein, & Shapiro, 1992), interstitial myocardial fibrosis (Renzi, Straus, & Glatstein, 1992), cardiac and pulmonary toxicities, brachial plexopathy and skin erythema (redness) (Truong, Olivotto, Whelan, & Levine, 2004). Fatigue has been reported as the most common side effect of radiation (Greenberg, Sawicka, Eisenthal, & Ross, 1992; Longman, Braden, & Mishel, 1996; Winningham, et al., 1994), but other side effects include lymphedema (Swedborg & Wallgren, 1981; Truong, Olivotto, Whelan, & Levine, 2004), chronic pain (Tasmuth, von Smitten, Hietanen, Kataja, & Kalso, 1995), brachial plexus neuropathies (Olsen, Pfeiffer, Johannsen, Schroder, & Rose, 1993) and rib fractures (Overgaard, 1988). Sugden et al., (1998) reported that radiation can cause (even months after radiation) cell death within subcutaneous tissues, which results in formation of microscopic areas of scar tissue that could purportedly “set” a shoulder that is not regularly taken through full ROM. Other authors have reported that radiation can add to the fibrous firm attachments made between muscle and tissue following surgery, further restricting ROM (Lauridsen M. C., Overgaard, Overgaard, Hessov, & Cristiansen, 2008). Near full ROM is critical for patients undergoing radiation treatments, as the arm must be put into almost full abduction and external rotation for precise radiation positioning (Sugden, Rezvani, Harrison, & Hughes, 1998). Hojris et al., (2000) compared patients treated with chemotherapy and with or

without radiation, and found that 52% of patients in the radiation group had impairment of shoulder movement (compared to 15% in the non-radiated group). Furthermore, 16% of radiated patients (compared to 2% of non-radiated patients) reported shoulder impairments that interfered with their work and ADL (Hojris, Andersen, Overgaard, & Overgaard, 2000). Sugden et al. (1998) compared morbidities caused by axillary dissection and radiation and reported that radiation at the axilla caused decreased shoulder ROM, and that radiation following axillary dissection increased the risk of developing lymphedema. Radiation has been reported to interfere with performance of ADL and return to work (Markes, Brockow, & Resch, 2006).

Section 2.1.5 Hormonal treatment

In some breast cancer patients, the presence of estrogen can promote cancer cell growth. Hormonal (endocrine) therapy is a form of cancer treatment that uses medication to block the way estrogen promotes the growth of estrogen receptor-positive breast cancers (Canadian Breast Cancer Foundation, 2010). In some cases hormonal therapy is therapeutically approached surgically, such as the removal of the ovaries (oophorectomy) (Schmitz, et al., 2010). Hormonal drug therapy is usually administered after surgery, chemotherapy and radiation are complete, and is often administered daily for many years. Hormonal treatments are known to cause fatigue, weight gain, and ovarian oblation leading to early menopause (Courneya, Mackey, & McKenzie, 2002), as well as lead to hot flashes, bone demineralization and psychosexual effects (Rutqvist, 2004). Early menopause may accelerate bone loss and result in osteopenia or osteoporosis (Swenson, Nissen, Anderson, Shapiro, Schousboe, & Leach, 2009), making this population of women more susceptible to bone fracture.

Section 2.2 Treatment-related sequelae

There are numerous treatment-related sequelae of breast cancer treatments. The side effects of cancer treatment can last days, months, and even years (Hsieh, Sprod, Hydock, Carter, Hayward, & Schneider, 2008).

Section 2.2.1 Physical factors

The physical sequelae from breast cancer treatments are numerous and diverse. Common toxicities include diarrhea, stomatitis, nausea, vomiting, and hand-foot syndrome (redness, burning and paining of the hands and feet) (Prado, et al., 2009). Other symptoms include weakness, edema, pain and decreased mobility (Kuehn, et al., 2000). Survivors also display decreased functional capacity, meaning they expend more effort (relative to their maximal ability) than normally required to perform usual activities, therefore leading to higher levels of fatigue (Mock, et al., 2005).

Breast cancer survivors are at a high risk for decreased bone mineral density due to chemotherapy (which contains bone wasting agents), use of glucocorticoids, resulting ovarian failure and lack of physical activity (Reichman & Green, 1994; Reyno, Levine, Skingley, Arnold, & Abu Zahra, 1992; Rodriguez-Rodriguez, et al., 2005; Shapiro, Manola, & Leboff, 2001; Shapiro & Recht, 1994; van Poznak & Sauter, 2005). Chemotherapy causes early menopause in 75% to 90% of female patients older than 40 years of age (Bines, Oleske, & Cobleigh, 1996), and endocrine therapies can also promote early menopause (Courneya, Mackey, & McKenzie, 2002). Early menopause means that these survivors have more years of estrogen depletion than postmenopausal women and therefore have more years of potential bone loss (Twiss, Waltman, Berg, Ott, Gross, & Lindsey, 2009). Breast cancer survivors are almost 5 times more likely to experience a vertebral fracture one year post-treatment compared to healthy women (Swenson, Henly, Shapiro, & Schroeder, 2005).

Section 2.2.2 Psychosocial factors

Treatment-related sequelae often involve psychosocial challenges, which can negatively influence QoL. Improvements in detection and treatment of breast cancer, and resultant increases in survival rates has caused an emphasis to be placed on addressing QoL issues within this population (Blanchard, Courneya, & Laing, 2001). Women suffer substantial psychological distress during cancer treatment, including symptoms of depression and anxiety, both of which are highly correlated with women suffering from breast cancer (Badger, Segrin, Dorros, Meek, & Lopez, 2007; Schreier &

Williams, 2004). Patients receiving chemotherapy or radiation report anxiety and depression before, during and after treatment as a result of treatment side-effects (Spiegel, 1997). Depression in cancer populations is estimated between 1.5% to 50% (Trask, 2004), and anxiety estimates range from 20% to 50% (Stark, Kiely, Smith, Velikova, House, & Selby, 2002). Kuehn et al., (2000) determined that surgery-related arm symptoms and fear of cancer recurrence were the most important long-term sources of distress for a sample of 396 breast cancer patients. This particular population also reports disturbances in body image (Kemeny, Wellisch, & Schain, 1988), and often describe negative consequences of the illness on themselves and their families (Manne, et al., 2003). Significant improvements in body image have been related to performing 12 weeks of supervised aerobic exercise (Pinto B. M., Clark, Maruyama, & Feder, 2003). Long term exercise can reduce anxiety in breast cancer patients (Mock, et al., 1997) and acute bouts of exercise may also be effective in reducing anxiety, especially if pre-exercise anxiety levels are high (Blanchard, Courneya, & Laing, 2001). Specifically, dragon boat racing has been reported to contribute to social, emotional, physical, spiritual and mental dimensions of health (Parry, 2007).

Section 2.3 Upper limb dysfunction related to breast cancer

Chronic arm morbidity is relatively understudied and is claimed to be one of the most troublesome long-term complications of breast cancer treatments (Kwan, Jackson, Weir, Dingee, McGregor, & Olivotto, 2002). Long term effects include side effects and complications that begin during or very shortly after treatment and persist afterward for which survivors must compensate; whereas late effects include those that appear months or years after treatment completion (Schmitz, et al., 2010). “Persistent effects” is a term used to describe both long term and late effects (Aziz & Rowland, 2003). Shoulder disability has been reported in 35% of patients as a late complication to early breast cancer treatments (Lauridsen, Overgaard, Overgaard, Hessov, & Cristiansen, 2008), and 30 - 70% of patients have been reported to suffer from at least mild arm and shoulder symptoms (Kwan, Jackson, Weir, Dingee, McGregor, & Olivotto, 2002). Common impairments post breast cancer treatment

include decreased shoulder ROM, numbness at the axilla and/or lateral chest wall, decreased grip strength, pain and increased arm volume (Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004). Adverse effects of cancer treatment may persist and last years after treatment is completed (Schmitz, et al., 2010). Late morbidities of the upper limb restrict ADL and negatively affect QoL (Rietman, et al., 2003). Factors thought to influence the development of shoulder morbidity include age of the patient, extent of axillary and breast surgery performed and the nature of the adjuvant treatments received (Lauridsen, Cristiansen, & Hessove, 2005).

Section 2.3.1 Range of motion

Range of motion is essential for effective performance of ADL and work. Decreased ROM is a well-known sequelae to breast cancer (Lauridsen, Cristiansen, & Hessove, 2005). It has been suggested that less than 100° to 120° of shoulder abduction or flexion is associated with reduced functional use (Badley, Wagstaff, & Wood, 1984). Humeral abduction, flexion and external rotation ROM is often limited in survivors (Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004). Near full ROM is essential for breast cancer patients undergoing chest radiation. The arm needs to be in an abducted and externally rotated posture (hand held above the head) for precise radiation positioning, and if motion is severely limited, this crucial treatment can be delayed or prevented (Sugden, Rezvani, Harrison, & Hughes, 1998).

The exact causes of restricted ROM associated with breast cancer are not completely understood, but is usually ascribed to surgical trauma and scarring caused by axillary dissection, plus the additional fibrosing effects caused by adjuvant radiation (Aitken, Gaze, Rodger, Chetty, & Forrest, 1989; Bentzen, Overgaard, & Thames, 1989; Box, Reul-Hirche, Bullock-Saxton, & Furnnival, 2002; Hack, Cohen, Katz, Robson, & Goss, 1999; Ivens, Hoe, Podd, Hamilton, Taylor, & Royle, 1992; Kolden, et al., 2002; Kuehn, et al., 2000; Lane, Jespersen, & McKenzie, 2005; Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004; Ryttov, Holm, Qvist, & Blichert-Toft, 1988). Decreases in shoulder mobility are not believed to be caused by changes in the

glenohumeral joint itself, but rather because of mechanical inhibition of movement caused by adhesions between the muscles, subcutaneous tissues and skin around the axilla and pectoralis major muscles, which can be further aggravated with adjuvant chemotherapy and radiation therapies which cause further firm fibrous attachments among these structures (Lauridsen, Cristiansen, & Hessove, 2005). A delay, reduction or lack of immediate post-surgical activity could also lead to muscle spasms around the glenohumeral joint, muscle atrophy and a tightened glenohumeral capsule, which could lead to short and long term mobility reductions and pain (Kilgour, Jones, & Keyserlingk, 2008).

Reductions in shoulder range of motion are commonly associated with individuals with breast cancer. Table 3 displays some long term restrictions in shoulder ROM as described by four studies. Although not outlined in Table 3, the variability of ROM restrictions was high. Kuehn et al. (2000), Rietman et al. (2004) and Hack et al. (1999) assessed long term shoulder ROM restrictions on 396, 55 and 222 patients, respectively, who had undergone axillary dissections followed by either MRM or BCT at approximately 32 months, 2.7 years and 33.2 months post-surgery. The mean differences in shoulder ROM compared to the contralateral (non-surgery side) for these three studies are outlined in Table 3. Hack et al. (1999) found that 73% of patients showed a difference between their affected and non-affected shoulder with respect to the sensation point of pain or discomfort, or the point of maximum arm and shoulder movement. Swedborg & Wallgren (1981) examined the shoulder ROM of three groups of patients at approximately 49 months post-surgery: Group A (N = 163) had received radiation before MRM; Group B (N = 168) had received radiation after MRM; and Group C (N= 144) consisted of MRM patients that had not received any radiation. The authors (Swedborg & Wallgren, 1981) presented ROM as a percentage of the non-affected arm ROM as described in Table 3.

Table 3 Restrictions in ROM associated with breast cancer

	Kuehn et al., (2000)*	Rietman et al., (2004)*	Hack et al., (1999)*	Swedborg & Wallgren (1981)§
abduction	-21°	-7.5°	-6.4° (P.O.P: -13.8°)	Grp A 85.2% Grp B 84.9% Grp C 91.7%
flexion	-12°	-5.7°	-4.3° (P.O.P: -10.2°)	Grp A 94.6% Grp B 94.9% Grp C 97.2%
external rotation	No restriction registered	-6.2°	\	Grp A 94.0% Grp B 93.5% Grp C 101.1%
internal rotation	No restriction registered	\	\	Grp A 95.1% Grp B 95.9% Grp C 101.7%
Extension	\	\	-1.3° (P.O.P: -2.2°)	\
horizontal abduction	\	\	-7.3° (P.O.P: -10.7°)	\
horizontal adduction	\	\	-1.0° (P.O.P: -1.4°)	\
external rotation at 90° abduction	\	\	\	Grp A 86.3% Grp B 87.4% Grp C 96.8%

*Mean difference in shoulder ROM compared to contralateral arm

§ROM expressed as a percentage of control arm

\ = not measured

P.O.P = sensation point of pain/discomfort

Differing assessment techniques and definitions of functional ROM complicate comparisons between studies, but several studies concur that surgery (axillary dissection, MRM and BCT) causes reductions in ROM. In a review of 6 studies that assessed early breast cancer patients who had received axillary clearance followed by either MRM or BCT, Rietman et al. (2003) concluded that the prevalence of decreased ROM ranged from 2 to 51% with severe restrictions (greater than 50% reduction) in 2% of patients. Shoulder ROM was less when the axilla was irradiated, and was worse with patients that received MRM compared to BCT (Rietman, et al., 2003). Bendz & Olsen (2002) assessed shoulder flexion, abduction, internal and external rotation of 205 patients who had undergone axillary dissections and either MRM or BCT at 2 weeks, 1 month and 2 years post-surgery. All movements decreased at the earlier time points and shoulder flexion and abduction were still significantly reduced at 2 years in both MRM and BCT patient groups (Bendz & Olsen, 2002).

Other studies have demonstrated that shoulder ROM restrictions are more frequent or severe in patients who have undergone MRM compared to BCT. Nesvold et al. (2008) compared the ROM of patients who had undergone axillary dissection and radiation as well as either MRM or BCT and determined that 24% and 38% of MRM patients had significantly restricted ROM in shoulder flexion and abduction compared to only 7% and 18% in the BCT group, respectively. In addition, subjective reports revealed that chest wall tightness and moderate to severe problems with arm function were reported in 16% and 58% of MRM patients, compared to 1% and 33% of BCT patients, respectively (Nesvold, Dahl, Lokkevik, Mengshoel, & Fossa, 2008). Lauridsen et al. (2008) assessed the ROM of 89 patients who had received axillary dissection followed by either BCT or MRM, and found that BCT patients were found to suffer less frequently from shoulder disability compared to patients that had received MRM (odds ratio = 8.5, $p = 0.002$). Sugden et al. (1998) assessed 93 BCT and MRM patients at baseline and approximately 18 months post radiation, defining relative shoulder movement as the ratio of ipsilateral movement to contralateral movement, multiplied by 100. Sugden et al. (1998) did not report specific measures of ROM, but did report objective reductions in at least one shoulder movement in 48% of patients (with 79% of these as MRM patients and 35% as BCT patients). The authors examined shoulder flexion, extension, abduction, internal and external rotation and warned that limiting examination to flexion and abduction motions would have caused them to miss more than half of all patients having mobility restrictions (Sugden, Rezvani, Harrison, & Hughes, 1998). The type of surgery (MRM or BCT) was the most important factor in the development of shoulder problems: with MRM displaying more problems than patients with BCT (79% versus 35%), but that radiation also restricted ROM and when combined with MRM, resulted in more complaints of swelling, pain and telangectasis (spider veins), and posed more difficulties with performance of ADLs (Sugden, Rezvani, Harrison, & Hughes, 1998).

Adjuvant radiation treatments are suspected to contribute to reduced shoulder ROM. Particularly, axillary dissection in combination with radiation therapy is thought to be the main

reason why patients surgically treated for breast cancer develop shoulder mobility restrictions on the operated side (Lauridsen, Overgaard, Overgaard, Hessov, & Cristiansen, 2008). Chemotherapy does not seem to cause restrictions in ROM. The effects of chemotherapy and radiation on ROM were investigated by Ryttov et al. (1988) by comparing three groups: patients with MRM (Group A), patients with MRM who underwent adjuvant chemotherapy and radiation (Group B), and patients with MRM who underwent only chemotherapy (Group C). The authors found that the frequency of impaired shoulder mobility significantly increased with radiation (38% in Group B versus 4% in Group A and 12% in Group C), and concluded that therefore, the administration of the systemic treatment of chemotherapy had no influence on the development of ROM restrictions (Ryttov, Holm, Qvist, & Blichert-Toft, 1988). Objective measures of shoulder movement impairment during long term follow-up (approximately 9 years) of 84 patients post mastectomy and chemotherapy indicated that 52% of irradiation patients developed some degree of ROM impairment, compared to only 15% of non-irradiated patients (Hojris, Andersen, Overgaard, & Overgaard, 2000). The timing of radiation administration apparently does not influence the effect radiation has on ROM. A comparison of patients (N = 928) who received radiation before or after surgery with those who did not receive radiation revealed that ROM was always less for patients that were irradiated compared to patients that did not receive radiation (Swedborg & Wallgren, 1981). Furthermore, the extent of axillary surgery combined with radiation has not been found to affect the impairment of shoulder mobility. Radiation was found to impair shoulder mobility regardless of the type of axillary surgery performed (node sampling or clearance) (Thompson, Air, Jack, Kerr, Rodger, & Chetty, 1995). Since the humeral head and glenohumeral joint are protected by barriers during radiation, Thompson et al. (1995) suggested that the reduction in mobility may reflect damage to the rotator cuff muscles. The supraspinatus (humeral abductor), infraspinatus and teres minor (humeral external rotators) insert on the greater tubercle of the humerus, and the subscapularis (humeral internal rotator) insert on the lesser tubercle of the humerus. It is possible that these tendon attachments could be damaged during radiation. Thompson et al. (1995) suggested that although axillary surgery alone can cause upper

limb morbidity (specifically more extensive surgeries can result in greater amounts of swelling), radiation can compound the problem by reducing shoulder girdle mobility.

Despite the considerable potential for rotator cuff involvement with restricted shoulder ROM, there has been limited information gathered regarding muscle activation or scapulothoracic kinematics in this population. Although several studies assess shoulder muscle strength, typically during basic chest press exercises (Ahmed, Thomas, Yee, & Schmitz, 2006; Battaglini, et al., 2007; Courneya K. S., et al., 2007; Lane, Jespersen, & McKenzie, 2005), there are no known studies that have investigated rotator cuff muscular activity in this population. Furthermore, likely due to the popular use of basic assessment tools such as goniometers, scapular movement is rarely assessed. Lauridsen et al. (2000) had physiotherapists visually assess 100 patients that received either BCT or MRM for scapular 'winging' (definite protrusion of the medial border of the scapula often attributed to a tight pectoralis major muscle or dysfunctional serratus anterior muscle) prior to and post exercise treatment. Eight patients displayed scapular winging prior to exercise therapy, and this number was reduced to 4 patients post exercise therapy, demonstrating that exercise can decrease the incidence of scapular winging (Lauridsen, Torsleff, Husted, & Erichsen, 2000). However, if the cause of scapular winging is due to severance of the long thoracic nerve which supplies the serratus anterior, winging is permanent (Tasmuth, von Smitten, Hietanen, Kataja, & Kalso, 1995). Reduced shoulder ROM may result in a change of upper body posture as individuals attempt to compensate for a reduction in mobility (Lauridsen, Torsleff, Husted, & Erichsen, 2000). There is a need for tracking of scapulothoracic and humerothoracic kinematics with 3-D motion capture in order to generate accurate and precise characterizations of shoulder movement and ability.

Section 2.3.2 Lymphedema

One complication of breast cancer treatment is lymphedema of the ipsilateral forearm and upper arm as depicted in Figure 11. Lymphedema is a chronic and progressive swelling of the arm, shoulder, neck and/or torso caused by compression or physical disruption of the axillary lymphatic channels

caused by surgery or radiation (Ahmed, Thomas, Yee, & Schmitz, 2006), which results in functional overload of the lymphatic system during which the lymph volume exceeds the transport capabilities, thereby causing a build-up of interstitial macromolecules (Petrek & Heelan, 1998). Clinical lymphedema is often described as a greater than 200 mL difference in volume between the ipsilateral arm and the non-affected arm (Kwan, Jackson, Weir, Dingee, McGregor, & Olivotto, 2002) or greater than a 10% increase in volume on the ipsilateral side (Bendz & Olsen, 2002; Kuehn, et al., 2000; Schmitz K. H., et al., 2009). Persistent swelling and stagnant protein can lead to fibrosis (or scarring: formation of excessive fibrous connective tissue), cellulitis (inflammation of skin) and lymphangitis (infection within lymphatic channels) (Petrek & Heelan, 1998). Symptoms commonly include a sensation of heaviness, achiness and tenderness (Moffatt, et al., 2003), and can lead to distress, depression and anxiety (Carter B. J., 1997). Lymphedema can affect performance of gross and fine motor skills (Rymal, 2001) and can impact activities at work and at home (Passik & McDonald, 1998). Treatments of lymphedema involve managing symptoms usually by use of complex decongestive therapy, which involves wearing compression garments, skin and wound care to reduce infection risk, physiotherapy and manual lymphatic drainage massage (Koul, et al., 2007).

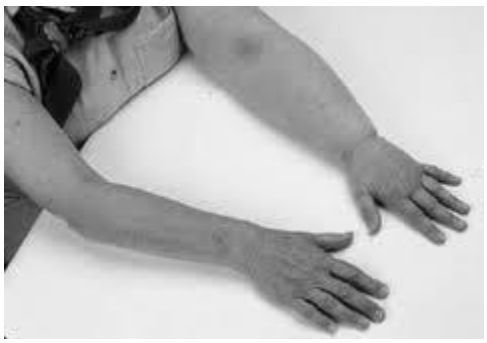


Figure 11 Lymphedema of the upper limb: left limb (ipsilateral breast cancer side) is swollen. Figure taken from (Phimaimedicine).

Lymphedema prevalence rates (number of survivors with lymphedema) range from 6% to 43% (Rietman J. S., et al., 2003), and incidence rates (frequency of developing lymphedema within a certain period of time) to range from 6% to 70%, depending on the criteria for defining lymphedema and the follow-up interval (Armer & Stewart, 2005; Ronka, Pamilo, von Smitten, & Leidenius, 2004;

Vignes, Arrault, & Dupuy, 2007). Ranges differ considerably between studies due to the diverse populations under study, and the differing methodology and timing of measurements (Petrek & Heelan, 1998). Lymphedema can develop at various times from initial cancer treatment (Petrek & Heelan, 1998) to 20 years post treatment (Petrek, Senie, Peters, & Rosen, 2001). There is a 50% probability that survivors will develop lymphedema at some point by 20 years post treatment (McKenzie & Kalda, 2003). However, incidence rates seem to be declining likely due to earlier detection and diagnosis, less advanced disease states and less extensive axillary surgeries (Petrek & Heelan, 1998). Factors believed to contribute to lymphedema include axillary dissection, radiation to the breast or axilla, pathological nodal status, obesity and the tumor stage (McKenzie & Kalda, 2003).

The type and extent of surgery and adjuvant treatment affect the development of lymphedema. Axillary dissection and radiation of the axilla are associated with much higher risks of lymphedema (Kwan, Jackson, Weir, Dingee, McGregor, & Olivotto, 2002; Rietman, et al., 2003): an odds ratio of 4.8 was determined for patients developing lymphedema following axillary dissection and radiation (Kwan, Jackson, Weir, Dingee, McGregor, & Olivotto, 2002). There is consensus that lymphedema occurs more frequently in patients that undergo MRM compared to those that undergo BCT (Nesvold, Dahl, Lokkevik, Mengshoel, & Fossa, 2008; Rietman, et al., 2003). Nesvold et al. (2008) examined 263 women and found that 8% of patients with BCT developed lymphedema, compared to 20% of MRM patients at approximately 47 months post-surgery. Ryttov et al. (1988) compared patients that had received axillary dissection and MRM (control group) with patients that had also had radiation and chemotherapy (Group 2) or solely chemotherapy (Group 3). The authors found that the frequency of lymphedema was significantly greater in the radiated Group 2 (seven times higher than the control group, which was equal to Group 3); therefore concluding that systemic treatment (chemotherapy) had no influence on the development of lymphedema (Ryttov, Holm, Qvist, & Blichert-Toft, 1988). Ryttov et al. (1988) suggested that radiation leads to subcutaneous

fibrosis and damage to the endothelial cells of small blood and lymph vessels, causing it to play a greater role in the development of lymphedema compared to the extensiveness of surgery.

Individuals with lymphedema have often been excluded from participating in exercise for fear of exacerbating the condition (Hayes, Reul-Hirche, & Turner, 2008). However, exercise should be encouraged amongst individuals with lymphedema. Limiting the use of the arm for fear of lymphedema may limit physical recovery and affect activity and work (Schmitz, et al., 2009). Further, there is evidence to suggest that exercise enhances lymphatic flow (Mortimer, 1990; Mortimer, 1995) and that increased pulmonary work (blood flow) associated with exercise also aids lymphatic flow (Brennan & Miller, 1998). Schmitz et al., (2009) performed a randomized controlled trial of progressive weightlifting for 1 year in 141 breast cancer survivors that demonstrated stable lymphedema of the arm, and found that slowly progressive weight training had no significant effect on limb swelling, and resulted in a decrease in exacerbations of lymphedema, reduced symptoms and increased strength compared to the control group. Ahmed et al. (2006) demonstrated that weight training twice a week for 6 months did not increase the incidence of lymphedema nor did it increase the signs and symptoms of lymphedema in breast cancer survivors compared to a control group. Similarly, Hayes et al. (2008) investigated the effects of exercise on breast cancer survivors that had developed unilateral upper limb lymphedema compared to a control group, and concluded that exercise was safe and did not exacerbate secondary lymphedema. Physical activity amongst lymphedema sufferers is encouraged to optimize physical and psychosocial recovery of cancer (Hayes, Reul-Hirche, & Turner, 2008), in conjunction with appropriate compression garments and close monitoring (Schmitz, et al., 2009).

Section 2.3.3 Strength

Strength is often reduced in breast cancer survivors, and is generally assessed with grip strength, one-repetition maximum tests or manual muscle tests. The side effects of cancer treatment can reduce functional capabilities such as aerobic capacity, muscular strength, flexibility and body composition,

which can decrease health-related QoL (Mustian, Katula, & Zhao, 2006). Reductions of strength in breast cancer survivors are logical due to potential neurological structural damage during surgery, muscle dysfunction caused by radiation or muscle atrophy caused by disuse. A review by Rietman et al. (2003) revealed that strength is often evaluated via a grip strength measure or through subjective reports of weakness, with a prevalence of strength decreases reported to range from 17% to 33% of survivors. Decreases in grip strength are significantly greater if the dominate side is operated on (Rietman, et al., 2003). Kuehn et al. (2000) systematically evaluated the long-term sequelae of 346 breast cancer survivors who had undergone axillary dissections and either BCT or MRM. Isotonic strength was assessed by measuring the angle to which a 3 kg dumbbell could be elevated with an outstretched arm, and at approximately 32 months post-surgery 43.4% of patients demonstrated a reduction in strength (Kuehn, et al., 2000). One-repetition maximum strength tests, often bench press and leg press exercises, are also used as an indication of overall strength (Kolden, et al., 2002; Schmitz, et al., 2009). One repetition maximum tests are considered safe for most populations if properly supervised (Barnard, Adams, Swank, Mann, & Denny, 1999; Shaw, McCully, & Posner, 1995) and are also specifically safe for breast cancer survivors with and at risk for lymphedema (Schmitz, et al., 2010). Other techniques to define one-repetition maximum include determining the maximal weight based on ratings of perceived difficulty during 4 to 6 repetitions of a 40 lbs leg press and a 5 lbs bench press, while continuing to add resistance until the participant rates maximal difficulty and refuses to attempt to lift anymore, is clearly unable to perform the lift properly, or reports a symptom that required stopping (Schmitz, et al., 2009). Exercise has proven to effectively increase upper and lower body muscle strength of breast cancer survivors (Ahmed, Thomas, Yee, & Schmitz, 2006; Herrero, et al., 2006; Mustian, Katula, & Zhao, 2006; Schmitz, et al., 2009; Twiss, Waltman, Berg, Ott, Gross, & Lindsey, 2009). Strength has also been assessed subjectively on a grading scale of 0 to 5 with the use of manual muscle tests which consisted of resisted movements in shoulder external rotation, flexion and abduction and increases in ER strength (higher scores) were seen in a BCP following exercise therapy (Kilgour, Jones, & Keyserlingk, 2008), but the literature is

limited regarding quantitative assessment of muscle-specific strength. It is difficult to compare and make population-based conclusions regarding strength using subjective assessments. By identifying specific exertions in which weakness is evident, it can be assumed to be attributed to muscle-specific strength deficits. Quantifying force levels will allow for comparisons between and within individuals and acquisition of this knowledge will help focus and direct therapeutic treatments and preventative techniques to reduce or eliminate these deficits.

Section 2.3.4 Cording

Axillary web syndrome, or cording, is a significant morbidity that occurs early in the post-operative stages (usually within the first post-operative month (Lauridsen, Cristiansen, & Hessove, 2005)) and is characterized by tight, painful, fibrous cords of tissue that extend from the axilla into the medial arm and sometimes extend distally to the antecubital fossa at the elbow and to the wrist or base of the thumb of the ipsilateral arm (Box, Reul-Hirche, Bullock-Saxton, & Furnnival, 2002; Lauridsen, Cristiansen, & Hessove, 2005; Moskovitz, Anderson, Yeung, Byrd, Lawton, & Moe, 2001; Tilley, Thomas-MacLean, & Kwan, 2009). These cords of tissue (usually 2 – 3 cords) are made taut and visible or palpable during shoulder abduction as depicted in Figure 12 (Moskovitz, Anderson, Yeung, Byrd, Lawton, & Moe, 2001).

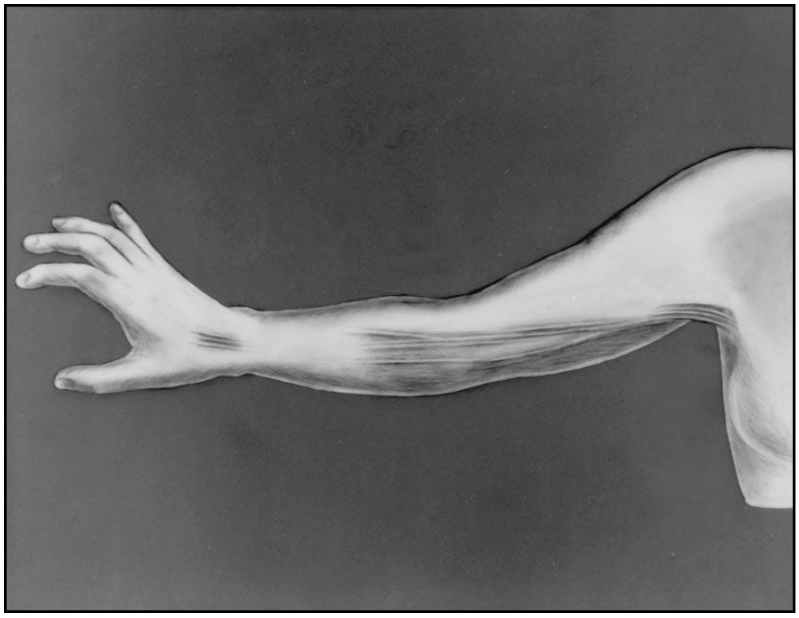


Figure 12 Cording: fibrous cords of tissue extend from the axilla into the medial arm and sometimes extend distally to the antecubital fossa at the elbow and to the wrist or base of the thumb. Figure taken from Moskovitz et al. (2001).

The interruption of axillary lymphatics appears to play an important role in the development of cording. Initially, it was hypothesized that the intercostobrachial nerve may be the origin of the palpable taut cords, but Moskovitz et al. (2001) demonstrated that of 44 patients that had developed cording, the intercostobrachial nerve had been preserved in 43% of these patients, suggesting that ligation of this nerve does not contribute to the development of cording. Rather, cording is hypothesized to result from a disruption to and/or damage of superficial lymphatics and vessels during axillary surgery, causing a disruption or ceasing of flow and resulting in hypercoagulation (Lacomba, del Moral, Zazo, Gerwin, & Goni, 2010; Moskovitz, Anderson, Yeung, Byrd, Lawton, & Moe, 2001). Surgical biopsies and histological analyses have been performed on these taut tissues, identifying these cords as lymphatic vessels without red blood cell components or hemosiderin pigments (which if these components had been identified in similar thin-walled vessels would be considered veins rather than lymphatics) (Moskovitz, Anderson, Yeung, Byrd, Lawton, & Moe,

2001). Although cording is a significant morbidity following breast cancer treatment, it has received little attention in the literature (Box, Reul-Hirche, Bullock-Saxton, & Furnnival, 2002).

Cording is painful and causes a significant reduction in ROM, but the effects of treatment are understudied. Moskovitz et al. (2001) investigated the ROM of 750 breast cancer patients over 16 years, and noted that 44 (6%) of these patients had developed cording and shoulder abduction was limited to 90° or less in 74% of patients with cording. Lacomba et al. (2010) assessed 116 women with breast cancer following axillary dissection and found that 56 (48%) of them had developed cording, and after 12 months of follow-up, the most frequent cause of pain was cording (n = 56), followed closely by myofascial pain syndrome (n = 52). The authors suggested that concurrence of cording and myofascial pain syndrome experienced in the pronator teres may reflect a protective splinting response of the muscle to avoid painful stretching of the tightened lymphatic vessels at the elbow (Lacomba, del Moral, Zazo, Gerwin, & Goni, 2010). The influence of cording on the recovery of shoulder movement of 65 breast cancer survivors assigned to either physiotherapy (n = 32) or control groups (n = 33) post-surgery, of which initially, 21.2% and 37.5% of survivors in the control and treatment groups, respectively, had developed cording was assessed by Box et al. (2002). ROM recovery for abduction and flexion at 3 months and 6 months were positively influenced by the presence of cording during early post-surgery stages, which may reflect the survivors increased attention to maintain shoulder movement after an initial difficult recovery post-surgery (Box, Reul-Hirche, Bullock-Saxton, & Furnnival, 2002). One case study described a patient that had regained full ROM immediately post-surgery, but developed cording 1 week later and had reduced ROM (135° and 123° of flexion and abduction, respectively) at 2 weeks post-surgery (Tilley, Thomas-MacLean, & Kwan, 2009). While this patient was being treated (stretched) by a physiotherapist, an audible ‘snap’ was heard, and immediately there was a relief of tension and an increase of ROM by 10° (Tilley, Thomas-MacLean, & Kwan, 2009). Further research is needed to determine the effects

of cording on ROM and performance of ADL and work tasks, and safe and effective treatment modalities need to be identified.

Section 2.3.5 Pain

Pain is commonly experienced by breast cancer patients and survivors. The prevalence of pain in patients with early stages of breast cancer that have received BCT or MRM range from 12% to 51% (Rietman, et al., 2003). The etiology of pain post cancer treatment varies and can include surgical damage, post-surgical complications or complications of radiation and chemotherapy (Lacomba, del Moral, Zazo, Gerwin, & Goni, 2010). Pain has been reported to be a side effect of axillary dissection (Hack, Cohen, Katz, Robson, & Goss, 1999; Kuehn, et al., 2000; Polinsky, 1994; Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004; Sugden, Rezvani, Harrison, & Hughes, 1998)), and can be caused by surgical scarring, radiation fibrosis, or intercostobrachial nerve damage (Sugden, Rezvani, Harrison, & Hughes, 1998). Pain can last months and even years after surgery (Kuehn, et al., 2000), and can affect mood and QoL (Keays, Harris, Lucyshyn, & MacIntyre, 2008).

Performance of activity may be restricted due to pain. Pain is worsened during certain activities, commonly reported as reaching out, carrying, working with the arm during household or handicraft tasks, or sleeping on the operated side (Rietman, et al., 2003). Pain is often reported in areas of the neck, arm and shoulder, as well as areas around the operative area and scar (Lauridsen, Overgaard, Overgaard, Hessov, & Cristiansen, 2008). Myofascial pain syndrome is a common source of pain during the first year post surgery in women undergoing breast cancer surgery that includes axillary dissection (Lacomba, del Moral, Zazo, Gerwin, & Goni, 2010). Myofacial pain syndrome is caused by active myofascial trigger points which cause hyperirritability and tenderness in palpable bands of taut skeletal muscle, which refer pain at a distance (Lacomba, del Moral, Zazo, Gerwin, & Goni, 2010). Lacomba et al. (2010) assessed the incidence of myofascial pain syndrome in 116 breast cancer survivors 12 months post-surgery (axillary dissection and BCT or MRM), and found 68 survivors reported pain, and the cause of pain was cording in 56 survivors, and myofascial pain

syndrome in 52 survivors (Lacomba, del Moral, Zazo, Gerwin, & Goni, 2010). The muscles (and incidence) involved with myofascial pain syndrome included: latissimus dorsi (25%), serratus anterior (24%), pectoralis major (20.7%), infraspinatus (19%), trapezius (13%), teres major (8.6%), teres minor (8.6%), pronator teres (5.2%), levator scapulae (0.9%) and supraspinatus (0.9%) (Lacomba, del Moral, Zazo, Gerwin, & Goni, 2010). Pain can restrict or discourage activity and use of full ROM, and continued disuse or fearful avoidance of full ROM can lead to further developments of ROM restrictions and muscle atrophy, further affecting performance of ADL and work.

Section 2.3.6 Fatigue

Cancer related fatigue is defined as a persistent and subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning (National Comprehensive Cancer Network, 2004). Cancer-related fatigue leads to a reduced capacity for work, causing sufferers to be less efficient while completing tasks due to feelings of weariness or tiredness (Stasi, Abriani, Beccaglia, Terzoli, & Amadori, 2003). The prevalence of fatigue post radiation ranges from 30% to 80% of patients (Jereczek-Fossa, Marsiglia, & Oreccchia, 2001), and ranges from 60% to 90% of patients post chemotherapy (Feyer & Steingraeber, 2001). Other reports have suggested that fatigue is the most prevalent and debilitating symptoms of breast cancer patients treated with chemotherapy or radiation (Mock, et al., 2005), affecting 70% to 100% of patients (Irvine, Vincent, Graydon, Bubela, & Thompson, 1994; Jacobsen, Hann, Azzarello, Horton, Balducci, & Lyman, 1999; Longman, Braden, & Mishel, 1996), and persisting for months or years (Andrykowski, Curran, & Lightner, 1998; Broeckel, Jacobsen, Horton, Balducci, & Lyman, 1998). Fatigue can cause a self-perpetuating condition such that patients may avoid activity in order to reduce symptoms of fatigue, but the resulting physical inactivity may induce muscle wasting and a loss of endurance, leading to easy fatigability, which can then discourage further activity as depicted in Figure 13 (Dimeo, Stieglitz, Novelli-Fischer, Fetscher, & Keul, 1999; Winningham, et al., 1994). In the fight to combat fatigue,

there has been a paradigm shift from encouraging rest, to encouraging exercise (Mock, et al., 2005). Aerobic exercise and relaxation training have been effective in improving fatigue of cancer patients post-surgery (Dimeo, Thomas, Raabe-Menssen, Propper, & Mathias, 2004), and physical activity and stress management education have been shown to improve fatigue, energy and emotional distress levels specifically of breast cancer survivors (Fillion, et al., 2008).

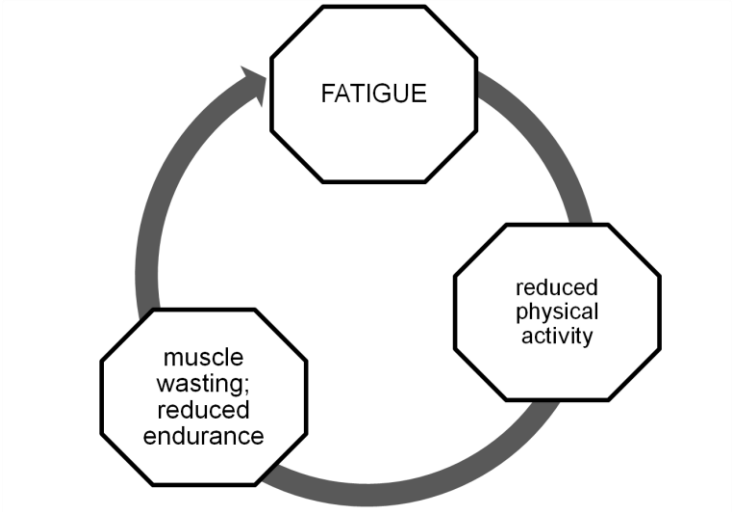


Figure 13 Fatigue: a self-perpetuating cycle

Section 2.3.7 Dysfunction progression

The self-perpetuating cycle of dysfunction is not only related to fatigue, but encompasses many other morbidities associated with the breast cancer population. Similar to symptoms of fatigue, pain, weakness, lymphedema and restricted ROM can also lead to reduced activity and resultant de-conditioning, which can result in further fatigue and inactivity. Often breast cancer patients undergoing adjuvant therapies become fearful of overexertion and are uncertain as to what they can safely perform, therefore they stop doing physical activity – and this inactivity further contributes to their debilitation (Segal, et al., 2001). Patients or survivors suffering from reduced mobility may alter their upper body posture as they attempt to compensate for their decreased ROM, and these compensations may lead to strained muscles and pain, discouraging the performance of activities,

and further contributing to disability (Lauridsen M. C., Overgaard, Overgaard, Hessov, & Cristiansen, 2008). Figure 14 demonstrates the progressive nature of dysfunction and the many variables that may promote the cyclic nature of disability.

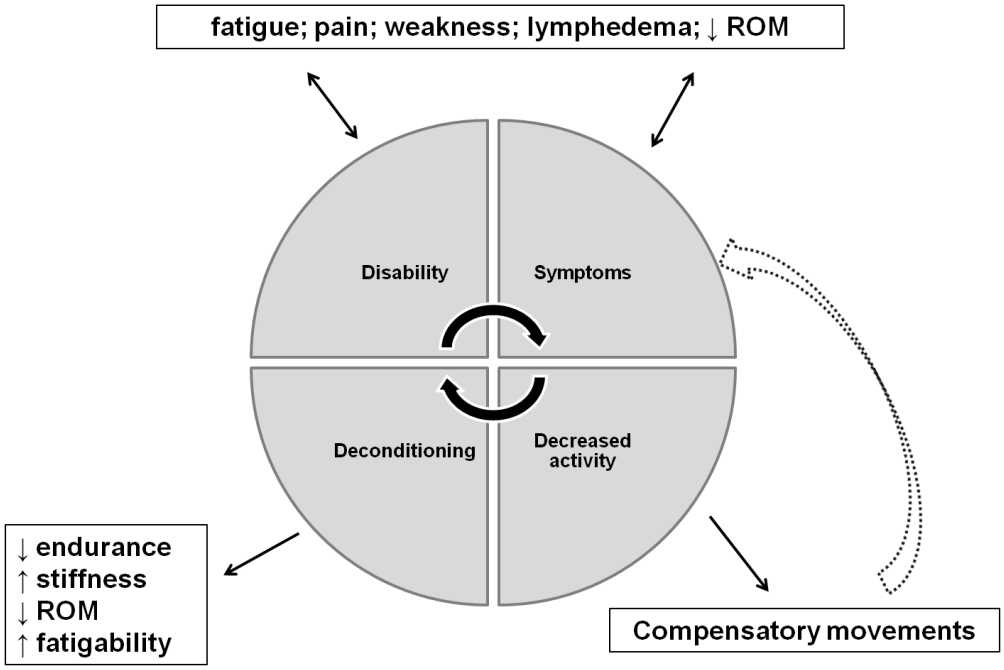


Figure 14 Cyclic progression of disability

Section 2.4 Quality of life

Quality of life is defined as an "individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (World Health Organization, 1997). The concept of QoL is said to be affected by 6 broad domains as demonstrated in Table 4. For the purposes and relevance of this thesis only the domains of physical health and level of independence will be directly addressed.

Table 4 Domains and associated facets of QoL. [Table taken from (World Health Organization, 1997).]

Domain	Facets incorporated within domains
Physical health	Energy & fatigue Pain & discomfort Sleep & rest
Psychological	Bodily image & appearance Negative feelings Positive feelings Self-esteem Thinking, learning, memory & concentration
Level of independence	Mobility Activities of daily living Dependence on medicinal substances & medical aids Work Capacity
Social relationships	Personal relationships Social support Sexual activity
Environment	Financial resources Freedom, physical safety & security Health & social care: accessibility & quality Home environment Opportunities for acquiring new information & skills Participation in & opportunities for recreation/leisure Physical environment (pollution/noise/traffic/climate) Transport
Spirituality/Religion/Personal beliefs	Religion /Spirituality/Personal beliefs

Section 2.4.1 Associations between performance of ADL and QoL

Physical health and an individuals' level of independence are directly related to each other and to QoL. The physical health of breast cancer survivors directly influences their performance of ADL and ability to perform work, and therefore, ultimately affects their level of independence. Researchers agree that managing symptoms and maintaining or resuming ADL are important components of QoL (Ferrell, Grant, Dean, Funk, & Ly, 1996; Graydon, 1994; Kiebert, de Haes, & van de Velde, 1991).

Investigations are scarce regarding the performance of ADL or work in the breast cancer population, and the relationship between performance of these activities and QoL are not well understood, but documented findings indicate that survivors have difficulty performing ADL and work post treatment. Box et al. (2002) investigated the changes in shoulder movement during

functional tasks (e.g. wash contralateral scapula, brush hair, reach overhead, push a grocery cart) of 65 patients after surgery to determine the effect of elective physiotherapy intervention. Abduction ROM returned to preoperative levels more quickly in the treatment group and the treatment group had more abduction at 3 months (+14°) and 24 months (+7°) compared to the control group. Mean shoulder ROM during functional tasks (assessed with a goniometer) and patient-rated scores of performance difficulty (scale of 1 (no difficulty) to 5 (unable to perform the task) indicated a trend of increased ratings of performance difficulty with decreased shoulder ROM (Box, Reul-Hirche, Bullock-Saxton, & Furnnival, 2002). The mean shoulder ROM of women who rated more than slight difficulty with task performance was less than 120° of abduction and ranged from 120° to 140° of flexion (Box, Reul-Hirche, Bullock-Saxton, & Furnnival, 2002). Hojris et al. (2000) compared subjective and objective measures of shoulder movement impairment and found that objective measures revealed 52% of irradiated patients and 15% of non-irradiated patients had some degree of impaired shoulder movement, while subjective reports revealed that only 16% of irradiated patients and 2% of non-irradiated patients felt their impairments of shoulder function interfered with work or daily activities. Wingate (1985) assigned 92 patients to either physiotherapy or control groups post-surgery, and assessed objective ROM and subjective ratings of performance difficulty (scale of 1 (no difficulty) to 5 (unable to perform the task). The physiotherapy group had far less difficulty performing functional tasks at 5 days and at 3 months postoperatively, compared to the control group, but a substantial percentage of patients in both groups experienced difficulty performing functional tasks, as indicated in Table 5. As the 5 and 10 year breast cancer survival rates continue to increase, impairments induced by treatment are increasingly important as they may influence performance of ADL and QoL (Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004).

Table 5 Percentage of patients with difficulty performing functional tasks 5 days and 3 months postoperatively [Data taken from (Wingate, 1985).]

Functional Task	% at 5 days		% at 3 months	
	Physiotherapy	Control	Physiotherapy	Control
Brush hair	34.7	43.9	0.0	2.4
Sweater over head	65.3	65.9	10.2	17.1
Pull on pants	26.5	34.1	0.0	4.9
Fasten bra	32.7	51.2	8.2	19.5
Back zipper	77.6	97.6	28.6	51.2
Ipsilateral scapula	40.8	68.3	16.3	26.8
Contralateral scapula	36.7	65.9	8.0	22.0
Reach over head	42.9	56.1	8.2	14.5
Make bed	44.9	61.0	4.1	17.1
Carry groceries	67.3	85.4	10.2	19.5

Section 2.4.2 Associations between physical health and QoL

The relationships between physical health (impairments, disabilities) and QoL in the breast cancer population are scarcely investigated (Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004). The number of chronic symptoms of late morbidity has been significantly correlated with anxiety and depression levels (Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004). Kuehn et al. (2000) emphasized the necessity of reducing functional impairments of the shoulder-arm complex since arm problems have a reported greater influence on QoL than the alteration of body shape, even in cases of mastectomy.

QoL has been reported to be associated with patient demographics, work status and physical symptoms. Liljegren & Holmberg (1997) proposed that patient age and employment state were strongly associated with arm symptoms found in breast cancer patients, and reported that 86% of patients under 65y were employed, suggesting that the patients' jobs may accentuate their symptoms. Voogd et al. (2003) investigated the associations between measures of arm circumference and shoulder abduction ROM and QoL in 332 breast cancer survivors approximately 4 years after axillary dissection, and found that in 26% of survivors, differences of circumference (>2 cm) and reduced ROM (>20°) were strong indicators of complaints (including difficulty performing

household chores, more likely to give up hobbies, felt more disabled, and were more likely to be treated by a physiotherapist). However, complaints also occurred in women without swelling or reduced shoulder abduction, indicating that these physical measures only identify some women whose ADL and well-being are affected (Voogd, Ververs, Vingerhoets, Roumen, Coebergh, & Crommelin, 2003). Rietman et al. (2003) reviewed the literature to evaluate the relationship of late morbidity to ADL in a breast cancer population, and found that there was a significant relationship between edema and restricted ROM and subjective assessments of functional impairments. Patients who underwent MRM had more difficulty performing ADL than patients who received BCT, but certain tasks were difficult for both groups, including: pulling a sweater overhead (20%), bra fastening (18%), doing up a back zipper (72%), reaching overhead (16%), and carrying heavy bags (29%) (Rietman, et al., 2003). The authors concluded that there is a significant relationship between late morbidity, restrictions of ADL and poorer QoL (Rietman, et al., 2003).

Long-term morbidity negatively affects QoL of the BCP. Long-term (≥ 8 years post-diagnosis) QoL of breast cancer survivors was compared with similarly aged women who had never experienced cancer, and results indicated disease-free survivors reported similar QoL to healthy women, except that the survivors reported more arm problems (specifically swelling and decreased sensation), worried more about their health and were less satisfied with their sexual life (Dorval, Maunsell, Deschenes, Brisson, & Masse, 1998). The authors emphasized that a non-negligible proportion of survivors still reported arm problems long-term, at more than 8 years post-diagnosis (Dorval, Maunsell, Deschenes, Brisson, & Masse, 1998). Kuehn et al. (2000) assessed the long-term morbidity associated with 346 survivors who had received BCT or mastectomies followed by axillary node dissections at approximately 32 months post-surgery. Surgery-related arm morbidities and fear of cancer recurrence were the most important long-term sources of distress for these survivors (29% and 22%, respectively) (Kuehn, et al., 2000). It is well-agreed that managing symptoms and maintaining and resuming ADL (physical and functional well-being) are important

components of QoL (Cella & Tulsky, 1990; Courneya & Friedenreich, 1997; Ferrell, Grant, Dean, Funk, & Ly, 1996; Graydon, 1994; Kiebert, de Haes, & van de Velde, 1991).

Section 2.5 Exercise effects

In the last two decades it has become clear that exercise plays a crucial role in cancer prevention and control (Courneya & Friedenreich, 2001; World Cancer Research Fund/American Institute for Cancer Research, 2007, p. 198-209). Exercise may extend breast cancer survival (Holmes, Chen, Kroenke, & Colditz, 2005; Irwin, et al., 2008) and exercise can increase physical functioning of patients during cancer treatments (Markes, Brockow, & Resch, 2006). Exercise is effective in increasing QoL, improving cardio-respiratory fitness, physical functioning and symptoms of fatigue in breast cancer patients and survivors (McNeely, Campbell, Rowe, Klassen, & Mackey, 2006), but it is unclear what type, amount, and frequency of exercise is most beneficial for specific outcomes (Pinto B. M., Clark, Maruyama, & Feder, 2003).

Section 2.5.1 Exercise benefits

Exercise has been proven to be a safe, feasible and beneficial QoL intervention for most BC patients and survivors (Courneya, Mackey, & Jones, 2000). There is strong evidence to suggest that aerobic exercise can reduce cancer-related fatigue and improve measures of cardiopulmonary function, global health, strength, sleep, self-esteem, weight gain, depression, anxiety and QoL (Kirshbaum, 2006).

Exercise positively influences both physical (weight gain, muscle strength, bone density, functional capacity) and psychosocial (social, emotional, mental) factors. Obesity is associated with an increased prevalence or recurrence of breast cancer and 50% to 96% of women experience weight gain during cancer treatment (Vance, Mourtzakis, McCargar, & Hanning, 2010). Weight gain is more common in pre-menopausal women that receive chemotherapy (Vance, Mourtzakis, McCargar, & Hanning, 2010). A review by Schmitz et al. (2010) examined randomized controlled trials that

investigated the effect of exercise to improve body size or body composition during (6 studies) or after (16 studies) cancer treatment, and found that during treatment the majority of studies indicate exercise results in significant reductions in percent body fat, body weight or improved lean muscle mass. After cancer treatments, the review indicated that about half of the studies demonstrated exercise had a positive effect on one or more variables related to body size or composition (Schmitz, et al., 2010). Aerobic weight bearing exercise has been shown to attenuate the decline in bone mineral density associated with the breast cancer population (Schwartz, Winters-Stone, & Gallucci, 2007). Bone loss in breast cancer patients may increase the risk of osteoporosis and bone fracture (Nikander, Sievanen, Ojala, Oivanen, Kellokumpu-Lehtinen, & Saarto, 2007). Long-term (1 – 2 year) strength and weight training can increase bone mineral density by increasing the tension on the bone and influencing bone formation during remodelling cycles (Twiss, Waltman, Berg, Ott, Gross, & Lindsey, 2009). Exercise increases functional capacity of cancer populations (Courneya K. S., Friedenreich, Sela, Quinney, Rhodes, & Handman, 2003; MacVicar, Winningham, & Nickel, 1989) and breast cancer patients that have received physiotherapy post-mastectomy obtain better functional outcomes than those who do not (Wingate, 1985). Conversational interviews with breast cancer survivors have revealed that exercise in the form of dragon boat racing contributes to social, emotional, physical, spiritual and mental dimensions of health (Parry D. C., 2007; Parry D. C., 2008). There is little doubt that exercise benefits breast cancer patients and survivors, but due to the heterogeneous population represented, differing methodologies, and limited research done in this area, it is difficult to attribute causal-effect relationships presently.

Section 2.5.2 Contraindications to exercise

Health contraindications or concerns, motivational and adherence factors may play a role in discouraging the BCP from exercising. Frequently a ‘sentinel life event’, such as a cancer diagnosis, may initiate self-evaluation of current lifestyle and provide an education opportunity for exercise promotion, which may motivate lifestyle change after initial diagnosis or treatment (Demark-

Wahnefried, Peterson, McBride, Lipkus, & Clipp, 2000; Jones & Courneya, 2002). However, exercise adherence (how well individuals adhere to their exercise prescription (Courneya, Mackey, & McKenzie, 2002)) is a challenge amongst this population: women who have regularly exercised before diagnosis are most prone to maintaining exercise programs (Pickett, Mock, Ropka, Cameron, Coleman, & Podewils, 2002). Exercise adherence is challenged by cancer treatment effects and resulting sequelae (Ingram, Wessel, & Courneya, 2010), and is influenced by pre-treatment exercise levels and readiness to change (Pickett, Mock, Ropka, Cameron, Coleman, & Podewils, 2002), motivational interviewing (Bennett J. A., Lyons, Winters-Stone, Nail, & Scherer, 2007), social support, goal setting, commitment and self-efficacy (Owens, Jackson, & Berndt, 2009), higher peak oxygen consumption, location of exercise centre (convenience), more advanced disease stage and less depression (Courneya K. S., et al., 2008). It seems logical that individuals who previously exercised regularly (likely representing those with higher peak oxygen consumption levels) would continue to do so after diagnosis, and that individuals who have more advanced disease would realize the seriousness of their health status and be more motivated to exercise to attempt to battle their prognosis.

Participation in and adherence to exercise is affected by cancer treatments, health concerns or fears and health contraindications. Fears that exercise will exacerbate arm swelling discourages some from exercising (Hayes, Reul-Hirche, & Turner, 2008), but several studies have demonstrated that exercise is safe and does not exacerbate lymphedema (Ahmed, Thomas, Yee, & Schmitz, 2006; Hayes, Reul-Hirche, & Turner, 2008; Schmitz, et al., 2009) and may actually improve lymphatic flow (Brennan & Miller, 1998; Mortimer, 1990; Mortimer, 1995; McKenzie & Kalda, 2003). Cancer treatments affect performance and adherence to exercise: adherence to a walking program was compromised during chemotherapy but improved after this treatment was complete (Swenson, Nissen, & Henly, 2010). Jansen et al. (1990) investigated the role of delayed (8 days post-surgery) shoulder exercises compared to immediate (1 day post-surgery) on wound drainage after axillary

dissection, and found that there was an increased trend toward more wound drainage (14% more; 701 ± 398 mL versus 600 ± 436 mL) with early start exercises, suggesting that exercises regimes start no sooner than 8 days post-surgery. Pre-exercise medical assessments should evaluate for peripheral neuropathies, musculoskeletal morbidities and cardiac toxicities secondary to cancer treatment, and individuals prescribed hormonal therapy should be evaluated for bone metastasis and fracture risk (Schmitz, et al., 2010). Exercise testing is not required before walking, flexibility or resistance training, and the American College of Sports Medicine guidelines for exercise testing should be followed before moderate to vigorous aerobic exercise (Schmitz, et al., 2010). Other factors that could warrant exercise prescription modification or cessation are listed in Table 6.

Table 6 Contraindications of exercise within a BCP.

Complications
severe fatigue
severe nausea
bone metastasis
hemoglobin < 8.0g/dL
fever > 38° C
ataxia, dizziness, peripheral sensory neuropathy
dyspnea
pain
dehydration
severe anaemia*
compromised immune function (exercising in public areas)*
chlorine exposure (if skin is irradiated)*
indwelling catheters (avoid water or other microbial exposures)*
Referenced from (Courneya, Mackey, & McKenzie, 2002) or * from (Doyle, et al., 2006)*

Section 2.5.3 Exercise during and after adjuvant treatment

A multitude of studies have been performed investigating the effects of exercise on various physiological measures during and after adjuvant cancer treatments. Several research and review papers have demonstrated exercise is safe, feasible and has a positive effect on various measures of physical function both during and after adjuvant therapies. Markes et al. (2006) reviewed the

literature regarding the effects of exercise on women with breast cancer receiving adjuvant therapy and reported that exercise has been found to statistically improve cardio-respiratory fitness, anxiety, and sleep disturbances and relieve nausea; however no significant improvements were found for fatigue, weight gain, QoL, depression, strength, immune function or mood. However, these results are based on a small number of studies, with limited sample sizes and considerable heterogeneity between studies (Markes, Brockow, & Resch, 2006). Another review by McNeely et al. (2006) similarly concluded that the literature suggests exercise improves cardio-respiratory fitness and has no significant effect on weight gain, but also contrarily concluded that exercise improves QoL, physical functioning and symptoms of fatigue in breast cancer patients and survivors. McNeely et al. (2006) also conceded these findings are based on a small number of studies with significant methodological weaknesses. A recent review by the American College of Sports Medicine (Schmitz, et al., 2010) reported high quality literature (randomized controlled trials with high internal validity) that demonstrated exercise is safe to perform during adjuvant breast cancer treatment (Battaglini, et al., 2007; Campbell, Mutrie, White, McGuire, & Kearney, 2005; Courneya & Friedenreich, 2001; Courneya, et al., 2008) and significantly improves:

- aerobic capacity (Adamsen, et al., 2009; Dimeo, Fetscher, Lange, Mertelsmann, & Keul, 1997)
- muscular strength (Courneya K. S., et al., 2007; Schwartz, Winters-Stone, & Gallucci, 2007)
- body size and composition (Segal, et al., 2001)
- QoL (Mutrie, et al., 2007)
- fatigue (Adamsen, et al., 2009)
- anxiety (Badger, Segrin, Dorros, Meek, & Lopez, 2007)

The review by Schmitz et al. (2010) also reported findings from randomized controlled trials of high internal validity that demonstrated exercise among survivors (post-treatment) is safe (Ahmed, Thomas, Yee, & Schmitz, 2006) and significantly improves:

- aerobic capacity (Basen-Engquist, et al., 2006; Bennett J. A., Lyons, Winters-Stone, Nail, & Scherer, 2007)
- strength (Berglund, Bolund, Gustafsson, & Sjoden, 1994)
- flexibility (Burnham & Wilcox, 2002)
- body size (Demark-Wahnefried W. , et al., 2007)
- QoL (Daley, Crank, Saxton, Mutrie, Coleman, & Roalfe, 2007)
- fatigue (Fillion, et al., 2008)
- depression (Daley, Crank, Saxton, Mutrie, Coleman, & Roalfe, 2007)
- anxiety (Burnham & Wilcox, 2002)

This review also reported other randomized controlled trials with high internal validity that found non-significant positive effects or no effect of exercise (Schmitz, et al., 2010). Table 7 provides an overview of evidence regarding the efficacy of exercise interventions for specific outcomes in breast cancer patients and survivors (Schmitz, et al., 2010). The conflicting findings and conclusions regarding the effect of exercise on breast cancer patients and survivors may be attributed to limited research and study limitations including small sample sizes and heterogeneity of samples and methodologies. McNeely et al. (2006) recommends methodologically rigorous studies examine different exercise regimens to understand the role of physical exercise among breast cancer populations, and that these studies include detail regarding the frequency, intensity, time and type of exercise, and that consensus be made regarding standardized methods of assessing physical fitness and body composition to allow for comparisons to be made across studies.

Table 7 Overview of evidence regarding efficacy of exercise interventions for breast cancer survivors [a] [Table taken from (Schmitz, et al., 2010)]

Outcome	During chemotherapy & radiation	After chemotherapy & radiation
Number of studies reviewed [b]	21	32
Safety (no exercise-related adverse events reported)	13	15
Physical function	2	4
Physical fitness Aerobic fitness Muscular strength Flexibility	 10 5	 10 6 5
Physical activity level	5	8
Body size (weight, BMI, body composition, muscle mass)	4	8
Bone health	2	1
Safety about lymphedema-related outcomes	2	7
QoL	4	12
Energy level or vigour/vitality	-	3
Fatigue	4	4
Sleep	1	
Depression	-	3
Anxiety	3	3
Symptoms/adverse effects (including pain)	3	3

[a] numbers in the table reflect the number of studies with a significant positive effect on the outcomes listed
[b] only randomized controlled trials with high internal validity were reviewed

Section 2.5.4 General exercise recommendations

Appropriate and safe exercise must be prescribed in order for breast cancer patients and survivors to benefit from it and adhere to it. Exercise location and format (supervised or self-directed) are equally important factors to consider as are frequency, type, intensity and duration of exercise. Finding the appropriate combination is highly dependent on individual preference, health, capability, and responsibilities at home and work.

The majority of cancer survivors prefer unsupervised exercises performed at home (Jones & Courneya, 2002). Exercises performed at home are generally cheaper, require less formal equipment

and are more convenient and less time consuming. In general, women are more likely to adhere to exercises at home and when it is convenient for them (Huberty, et al., 2008). Several studies have shown that unsupervised home-based exercises are effective. Mock et al. (1997) found that self-paced walking programs performed at home helped to manage symptoms and improve physical function of breast cancer populations treated with radiation. Home-based walking exercise programs have also been shown to be safe and effective in increasing short-term physical activity levels, even of individuals who were not previously active on a regular basis (Matthews, et al., 2007). Segal et al. (2001) compared the effects of self-directed and supervised exercise to usual care breast cancer patients and found that the self-directed exercises group had moderate-large significant increases (increased 5.7 points) in physical function (compared to usual care (decreased 4.1 points)) compared to smaller improvements (increased 2.2 points) seen in the supervised exercise group (compared to usual care), despite adherence being the same between both exercise groups.

Various types of exercise including aerobic, resistance and flexibility all provide potential benefits to different aspects of health such as cardiopulmonary fitness, muscle and bone strength and stretching of tight muscles, tendons or scar tissue, respectively. Women with or at risk of lymphedema should wear a well-fitted compression garment during exercise (Schmitz, et al., 2010). It has been recommended that survivors start with a supervised exercise program at very low resistance, progressing at small increments with no upper limit on the amount of weight to which they can progress (Schmitz, et al., 2010). If a break is taken, the level of resistance should be decreased by 2 weeks' worth for every week of rest (e.g. 1 week vacation = back off to resistance used 2 weeks ago) (Schmitz, et al., 2010). Specific exercise recommendations are outlined in Table 8 (Courneya, Mackey, & McKenzie, 2002). To promote psychological health, exercises should be included that are enjoyable, help to develop new skills, promote social interaction and that occur in a stimulating environment (Courneya, Mackey, & McKenzie, 2002).

Table 8 General aerobic exercise recommendations for cancer survivors and early-stage cancer patients. [Table taken from (Courneya, Mackey, & McKenzie, Exercise for breast cancer survivors, 2002).]

Parameter	Recommendation & Comment
Mode	Most exercises involving large muscle groups are appropriate, but walking and cycling are especially recommended. The key is to modify exercise mode based on acute or chronic treatment effects from surgery, chemotherapy, and/or radiation therapy.
Frequency	At least 3-5 times/week, but daily exercise may be preferable for deconditioned cancer patients performing lighter-intensity and shorter-duration exercises
Intensity	Moderate intensity, depending on patient's current fitness level and severity of side effects from treatments. Guidelines include 50%-75% VO_2max or $HR_{reserve}$, 60%-80% HR_{max}, or an RPE of 11-14. $HR_{reserve}$ is the best guideline if HR_{max} is estimated rather than measured. *
Duration	At least 20-30 min of continuous activity, but this goal may require multiple intermittent shorter bouts (e.g. 5-10 min) with rest intervals in deconditioned patients or those experiencing severe side effects of treatment.
Progression	Initial progression should be in frequency and duration. Only when these goals are met should intensity be increased. Progression should be slower and more gradual for deconditioned patients or those with severe side effects of treatment.
*$HR_{reserve}$ = maximal heart rate (HR_{max}) minus standing resting heart rate (HR_{rest}). Multiply $HR_{reserve}$ by 0.60 and 0.80. Add each of these values to HR_{rest} to obtain the target heart rate range. HR_{max} can be estimated as 220 minus age in years. HR = heart rate; RPE = rating of perceived exertion	

Section 2.6 Unknown aspects of breast cancer survivorship addressed by this thesis

In summary, the breast cancer research literature demonstrates that upper arm dysfunction is a common and serious consequence of cancer treatment among the breast cancer population. It demonstrably adversely affects independence and function. However, the specific upper limb capabilities and dysfunction in terms of 3-dimensional kinematics, muscle activation and muscle-specific strength of this population during ROM, ADL and work are inadequately described. Quantitative detail and description of survivor joint motion, muscle strategies and strength will help identify differences (indicative of dysfunction) between healthy and affected sides, which will be

useful in recommending more focused and accurate treatment and preventative therapies. The main unascertained themes in literature relating to the purposes of this thesis are as follows:

1. Lack of standardized assessments and quantification of upper limb morbidities, including:
    a. 3-D upper limb ROM
    b. muscle activation (EMG)
    c. muscle-specific strength (defined as maximal force production during functional exertions)
2. The relationship between physical dysfunction (in terms of muscle activation) and QoL and disability scores are unknown.
3. Specific exercises which are appropriate and beneficial to breast cancer survivors are unidentified.

This thesis aims to directly address the first two gaps in literature, and the findings from this research will be used in the future to address the third gap of determining appropriate exercises for this population.

Breast cancer survivors are a challenging population to research. Investigating cancer survivors is difficult as the group is extremely heterogeneous in terms of their demographics, behavioural profiles, disease pathology, treatment protocols and symptoms (McNeely, Campbell, Rowe, Klassen, & Mackey, 2006). This population generally feels unwell and has limited time or energy for activities outside of their medical treatment, and therefore, recruitment is difficult and most studies have a limited sample size and significant attrition of participants. Comparisons between studies are difficult to make due to differing methodologies, heterogeneous groups and methodological weaknesses (e.g. failure to blind participants and researchers during randomized controlled trials). Late morbidity may interfere with ADL and QoL, but it is not clear how strong the relationships are between late morbidity (pain, edema, decreased ROM, weakness) and ADL and

QoL (Rietman, et al., 2003). It is not known what type, duration, intensity or frequency of exercise is most beneficial for specific health and physical functioning outcomes in the breast cancer population (Courneya, Mackey, & McKenzie, 2002; Pinto B. M., Clark, Maruyama, & Feder, 2003). Current programs in cancer rehabilitation are mainly focused on psychotherapy or social support and do not address the physical limitations faced by this population (Mutrie, et al., 2007). Determining the role of different exercise regimens (McNeely, Campbell, Rowe, Klassen, & Mackey, 2006) and exercise prescription for breast cancer survivors are important for future research (Courneya, Mackey, & McKenzie, 2002).

Upper limb morbidity has rarely been accurately documented (Thompson, Air, Jack, Kerr, Rodger, & Chetty, 1995) but few studies have investigated the mechanisms of change or the mediating mechanisms between exercise and QoL of breast cancer survivors (Courneya K. S., Friedenreich, Sela, Quinney, Rhodes, & Handman, 2003). There is substantial variability in the instruments used for assessing impairments, and no standardized criteria exist for identifying pain, ROM, arm volume, or muscle strength impairments (Rietman, et al., 2003). Current quantitative measures of physical capacity of breast cancer populations consist of basic evaluations, such as manual goniometric measures of joint ROM. Only three groups have investigated 3-D scapular kinematic during basic motions of flexion, abduction and scaption (Borstad & Szucs, 2012; Crosbie, et al., 2010; Shamley, Srinaganathan, Oskrochi, Lascurain-Aguirrebena, & Sugden, 2009; Shamley, Lascurain-Aguirrebena, Oskrochi, & Srinaganathan, 2012) and only two groups have reported electromyographic measures (during a writing task and during scaption) on this population (Galiano-Castillo, Fernandez-Lao, Cantarero-Villanueva, Fernandez-de-las-Penas, Menjon-Beltran, & Arroyo-Morales, 2011; Shamley, et al., 2007; Shamley, Lascurain-Aguirrebena, Oskrochi, & Srinaganathan, 2012). Limited information regarding kinematics, electromyography, muscle-specific strength or muscle coordination has been documented or related to ADL or work on this population. No known theoretical modelling attempt has assessed internal/external rotation muscle strategies demonstrated

by breast cancer survivors. This thesis aims to address these gaps in literature by thoroughly and accurately quantifying the capabilities and dysfunction of breast cancer survivors both empirically and theoretically. The specifics regarding methodology of biomechanical procedures used to investigate these gaps in literature will be addressed in the following chapter.

Chapter 3 General review of biomechanical methods and research considerations

This chapter provides a summary of the biomechanical methodological procedures, justifying their use through a review of literature of previously used, currently recommended, or identified inadequate techniques.

Section 3.1 Data acquisition from a breast cancer population

Data acquisition from the BCP introduces challenges absent in collections from healthy persons. Ability and endurance of this population is compromised due to the primary disease and associated treatment morbidities. Collections intentionally focused on safe and feasible measurements that accommodated for individual needs (e.g. rest periods), while specific and novel data was acquired (e.g. intramuscular EMG, 3-D kinematics, strength) during a wide range of tasks and intensities (total of 142 exertions).

Section 3.1.1 Population precautions

Precautions must be taken against spreading infections when performing research on a breast cancer population. This population has a compromised immune system due to their cancer treatments and are therefore susceptible to infection. Such acquired infection (e.g. common cold) could traumatically and dramatically deteriorate their health. Precautions were taken to ensure that participants were not exposed to any known acquired illnesses. A sign outside the laboratory was posted to alert people that were knowingly ill (cold or flu-like symptoms) to stay out of the room. Hand sanitation stations were placed in the laboratory, so that the participant and researchers could regularly sanitize their hands to avoid the spread of germs. Intramuscular electrode insertions were performed under sterilized conditions, as is discussed in more depth in the corresponding study methodology. Ethics was received from the University of Waterloo Office of Research Ethics, and permission was granted from the Grand River Hospital. In principle, these participants were not

exposed to any additional immune risk than would be associated with having blood taken at the doctors' office.

Cancer survivors are a heterogeneous population in terms of their demographics, behavioural profiles, disease pathology, treatment protocols and symptoms (McNeely, Campbell, Rowe, Klassen, & Mackey, 2006). As such, each individual had different health concerns and physical limitations and levels of endurance. The experimental protocol was modified according to the specific needs of each participant, including provision of appropriate rest periods or negating performance of certain study elements (e.g. adjusting positioning of testing for comfort, declining insertion of intramuscular electrodes) if the participant was unable or unwilling to perform them. One-repetition maximum strength tests have been shown to be safe amongst the breast cancer population, even those with or at risk of lymphedema (Schmitz, et al., 2010). However, if these or other measures were painful or uncomfortable for the participant, or if additional risks prohibited a specific activity (e.g. increased risk of fracture), commensurate accommodations (modifications or neglect) were made.

Deliberate timing of recruitment was important to ensure survivors were at low risk of infection during participation in the study. Breast cancer survivors were recruited at least 3 months following adjuvant treatments. This time should have allowed survivors to start regaining their health such as increased immune response and decreased skin sensitivities caused by radiation. In previous work, 'recent' breast cancer survivors were considered those that are 4-36 months post adjuvant therapy (Schmitz K. H., Ahmed, Hannan, & Lee, 2005). In this thesis distinctions were not made between survivors and end-range of post adjuvant therapy, due to recruitment complications and lack of participant availability. Adjustments have been made in previous work to accommodate for recruitment issues. Sandel et al. (2005) initially recruited breast cancer patients who had surgery 18 months prior, but had trouble recruiting enough participants so later extended their criteria to 5 years post-surgery to attain an appropriate sample size. Further, these authors did not exclude participants with differing treatment regimens (surgery type, chemotherapy, radiation etc.), as obtaining

homogenous groups within this population is extremely difficult and would take a tremendous amount of resources and time. This thesis similarly involved a wide inclusion criteria and narrow exclusion criteria so as to promote recruitment.

Section 3.1.2 Range of motion measurement

Range of motion among a breast cancer population has most commonly been reported via subjective measures (Lauridsen, Overgaard, Overgaard, Hessov, & Cristiansen, 2008) or by physical examination using goniometry (Box, Reul-Hirche, Bullock-Saxton, & Furnnival, 2002; Hack, Cohen, Katz, Robson, & Goss, 1999; Nesvold, Dahl, Lokkevik, Mengshoel, & Fossa, 2008; Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004; Ryttov, Holm, Qvist, & Blichert-Toft, 1988; Sugden, Rezvani, Harrison, & Hughes, 1998; Swedborg & Wallgren, 1981; Tasmuth, von Smitten, Hietanen, Kataja, & Kalso, 1995). Often only a single motion is assessed (e.g. shoulder abduction) and is assumed to be indicative of restricted shoulder motion, even though there is evidence that some patients can have full abduction, but decreased flexion ROM (Lauridsen, Overgaard, Overgaard, Hessov, & Cristiansen, 2008). This emphasizes the importance of assessing several planes of shoulder motion. It appears that only three groups have recorded 3-D kinematics of this population, which included scapulothoracic motion during scaption (humeral elevation in the scapular plane), flexion and abduction (Borstad & Szucs, 2012; Crosbie, et al., 2010; Shamley, Srinaganathan, Oskrochi, Lascurain-Aguirrebena, & Sugden, 2009). Three-dimensional motion tracking to record kinematics is essential to obtain accurate assessments of ROM. It is difficult to visually assess and quantify the highly dynamic 3-D motions of the shoulder, including scapulothoracic angles (scapular winging is a potential complication amongst the breast cancer population (Lauridsen, Torsleff, Husted, & Erichsen, 2000)).

Accurate assessment tools and standardized definitions of functional ROM are needed in order to achieve consistent inter-subject measures of ROM and allow for comparisons between studies. There is some consensus that ‘functional’ shoulder ROM (ROM required to perform most

ADL) is defined as 145° abduction, 160° flexion and 80° degrees external rotation (Ryttov, Blichert-Toft, Madsen, & Weber, 1983; Ryttov, Holm, Qvist, & Blichert-Toft, 1988; Gerber, et al., 1992). However, there is considerable disagreement in the literature as to what defines impaired ROM. Nesvold et al., (2008) claimed clinical experience revealed that a decreased ROM of 10° - 20° did not limit ADL, and therefore chose ≥25° difference of affected arm to non-affected side as the definition of impaired shoulder function. Box et al. (2002) defined shoulder impairment as a post-operative loss of 20° of shoulder abduction or flexion. Rietman et al. (2004) defined impaired ROM as ≥20° difference between sides, whereas Ryttov et al. (1988) defined impaired ROM as <170° of shoulder flexion or abduction. Sugden et al. (1998) defined functional impairment to be >90% when ipsilateral movement is divided by contralateral movement. Much smaller changes in scapular kinematics have been reported to be clinically meaningful by Shamely et al. (2009) (10° increase in scapular protraction) and Borstad & Szuks (2012) (11.5° increase in scapular protraction). Lack of consensus regarding the definition of functional impairment makes it difficult to make comparisons between studies regarding the physical capability of the breast cancer population. For this thesis, a definition of impairment will be defined as a significant difference in degrees between health and affected sides.

This thesis used 3-D motion capture to record scapulothoracic and humerothoracic kinematic measures of the BCP. Assessments included motions in several planes, including measures of flexion, extension, abduction, external and internal rotation, as well as a variety of functional ADL and work tasks. Measures of this detail and accuracy, in this number of planes and for such a diversity of active tasks is unprecedented within the BCP.

Section 3.1.3 Muscle activation measures

Very little is known about shoulder muscle activation amongst the breast cancer population. Only two groups have investigated surface EMG of the BCP. Galiano et al. (2011) recorded surface EMG from the sternocleidomastoid, upper trapezius and deltoid during a functional writing task and

reported increased activation of the upper trapezius bilaterally (up to 20% and 4% increases on affected and unaffected side, respectively) and sternocleidomastoid muscles (up to 31% increase on affected side) of survivors compared to a healthy control group. Shamley et al., (2007) investigated surface EMG of the pectoralis major, pectoralis minor, rhomboid and serratus anterior of the BCP performing scaption. The authors indicated that there was a general loss of muscle activity of the affected arm during humeral elevation (significant loss on downward movement of arm; greatest loss at the highest point of elevation) compared to the unaffected arm, which would concur with diminished ability to perform ADLs. However, the interpretation of these results is difficult because EMG was not normalized; rather comparisons were made based on frequency of data points above or below those from the muscles of the unaffected contralateral arms. Past work has demonstrated because of the inherent signal variability, surface EMG requires normalization for physiologic interpretation and comparison between bilateral muscles and between the same muscle at different time points or across participants (Lehman & McGill, 1999). Later, Shamley et al. (2012) re-examined normalized muscle activity of pectoralis major, serratus anterior, rhomboids and upper trapezius during scaption of a BCP with mastectomy or wide local excision. With the exception of upper trapezius in the mastectomy group, the authors reported an increase in activity of all muscles on the left affected side of patients with either mastectomy or wide local excision compared to the left side of a healthy control group; and reported greater activation of the upper trapezius, rhomboids and serratus on the right affected side of patients with mastectomy compared to the right side of a healthy control, suggesting the BCP was working at a higher level of percent capability. Shamley et al. (2012) also reported a decrease in pectoralis major activity and an increase in serratus anterior activity on the affected side compared to the unaffected side.

Section 3.1.3.1 Intramuscular electrodes

EMG has not been recorded directly from the rotator cuff within the breast cancer population, but has been recorded from some surrounding shoulder musculature via surface electrodes (Galiano-Castillo,

Fernandez-Lao, Cantarero-Villanueva, Fernandez-de-las-Penas, Menjon-Beltran, & Arroyo-Morales, 2011; Shamley, et al., 2007; Shamley, Lascurain-Aguirrebena, Oskrochi, & Srinaganathan, 2012). Thompson et al., (1995) suggested that the reduction in mobility may reflect damage to the rotator cuff muscles. Due to the depth and small size of these muscles, intramuscular electrodes are the gold standard for obtaining muscle activity information. The author of this thesis received intramuscular electrode training and a note of delegation from a medical doctor to perform this task without medical supervision. The author of this thesis also received ethics consent from the University of Waterloo Office of Research Ethics to perform this task. This thesis work incorporated intramuscular EMG measures of rotator cuff muscles, and surface EMG measures of other shoulder, neck and trunk muscles of healthy participants and breast cancer survivors.

Section 3.1.3.2 Co-activation quantification

This thesis described the empirical co-activation relationship between humeral internal and external rotators in healthy and breast cancer survivor populations. Co-activation has been measured between antagonist and agonist muscles at the ankle (Granata, Wilson, Massimini, & Gabriel, 2004), knee (Kellis, Arabatzi, & Papadopoulos, 2003; Kingma, Aalbersherg, & van Dieen, 2004), trunk (Lee, Rogers, & Granata, 2006) and elbow (Brookham, Middlebrook, Grewal, & Dickerson, 2011; Doheny, Lowery, Fitzpatrick, & O'Malley, 2008; Gottlieb, 1998; Praagman, Chadwick, van der Helm, & Veeger, 2010; Solomonow, Guzzi, Baratta, Shoji, & D'Ambrosia, 1986). Co-activation occurs for the purposes of limb or end effector motion control, joint or whole body stabilization and limb stiffness (Granata, Wilson, Massimini, & Gabriel, 2004; Latash, 1992; Milner & Cloutier, 1993; Zhang & Eymer, 1997). In biomechanical modeling, optimization procedures often involve simplifying assumptions, including that the body selectively activates specific muscles for a given activity according to some criterion (for example, minimum muscle stress or minimum physiological cost) (Crowninshield & Brand, 1981). In the mathematical formulation of these objective functions, antagonistic contraction is counterproductive - producing moments that do not contribute to

production of the required net joint moments, but increasing physiological cost. Therefore, optimization models that apply efficiency-based objective functions often negate or underestimate antagonist co-activation (Collins, 1995; Dickerson, 2008; Hughes & Chaffin, 1988; Zajac & Gordon, 1989). Defining and applying co-activation relationships to biomechanical models could potentially improve model predictions, and could have additional utility for identifying muscular activation changes in a patient population compared to a healthy group. Identification of specific co-activation changes within breast cancer survivors could direct preventative and therapeutic interventions and define differential strategies of this population.

Co-activation index ratios were calculated to determine the relative activation of humeral internal rotation activation to internal and external rotation about the shoulder. A similar ratio was described by Kellis et al., (2003), and was used previously to describe co-activation at the elbow (Brookham, Middlebrook, Grewal, & Dickerson, 2011). A secondary ratio was calculated which was weighted according to physiological cross-sectional area (PCSA) for each respective muscle. PCSA data has been measured directly (Fick, 1911; Poppen & Walker, 1978; Shiino, 1913) and calculated (Bassett, 1983; Fick, 1911; Howell, Imobersteg, Segar, & Marone, 1986; Wood, Meek, & Jacobsen, 1989) in past literature. Veeger et al., (1991) compares PCSA data for shoulder muscles across studies as demonstrated in Table 9. PCSA data inserted into the weighted co-activation ratios was from Veeger et al., (1991) and van der Helm (1994).

Table 9 Comparison of shoulder muscle PCSA data for past literature. [Table duplicated from Veeger et al., (1991)]

	Physiological cross-sections (cm^{-2})									
	Weber (1851)	Fick (1911)	Shiino (1913)	Poppen and Walker (1978)	Bassett ‖(1983)	Howell *et al.* (1986)	Wood *et al.* (1989)	Wood *et al.* (1989)	This study	
No. of shoulder specimen		(N=6)	(N=3)	(N=2)*	(N=2×2+1)	(N=5)	(N=1)‖	(N=1)¶	(N=7×2)	s.d.
Biceps cap. med.	9.15	6.55	5.90		2.04		3.2	1.3	3.08	1.01
Biceps cap. lat.			5.10		2.16		7.1	1.9	3.21	1.07
Triceps	15.98†	4.75	15.00†		11.93		7.1†	3.8†	6.84†	1.58
Coracobrachialis	5.79	5.79§	5.50				1.3	1.2	2.51	0.91
Levator scapulae	2.58								2.82	0.50
Rhomboideus	6.52						12.3	12.9	6.27	1.94
Lat. dorsi	9.43		8.20	7.39	12.33		12.9	5.8	8.64	3.05
Trapezius	12.68						27.7	2.6	15.99	3.35
Teres major	9.81	9.81§	10.50		8.49		8.4	5.8	10.02	4.29
Teres minor	‡				‡		2.6	2.5	2.92	1.01
Infraspinatus	16.47‡	16.47§	13.20	11.36	13.59‡	17.57	8.4	5.8	9.51	2.97
Supraspinatus	7.71	7.71§	9.30	6.21	5.74	9.52	5.2	4.5	5.21	1.76
Subscapularis	25.24	25.24§	21.00	13.85	15.89	16.00	13.6	9.7	13.51	3.49
Deltoideus	25.31	25.30§	34.00	37.69	23.13	26.72	29.0	21.9	25.90	4.28
Pect. major	17.36		12.90		13.61		18.7	13.5	13.65	3.00
Pect. minor	4.18						4.5	3.8	3.74	0.99
Serratus anterior	12.80						13.6	13.0	13.93	3.46
Total	181.00						175.5	132.3	147.57	

*Two specimens combined with Fick's data.
†Long head only.
‡Infraspinatus + teres minor.
§Data from Weber.
¶Calculated with the use of Coons surface grids.
‖Calculated as volume/muscle length.

This thesis focused on simplified co-activation of the shoulder: including internal and external rotators. The internal rotators (specifically the pectoralis major), located on the anterior aspect of the chest, are most likely to be affected in a breast cancer population due to the directed radiation field and location of surgery. Radiation can cause secondary damage to adjacent healthy tissues which may affect muscle contraction efficiency. Damage to the internal rotators may result in significant changes in the co-activation relationships between internal and external rotation activity. Determination and investigation of theses co-activation relationships has not yet been examined among breast cancer survivors.

Section 3.1.4 Lymphedema measures

Arm volume measurements can be used to monitor edema and the incidence of lymphedema. The gold standard for arm volume measurement is the water displacement method (Lette, 2006). Often edema is quantified using circumference measurements of the arm at different levels, but this measurement type is unreliable because of inter-subject variability of arm shape and differences in arm shape before and after swelling (Swedborg & Wallgren, 1981), and inaccurate measures due to

tape constriction (Petrek & Heelan, 1998). Water displacement is more accurate but rarely used (Petrek & Heelan, 1998). Water displacement arm volumeters are commonly large, cumbersome, fragile and expensive, and often inaccessible to patients (Lette, 2006). Lette (2006) designed a simple and inexpensive water displacement arm volumeter to measure arm volume, and found it to be a highly accurate measure of volume. This thesis work has duplicated Lette's (2006) design and constructed two arm volumeters and tested their accuracy with known volumes. These volumeters were used to measure arm volume of breast cancer survivors as demonstrated in Figure 15.

There is some variation in volumetric measuring procedures used in literature. In particular, the depth to which the arm is inserted within a volumeter varies between studies. Lette (2006) recommended participants insert their straight arm until the middle finger reached the bottom of the volumeter. Lane et al., (2005) and McKenzie & Kalda (2003) had participants insert the arm until a depth of 45 cm proximal to the styloid process of the ulna. Lane et al., (2005) recommended participants slowly immerse the arm and measure the displaced water (read on a graduated cylinder as the volume to the nearest 10 mL) once the water drips less than once per second. On the contrary, Lette (2006) recommends weighing the displaced water, assuming the amount of water displaced is equivalent to its volume (1 L of water weighs 1 kg), since it is difficult to purchase large enough jugs with precise graduations and smaller variations in volume are more easily and accurately gauged by weighing. In this thesis, the participant's arm was immersed until 20 cm above the lateral epicondyle, and the displaced water was weighed on a balance that was accurate to 0.01 g.

The definition of lymphedema varies between studies. Nesvold et al. (2008) defined lymphedema as ≥10% volume difference between arms or >2 cm increase of any circumference measure compared to the opposite arm, and defined severe lymphedema as >20% volume difference between arms. Similarly, Rietman et al. (2004) and Sugden et al. (1998) defined lymphedema as a volume difference between arms of ≥10%. Ryttov et al. (1988) defined lymphedema as ≥2.5 cm circumference difference between arms. Upper limb volume increases of 200 mL are considered

clinically significant and potentially disabling (Kissin, Querci della Rovere, Easton, & Westbury, 1986; Hoe, Iven, Royle, & Taylor, 1992; Tracy, Reeve, Fritzsimmons, & Rundle, 1961). In this thesis, volume was recorded for all participants, and lymphedema was defined as ≥200 mL difference between arms.

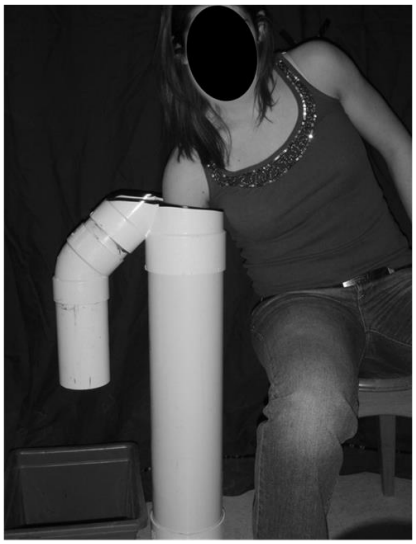


Figure 15 Arm volumeter used to measure arm volume via water displacement. Instrument designed by Lette (2006).

Section 3.1.5 Strength measures

Measures of muscle-specific strength, especially around the shoulder, within a breast cancer population have not been adequately quantified and lack of standardization in the measures makes comparisons between studies challenging. A review by Rietman et al. (2003) revealed that strength is commonly assessed using grip strength data or through subjective reports of weakness. Impaired grip strength has been defined as ≥10% difference between sides (Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004). Muscle strength has been assessed using submaximal muscle endurance protocols that predict one-repetition maximum during leg extension, seated leg curl, lateral pull down and seated chest press exercises (Battaglini, et al., 2007). Muscle strength has been defined as the peak torque achieved divided by participant body weight during hip, knee and

wrist flexion/extension, and mean baseline values for 249 postmenopausal breast cancer survivors have been determined (Twiss, Waltman, Berg, Ott, Gross, & Lindsey, 2009). This thesis determined muscle-specific strength measures (maximal force achieved during manual muscle tests found to maximally functionally isolate specific muscles) of breast cancer survivors. These forces were recorded with a hand-held digital dynanometer. Previous work by Brookham et al., (2010) has defined manual muscle testing positions which maximally functionally isolate the rotator cuff muscles, and also identified a variety of position-modified tests. These tests may be appropriate to use with breast cancer survivors with reduced ROM, who are not able to move into standard recommended muscle testing positions.

Section 3.1.6 Quality of life measures

There is no standardized method for assessing QoL of the breast cancer population, and often tools that are used are not validated. A review by Rietman et al. (2003) reviewed ADL and QoL among a breast cancer population and found that these measures were often assessed with questionnaires and rating scales, but that the tools were often not validated or reliable instruments. Another limitation to findings regarding QoL is often attributed to a lack of statistical power. One work that investigated the relationship between QoL and physical impairments cautioned against interpretation of the associations made (pain, grip strength and arm volume predicted QoL) due to a low sample size and lack of statistical power (Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004). Many studies are based on physical measures, but fail to ask patients how physical complaints affect their performance of ADL, including tasks at work, home, sports and hobbies (Voogd, Ververs, Vingerhoets, Roumen, Coebergh, & Crommelin, 2003). The Functional Assessment of Cancer Therapy – Breast (FACT-B) questionnaire is a multidimensional health-related QoL instrument designed specifically for breast cancer populations which has been proven to be a valid and reliable tool that is easy to administer, doesn't take long to complete and is sensitive to change (Brady, et al., 1997). The FACT-B has been used extensively in studies (Campbell, Mutrie, White, McGuire, &

Kearney, 2005; Courneya K. S., Mackey, Bell, Jones, Field, & Fairey, 2003; Daley, Crank, Saxton, Mutrie, Coleman, & Roalfe, 2007; Mutrie, et al., 2007; Sandel, Judge, Landry, Faria, Ouellette, & Majczak, 2005; Segal, et al., 2001; Vallance, Courneya, Plotnikoff, Yasui, & Mackey, 2007) and baseline FACT-B scores for 377 breast cancer survivors are reported by Vallance et al., (2007). These baseline scores were used to compare the baseline FACT-B scores obtained in the present thesis work. This current thesis work incorporated a detailed medical history questionnaire, a disability questionnaire (QuickDASH) and a FACT-B quality of life questionnaire.

Section 3.2 Biomechanical modeling

Biomechanical models are useful for predicting moments, joint and muscle forces that cannot feasibly be empirically measured. Link-segment models can be implemented to calculate these parameters using inverse methods. Numerical optimization approaches are commonly used to determine moment load sharing amongst muscles.

Section 3.2.1 Link-segment models

Link-segment modelling is the process by which net joint forces and moments are calculated (Winter, 2009). Five assumptions are commonly associated with link segment models, as outlined by Winter (2009):

1. Each segment has a fixed mass located as a point mass at its centre of mass (COM).
2. The location of each segment's COM remains fixed (relative to the segment) during movement.
3. The joints are considered hinge or ball-and-socket joints.
4. The mass moment of inertia of each segment is about its mass centre or either proximal or distal joints, and is constant during movement.
5. The length of each segment remains constant during movement.

Gravity, external forces and muscle and ligament forces act on the link-segment model. However, often the contribution of passive structures is ignored as these are incompletely described across postures, especially at the shoulder (Veeger & van der Helm, 2007). The situation is simplified by replacing every force that acts across the joint with an equivalent force and moment about a common axis (Robertson, Caldwell, Hamill, Kamen, & Whittlesey, 2004). Muscle forces are the main contributors to net moments as ligament and bone-on-bone forces contribute mainly during end ROM (Robertson, Caldwell, Hamill, Kamen, & Whittlesey, 2004). In this thesis a previously-built optimization-based muscle force prediction model of the shoulder, termed the Shoulder Loading Analysis Modules (SLAM) (Dickerson, 2005; Dickerson, Chaffin, & Hughes, 2007; Dickerson, 2008) was modified to include co-activation constraints and strength inputs determined from the BCP, during static postures of humeral IR and ER exertions. The force equilibrium calculation, derived from the linear form of Newton's second law of motion was applied for each segment using the equilibrium for each segment as described in Equation 1.

Equation 1 Force equilibrium calculation. Where *F* are the forces; *m* is the mass of segment and *a* is the acceleration of segment COM. External forces are the hand forces and weights of the segments. Solving the resulting equation achieves the external joint load at each proximal joint segment.

$$\sum F = m_{segment} \times a_{COM,segment}$$

To calculate moment values, the angular analog of Newton's second law is applied to each segment as shown in Equation 2:

Equation 2 Moment equilibrium calculation. Where *M* is external moment and Ḣ is the rate of change of segmental angular momentum. Ḣ is calculated based on segmental moments of inertia and the segmental velocities and accelerations. External moments are calculated based on the cross products of the produced forces and their moment arms. Moments are calculated at the proximal ends of each segment.

$$\sum M = \dot{H}$$

Static equilibrium equations (Equation 3, Equation 4) were applied in the link-segment model to solve for net segmental forces and moments, which represented the summed effect of all structures producing moments and force across the joint. These equilibrium equations were solved using

inverse simulations, and allowed for the determination of muscle force, which could be compared with experimental EMG recordings.

Equation 3 Translational equilibrium equation. Where $F_{m,i}$ are the muscles active on segment i, J_{i-1} is the joint contact force on the distal joint, J_i is the joint contact force on the proximal joint and F_E are any external forces unaccounted for in the previous segmental calculations.

$$\sum F_{m,i} + J_{i-1} + J_i = \sum F_E$$

Equation 4 Rotational equilibrium equation. Where ma_i is the moment arm of the i^{th} muscle, $F_{m,i}$ are the muscles active on segment i, M_{i-1} is the moment acting about the distal joint, M_i is the moment acting about the proximal joint and M_E are any external moments unaccounted for in the previous segmental calculations.

$$\sum (ma_i \times F_{m,i}) + M_{i-1} + M_i = \sum M_E$$

Section 3.2.2 Inverse solutions

The majority of kinetic analysis of human movement has been performed using inverse dynamics (Winter, 2009). Inverse simulations are performed when kinematics, anthropometric measures and external forces are known or measured, resulting in the calculation of joint reaction forces and moments. In this thesis, the force produced at the hands was measured with a force transducer, individual anthropometrics (segment lengths and body mass) were measured for each participant, and segment parameters (segment mass, COM locations, muscle moment arms, and PCSA values) were determined from a previously described upper limb model termed Shoulder Loading Analysis Modules (SLAM) (Dickerson, 2005; Dickerson, Chaffin, & Hughes, 2007; Dickerson, 2008). In a dynamic model linear and angular accelerations would normally be calculated by double differentiating positional data, which can be recorded with motion capture, or assumed with goniometric confirmation. In this thesis, linear and angular accelerations were zero, as static positions were assumed, and goniometry was used to determine these static joint positions. A graphical depiction of traditional inverse simulation methods adapted from Buchanan et al., (2004), as well as modified inverse-type simulation used in this thesis is shown in Figure 16.

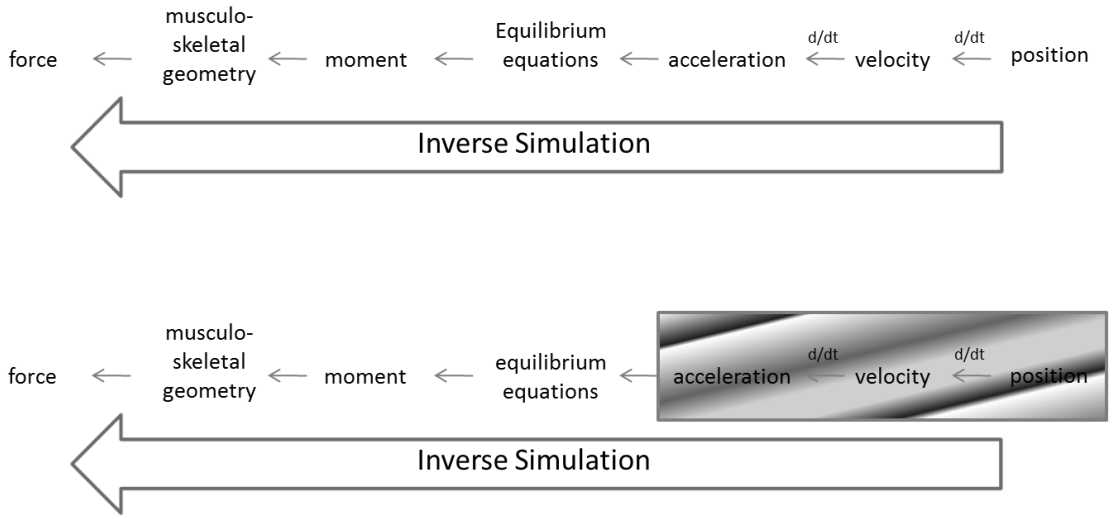


Figure 16 Traditional inverse simulation procedures (top) and inverse-type simulation (bottom) performed in this thesis [gray area represents steps excluded].

Muscle force is most simply determined by assuming a single-muscle equivalent model, during which only one muscle or group of muscles with one line of action and moment arm is assumed to actuate the movement at the joint (e.g. only the biceps is assumed to contribute to elbow flexion). This assumption does not allow for consideration of other contributing muscles, including antagonistic muscles that do not contribute to the net joint moment. This assumption is not always appropriate, particularly, at the glenohumeral joint where there are 6 degrees of freedom and many muscles crossing the joint. To improve physiological realism, a model should include other muscle contributions, including co-activation of antagonistic muscles, in the determination of net joint force. In Study 4 of this thesis, 38 muscle portions were modeled, of which seven muscles (11 muscle portions) were used to create the co-activation constraint and from which predicted muscle forces were compared directly with experimentally recorded EMG. In order to determine load sharing between muscles, an optimization approach was used.

Section 3.2.3 Optimization

Estimating muscle force at the glenohumeral joint is difficult because the solution is indeterminate, meaning that there are more unknowns (many muscles contributing to the net moment) then there are independent equations. Many models use optimization at various joints to determine muscle force (Crowninshield & Brand, 1981; Dickerson, Chaffin, & Hughes, 2007; Hughes, Bean, & Chaffin, 1995). Optimization assumes that the musculoskeletal system allocates certain muscles to generate the required net muscle moment in a mathematically describable manner, which usually involves minimizing some objective function, such as physiological cost (Dickerson, 2008b). The objective function used in this thesis was the minimization of the sum of the cubed muscle stresses, as has been used previously in the lower extremity, elbow and shoulder (Crowninshield & Brand, 1981; Brookham, Middlebrook, Grewal, & Dickerson, 2011; Dickerson, Chaffin, & Hughes, 2007). This simplifying assumption assumes that antagonistic contraction is counterproductive, producing moments that do not contribute to the net joint moment while increasing physiological cost. Therefore, optimization models that apply efficiency-based objective functions often underestimate or negate antagonistic co-activation (Collins, 1995; Dickerson, 2008b). Co-activation occurs for the purposes of limb or end effector motion control, stabilization and stiffness (Granata, Wilson, Massimini, & Gabriel, 2004; Latash, 1992; Milner & Cloutier, 1993; Zhang & Eymer, 1997). Co-activation occurs at the shoulder as previous literature has reported that the rotator cuff muscles are simultaneously active and cannot be independently isolated (Brookham, McLean, & Dickerson, 2010). Therefore, to improve physiological realism, optimization procedures were used to determine load sharing amongst muscles and survivor humeral rotator co-activation relationships (determined from Study 3) were added as constraints to this model. A similar study has enforced flexion/extension co-activation constraints in a 2-D model of the elbow (Brookham, Middlebrook, Grewal, & Dickerson, 2011). The constraints will enforce an *a priori* level of humeral rotator co-activation during optimization. Prediction accuracy will be evaluated by correlating muscle force predictions to empirical measurements of muscle activity and determining magnitude differences

between predicted muscle levels and measured EMG. This analysis was similar to that performed by Dickerson et al. (2008) during which model muscle force predictions were compared with experimentally collected EMG from a healthy population. Comparisons of muscle force predictions to empirically measured EMG is a form of face validation, during which the model outcomes are compared to the expected behavior with respect to past historical data (Lewandowski, 1982). These methods describe a careful attempt to simulate muscle strategy related to muscle dysfunction in a BCP, which has been not been examined to date in the literature.

Chapter 4 Study 1 – Quantification of upper limb capabilities and dysfunction of breast cancer survivors, and relationship to quality of life (QoL) and performance of activities of daily living (ADL) and work tasks

Section 4.1 Introduction

One in nine Canadian women will develop breast cancer in her lifetime (Canadian Breast Cancer Foundation, 2010). The five year survival rate is 88% (Canadian Cancer Society, 2014) and as the survival rates increase, more research needs to focus on life after diagnosis and treatment (Sandel, Judge, Landry, Faria, Ouellette, & Majczak, 2005). Treatment-related sequelae of breast cancer affect 30% - 82% of patients, commonly including reduced ROM, weakness, pain, numbness and swelling (Kwan, Jackson, Weir, Dingee, McGregor, & Olivotto, 2002; Lauridsen, Overgaard, Overgaard, Hessov, & Cristiansen, 2008; Maycock, Dillon, & Dixon, 1998; Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004). Cancer treatment side effects can last days, months, and even years (Schmitz, et al., 2010).

Current detailed knowledge of upper limb physical capabilities of breast cancer survivors is limited. Some have reported that late upper limb morbidities restrict and interfere with completing ADL and return to work, negatively affecting QoL (Markes, Brockow, & Resch, 2006; Rietman, et al., 2003). However, upper limb morbidity has rarely been accurately documented (Thompson, Air, Jack, Kerr, Rodger, & Chetty, 1995). The relationships between impairments, disability, performance of tasks and QoL of breast cancer patients have only scarce documentation (Rietman, et al., 2003; Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004). Current quantitative measures of physical capacity of breast cancer populations consist of basic evaluations that thwart meaningful interpretations. Variability of the assessment methods of impairments is high, and no uniform criteria exist for ROM, muscle strength, pain and arm volume measures (Rietman, et al., 2003). Further, muscle coordination, muscle-specific strength measures and 3-D kinematic

assessments of this population during ADL and work tasks have not been assessed. Only a few groups have investigated 3-D scapulothoracic kinematics of this population during scaption, flexion and abduction (Borstad & Szucs, 2012; Crosbie, et al., 2010; Shamley, Srinaganathan, Oskrochi, Lascurain-Aguirrebena, & Sugden, 2009; Shamley, Lascurain-Aguirrebena, Oskrochi, & Srinaganathan, 2012). This stark lack of description of upper limb disability requires immediate attention.

Upper limb dysfunction within this population has not been systematically evaluated and therefore, specific and effective preventative and treatment strategies do not exist to promote return to function and work. Effective rehabilitation and reduction of symptoms could potentially lower the social and economic burdens of survivor aftercare and dramatically enhance quality of life. Improving the health of this population will allow these survivors not just the ability to live – but to live highly functional and independent lives. A prerequisite for creating these preventative and treatment strategies is rigorous quantification of the physical capabilities typical within this population. This study described these upper limb capacities and dysfunctions in female breast cancer survivors in terms of scapulothoracic and humerothoracic kinematics, muscle coordination and strength during ROM, ADL and simulated work activities. These findings will enable future projects, intended to improve the eventual return to work of breast cancer survivors through improved rehabilitation and treatment strategies.

The two purposes of this study were to:

1. Describe the upper limb capabilities and dysfunction of breast cancer survivors in terms of 3-D upper limb kinematics (specifically, motions of the humerus and scapula with respect to the thorax), muscle activation patterns (electromyography), and muscle-specific strength (force).

2. Determine relationships between total muscle effort (a physical muscle activation quantity of (dys)function) with subjective measures of function (QoL and disability scores) during ROM, ADL and work task performance.

The hypotheses of this study were as follows:

1. Three-dimensional kinematic description of breast cancer survivors will reveal survivors have reduced humeral angle of elevation and external rotation range of motion, but increased scapular protraction range of motion on their affected side compared to the contralateral limb.

Past literature have reported reduced angles of elevation during humeral abduction and flexion ROM (Hack, Cohen, Katz, Robson, & Goss, 1999; Isaksson & Feuk, 2000; Kuehn, et al., 2000; Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004; Swedborg & Wallgren, 1981), reduced external rotation ROM (Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004; Swedborg & Wallgren, 1981), and increased scapular winging (protraction) (Lauridsen, Torsleff, Husted, & Erichsen, 2000) amongst the breast cancer population. These measures have been recorded manually with goniometry and inclinometer tools or have been reported via clinicians' visual assessment. Two studies have recorded 3-D scapulothoracic kinematics with electromagnetic tracking, and have reported increase in scapular protraction on the affected side of survivors (Borstad & Szucs, 2012; Shamley, Srinaganathan, Oskrochi, Lascurain-Aguirrebena, & Sugden, 2009).

2. Breast cancer survivors will demonstrate reduced strength and increased muscle activity (enhanced EMG amplitude) on the affected side when performing muscle specific strength tests, ROM, ADL and work tasks compared to their unaffected side.

Reductions in strength are commonly reported amongst the breast cancer population (Isaksson & Feuk, 2000; Kuehn, et al., 2000; Rietman, et al., 2003), but often measures include subjective reports or quantitative measures of grip strength. Quantification of muscle-specific weakness is scarce amongst this population. There is discrepancy of findings of the two groups that reported muscle activation in survivors. Shamley et al. (2007) reported decreased activation of shoulder muscles on the affected side during scaption; whereas increased activation of the upper trapezius was found in

survivors performing a functional writing task by Galiano-Castillo et al. (2011). Later, Shamley et al. (2012) re-examined normalized muscle activity of pectoralis major, serratus anterior, rhomboids and upper trapezius during scaption of a BCP with mastectomy or wide local excision. With the exception of upper trapezius in the mastectomy group, the authors reported an increase in activity of all muscles on the left affected side of patients with either mastectomy or wide local excision compared to the left side of a healthy control group; and reported greater activation of the upper trapezius, rhomboids and serratus on the right affected side of patients with mastectomy compared to the right side of a healthy control, suggesting the BCP was working at a higher level of percent capability. Shamley et al. (2012) also reported a decrease in pectoralis major activity and an increase in serratus anterior activity on the affected side compared to the unaffected side.

3. As physical data indicates increased dysfunction (increased total muscle effort), there will be decreased QoL scores (FACT-B) and increased disability (QuickDASH) scores.

The number of chronic symptoms of late morbidity of breast cancer survivors has been reported to be significantly correlated with anxiety and depression levels (Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004). Decreased muscular activity of the upper trapezius and rhomboid muscles have been associated with increased Shoulder Pain and Disability Index scores in breast cancer survivors (Shamley, et al., 2007). Box et al. (2002) reported a trend of decreased shoulder ROM associated with breast cancer patients' increased rating of performance difficulty while performing functional tasks.

Section 4.2 Methods

Anthropometrics (including arm volume), a brief medical history, disability and QoL scores were assessed from 50 breast cancer survivors. Survivors performed a total of 88 tasks including ROM, ADL and work tasks. Forty four unique tasks were performed twice each. Eighty tasks were performed unilaterally and 8 were performed bilaterally. Electromyography and kinematic data was recorded and muscle-specific force exertions were used to assess strength. The association between

physical capability (in terms of total muscle effort) and subjective QoL and disability scores were evaluated statistically. An outline of methods is described in Figure 17.

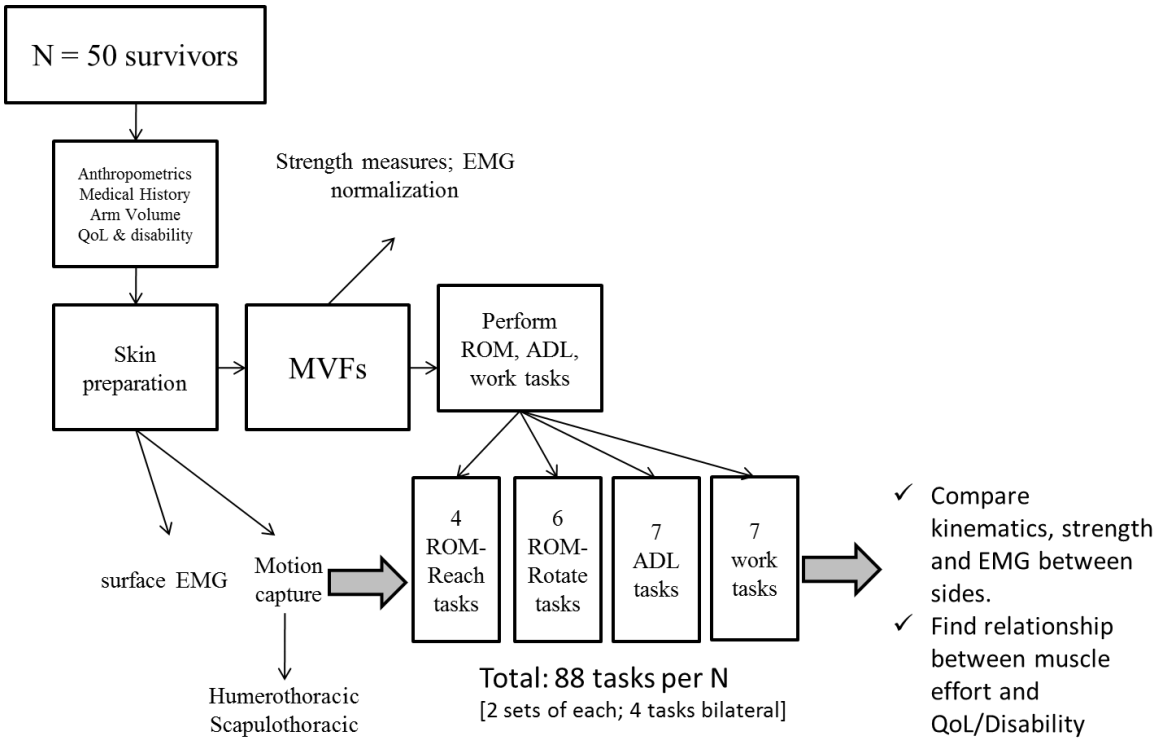


Figure 17 Flow chart depicting methods of Study 1. Brief medical and demographic information was obtained from the BCP and skin was prepared for EMG and motion capture. Maximal voluntary force exertions were performed to obtain strength measures and allow for normalization. Participants performed a total of 88 tasks. Outputs included kinematics, strength and muscle activation information, as well as scores of QoL and disability.

Section 4.2.1 Participants

Participants included 50 female breast cancer survivors who were previously diagnosed with stages I, II or III unilateral breast cancer and who had completed cancer therapies including surgery, radiation and/or chemotherapy at least 3 months prior to participation. Participants had a mean age of 59.4 yr [+/- 9.7 yr; range 31-83 yr], mean height of 1.7 m [+/- 0.1 m; range 1.5-1.8 m], mean weight of 71.7 kg [+/- 11.8 kg, range 51.4-97.7 kg] and were predominately right-hand dominant (n = 47). Cancer was on the left breast for 27 participants. Twenty seven participants had mastectomies (16 prophylactic bilateral); 34 had lumpectomies and 48 had axial node dissection surgeries. Thirty four

participants had received hormone replacement therapy, 34 had received chemotherapy and 37 had received radiation treatments. Average time since diagnosis was 74.9 months (+/-59.6 months; range 12-228 months]. Participants were able to communicate freely in English and had sufficient cognitive ability to participate and give informed consent. Participants were excluded if they had any of the following health disorders: blood clotting disorders, HIV, Hepatitis B or C, allergies to isopropyl alcohol, latex or nickel. Participants were recruited from the Kitchener-Waterloo area. This study received ethics clearance through the Office of Research Ethics at the University of Waterloo. Participants received a gift basket valued at $30 in appreciation for their time and efforts, as well as a summary of their ROM and strength results compared to normative data.

Due to limited study and discrepancy in the literature regarding the definition of impaired ROM, it was difficult to perform a power analysis *a priori* since an appropriate effect size (discrepancy between the null hypothesis (there is no difference in ROM = unaffected, 'normal' ROM) and alternative hypothesis (restricted ROM) was unclear. Two groups have defined impaired shoulder ROM as a loss of 20° compared to the unaffected limb (Box et al., 2002, Rietman et al, 2004), therefore it was assumed that the expected response of the unaffected arm ($\pi 1$) is 1.0 (no loss in ROM) and the expected response of the affected arm ($\pi 2$) is 0.8 (20% loss of ROM). The α level (probability of a Type I error – claiming there was a difference in ROM when in fact there was not) was set conservatively to 0.05. The β level (probability of a Type II error – claiming there was no difference when in fact there was) was set to 0.2, meaning the power (1-β) was 0.8. With the $f_{(\alpha,\beta)} = 7.9$, the sample size was estimated using Equation 5.

Equation 5 Sample size equation

$$N = \frac{\pi 1(1-\pi 1) + \pi 2(1-\pi 2)}{(\pi 1 - \pi 2)^2} \cdot f_{(\alpha,\beta)} = 31.6\, participants$$

Due to the anticipated heterogeneity likely to be recruited amongst the breast cancer survivor participants (differing cancer treatments, time since diagnostic etc.), the recommended sample of 31.6 participants was increased to 50 participants.

Section 4.2.2 Surface electromyography

In preparation for the surface electrodes, the skin overlying the muscle of interest was shaved of hair and cleansed with isopropyl alcohol. Disposable bipolar Ag/AgCl surface electrodes (Product #272, Noraxon, USA, Inc., Arizona, USA) were placed on both sides of the body over the pectoralis major (clavicular and sternal insertions), posterior deltoid, latissimus dorsi, supraspinatus, infraspinatus, serratus anterior and upper trapezius. The electrode placements are described in Appendix E. A reference electrode was placed over the sternum, just inferior to the suprasternal notch. A wireless Noraxon TeleMyo 4200T G2 (Noraxon 2 USA Inc., Arizona, USA) sampled EMG channels at 3000 Hz. This system had a 16-bit resolution on all analog inputs with a band-pass filter from 10-1500 Hz, an input impedance > 100 MΩ, a common mode rejection ratio > 100 dB and a base gain of 500.

Section 4.2.3 Motion capture

Three-dimensional kinematics were recorded using an 8-camera (2 MP) optoelectronic Vicon MX20+ motion tracking system (sampling rate 50 Hz) (Vicon, Oxford, UK). Light emitting diode cameras surrounded the collection area in which the participants moved. Prior to participant arrival, the space was calibrated using Vicon Nexus 1.2 software (Vicon, Oxford, UK) and the origin of the collection space was set on the floor, to the rear and right side of the participants chair (the participants were seated facing the positive global X-axis, with the positive global Z-axis pointing to the participants right and positive global Y pointing up). Twenty eight individual reflective markers (diameter = 9.0 mm) including 2 sets of marker clusters (3 markers each) affixed to rigid-plates were placed over anatomical landmarks and segments on both sides of the body as described in Table 10. Using an acromial marker cluster is a valid method of measuring scapular movement during arm elevation less than 90° and has been used to quantify scapular orientation in healthy individuals

(Picco, Fischer, & Dickerson, 2010; van Andel, van Hutten, Eversdijk, Veeger, & Harlaar, 2009). The acromial marker cluster was placed over the flat part of the posterior-lateral acromion, just medial to the origin of the deltoid when the shoulder was abducted 90° as per previous literature (Karduna, McClure, Michener, & Sennett, 2001; Ludewig & Cook, 2000; van Andel, van Hutten, Eversdijk, Veeger, & Harlaar, 2009). The cameras recorded the 3-D global positions of the markers. With the participant standing in the anatomical position, a static calibration frame was taken before experimental testing and was used to establish the relationship between rigid clusters and calibration markers over anatomical landmarks on a template formed using Vicon Nexus 1.2 software (Vicon, Oxford, UK). Six additional static calibration frames were taken with the stylus tip (diameter = 2.0 mm) palpating each of the three scapula anatomical landmarks (acromial angle, trigonum spinae and inferior angle) on both left and right sides. This data was used to calculate joint centers and segment coordinate systems, as described later in Section 4.3.2.

Table 10 Description of reflective markers used during motion capture: their anatomical location and associated body segment.

<table>
<tr><th>Number of Markers</th><th>Marker Name</th><th colspan="2">Location</th><th colspan="2">Associated Segment</th></tr>
<tr><td>1, 2</td><td>(L/R)ME</td><td colspan="2">Medial epicondyle</td><td rowspan="4">Upper Arm</td><td></td></tr>
<tr><td>3, 4</td><td>(L/R)LE</td><td colspan="2">Lateral epicondyle</td><td rowspan="11">Scapula</td></tr>
<tr><td>5, 6</td><td>(L/R)Acr</td><td colspan="2">Acromion (midpoint, centred over GHJ)</td></tr>
<tr><td>Stylus (calibration) 7, 8</td><td>(L/R)AA</td><td colspan="2">Acromial angle (most latero-dorsal point of scapula)</td></tr>
<tr><td>Stylus (calibration) 9, 10</td><td>(L/R)TS</td><td colspan="2">Trigonum Spinae Scapulae (Root of scapular spine; medial border in line with scapular spine)</td><td rowspan="6"></td></tr>
<tr><td>Stylus (calibration) 11, 12</td><td>(L/R)IA</td><td colspan="2">Inferior angle of scapula</td></tr>
<tr><td>13, 14</td><td>(L/R)SC1</td><td>Scapula Cluster I</td><td rowspan="3">Scapula cluster: rigid plate placed over posterior-lateral acromion</td></tr>
<tr><td>15, 16</td><td>(L/R)SC2</td><td>Scapula Cluster II</td></tr>
<tr><td>17, 18</td><td>(L/R)SC3</td><td>Scapula Cluster III</td></tr>
<tr><td>19</td><td>C7</td><td colspan="2">Spinous process of 7th cervical vertebra*</td><td colspan="2" rowspan="4">Thorax</td></tr>
<tr><td>20</td><td>SS</td><td colspan="2">Suprasternal notch*</td></tr>
<tr><td>21</td><td>XP</td><td colspan="2">Xyphoid process*</td></tr>
<tr><td>22</td><td>T8</td><td colspan="2">Spinous process of the 8th thoracic vertebra*</td></tr>
<tr><td>23, 24</td><td>(L/R)UAC1</td><td>Upper Arm cluster I</td><td rowspan="3">Upper arm cluster: rigid plate placed midway on upper arm</td><td colspan="2" rowspan="3"></td></tr>
<tr><td>25, 26</td><td>(L/R)UAC2</td><td>Upper Arm cluster II</td></tr>
<tr><td>27, 28</td><td>(L/R)UAC3</td><td>Upper Arm cluster III</td></tr>
<tr><td colspan="6">Markers placed bilaterally except in the instances as indicated by *.
The glenohumeral joint centre (GH) was estimated to be 4 cm inferior to the midpoint of the acromion and acromial angle, along the long axis of the torso (Nussbaum & Zhang, 2000).</td></tr>
</table>

Section 4.2.4 Pre-experimental protocol

Prior to testing, anthropometric measurements (stature, body weight, upper arm length (tip of acromion to lateral epicondyle) and lower arm length (lateral epicondyle to ulnar styloid)) were recorded and the participants completed a brief demographic and medical questionnaire (Appendix

B), a Disability of Arm, Shoulder and Hand (QuickDASH) questionnaire (Appendix D) and an assessment of QoL using the FACT-B scale (Appendix C). Arm volume of each arm was measured using the water displacement method. The volumeter used was built following the protocol designed by Lette (2006), and is highly accurate ($R^2 = 0.9999$ when compared with known volumes). Participants slowly inserted their bare arm into the volumeter until the upper arm was immersed 20 cm above the lateral epicondyle. The displaced water was weighed on a digital balance, assuming 1kg is equivalent to 1 L (at 4°C pure water has a density of approximately 1Kg/L). Lymphedema was defined as a volume difference of ≥ 200 mL difference between arms. Bilateral hand grip strength was assessed using a hand dynamometer (JAMAR, USA).

Two sets of each maximal voluntary force exertion (MVF) described in Table 11 were performed on both sides against a digital hand-held dynamometer (ergoFET300™, Utah, USA). MVFs were 3 s in duration, with at least two minutes of rest given between tests. The MVFs were used to obtain a measure of maximal force obtained during functionally-specific muscle tests and were also used for normalization of EMG. Ratings of perceived discomfort (RPD) were reported for each MVF, where a rating of zero indicated no discomfort and a rating of 100% indicated the "worst discomfort imaginable". Data was transferred from the receiver to a personal computer, and analysed using Matlab™ R2010a (Mathworks Inc., USA).

Table 11 Study 1 Maximal voluntary force exertion protocol

Muscle (tested on both arms)	**Test Contraction**
Supraspinatus	Subject is seated. Shoulder is abducted to 5° with elbow extended (thumb pointing up). Abduction is resisted.
Infraspinatus	Subject is seated. Arm is at side with elbow bent to 90°. External rotation of the arm is resisted.
Subscapularis	Subject is seated. Arm is at side with elbow bent to 90°. Internal rotation of the arm is resisted.
Latissimus Dorsi	Subject is seated with shoulder horizontally abducted and externally rotated to 90° and elbow flexed to 90° (fingers point to ceiling). Shoulder adduction is resisted.
Pectoralis Major (sternal and clavicular insertions)	Subject is seated with shoulder horizontally abducted and externally rotated to 90° and elbow flexed to 90° (fingers point to ceiling). Shoulder horizontal adduction is resisted.
Posterior Deltoid	Subject is seated. Resistance is provided to shoulder extension when shoulder is abducted to 90° and externally rotated, with elbow flexed to 90° (fingers point to ceiling).
Serratus Anterior	Subject is seated. Subject protracts scapula with arm at 90° flexion. Resistance is provided at the hand.
Upper Trapezius	Subject is prone with head turned to right side. Participant resists shoulder abduction at 90º with elbow extended, thumb down to floor.

Section 4.2.5 Experimental protocol

EMG and 3-D kinematics were recorded as participants performed 88 tasks (2 sets of 20 unilateral tasks and 2 sets of 4 bilateral tasks) These tasks included 10 tasks of shoulder ROM (as a measure of full ROM capacity), 7 ADL tasks (involving personal body care activities) and 7 work tasks (reaching tasks with and without loads). These tasks were similar to those described previously within healthy and elderly populations (Hall, Middlebrook, & Dickerson, 2011; Magermans, Chadwick, Veeger, & van der Helm, 2005; Murray & Johnson, 2004)). These tasks are described in Table 12, Table 13 and Table 14. Participants were given 6 seconds to complete the tasks and were asked to perform each task as naturally as possible.

Table 12 Range of Motion tasks performed by survivors during experimental protocol

Test #	ROM tasks (performed separately with each arm)	Description
1	Humeral flexion	Participants are instructed to elevate their arm anteriorly in the sagittal plane (elbow extended) to full range. Start/End position was arm at side.
2	Humeral extension	Participants are instructed to elevate their arm posteriorly in the sagittal plane (elbow extended) to full range. Start/End position was arm at side.
3	Humeral abduction	Participants are instructed to elevate their arm in the frontal plane (elbow extended) to full range. Start/End position was arm at side.
4	Humeral ER at 45° elevation	With the elbow flexed to 90° and arm abducted to 45°, participants are instructed to externally rotate their humerus to full range.
5	Humeral IR at 45° elevation	With the elbow flexed to 90° and arm abducted to 45°, participants are instructed to internally rotate their humerus to full range.
6	Scaption	Participants are instructed to elevate their arm (elbow extended) in the scapular plane (30° anterior to the frontal plane) to full range. Start/End position was arm at side.
7	Neutral Scapular Orientation*	Participants are instructed to identify the most comfortable neutral scapular posture while actively protracting and retracting the scapula. (Smith, Kotajarvi, Padgett, & Eischen, 2002) Start/End position was with hands resting on table in front of them.
8	Scapular Protraction*	Participants are instructed to protract the scapula (move the scapula in an anterior-lateral direction, moving the scapular border away from the vertebral column). (Solem-Bertoft & Wresterberg, 1993) Start/End position was with hands resting on table in front of them.
9	Scapular Retraction*	Participants are instructed to retract the scapula (move the scapula in a posterior-medial direction, moving the scapular border towards the vertebral column). (Solem-Bertoft & Wresterberg, 1993) Start/End position was with hands resting on table in front of them.
10	Winging Scapula Test	Flex humerus to 30° against inferiorly-directed resistance.
*bilateral task. For later analysis, ROM tasks were further subdivided into 2 groups: "ROM – Reach Tasks" included [unshaded] Tests 1, 2, 3 and 6; and "ROM – Rotation Tasks" included [shaded] Tests 4, 5, 7, 8, 9 and 10.		

Table 13 Activities of daily living tasks performed by survivors during experimental protocol

Test #	**ADL tasks** (performed separately with each arm)	**Description** (all tasks are performed seated and begin and end with hand on the table)
11	Comb hair	Participant combs the right, center and left side of the head once.
12	Anterior reach to contralateral scapula	Participant reaches across chest and over opposite shoulder to wash contralateral scapula.
13	Posterior reach to contralateral scapula	Participant reaches behind back and up to contralateral scapula.
14	Wash opposite axilla	Participant reaches across chest to wash contralateral axilla.
15	Eat with spoon	Participant brings a spoon to the mouth.
16	Perineal care	Participant reaches behind back and places hand on sacrum.
17	Posterior bra unfasten	Participant is instructed to simulate unfastening a bra at the spine height of the inferior angle of the scapula.
All tasks were performed with participant seated in 43 cm high backless chair behind a 66 cm high table. Participants started and ended task with hand placed on table.		

Table 14 Work tasks performed by survivors during experimental protocol

Test #	**Work tasks** (performed separately with each arm)	**Description**
18	Seated reach above shoulder (no load)	Participant reaches towards a target which is 1.5 m vertical from the ground and centered in front of the participant's body. [Task simulates reaching up to a shelf.]
19	Seated reach above shoulder (1 kg load)	Same as Test#18 with 1 kg load.
20	Seated reach above shoulder – scaled to torso-reach height with (no load)	Prior to collection, the researcher measures the 'torso-reach' distance, defined as the distance from participant's greater trochanter of the hip to the tip of the fingers when the arm is raised vertically. A target is placed in front (centre) of the participant at a height of 80% of torso-reach distance plus the height of the chair. The participant reaches towards the target. [Task simulates reaching up to a shelf.]
21	Seated reach above shoulder – scaled to torso-reach height (1 kg load)	Same as Test#20 with 1 kg load.
22	Seated side reach at shoulder height (no load)	Participant reaches out to side (in frontal plane) at shoulder height with extended arm.
23	Seated side reach at shoulder height (1 kg load)	Same as Test#22 with 1 kg load.
24	Standing 2-handed lift (4 kg load)*	Participant (standing) reaches for 4 kg load placed on floor in front of them. Participant lifts load and places it on table in front of them. [Simulates lifting a load equivalent to a 4 L milk bag.]
All tasks (except Test 24 Standing 2-handed lift) were performed with participant seated in 43 cm high backless chair behind a 66 cm high table. Participants started and ended task with hand placed on table. *bilateral task		

Section 4.3 Analysis

EMG and upper limb kinematic data were processed using custom-built scripts written in MATLAB™ R2010a (Mathworks, USA). Statistical analysis was performed in JMP 11® (SAS Institute Inc., Cary, NC).

Section 4.3.1 EMG data processing

Raw EMG was high pass filtered (Fc 30Hz as recommended by Drake & Callaghan (2006)) to remove potential heart rate or motion artifact, and then linear enveloped with a single-pass Butterworth LPF (Fc = 2.5 Hz as determined by residual analysis on a random sample of more than 20 exertions and participants for all channels). A 500 ms moving window average of linear enveloped MVC trials was calculated and the highest moving window average from the two sets (for each specific muscle and individual) was defined as maximal percent activation from which respective channels were normalized to. Integrated EMG (area under each 6 s test curve) was calculated for all channels and tests. Total muscle effort was defined as the summation of integrated EMG on affected and unaffected sides [Equation 6 and Equation 7]. The sum of all mean muscle activities has been used previously as an estimate of total shoulder effort in healthy individuals (Chopp, Fischer, & Dickerson, 2010).

Equation 6 Total muscle effort on affected side. Where i = 1-8 are eight muscles on the affected side recorded with surface EMG. Integrated normalized EMG of these muscles was summed.

$$TME_{aff} = \sum_{i=1}^{8} integrated\ EMG$$

Equation 7 Total muscle effort on unaffected side. Where i = 9-16 are the eight muscles on the unaffected side recorded with surface EMG. Integrated normalized EMG of these muscles was summed.

$$TME_{unaff} = \sum_{i=9}^{16} integrated\ EMG$$

Section 4.3.2 Kinematic data processing

Raw kinematic data was initially processed using the Vicon Nexus 1.2 software (Vicon, Oxford, UK), which was used to confirm proper marker labelling and pattern-fill any gaps (missing marker data) by reconstructing the marker trajectory using locations of other markers on defined segments. Further data reduction of kinematic data was performed in a custom-built software program developed using MATLAB R2010a (Mathworks, USA). Kinematic data was dual-pass filtered with a Butterworth low pass filter (LPF) with a cut-off frequency (Fc) of 4 Hz.

Using the global positions of the reflective markers, local coordinate systems were defined for each segment according to the International Society of Biomechanics recommendations (Johnson, Bogduk, Nowitzke, & House, 1994) during static calibration as described for the right side in Table 15 (Wu, et al., 2005). For development of local coordinate systems on the left side, the same anatomical landmarks were used as expressed in Table 15; however directions were reversed when required to maintain the Z axis pointing to the right, the Y axis pointing superiorly and the X axis pointing anteriorly. Three non-collinear anatomical landmarks were required on each segment to construct a local coordinate system. The global coordinates of the left and right scapula landmarks (AA, IA, TS) were identified using the position of the digitizing stylus tip in each of the six calibration tests (one calibration per digitized landmark) as demonstrated in Equation 8:

Equation 8 Determining scapular landmarks. Where $T_{X,GLOBAL}$, $T_{Y,GLOBAL}$, and $T_{Z,GLOBAL}$ is the position vector of the stylus tip (and therefore scapular landmark) in the global system; $O_{SX,GLOBAL}$, $O_{SY,GLOBAL}$, and $O_{SZ,GLOBAL}$ is the position vector of the origin of the LCS of the digitizing stylus during the landmark calibration in the global system; [R] is the stylus LCS to global rotational matrix; $T_{X,stylus}$, $T_{Y,stylus}$, and $T_{Z,stylus}$ are the position coordinates of the vector between the stylus tip and the origin of the stylus LCS in the global.

$$\begin{bmatrix} T_{X,GLOBAL} \\ T_{Y,GLOBAL} \\ T_{Z,GLOBAL} \end{bmatrix} = \begin{bmatrix} O_{SX,GLOBAL} \\ O_{SY,GLOBAL} \\ O_{SZ,GLOBAL} \end{bmatrix} + [R]^{stylus}_{GLOBAL} \cdot \begin{bmatrix} T_{X,stylus} \\ T_{Y,stylus} \\ T_{Z,stylus} \end{bmatrix}$$

Static calibration tests were used to determine the position of the scapular landmarks relative to the acromial cluster, and the humeral landmarks relative to the humeral cluster, as demonstrated in Equation 9.

Equation 9 Relationship between cluster and anatomical landmark. Where $V_{X,cluster}$, $V_{Y,cluster}$, and $V_{Z,cluster}$ are the coordinates of the vector between the (acromial or humeral) cluster and a respective (scapular or humeral) landmark (AA, IA, and TS for the scapula, or ME and LE for the humerus); [R] is the global to cluster rotational matrix; $V_{X,GLOBAL}$, $V_{Y,GLOBAL}$, and $V_{Z,GLOBAL}$ are the global coordinates of the position vector of the (scapula or humeral) landmark; $O_{X,GLOBAL}$, $O_{Y,GLOBAL}$, and $O_{Z.GLOBAL}$ are the global coordinates of the position vector of the origin of the cluster.

$$\begin{bmatrix} V_{X,\,cluster} \\ V_{Y,\,cluster} \\ V_{Z,cluster} \end{bmatrix} = [R]_{cluster}^{GLOBAL} \cdot \begin{bmatrix} V_{X,GLOBAL} & O_{X,GLOBAL} \\ V_{Y,GLOBAL} - O_{Y,GLOBAL} \\ V_{Z,GLOBAL} & O_{Z,GLOBAL} \end{bmatrix}$$

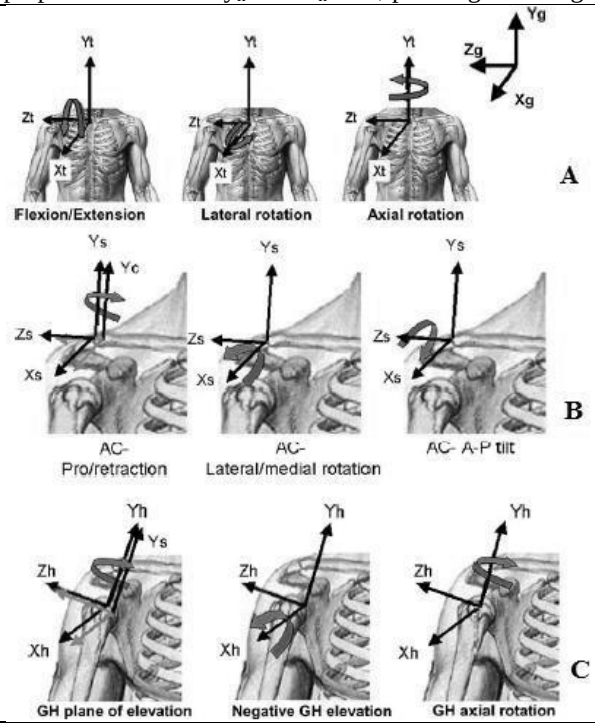
These relationships were used to generate virtual scapular and humeral landmarks during dynamic tests, as described in Equation 10.

Equation 10 Calculating virtual markers. Where $VV_{X,GLOBAL}$, $VV_{Y,GLOBAL}$, and $VV_{Z,GLOBAL}$ is the position vector of the virtual landmarks in the global system; $O_{X,GLOBAL}$, $O_{Y,GLOBAL}$, and $O_{Z,GLOBAL}$ are the global coordinates of the position vector of the origin of the cluster; [R] is the cluster to global rotational matrix; $V_{X,cluster}$, $V_{Y,cluster}$, and $V_{Z,cluster}$ are the coordinates of the vector between the (acromial or humeral) cluster and a respective (scapular or humeral) landmark (AA, IA, and TS for the scapula, or ME and LE for the humerus).

$$\begin{bmatrix} VV_{X,GLOBAL} \\ VV_{Y,\,GLOBAL} \\ VV_{Z,GLOBAL} \end{bmatrix} = \begin{bmatrix} O_{X,GLOBAL} \\ O_{Y,GLOBAL} \\ O_{Z,GLOBAL} \end{bmatrix} + [R]_{GLOBAL}^{cluster} \cdot \begin{bmatrix} V_{X,\,cluster} \\ V_{Y,\,cluster} \\ V_{Z,cluster} \end{bmatrix}$$

Using virtual markers, local coordinate systems for the humerus, thorax and scapula were defined during dynamic tests (with the same procedures as done during static calibration). The relative rotation matrices were found by multiplying the distal segment (scapula or humerus) by the transpose of the proximal segment (thorax).

Table 15 Right side segment local coordinate systems as recommended by ISB and described by Wu et al., (2005). X,Y and Z axis descriptions are provided for each segment. Figures A, B and C represent the thorax, scapula and humerus local coordinate systems, respectively. Refer to Table 10 for definitions of short-form terminology.

Description of Local Coordinate System
Thorax - $x_t y_t z_t$ Origin: The origin coincident with SS. y_t: The line connecting the mid-point between XP and T8 and the mid-point between SS and C7, pointing upward. z_t: The line perpendicular to the plane formed by SS, C7, and midpoint between SS, C7 and the midpoint between XP and T8 pointing upward. x_t: The common line perpendicular to z_t- and y_t-axis, pointing forwards
Scapula - $x_s y_s z_s$ Origin: The origin coincident with AA. z_s: The line connecting TS and AA, pointing to AA. x_s: The line perpendicular to the plane formed by IA, AA, and TS, pointing forward. y_s: The common line perpendicular to the x_s- and z_s-axis pointing upward.
Humerus – $x_h y_h z_h$ Origin: The origin coincident with GH. y_h: line connecting GH and the midpoint of the EL and EM, pointing to GH x_h: line perpendicular to the plane formed by EL, EM, and GH, pointing forward z_h: common line perpendicular to the y_h- and z_h-axis, pointing to the right


The scapular and humeral local coordinate systems were described with respect to the thorax local coordinate system as demonstrated by Figures B and C in Table 15. Scapulothoracic and humerothoracic joint descriptions were based on the Euler YXZ and YXY' rotation sequences, respectively, as recommended by the International Society of Biomechanics (Wu, et al., 2005) and

described in Table 16. Euler decomposition and rotational transformation matrices are depicted in Appendix G.

Table 16 Description of segment rotations using Euler angles according to recommendations by the International Society of Biomechanics (Wu, et al., 2005). Scapulothoracic rotations were described using the YXZ Euler sequence, and humerothoracic rotations were described using the YXY' Euler sequence.

Segment	Rotation Sequence
Motion of the scapula relative to the thorax (scapulothoracic rotations) **Y-X-Z**	e1: axis fixed to the thorax and coincident with the Y_t-axis of the thorax coordinate system. *Rotation (γ_{ST}):* retraction (negative) or protraction (positive) e3: axis fixed to the scapula and coincident with the Z_s-axis of the scapular coordinate system. *Rotation (α_{ST}):* anterior (negative) or posterior (positive) tilt. e2: common axis perpendicular to e1 and e3. *Rotation (β_{ST})*: lateral (negative) or medial (positive) rotation.
Motion of the humerus relative to the thorax (humerothoracic rotations) **Y-X-Y'**	e1: axis fixed to the thorax and coincident with the Y_t-axis of the thorax coordinate system. *Rotation (γ_H):* GH plane of elevation (0^o is abduction, 90^o is forward flexion) e3: axial rotation around the Y_h-axis. *Rotation (γ_H)$_2$:* GH-axial rotation, internal (positive) or external (negative) rotation e2: axis fixed to the humerus and coincident with the X_h-axis of the humerus coordinate system. *Rotation (β_{GH})*: elevation (negative)

The orientation of the scapula with respect to the thorax was quantified by extracting the Euler angles from Equation 11 where x_s, y_s and z_s are the axes of the scapula local coordinate system and x_t, y_t and z_t are the axes of the thorax local coordinate system. The transformation matrix was derived using the Y-X-Z Euler sequence (described in Table 16 and Appendix G). The scapulothoracic rotations for both left and right sides were described as +upward/-downward rotation (β, about the X axis), +anterior/-posterior tilt (α, about the Z axis), and +retraction/-protraction (γ, about the Y axis). Scapular kinematics were reported as absolute values with respect to the local coordinate systems (the neutral "zero" position was defined as the alignment of the local coordinate systems of the scapula and the thorax).

Equation 11 Scapulothoracic transformation matrix

$$\begin{Bmatrix} x_s \\ y_s \\ z_s \end{Bmatrix} = \begin{bmatrix} (\cos\alpha\cos\gamma - \sin\gamma\sin\alpha\sin\beta) & -\cos\beta\sin\alpha & \sin\alpha\sin\beta\cos\gamma + \cos\alpha\sin\gamma \\ \cos\alpha\sin\beta\sin\gamma + \sin\alpha\cos\gamma & \cos\beta\cos\alpha & \sin\alpha\sin\gamma - \cos\alpha\sin\beta\cos\gamma \\ -\sin\gamma\cos\beta & \sin\beta & \cos\beta\cos\gamma \end{bmatrix} \begin{Bmatrix} x_t \\ y_t \\ z_t \end{Bmatrix}$$

The orientation of the humerus with respect to the thorax was quantified by extracting the Euler angles from Equation 12, where x_h, y_h and z_h are the axes of the humerus local coordinate system and x_t, y_t and z_t are the axes of the thorax local coordinate system. The transformation matrix was derived using the Y-X-Y' Euler sequence (described in Table 16 and Appendix G). The humerothoracic rotations were described as magnitude of elevation (β, about the X axis), plane of elevation (γ, about the Y axis), and humeral rotation (γ2, about the Y axis). For both left and right sides, elevation was positive, plane of elevation was described as -90° in forward flexion and 0° in abduction, and humeral ER was positive and IR was negative as shown in Figure 18. Humerothoracic kinematics were reported as absolute values with respect to the local coordinate systems (the neutral "zero" position was defined as the alignment of the local coordinate systems of the humerus and the thorax).

Equation 12 Humerothoracic transformation matrix

$$\begin{Bmatrix} x_h \\ y_h \\ z_h \end{Bmatrix} = \begin{bmatrix} (\cos\gamma\cos\gamma_2 - \sin\gamma\sin\gamma_2\cos\beta) & \sin\beta\sin\gamma_2 & \cos\gamma_2\sin\gamma + \cos\beta\cos\gamma\sin\gamma_2 \\ \sin\beta\sin\gamma & \cos\beta & -\cos\gamma\ \sin\beta \\ -\cos\gamma\sin\gamma_2 - \cos\beta\cos\gamma_2\sin\gamma & \cos\gamma_2\sin\beta & \cos\beta\cos\gamma\cos\gamma_2 - \sin\gamma_2\ \sin\gamma \end{bmatrix} \begin{Bmatrix} x_t \\ y_t \\ z_t \end{Bmatrix}$$

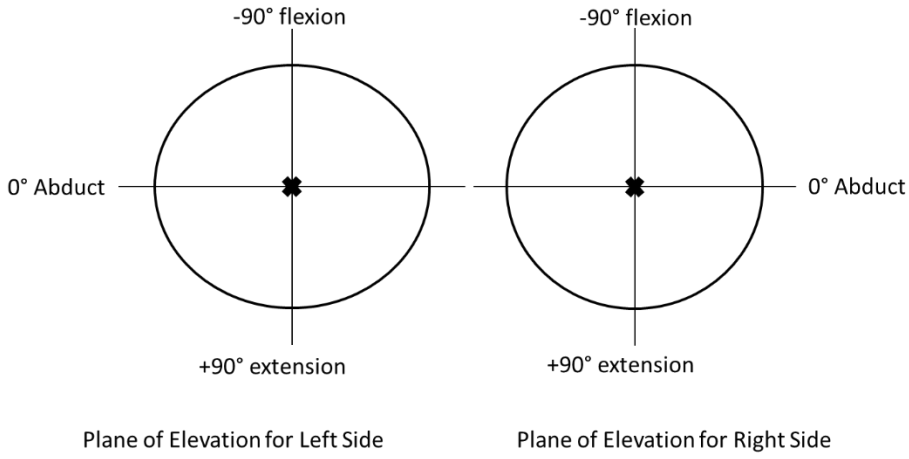


Figure 18 Humerothoracic plane of elevation (rotation about gamma) for left and right sides. Abduction represents a plane of elevation of 0° and forward flexion is -90°.

Section 4.3.3 Statistical testing

The maximal and minimal angles achieved during each functional task were determined, and averaged for each of the 2 sets of repeated tasks. Range of motion (minimal subtracted from maximal angle) was reported, similar to Hall et al. (2011). To investigate differences in range of motion of humerothoracic (β, γ, γ2) and scapulothoracic (β, γ, α) angles between affected and unaffected sides, repeated measures ANOVA were performed with ROM, maximal and minimal humerothoracic and scapulothoracic angle components named the dependent variables, with task performance side (affected or unaffected) with subject as a random variable named the independent variables, and the within ('by') variable was listed as the task group (ROM-Reach, ROM-Rotation, ADL and work tasks).

For all tasks, a repeated measures ANOVA was used to determine the effects of task performance side (affected or unaffected side) on TME, within task type (ROM-Reach, ROM-Rotation, ADL or work task). The average TME was named the dependent variable, and the task performance side (affected or unaffected) and subject as a random variable were listed as the

independent variables. The within ('by') variable was listed as the task type (ROM-Reach, ROM-Rotation, ADL, work).

To determine what specific muscles had higher levels of activation during unilateral tasks, eight repeated measures ANOVA were performed to determine the effect of task performance side on integrated EMG within the task groups. The integrated EMG for the 8 muscles collected were named the dependent variables, the task performance side (affected or unaffected) with subject as a random variable were named the independent variables, and the within ('by') variable was listed as the task group (ROM-Reach, ROM-Rotation, ADL, work).

To identify differences in MVF values between affected and unaffected sides, seven repeated measures ANOVA were performed. The dependent variables were listed as the MVF for seven muscles (latissimus dorsi, pectoralis major, posterior deltoid, serratus anterior, infraspinatus, supraspinatus and upper trapezius) and the independent variables were listed as task performance side (affected or unaffected) and subject as a random variable.

To investigate differences in ratings of perceived discomfort (RPD) between sides, repeated measures ANOVA with RPD for each of the seven muscles were listed as the independent variables, with side (affected or unaffected) and subject as a random variable listed the dependent variables.

Total muscle effort per participant was calculated as the summation of affected side TME during all tasks. To determine if a quantitative measure of physical function (total muscle effort during all tasks) was related to quality of life or disability scores, linear and polynomial correlations were explored. Specifically, total muscle effort values were plotted against FACT-B and QuickDASH scores.

Post hoc analysis included Student's T tests that were used to identify significant differences between groups.

Section 4.4 Results

Section 4.4.1 Kinematic results

In general, unaffected scapulothoracic ROM was greatest in upward/downward rotation (24.7° [SD±19.0°]), followed by retraction/protraction (16.3° [SD±15.3°]) and then anterior/posterior tilt (14.3° [SD±15.0°]). In general, affected scapulothoracic ROM was greatest in upward/downward rotation (24.4° [SD±18.6°]), followed by retraction/protraction (15.9° [SD±17.8°]) and then anterior/posterior tilt (15.2° [SD±16.2°]). Analysis of scapulothoracic kinematics revealed there were some statistically significant differences in ROM between unaffected and affected sides within some groups of tasks (Figure 19):

- During ADL and work tasks, the affected side demonstrated more anterior/posterior tilt ROM compared to the unaffected side (16.2° vs. 14.4°, p = 0.0428; and 16.6° vs. 14.6°, p = 0.0307), respectively.

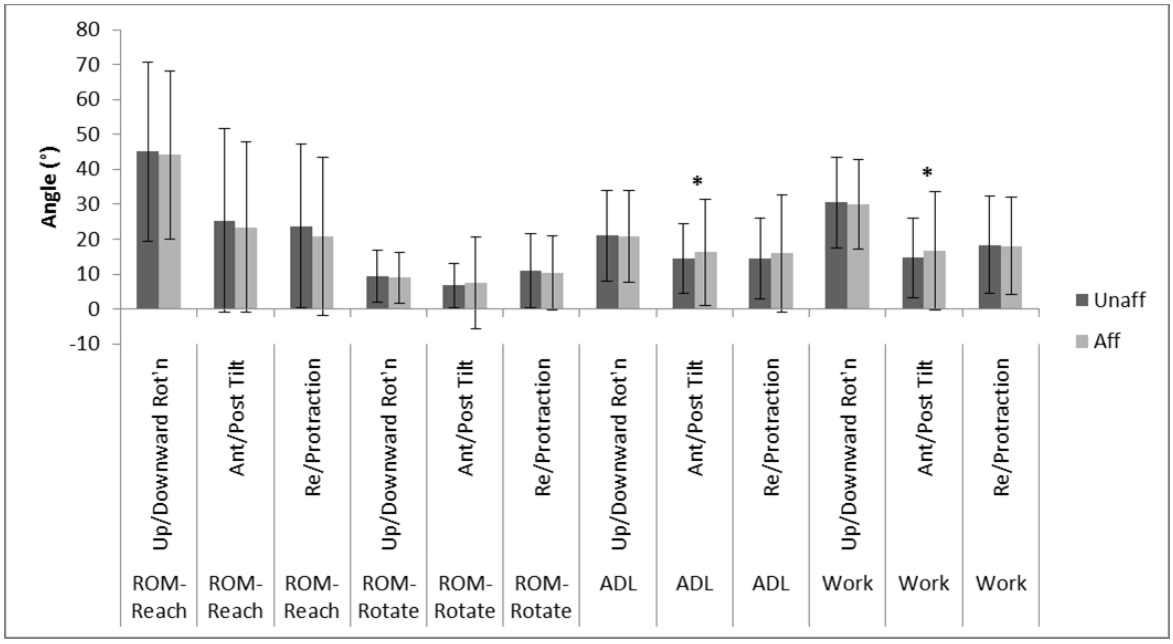


Figure 19 Comparison of scapulothoracic ROM (maximum minus minimum angle) between unaffected and affected sides during four types of tasks (ROM-Reach, ROM-Rotate, ADL and work tasks). LSM±SD. Significance (*) between sides is indicated.

On average, unaffected humerothoracic ROM was greatest in humeral rotation (42.4° [SD±40.4°]), followed by elevation (38.5° [SD±28.7°]) and then plane of elevation (32.5° [SD±27.1°]). On average, affected humerothoracic ROM was greatest in humeral rotation (47.1° [SD±45.8°]), followed by elevation (40.6° [SD±32.5°]) and then plane of elevation (28.7° [SD±26.5°]). Analysis of humerothoracic kinematics revealed there were some statistically significant differences in ROM between unaffected and affected sides within some groups of tasks (Figure 20):

- During ROM-Reach tasks, the affected side demonstrated reduced ROM in the plane of elevation (32.3° vs. 39.0°, $p = 0.0034$)
- During ROM-Rotate tasks, the affected side demonstrated reduced ROM in elevation angle and in the plane of elevation (9.7° vs. 12.0°, $p = 0.0121$; and 15.3° vs. 18.6°, $p = 0.0440$); but increased ROM in humeral rotation (33.6° vs. 26.5°, $p = 0.0036$) compared to the unaffected side.
- During work tasks, the affected side demonstrated more ROM in elevation compared to the unaffected side (56.5° vs. 51.2°, $p = 0.0037$).

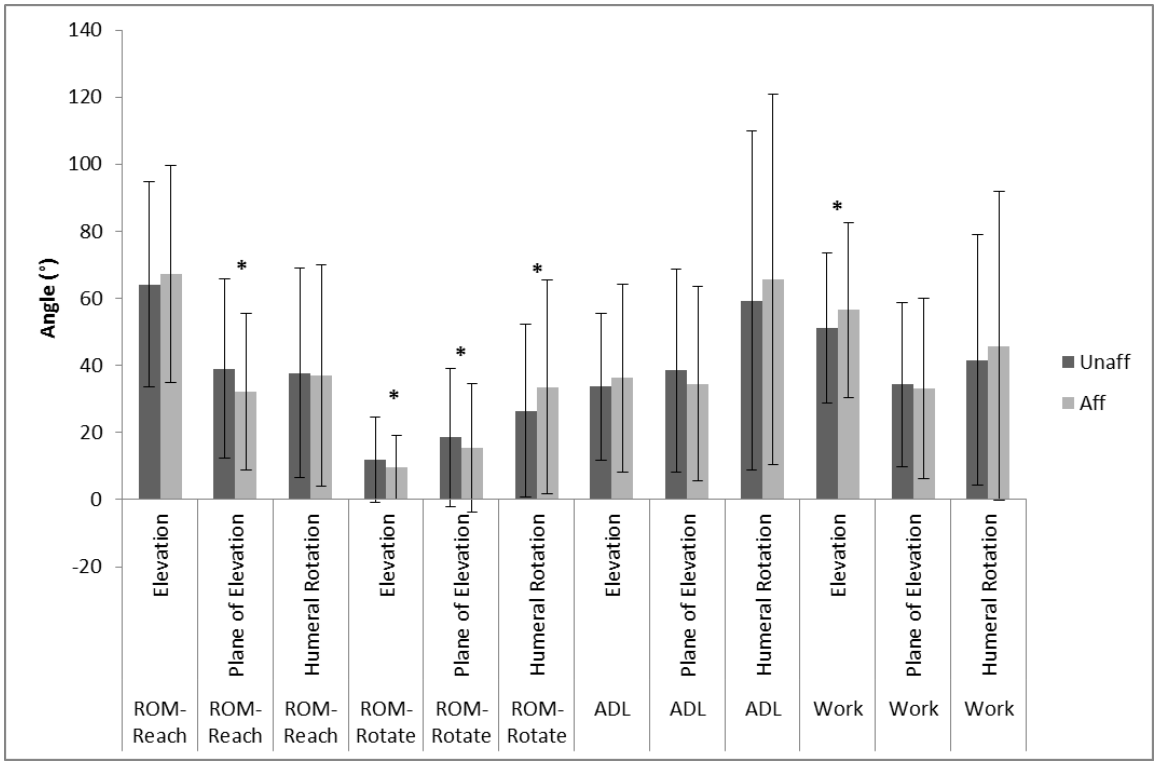


Figure 20 Comparison of humerothoracic ROM (maximum minus minimum angle) between unaffected and affected sides during four types of tasks (ROM-Reach, ROM-Rotate, ADL and work tasks). LSM±SD. Significance (*) between sides is indicated.

For all tasks, the unaffected scapulothoracic maximal angles demonstrated that on average the scapula was upwardly rotated at 18.0° [SD± 22.7°]), anteriorly tilted at 17.5° [SD±20.0°], and protracted at -28.6° [SD±20.9°]. For all tasks, the affected scapulothoracic maximal angles demonstrated that on average the scapula was upwardly rotated at 19.9° [SD± 22.4°]), anteriorly tilted at 16.6° [SD±23.3°], and protracted at -26.1° [SD±26.8°]. Analysis of scapulothoracic kinematics revealed there were some statistically significant differences in maximal angles between unaffected and affected sides within some groups of tasks (Figure 21):

- During ROM-Rotate tasks, the affected side demonstrated more upward rotation compared to the unaffected side (7.0° vs. 4.2°, p = 0.0050).

- During ADL and work tasks, the affected side demonstrated less protraction compared to the unaffected side (-28.4° vs. -31.8°, p = 0.0111; and -26.3° vs. -30.2°, p = 0.0136, respectively).

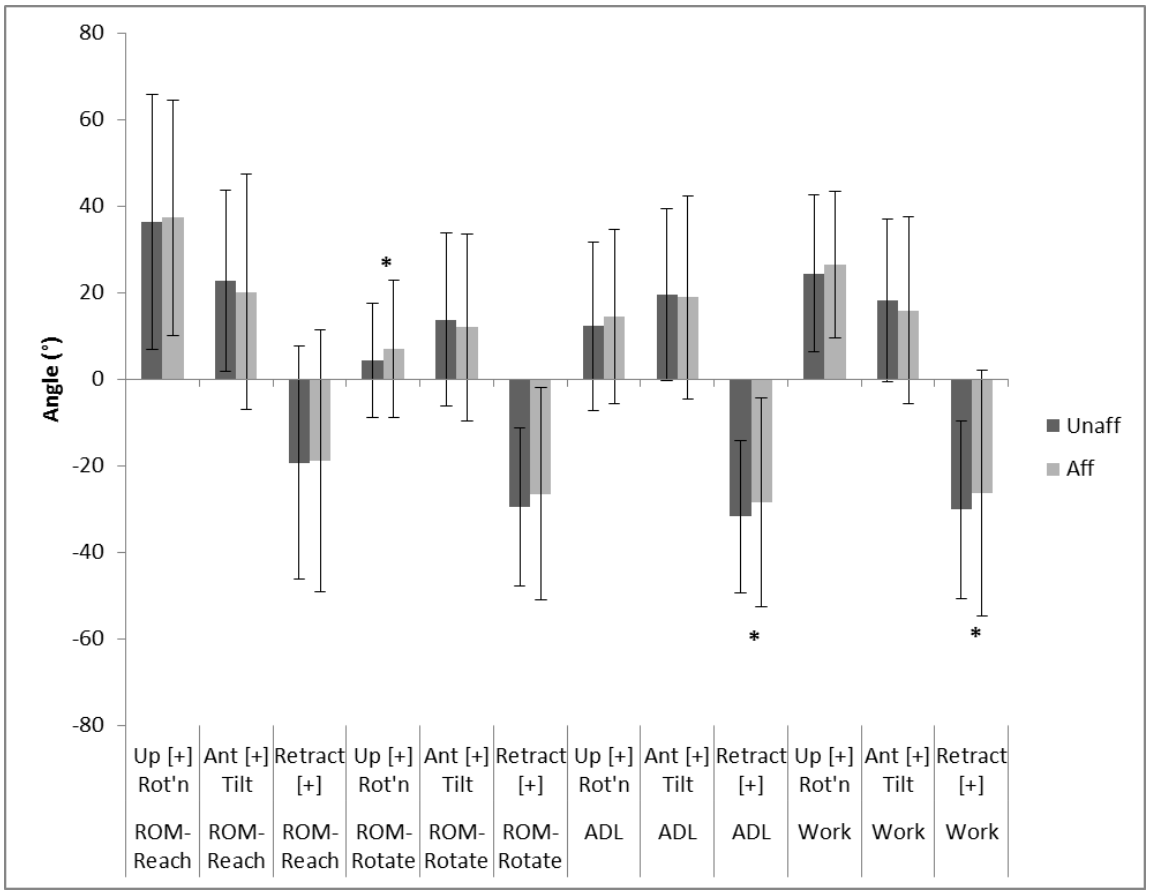


Figure 21 Comparison of scapulothoracic maximal angles between unaffected and affected sides during four types of tasks (ROM-Reach, ROM-Rotate, ADL and work tasks). Upward rotation, anterior tilt and retraction are shown as positive values. Downward rotation, posterior tilt and protraction are shown as negative values. LSM±SD. Significance (*) between sides is indicated.

The unaffected humerothoracic maximal angles demonstrated that on average the humerus was elevated to 76.8° [SD± 27.5°]), externally rotated to 4.4° [SD±37.6°], and in a plane of elevation of -9.7° [SD±34.5°] during all tasks. The affected humerothoracic maximal angles demonstrated that on average the humerus was elevated to 75.3° [SD± 31.7°]), externally rotated to 0.7° [SD±42.3°], and in a plane of elevation of -13.2° [SD±34.8°] during all tasks. Analysis of humerothoracic kinematics

revealed there were some statistically significant differences in maximal angles between unaffected and affected sides within some groups of tasks (Figure 22):

- During ROM-Rotate tasks, the affected side demonstrated a reduced angle of elevation compared to the unaffected side (48.4° vs. 54.9°, $p < 0.0001$). The affected side humerus was kept in a plane of elevation that was more anterior to abduction, compared to the unaffected humerus which was kept closer to the abduction plane (-21.1° vs. -17.2°, $p = 0.0449$).
- During work tasks, the affected side demonstrated a more neutral humeral rotation compared to the more externally rotated unaffected side (0.4° vs. 9.3°, $p = 0.008$).

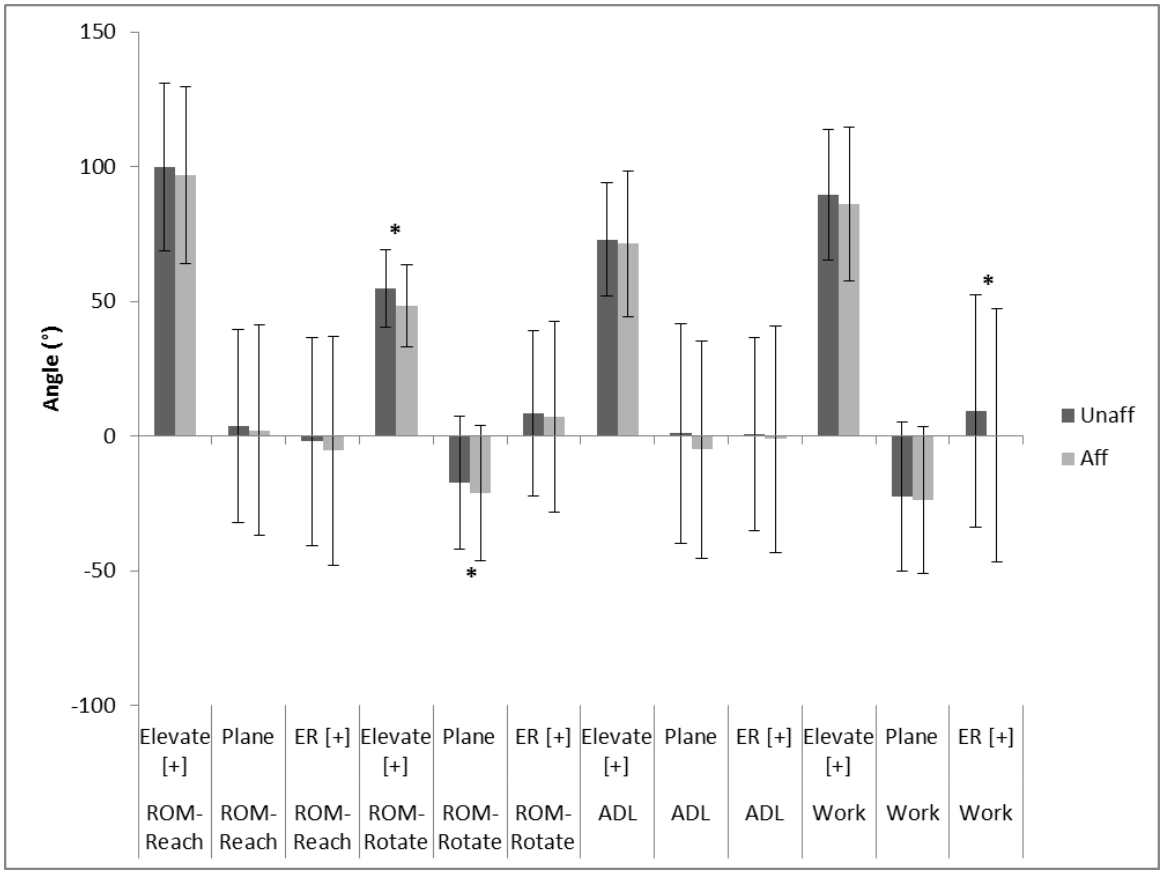


Figure 22 Comparison of humerothoracic maximal angles between unaffected and affected sides during four types of tasks (ROM-Reach, ROM-Rotate, ADL and work tasks). Elevation and external rotation are shown as positive values. Internal rotation is shown as negative values. Plane of elevation is 0° at abduction and -90° in flexion. LSM±SD. Significance (*) between sides is indicated.

Average minimum angles during all tasks indicated the unaffected scapula was downwardly rotated at -7.1° [SD± 13.0°]), anteriorly tilted at 3.0° [SD±20.1°], and protracted at -45.2° [SD±17.9°]; similar to the affected side scapula which was downwardly rotated at -4.5° [SD± 14.7°]), anteriorly tilted at 1.4° [SD±24.5°], and protracted at -42.0° [SD±22.2°]. Analysis of scapulothoracic kinematics revealed there were some statistically significant differences in minimal angles between unaffected and affected sides within some groups of tasks (Figure 23):

- During ROM-Reach and ROM-Rotate tasks, the affected side scapula demonstrated less downward rotation compared to the unaffected side (-6.7° vs. -10.1°, $p = 0.0003$; and -1.9° vs. -5.4°, $p < 0.0001$, respectively).
- During ROM-Rotate tasks, the affected side scapula demonstrated less protraction compared to the unaffected side (-37.1° vs. -40.7°, $p = 0.0066$).
- During ADL tasks, the affected side scapula demonstrated less downward rotation compared to the unaffected side (-6.3° vs. -9.2°, $p = 0.0010$).
- During Work tasks, the affected side scapula demonstrated less downward rotation, more posterior tilting and less protraction compared to the unaffected side (-3.5° vs. -6.7°, $p < 0.0001$; -0.7° vs. 3.4°, $p = 0.0026$; and -44.7° vs. -49.1, $p = 0.0003$, respectively).

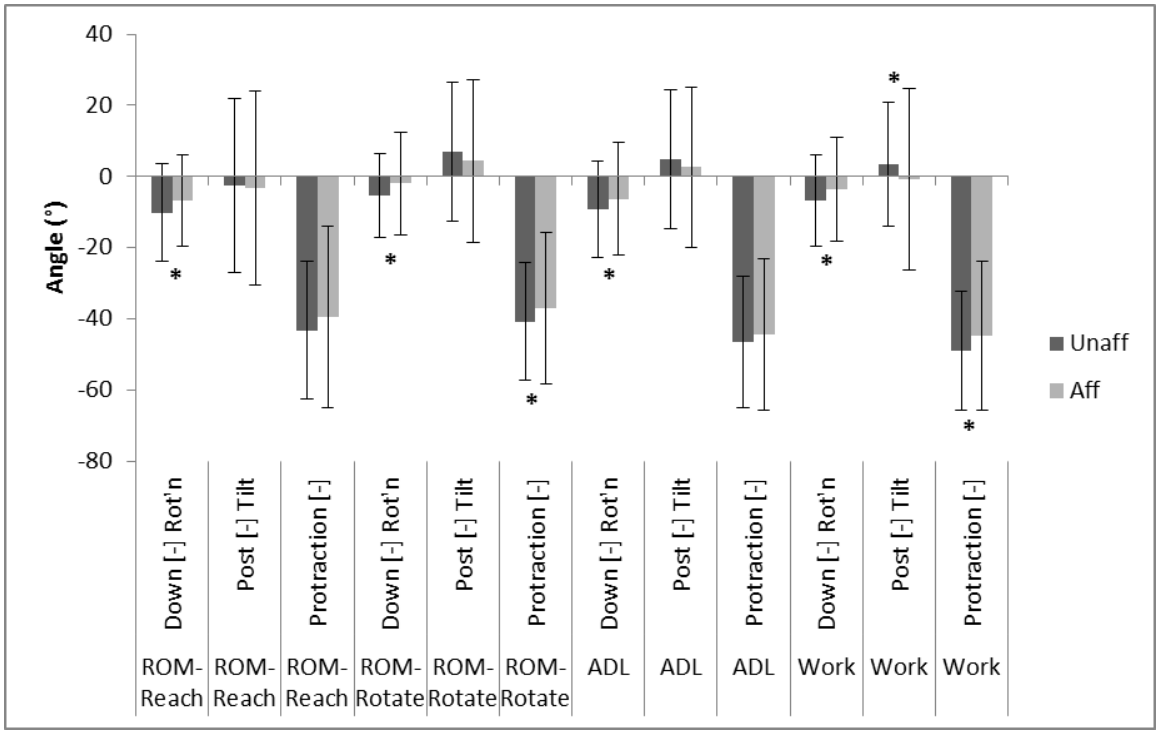


Figure 23 Comparison of scapulothoracic minimum angles between unaffected and affected sides during four types of tasks (ROM-Reach, ROM-Rotate, ADL and work tasks). Upward rotation, anterior tilt and retraction are shown as positive values. Downward rotation, posterior tilt and protraction are shown as negative values. LSM±SD. Significance (*) between sides is indicated.

The average unaffected humerothoracic minimal angles during all tasks demonstrated that the humerus was minimally elevated to 37.8° [SD± 14.8°]), internally rotated to -39.1° [SD±39.1°], and in a minimal plane of elevation of -42.8° [SD±36.1°]. The affected humerothoracic minimal angles demonstrated that on average the humerus was minimally elevated to 34.7° [SD± 16.6°]), internally rotated to -47.4° [SD±39.7°], and in a minimal plane of elevation of -42.0° [SD±33.6°] during all tasks. Analysis of humerothoracic kinematics revealed there were some statistically significant differences in minimal angles between unaffected and affected sides within some groups of tasks (Figure 24):

- During ROM-Reach and ROM-Rotate tasks, the humerus reached lower angles of elevation on the affected side (29.5° vs 35.2°, $p = 0.0001$; 38.5° vs. 42.7°, $p < 0.0001$, respectively).

- During ROM-Rotate tasks, the humerus was more internally rotated on the affected side (-26.5° vs. -18.6°, p = 0.0124).
- During ADL tasks, compared to the unaffected side, the affected side humerus reached a lower minimum angle of elevation (35.1° vs. 39.0°, p = 0.0003), and was more internally rotated (-69.5° vs. -61.0°, p = 0.0073).
- During work tasks, the affected side humerus was also more internally rotated compared to the unaffected side (-46.7° vs. -33.6°, p < 0.0001).

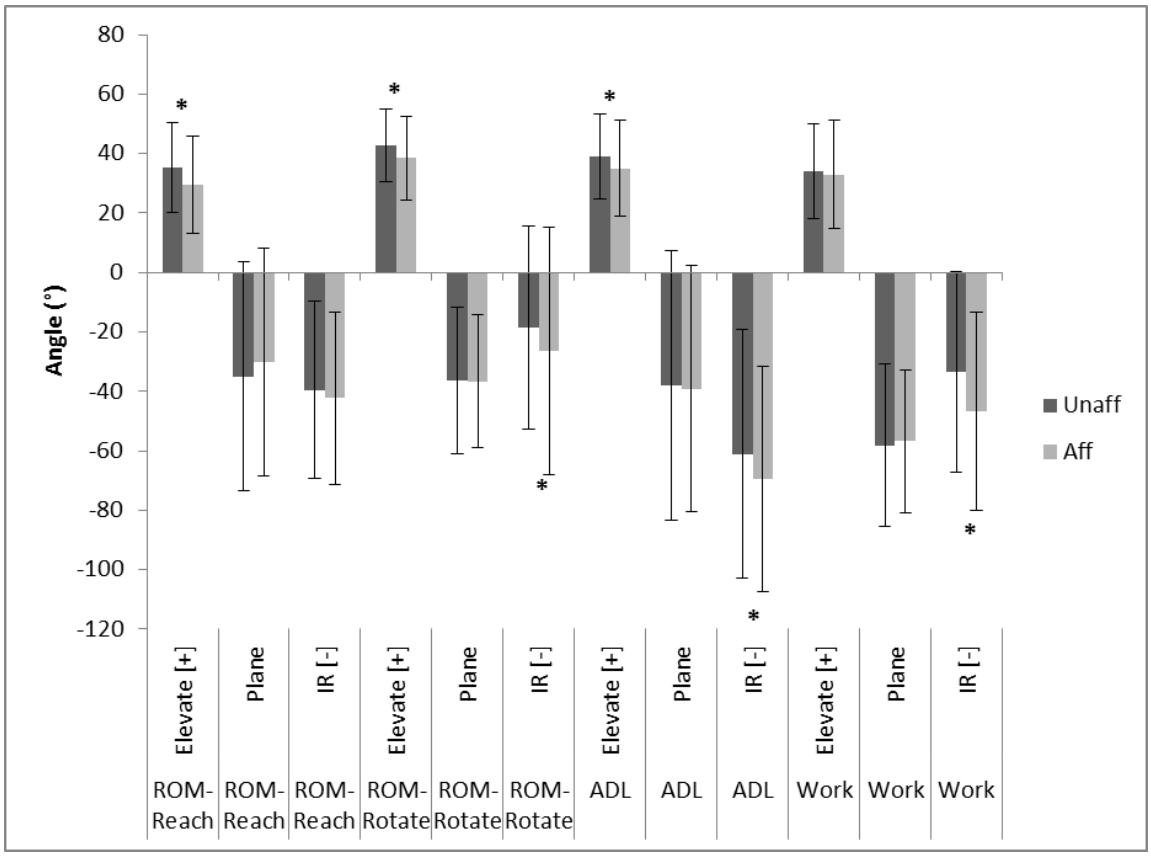


Figure 24 Comparison of humerothoracic minimum angles between unaffected and affected sides during four types of tasks (ROM-Reach, ROM-Rotate, ADL and work tasks). Elevation and external rotation are shown as positive values. Internal rotation is shown as negative values. Plane of elevation is 0° at abduction and -90° in flexion. LSM±SD. Significance (*) between sides is indicated.

Mean scapulothoracic and humerothoracic angles for unaffected and affected sides of all subjects during ROM-Reach, ROM-Rotation, ADL and work tasks are shown in Table 17 and Table 18. Mean scapulothoracic and humerothoracic angles for all subjects, for each of the 24 tests are outlined in Appendix H in Table 41,Table 42, Table 43, Table 44, Table 45 and Table 46. Due to an irrecoverable software issue, all kinematic data was lost for 1 subject (both sides); and due to an unrelated wrist injury on the unaffected side, kinematics were collected for only the affected side for one other subject. Typical time-series profiles of scapulothoracic and humerothoracic kinematics are shown in Figure 25 and Figure 26.

Table 17 Mean scapulothoracic angles during ROM-Reach, ROM-Rotation, ADL and Work Tasks for unaffected and affected [shaded cells] sides. Angles shown are ROM angles (maximum minus minimum angles); maximum angles (upward rotation, anterior tilt and retraction angles are denoted as positive values); and minimum angles achieved (downward rotation, posterior tilt and protraction angles are denoted as negative values). Angles are in degrees.

	Mean	SD±	Mean	SD±	Mean	SD±
	Scapulothoracic Beta ROM Angles (max-min)		**Scapulothoracic Beta Max Angles (Upward Rot'n = [+])**		**Scapulothoracic Beta Min (Downward Rot'n = [-])**	
ROM-Reach Tasks	45.6	25.7	36.4	29.5	-9.2	13.7
	44.1	24.0	37.3	27.2	-6.8	12.9
ROM-Rotate Tasks	9.4	7.3	4.4	13.2	-5.0	11.7
	9.0	7.3	7.0	15.9	-2.0	14.3
ADL Tasks	21.2	13.0	12.5	19.5	-8.7	13.6
	20.6	13.1	14.4	20.2	-6.3	15.7
Work Tasks	30.4	13.0	24.5	18.1	-5.9	12.8
	30.0	12.9	26.4	17.0	-3.6	14.6
	Scapulothoracic Alpha ROM Angles (max-min)		**Scapulothoracic Alpha Max Angles (Ant. Tilt = [+])**		**Scapulothoracic Alpha Min Angles (Posterior Tilt = [-])**	
ROM-Reach Tasks	26.0	26.2	22.3	20.9	-3.7	24.5
	23.1	24.3	20.2	27.3	-2.9	27.2
ROM-Rotate Tasks	6.9	6.3	12.9	19.9	6.0	19.6
	7.4	13.2	12.1	21.6	4.6	22.9
ADL Tasks	14.5	9.9	18.8	19.9	4.3	19.5
	16.1	15.1	18.9	23.6	2.8	22.5
Work Tasks	14.3	11.4	17.4	18.8	3.1	17.4
	16.5	16.8	16.0	21.5	-0.5	25.6
	Scapulothoracic Gamma ROM Angles (max-min)		**Scapulothoracic Gamma Max Angles (Retraction = [+])**		**Scapulothoracic Gamma Min Angles (Protraction = [-])**	
ROM-Reach Tasks	24.2	23.4	-19.5	27.0	-43.7	19.3
	20.6	22.6	-19.1	30.3	-39.7	25.5
ROM-Rotate Tasks	11.2	10.7	-29.3	18.3	-40.5	16.6
	10.4	10.5	-26.8	24.5	-37.1	21.2
ADL Tasks	14.5	11.6	-32.0	17.6	-46.4	18.5
	15.8	16.8	-28.7	24.2	-44.5	21.3
Work Tasks	18.9	13.9	-29.9	20.6	-48.9	16.7
	18.2	13.9	-26.9	28.5	-45.1	21.1

Table 18 Mean humerothoracic angles during ROM-Reach, ROM-Rotation, ADL and Work Tasks for unaffected and affected [shaded cells] sides. Angles shown are ROM angles (maximum minus minimum angles); maximum angles (elevation and external rotation angles are denoted as positive values); and minimum angles achieved (internal rotation angles are denoted as negative values). Plane of elevation was 0° at abduction and -90° in forward flexion. Angles are in degrees.

	Mean	SD±	Mean	SD±	Mean	SD±
	Humerothoracic Beta ROM Angles (max-min)		**Humerothoracic Beta Max Angles (Elevation = [+])**		**Humerothoracic Beta Min Angles (Elevation = [+])**	
ROM-Reach Tasks	64.9	30.6	100.1	31.3	35.2	15.1
	67.2	32.3	97.0	32.7	29.8	16.3
ROM-Rotate Tasks	12.2	12.7	54.7	14.4	42.5	12.2
	9.6	9.5	48.7	15.2	39.1	14.2
ADL Tasks	34.1	21.8	73.0	21.0	38.9	14.2
	36.1	27.9	71.6	27.1	35.4	16.1
Work Tasks	51.9	22.4	86.2	24.2	34.3	16.0
	56.2	26.0	89.4	28.5	33.1	18.2
	Humerothoracic Gamma ROM Angles (max-min)		**Humerothoracic Gamma Max Angles (Plane of Elevation: -90 = flexion, 0 = abduction)**		**Humerothoracic Gamma Min Angles (Plane of Elevation: -90 = flexion, 0 = abduction)**	
ROM-Reach Tasks	39.1	26.7	3.9	35.8	-35.2	38.6
	32.2	23.4	2.2	39.0	-30.1	38.1
ROM-Rotate Tasks	19.0	20.5	-17.0	24.7	-36.0	24.7
	15.3	19.2	-20.9	25.1	-36.2	22.4
ADL Tasks	38.8	30.3	0.9	40.6	-38.0	45.3
	34.3	29.0	-4.8	40.4	-39.1	41.3
Work Tasks	35.6	24.5	-22.1	27.7	-57.6	27.2
	32.8	26.8	-23.8	27.2	-56.7	24.0
	Humerothoracic Gamma2 ROM Angles (max-min)		**Humerothoracic Gamma2 Max Angles (ER = [+])**		**Humerothoracic Gamma2 Min Angles (IR = [-])**	
ROM-Reach Tasks	38.1	31.3	-2.1	38.7	-40.2	29.8
	37.0	33.0	-5.3	42.5	-42.3	29.0
ROM-Rotate Tasks	26.9	25.8	8.1	30.8	-18.8	34.3
	33.6	31.8	7.0	35.6	-26.6	41.6
ADL Tasks	61.4	50.6	0.4	35.7	-61.0	41.8
	68.3	55.3	-1.2	42.1	-69.5	38.0
Work Tasks	43.0	37.3	8.8	43.0	-34.2	33.8
	47.3	46.0	0.4	47.1	-46.9	33.4

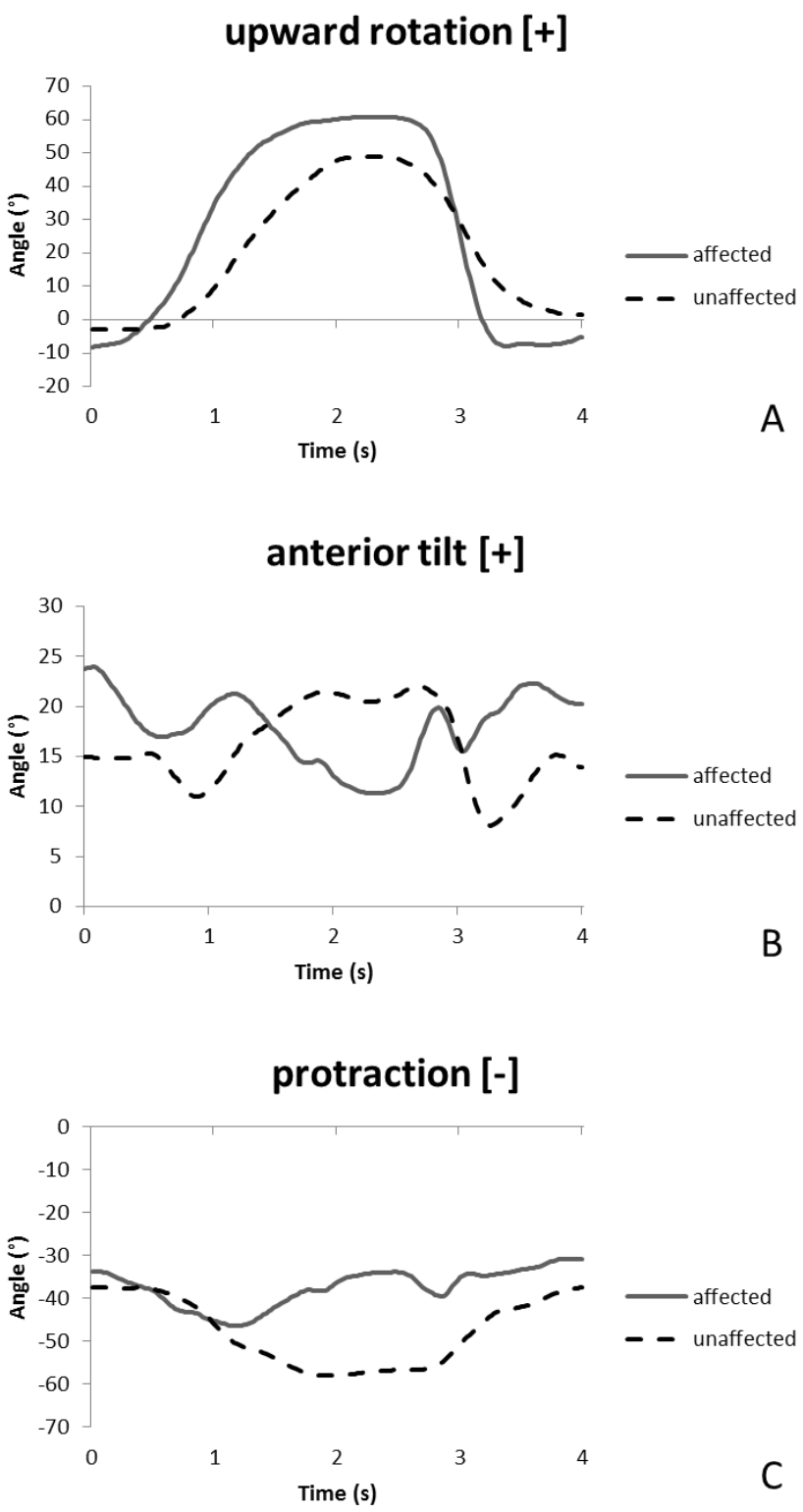


Figure 25 Representative comparison of scapulothoracic angles during flexion between affected and unaffected sides of one participant. Upward rotation [A] and anterior tilt [B] angles are denoted as positive values. Protraction angles [C] are denoted as negative values.

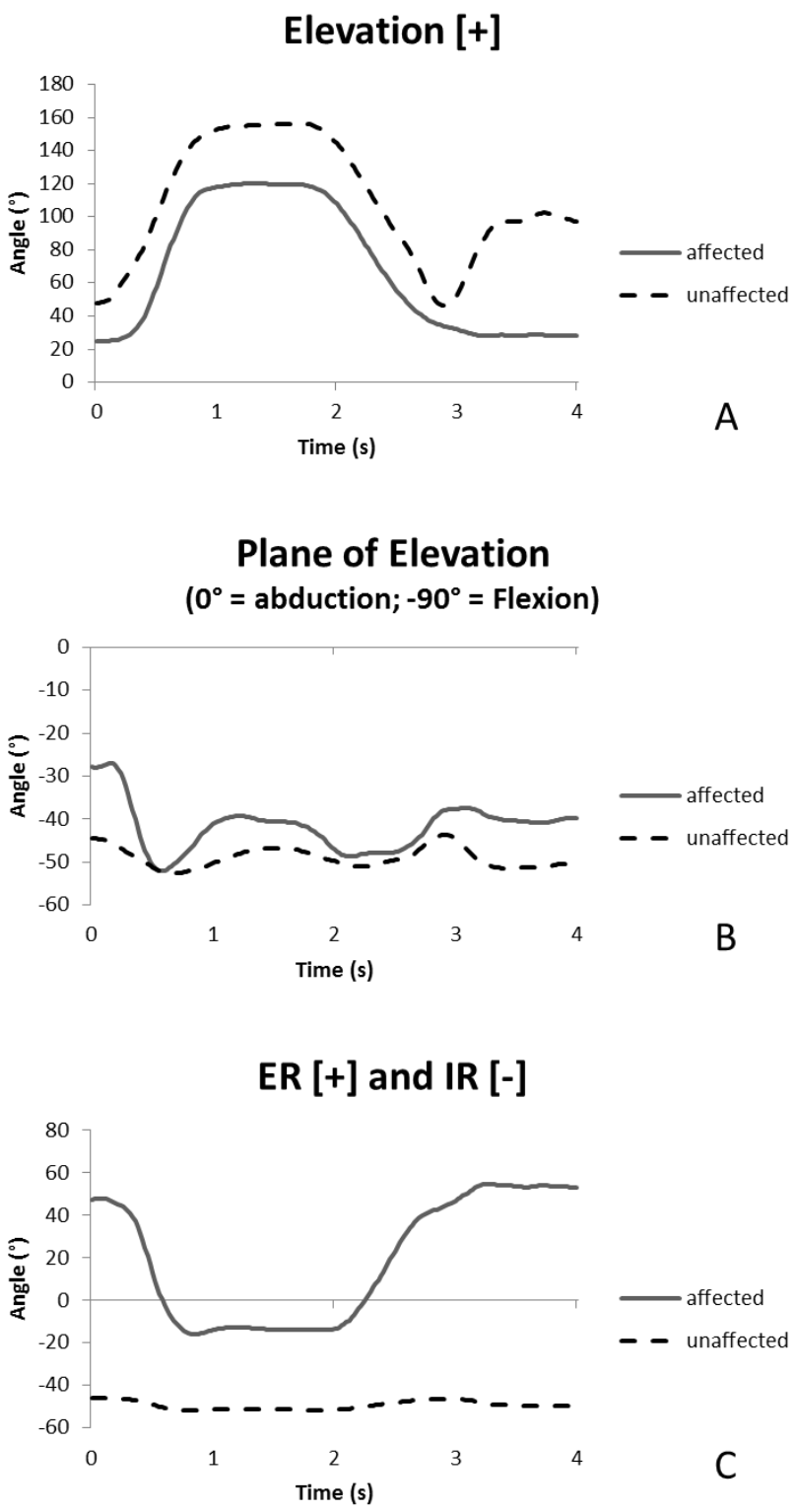


Figure 26 Representative comparison of humerothoracic angles during flexion between affected and unaffected sides of one participant. Elevation [A] and external rotation [C] angles are denoted as positive values. Internal rotation angles [C] are denoted as negative values. Plane of elevation [B] is described as 0° at abduction and -90° at forward flexion.

Section 4.4.2 Total muscle effort

The TME of the affected side was greater than the unaffected side during work tasks (p = 0.0258); there was no statistically identifiable difference of TME between sides within the ROM-Reach group (p = 0.1750), ROM-Rotation group (p = 0.4099) or ADL tasks (p = 0.1368) [Figure 27], though the mean values were higher on the affected side for each group. Mean TME for all subjects are shown in Appendix F [Table 40].

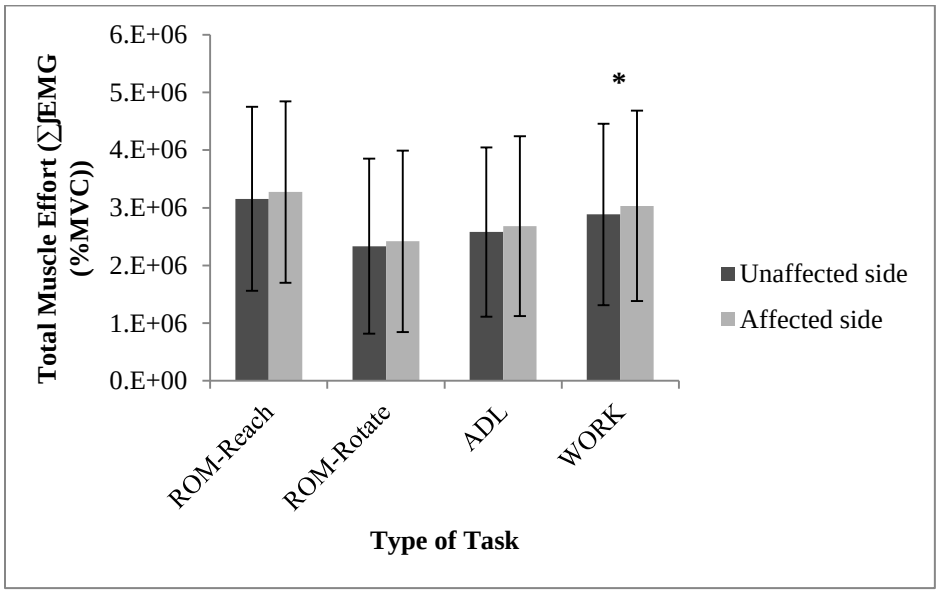


Figure 27 Comparison of TME between sides. LSM ±SD. Asterix (*) indicates significant differences between sides.

Section 4.4.3 Integrated EMG

Analysis of iEMG revealed there were differences between unaffected and affected sides within certain muscles and groups of tasks:

1. For ROM-Reach tasks
    a. iEMG affected > unaffected for posterior deltoid and supraspinatus [p values = 0.0116 and 0.0161, respectively.]
    b. iEMG unaffected > affected for pectoralis major sternal, infraspinatus [p values = 0.0008 and 0.0154, respectively.]

    c. No difference in iEMG between sides for pectoralis major clavicular, latissimus dorsi, upper trapezius or serratus anterior [p values = 0.1880,0.5361, 0.0586 and 0.0594, respectively.]
2. For ROM-Rotation tasks
    a. iEMG affected > unaffected for posterior deltoid [p = 0.0032]
    b. iEMG unaffected > affected for pectoralis major sternal and infraspinatus [p = 0.0032 and 0.0328, respectively.]
    c. No difference in iEMG between sides for pectoralis major clavicular, latissimus dorsi, serratus anterior, upper trapezius and supraspinatus [p = 0.6650, 0.8349, 0.0714, 0.0955, 0.0520, respectively.]
3. For ADL tasks
    a. iEMG affected > unaffected for posterior deltoid, upper trapezius, supraspinatus [p values = 0.0065, 0.0486 and 0.0380, respectively.]
    b. iEMG unaffected > affected for pectoralis major sternal [p values = 0.0230, respectively.]
    c. No difference in iEMG between sides for pectoralis major clavicular, latissimus dorsi, serratus anterior, infraspinatus [p values = 0.6972, 0.6833, 0.0533 and 0.4327, respectively.]
4. For work tasks
    a. iEMG affected > unaffected for posterior deltoid, serratus anterior, upper trapezius, supraspinatus [p values = <0.0001, 0.0019, 0.0009, and 0.0003, respectively.]
    b. iEMG unaffected > affected for pectoralis major sternal, infraspinatus [p values = <0.0001 and 0.0002, respectively.]
    c. No difference in iEMG between sides for pectoralis major clavicular, latissimus dorsi [p values = 0.6717 and 0.4330, respectively.]

These relationships are demonstrated in Figure 28. Mean integrated EMG values for all subjects are shown in Appendix E [Table 40].

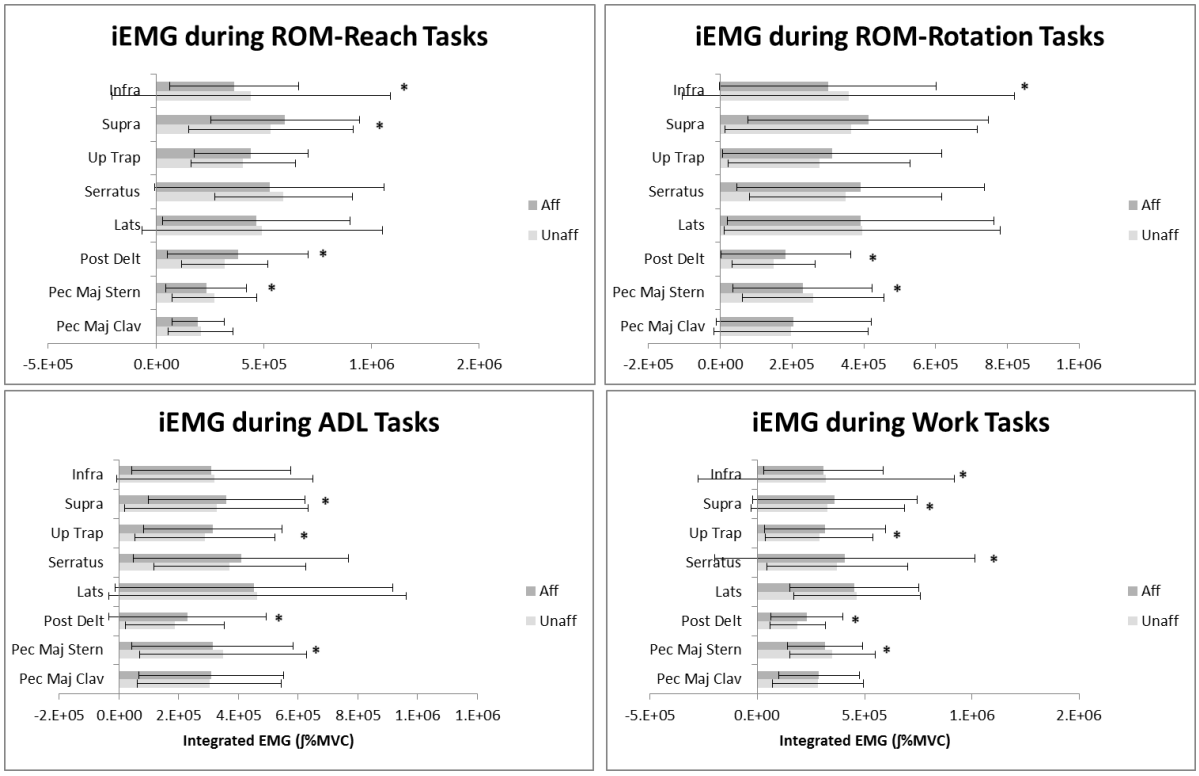


Figure 28 Least squared mean iEMG during ROM-Reach, ROM-Rotation, ADL and work tasks (LSM±SD and Significance* between sides are shown)

Section 4.4.4 Strength

The strength of the infraspinatus, supraspinatus and upper trapezius were weaker on the affected side (p values were 0.0028, 0.0057, and <0.0001, respectively). There was no difference in strength (MVF values) between sides for the latissimus dorsi (p = 0.2179), pectoralis major (p = 0.6860), posterior deltoid (p = 0.2333) or serratus anterior (p = 0.7036). Least mean squared MVFs and significant differences are demonstrated in Figure 29 and average strength values for all participants are shown in Table 19.

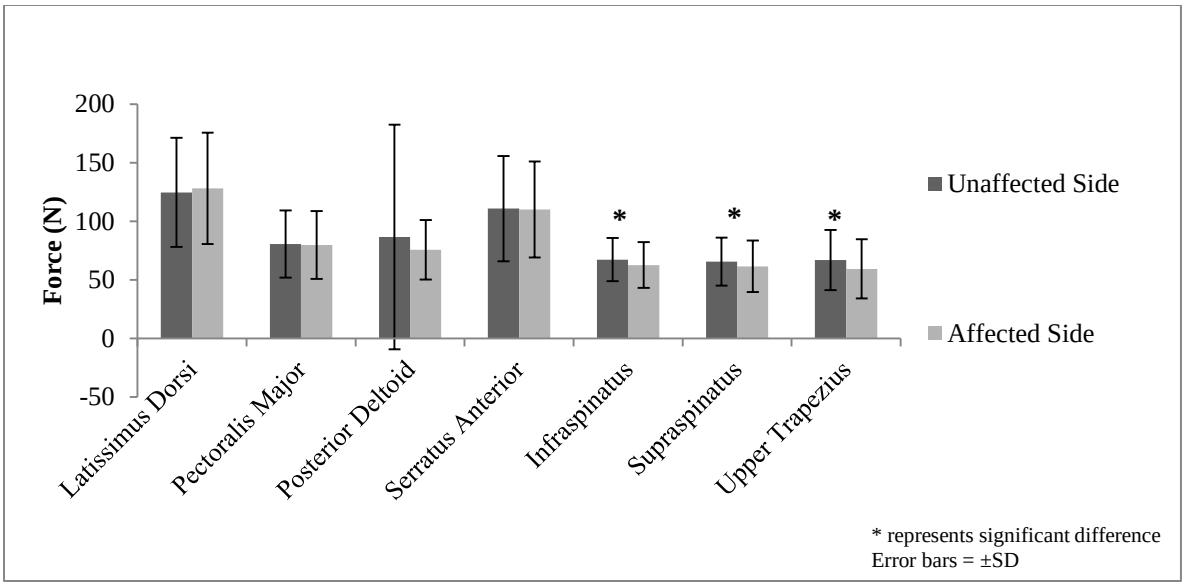


Figure 29 Muscle strength (MVF values) of unaffected compared to affected sides

Table 19 Mean strength (MVF values) for all participants during maximal voluntary force exertions. Affected [shaded] and unaffected sides are listed. Standard deviation and range (minimum and maximum) values are listed. Note: bilateral comparisons were not collected for subscapularis.

Muscle	Median	Avg	SD	Min	Max
R Grip (kg)	22	22	5	11	38
L Grip (kg)	20	21	5	9	36
Subscapularis MVF (N)	85	87	24	35	129
Infraspinatus MVF (N)	59	63	19	32	118
Infraspinatus MVF (N)	64	67	18	29	292
Latissimus Dorsi MVF (N)	126	128	48	43	151
Latissimus Dorsi MVF (N)	123	125	47	43	306
Pectoralis Major MVF (N)	78	80	29	5	122
Pectoralis Major MVF (N)	80	81	29	25	161
Supraspinatus MVF (N)	61	62	22	19	125
Supraspinatus MVF (N)	66	66	20	16	120
Posterior Deltoid MVF (N)	78	76	25	21	123
Posterior Deltoid MVF (N)	78	87	96	32	994
Upper Trapezius MVF (N)	56	60	25	8	262
Upper Trapezius MVF (N)	65	67	26	16	145
Serratus Anterior MVF (N)	112	110	41	36	133
Serratus Anterior MVF (N)	108	111	45	28	290

Section 4.4.5 Ratings of perceived discomfort, quality of life and disability scores

In general, the ratings of perceived exertions reported during MVC testing revealed the affected side discomfort to be higher than the unaffected side, although significantly so only during infraspinatus and posterior deltoid maximal exertions (4% vs. 2% RPD, $p = 0.018$; 6% vs. 3% RPD, $p = 0.0064$, respectively) (Figure 30).Mean, variability and range of RPD scores for all participants are outlined in Table 20.

Table 20 Mean ratings of perceived discomfort for all subjects during maximal voluntary contraction testing. Minimum, maximum and standard deviations are listed. Affected side [shaded] vs. unaffected sides. Note: bilateral comparisons were not collected for subscapularis.

Muscle	Avg	SD	Min	Max
Subscapularis RPD	6	15	0	85
Infraspinatus RPD	4	11	0	70
Infraspinatus RPD	2	8	0	60
Latissimus Dorsi RPD	5	15	0	70
Latissimus Dorsi RPD	4	9	0	40
Pectoralis Major RPD	5	13	0	70
Pectoralis Major RPD	4	12	0	50
Supraspinatus RPD	8	15	0	70
Supraspinatus RPD	5	14	0	75
Posterior Deltoid RPD	6	14	0	80
Posterior Deltoid RPD	3	10	0	70
Upper Trapezius RPD	6	16	0	80
Upper Trapezius RPD	5	15	0	75
Serratus Anterior RPD	3	13	0	70
Serratus Anterior RPD	2	8	0	40

The average QuickDASH score was 19 (out of a total score of 100, with 0 indicating no disability and 100 indicating severe disability). The average FACT-B Trial Outcome Index Score was 70 (out of a total score of 92); the average FACT-G total score was 89 (out of a total score of 108) and the average FACT-B total score was 114 (out of a total score of 144), with a higher score indicating better quality of life. Mean, standard deviations and ranges of disability and QoL scores for all participants are outlined in Table 21. The average difference in volume between limbs was 131.40 mL (SD±252.66 mL; range 0.2 mL-1673.14 mL). Lymphedema was defined as a difference of 200 mL or more between sides, and 5 participants had lymphedema as per this definition. Additional self-reported participant characteristics are outlined in Table 22.

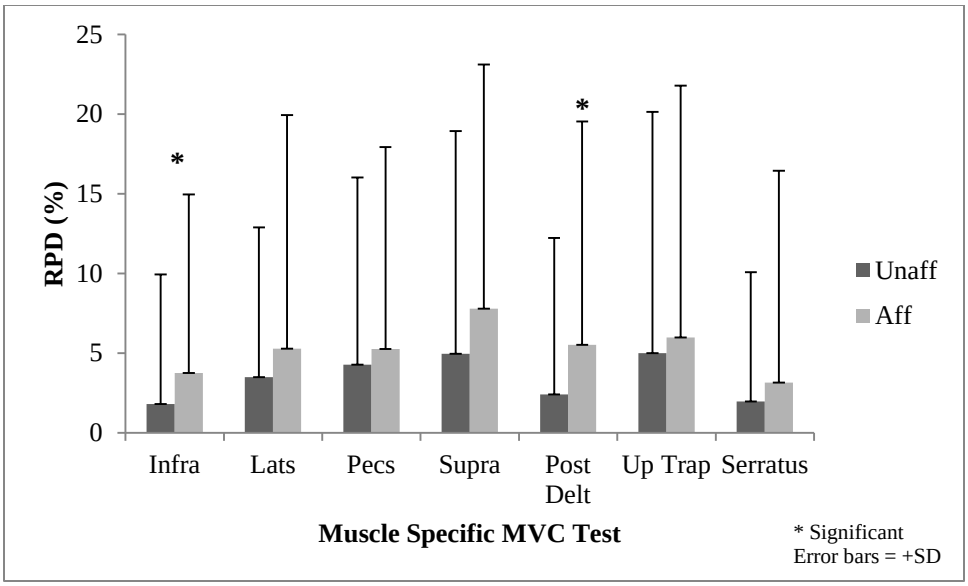


Figure 30 Comparison of rating of perceived discomfort between sides during MVC tests

Table 21 Summary of mean disability (QuickDASH) and quality of life (FACT-B) scores for all participants. A higher QuickDASH score indicates more severe disability. A higher FACT-B scores indicates better quality of life.

Score	Avg	SD	Min	Max
QuickDASH	19	18	0	84
FACT-B score (Trial Outcome Index Score: range 0-92)	70	14	21	89
FACT-B score (FACT-G Total Score: range 0-108)	89	16	35	105
FACT-B score (FACT B Total Score: range 0-144)	114	20	35	140

Table 22 Participant self-reported characteristics

Description	N
Employment Status:	
Unemployed or retired	27
Full-time	17
Part-time	6
Exercise Status:	
Sedentary	6
Exercise <= 3 d/wk	9
Exercise >= 4 d/wk	35
Subjective Scores:	
reported compromised ADL performance	16
reported affected chest/shoulder tightness	30
reported affected ROM was reduced	26
reported consistent pain on affected side	26
reported weaker on affected side	24
reported swelling on affected side	25
reported cording on affected side	9
reported numbness on affected side	31
Routinely wore compression garments	10
Had Reconstructive Surgery	11

Section 4.4.6 Relationship between total muscle effort and quality of life and disability scores

Correlation analysis revealed modest linear relationships between disability and QoL scores with summation of affected side TME for all exertions [Equation 13, Equation 14]:

Equation 13 Relationship between muscle effort and disability score

$$TME = 672{,}709(QuickDASH) + 5^{E+07} \qquad R^2 = 0.1465$$

Equation 14 Relationship between muscle effort and quality of life score

$$TME = -329{,}310(FACT.B) + 9^{E+07} \qquad R^2 = 0.0315$$

Non-linear relationships were also investigated, but these relationships greatly complicated interpretation while failing to greatly improve correlations, as shown in Figure 31 and Figure 32.

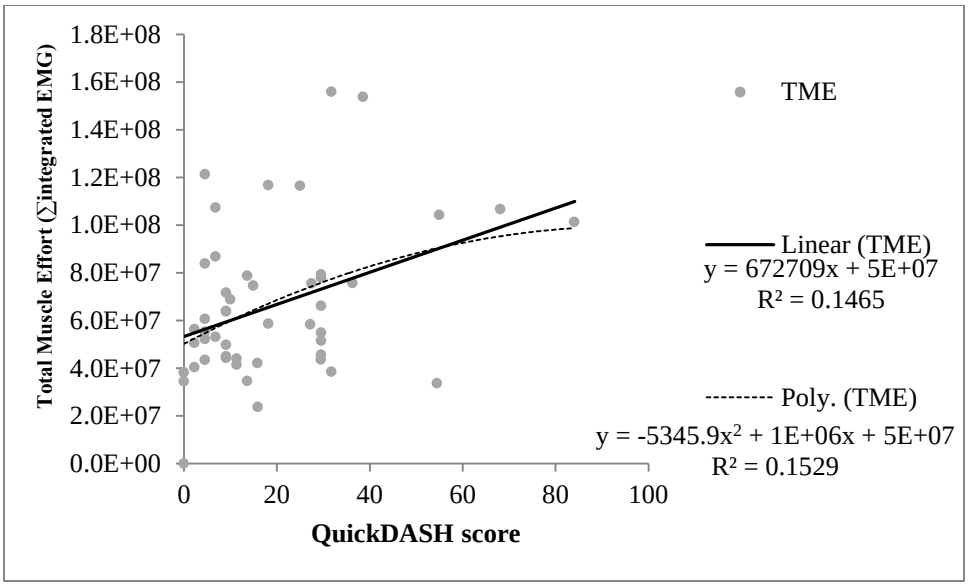


Figure 31 Relationships between summation of affected side TME during all exertions with disability scores (QuickDASH). Linear and polynomial relationships are shown.

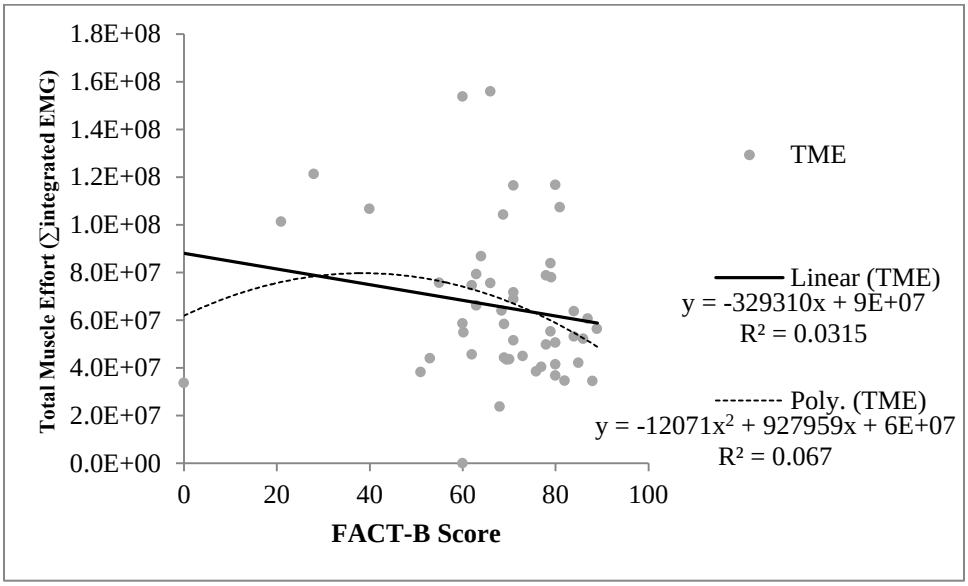


Figure 32 Relationship between summation of affected side TME during all exertions with quality of life (FACT-B) scores. Linear and polynomial relationships are shown.

Section 4.5 Discussion

The purposes of this investigation were to describe upper limb capabilities and dysfunction of breast cancer survivors in terms of 3-D upper limb kinematics, muscle activation patterns and strength; and to determine the relationships between a physical quantity of function (total muscle effort) with subjective functional measures (QoL and disability scores). Accurate documentation of physical capability and dysfunction is the first step towards developing targeted treatment and preventative strategies for this disabled population. In general, the kinematic findings demonstrated reduced angle of elevation and increased internal rotation on the affected side humerus; and reduced protraction, less downward rotation, and more posterior tilting on the affected side scapula. These kinematic changes coincided with other factors suggestive of dysfunction on the affected side, including: weakness (reduction in muscle-specific strength), enhanced muscle effort (increased activity levels insinuating increased effort required or increased fatigue due to damage or dysfunction), reduced muscle capability (reduced activity levels due to damage or dysfunction) and discomfort (increased RPD scores).

Section 4.5.1 Addressing the hypotheses

Revisiting Hypothesis 1: It was hypothesized that survivors would demonstrate reduced humeral angle of elevation and external rotation range of motion, but increased scapular protraction range of motion on their affected side compared to the contralateral limb.

The humerothoracic kinematic results **confirmed** the hypotheses and demonstrated that survivors averaged 3.9° - 6.5° reductions in humeral elevation and 8.9° less humeral external rotation on the affected side. Further, survivors were 7.9° - 13.1° more internally rotated.

The scapulothoracic kinematic results **partly confirmed** the hypotheses and demonstrated that although both sides of survivors were always in a state of protraction during all tasks, the affected side demonstrated reduced scapular protraction compared to the degree of protraction on the

unaffected side during ROM and work tasks. Specifically, 3.4° less of protraction compared to the unaffected side during ADL and work (maximal angles), and 3.6° and 4.4° less protraction during ROM-Rotate and work tasks (minimal angles). Increased protraction ('winged scapula') have been documented previously (as determined by visual clinical assessment and classified as either 'winged' or 'normal') in the BCP (Lauridsen, Torsleff, Husted, & Erichsen, 2000). In a previous study of 11 participants performing scaption, increases of scapular protraction by 3.9° were displayed on the affected arm, compared to the unaffected arm post-surgery.

Revisiting Hypothesis 2: It was hypothesized that survivors would demonstrate reduced strength and increased muscle activity on the affected side.

Total muscle effort was significantly greater on the affected side during work tasks, **confirming** the hypothesis of increased muscle activity. In **partial support** of the hypothesis, reductions in muscle-specific strength of the affected side of 4 N, 4 N and 7 N were seen in only the infraspinatus, supraspinatus and upper trapezius exertions, respectively.

Revisiting Hypothesis 3: It was hypothesized that as total muscle effort increased, there would be a decrease in quality of life (FACT-B scores) and an increase in disability (QuickDASH) scores.

This hypothesis was **confirmed**, and small correlations were found between quantitative and subjective measures of function, affirming poorer ratings of quality of life and higher ratings of disability with higher levels of total muscle effort.

Section 4.5.2 Kinematics

All three angle calculations (maximum and minimum achieved angles and total ROM (the difference between maximum and minimum angles)) should be considered when interpreting bilateral changes in scapulothoracic and humerothoracic kinematics. A wider task ROM calculation (maximum minus minimum angles) could reflect variability of movement strategies used, or relate to available range. Maximum and minimum angles must be carefully interpreted based on their polarity in the context of

the task being investigated (e.g. a negative humeral rotation angle would be expected during perineal care tasks, but not during an external rotation exertion).

Section 4.5.2.1 Interpretation of ROM calculations

There was little difference in the overall scapulothoracic and humerothoracic task ROM (the difference between maximum and minimum achieved angles) between unaffected and affected sides. The affected side demonstrated reduced ROM only in elevation angle during ROM-Rotate tasks (-2.3°) and in plane of elevation during ROM-Reach (-6.7°) and ROM-Rotate tasks (-3.3°). A reduced ROM in plane of elevation could suggest the BCP was less variable in their movement strategies between planes, keeping movements in a tighter range of planes. In many instances, the affected side demonstrated movement through a greater ROM: 1.8° and 2.0° more ROM in anterior/posterior tilt during ADL and work tasks, respectively; 7.1° more humeral rotation ROM during ROM-Rotate tasks, and 5.3° more ROM in elevation during work. Past clinical assessments have reported reductions in elevation angle ROM on the affected side during abduction (-6.4°, -7.5° and -21°) and flexion (-4.3°, -5.7°, -12°), as well as reduced external rotation ROM (-6.2°) (Hack, Cohen, Katz, Robson, & Goss, 1999; Kuehn, et al., 2000; Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004). However, maximum and minimum absolute angle values must be considered before making any conclusions regarding affected side having greater ROM, as enhanced total ROM is sometimes explained by a lower minimum starting angle (e.g. the affected side reached lower maximum elevation angles, but started at lower humeral elevation angles, resulting in a greater overall ROM). It is difficult to compare ROM values between previous studies as it is unknown if the starting position was consistent within tasks and studies, and if that starting position was similar to the current thesis study. Detail regarding the minimum and maximal angles, as is described in the next section, provides further insight into the movement differences between sides.

Section 4.5.2.2 Interpretation of the scapulothoracic angles in terms of maximum and minimum angles and comparison with previous literature

Both minimum and maximum angles revealed that the affected side scapula was less protracted, more upwardly rotated, less downwardly rotated, and more posteriorly tilted. The significance of these relationships was dependent on the group of tasks being performed. The affected scapula displayed 3.4° - 3.9° less protraction compared to the unaffected side during ADL and work tasks (according to maximum angles), respectively; and 3.6° – 4.4° less protraction during ROM-Rotate and work tasks (according to minimum angles). The scapula demonstrated 2.8° more upward rotation on the affected side during ROM-Rotate tasks, and non-significant trends indicated increases in upward rotation (0.9° – 2.6° more) for all other groups of tasks. Interpretation of the minimum angles revealed that the affected scapula displayed 2.9°– 3.5° less downward rotation compared to the unaffected side during all four groups of tasks. The affected side scapula demonstrated 4.1° more posterior tilt during work tasks.

These kinematic findings partly contrast with previous reports, although it is difficult to make direct comparisons between scapulothoracic changes reported in the BCP due to the limited number of studies available and the differing methodologies used (population characteristics, type and timing of treatment and measurements, recording methods and exertions examined). A recent study investigated scapulothoracic kinematics of the BCP during bilateral flexion, abduction and scaption, and reported that women with dominant-side mastectomies exhibited greater upward rotation during arm elevation during scaption (5.0° – 9.3° more) and abduction (5.5° – 11.9° more) on the affected side compared to a healthy control group (Crosbie, et al., 2010). Shamley et al. (2009) compared affected left and right-sided scapulothoracic changes in the BCP post-surgery, and found that the both sides displayed increased posterior tilt (~2° and depended on the angle of elevation) but left-affected scapulothoracic changes included increased protraction (~10° and depended on the angle of elevation) and decreased upward rotation; whereas right-affected

dysfunction included increased retraction and increased upward rotation. Later, Shamley et al. (2012) compared the scapular kinematics of survivors during scaption to healthy controls, and reported that patients demonstrated greater upward rotation on the affected side ($p<0.0001$, CI 4.82 – 8.51 for left affected side; CI 3.91 – 7.71 for right affected side) (associated with a decrease in pectoralis major activity and an increase in serratus anterior activity) and a non-significant increase in posterior tilt. Borstad and Szucs (2012) investigated scapular kinematics of the BCP 2 months post-surgery while performing scaption and reported scapular protraction increased post-surgery by 8.1° and was increased on the affected arm by 3.9°. Trends indicated increases of 3.4° in upward rotation and increases of 3.5° in anterior tilt on affected arm, but there was no significant change in scapular rotation or tilt (Borstad & Szucs, 2012). Despite a lack of data available for comparison (especially for the range of tasks investigated in the current study), there was general agreement between the current study and previous work that the affected side of the BCP demonstrated more scapular posterior tilting (Shamley, Srinaganathan, Oskrochi, Lascurain-Aguirrebena, & Sugden, 2009), increased upward rotation (Crosbie, et al., 2010; Shamley, Lascurain-Aguirrebena, Oskrochi, & Srinaganathan, 2012).

Differences in findings within and between past research and the current study may be due to methodological differences. Crosbie et al. (2010) and Shamley et al. (2012) reported increased upward rotation on the affected side during flexion, abduction and scaption, but in the current study upward rotation was significantly greater during only ROM-Rotate tasks, although trends suggested increases in all tasks. Crosbie et al. (2010), Shamley et al. (2009; 2012) and Borstad & Szucs (2012) used electromagnetic tracking devices to record kinematics, but the acromion tracking technique used in the optoelectronic recording method of the current study underestimates upward rotation (Karduna, McClure, Michener, & Sennett, 2001). Grewal (2011) further confirmed that the acromial tracking technique underestimated upward rotation by about 9° – 11° compared to other methods. Conflicting reports of posterior tilt and protraction angles may also be due to differing

methodologies. Grewal (2011) recommended the acromial tracking technique to measure scapular orientation, but cautioned interpretation of results since the method overestimated posterior tilt at overhead elevation angles [recall significant increases in posterior tilt were seen during work tasks of elevated reaching in the current study] and underestimated it at low elevation angles; and underestimated protraction in the frontal plane at low elevation angles, but overestimated it for all other postures, with errors increasing with internal rotation and elevation angle [recall survivors were always in a state of protraction in the current study]. Other investigators have similarly reported the inaccuracy of scapular protraction measures using the acromial tracking techniques at higher elevation angles (Karduna, McClure, Michener, & Sennett, 2001; van Andel, van Hutten, Eversdijk, Veeger, & Harlaar, 2009). These methodological differences could partly influence the kinematic discrepancies reported between scapulothoracic ranges of motion displayed by Shamley et al. (2009) during scaption (~12° ROM in protraction/retraction, ~45° ROM in upward/downward rotation and ~10° ROM in anterior/posterior tilt) compared to the mean ranges of motion found during the current study's ROM-Reach tasks (20.6° ROM in protraction/retraction, 44.1° ROM in upward/downward rotation 23.1° ROM in anterior/posterior tilt). Future study of this population should incorporate standardized methods so that kinematics can be accurately compared.

Adaptive changes may reflect the scapulothoracic kinematic changes seen between sides. It has been speculated that the altered motor patterns of the scapula may be evidence of an adaptation made due to reduced frequency and amplitude of arm elevation following surgery (Crosbie, et al., 2010). Following surgery, a drain is often inserted into the chest wall to reduce risk of seroma formation and women are recommended to limit arm elevation and guard their limb (disallowing even blood pressure measurements on the affected side), in order to reduce incidence of lymphedema. Further, patients receiving chemotherapy may have a port catheter surgically inserted under the skin of the chest wall (usually on the right side at the location of the internal jugular vein), and associated risks and complications may cause some patients to limit mobility and experience

pain even after it has been removed. In the current study the BCP was found to be in a consistent state of scapular protraction on both sides. The participants also exhibited more upward rotation and less downward rotation on the affected side, which may reflect adaptive changes to motor patterns and learned usage as suggested by Crosbie et al. (2010). Increased upward rotation could also reflect a compensatory change due to postures of increased scapular protraction. Healthy populations in slouched trunk postures were found to have more upward rotation and less posterior tilting of the scapula compared to erect posture (Kebaetse, McMclure, & Pratt, 1999). Increases in posterior tilt seen in the current study may reflect a compensatory movement to increase the subacromial space (reducing risk of impingement) due to the degree of protraction and reduction in downward rotation. Decreased scapular upward rotation and posterior tilting, and increased protraction have all been associated with subacromial impingement syndrome (Ludewig & Reynolds, 2009). These adaptative kinematic changes seen in the scapula suggest the body may be compensating to guard against movements that are difficult, cause pain, or infer risk of subacromial impingement.

Section 4.5.2.3 Interpretation of humerothoracic angles in terms of maximum and minimum angles and comparison with previous literature

Interpretation of both minimum and maximum angles revealed that the affected side humerus reached lower elevation angles, maintained a more anterior plane of elevation and was less externally rotated and more internally rotated. The significance of these relationships depended upon the group of tasks being performed. Trends indicated the affected humerus reached lower maximal angles of elevation for all tasks, although only significantly so during ROM-Rotate tasks. The affected humerus reached 6.5° lower maximal angles of elevation and was maintained in a more anterior plane of elevation (-21.1° vs -17.2°) during ROM-Rotate tasks compared to the unaffected limb. Three-dimensional humerothoracic kinematics of the BCP have not been described previously, but clinical assessments have reported similar reductions in elevation angles (-6.4 and -7.5 during abduction; -4.3 and -5.7 during flexion) (Hack, Cohen, Katz, Robson, & Goss, 1999; Rietman,

Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004). With the exception of the work task group, the affected side humerus reached 3.9° – 5.7° lower minimum angles of elevation during all other groups of tasks. During work tasks of the current study the humerus was 8.9° less externally rotated, which is similar to past research which reported reductions of external rotation of -6.2° on the affected side (Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004). With the exception of the ROM-Reach tasks, the affected humerus was 7.9° – 13.1° more internally rotated during all other groups of tasks.

This is the first published study to report 3-D humerothoracic angles of the BCP so direct comparisons are challenging, but many studies have described clinical assessments of humeral angles from which comparisons can be made. Similar to the findings of the current study, previous clinical investigations have determined reductions in elevation angle and external rotation amongst the BCP. In the current study survivors maximal end reach height was reduced on the affected side humerus by 6.5° during ROM-Reach tasks, and survivors started tasks with their arm closer to their side (3.9° - 5.7° reduced minimal angle) during ROM-Reach, Rom-Rotate and ADL tasks. Clinical assessments using goniometry have reported reductions in elevation angles of survivors during flexion and abduction with differences in range of motion between sides from 4° to 6° (Hack, Cohen, Katz, Robson, & Goss, 1999), 12° and 21°(Kuehn, et al., 2000), and 6° to 8°, respectively (Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004). In the current study, the affected humerus externally rotated 8.9° less than the unaffected limb during work tasks, and internally rotated 7.9°, 8.5° and 13.1° more ROM-Rotate, ADL and work tasks, respectively. Reductions of 6° external rotation have been reported previously during clinical examination of survivors (Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004). Smaller magnitudes of maximal elevation angles reported in the current work from some previous clinical assessments may be due to the fact that angles extracted from recorded motion tracking tend to underestimate angles as the arm elevates, which has been attributed to trunk tilting during arm elevation (Grewal, 2011). McClure et

al. (2001) similarly reported extracted angles underestimating goniometer measurement of humeral elevation by about 15°. In the current study, neutral trunk posture was encouraged, but it was not constrained and participants were seated on a backless stool. Extracted angles also tend to overestimate elevation angles at lower (more neutral) arm postures, due to surrounding soft tissue of the arm and thorax which disallows alignment of the two local y-axes (Grewal, 2011). Further, the definition of "zero" between clinical assessments with the current work may limit direct comparison of data. Often, neutral or zero positions are defined as the anatomical stance in clinical settings, whereas zero was defined as the alignment of the humerus and thorax local coordinate systems in the current study.

The maximal angles of elevation were on average lower on the unaffected side compared to healthy populations performing similar exertions, suggesting bilateral kinematic changes occur in the BCP. Humerothoracic kinematics had been examined for a similar battery of exertions examined in this body of work in elderly healthy and impingement populations by Hall et al. (2011). Hall et al. (2011) reported the maximal humerothoracic elevation angles during flexion and abduction as: 145° [±24°] (healthy, flexion) and 108° [±28°] (impinged, flexion), 140° [±20°] (healthy, abduction) and 96° [±30°] (impinged, abduction). The BCP of the current study achieved maximal elevation angles more similar to the impingement population, with lower angles of elevation on even the unaffected side compared to the healthy group: 115.1° [±25.3°] (BCP unaffected side, flexion) and 114.5° [±24.7°] (BCP affected side, flexion), 110.5° [±25.5°] (BCP unaffected side, abduction) and 107.0° [±24.8°] (BCP affected side, abduction) (as described in Table 44). Bilateral changes have been reported by Shamely et al. (2012), who identified scapular kinematic and muscle activation changes in both arms of unilateral BCP when compared to healthy participants. Compensatory changes on the unaffected arm (due to overuse, radiated pain and overflow effects of radiation or surgery), as well as prophylactic bilateral mastectomy (N=16 participants in the current study) may have altered the 'unaffected' side and resulted in bilateral changes.

Section 4.5.2.4 Kinematic changes between sides are small but meaningful

Despite modest magnitudes of kinematic differences (2.8° – 13.1°) found between sides in the current study, these differences are believed to be important. These differences are believed to be important because they are thought to demonstrate biological and clinical relevance, as well as mathematical (statistical) significance. Statistical significance is distinct from biological and clinical significance. Statistical significance is determined mathematically and describes the likelihood of a chance finding that will not hold up in future replications, but does not provide information regarding if that difference was biologically or clinically relevant. Biological significance determines if the differences identified have some biological affect. For example, the results indicated the affected limb demonstrated a 9° reduction in humeral ER in comparison to the contralateral limb: it is necessary to know if this reduction in ER would result in lower muscle activation of the infraspinatus. The results did in fact show synchronous reductions in infraspinatus muscle activation that coincided with the reductions in ER ROM. However, yet even another level needs to be examined as it should be determined if the magnitude of reductions in infraspinatus activity are important in clinical terms – such as if this lack of ER ROM, reduced muscle activation and subsequent reduction in muscle force disallows an individual from performing a routine functional task (eg. dressing, driving a manual shift vehicle). The remainder of this section and the following section will describe how the modest differences identified were associated with synchronous biological changes (EMG, strength, RDP) which could lead to basic functional impairment, and will refer to other literature that has reported similar magnitude changes interpreted as being clinically meaningful.

Some groups have defined impaired shoulder ROM as a loss of 20° compared to the unaffected limb (Box, Reul-Hirche, Bullock-Saxton, & Furnnival, 2002; Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004), however other groups have shown that much smaller changes are clinically meaningful. Ludewig & Cook (Ludewig & Cook, 2000) demonstrated

the clinical importance of modest angular kinematic differences, showing that 4° – 6° difference in scapular kinematics distinguished between healthy and impinged populations. Similarly, Ebaugh et al. (2005) demonstrated 4° - 5° of scapular kinematic differences were important in assessing the effects of muscle activity on kinematics; and Lukasiewicz et al. (1999) reported a 5° difference between healthy and impingement groups to be clinically meaningful. Borstad and Szuks (2012) reported a clinically meaningful increase of 11.5° protraction of breast cancer survivors post-surgery. The considerable variability seen in the current work is not surprising due to the wide variety of tasks performed and differing participant factors (e.g. cancer severities, treatments, timing). Shamley et al. (2012) indicated that larger movement deviations (and greater pain) were seen in scapulothoracic kinematics of survivors that had mastectomies compared to those with local wide excision. Shoulder kinematics are highly variable across even healthy individuals, and it has been demonstrated that several measures of variability as indicated by the standard deviations exceed 100% of the recorded ROM (Picco B. , 2012). Hall et al. (2011) reported considerable variability in range of humeral elevation and rotational angles during ADL tasks of elderly healthy adults (±30° variation in elevation angle and ±36° variation in humeral rotation angle), which was almost average to the variability observed of the BCP in the current study during similar tasks (elevation: ±21.8° (unaffected) and ±27.9° (affected); rotation: ±50.6° (unaffected) and ±55.3° (affected)). Significant differences in kinematics were found despite considerable variability, emphasizing their importance. Small magnitude differences found between sides of the BCP emphasize the need for quantification of 3-D scapulothoracic and humerothoracic kinematics, as these changes may be difficult to evaluate using clinical assessment tools.

Section 4.5.3 Interpretations of kinematic changes are enhanced when RPD scores, strength and EMG results are considered

The kinematic data corresponds synchronously to the RPD scores, strength and EMG results, aiding in the explanation of the dysfunctions identified. Total muscle effort was significantly greater on the

affected side during work tasks, and reductions in muscle-specific strength during tasks thought to functionally isolate muscles were seen on the affected infraspinatus, supraspinatus and upper trapezius. Weakness in the affected side infraspinatus (a primary ER) and supraspinatus (involved in abduction and ER) could result in reductions in humeral elevation angles, as well as reduced external rotation. Weakness or dysfunction of the affected side infraspinatus was reflected subjectively by a higher RPD score. Higher RPD scores during the posterior deltoid MVC testing position may also reflect weakness of the supraspinatus, infraspinatus and upper trapezius weakness as each of these muscles would also be recruited in the testing position of resisted humeral abduction and extension during external rotation. Total muscle effort was greatest during ROM-Reach tasks (when moment arms would be extended to allow for maximal reach), followed by work tasks, suggesting more effort was required of these muscles; or increased amplitudes were indicative of fatigue of damaged or deconditioned muscles. Since the work tasks involved greater moment arms during extended reaching and in some cases lifting external loads, these tasks were assumed to be more muscularly demanding compared to ADL and ROM-Rotate tasks. The iEMG was greater on the affected side posterior deltoid, upper trapezius and supraspinatus during all tasks – again suggesting that these muscles may have had some level of dysfunction (requiring them to activate to higher levels and produce more effort to result in the same movement as the unaffected side) or the response was indicative of compensatory changes (muscle was working at a greater extent because it was able to, and needed to compensate for other muscles that were less functional). Previous works have indicated that survivors experience decreased functional capacity, meaning they exert more effort relative to their maximal ability to perform usual activities, therefore leading to higher levels of fatigue (Mock, et al., 2005). Recently, the activation of the upper trapezius in breast cancer survivors during a functional writing task was found to be greater on the affected side, and greater in both sides compared to a control group (Galiano-Castillo, Fernandez-Lao, Cantarero-Villanueva, Fernandez-de-las-Penas, Menjon-Beltran, & Arroyo-Morales, 2011). Survivors with greater shoulder pain scores exhibited greater EMG amplitude within the affected upper trapezius, suggesting that increases in

EMG may be due to pain (resulting in muscle tension) or the fear of pain (Galiano-Castillo, Fernandez-Lao, Cantarero-Villanueva, Fernandez-de-las-Penas, Menjon-Beltran, & Arroyo-Morales, 2011). Patients with chronic neck pain exhibit increased upper trapezius and sternocleidomastoid muscle activation (Falla, Bilenkij, & Jull, 2004).

The serratus anterior was suspected to have some level of dysfunction due to the persistent presence of scapular protraction evident in both sides of the BCP, and the reduction of protraction demonstrated on the affected side. The serratus anterior is primarily responsible for scapular protraction and is active during anterior reaching (Moore, Dalley II, & Agur, 2014). Greater muscle activation levels (iEMG) of the serratus anterior were only evident during work tasks, which did involve some anterior reach tasks with and without external loads. Increased activity in the serratus anterior has been seen previously in affected shoulders of breast cancer survivors during scaption, compared to a healthy population (Shamley, Lascurain-Aguirrebena, Oskrochi, & Srinaganathan, 2012). Ebaugh et al. (2005) demonstrated the important role serratus and upper trapezius have in producing upward rotation of the scapula, especially during mid-range of arm elevation. In a healthy population, an increase in muscle activity resulted in more scapular retraction and more upward rotation when the arm was elevated (Ebaugh, McClure, & Karduna, 2005). These findings are consistent with the current study's results. The serratus was relied upon heavily during work groups tasks as these tasks involved several outstretched arm reaches with some external loads, whereas the serratus would be recruited less during ADL tasks when the hand was often kept close to the body. Although ROM-Reach tasks involved several outstretched arm reaches, no external loads were applied and it is assumed that the serratus was not relied upon to the same extent it was during work tasks. Scapular kinematics demonstrated that on average the survivor population was always in a state of scapular protraction (even on the unaffected side). The survivors may have exhibited some thoracic flexion (kyphosis or slouching) while seated: they were seated on a backless stool and often had their hands placed in front of them on a table. Thoracic kyphosis increases in healthy women

over the age of 40 years, and raises from 43° between 55 to 60 years of age to 52° in women 76 to 80 years old (Ensrud, Black, Harris, Ettinger, & Cummings, 1997). The current study's environmental seating factors, increased participant age, and also anteriorly directed task demands would encourage a tendency of thoracic slouching and a posture of scapular protraction – especially if the participant became weary during the duration of the study. Habitual scapular protraction even during standing can be resultant of every day anteriorly directed tasks (eg. sitting, driving, computer work). A portion of this population may also exhibit scapular protraction as a self-conscious response in attempt to hide the sometimes rather obvious results of mastectomy. Prosthetic breasts are available, but are expensive, cumbersome and uncomfortable. The affected side serratus anterior had to produce more effort (higher activation) and demonstrated a reduction in protraction range, which is suggestive of some level of serratus anterior dysfunction that could be a result of nerve damage. Forty eight of the fifty participants had axillary node dissections. The serratus anterior is supplied by the long thoracic nerve, which is susceptible to damage during axillary node dissections (Lauridsen, Torsleff, Husted, & Erichsen, 2000), and this potential damage could explain the dysfunction seen. Galiano-Castillo et al. (2011) also suggested that chemotherapy and/or neuropathy could induce muscle damage which would promote changes in muscle recruitment and result in alterations to exhibited motor strategies.

Loss of tissue and damage to the pectoralis major sternal muscle may explain reduced activation seen during all tasks. Reduction in pectoralis major activity has been seen previously in affected shoulders of breast cancer survivors during scaption, compared to a healthy population (Shamley, Lascurain-Aguirrebena, Oskrochi, & Srinaganathan, 2012). Dysfunction was expected in the pectoralis major sternal portion as it is highly susceptible to surgical and radiation exposure (Dalberg, Krawiec, & Sandelin, 2010; Sugden, Rezvani, Harrison, & Hughes, 1998) . Scar tissue and adhesions to the anterior chest wall can inhibit smooth muscle and tissue movement (Lauridsen, Overgaard, Overgaard, Hessov, & Cristiansen, 2008) and may dampen the electromyographic signal from the underlying muscle. Residual effects (surgical scarring, fibrosis) could affect movement

mechanics through tethering soft-tissue or inhibiting movement due to pain (Crosbie, et al., 2010). The pectoralis major is supplied by the pectoral nerve, which is also susceptible to damage during axillary node dissections (Lauridsen, Torsleff, Husted, & Erichsen, 2000), and may be a partial cause of the reduction in muscle activation seen in this muscle. The affected side pectoralis major and minor muscles were measured with MRI and found to be significantly smaller in size (mean muscle area) following various breast cancer treatments (Shamley, et al., 2007). Reduction in length of the pectoralis major may affect the patients' ability to reach up and elevate the arm (Shamley, et al., 2007). Dysfunction in the pectoralis major sternal muscle may explain reduced humerothoracic elevation angles. Further possible implications of the reduced capacity of the pectoralis major muscle were investigated in Study 4 of this thesis.

Section 4.5.4 Secondary changes associated with BCP

It is apparent that some dysfunction associated with the survivors is not due to direct surgical or radiation damage, but may be reflective of compensatory changes due to kinematic differences. Despite predominate anteriorly-directed treatments to the chest (ex. lumpectomies, mastectomies, anteriorly-directed radiation), posterior chest muscles also demonstrated dysfunction as evidenced by:

- weakness in the supraspinatus, infraspinatus, and upper trapezius;
- increased muscle effort required by posterior deltoid, upper trapezius and supraspinatus;
- reduced muscle contribution (decreased activation) demonstrated by the infraspinatus during ROM-Reach, ROM-Rotate and work tasks;
- elevated RPD scores during infraspinatus and posterior deltoid maximal testing.

Anterior chest wall damage and resultant scar tissue may be the factor that limits range of humeral external rotation and elevation angle. The survivors may be demonstrating a compensatory or protective posture of increased internal rotation, during which the humerus is forced into internal

rotation due to adhesions, or voluntarily held in that position to reduce external rotation motions that result in painful pulling on tender tissues due to surgical or radiation damaging effects. Lower angles of elevation and reduction in external rotation motions would mean that the humeral abductors, extensors and external rotators are relied upon less frequently, and therefore may become weak due to disuse. Further, postures involving more internal rotation and humeral elevation would mean the external rotator muscles are fully lengthened and at a non-optimal length (minimizing the overlap between actin and myosin filaments), disallowing maximal tension. This scenario could explain the weakness of the infraspinatus and reduced capacity of the infraspinatus (humeral ER), the weakness and increased muscle effort required of the supraspinatus (humeral abductor and ER), and the discomfort and increased effort required of the posterior deltoid. The upper trapezius acts to draw the scapula and clavicle backward, or raise the scapula by rotating the clavicle about the sternoclavicular joint (Johnson, Bogduk, Nowitzke, & House, 1994). The affected upper trapezius was weaker (produced less force), and demonstrated greater levels of activation during all tasks. Since all survivors demonstrated a consistent posture of scapular protraction, the upper trapezius dysfunction (weakness, increased effort demands) may also be a result of disuse, as it is recruited less to draw the scapula backward, but rather is often in a state of semi-eccentric contraction in a position of scapular protraction. Increased upper trapezius activity has been observed previously in the breast cancer population (Galiano-Castillo, Fernandez-Lao, Cantarero-Villanueva, Fernandez-de-las-Penas, Menjon-Beltran, & Arroyo-Morales, 2011; Shamley, Lascurain-Aguirrebena, Oskrochi, & Srinaganathan, 2012), as well as in patients with impingement (Ludewig & Cook, 2000) and adhesive capsulitis (Lin, Wu, Wang, & Chen, 2005). Shamley et al. (2007) reported ‘primary’ expected changes in the pectoralis muscle and serratus anterior due to their location in the field of surgery and radiation, but also recognized ‘secondary effects’ in muscles outside the line of surgery or radiation (reduced upper trapezius and rhomboid activity) that persist for years and are associated with an inability to perform pain-free functional tasks. Shamley et al. (2007) recommended that

exercise programs should include postural correction and education of potential long-term effects, as well as ROM programs.

Section 4.5.5 Caution with generalization of results and recommendations for future works

Due to the heterogeneity of the population understudy, caution must be used in interpretation and generalization of findings. The survivors in the current study reported similar, but slightly higher levels of disability than those recorded previously. Crosbie et al. (2010) studied survivors with mastectomies who reported DASH scores of 10.12 (±9.39) – 12.97 (±11.60) compared to a healthy control score of 3.29 (± 4.75), whereas the BCP from the current study reported scores of 19 (±18). The 50 survivors in the current study reported very similar FACT-B scores (114 (±20)) to the baseline FACT-B scores of 377 survivors reported by Vallance (2007) (115.1 – 117.5 (±17.3 – 19.7)). Increases in total muscle effort were lightly correlated with increased QuickDASH scores (higher disability) and lower FACT-B scores (poorer quality of life), demonstrating that these subjective measures are not sufficient in identifying physical dysfunction, and confirming the need for further quantitative analysis of survivor dysfunction. It is not surprising that a quantitative measure of physical function (TME) was not strongly related to a multifaceted measure of disability or quality of life which considered many other parameters (e.g. social, emotional, relationship) besides physical function.

Potential treatment effects, including possible bilateral changes, may have complicated results and compromised interpretation of findings. Hand dominance was not controlled for, nor was side affected by cancer, and it is possible these factors may have had an effect on kinematics and muscle activation. Shamley et al. (2014) reported the BCP demonstrated a different movement dysfunction depending on whether the left or right shoulder was affected, and concluded left affected wide local excision and/or mastectomy patients should be considered high risk for developing shoulder complications after treatment. Due to the sample size and wide variation of treatments received it was not possible to group our participants into treatment groups (nor was it the proposed purpose of

this work). By recruiting a much larger sample size, future works could examine specific treatment effects. The results of this study provide a broad sense of capability and dysfunction of survivors in general, and are not specific to treatments received. In the current study, the affected side was compared to the unaffected 'healthy' limb as has been done previously (Hack, Cohen, Katz, Robson, & Goss, 1999; Kuehn, et al., 2000; Lauridsen, Torsleff, Husted, & Erichsen, 2000; Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004; Shamley, Srinaganathan, Oskrochi, Lascurain-Aguirrebena, & Sugden, 2009), and as a result it is possible that some dysfunction could go unrecognized. In the current population under study there were 16 survivors that received bilateral (prophylactic) mastectomy, and it is plausible that some dysfunction would have occurred on the unaffected side of these individuals. Shamley et al. (2012) demonstrated altered muscle activity and shoulder kinematics on both sides of unilateral breast cancer survivors compared to healthy populations. It is possible that presence of pain may have limited maximal voluntary contractions and therefore affected the normalization of EMG data: lower maximums could be associated with higher muscle activation levels. The classification of tasks into groups was useful to ease interpretation and provide a general overview of survivor capacity, however this division may have diminished findings by failing to recognize differences between tasks within a group. The ROM-Reach and ADL task classifications were similar to Hall et al. (2011). Some changes suggestive of dysfunction (increased TME, iEMG and kinematic differences) were more obvious within the ROM-Reach and work tasks groups during which there was assumed to be more muscularly demanding tasks since it involved extended moment arms (maximal reaches) and lifting external loads. Further works should continue to examine a broader range of functional tasks with varied reach distances and external loads. Future works should also expand the survivor sample size, narrow (or match groups based by) disease characteristics and treatment variability, and compare results with an age-matched healthy population, as well as between sides. Animal studies may be useful in future investigations of specific treatment effects and efficacy of proposed rehabilitation (eg. irradiate tissue, record

muscular and ROM changes before and after exercise treatments), and would be useful to determine if EMG is an accurate reflection of muscle changes.

Section 4.5.6 Summary of study contributions and recommendations for the treatment

This investigation has produced the most comprehensive collection of 3D humerothoracic and scapulothoracic kinematics and electromyographic recordings for the BCP. Details regarding physical function during a wide variety of exertions that have not yet been examined in the literature have been provided, and the changes discovered reinforce the need for further laboratory examinations as these differences would be difficult to assess in a clinical examination. Prior to this study, humerothoracic kinematics in a breast cancer population had not been examined, and scapulothoracic kinematics had been examined only during scaption (Borstad & Szucs, 2012; Crosbie, et al., 2010; Shamley, Srinaganathan, Oskrochi, Lascurain-Aguirrebena, & Sugden, 2009), flexion and abduction (Crosbie, et al., 2010). This study provides details regarding survivor capability and dysfunction that have never been examined before, and further research must continue to allow for generalizability of results and population-specific recommendations. In general, the results demonstrate the need to focus on secondary changes following breast cancer treatment. Although muscles within the field of surgery and radiation are affected (pectoralis major and serratus), additional long-lasting morbidity continues in muscles outside this field. Despite the need for strengthening, stretching and ROM of anterior chest muscles, posterior shoulder muscles should not be ignored. In particular, therapies should focus on postural control (scapular retraction), strengthening of the posterior rotator cuff and upper trapezius muscles, and encourage movements involving external rotation.

Section 4.5.7 Study contribution to science and health

This study has contributed to science by furthering the knowledge that is currently understood about breast cancer survivor muscle activation, strength and kinematic patterns during ROM, ADL and work tasks and how these relate to QoL and disability. This investigation has contributed to health

advancement of the breast cancer population by accurately quantifying and assessing physical capability and dysfunction during a wide range of functional tasks – a feat which previous to this work had not yet been performed. Accurate documentation of physical capability and dysfunction is the first step towards developing targeted treatment and preventative strategies for this disabled population.

Chapter 5 Study 2 –Empirical quantification of internal and external rotation muscular co-activation in healthy shoulders

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Section 5.1 Introduction

Shoulder pain is common in industrial workers, but using high resolution laboratory techniques to measure shoulder loading (to estimate risk of injury) is not always feasible in occupational environments. Instead, mathematical biomechanical models are often used to replicate exposures and estimate shoulder joint and tissue loads. However, in making these predictions, the models frequently indicate that antagonistic muscles are inactive or underestimate their contribution (Collins, 1995; Dickerson, 2008; Hughes & Chaffin, 1988; Zajac & Gordon, 1989). Optimization procedures often involve simplified assumptions, such that the body activates muscles specifically according to the minimum total muscle stress (Crowninshield & Brand, 1981). Using this assumption, antagonistic contraction is mathematically counterproductive (as it generally produces moments that fail to contribute to the net joint moment, but increase physiological cost) and is therefore discouraged by the optimization algorithms. By mischaracterizing the physiologically known co-activation of opposing muscles, these models underestimate individual and corporate muscle activity predictions, which cascades into low estimates of joint contact forces.

Though previous research into documenting co-activation in human joints exists, few efforts have focused on the shoulder. Co-activation has been measured at the ankle (Granata, Wilson, Massimini, & Gabriel, 2004), knee (Kellis, Arabatzi, & Papadopoulos, 2003; Kingma, Aalbersberg, & van Dieen, 2004), trunk (Lee, Rogers, & Granata, 2006) and elbow (Brookham, Middlebrook, Grewal, & Dickerson, 2011; Doheny, Lowery, Fitzpatrick, & O'Malley, 2008; Praagman, Chadwick, van der Helm, & Veeger, 2010; Solomonow, Guzzi, Baratta, Shoji, & D'Ambrosia, 1986). Shoulder co-activation relationships need to be quantified so that they can be included in biomechanical

models to increase physiological realism and promote more accurate model predictions. Further, the definition of a data base of normative co-activation behaviours could be used to compare against injury population groups. This comparison may enhance current clinical assessments of muscular dysfunction and inform more effective therapeutic and preventative strategies.

Physiological cross-sectional area (PCSA) should arguably be considered in co-activation calculations to account for known differences in muscle size. Previous examinations of co-activation at the knee and elbow have used linear enveloped electromyography (EMG) to define co-activation as a ratio of the contribution of one group of muscles activation to the total of that group of muscles activation combined with the activation of a defined group of antagonistic muscles (Brookham, Middlebrook, Grewal, & Dickerson, 2011; Kellis, Arabatzi, & Papadopoulos, 2003). In this traditional non-weighted approach, muscles are equally weighted with respect to contributions to co-activation. However, muscles at the shoulder vary greatly in size, and therefore, may vary greatly in their contribution to activation. PCSA is a measure of the number of sarcomeres in parallel with the angle of pull of the muscles (Winter, 2009). The PCSA of the rotator cuff and shoulder muscles that individually contribute to internal and external rotation vary greatly. Previous authors have reported through the direct measurements of PCSA of humeral rotator muscles, that these values can range from less than 2 cm^2 (teres minor) to greater than 13 cm^2 (subscapularis) (Veeger, van der Helm, van der woude, Pronk, & Rozendal, 1991). Shoulder co-activation descriptions should consider muscle specific PCSAs to prevent contribution biasing of muscles in activation equations, by allowing for quantification of scaled muscle contributions.

The primary purpose of this study was to quantify the co-activation relationships of humeral internal and external rotators in young healthy adults during a subset of isometric exertions varying in intensity and in posture (humeral abduction and rotation angles). These co-activation relationships were defined using traditional and novel definitions. First, co-activation was defined using a non-weighted co-activation index ratio similar to those methods of Kellis et al. (2003) and Brookham et al. (2011). Secondly, co-activation was defined using a novel PCSA-weighted co-activation index

ratio. It was hypothesized that the novel PCSA-weighted co-activation prediction models will better represent empirically measured co-activation (with predictions yielding higher r^2 values) compared to the traditional non-weighted co-activation prediction models.

Secondary (unpublished) study purpose:

[***The secondary purpose and results of this study have not yet been published, and is not part of the*** (Brookham & Dickerson, 2014) ***publication. The results and discussion have been included in separate sections.]***

A secondary purpose of this study was to determine if the co-activation relationships defined from a subset of exertions can be extrapolated to other additional postures and intensities. It was hypothesized that the co-activation relationship determined for a subset of postures (original data set) would be appropriately extrapolated to a unique subset of exertions (extrapolated data set). Recent work has demonstrated that extrapolation of the co-activation relationships for elbow flexion and extension defined by Brookham et al. (2011) to a subset of novel exertions of increased intensity and different postures is appropriate (Middlebrook, Brookham, & Dickerson, 2013).

Section 5.2 Methods

Twenty healthy participants performed 82 isometric humeral rotation exertions, half of which were internal and half of which were external rotations, at various shoulder postures and work intensities. Intramuscular electrodes were inserted into the rotator cuff muscles, and surface electrodes were placed over surrounding shoulder musculature. Electromyographic data were used to calculate non-weighted and PCSA-weighted co-activation index ratios, and the influence of arm posture, load and subject anthropometric factors were assessed through multiple regression analyses.

Section 5.2.1 Participants

Participants included 20 (10 male, 10 female) healthy, right-handed individuals (mean [range]: age (years) 22 [18-32], stature (m) 1.7 [1.6-1.8]; weight (kg) 66.6 [48.5-85.0]) which were recruited from

a university population. Participants were excluded from the study if they had any of the following known health disorders: blood clotting disorders, HIV, Hepatitis B or C, chronic (lasting more than 6 months) or acute (within the past 6 months) shoulder, elbow, and/or wrist injury, allergies to isopropyl alcohol, latex or nickel. Participants gave informed consent before participation in the study. This study received institutional ethics clearance. Participants received $30 CAD remuneration for completing this study.

Section 5.2.2 Surface electromyography

In preparation for the surface electrodes, the skin overlying the muscle of interest was shaved of hair and cleansed with isopropyl alcohol. Disposable bipolar Ag/AgCl surface electrodes (Product #272, Noraxon, USA, Inc., Arizona, USA) were placed on the right side over the supraspinatus, infraspinatus, pectoralis major (clavicular and sternal insertions), posterior deltoid and latissimus dorsi (placements are described in Appendix D). Surface supraspinatus and infraspinatus data were only used to replace their respective indwelling signals when these latter signals were compromised due to artifact, as is described in Section 5.3.1. A reference electrode was placed over the sternum, just inferior to the suprasternal notch. A wireless Noraxon TeleMyo 4200T G2 (Noraxon 2 USA Inc., Arizona, USA) sampled EMG channels at 4000 Hz. This system had 16-bit resolution on all analog inputs with a band-pass filter from 10-1500 Hz, an input impedance > 100 MΩ, a common mode rejection ratio > 100 dB and a base gain of 500.

Section 5.2.3 Intramuscular electromyography

In preparation for intramuscular electrode insertion, hair surrounding the area of the muscle of interest was shaved off, and the skin was cleansed with isopropyl alcohol. Four intramuscular electrodes were inserted into one of each of the rotator cuff muscles on the right side: supraspinatus, infraspinatus, teres minor and subscapularis. Sterile single-use hypodermic needles of 33 mm in length and 25 gauge (~0.55 mm) (Product # 000-318-30, Motion Lab Systems, Inc., Baton Rouge, LA) were inserted into the supraspinatus, teres minor and infraspinatus using published instructions

from Geiringer (1999). Sterile single-use hypodermic needles of 50 mm length and 25 gauge (Product # 000-318-50, Motion Lab Systems, Inc., Baton Rouge, LA) were inserted into the subscapularis using published instructions from Nemeth et al., (1990). Each hypothermic needle contained two very thin wires (0.051 x 200 mm) which were insulated and hooked at the ends with bare-wire terminations. Inter-electrode distance was approximately 1mm. The supraspinatus and infraspinatus indwelling electrodes were inserted between (but not under) the bipolar placements of the surface electrodes. The relationship between the surface and indwelling electrode placements is demonstrated in Figure 33. The wires remained in the muscle for the duration of the study, and then were removed with a quick tug. A wireless Noraxon TeleMyo 4200T G2 (Noraxon 2 USA Inc., Arizona, USA) sampled EMG channels at 4000 Hz. Further detail regarding insertion procedures are listed in Appendix A.

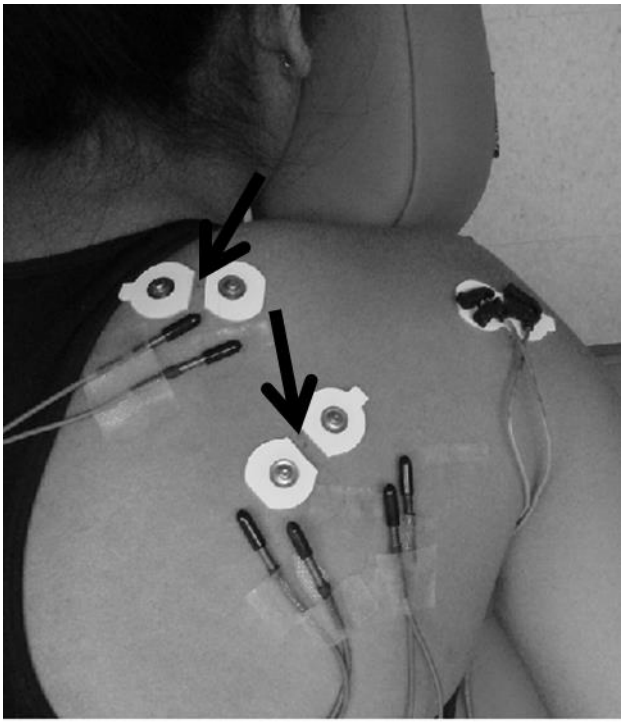

Figure 33 The indwelling electrodes of supraspinatus and infraspinatus were placed in between (but not under) their respective bipolar surface arrangements. (Indwelling electrode placements are highlighted by the arrows)

Section 5.2.4 Pre-experimental protocol

Prior to testing, anthropometric measurements were recorded and the participants exerted maximal voluntary forces (MVF) during isometric humeral internal and external rotation (3 sets each) while standing with the arm at the side and the elbow flexed to 90°. MVF were performed against a tri-axial force transducer which sampled at 1024 Hz with a gain of 1000 (MC3-6-500, Advanced Mechanical Technology Inc., Watertown, Massachusetts). If greater than 5% difference was seen between the 3 sets of MVFs, the MVFs were repeated. MVFs were 6 s in duration, and 2 min of rest was given between MVFs. An average of the three resultant force trials for each exertion direction was defined as the final MVF. The final MVFs were used to calculate the specific target force intensities each participant exerted in each trial (ranging from 10% - 80% MVF). A custom-made program (Labview 8.5, National Instruments Inc., Texas, USA) displayed visual force feedback to participants during experimental trials (Figure 34). Participants were given opportunity to practice achieving appropriate forces using the visual feedback before experimental trials began. Muscle-specific maximal voluntary contractions (MVCs) were performed against manual resistance as described in Table 23. MVCs were 6s in duration and participants were asked to ramp up to their maximal strength and maintain it from seconds 2 – 4, and then relax. MVCs were repeated 3 times and the peak from a 500ms moving window average of linear enveloped data was used to normalize respective linear enveloped EMG channels.

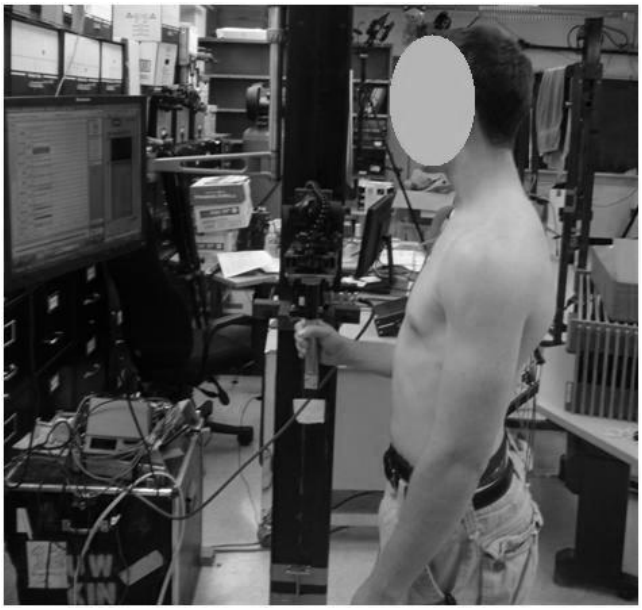

Figure 34 A participant grasps the handle attached to the tri-axial force cube and exerts a rotational force - meeting a target displayed by visual force feedback on the computer monitor

Table 23 Maximal voluntary contraction testing protocol

Muscle	Test Contraction:
Supraspinatus	Subject is standing. Shoulder is abducted to 5° with elbow extended (thumb pointing up). Abduction is resisted.
Infraspinatus & Teres Minor	Subject is standing. Arm is at side with elbow bent to 90°. External rotation of the arm is resisted.
Subscapularis	Subject is standing. Arm is at side with elbow bent to 90°. Internal rotation of the arm is resisted.
Latissimus Dorsi	Subject is sitting with shoulder horizontally abducted and externally rotated to 90° and elbow flexed to 90° (fingers point to ceiling). Shoulder adduction is resisted.
Pectoralis Major (sternal insertion)	Subject is sitting with shoulder horizontally abducted and externally rotated to 90° and elbow flexed to 90° (fingers point to ceiling). Shoulder horizontal adduction is resisted.
Posterior Deltoid	Subject is sitting. Resistance provided to shoulder extension when shoulder is abducted to 90° and externally rotated, with elbow flexed to 90° (fingers point to ceiling).
Pectoralis Major (clavicular insertion)	Subject is sitting with elbow and shoulder flexed to 90°, and is horizontally adducting and flexing their shoulder. Resistance is provided (from above) proximal to elbow joint in a downward and outward direction.

Section 5.2.5 Experimental protocol

Each participant performed a total of 82 trials of isometric shoulder internal or external rotation exertions at varying intensities (10%-80% MVF), humeral rotation angles (absolute angles relative to a vertical plane through the humerus: 0°, -45°, 45°) and humeral abduction angles (elevation angles in the frontal plane: 0°, 45°, 90°) with the elbow flexed to 90°, as described in Table 24 and Table 25. In an attempt to reduce the possibility of contribution from the trunk or other muscles, the participants were instructed to stand erect with both feet flat on the floor, not to bend or lean, but only perform humeral internal or external rotation. Test trials were of 6 s duration. A goniometer was used to verify postures. The wrist was maintained in a neutral posture during all exertions, facilitated by a fully moveable handle that was locked into position and attached to a tri-axial force transducer (MC3-6-500, Advanced Mechanical Technology Inc., Watertown, Massachusetts). Fifty four trials were designated as 'original' and served as a basis to create the co-activation multiple regression prediction models (*primary study purpose)* (Table 24). The remaining 28 trials were considered 'extrapolated' postural data, and were used to assess if the co-activation relationship (defined from the original data set) could be generalized to the extrapolated data set *(secondary study purpose)* (Table 25). The order of exertions was randomized. Force and EMG were collected simultaneously with a trigger during all MVCs and test trials. The entire study protocol lasted approximately 2.5 hours. A flow chart depicting study procedures is depicted in Figure 35.

Table 24 Description of test exertions of the original data set. Test 1-27 represent external rotation type exertions. These 27 postures are repeated and performed during internal rotation exertions for tests 28-54 (not shown). Co-activation relationships were determined using data from these exertions.

Test Number	Exertion Type (ER= external rotation; IR= internal rotation)	Humeral Abduction (degrees from vertical axis)	Humeral Rotation (degrees)	Intensity (% of MVF)
1	ER	0	0	20
2	ER	45	0	20
3	ER	90	0	20
4	ER	0	-45IR	20
5	ER	45	-45IR	20
6	ER	90	-45IR	20
7	ER	0	+45ER	20
8	ER	45	+45ER	20
9	ER	90	+45ER	20
10	ER	0	0	40
11	ER	45	0	40
12	ER	90	0	40
13	ER	0	-45IR	40
14	ER	45	-45IR	40
15	ER	90	-45IR	40
16	ER	0	+45ER	40
17	ER	45	+45ER	40
18	ER	90	+45ER	40
19	ER	0	0	60
20	ER	45	0	60
21	ER	90	0	60
22	ER	0	-45IR	60
23	ER	45	-45IR	60
24	ER	90	-45IR	60
25	ER	0	+45ER	60
26	ER	45	+45ER	60
27	ER	90	+45ER	60
Tests 28-54: Repeat above abduction, rotation and intensity combinations for IR type exertions for the remainder of Original Data Set Exertions.				

Table 25 Description of test exertions from extrapolated data set. The generalizability of the defined co-activation relationships were tested using data from these exertions.

Test Number	Exertion Type (ER= external rotation; IR= internal rotation)	Humeral Abduction (degrees from vertical axis)	Humeral Rotation (degrees)	Intensity (% of MVF)
55	ER	0	0	10
56	ER	0	0	30
57	ER	0	0	50
58	IR	0	0	10
59	IR	0	0	30
60	IR	0	0	50
61	ER	45	0	10
62	ER	45	0	30
63	ER	45	0	50
64	IR	45	0	10
65	IR	45	0	30
66	IR	45	0	50
67	ER	90	0	10
68	ER	90	0	30
69	ER	90	0	50
70	IR	90	0	10
71	IR	90	0	30
72	IR	90	0	50
73	IR	0	0	80
74	ER	0	0	80
75	IR	135	0	10
76	IR	135	0	20
77	IR	135	0	30
78	IR	135	0	40
79	ER	135	0	10
80	ER	135	0	20
81	ER	135	0	30
82	ER	135	0	40

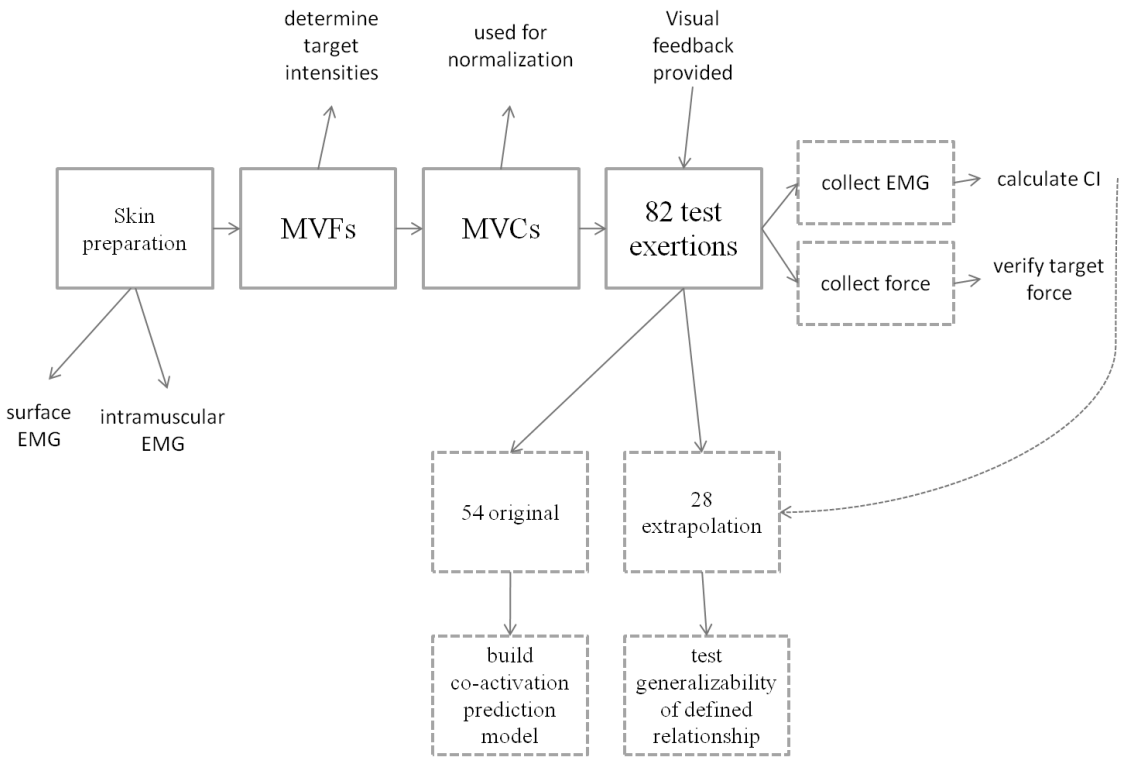

Figure 35 Flow-chart of experimental procedures for Study 2. Participants were prepared for surface and intramuscular EMG, and maximal voluntary force exertions (MVFs) and maximal voluntary contractions (MVCs) were performed, followed by the 82 test exertions. Co-activation prediction models were created from data obtained during the 54 original exertions, and these relationships were tested for generalizability using the 28 extrapolated test exertions.

Section 5.3 Analysis

Co-activation ratios were calculated, EMG was linear enveloped and normalized and force was filtered and converted to newtons. All data processing was performed in MATLAB™ R2010a (Mathworks, USA). Co-activation ratios were inputted into JMP 11® (SAS Institute Inc., Cary, NC) where statistical analyses were performed to build co-activation prediction models.

Section 5.3.1 Data processing

Force was filtered with a dual-pass Butterworth low pass filter (LPF) at a cutoff of 3 Hz. Force (collected in volts) was converted to Newtons using a shunt calibration. The resultant force was calculated using Equation 15. Raw EMG was high pass filtered (Fc 30Hz as recommended by Drake & Callaghan (2006)) to remove any heart rate or motion artifact. High pass filtered EMG was linear

enveloped with a single-pass Butterworth LPF (Fc 2.5Hz, which was confirmed with residual analysis). A 500ms moving window average of linear enveloped MVC trials were calculated and the highest moving window average from the three sets (for each specific muscle and individual) was defined as maximal percent activation. Linear enveloped channels within test trials were normalized to their respective MVC. Integrated and normalized EMG (between 2 - 4 s of each trial) was used in the calculation of a non-weighted co-activation index ($CI_{non\text{-}wght}$) and a PCSA-weighted co-activation index (CI_{PCSA}) (Equation 16 & Equation 17, respectively). The CI_{PCSA} were calculated for all trials and participants in the original data set (n = 1080); and the $CI_{non\text{-}wght}$ were calculated for all trials and participants in both the original and extrapolation data sets (n = 1640). PCSA data used (Table 26) in Equation 17 were reported by Veeger et al. (1991), except for the pectoralis major, which was reported by van der Helm et al. (1994).

Equation 15 Resultant force calculation

$$\text{Resultant Force} = \sqrt{(Force_x)^2 + (Force_y)^2 + (Force_z)^2}$$

Equation 16 Non-weighted co-activation index calculation. Where E = linear enveloped and normalized EMG; $R_{1\text{-}4}$ = Internal rotators: subscapularis, pectoralis major clavicular / sternal heads and latissimus dorsi, respectively; $R_{5\text{-}7}$ = External rotators: infraspinatus, posterior deltoid and supraspinatus, respectively.

$$CI_{non-wght} = \frac{\int_{t1}^{t3} \left[\frac{\sum_{i=1}^{4} E_{R_i}}{4}\right](t)dt}{\int_{t1}^{t3} \left[\left[\frac{\sum_{i=1}^{4} E_{R_i}}{4}\right] + \left[\frac{\sum_{i=5}^{7} E_{R_i}}{3}\right]\right](t)dt}$$

Equation 17 PCSA-weighted co-activation index calculation. Where E = linear enveloped and normalized EMG; $R_{1\text{-}4}$ = Internal rotators: subscapularis, pectoralis major clavicular / sternal heads and latissimus dorsi, respectively; $R_{5\text{-}7}$ = External rotators: infraspinatus, posterior deltoid and supraspinatus, respectively. PCSA is physiological cross-sectional area of muscle i.

$$CI_{PCSA} = \frac{\int_{t1}^{t3} \left[\frac{\sum_{i=1}^{4} E_{R_i} \cdot PCSA_i}{\sum_{i=1}^{4} PCSA_i}\right](t)dt}{\int_{t1}^{t3} \left[\left[\frac{\sum_{i=1}^{4} E_{R_i} \cdot PCSA_i}{\sum_{i=1}^{4} PCSA_i}\right] + \left[\frac{\sum_{i=5}^{7} E_{R_i} \cdot PCSA_i}{\sum_{i=5}^{7} PCSA_i}\right]\right](t)dt}$$

Table 26 PCSA values used as inputs into the PCSA-weighted co-activation index calculations

Muscle	PCSA (cm^2)
Subscapularis	13.51
Pectoralis major (clavicular insertion)	3.55
Pectoralis major (sternal insertion)	8.68
Latissimus dorsi	8.64
Infraspinatus	9.51
Posterior deltoid	13.51
Supraspinatus	5.21

The $CI_{non\text{-}wght}$ provides a relative measure of internal rotation (IR) contribution to total activation (IR and external rotation (ER) activation) about the shoulder. The CI_{PCSA} also provides a relative measure of IR activation to total activation about the shoulder, but each muscle's contribution to co-activation is limited to its respective PCSA. A CI (either non-weighted or PCSA-weighted) of 0 indicates no co-activation (IRs are not activated); a CI of 0.5 indicates full co-activation (both IRs and ERs are activated equally relative to maximum) and a CI of 1.0 indicates no co-activation (the ERs are not activated). Some trials were excluded from analysis due to EMG artifact or errors in target force levels. All EMG trials were visually inspected for motion artifact, which was determined by a large spike in EMG amplitude. Channels determined to have artifact were removed from the CI ratios, and the denominators of such ratios were scaled accordingly to reflect this removal. Trials with supraspinatus or infraspinatus wire artifact were replaced with surrogate surface electrode data. The actual force produced by each participant was compared to the target force for each trial. This comparison ensured removal of trials containing error >5% MVF or >5 N difference between actual and target force. Any trials exceeding this error were removed from further analysis and therefore a CI was not calculated for such trials.

Section 5.3.2 Statistical analysis pertaining to the original data set (*primary study purpose*)

Statistical analyses were performed in JMP 11® (SAS Institute Inc., Cary, NC). Potential predictor variables (height, weight, upper arm length, lower arm length, age, task intensity (%MVF), humeral

abduction angle, humeral rotation angle, MVF and gender) were analyzed for inter-correlations and redundant variables (variables highly correlated (r>0.7)) were removed. Preliminary stepwise multiple linear regression analysis determined which predictors variables should be included in each of the co-activation prediction models. The stepwise direction was mixed (forward and back) with a stopping rule p-value threshold of 0.25 to enter and 0.25 to leave. Prediction models were developed for non-weighted and PCSA-weighted CIs, separately for both IR and ER type exertions ($CI_{non\text{-}wght,\ IR}$, $CI_{non\text{-}wght,\ ER}$, $CI_{PCSA,\ IR}$, and $CI_{PCSA,\ ER}$) for the original CI data and the extrapolation data sets using a repeated measures analysis of variance. In the repeated measures multiple analysis of variance test (ANOVA) the $CI_{non\text{-}wght}$ and CI_{PCSA} were considered dependent variables, and the independent variables included all predictor variables identified as significant during stepwise multiple linear regression analysis. Both main and interaction effects were considered.

Section 5.3.3 Results pertaining to the original data set (*primary study purpose*):

The most parsimonious models for non-weighted co-activation ($CI_{non\text{-}wght}$) and PCSA-weighted co-activation (CI_{PCSA}) during humeral IR exertions were (Equation 18 & Equation 19):

Equation 18 Non-weighted co-activation index calculation for internal rotation exertions. Where *humeral abduction* angle is in degrees, and *intensity* is individual %MVF; whole model p value <0.0001; $r^2 = 0.70$; independent variable p values = <0.0001, <0.0001, respectively; independent variable F ratios = 757.99, 131.34, respectively.

$$CI_{non-wght,IR} = 0.70 - [0.0036 \cdot humeral\ abduction] + [0.0034 \cdot intensity]$$

Equation 19 PSCA-weighted co-activation index calculation for internal rotation exertions. Where *humeral abduction* angle is in degrees, and *intensity* is individual %MVF; whole model p value <0.0001; $r^2 = 0.62$; independent variable p values = <0.0001, <0.0001, respectively; independent variable F ratios = 467.49, 106.11, respectively.

$$CI_{PCSA,IR} = 0.72 - [0.0032 \cdot humeral\ abduction] + [0.0034 \cdot intensity]$$

The most parsimonious models for non-weighted co-activation ($CI_{non\text{-}wght}$) and PCSA-weighted co-activation (CI_{PCSA}) during humeral ER exertions were (Equation 20 & Equation 21):

Equation 20 Non-weighted co-activation index calculation for external rotation exertions. Where *humeral abduction* angle is in degrees; whole model p value <0.0001; r^2 = 0.35; independent variable p value = <0.0001; independent variable F ratio = 22.09.

$$CI_{non-wght,ER} = 0.22 - [0.00047 \cdot humeral\ abduction]$$

Equation 21 PCSA-weighted co-activation index calculation for external rotation exertions. Where *humeral abduction* angle is in degrees, and *intensity* is individual %MVF; whole model p value <0.0001; r^2 = 0.42; independent variable p values = <0.0001, 0.0205, respectively; independent variable F ratios = 23.61, 5.40, respectively.

$$CI_{PSCA,ER} = 0.29 - [0.00060 \cdot humeral\ abduction] - [0.00064 \cdot intensity]$$

Analyses of interaction effects were performed, but inclusion of these effects provided no or little improvement in explained variance. Specifically, the inclusion of these interactions had the following effects when compared to inclusion of only main effects:

- For $CI_{non\text{-}wght}$ during IR exertions: interaction model explained 1% more variance (r^2 = 0.71).
- For CI_{PCSA} during IR exertions: no interactions were significant.
- For $CI_{non\text{-}wght}$ during ER exertions: interaction model explained 2% more variance (r^2 = 0.37).
- For CI_{PCSA} during ER exertions: interaction models explained 1% less variance (r^2 = 0.41).

Hence, the authors chose prediction equations that included only main effects to enhance parsimony and to improve the ease of application of these relationships during future modelling employments.

Table 27 outlines the channels and muscles that were excluded from analysis due to signal artifact. The teres minor EMG was excluded from this study due to the unstable nature of the signal obtained (it was not included in any CI calculations). The teres minor signals were often compromised by artifact (17% of trials), which may be attributed to wire movement during changes of arm postures required during the experimental protocol, as well as difficulty landmarking and inserting the electrode into such a thin small muscle moving along the lateral border of the scapula.

Since we obtained good signal from the infraspinatus, we felt we had adequate representation of the humeral external rotators and felt it most prudent to exclude teres minor from the analysis.

Table 27 Channels removed due to motion artifact in EMG

	Supraspinatus (Wire)	Infraspinatus (Wire)	Teres Minor (Wire)	Subscapularis (Wire)	Pectoralis Major Sternal (Surface)
# trials removed	53	42	179	115	1
Percentage of trials removed (Total = 1080)	5%	4%	17%	11%	0.09%
A total of 15 trials (1.4% of total trials) were removed due to erroneous force values.					

Section 5.3.4 Discussion pertaining to the original data set (primary study purpose)

Co-activation relationships (using both traditional non-weighted and PCSA-weighted approaches) of humeral rotators were defined for a subset of isometric exertions varying in intensity and posture. Regression models were able to predict these co-activation relationships well during humeral IR exertions, but only moderately well during humeral ER exertions. In partial support of the hypothesis, when compared to non-weighted co-activation predictions, PCSA-weighted predictions were modestly more representative of empirically measured co-activation only during ER exertions.

The intercepts of each regression equation demonstrate the overall behavior of muscle activation during IR and ER exertions. The intercepts of both $CI_{non\text{-}wght}$ and CI_{PCSA} are larger (0.70 – 0.72) during IR exertions than those during ER exertions (0.22- 0.29). Recall that balanced co-activation between the IR and ER muscles occurs at a CI of 0.50. The magnitudes of these intercepts are intuitive in that they indicate an increase in activation of the IR musculature during IR exertions, and an increase in activation of the ER muscles during ER exertions. It is important to recall that the lowest intensity upon which these models were built was 20% MVC, and assuming for simplicity that humeral abduction is at 0°, this intensity would reduce the CI_{PCSA} bias to 0.277 during ER

exertions. Greater intensities would further reduce this bias, indicating increased activation of the ER muscles during ER exertions. The relative magnitude of the intercepts compared to the coefficients is large, indicating model stability. Due to small magnitudes of the coefficients on the other modifying factors, changes in humeral abduction angle and task intensity have modest effects on CI predictions and importantly do not substantially modify the overall behavior of the model.

The explanations of variance of co-activation relationships during ER exertions were less comprehensive than those during IR exertions. This reduction of r^2 may be indicative of more variable muscle activation strategies occurring during ER exertions, as the body attempts to preserve glenohumeral joint stability. Glenohumeral dislocations are most commonly anterior, occurring when the humerus is abducted and externally rotated. The dynamic stabilizing roles that muscles play change as posture is adjusted. McKernan et al (1990) demonstrated that the subscapularis is an important anterior shoulder stabilizer when the humerus is abducted and at neutral rotation, but that it becomes less important when the humerus externally rotates. Lee et al (2000) found that in the mid-range of motion (neutral rotation with the humerus positioned at 60° abduction and 45° extension), the supraspinatus and subscapularis provided more stability than the other rotator cuff muscles, but at end ranges of motion (90° external rotation with the humerus positioned at 60° abduction and 45° extension), the subscapularis, infraspinatus and teres minor provided more stability than the supraspinatus. Ligaments are tightened at end ranges of motion, which can provide further passive stabilization and alter the surrounding muscle activation requirements. During external rotation, the inferior ligament is tightened and upward elevation is limited (Itoi, Morrey, & An, 2009). Differing from the IR exertions, the ER exertions of this current study would be more representative of end range of motion postures, during which passive ligament constraints may attribute to joint stability. Marked variability of joint laxity has been noted among subjects with healthy shoulders (Harryman, Sidles, Harris, & Matsen, 1992). The addition of passive stability constraints (their contribution variable due to inter-subject differences in laxity) to dynamic (muscular) constraints, could affect the

both the selection and magnitude of muscle-specific control. Therefore, during ER exertions (especially involving levels of humeral abduction when the humerus is more susceptible to glenohumeral dislocation), variability of muscle activation strategies may be large causing co-activation to be less predictable.

Initially it was hypothesized that PCSA-weighted prediction equations (compared to non-weighted) would better represent the empirically measured co-activation, however this was only the case during ER exertions (7% more explained variance, although the explained variance remained moderate). The inclusion of PCSA weightings lowered the explained variance by 8% in IR exertions (although the variance was explained well). The PCSA of anterior (subscapularis) and posterior (infraspinatus and teres minor) rotator cuff muscles are approximately equal (Basset, Browne, Morrey, & An, 1990). Therefore, the inclusion of PCSA weightings used in this current study may not be that beneficial since the summation of IR muscle PCSAs and ER muscle PCSA used were approximately equal (34.38 cm^2 vs. 31.15 cm^2) as well, nearly balancing their effects in the equation. The differences in explanation observed between non-weighted and PCSA-weighted (but nearly balanced) prediction equations may then be partly contributed to non-generalizability of the PCSA values taken from cadaveric data on this sample of young adults.

Co-activation during humeral rotation is known to be sensitive to changes in humeral abduction and task intensity, which both appear in three of the four prediction equations, and solely humeral abduction occurring in the fourth. These factors are quite influential ($p<0.0001$ for all but one instance), and according to the F ratios, humeral abduction always had the largest effect size, followed by intensity. Therefore, co-activation is foremost affected by humeral abduction posture, followed by task intensity. Despite small coefficients, signs indicate the directional effects each factor has on co-activation indices. For instance, in Equation 20, at 100° of humeral abduction the intercept changes from 0.22 to 0.173, which is not vastly different, but indicates how muscles are activated with respect to each other. As humeral abduction angle increased during IR and ER

exertions, both $CI_{non\text{-}wght}$ and CI_{PCSA} decreased, indicating an increased activation of external rotators relative to total muscular activation. Prediction equations also indicated that in general (with the exception of CI_{PCSA} for ER exertions), co-activation index ratios increased as task intensity increased, representing increases in activation of humeral internal rotators to total rotational activation. The negative coefficient associated with intensity in Equation 21 is not as strong as the positive coefficients of intensity associated with IR type exertions. Subscapularis (a humeral internal rotator) has been reported to be an important anterior stabilizer during humeral abduction with neutral rotation (McKernan, et al., 1990). Subscapularis also has the greatest contribution potential to internally rotate, as it has the largest PCSA of the 4 internal rotators identified in the CI indices. It is suggested that increases in IR activation related to increased task intensity could be identified as a protective response of dynamic stabilizers, as the internal rotators (primarily subscapularis, which increases anterior joint stability as previously mentioned), attempt to protect against large forces which could compromise joint stability, namely anterior dislocations, which are more common during forceful exertions at postures of humeral external rotation and abduction.

The developed predictions equations are germane to the subset of exertions for which they were designed. Currently, the feasibility of extrapolating these relationships to other postures and intensities is unknown. However, recent work has demonstrated that extrapolation of co-activation relationships defined for elbow flexion and extension defined by Brookham et al. (2011) to a subset of novel exertions of increased intensity and different postures was associated with high consistency (Middlebrook, Brookham, & Dickerson, 2013). Elbow co-activation was sensitive to changes in posture and applied load, and during elbow flexion and extension tasks the explained variance for CI models were 46% and 31%, respectively (Brookham, Middlebrook, Grewal, & Dickerson, 2011). Comparatively, the non-weighted CI models for the present study were also sensitive to changes in posture and load (task intensity), and models provided similar explained variance during ER exertions (35%), but substantially more explained variance during IR exertions (70%). Limitations of

this study included the small participant sample size from which these equations were built, and the minimal data lost due to the occurrence of motion artifact in some of the intramuscular EMG channels. It is possible that the inclusion of resting EMG activation levels may have a limited effect on the CI calculations. For future studies considering co-activation of similar exertions sets, we recommend against consideration of PCSA in analysis, as this inclusion provided little benefit. Further efforts should continue to examine the sensitivity of these relationships during additional postures and intensities, as well as to examine the influence of multifunctional muscles on the nature of the co-activation relationships. It should be determined whether inclusions of co-activation relationships improve model predictions on novel exertions. Future works that encompass these multiple scenarios should produce a robust co-activation description that is of utility for a wide range of exertions that include axial humeral rotation. This is the first known attempt to empirically quantify humeral rotational co-activation relationships. Humeral rotational co-activation is strongly dependent upon humeral abduction angle, followed by individual task intensity. Evaluation of the use of these constraints in biomechanical modelling must be assessed to determine if their inclusion improves predictions of muscle forces and joint loads.

Section 5.3.5 Statistical analysis and results pertaining to the extrapolated data set (*secondary study purpose)*

The empirical calculation of $CI_{non\text{-}wght}$ (as was described in Section 5.3.1 and Equation 16) was performed for tests 55-82 (the extrapolated data set). These calculated co-activation values were used to create $CI_{extrap,\ IR}$ and $CI_{extrap,\ ER}$ prediction equations using repeated measures ANOVA. The $CI_{non\text{-}wght}$ was considered the dependent variable, and the independent variables included all predictor variables identified as significant during stepwise multiple linear regression analysis, as was described previously in Section 5.3.2. Main and interaction effects were considered. The most parsimonious models built from the extrapolation data set for non-weighted co-activation during humeral IR and ER exertions ($CI_{extrap,\ IR}$ [Equation 22] and $CI_{extrap,\ IR}$ [Equation 23], respectively) were:

Equation 22 Extrapolation data set co-activation index prediction equation during IR type exertions. Where *humeral abduction* angle is in degrees, and *intensity* is individual %MVF; whole model p value is p<0.0001; r^2=0.76; independent variable p values = p<0.0001, p<0.0001, respectively, and F ratios = 352.80, 87.69, respectively.

$$CI_{extrap,IR} = 0.63 - (0.0029 \cdot humeral\ abduction) + (0.0040 \cdot intensity)$$

For IR type exertions, a significant interaction was found between humeral abduction and intensity, however it complicated the interpretation of the prediction equation and failed to improve the explanation of variance (r^2 remained to be 0.76). Therefore, only the main effects were considered.

Equation 23 Extrapolation data set co-activation index prediction equation during ER type exertions. Where whole model p < 0.0001; r^2=0.40.

$$CI_{extrap,ER} = 0.21$$

The actual humeral abduction angles and intensity data for the extrapolated data set (Tests 55-82) were inserted into the extrapolated co-activation index prediction equation for internal rotation exertions (Equation 22). All ER type exertions were designated at 0.21, as per Equation 23. These calculated co-activation indices were denoted as "CI_{extrap_calc}". These CI calculated values were the same for all 20 participants, since each participant performed the same task set.

Using the non-weighted prediction equations developed from the original data set, as described in Equation 18 and Equation 20, humeral abduction angles and intensity values for the extrapolated data (Tests 55-82) were inserted into their respective IR or ER type exertion equations. These calculated co-activation indices were termed "$CI_{original\_calc}$". These co-activation calculations were the same for all 20 participants, since each subject performed the same task set.

The empirical calculation of co-activation indices using the EMG from the original data set, (which was used to create the original prediction equations ($CI_{original,IR}$ [Equation 18] and $CI_{original,ER}$ [Equation 20]) were termed CI_{EMG_calc}.

Therefore, there were 3 types of co-activation indices:

1. CI_{EMG_calc}
2. $CI_{original\_calc}$
3. CI_{extrap_calc}

To determine if the co-activation relationship determined in the primary purpose of this study could be extrapolated to a novel task set, a repeated measures ANOVA was run with the co-activation index calculations as the dependent variable, the type of CI calculation method (Type 1, 2, or 3) as the independent variables with subject as a random variable, by exertion type (humeral internal and external rotation). Both main and interaction effects were considered.

Post hoc analysis (Student's T test) revealed that for IR type exertions; there was no difference between CI_{EMG_calc}, CI_{orig_calc} or $CI_{extrap\_calc.}$ No significant difference was found between the values of CI magnitude for these 3 calculation methods to extrapolative tests of IR exertions [p values: CI_{orig_calc} vs. CI_{extrap_calc} p=0.8550; CI_{orig_calc} vs. CI_{EMG_calc} p=0.8593; CI_{EMG_calc} vs. CI_{extrap_calc} p = 0.9963], as demonstrated in Figure 36.

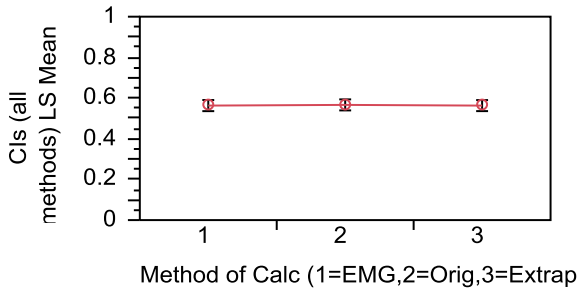

Figure 36 Least square means plot of co-activation ratios during IR exertions for three calculation methods: EMG (1), Original (2) and Extrapolation (3).

During ER type exertions, post hoc analysis (Student's T test) revealed the following significant differences: CI_{EMG_calc} and CI_{extrap_calc} significantly overestimated ($p<0.0001$, $p<0.0001$) the CIs for exertions in the extrapolative tests of ER exertions as compared to CI_{orig_calc} calculation method, as demonstrated in Figure 37.

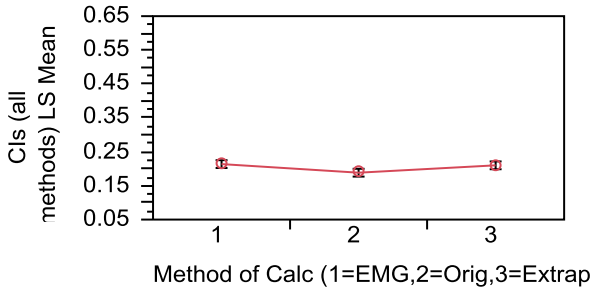

Figure 37 Least square means plot of co-activation ratios during ER exertions for three calculation methods: EMG (1), Original (2) and Extrapolation (3).

A 500 ms moving window average of linear enveloped test trials were calculated between 2 – 4 seconds of each test, for all participants as shown in Appendix I Table 47 (means) and Table 48 (standard deviations). This data will be used for comparison in Study 3 of this thesis.

Section 5.3.6 Discussion pertaining to the extrapolated data set (*secondary study purpose)*

In partial support of the hypothesis, the co-activation relationship defined through the primary purpose and results of this study (published by Brookham & Dickerson (2014)) was extrapolated successfully to a novel task set of IR exertions. However, this relationship was not extrapolated successfully during ER type exertions.

The prediction equation developed from the extrapolated data set for IR type exertions (Equation 22) was very similar to that predicted from the original data set (Equation 18). The intercept was slightly lower (0.63 vs. 0.70) than the original, but was still larger than the ER intercept (0.21), and indicated that there was an increase in IR muscle activation during IR type exertions. The same predictor variables were present: humeral abduction and intensity, and their magnitudes were

similar to those of Equation 18. The magnitude of the coefficient of humeral abduction was slightly smaller (0.0029 vs. 0.0036), but the direction (and interpretation) was the same, indicating an increase in ER muscle activation to total rotation activation as humeral abduction angle increased. The magnitude of the coefficient of intensity was slightly larger (0.0040 vs. 0.0034) than the original, but the direction was the same, indicating an increase in IR muscle activation to total rotational activation as intensity increased. The relative magnitude of the intercept compared to the coefficients was large, indicating that there was only modest effect on CI predictions with changes in humeral abduction and intensity. The effect size of the model effects reflected that co-activation was foremost affected by posture (humeral abduction) and then by intensity, as was shown in the original prediction equations. The explained variance of the prediction model built with extrapolation data was greater than that from the original data set ($r^2 = 0.76$ vs. $r^2 = 0.70$) – indicating that the prediction model created using the CI's calculated from the EMG of Tests 55-82 explained 6% more variance than the model created from the EMG data from Tests 1-54. This improvement in explanation may be due to the specific exertions classed within the extrapolative set, which had less variable changes in posture and intensity (only 14 different postures, of which humeral rotation always remained unchanged versus 27 different postures in the original data set).

Stepwise multiple regression analysis identified shoulder abduction and intensity as potential predictor variables during ER type exertions. However, repeated measures ANOVA revealed that neither of these main or interaction model effects was significant in the prediction of CI during ER type exertions and their inclusion did not improve explained variance. Therefore, we did not have any variables that accounted for prediction of CI, and as a result CI was set to 0.21for all ER type exertions. As a result, the CI was always predicted to be 0.21 regardless of postural or intensity changes. The static nature of this prediction equation may explain why the relationship did not extrapolate well; since the extrapolation data set contained some very diverse postures (ex. 135 degrees humeral abduction versus 0 degrees abduction). The magnitude of the intercept was very similar to that of the prediction equation based on the original data set in Equation 20 (0.22),

however negated the involvement of the humeral abduction or intensity coefficients. The explained variance of the extrapolated prediction model was 40%, which was a 5% improvement from that explained in the original prediction model, but still represented only a modest ability to predict co-activation during ER exertions. As was discussed previously, muscles' roles change as posture changes (Lee, Kim, O`Driscoll, Morrey, & An, 2000; McKernan, et al., 1990) and variable muscle strategies may be used during ER exertions (especially involving abduction) in order to preserve glenohumeral stability, causing the co-activation relationships to be less predictable. Further, the exertions in the extrapolation data set did involve a near-end range of motion posture (135 degrees of abduction), which likely resulted in ligament involvement and further change to muscle requirements to maintain glenohumeral stability.

In conclusion, the co-activation relationship defined for IR exertions during the primary purpose of this study can be successfully extrapolated to novel IR tasks with confidence. However, the co-activation relationship defined for humeral ER type exertions has modest prediction ability and cannot be successfully extrapolated to novel ER task sets. Future works should encompass more diverse data sets and a larger sample size in attempts to develop more predictable relationships of co-activation during ER exertions, and determine the ability of this relationship to predict appropriately in novel task sets.

Section 5.3.7 Study contribution to science and health

The findings of this study contribute to science by furthering the knowledge that is currently understood about shoulder muscle co-activation. Previous to this work, shoulder internal/external rotation co-activation relationships had not yet been quantified. It was demonstrated that these newly defined relationships are successfully extrapolated in humeral internal rotation exertions, but further quantification of co-activation is required in humeral external rotation type exertions. Successful extrapolation supports use of these relationships in biomechanical muscle force prediction models replicating similar task sets. The inclusion of these relationships may further the advancement of

these models by enforcing muscle co-activation - improving physiological realism and possibly improving accuracy of predictions. The knowledge gained from this study will also indirectly contribute to health advancement of breast cancer survivors, by allowing for comparison of co-activation relationships between survivor and healthy populations, which will be useful in identifying dysfunction (discussed in Study 3). This process may be transferred to other patient populations (such as different injury groups), assisting in dysfunction identification and promotion of effective treatment protocols.

Chapter 6 Study 3 – Comparison of humeral rotation co-activation of breast cancer survivors and healthy shoulders

Section 6.1 Introduction

Upper limb morbidities are common amongst breast cancer survivors, resulting in disabilities that affect independence, work and life. Decreased strength is prevalent in 17% to 33% of survivors (Rietman, et al., 2003). Strength reductions in breast cancer survivors may be the result of iatrogenic neurological structural damage, muscle dysfunction caused by radiation or muscle atrophy caused by disuse. These impairments interfere with survivors' ability to perform ADL and return to work (Markes et al., 2006). However, very little research has been performed to investigate the electromyographic activity amongst the breast cancer population.

It appears only two groups have described shoulder electromyographic activity of the breast cancer population. The activity of the pectoralis major, rhomboids, upper trapezius and serratus anterior was recorded with surface electrodes as survivors (ranging from 6 months – 6 years post cancer surgery) elevated their arms in the scapular plane (Shamley, et al., 2007). No other motions or muscles were monitored. EMG was not normalized (MVCs were neglected due to pain) and the frequency of raw data points from muscles were compared between affected and unaffected sides (Shamley, et al., 2007). The authors reported a generalized loss of activity in these four shoulder muscles during elevation on the affected side (Shamley, et al., 2007). However, failing to normalize EMG, to even a submaximal voluntary contraction (subMVC), could have compromised interpretation of findings. Normalization is vital for temporal EMG (Ball & Scurr, 2010) as past literature has demonstrated un-normalized EMG can be misinterpreted (Lehman & McGill, 1999). Later, Shamley et al. (2012) re-examined normalized muscle activity of pectoralis major, serratus anterior, rhomboids and upper trapezius during scaption of a BCP with mastectomy or wide local excision (WLE). With the exception of upper trapezius in the mastectomy group, the authors

reported an increase in activity of all muscles on the left affected side compared to the left side of a healthy control group (UpTrap $p < 0.05$, CI 2.38 – 15.01 for WLE; Pec $p < 0.001$, Rhomb $p < 0.001$, Serr $p < 0.001$, CI 6.09 – 12.9 for WLE and $p < 0.05$, CI 1.02 – 9.02 for mastectomy) and reported greater activation of the upper trapezius ($p < 0.001$, CI 9.8 – 21.51), rhomboids ($p < 0.001$, CI 11.1-15.71) and serratus ($p < 0.001$, CI 7.16 – 16.26) on the right affected side of patients with mastectomy compared to the right side of a healthy control, suggesting the BCP was working at a higher level of percent capability. Shamley et al. (2012) also reported a decrease in pectoralis major activity and an increase in serratus anterior activity on the affected side compared to the unaffected side. Galiano et al. (2011) recorded surface EMG from the sternocleidomastoid, upper trapezius and deltoid during a functional writing task and reported increased activation of the upper trapezius bilaterally (up to 20% and 4% increases on affected and unaffected side, respectively) and sternocleidomastoid muscles (up to 31% increase on affected side) of survivors compared to a healthy control group. Galiano-Castillo et al. (2011) suggested 3 possible reasons for increases in EMG: increases may be due to pain or fear of pain; or perhaps cancer treatment or neuropathy resulting in muscle damage has caused changes in muscle recruitment; or perhaps participants are exhibiting altered motor strategies. Others have suggested that reduced mobility amongst the breast cancer population could reflect damage to rotator cuff muscles (Thompson, Air, Jack, Kerr, Rodger, & Chetty, 1995). Due to the depth, location and size of the rotator cuff muscles, electromyography is best recorded with intramuscular electrodes. Further research is needed to investigate activity of shoulder muscles of survivors, specifically those of the rotator cuff, during a variety of postures.

Humeral internal and external rotator co-activation relationships amongst breast cancer survivors are unknown. These relationships need to be quantified and compared with co-activation relationships defined in a healthy population. Differences observed between population groups may assist in clinical interpretation of dysfunction, which could lead to more evidence-based therapeutic and preventative interventions within the breast cancer population. If proven interpretable, this process may be transferred to other patient populations (such as different injury groups), assisting in

dysfunction identification and promotion of effective treatment protocols. Furthermore, quantification of co-activation relationships amongst breasts cancer survivors could be useful to include in biomechanical models which predict muscle force and demand. These models often negate antagonistic co-activation, and including these relationships would increase physiological realism of the models and may promote more accurate model predictions. These models could play an essential role in the assessment and integration of breast cancer survivors into safe, effective and sustainable return to work.

The two purposes of this study are to:

1. Quantify the co-activation relationships of humeral internal and external rotators in breast cancer survivors
2. Compare the survivor co-activation relationship with those of a healthy population (as defined in Study 2 of this thesis)

It is hypothesized that muscle-activation patterns of breast cancer survivors will reveal survivors have a reduced internal/external humeral rotation co-activation ratio compared to healthy individuals during IR exertions (reflecting a decrease in pectoralis major activation). The co-activation ratio provides a relative measure of internal rotation (IR) contribution to total activation (IR and external rotation (ER) activation) about the shoulder. Due to the location of the breast cancer treatment (surgery and radiation is typically directed to the anterior aspect of the chest), the pectoralis muscles are primarily in the field of disturbance. It is hypothesized that these anterior chest muscles (humeral internal rotators) will be unable to produce force, causing a reduction in total activation of the internal rotator muscles in relation to the posteriorly located humeral external rotators. It was hypothesized that this dysfunction would present as a reduction in magnitude of the numerator of the co-activation ratio, compared to the ratio of a healthy population.

Section 6.2 Methods

Fifty breast cancer survivors performed 22 isometric humeral internal or external rotation exertions at various shoulder postures and intensities. Intramuscular electrodes were inserted into three rotator cuff muscles, and surface electrodes were placed over surrounding shoulder musculature. Electromyographic data was used to calculate co-activation index ratios, and these relationships were further predicted using multiple regression analysis. Finally, co-activation relationships of breast cancer survivors were compared to those relationships defined in a healthy population (described in Study 2 of this thesis).

Section 6.2.1 Participants:

Participants included 50 female breast cancer survivors with a mean age of 59.4 yr [+/- 9.7 yr; range 31-83 yr], mean height of 1.7 m [+/- 0.1 m; range 1.5-1.8 m], mean weight of 71.7 kg [+/- 11.8 kg, range 51.4-97.7 kg]. Twenty seven participants had mastectomies (16 bilateral); 34 had lumpectomies and 48 had axial node dissection surgeries. Thirty four participants had received hormone replacement therapy, 34 had received chemotherapy and 37 had received radiation treatments. Average time since diagnosis was 74.9 months (+/-59.6 months; range 12-228 months]. Participants were excluded from the study if they had any of the following health disorders: blood clotting disorders, HIV, Hepatitis B or C, allergies to isopropyl alcohol, latex or nickel. Participants were recruited from the Kitchener-Waterloo area. Participants provided informed consent before participation in the study. This study received ethics clearance through the Office of Research Ethics at the University of Waterloo. Participants received a gift basket valued at $30 in appreciation for their time and efforts. Sample size justification is given in Study 1 in Section 4.2.1 and Equation 5. Data collection for Studies 1 and 3 were collected simultaneously and participants were shared.

Section 6.2.2 Surface electromyography

In preparation for the surface electrodes, the skin overlying the muscle of interest was shaved of hair and cleansed with isopropyl alcohol. Disposable bipolar Ag/AgCl surface electrodes (Product #272,

Noraxon, USA, Inc., Arizona, USA) were placed on the affected side (side affected by breast cancer) over the pectoralis major (clavicular and sternal insertions), posterior deltoid, latissimus dorsi, supraspinatus and infraspinatus. Surface supraspinatus and infraspinatus data were only used to replace their respective intramuscular signals if these latter signals were compromised due to artifact, as is described in Section 5.3.1, or when the participants did not provide consent to insertion of intramuscular electrodes. A reference electrode was placed over the sternum, just inferior to the suprasternal notch. Electrode placements are described in Appendix D. A wireless Noraxon TeleMyo 4200T G2 (Noraxon 2 USA Inc., Arizona, USA) sampled EMG channels at 3000 Hz. This system has 16-bit resolution on all analog inputs with a band-pass filter from 10-1500 Hz, an input impedance > 100 MΩ, a common mode rejection ratio > 100 dB and a base gain of 500. EMG was recorded on the computer using the Vicon Nexus 1.2 software (Vicon, Oxford, UK).

Section 6.2.3 Intramuscular electromyography

In preparation for intramuscular electrode insertion, hair surrounding the area of the muscle of interest was shaved off, and the skin was cleansed with isopropyl alcohol. Three intramuscular electrodes were inserted into one of each of the following rotator cuff muscles on the affected side: supraspinatus, infraspinatus, and subscapularis. Sterile single-use hypodermic needles of 33 mm in length and 25 gauge (~0.55 mm) (Product # 000-318-30, Motion Lab Systems, Inc., Baton Rouge, LA) were inserted into the supraspinatus and infraspinatus using published instructions from Geiringer (1999). Sterile single-use hypodermic needles of 50 mm length and 25 gauge (Product # 000-318-50, Motion Lab Systems, Inc., Baton Rouge, LA) were inserted into the subscapularis using published instructions from Nemeth et al., (1990). Further detail regarding insertion procedures are listed in Appendix A. A wireless Noraxon TeleMyo 4200T G2 (Noraxon 2 USA Inc., Arizona, USA) sampled EMG channels at 3000 Hz.

Section 6.2.4 Pre-experimental protocol

Prior to testing, anthropometric measurements (stature, body weight, upper and lower arm length) were recorded and the participants exerted maximal voluntary forces (MVF) with the affected arm during isometric humeral internal and external rotation (2 sets each; standing, humerus at the side and the elbow flexed to 90°). MVF were performed against a digital hand-held dynamometer (ergoFET300^{TM}, Utah, USA). MVFs were 3 s in duration, and at least two minutes of rest were given between MVFs. An average of the two trials was defined as the final MVF, which was used to calculate the specific target force intensities for each trial (ranging from 10% - 60% MVF). A custom-made program (Labview 8.5, National Instruments, Texas, USA) was built to display visual force feedback to participants during testing trials. Participants were given an opportunity to practice achieving specified forces using the visual feedback before testing trials began. Muscle-specific maximal voluntary contractions (MVCs) were performed on the affected side. MVCs were 3 s in duration (2 sets) and participants were asked to ramp up to their maximal strength and then relax. The peak from a 500 ms moving window average of linear enveloped data was used to normalize respective linear enveloped EMG channels. The MVC testing protocol is outlined in Table 28.

Table 28 Study 3 Description of maximal voluntary contraction tests

Muscle	Maximal Test Contraction:
Supraspinatus	Subject is seated. Shoulder is abducted to 5° with elbow extended (thumb pointing up). Abduction is resisted.
Infraspinatus	Subject is seated. Arm is at side with elbow bent to 90°. External rotation of the arm is resisted.
Subscapularis	Subject is standing. Arm is at side with elbow bent to 90°. Internal rotation of the arm is resisted.
Latissimus Dorsi	Subject is seated with shoulder horizontally abducted and externally rotated to 90° and elbow flexed to 90° (fingers point to ceiling). Shoulder adduction is resisted.
Pectoralis Major (sternal and clavicular insertions)	Subject is seated with shoulder horizontally abducted and externally rotated to 90° and elbow flexed to 90° (fingers point to ceiling). Shoulder horizontal adduction is resisted.
Posterior Deltoid	Subject is seated. Resistance provided to shoulder extension when shoulder is abducted to 90° and externally rotated, with elbow flexed to 90° (fingers point to ceiling).

Section 6.2.5 Experimental protocol

Each participant performed 22 trials of isometric shoulder internal or external rotation exertions at varying intensities (10%-60% MVF) and humeral abduction angles (0°, 45°, 90°) as described in Table 29. Tests 19 – 22 are primarily used for the purposes of Study 4 of this thesis and will not be included in analysis of this current study. Test trials were 6 s in duration. A goniometer was used to ensure correct posture. The wrist was maintained in a neutral posture during all exertions, facilitated by a fully moveable handle attached to a tri-axial force transducer (MC3-6-500, Advanced Mechanical Technology Inc., Watertown, Massachusetts). The order of exertions was randomized. Force and EMG were collected simultaneously. A custom-built program in Labview 8.5 (National Instruments Inc., Texas, USA) provided participants real-time visual force feedback, allowing them to produce the required target intensity for each specific exertion. The entire study protocol was approximately 2 hours in duration. Experimental methods are outlined in Figure 38.

Table 29 Test exertions performed by the breast cancer population, used to define co-activation of survivors.

Test	Intensity (% MVF)	Humeral abduction angle (°)	Exertion type
1	10	0	IR
2	20	0	IR
3	30	0	IR
4	40	0	IR
5	50	0	IR
6	60	0	IR
7	10	0	ER
8	20	0	ER
9	30	0	ER
10	40	0	ER
11	50	0	ER
12	60	0	ER
13	20	45	IR
14	40	45	IR
15	20	45	ER
16	40	45	ER
17	30	90	IR
18	30	90	ER
19	40 N	0	IR
20	40 N	0	ER
21	19.6 N	0	IR
22	19.6 N	0	ER

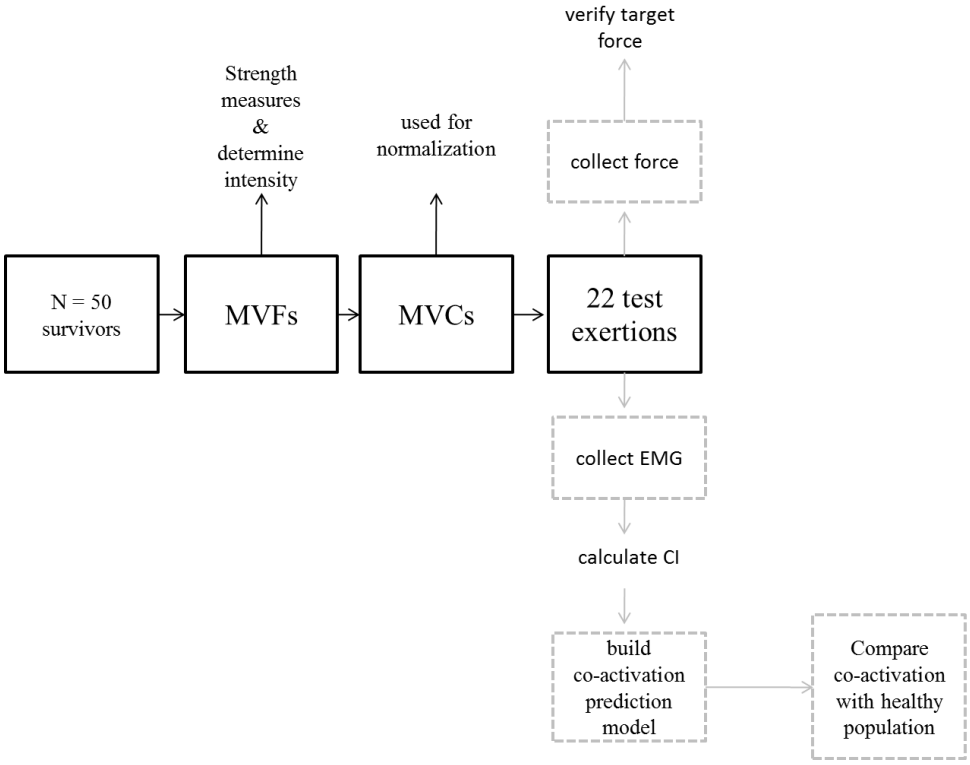

Figure 38 Flow-chart depicting methodology for Study 3. Solid boxes indicate methodological protocol and dashed lines indicate outputs and analysis.

Section 6.3 Analysis

Data was transferred from the receiver to a personal computer, and analysed using Matlab™ R2010a (Mathworks Inc., USA). Co-activation ratios were calculated, EMG was linear enveloped and normalized, and force was filtered and converted to Newtons. These co-activation ratios were assessed in JMP 11® (SAS Institute Inc., Cary, NC) to build co-activation prediction models.

Section 6.3.1 Data processing

Raw force signals were filtered with a dual-pass Butterworth low pass filter (LPF) with a cutoff of 3 Hz. Force (collected in volts) was converted to Newtons using a shunt calibration. The resultant force was calculated using Equation 15 defined in Study 2. Raw EMG was high-pass filtered (Fc 30Hz) and linear enveloped with a single-pass Butterworth LPF (Fc = 2.5 Hz, confirmed with residual

analysis). EMG was normalized to maximal contractions as was discussion in Section 6.2.4. Integrated and normalized EMG (between 2 - 4 s of each trial) magnitudes were used in the calculation of a co-activation index (CI) which was separately calculated for all trials and participants as shown in Equation 24. The CI provides a relative measure of IR contribution to total IR and ER activation about the shoulder. A CI of 0% indicates no co-activation (IRs are not activated); a CI of 50% indicates full co-activation (both IRs and ERs are activated in equal amounts); and a CI of 100% indicates no co-activation (the ERs are not activated).

Equation 24 Co-activation index calculation for the BCP. Where E = linear enveloped and normalized EMG; $R_{1\text{-}4}$ = Internal rotators: subscapularis, pectoralis major clavicular / sternal heads and latissimus dorsi, respectively; $R_{5\text{-}7}$ = External rotators: infraspinatus, posterior deltoid and supraspinatus, respectively.

$$CI_{cancer} = \frac{\int_{t1}^{t3}\left[\frac{\sum_{i=1}^{4} E_{Ri}}{4}\right](t)dt}{\int_{t1}^{t3}\left[\left[\frac{\sum_{i=1}^{4} E_{Ri}}{4}\right]+\left[\frac{\sum_{i=5}^{7} E_{Ri}}{3}\right]\right](t)dt}$$

Some trials were excluded from analysis due to EMG motion artifact or error in target force levels. All EMG trials were visually inspected for motion artifact, which was identified by a large spike in amplitude. Channels determined to have artifact were removed from the CI ratios. The actual force produced by each participant was compared to the target force for each trial. Any force trials containing error >5% MVF or >5 N difference between actual and target force were removed from further analysis.

Section 6.3.2 Statistical analysis

Statistical analyses were performed in JMP 11® (SAS Institute Inc., Cary, NC). Potential predictor variables (height, weight, upper arm length, lower arm length, age, task intensity (%MVF), humeral abduction angle, and MVF) were analyzed for inter-correlations and redundant variables (variables highly correlated (r>0.7)) were removed. Preliminary stepwise multiple linear regression analysis determined which predictor variables should be included in each of the co-activation prediction models. The stepwise direction was mixed (forward and back) with a stopping rule p-value threshold

of 0.25 to enter and 0.25 to leave. Prediction models were developed separately for both IR and ER type exertions ($CI_{cancer,IR}$, $CI_{cancer,ER}$) from Tests 1-18, using a repeated measures ANOVA. The $CI_{cancer,IR}$ and $CI_{cancer,ER}$ values were considered dependent variables, and the independent variables included all predictor variables identified as significant during stepwise multiple linear regression analysis. Both main and interaction effects were considered.

To assess differences in muscle strategy used between healthy and breast cancer populations, muscle activation levels (normalized, mean moving average activation between 2 – 4 s of each 6 second duration test) were compared for Tests 1 – 18. Tests 1 – 18 were identical between populations, defined by the same intensity, posture and exertion type combinations. Nine repeated measures ANOVAs were performed with muscle activation level (for each of the nine muscles) as the dependent variables, by exertion type (IR or ER), with population group (healthy or cancer survivor) and subject as a random variable termed the independent variables. Post hoc Student's T tests were performed to identify significant difference between population groups for each muscle and exertion type.

Section 6.4 Results

Co-activation relationships were determined using multiple regression analysis for humeral IR and ER exertions for the breast cancer and healthy populations (Study 2).

Section 6.4.1 Co-activation relationships during internal rotation exertions

The most parsimonious model for co-activation during humeral IR exertions for the breast cancer population was [Equation 25]:

Equation 25 Co-activation prediction equation for a breast cancer population during IR exertions. Where *humeral abduction* angle is in degrees, and *intensity* is individual %MVF; whole model p value is p<0.0001; r^2=0.77; independent variable p values = p<0.0001, p<0.0001, respectively and independent F ratios = 553.67, 41.78, respectively.

$$CI_{cancer,IR} = 0.71 - (0.0033 \cdot humeral\ abduction) + (0.0018 \cdot intensity)$$

As determined in Study 2, the most parsimonious models for co-activation of a healthy population during humeral IR exertions ($CI_{healthy,\ IR}$) was [Equation 26]:

Equation 26 Co-activation prediction equation for a healthy population during internal rotation exertions. Where *humeral abduction* angle is in degrees, and *intensity* is individual %MVF; whole model p value <0.0001; $r^2 = 0.70$; independent variable p values = <0.0001, <0.0001, respectively and independent variable F ratios = 757.99, 131.34, respectively.

$$CI_{healthy,IR} = 0.70 - [0.0036 \cdot humeral\ abduction] + [0.0034 \cdot intensity]$$

Section 6.4.2 Co-activation relationships during external rotation exertions

The most parsimonious model for co-activation during humeral ER exertions for the breast cancer population was [Equation 27]:

Equation 27 Co-activation prediction equation for a breast cancer population during ER exertions. Where *humeral abduction* angle is in degrees, and *intensity* is individual %MVF; whole model p value is p<0.0001, $r^2 = 0.77$; independent p values = <0.0001, <0.0001, 0.0047 respectively and independent F ratios = 85.36, 111.52, 8.77 respectively.

$$CI_{cancer,ER} = 0.18 - (0.00099 \cdot humeral\ abduction) - (0.0023 \cdot intensity) + (0.0038 \cdot body\ mass)$$

The most parsimonious models for co-activation of a healthy population during humeral ER exertions ($CI_{healthy,\ ER}$) was [Equation 28]:

Equation 28 Co-activation prediction equation for a healthy population during external rotation exertions. Where *humeral abduction* angle is in degrees; whole model p value <0.0001; $r^2 = 0.35$; independent variable p value = <0.0001; independent variable F ratio = 22.09

$$CI_{healthy,ER} = 0.22 - [0.00047 \cdot humeral\ abduction]$$

Analysis of interaction effects were performed, but these effects were not significant for either exertion type so therefore only the main effects were considered. Twenty four participants agreed to have intramuscular electrodes inserted into the rotator cuff muscles, and the remaining 26 participants declined the needles and opted to have only surface electrodes record EMG. A total of 22 tests were removed due to erroneous force values, and 50 channels of subscapularis intramuscular EMG were removed due to artifact, as outlined in Table 30. When EMG artifact was present, or

when subscapularis wire data was not available (participants that declined needles) CI calculations were adjusted to reflect the exclusion of subscapularis from the equation (the IR denominator was reduced from four to three).

To investigate the effects of resting EMG levels on CI calculations, the resting EMG was subtracted from raw signals, before linear enveloping and normalizing the EMG. This was done for 25 participants. The CIs were calculated using both processing methods (Method 1 = no removal of resting EMG; Method 2 = subtraction of resting EMG) and compared using a T test. The CI was the dependent variable and the independent variables included the method of processing (1 or 2) with subjects as a random variable. Results indicated that there was no significant difference between the CIs calculated between processing methods ($p = 0.7135$). The least square means of the CI for Method 1 was 0.5313, compared to 0.5267 for Method 2. Since it was demonstrated that subtraction of resting EMG had no significant effect on the CI calculations, the EMG processing methods were kept the same as the Brookham & Dickerson (2014) publication, and all CIs were calculated for all participants using Method 1 (no removal of resting EMG).

Table 30 Tests affected by force error and EMG artifact

	Tests removed due to erroneous force	**Subscapularis channels removed due to artifact**
Number of tests/channels affected	n = 22/1100	n = 50/528 [24 participants had intramuscular EMG]
Percentage of tests affected	2.0%	9.5%
Number of participants affected	N = 10	N = 3

Mean EMG (calculated by taking a 500 ms moving window average of linear enveloped data calculated between 2 – 4 seconds of each test) of all participants are shown in Appendix J, Table 49. Comparisons of least square mean activation levels between healthy (from Study 2) and breast cancer populations for IR and ER type exertions are shown in Table 31.

Table 31 Comparison of EMG activation levels (mean and SD) between healthy and cancer populations. Significance (p<0.05) are denoted with an asterix (*).

For ER Type Exertions					
Muscle	**Healthy Population Activation Level (%MVF)**		**Cancer Population Activation Level (%MVF)**		**Significance Level**
	mean	**SD**	**mean**	**SD**	
Pectoralis Major Clavicular	3.1	3.4	7.4	5.9	**p < 0.01***
Pectoralis Major Sternal	3.1	1.8	11.9	10.0	**p < 0.01***
Posterior Deltoid	10.8	9.6	18.2	15.4	**p < 0.01***
Latissimus Dorsi	7.4	8.3	23.7	19.6	**p < 0.01***
Supraspinatus (surface)	27.4	16.0	28.6	19.7	p = 0.68
Infraspinatus (surface)	28.1	24.9	29.3	18.8	p = 0.72
Supraspinatus (wire)	24.6	18.2	40.7	23.4	**p < 0.01***
Infraspinatus (wire)	31.4	24.9	29.2	20.5	p = 0.64
Subscapularis (wire)	10.4	12.6	24.5	30.1	**p = 0.03***
For IR Type Exertions					
	Healthy LSM (%MVF)		**Cancer LSM (%MVF)**		**Significance Level**
	mean	**SD**	**mean**	**SD**	
Pectoralis Major Clavicular	16.7	15.6	24.8	23.8	**p = 0.03***
Pectoralis Major Sternal	23.2	20.9	32.0	28.2	**p = 0.03***
Posterior Deltoid	2.7	2.5	7.2	6.2	**p < 0.01***
Latissimus Dorsi	9.6	12.3	26.5	23.8	**p < 0.01***
Supraspinatus (surface)	1.6	6.8	10.5	11.4	p = 0.11
Infraspinatus (surface)	6.8	6.1	10.6	10.9	**p = 0.05***
Supraspinatus (wire)	7.8	8.1	16.7	14.4	**p < 0.01***
Infraspinatus (wire)	3.3	4.1	4.3	6.3	p = 0.39
Subscapularis (wire)	28.8	30.9	40.2	35.3	p = 0.08

Section 6.5 Discussion

Co-activation relationships of humeral rotators were defined in a breast cancer survivor population for a subset of isometric exertions varying in intensity and posture. Regression models were able to predict co-activation well during both IR and ER type exertions (77% explained variance). There was improvement in explained variance of co-activation for the survivor population compared to the healthy population, especially during ER type exertions. Co-activation of the breast cancer population was defined very similarly to that of the healthy population, reflecting similar joint level strategies for maintenance of GH stability, which was supported by various changes in survivor muscle. Contrary to the hypothesis, muscle-activation patterns of breast cancer survivors did not demonstrate a reduced internal/external humeral rotation co-activation ratio compared to healthy individuals during IR exertions (reflecting a decrease in pectoralis major activation). In contrast, compared to a healthy population, the survivors demonstrated significant increases in activation of the pectoralis major.

The CI prediction equations of the breast cancer survivor population were similar to those predictions of a healthy population as described in Study 2 and outlined in Equation 18 and Equation 20. The intercept magnitudes were very similar between the population groups; the survivor intercept was slightly higher during IR exertions (0.71 vs. 0.70) and slightly lower during ER type exertions (0.18 vs. 0.22). The intercepts of each regression equation demonstrated the overall behavior of muscle activation during IR and ER exertions. The larger intercept during IR exertions (0.71) and smaller intercept during ER exertions (0.18) demonstrated an increase in activation of the IR musculature during IR exertions, and an increase in activation of the ER muscles during ER type exertions. The subtle magnitude differences of intercepts between populations indicate that the survivors had slightly higher activation of IR musculature during IR exertions, and slightly higher activation of ER musculature during ER exertions. In summary, compared to a healthy population, the survivor population group had higher levels of rotator muscle activation in their respective

rotation-type exertions. Higher levels of activation in the BCP is suggestive of increased effort required and increases in amplitude may also be indicative of fatigue. Survivors are known to experience decreased functional capacity, meaning they exert more effort relative to their maximal ability to perform usual activities, therefore leading to higher levels of fatigue (Mock, et al., 2005). Previous researchers have identified increased levels of activation of shoulder muscles in the BCP compared to healthy controls during scaption (Shamley, Lascurain-Aguirrebena, Oskrochi, & Srinaganathan, 2012) and functional writing tasks (Galiano-Castillo, Fernandez-Lao, Cantarero-Villanueva, Fernandez-de-las-Penas, Menjon-Beltran, & Arroyo-Morales, 2011). Findings from Study 1 of this thesis similarly found that total muscle effort (summation of integrated EMG of 8 shoulder muscles) was greater on the affected side compared to the unaffected side during reaching and lifting tasks. Results from Study 1 also indicated increases in activation of the external rotators (supraspinatus and posterior deltoid) during all tasks. Identifying the changes in muscle activation is useful to identify muscle strategies used by the BCP in order to preserve glenohumeral joint stability, as evidenced by the similar CI relationships. These strategies are further discussed below.

Humeral abduction followed by intensity were significant factors in the prediction of CI in the survivor population, which mirrored the healthy CI results. During IR exertions, the coefficient magnitudes were slightly lower for the survivor population (BCP: -0.0033 vs. H: -0.0036 for humeral abduction; BCP: 0.0018 vs. H: 0.0034 for intensity), indicating that changes in posture and intensity had slightly less effect on CI for the survivor groups. This was also reflected by the smaller effect size of these coefficients in the survivor group compared to the healthy population (F ratios = 553.67 vs. 757.99 for humeral abduction; 41.78 vs. 131.34 for intensity). During ER exertions, the coefficient of humeral abduction was greater in the survivor CI prediction (-0.00099 vs. -0.00047), albeit still small. Humeral abduction angle (or angle of elevation) was demonstrated to affect muscle activation of the BCP during Study 1 of this thesis: total muscle effort (summation of iEMG of 8 shoulder muscles) was greatest during ROM-Reach tasks in which the participant was maximally

elevating the humerus in several difference planes, compared to other tasks with reduced reach heights. Shamley et al. (2007) reported loss of muscle activity (in terms of frequency of data points) of the pectoralis major, minor, rhomboid and serratus in the BCP to be greatest (most reduction) during highest angles of elevation during scaption. The survivor CI prediction for ER exertions also contained two additional predictors (intensity and body mass) compared to the healthy group prediction. In general, the relative magnitude of the intercepts compared to the coefficients was large, indicating model insensitivity to other factors. The small magnitudes of the coefficients suggest that changes in humeral abduction angle, intensity or body mass have only modest effects on CI predictions and do not substantially modify the overall behavior of the model. For example, during internal rotation exertions, if humeral abduction changes by 45°, the CI is reduced by only 0.1. The inclusion of a new predictor variable, body mass, in the prediction of CI during ER for the survivor population may be due to the difference and variance in demographics compared to the healthy population. The healthy population consisted of a tighter demographic consisting of young males and females (gender did not affect CI) with a mean body mass of 66.6 kg [range 48.5-85.0, SD 10.9] and mean BMI of 23.0. The survivor group consisted of a wider range demographic of older, heavier females (71.7 kg [range 51.4-97.7, SD 11.8]), with a mean BMI 26.3. Intensity may play a more important role during ER of the breast cancer population due to dysfunctional changes that limit humeral ER ROM and increase humeral IR ROM as demonstrated by the kinematic findings of Study 1. Study 1 demonstrated weakness and increased effort required in posterior rotator cuff and shoulder muscles (which may be the cause or effect of reduced ER movements), and these changes were more evident during work tasks, which involved external loads and were higher intensity tasks compared to the other ADL tasks performed in Study 1. In the current study, it was evident that intensity was an important factor that was considered in maintaining GH stability through co-activation.

There was a 42% improvement in explained variance of the CI prediction of the survivor group compared to that of the healthy population for ER exertions, suggesting that survivor CI was more predictable. This improved explanation of variance for ER exertions is likely due in part to the increased sample size (50 survivors vs. 20 healthy) and reduced task set (9 ER tests vs. 27 ER tests) upon which the regression equation was built. Also, there may be less variability in the muscle strategies that are used or available for use in the survivor population, causing survivor CI to have greater explanation of variance. It is known that muscle strategies change with postural changes in a healthy population (Lee, Kim, O`Driscoll, Morrey, & An, 2000; McKernan, et al., 1990), but the roles of shoulder muscles in co-activation of a breast cancer population have not yet been investigated. Future discrimination between levels of disability may allow further improvements in explained variance when defining co-activation within this population.

Differing muscle strategies used by the survivor population may help explain how glenohumeral stability is maintained, as was represented by the CI predictions presenting so similar to that of the healthy population. In general, results indicated that survivor activation levels are higher than those of a healthy population. Specifically, during both IR and ER type exertions, the survivors had significantly higher activation in the following four muscles: pectoralis major clavicular, pectoralis major sternal, latissimus dorsi, posterior deltoid and supraspinatus (wire). These muscle activation patterns agree partially with previous works. In Study 1 of this thesis; during which the muscle activation of the unaffected limb was considered the ‘healthy control’ that was compared to the affected limb, there was increased Total Muscle Effort (summation of integrated EMG) during work tasks on the affected side. Similarly, Study 1 also demonstrated significant increases in activation of posterior deltoid and supraspinatus on the affected side during ROM-Reach, ROM-Rotate (excluding supraspinatus, $p=0.0520$), ADL and work tasks. However, in contrast to the current study findings, Study 1 results demonstrated a reduction in pectoralis major sternal activation on the affected side during ROM, ADL and work tasks. This discrepancy could be

due to methodological differences or population baseline comparison differences. Firstly, the muscle activation may be different due to the vastly different exertions being considered. Reduced pectoralis major sternal activation was seen in Study 1 during highly dynamic, functional tasks, which involved significant reach distance, extending the moment arm of pectoralis major. Increased pectoralis major (sternal and clavicular portions) activation was seen during static postures of IR and ER, during which the majority (67%) of exertions were performed with the arm at the side (for only 2% and 1% of tests was the humerus elevated to 45° and 90°, respectively). It may be that the pectoralis major is more capable of producing activation at lower elevation angles, but that muscle dysfunction is more evident in more extreme postures. Scar tissue formation and anterior chest wall tightness is evident in this population (Lauridsen, Cristiansen, & Hessove, 2005), and Study 1 kinematics have demonstrated the survivors tend to keep the affected arm closer to the side and more internally rotated. This may reflect an adaptive change due to a dysfunction in the pectoralis major which is more evident at extreme ranges. Increased activation found in these extreme ranges may reflect increased levels of pain due to stretching or tearing of tight or damaged tissues. Galiano-Castillo et al. (2011) suggested increases in survivor EMG may be due to pain or fear of pain and Shamley et al. (2012) demonstrated that pain was associated with higher levels of muscle activation in survivors. Secondly, the discrepancy of pectoralis major activity may be due to the fact that the current study was comparing activation levels of survivor and healthy populations; whereas activation levels between unaffected and affected limbs of survivors were compared in Study 1. Shamley et al. (2012) compared muscle activity and scapulothoracic kinematics of both shoulders of survivors and also compared to healthy women, and reported bilateral changes of shoulder morbidity. Shamley et al. (2012) found that survivors that had mastectomies demonstrated higher pectoralis major activity on the affected side compared to a healthy control, but in contrast, survivors that had wide local excision demonstrated decreased pectoralis major activity on the affected side compared to a healthy control. The discrepancies found in pectoralis major muscle activation may reflect different muscle strategy adaptations occurring due to type of movement performed and type of surgery received, and

consideration should be taken when comparing within or between populations. In addition, the activation of the subscapularis of the survivor group was higher during ER exertions. This is of particular interest as it may suggest survivors increased reliance on subscapularis as a primary internal rotator to help stabilize the glenohumeral joint during ER exertions (and maintain the CI ratio), due to reduced function of the pectoralis major assumed to be adversely affected by adjuvant treatments.

Interpretation of some results is compromised due to conflicting findings between respective surface and intramuscular EMG activation levels. Specifically, there is difficulty in interpretation of the strategies used by survivors in activation of the supraspinatus during ER exertions, and activation of the supraspinatus and infraspinatus during IR type exertions. During ER exertions, the survivors had higher levels of supraspinatus activation recorded intramuscularly, but there was no significant difference between surface recordings. During IR exertions, the survivors had higher levels of infraspinatus (surface) and supraspinatus (wire) signals, but there was no significant difference in activation levels between their respective wire and surface recordings. Intramuscular electrodes are recommended for recording EMG from the rotator cuff (Waite, Brookham, & Dickerson, 2010), but it is not always feasible to use them. Almost half (24) of the participants agreed to insertion of intramuscular electrodes, but the remaining individuals declined due to fear of complications or risk of lymphedema, so surface electrodes were used to record rotator cuff activity of these participants. Surface electrodes have been shown to reasonably reflect activation patterns of their respective intramuscular recordings in both maximal (Waite, Brookham, & Dickerson, 2010) and submaximal (Allen, Brookham, Cudlip, & Dickerson, 2013) exertions of healthy participants. Surface electrodes better represent their intramuscular counterparts during submaximal exertions, compared to maximal exertions (Allen, Brookham, Cudlip, & Dickerson, 2013). The exertions of the current study were submaximal, and it was assumed that the surface electrode would reasonably reflect the activation recorded by the intramuscular (gold standard) electrode. Surface recordings generally overestimate

intramuscular recordings, likely in part due to cross-talk contamination of overlying muscles. Waite et al. (2010) reported 4 – 11% cross-talk between infraspinatus and upper and middle trapezius, posterior deltoid and infraspinatus; and reported 9 - 17% cross-talk between supraspinatus and posterior deltoid and upper trapezius during maximal exertions. Other differences between surface and intramuscular recordings have been attributed to muscle size and location (which can affect the reliable placement of electrodes (Waite, Brookham, & Dickerson, 2010)); posture, intensity and whether the muscle was a primary mover (Allen, Brookham, Cudlip, & Dickerson, 2013). The statistical differences found between activation levels of surface and intramuscular recordings of supraspinatus and infraspinatus may be a result of these above mentioned factors, or could be a reflection of the variance seen in the signals (Table 31). Further, the relationships between these electrode types has not been examined in a survivor population, and changes in muscle characteristics due to surgery and adjuvant treatments could impact these relationships. Although the statistical significance of the differences was not consistent, the general findings agreed that activation levels of supraspinatus and infraspinatus for both surface and wire recordings were higher in the survivor population compared to the healthy.

This is the first study to define co-activation patterns of breast cancer survivors. Regression models were able to predict survivor CI well during static IR and ER exertions, demonstrating greater explanation of variance compared to CI regression models of a healthy population (defined in Study 2 of this thesis). There was good agreement between healthy and survivor CI, indicating similar joint level strategies for maintenance of GH stability, which was supported by various changes in survivor muscle strategies. In general, the survivors demonstrated greater activation in the pectoralis major, posterior deltoid, latissimus dorsi and supraspinatus, compared to the healthy group. Muscle activation strategies deployed by the survivors were generally coincident with EMG and kinematic findings from Study 1 and that of previous work. Differences in study methodologies including; exertions examined (type, intensity), population comparisons made (contralateral limb vs.

healthy control) and electrode types used (surface vs. intramuscular) made some comparisons difficult, and may have confounded some findings. The results of this study are not generalizable to other exertions. Due to the nature and location of surgery and radiation, the IRs located on the anterior chest wall (pectoralis major clavicular and sternal insertions) are commonly affected (Dalberg, Krawiec, & Sandelin, 2010; Sugden, Rezvani, Harrison, & Hughes, 1998), causing pectoralis major capability and humeral internal-external rotation exertions to be of most interest within this population. Future works should continue to examine breast cancer co-activation by attempting to extrapolate this relationship to a wider range of tasks and intensities.

Section 6.6 Study contribution to science and health

This study contributes to both science and health by furthering knowledge about shoulder muscle activation and coordination in a breast cancer survivor population. This first attempt at quantification of these co-activation relationships has provided insight into how survivor muscles compensate during dysfunction. Continued advancement of this knowledge could allow knowledge translation to clinicians to improve diagnostic capabilities, providing a more thorough understanding of what dysfunction is occurring and which muscles are affected, and may promote the generation of evidence-based therapeutic preventative and treatment interventions to treat these identified dysfunctions. These defined relationships will be used in Study 4 of this thesis in a computational shoulder model, to investigate changes to muscle strategy with inclusion of co-activation constraints, and adjustments of pectoralis major capability.

Chapter 7 Study 4 – Modelling changes in humeral internal and external rotation strength of breast cancer survivors to investigated employed muscle strategies

Section 7.1 Introduction

Biomechanical models are useful for predicting biophysical magnitudes such as moments, joint and muscle forces that are difficult, infeasible, or unethical to measure empirically. Biomechanical analyses of the upper limb are at a relatively early stage compared to gait and low back biomechanics (Dickerson, 2008b). A summary of ten shoulder biomechanical models is provided by Dickerson (2008b). Specifically, the Shoulder Loading Analysis Modules (SLAM) is a 3-D, inverse dynamic link-segment model of the right upper limb (38 muscle segments) which is not dependent on experimental data, includes dynamics and is population scalable (Dickerson, 2005; Dickerson, Chaffin, & Hughes, 2007). Mathematical biomechanical models frequently negate co-activation of antagonistic muscles (Collins, 1995; Dickerson, Hughes, & Chaffin, 2008; Hughes & Chaffin, 1988; Zajac & Gordon, 1989), often because optimization procedures employed assume the body activations muscles according to the minimal total muscle stress (Crowninshield & Brand, 1981). In these instances, antagonistic contraction would be considered mathematically counterproductive. By mischaracterizing the co-activation characteristics of muscles, the models underestimate muscle activity predictions, which results in low estimates of joint contact forces. Inclusion of co-activation predictions will increase physiological realism of models, and should enhance accuracy of model predictions. Humeral IR and ER co-activation has been defined at the shoulder in a healthy population (Brookham & Dickerson, 2014), and was defined in a breast cancer population in Study 3 of this thesis.

There is a need for models that provide insight into the mechanisms of specific muscle disability, such as those experienced within a breast cancer population. It is important to have models that can predict strength and link it back to specific tissue injuries. Models which can successfully achieve this goal could be useful in the return to work of injured populations (not just exclusively

breast cancer survivors) by evaluating the capacity of workers and assessing this capacity in the context of workplace task demands. By modifying inputs to an existing advanced upper limb biomechanical model to reflect specific muscle deficits, strength and anthropometrics of a survivor population, predictions of muscle strategy and function could be useful in providing insight into mechanisms of specific muscle disability. Understanding the mechanisms of disability is an essential first step to treating and preventing the disability.

Capability of the pectoralis major has been shown to be consistently compromised in a breast cancer survivor population (Dalberg, Krawiec, & Sandelin, 2010; Rietman, et al., 2003; Sugden, Rezvani, Harrison, & Hughes, 1998). Previous investigations have demonstrated that the pectoralis major demonstrates changes and dysfunction on the affected side of survivors, thought to be due to surgery or cancer treatments. Shamley et al. (2007) used MRI to measure the size of the unaffected and affected side pectoralis major and minor, rhomboids and serratus anterior muscles of 57 female breast cancer survivors ranging from 6 months to 6 years post-surgery. Pectoralis major and minor demonstrated a significant decrease in size on the affected side, which authors reported was not surprising due to its location in the field of surgery and radiation (Shamley, et al., 2007). Shamley et al. (2007) surmised that reduction in size of the pectoralis major may affect the survivor's ability to reach up, since extensibility of the muscle is required to allow for full humeral elevation. Reductions in elevation angle have been reported in previous works (Hack, Cohen, Katz, Robson, & Goss, 1999; Kuehn, et al., 2000; Rietman, Dijkstra, Debreczeni, Geertzen, Robinson, & De Vries, 2004), including the results of Study 1 of this thesis. Reduction in pectoralis major activity has been seen previously in the affected shoulder of survivors during scaption, compared to a healthy population (Shamley, Lascurain-Aguirrebena, Oskrochi, & Srinaganathan, 2012). Similarly, results from Study 1 of this thesis reported reductions in survivor pectoralis major sternal activation during ROM, ADL and work tasks. Activation of the pectoralis major can further be compromised by damage to the supplying pectoral nerve, which is susceptible to harm during axillary node dissections (Lauridsen,

Torsleff, Husted, & Erichsen, 2000). Due to the nature and location of surgery and radiation treatment of breast cancer, the internal rotators located on the anterior chest wall (pectoralis major clavicular and sternal insertions) are commonly affected, causing pectoralis major capability and humeral internal-external rotation exertions to be of most interest within this population. Modeling internal and external rotation strength of breast cancer survivors provides a conceptual understanding of what type and amount of muscle force decrements most affect functional outcomes. As the pectoralis major (sternal and clavicular) muscle force capabilities were reduced and disabled, the effect of these simulated changes in muscle strategy were evaluated. The predicted outcomes generated an understanding of what functional changes in muscle strategy occur when certain pectoralis portions are decremented or disabled.

The purposes of this study were to modify an existing 3-D, inverse dynamic link-segment model of the right upper limb (specifically, the Shoulder Loading Analysis Modules (SLAM) (Dickerson, 2005; Dickerson, Chaffin, & Hughes, 2007)) in terms of survivor pectoralis major capability, co-activation (defined from Study 3 of this thesis) and population anthropometrics to determine the following:

1) Determine how muscle strategy is affected by specific muscle dysfunction (using an inverse-type simulation). Specifically, compare how closely SLAM muscle force predictions represent empirically measured survivor EMG during IR and ER exertions.

2) Determine if inclusion of survivor IR and ER exertion type co-activation constraints improve the physiological realism of the muscle force predictions (more closely represent the empirically recorded EMG).

It was hypothesized that:

1. SLAM muscle force predictions will be more closely associated with empirically measured EMG activation levels during states of reduced pectoralis major capability. Specifically,

correlations between EMG and muscle force predictions will be highest when the pectoralis major capability is set to 0.25, 0.50 and 0.75; and correlations will be lowest when capability is set to 0.0 or 1.0. Similarly, it is assumed that differences between predicted and actual values of activation will be smallest when the pectoralis major capability is set to 0.25, 0.50 and 0.75; and differences will be greatest when capability is set to 0.0 or 1.0.

Due to the nature of surgeries and adjuvant treatments received in the population under study, and the resultant evidence of dysfunctional changes prevalent in this population (as demonstrated by muscle activation and kinematic changes in Study 1 of this thesis), it is assumed that survivors will neither have total disability (pectoralis major capability of 0) nor total capability (100% capable of producing maximal force) of the pectoralis major muscles. It is hypothesized that survivors maintain 0.25-0.75 ability of the pectoralis major capability, which will be reflected by higher correlations between EMG and model predictions and lower activation differences during these conditions.

2. Inclusion of the co-activation constraint would result in the muscle force predictions more closely representing the empirically recorded muscle activation. Specifically, correlations will be greater and activation differences will be smaller when co-activation is enforced.

Previously, elbow flexor and extensor co-activation constraints were included in an optimization muscle force prediction model of the elbow, and results demonstrated that inclusion of these constraints improved the model predictions, bringing them closer to the empirically measured activation levels (Brookham, Middlebrook, Grewal, & Dickerson, 2011).

Section 7.2 Methods

Survivor anthropometrics, posture and hand forces were inputted into the SLAM model. Capability of pectoralis major sternal and clavicular portions was adjusted, and survivor IR and ER co-activation ratios were added as constraints to the inverse-type simulation. Predictions of muscle strategy were compared with experimentally collected EMG.

Section 7.2.1 Background of the SLAM model

Before details can be provided regarding modifications made to the SLAM model, the reader must be provided a basic overview of what the SLAM model entails. SLAM is a 3-D inverse dynamic link-segment model of the right upper limb developed by Dickerson (2005) and further detailed by Dickerson et al. (2007; 2008). The SLAM model is comprised of 3 major components: 1) a geometric model representing shoulder muscles and bones; 2) an external dynamic shoulder torque model; and 3) an internal muscle force prediction model. For the purpose of this thesis, only aspects of the geometric model and the muscle force prediction model applicable to this thesis' study will be discussed.

The SLAM geometric model accepts motion files as input. The static posture of interest of the current study was with the arm at the side (0° humeral elevation) and the elbow bent to 90°. This posture was initially created in the University of Michigan's 3-D Static Strength Prediction Program (3DSSPP) software (described in by Chaffin, Andersson & Martin (1999)), and the orientation and relative position of each shoulder bone was transferred to the SLAM model. The SLAM geometric model then defined bone parameters (scapula, clavicle, humerus and torso), muscle lines-of-action and moment arms for 38 muscle elements represented in the model. (A total of 23 shoulder muscles are represented in the model, but some muscles have multiple contributors and are modeled as having more than one line of action.) Muscle attachment sites and muscle lines of action were numerically determined in the SLAM geometric model. Segment lengths for each bone were calculated based on torso length with published proportions (Makhsous, 1999). Muscle attachment sites were based on a cadaver study (Hogfors, Sigholm, & Herberts, 1987), and were represented on each bone mathematically as a fractional distance along each axis, relative to segment length. Muscle line-of-actions were wrapped using variations of spherical and cylindrical geometric wrapping techniques as is further detailed in Dickerson (2007).

The SLAM muscle force prediction model implements optimization procedures to solve the load distribution problem among the muscles that are required to resist external forces, while maintaining shoulder stability. Dickerson (2005) described five key elements used to determine one unique solution to the load-sharing problem, as described briefly here:

1. *Mechanical equilibrium constraints:* sum of forces and moments equal zero
2. *Force bounds for individual muscles:* muscles cannot transmit force in tension; upper and lower bound for muscle tension are defined
3. *A glenohumeral contact, non-dislocation constraint:* stability ratios (directional shear to compressive force) of joint dislocation tolerances are used
4. *An objective function* to minimize the sum of the cubed muscle stresses
5. *A solution methodology:* to minimize the objective function using linear equality constraints

The outputs of the muscle force prediction model include the prediction of individual muscle forces at distinct time points throughout a dynamic exertion (or one static posture as was the case of this thesis' study). These predictions were provided as normalized muscle forces (percentages of maximum prediction muscle force). For the purposes of this thesis' study, only 11 of the 38 muscle components force predictions were of interest (to allow for comparison of those 7 muscles EMG was recorded from in Study 3). The 11 muscle components of interest are outlined in Table 32.

.

Table 32 List of muscle portions modeled that were compared with experimental results from Study 3

Number	Muscle Modeled (Muscle Portion)
1	Latissimus Dorsi I (Upper)
2	Latissimus Dorsi II (Lower)
3	Pectoralis Major I (Sternal Insertion)
4	Pectoralis Major II (Clavicular Insertion)
5	Posterior Deltoid
6	Infraspinatus I (Upper)
7	Infraspinatus II (Lower)
8	Subscapularis I (Upper)
9	Subscapularis II (Middle)
10	Subscapularis III (Lower)
11	Supraspinatus

Section 7.2.2 Modifications made to the SLAM model

Specific inputs and adjustments were necessary to customize the SLAM model to allow survivor net glenohumeral internal/external moment to be transformed to specific muscle forces using optimization procedures in the posture of interest. Inputs included:

1. *The posture:* arm at side at 0° elevation, elbow flexed to 90°
2. *Breast cancer survivor anthropometrics:* stature and body mass for 50 survivors (measured during Study 3). These parameters were used to generate population-specific bone length parameters which were used during link-segment inverse calculations to transform hand force to net glenohumeral internal/external moment.
3. *Hand forces:* 19.6 N IR, 19.6 N ER, 40 N IR and 40 N ER. These exertions were performed by survivors in Study 3 of this thesis: the force produced at the hand was measured with a tri-axial force transducer (MC3-6-500, Advanced Mechanical Technology Inc., Watertown, Massachusetts) and confirmed with visual force feed-back of breast cancer survivors, as detailed in Study 3. It should be noted that the affected (cancer) side was on the right for 23 participants; and the affected side was on the left for 27 participants. For the left-affected participants, forces were mirrored to represent forces acting on the right side so they could

be inputted into the right-handed SLAM model. It was assumed that muscle behavior would be consistent on either side.

4. *Survivor humeral rotator co-activation constraints:* These relationships were defined during IR and ER type exertions in Study 3 (Equation 25 and Equation 27). The model was run when no co-activation was enforced, and when co-activation was enforced.
5. *Pectoralis major force capability:* The force capability of the pectoralis major sternal and clavicular muscle portions was adjusted to reflect total disablement, fractions of capability, and total capability, as described in Equation 29. This modification simulated reduced pectoralis major contribution due to muscle damage resulting from cancer treatments.

Equation 29 Muscle force capability. Where PCSA is physiological cross-sectional area; ST is specific muscle tension for muscle, *i*; and M is a multiplier that was set at 0 (muscle is disabled), 0.25, 0.50, 0.75 and 1.0 (maximal force capability of muscle, *i*).

$$F_i = PCSA_i \cdot ST_i \cdot M$$

As mentioned above, optimization was used to solve for specific muscle forces. The objective function which was implemented was the sum of the cubed muscle stresses (Equation 30), which has been used in several models (Crowninshield & Brand, 1981; Brookham, Middlebrook, Grewal, & Dickerson, 2011; Dickerson, 2005; Dickerson, Chaffin, & Hughes, 2007).

Equation 30 Objective function: Sum of the cubed muscle stresses. Where Θ is the objective function, f_i is the force prediction in an individual muscle *i*, and $PCSA_i$ is the physiological cross-sectional area of the same muscle *i*.

$$\Theta = \sum_{i=1}^{11} \left(\frac{f_i}{PCSA_i} \right)^3$$

The format of constraints (Equation 31) and set of constraints associated with minimization of the objective function within the SLAM model were as follows and were similar to Dul et al., (1984) (Equation 32, Equation 33, Equation 34, Equation 35, and Equation 36)

Equation 31 Minimization of the objective function (Θ) using linear equality constraints

$$\textbf{Minimize } \boldsymbol{\Theta}, \quad \text{such that } \mathbf{Ax} = \mathbf{B}$$

Equation 32 Constraint 1: Muscle (*i*) can only develop tensile force (F)

$$\textbf{Minimize } \boldsymbol{\Theta}, \quad \text{such that } \mathbf{F}_i \geq \mathbf{0}$$

Equation 33 Constraint 2: Force (F) equilibrium must be maintained. Where *F* are the forces; *m* is the mass of segment and *a* is the acceleration of segment COM. External forces are the hand forces and weights of the segments. Solving the resulting equation achieves the external joint load at each proximal joint segment.

$$\textbf{Minimize } \boldsymbol{\Theta}, \quad \text{such that } \sum \mathbf{F} = \boldsymbol{m_{segment}} \times \boldsymbol{a_{COM,segment}} = \mathbf{0}$$

Equation 34 Constraint 3: Moment (M) equilibrium must be maintained. Where *M* is external moment and Ḣ is the rate of change of segmental angular momentum. Ḣ is calculated based on segmental moments of inertia and the segmental velocities and accelerations. External moments are calculated based on the cross products of the produced forces and their moment arms. Moments are calculated at the proximal ends of each segment.

$$\textbf{Minimize } \boldsymbol{\Theta}, \quad \text{such that } \sum \mathbf{M} = \dot{\boldsymbol{H}} = \mathbf{0}$$

Equation 35 Constraint 4: Specific muscle (i) force (F) is limited by maximal (max) muscle force capacity

$$\textbf{Minimize } \boldsymbol{\Theta}, \quad \text{such that } \mathbf{F}_i < \mathbf{F}_{i_{max}}$$

Equation 36 Constraint 5: Co-activation constraint (k) between IR muscle (*IR*) and ER muscle (*ER)* forces (F)

$$\textbf{Minimize } \boldsymbol{\Theta}, \quad \text{such that } \sum \boldsymbol{F_{IR}} = \mathbf{k} \cdot \sum \boldsymbol{F_{ER}}$$

Optimization procedures resulted in predictions of specific muscle forces which were then compared directly with experimentally measured EMG of survivors (which was recorded during Study 3). The model was run for 2000 iterations, accommodating for 50 survivors, 2 co-activation constraints (none or included); 5 force capability constraints for two pectoralis major muscles; during 4 hand forces (19.6 N and 40 N of IR and ER) as is depicted in Figure 39. The study methods and general model inputs and outputs are depicted in Figure 40.

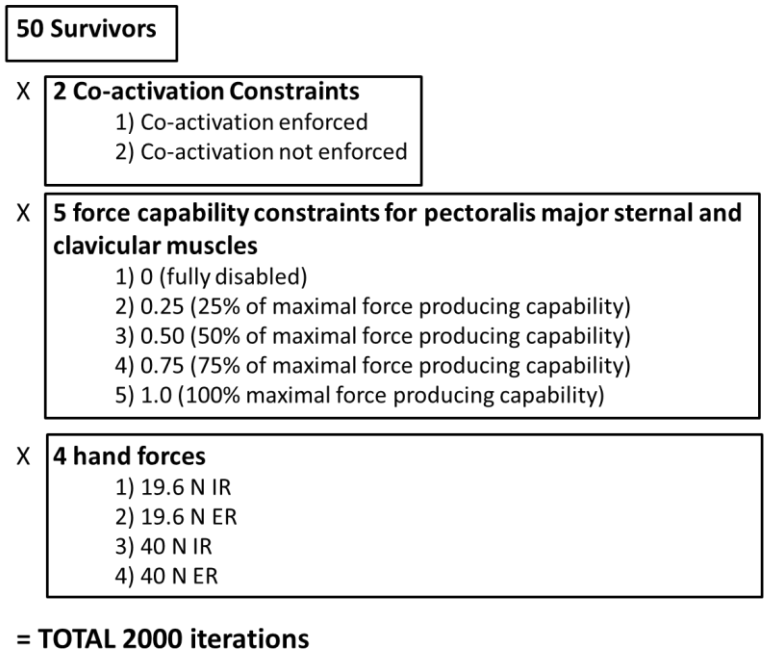

Figure 39 Break-down of model iterations: model was run for 2 co-activation constraints, 5 force capability constraints and 4 hand forces for 50 breast cancer survivors.

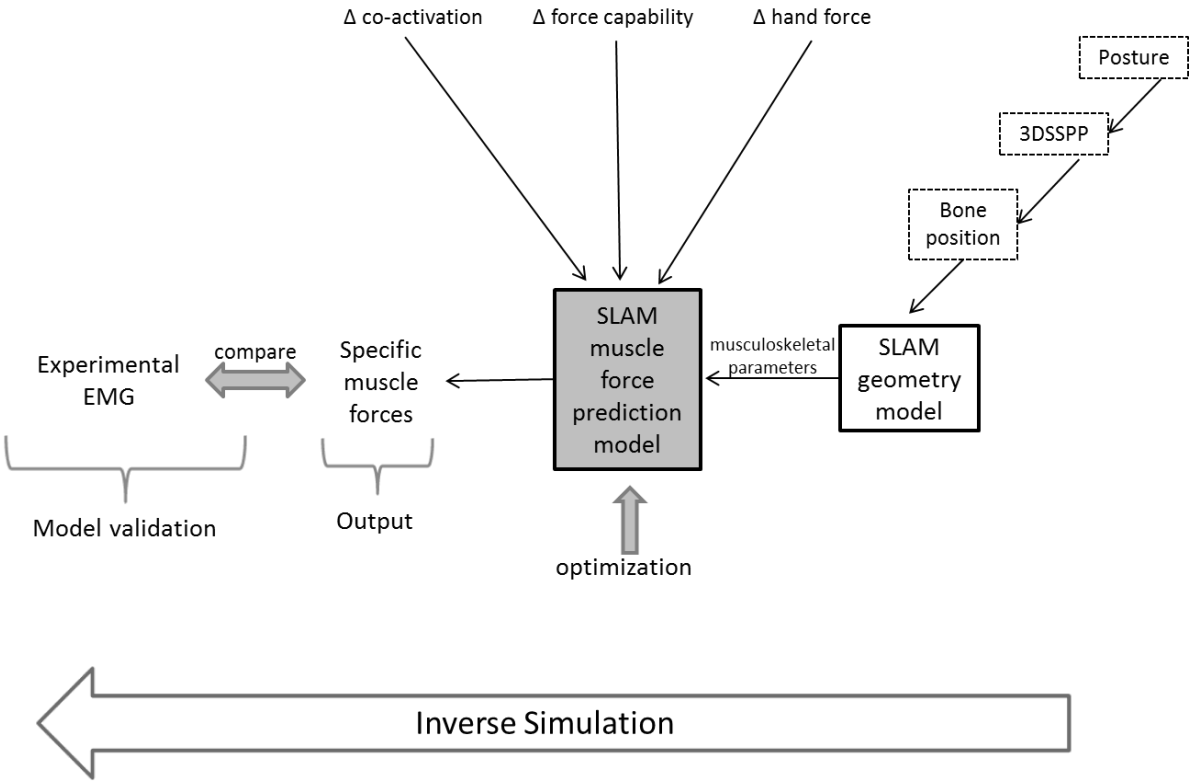

Figure 40 Study 4 Methods and general inputs and outputs: Posture was recreated in 3DSSP and bone positions were implemented into SLAM. Hand force, force capability and co-activation conditions were modified and muscle force predictions were solved using optimization procedures. Muscle force predictions were compared with experimentally recorded muscle activation.

Section 7.2.3 Predicted muscle force assessment

Correlation coefficients were calculated to compare model and experimental values, and describe the degree (strength and direction) of linear association present. Specifically, 1000 correlations were calculated between the model muscle force predictions (% MVF) and experimental EMG (%MVC) of internal and external rotator type muscles, grouped by pectoralis major capability (0, 0.25, 0.50, 0.75, 1.0) and co-activation status (enforced or no co-activation). Similar to Study 2 and 3 of this thesis, the internal rotators were defined as the subscapularis, pectoralis major clavicular / sternal heads and latissimus dorsi; and the external rotators were considered the infraspinatus, posterior deltoid and supraspinatus muscles.

To investigate closeness of magnitudes of muscle force predictions with EMG, average normalized muscle force predictions (model output) were compared with average empirical measures of normalized muscle activation using a simple difference calculation (Equation 37).

Equation 37 Activation difference calculation. Where MFP = model muscle force prediction (normalized to percent maximal force) and EMG = measured muscle activation (normalized to percent maximal exertion).

$$Diff_{activation} = MFP - EMG$$

Section 7.3 Analysis

Model muscle force predictions were compared with experimental electromyographic data in JMP 11® (SAS Institute Inc., Cary, NC) for 2 muscle types (IR/ER), 2 co-activation constraint conditions, 4 hand force conditions and 5 pectoralis major capability constraints.

Section 7.3.1 Statistical analysis

To determine any differences in correlation coefficients between groups, an ANOVA was run with the correlation coefficients as the dependent variable, and the independent variables included subject as a random variable, muscle type (IR/ER), CI constraint (on/off) and pectoralis major capability (5 conditions). Main and interaction effects were analyzed.

To determine any differences in magnitudes of predictions and EMG between groups, an ANOVA was run with the activation difference (Equation 37) listed as the dependent variable, and the independent variables included subject as a random variable, muscle type (IR/ER), CI constraint (on/off), hand force (19.6 N IR/ER, 40 N IR/ER) and pectoralis major capability (5 conditions). Main and interaction effects were analyzed.

Post hoc analyses were performed using Student's t-tests (for differences in correlation coefficients between two-level conditions) and Tukey's Honestly Significant Differences tests (for differences in correlation coefficients and activation differences between groups with more than 2

levels). Mean and standard deviations of correlation coefficients for all subjects were calculated for muscle types between groups (CI constraint and pectoralis major capability).

Section 7.4 Results

The ability of the model to predict muscle activation was influenced by muscle type, the CI constraint condition, hand force and pectoralis major capability; as well as some interactions of these factors.

Section 7.4.1 Main effect results for correlation coefficients

The correlations between model predictions and empirically measured muscle activation were significantly higher for external rotator muscles compared to internal rotators ($r = 0.567$ [±0.264] vs. 0.347 [±0.254], respectively; $p < 0.0001$; F ratio 272.42. Whole model $p < 0.0001$.), as depicted in Figure 41.

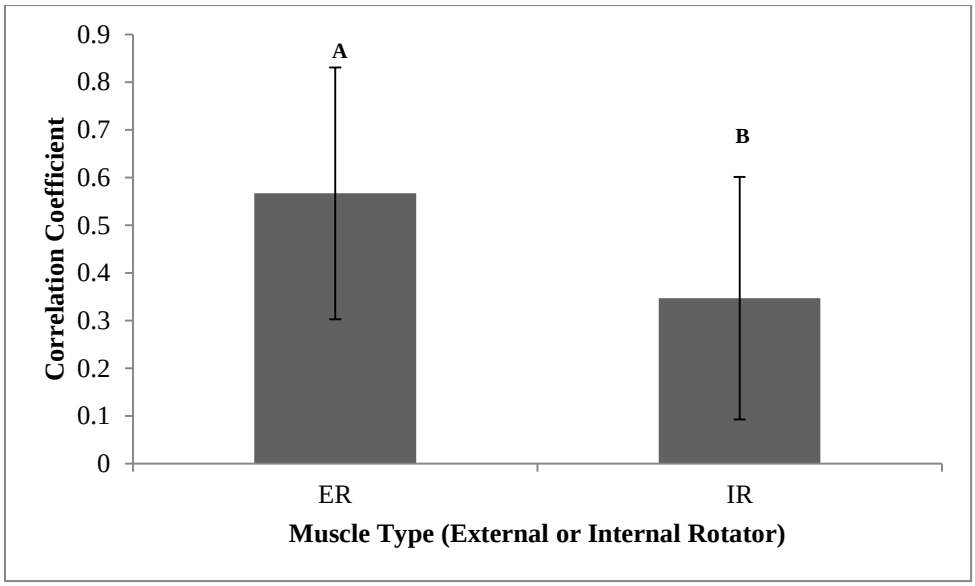

Figure 41 Prediction ability between muscle type. LSM±SD are shown. Levels not connected by same letter are significantly different.

The correlations between model predictions and empirically measured muscle activation were significantly higher when the CI constraint was not enforced (r = 0.580 [±0.286] vs. 0.333 [±0.214], respectively; p < 0.0001; F ratio 342.35. Whole model p< 0.0001.), as depicted in Figure 42.

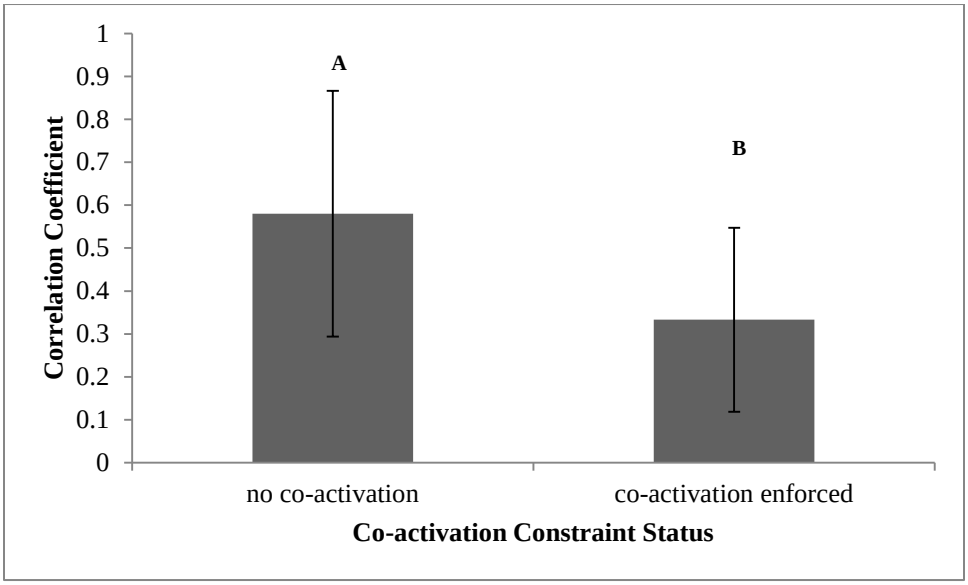

Figure 42 Prediction Ability between co-activation constraints. LSM±SD are shown. Levels not connected by same letter are significantly different.

The correlations between model predictions and empirically measured muscle activation were significantly higher during pectoralis major capability intermediate levels compared to correlations during total disability or total capability (p = 0.0015, F ratio 4.41):

- r during 0.25, 0.5, 0.75 (r = 0.46 – 0.48) > r during 0 pectoralis capability (r = 0.40)

Description of significant differences between levels is depicted in Figure 43.

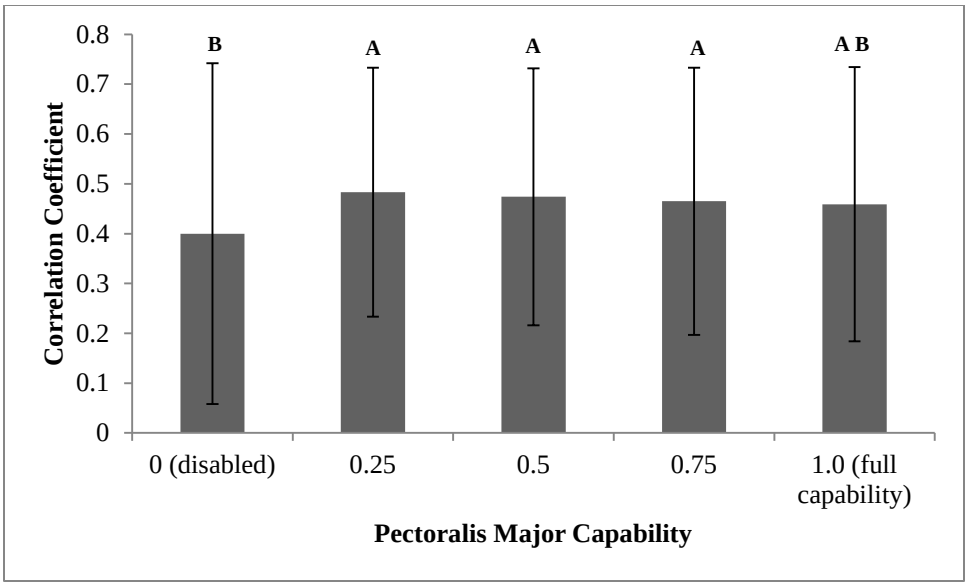

Figure 43 Prediction ability between pectoralis major capability constraints. LSM±SD are shown. Levels not connected by same letter are significantly different.

The effect size of main effects variables was in the following descending order:

CI constraint > Muscle Type > Pectoralis Major Capability

The ANOVA assumptions were not violated as the independence of variables were ensured through random sampling, and normality and equal variance was confirmed (mean 0.04, SD = 0.002).

Section 7.4.2 Main effect results for activation differences

The activation differences between model predictions and empirically measured muscle activation were significantly less for external rotator muscles compared to internal rotators (LSM = -20.3% [±23.4] vs. -21.7% [±34.0], respectively; p=0.0010; F ratio 10.9. Whole model p< 0.0001.), as depicted in Figure 44. Negative values indicate the model predictions were lower (underestimated) actual measurements of muscle activation.

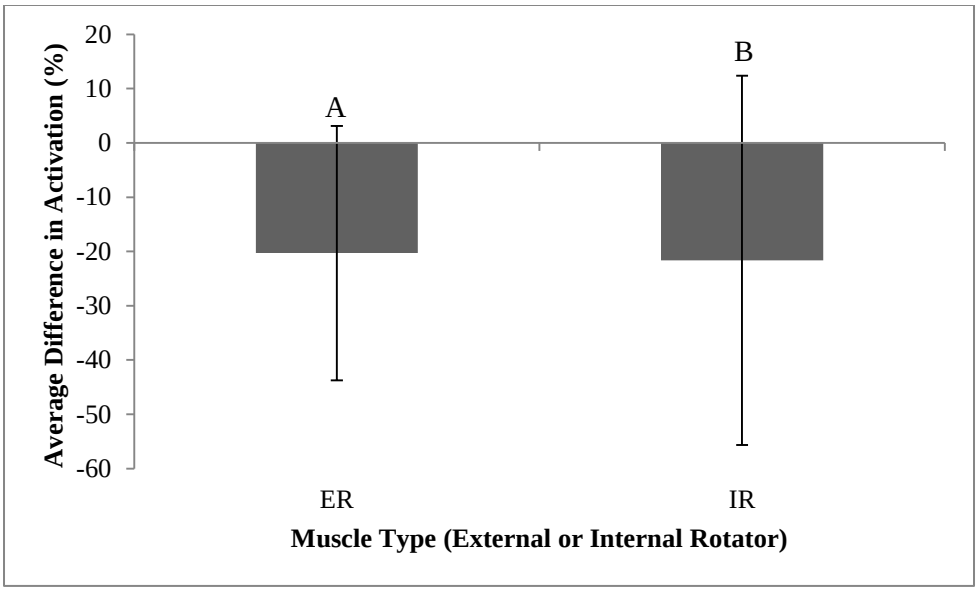

Figure 44 Difference between predicted and actual muscle activation: between muscle types. LSM±SD are shown. Levels not connected by same letter are significantly different.

The activation differences between model predictions and empirically measured muscle activation were significantly less when the co-activation constraint was enforced compared to predictions without co-activation (LSM = -18.4% [±31.9] vs. -23.5% [±27.6], respectively; $p < 0.0001$; F ratio 164.1. Whole model $p < 0.0001$.), as depicted in Figure 45.

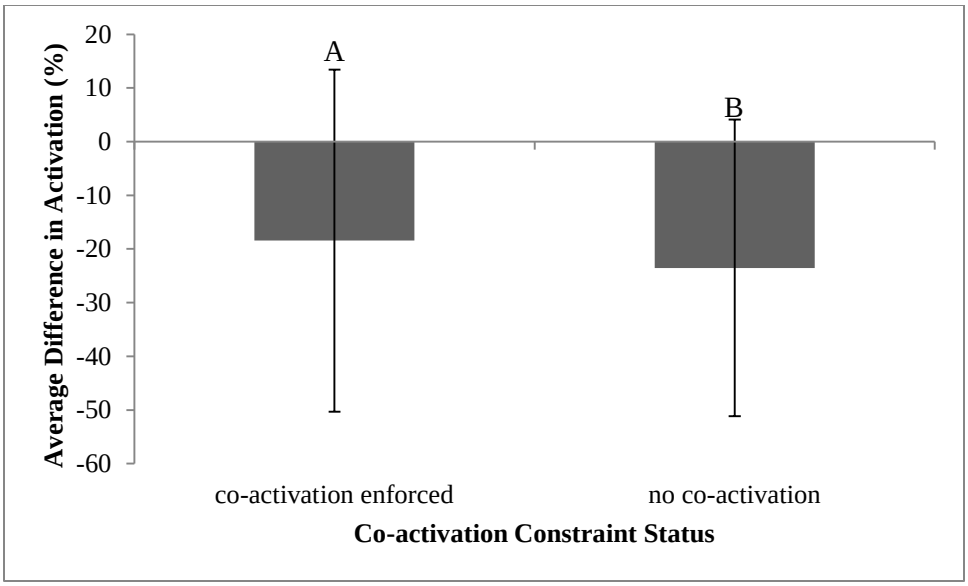

Figure 45 Difference between predicted and actual muscle activation: between co-activation constraints. LSM±SD are shown. Levels not connected by same letter are significantly different.

The activation differences between model predictions and empirically measured muscle activation were significantly less when the pectoralis major capability constraint was set to 0.25 compared to other capability levels (LSM = -19.0% [±31.2] vs. -20.9 - -21.89% [±29.5-29.9], respectively; $p < 0.0001$; F ratio 6.8. Whole model $p < 0.0001$.), as depicted in Figure 46.

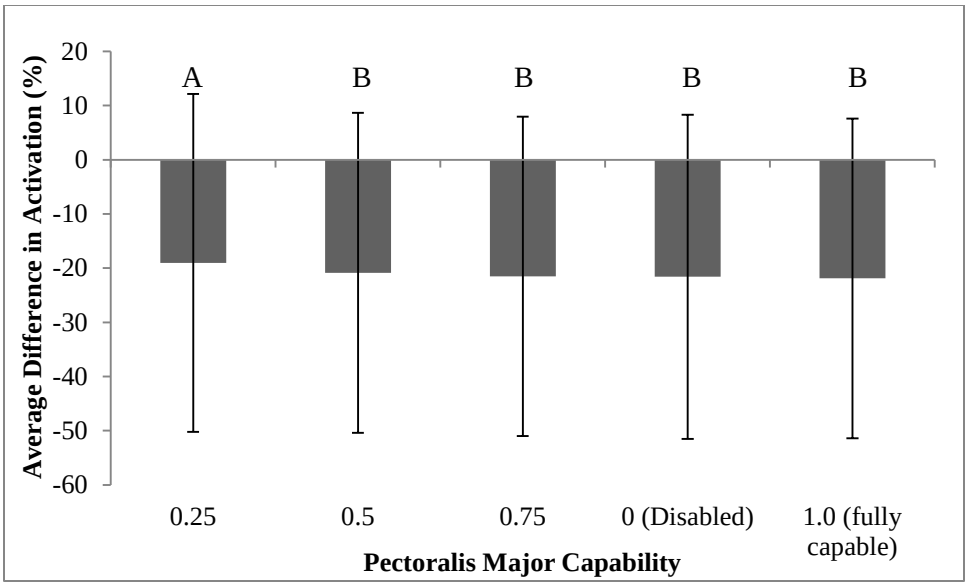

Figure 46 Difference between predicted and actual muscle activation during various pectoralis major capability constraints (0 (disabled) – 1.0 (fully capable) pectoralis major contributions). Mean differences in activation and standard deviations are shown. Levels not connected by same letter are significantly different.

The activation differences between model predictions and empirically measured muscle activation were significantly less for lower hand forces (19.6 N) and internal rotation exertions, compared to higher hand forces (40 N) and external rotation exertions (LSM = -13.5% [±23.0], -15.8% [±25.8] vs. -24.17% [±31.9], -30.41% [±36.4] respectively; $p < 0.0001$; F ratio 358.4. Whole model $p < 0.0001$.), as depicted in Figure 47.

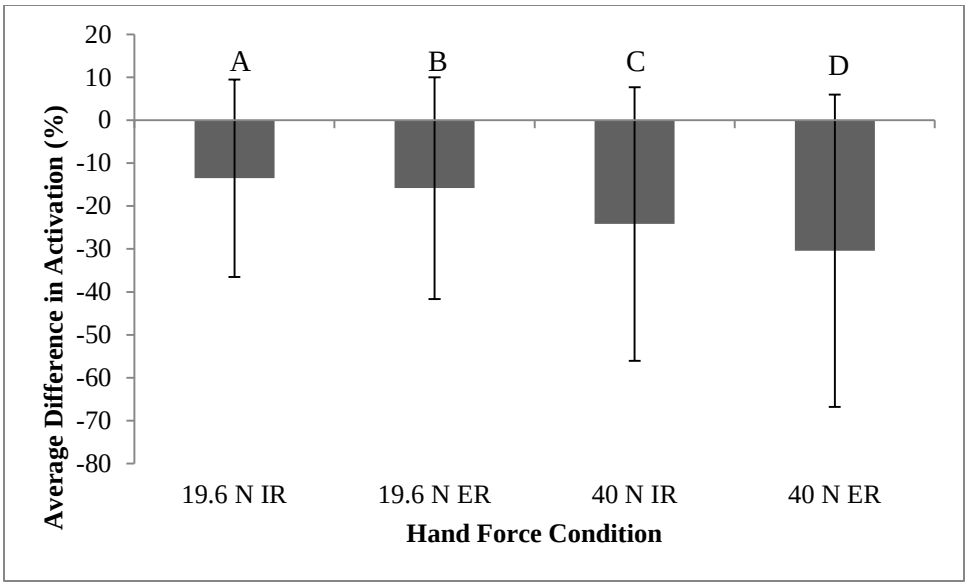

Figure 47 Difference between predicted and actual muscle activation: between hand force conditions. LSM±SD are shown. Levels not connected by same letter are significantly different.

The effect size of main effects variables was in the following descending order:

Hand force > co-activation constraint > muscle type > pectoralis major capability

Section 7.4.3 Interaction effect results for correlation coefficients

There were significant interaction effects between muscle type and pectoralis major capability correlations ($p<0.0001$; F ratio = 12.93. Whole model $p<0.0001$) as depicted in Figure 48.

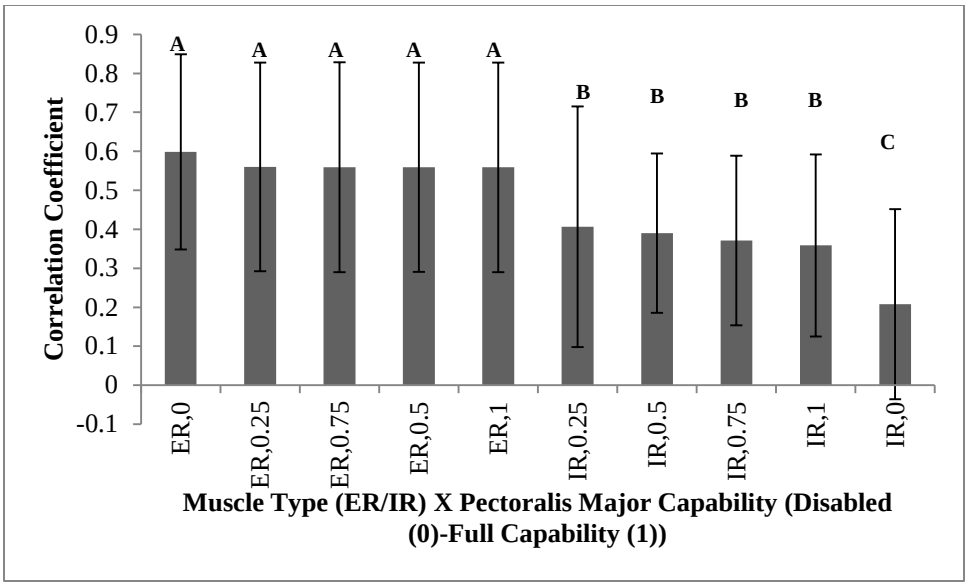

Figure 48 Prediction ability by muscle type interacted with pectoralis major capability. LSM±SD are shown. Levels not connected by same letter are significantly different.

There were significant interaction effects between co-activation constraint and pectoralis major capability correlations ($p=0.0021$; F ratio = 4.24. Whole model $p<0.0001$) as depicted in Figure 49.

The effect size of interaction effects variables was in the following descending order:

muscle type X pectoralis major capability > co-activation constraint X pectoralis major capability

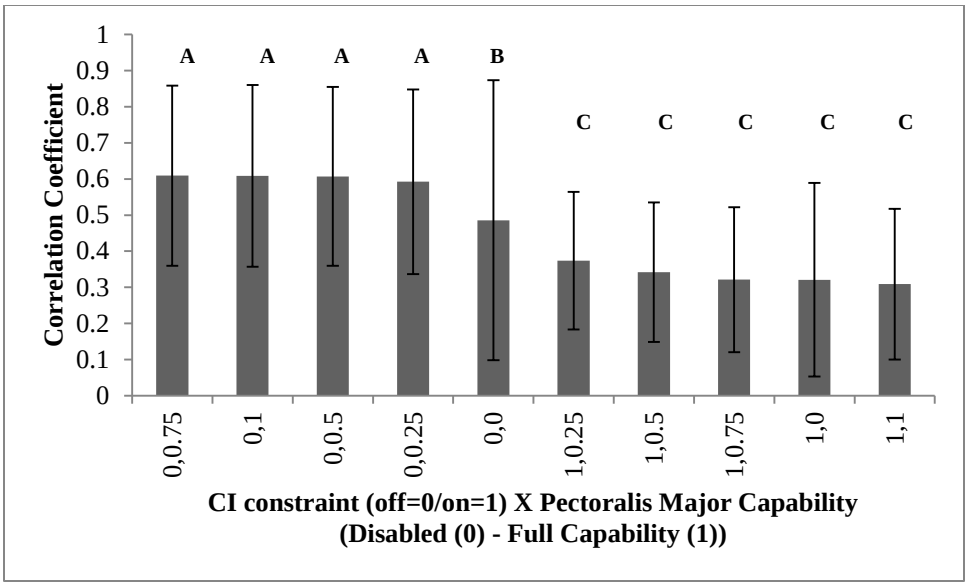

Figure 49 Prediction ability by CI constraint interacted with pectoralis major capability. LSM±SD are shown. Levels not connected by same letter are significantly different.

Section 7.4.4 Interaction effect results for activation differences

There were significant interaction effects between activation differences of muscle type and pectoralis major capability constraints ($p=0.0001$; F ratio = 5.7. Whole model $p<0.0001$) as detailed in Table 33.

Table 33 Interaction effects between activation differences (MFP-EMG) of muscle type X pectoralis major capability constraints. Muscle type included internal rotator muscles (IR) and external rotator muscles (ER). Pectoralis major capability constraints included 0 (disabled) – 1.0 (fully capable) conditions.

Level				MFP-EMG	SD
0.25,IR	A			-18.2	35.9
0.75,ER	A	B		-20.4	23.5
0.5,ER	A	B		-20.4	23.5
1,ER	A	B		-20.5	23.5
0.25,ER	A	B		-20.5	23.5
0,ER		B	C	-21.0	23.2
0.5,IR		B	C	-21.5	33.3
0,IR		B	C	-22.2	34.1
0.75,IR		B	C	-22.6	33.2
1,IR			C	-23.2	33.2

There were significant interaction effects between activation differences of hand force and co-activation constraints ($p<0.0001$; F ratio = 20.6. Whole model $p<0.0001$) as detailed in Table 34.

Table 34 Interaction effects between activation differences (MFP-EMG) of hand force X co-activation constraints. Hand forces include 19.6 N and 40 N internal (negative values) and external (positive values) rotation exertions. Co-activation was enforced (1) or not enforced (0).

Level						MFP-EMG	SD
-19.6,1	A					-12.0	23.4
-19.6,0	A					-13.4	22.6
19.6,1	A					-13.7	28.1
19.6,0		B				-19.7	22.8
-40,1		B	C			-21.4	32.6
-40,0			C			-23.6	31.1
40,1				D		-27.9	41.0
40,0					E	-36.6	30.1

There were significant interaction effects between activation differences of hand force and pectoralis major capability constraints ($p=0.0071$; F ratio = 2.3. Whole model $p<0.0001$) as detailed in Table 35.

Table 35 Interaction effects between activation differences (MFP-EMG) of hand force X pectoralis major capability constraints. Hand forces include 19.6 N and 40 N internal (negative values) and external (positive values) rotation exertions. Pectoralis major capability constraints included 0 (disabled) – 1.0 (fully capable) conditions.

Level						MFP-EMG	SD
-19.6,0.25	A					-10.4	24.0
-19.6,0.5	A					-12.5	22.5
-19.6,0.75	A	B				-13.3	22.5
-19.6,0	A	B				-13.6	23.1
-19.6,1	A	B				-13.6	22.6
19.6,1		B	C			-16.7	25.8
19.6,0.25		B	C			-16.7	25.9
19.6,0.75		B	C			-16.7	25.8
19.6,0.5		B	C			-16.7	25.8
19.6,0		B	C			-16.8	25.8
-40,0.25			C			-18.0	35.4
-40,0.5				D		-22.4	30.6
-40,0				D		-23.8	31.8
-40,0.75				D		-23.9	30.3
-40,1				D		-24.6	30.5
40,0.5					E	-32.0	36.4
40,0.75					E	-32.2	36.4
40,0.25					E	-32.3	36.4
40,1					E	-32.4	36.4
40,0					E	-32.4	36.3

There were significant interaction effects between activation differences of hand force and muscle type ($p=0.0071$; F ratio = 798.4. Whole model $p<0.0001$) as detailed in Table 36.

Table 36 Interaction effects between activation levels (MFP-EMG) of hand force X muscle type. Hand forces include 19.6 N and 40 N internal (negative values) and external (positive values) rotation exertions. Muscle type included internal rotator muscles (IR) and external rotator muscles (ER).

Level							MFP-EMG	SD
-19.6,ER	A						-5.7	7.8
19.6,IR		B					-10.7	25.4
-40,ER		B					-10.7	9.7
-19.6,IR			C				-19.6	28.5
40,IR			C	D			-21.5	39.3
19.6,ER				D			-22.8	24.5
-40,IR					E		-34.3	38.2
40,ER						F	-43.1	27.5

There were significant interaction effects between activation differences of co-activation constraints and muscle type ($p<0.0001$; F ratio = 126.3. Whole model $p<0.0001$) as detailed in Table 37.

Table 37 Interaction effects between activation differences (MFP-EMG) of co-activation constraints X muscle type. Muscle type included internal rotator muscles (IR) and external rotator muscles (ER). Co-activation was enforced (1) or not enforced (0).

Level				MFP-EMG	SD
1,IR	A			-17.1	36.3
1,ER		B		-20.4	24.7
0,ER		B		-20.8	22.1
0,IR			C	-25.9	30.9

There were significant interaction effects between activation differences of hand force and co-activation constraints and muscle type ($p<0.0001$; F ratio = 85.7. Whole model $p<0.0001$) as detailed in Table 38.

Table 38 Interaction effects between activation differences (MFP-EMG) of hand force X co-activation constraints X muscle type. Muscle type included internal rotator muscles (IR) and external rotator muscles (ER). Co-activation was enforced (1) or not enforced (0). Hand forces include 19.6 N and 40 N internal (negative values) and external (positive values) rotation exertions.

Level										MFP-EMG	SD
19.6,1,IR	A									-3.8	27.0
-19.6,1,ER	A									-4.4	7.9
-19.6,0,ER	A	B								-7.0	7.4
-40,1,ER		B	C							-8.6	10.7
40,1,IR			C	D						-11.0	43.1
-40,0,ER				D						-12.9	8.0
19.6,0,IR					E					-17.6	21.5
-19.6,1,IR					E	F				-19.6	28.7
-19.6,0,IR					E	F				-19.7	28.3
19.6,0,ER						F	G			-21.9	24.1
19.6,1,ER							G			-23.7	25.0
40,0,IR								H		-32.0	31.7
-40,1,IR								H		-34.3	38.4
-40,0,IR								H		-34.4	38.0
40,0,ER									I	-41.3	26.7
40,1,ER									I	-44.8	28.1

There were significant interaction effects between activation differences of hand force and muscle type and pectoralis capability constraints ($p=0.0189$; F ratio = 2.0. Whole model $p<0.0001$) as detailed in Table 39.

Table 39 Interaction effects between activation differences (MFP-EMG) of hand force X muscle type X pectoralis major capability constraints. Muscle type: internal (IR) and external rotators (ER). Hand forces: 19.6 N and 40 N IR [-] and ER [+] exertions. Pectoralis major capability constraints: 0 (disabled) – 1.0 (fully capable) condition.

Level								MFP-EMG	SD
-19.6,0.5,ER	A							-5.5	7.8
-19.6,1,ER	A							-5.5	7.8
-19.6,0.75,ER	A							-5.5	7.8
-19.6,0.25,ER	A							-5.6	7.8
-19.6,0,ER	A							-6.3	7.9
-40,1,ER	A	B						-10.4	9.9
-40,0.75,ER	A	B						-10.4	9.9
-40,0.5,ER	A	B						-10.4	9.8
-40,0.25,ER	A	B						-10.4	9.8
19.6,0.25,IR	A	B						-10.5	25.4
19.6,0.5,IR	A	B						-10.6	25.3
19.6,1,IR	A	B						-10.7	25.4
19.6,0.75,IR	A	B						-10.7	25.4
19.6,0,IR	A	B						-10.8	25.4
-40,0,ER	A	B						-11.8	8.9
-19.6,0.25,IR		B	C					-15.2	30.6
-19.6,0.5,IR			C	D				-19.5	27.9
-19.6,0,IR			C	D	E			-20.8	28.6
-19.6,0.75,IR				D	E			-21.0	27.5
40,0.5,IR				D	E			-21.2	39.2
40,0.25,IR				D	E			-21.4	39.3
40,0.75,IR				D	E			-21.5	39.4
40,1,IR				D	E			-21.6	39.3
40,0,IR				D	E			-21.6	39.2
-19.6,1,IR				D	E			-21.7	27.5
19.6,1,ER				D	E			-22.7	7.8
19.6,0.75,ER				D	E			-22.7	24.6
19.6,0,ER				D	E			-22.8	24.5
19.6,0.5,ER				D	E			-22.8	24.6
19.6,0.25,ER				D	E			-22.9	24.6
-40,0.25,IR					E			-25.6	44.8
-40,0.5,IR						F		-34.4	36.2
-40,0,IR						F		-35.8	38.2
-40,0.75,IR						F	G	-37.3	34.9
-40,1,IR						F	G	-38.7	34.7
40,0.5,ER							G	-42.8	27.6
40,0.75,ER							G	-42.8	27.6
40,0.25,ER							G	-43.2	27.4
40,0,ER							G	-43.2	27.5
40,1,ER							G	-43.2	27.4

The effect size of interaction effects variables was in the following descending order:
Hand force X muscle type > CI X muscle type > hand force X CI X muscle type > hand force X CI > pectoralis capability X muscle type > hand force X pectoralis capability > hand force X pectoralis capability X muscle type.

Section 7.4.5 General descriptive findings

Mean correlation coefficients and associated standard deviations for ER and IR type muscles, by co-activation constraints and pectoralis major capability constraints are depicted in Figure 50. A typical scatterplot matrix of EMG and muscle force predictions for external and internal rotators by co-activation constraints and pectoralis major capabilities is shown for one subject in Figure 51.

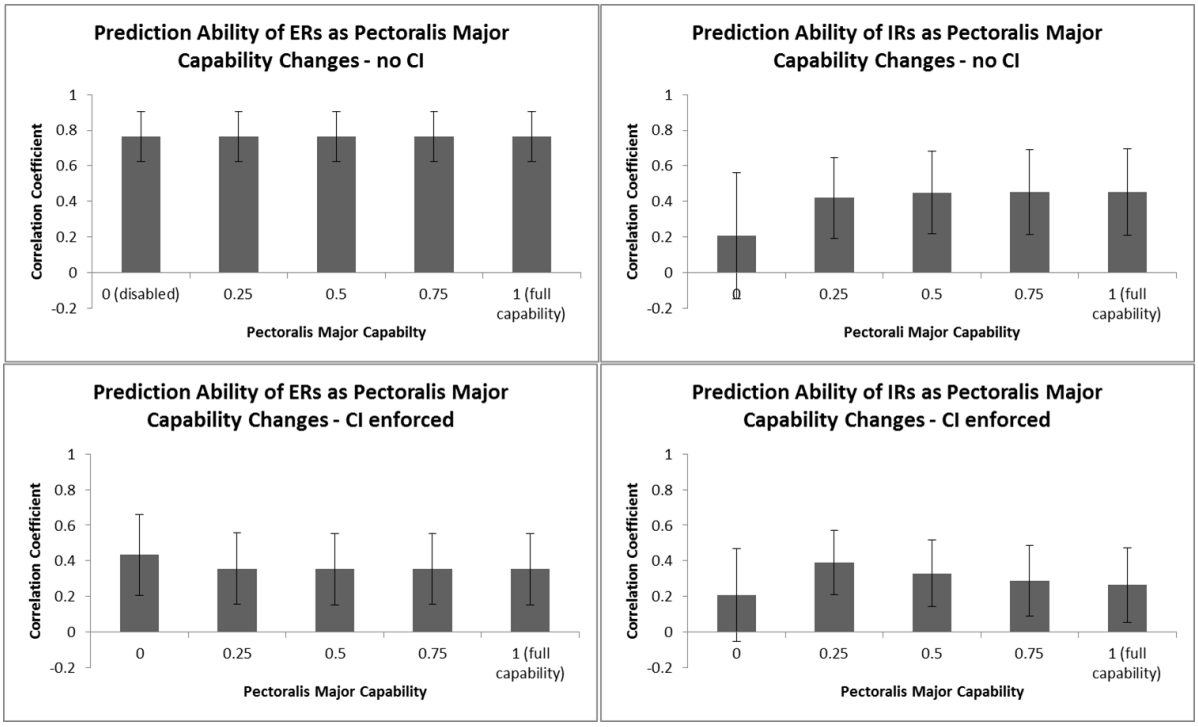

Figure 50 Mean (SD) Correlation Coefficients for all Subjects by muscle type (ERs = A, B; IRs = C, D), CI constraint (none = A, B; enforced = C, D) and pectoralis major capability condition.

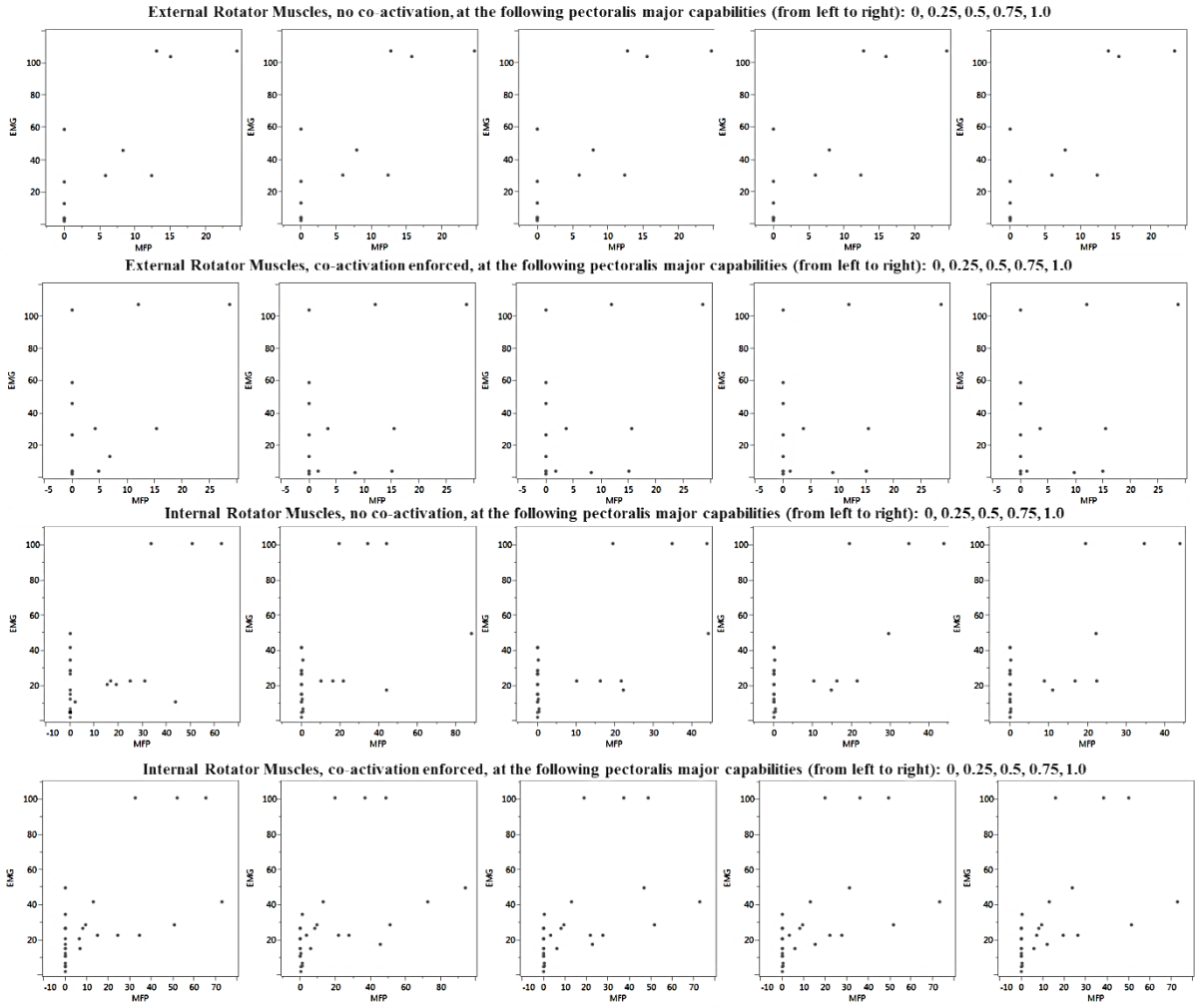

Figure 51 Typical scatterplot matrix of EMG (%MVC) [Y axis] and muscle force prediction (% maximal force) [X axis] of internal and external rotator muscles, by co-activation constraint and pectoralis major capability is shown for one subject.

Section 7.5 Discussion

The purposes of this study were to modify an optimization-based muscle force prediction model in terms of survivor pectoralis major capability, co-activation and population anthropometrics to determine how muscle strategy was affected by specific muscle dysfunction (how closely model muscle force predictions were associated to empirically measured survivor EMG); and to determine if inclusion of survivor IR and ER exertion type co-activation constraints improved the physiological

realism of the muscle force predictions (are model predictions more closely associated with EMG when co-activation constraints were enforced). In general, the model underestimated actual muscle activity but was able to predict external rotator muscle activity more closely than for internal rotators. Predictions were influenced by muscle type, co-activation constraints, hand force and pectoralis major capability. The model predictions were closer to empirical measures of muscle activation when the co-activation constraint was enforced.

Section 7.5.1 Addressing the hypotheses

Revisiting Hypothesis 1: It was hypothesized that model predictions would be more closely associated (higher correlation and lower activation difference) with EMG during states of reduced pectoralis major capability, and lowest (lower correlation and greater activation difference) during total disability or total capability constraints. This hypothesis was **partly confirmed**. Confirming the hypothesis, correlation coefficients were higher during 0.25, 0.50 and 0.75 pectoralis major capability constraints, compared to totally disabled or totally capable conditions. Partly confirming the hypothesis, activation differences (MFP – EMG) were significantly smaller only during 0.25 pectoralis major capability constraints, compared to all other conditions; and activation differences were greatest during fully disabled and fully capable conditions, however there was no significant difference between 0, 0.5, 0.75 or 1.0 pectoralis capability conditions.

Revisiting Hypothesis 2: It was hypothesized that the inclusion of the co-activation constraint would improve the association between model predictions and EMG. This hypothesis was **partly confirmed.** The differences in activation between predicted muscle force and measured muscle activation were significantly smaller (indicating closer predictions) when co-activation was enforced. However, in terms of correlation coefficients, the linear association between EMG and muscle force predictions worsened when co-activation was enforced.

Section 7.5.2 Comparison of model predictions with empirical measures

The modeled muscle force predictions were more closely linearly associated to empirically recorded muscle activation levels for external rotator muscles, compared to internal rotators ($r = 0.567$ [±0.264] vs. 0.347 [±0.254], respectively; $p < 0.0001$). Similarly, despite small magnitude of differences, the activation differences were significantly less for external rotator muscles compared to internal rotators (LSM differences = -20.3% [±23.4] vs. -21.7% [±34.0], respectively). The results of the current study suggest that the ER muscle strategies used by survivors are more predictable (more consistent), compared to the strategies employed by IR muscles. Contrarily, in a healthy population ER muscle strategies were found to be more variable compared to IR muscles (Brookham & Dickerson, 2014). It was demonstrated in Studies 2 and 3 of this thesis that compared to a healthy population, co-activation relationships of survivors during external rotation exertions are 42% more predictable ($r^2 = 0.77$). The healthy population was thought to exhibit more variable activation strategies during ER exertions in attempt to preserve glenohumeral stability. The glenohumeral joint is more susceptible to dislocation during humeral elevation and ER. Muscle stabilization roles change with posture (Lee, Kim, O`Driscoll, Morrey, & An, 2000; McKernan, et al., 1990), and external rotation exertions often involve extreme or end ranges of motion, during which passive ligaments contribute to stability, affecting the selection and magnitude of required muscle control. It appears there is a reduction in external rotator muscle strategies used (or available for use) in the survivor population, which could be explained by dysfunctional changes and limits to these muscles. Study 1 of this thesis demonstrated that survivors exhibit dysfunctional changes (including weakness, increased required muscle effort and increased ratings of discomfort) in posterior chest muscles, including the posterior rotator cuff (external rotators), posterior deltoid and upper trapezius during dynamic, functional tasks. These changes may limit the number of strategies available to ERs for the purposes of maintaining joint stability. Consistent ER muscle strategy between survivors would allow the model to reflect EMG more closely. Reduced prediction accuracy of IR muscles may be due to variability in survivor IR muscle health and may also reflect the exertion and posture under

investigation. Heterogeneity of survivors (as described in Studies 1 and 3 of this thesis) was evidenced by various type and timing of treatment and interventions. Past works have demonstrated pain and movement deviations are greater in survivors who had undergone mastectomy surgeries, compared to those who had received wide local excision (Shamley, Lascurain-Aguirrebena, Oskrochi, & Srinaganathan, 2012). Variability of IR muscle strategy was demonstrated in Studies 1 and 3 of this thesis during which survivors demonstrated reduced activation of the pectoralis major sternal muscle during dynamic ROM, ADL and work tasks; but increased activity of the clavicular and sternal portions during static IR and ER exertions (the majority of static exertions performed with the arm at the side – similar to the modeled exertion posture of the current study). Dysfunction of the pectoralis major muscles may be more evident during postures which require larger moment arms. Therefore, in the modeled posture, dysfunction may be less obvious and survivors may have more strategies available for use causing an increase in variability of activation and a reduction in prediction accuracy. Palmerud et al. (1995) demonstrated that in a healthy population, different subjects may use different muscle strategies, and could voluntarily redistribute muscle activity at the shoulder. Posture, task type and inconsistent IR muscle health could cause increased variability in IR muscle strategies used and available for use by survivors, and would explain reduced prediction accuracy and increased activation differences between modeled muscle forces and EMG.

The model predictions were most closely associated with EMG during reduced (but not disabled) pectoralis major capability. Activation differences also confirmed that modeled predictions were closest to EMG measurements during a state of reduced pectoralis major capability (25% capability). This confirms the hypothesis, and suggests survivors did have some degree of pectoralis major dysfunction, but were not totally disabled. It is not surprising that predictions would be worse at fully disabled and fully capable conditions, due to the subject pool and displayed abilities. Every subject had some type of intervention or treatment that was likely to compromise pectoralis major function to some degree, but each participant demonstrated some ability in terms of strength, muscle

activation and kinematics to negate suggestions of total disability. Radiation is thought to cause vascular changes that result in muscle ischemia (Soulen, Romero, Chuba, Evelhouch, Simpson, & Forman, 1997; Wedgewood & Benson, 1992), which when accompanied with connective tissue constraints may affect the efficacy of muscle contraction (Blomlie, Rofstad, Tvera, & Lien, 1996; Gutman, Kersz, Barzilai, Haddad, & Reiss, 1990). MRI scans have shown pectoralis major and minor to be smaller on the affected side, suggesting induced muscle morbidity (Shamley, et al., 2007). There was no difference between correlation coefficients within 25-75% pectoralis major capability conditions, and no difference in activation between modeled and predicted values within 0% and 50% - 100% pectoralis major capability conditions (despite fully disabled and fully capable conditions demonstrating the greatest non-significant differences). These results suggest that in general the survivors under study best reflected a population with only 25% pectoralis capability; and that the muscle strategies used by survivors with dysfunction did not differ between most reduced capability levels. The prediction ability of the model during pectoralis major capability constraints is encouraging, as it demonstrates that specific muscle dysfunction can be modeled and that predictions sufficiently ($r = 0.465 – 0.483$; underestimated actual values by 19.0% - 21.9%) represent empirically measured activation levels. This shows promise for continued investigations, which should incorporate a larger sample size and data set, that would allow for individual muscle (rather than grouped) comparisons between tasks types. This method could also be expanded to investigate other disabilities or injuries: MRI studies have demonstrated muscle morbidity in cervical cancer (Blomlie, Rofstad, Tvera, & Lien, 1996) and prostate cancer (Soulen, Romero, Chuba, Evelhouch, Simpson, & Forman, 1997).

In support of the hypothesis, predictions were closer to actual values when co-activation constraints were enforced. The model predictions underestimated actual values by 18.4% [±31.9] when co-activation was enforced, but this difference was significantly greater when co-activation was not enforced (-23.5% [±27.6]). It was hypothesized that the inclusion of a survivor co-activation

constraint would improve the physiological realism of the model, and resultantly improve model predictions. A previous study demonstrated inclusion of elbow flexion/extension co-activation constraints into an optimization-based muscle force prediction model of the elbow improved model predictions of a healthy population, bringing them closer to empirically measured activation levels (Brookham, Middlebrook, Grewal, & Dickerson, 2011). Enforcing co-activation enhanced the physiological realism of the model (Study 3 demonstrated that this co-activation does exist), and the smaller magnitude of activation differences demonstrated that inclusion of this information does improve model predictions, bringing them closer to actual values. Contrary to hypothesis, linear association between predicted and actual values was weaker when co-activation was enforced (0.333 [±0.214] vs. $r = 0.580$ [±0.286], respectively; $p < 0.0001$). The decrease in correlation when co-activation was enforced emphasizes the nonlinearity of muscle demand. The relationship between the myoelectric signal and force is not a truly linear relationship, as has been shown by Lawrence & De Luca (1983). The predictions could perhaps be further improved (in terms of further reducing prediction underestimations, and strengthening correlations between actual and predicted values) by refining the co-activation constraint. The misestimated predictions during enforcement of the constraint may be explained by a limit in the generalizability of the defined co-activation. The survivor co-activation defined in Study 3 was built off of 18 static exertions of IR or ER at various intensity levels ranging from 10 – 60% individual MVF, during which the majority (67%) of exertions were performed with the arm at the side (for only 2% and 1% of tests was the humerus elevated to 45° and 90°, respectively). Despite good explained variance within the tasks upon which it was built, this co-activation constraint was then applied to this model and its use was generalized to absolute values of intensity (19.6 and 40 N of IR and ER), upon which its extrapolative ability was untested. It's obvious that the co-activation constraints did extrapolate reasonably well (as evident by the reduction in activation differences) to these new intensities (which would have varied drastically between survivors, depending on individual strength), but it's possible that further refinement of the co-activation constraint could have been useful in allowing it to more adequately represent survivor

co-activation for the exertions being modeled. Future works should continue refining definitions of survivor co-activation by expanding sample size, postures and intensities, and assessing ability of the defined relationships to extrapolate to novel tasks sets (as was similarly performed in a healthy population described in Study 2 of this thesis).

In terms of correlation coefficients, prediction ability was most strongly influenced by the main effects of co-activation ($F = 342.4$) and muscle type ($F = 272.4$), but it was also influenced by interaction effects between muscle type and pectoralis major capability ($p<0.0001$; F ratio = 12.93); and between co-activation and pectoralis major capability constraints ($p<0.0021$; F ratio = 4.24). The interaction effects outlined a similar message as the main effects: correlation coefficients were greater for ER muscles during all capability levels, compared to IR muscles during all capability levels. The lowest correlation occurred for internal rotator muscles defined to be totally disabled. Morbidity of the pectoralis major can be caused by radiation or nerve damage. Complete severance of the pectoral nerve is possible during surgery, but the introduction of sentinel node biopsies has reduced the morbidity rates associated with dissection (Lauridsen, Overgaard, Overgaard, Hessov, & Cristiansen, 2008; Rietman, et al., 2003). Total disablement of the pectoralis major was unlikely, and lower associations were likely to occur when the pectoralis major was considered totally disabled as all subjects demonstrated some muscle activity in the pectoralis major during all conditions. Further, as discussed previously, pectoralis major dysfunction may be less evident in a posture lacking an extended moment arm, and as a result the survivors may have had more muscle strategies available to them. Increased variability of muscle strategies used between survivors would result in lower correlations with model predictions. The interaction between co-activation and pectoralis major capability constraints demonstrated lower correlation coefficients when co-activation was enforced (no difference between capability levels) compared to when there was no co-activation. Compared to other capability levels with no co-activation, there were significantly lower correlations when there was no co-activation and the pectoralis was disabled. This again demonstrated how the total

disability constraint influenced the magnitude of the correlation coefficients, as no participant ever exhibited 0% MVF of pectoralis major activity (as was displayed in Figure 51).

In terms of activation differences, prediction ability was influenced by several main and interaction effects, the strongest including hand force X muscle type (F = 798.4), hand force (F = 358.4), co-activation (F = 164.1), co-activation X muscle type (F = 126.3) and hand force X co-activation X muscle type (F = 85.7). Main effect results demonstrated how predicted values were closest to actual values during lower intensity exertions and during IR exertions. Despite predictions being closest for ER type muscles, it was interesting to note that predictions were closest during IR exertions, when ER muscles would not be primary movers. This antagonistic activation would largely be negated in models that did not include co-activation (Collins, 1995; Dickerson, Hughes, & Chaffin, 2008; Hughes & Chaffin, 1988; Zajac & Gordon, 1989). Interaction effects demonstrated that as predictions were closest in ER type muscles during low intensity IR exertions (underestimated actual values by only 5.7%); and worst at high intensity exertions (underestimated actual values by 34.3% and 43.1% for IR and ER type muscles, respectively). These results suggest that dysfunction was more evident as muscle demand increased (as mentioned previously with regards to lengthened moment arm). The interaction between muscle type, hand force and co-activation again reiterated the improvement of predictions with the enforcement of co-activation (predictions underestimated actual values by only 3.8% - 4.4%. during low intensity exertions of IR and ER type muscles, respectively).

The misestimate of muscle forces is likely attributed to model assumptions, population and experimental factors. The SLAM models' prediction ability was evaluated previously during static hold and dynamic reach tasks in a healthy population, and predictions correlated positively with EMG and demonstrated good correlations for prime movers (r = 0.53 - 0.63) (Dickerson, Hughes, & Chaffin, 2008). In the current study, all predictions correlated positively over all subjects with EMG, and the predicted force of the external rotator muscles was similarly sufficient (r = 0.567), although internal rotators had lower correlation coefficients (r = 0.347), and variations existed across co-

activation and pectoralis major capability constraints. Although variations existed across main and interaction conditions, at best the model predictions underestimated actual values by only 3.8% - 4.4% (when co-activation was enforced during low intensity exertions of IR and ER type muscles, respectively). The model assumes consistent subject characteristics including segment scaling and muscle attachment sites (based on bone length). Ignoring intersegment length variations and changes to muscle moment arms could magnify muscle force prediction accuracies. The upper force bounds limiting a muscle are based on PCSA values taken from a cadaveric data set (Hogfors, Sigholm, & Herberts, 1987) and since the morphological characteristics have been reported to change due to factors such as shrinkage (Friedrich & Brand, 1990), they may not be representative of the survivor population. Shamley et al. (2007) performed paired t-tests for total mean muscle area (cm^3) determined from the MRI of 57 breast cancer patients and reported a significant decrease in size of the pectoralis major on the affected side ($t = 2.177$, $p = 0.034$). With future acquisition of accurate PCSA data for the BCP, the co-activation ratios should be weighted accordingly. Misestimates of true capabilities would impact the model predictions. Pain could inhibit force production in reality, but the objective function used in optimization procedures (minimized cubed muscle stresses) is not sensitive to that inhibition, and as a result, may provide higher estimates of force capabilities than were physiologically likely. Controlling for pain mathematically would be an extremely speculative process. Related to that, experimental and population factors can affect prediction accuracy. In particular, muscle force predictions and EMG comparisons rely on consistent normalization techniques. Although standardized testing protocols were used (and similar to those tested in a healthy population), true maximal exertions may not have been achieved. Survivors may have been involuntarily limited from, or may have voluntarily refrained from true maximal exertions due to pain, fear of pain or mechanical constraints (scar tissue formation limiting ROM, muscle dysfunction as evidenced in Studies 1 and 3). Improper normalization would have affected the correlation between recorded percent muscle activation and percent muscle force predictions. Further, there is limited confidence that the same proportion of maximum muscle activity results in identical muscle

forces for different individuals (Cram & Kasman, 1998). As discussed previously, the possible lack of generalizability of the co-activation constraint to the exertion modeled may have also contributed to misestimates.

This is the first known attempt to model potential specific muscle dysfunction of a breast cancer survivor population. EMG data was used to assess muscle force predictions generated by a mathematical model. Overall the model effectively estimated muscle activity in the ERs, and provided some insight into how IR and ER muscle strategy was affected by specific muscle dysfunction. The model's ability to approximate EMG was greatest for the ER muscle group, and demonstrated some difficulty predicting muscle force for the IR muscle group. The model predictions were more closely associated with EMG during reduced (but not dysfunctional) pectoralis major capability conditions. Inclusion of survivor co-activation constraints improved predictions, emphasizing the importance of including co-activation in biomechanical muscle force prediction models. Future works should incorporate a larger, more homogenous sample upon which the co-activation relationship was built, and should incorporate more postures and intensities from which EMG can be compared from. Further refinement and testing of the generalizability of population specific definitions of co-activation is advised. Future works should continue investigating modelled dysfunction in this and other patient populations, as predicted outcomes will generate an understanding of muscle strategies used during disability, which can be useful in the development of treatment plans.

Section 7.5.3 Study contributions to science and health

This study has contributed to science by expanding the current biomechanical modeling procedures to a breast cancer survivor population, modelling predicted muscle strength during specific muscle dysfunction. Advancements of this work could include other patient populations, which could be useful in the return to work of injured populations by evaluating the capacity of workers and assessing this capacity in the context of workplace task demands. Additional study with the survivor

population will specifically contribute to the advancement of health of breast cancer survivors, by providing a conceptual understanding of what type and amount of muscle force decrements most affect functional outcomes. Definition of the problem is the first step towards designing effective and targeted rehabilitative and preventative interventions.

Chapter 8 Summary

This chapter will address the global thesis objectives and revisit the associated hypotheses. Novel contributions of this work and their significance to science and health will be reviewed and future research directions will be suggested.

Section 8.1 Addressing the global thesis objectives and hypotheses

Study 1 Objectives:

1. Describe the upper limb capabilities and dysfunction of breast cancer survivors in terms of 3-D scapulothoracic and humerothoracic kinematics, muscle activation patterns, and muscle-specific strength.
2. Determine relationships between total muscle effort (a physical muscle activation quantity of (dys)function) with subjective measures of function (QoL and disability scores) during ROM, ADL and work task performance.

Study 1 Hypotheses:

1. Three-dimensional kinematics will reveal survivors have reduced humeral elevation angles and external rotation range of motion, but increased scapular protraction range of motion on their affected side compared to the contralateral limb.
2. Breast cancer survivors will demonstrate reduced strength and increased muscle activity on the affected side when performing muscle-specific strength tests, ROM, ADL and work tasks compared to their unaffected side.
3. As physical data indicates increased dysfunction (increased total muscle effort), there will be decreased QoL scores (FACT-B) and increased disability scores (QuickDASH).

Study 1 Main Findings:

In general, survivors demonstrated kinematic and muscle activation changes on the affected side including:

- **reduced humeral elevation angle:** trends indicated reduced maximal elevation angle on the affected side during all tasks, although only significant less (-6.5°) during ROM-Rotate tasks.
- **reduced humeral external rotation:** 8.9° less externally rotated during work tasks
- **increased humeral internal rotation:** 7.9° – 13.1° more internally rotated during ROM-Rotation, ADL and work tasks
- **reduced scapular protraction (although both sides were protracted):** 3.4° - 3.9° less protraction during ADL and work tasks (according to maximum angles), respectively; and 3.6° – 4.4° less protraction during ROM-Rotate and work tasks (according to minimum angles).
- **increased scapular posterior tilting:** 4.1° more during work tasks
- **increased scapular upward rotation:** trends indicated increased upward rotation during all tasks, although only significantly more (+2.8°) during ROM-Rotate tasks.
- **less downward rotation:** 2.9°– 3.5° less during all tasks

Some muscles on the affected side exhibited changes suggestive of dysfunction as evidenced by:

- **increased total muscle effort (summation of integrated EMG):** affected side TME was significantly greater during work tasks
- **increased effort/activation levels:** posterior deltoid was increased during all tasks, as was supraspinatus with the except of ROM-Rotate tasks ($p = 0.052$). Upper trapezius and serratus anterior also showed increases in activation that were depended upon task performance.
- **reduced activation:** Pectoralis major sternal muscle was significantly reduced during all tasks; infraspinatus was reduced in all tasks excepting ADL tasks
- **weakness:** infraspinatus, supraspinatus and upper trapezius demonstrated reduced force during functional testing

- **increased discomfort scores:** RPD scores were greater during infraspinatus and posterior deltoid maximal functional exertions on the affected side.

Both primary and secondary muscles (outside of the field of surgery and radiation) were affected. Total muscle effort was only modestly related to disability and QoL scores.

Study 2 Objectives:

1. Quantify co-activation relationships of humeral internal and external rotators in young healthy adults using non-weighted and PCSA-weighted co-activation index ratios.
2. Determine if the co-activation relationships defined from a subset of exertions can be extrapolated to other additional postures and intensities.

Study 2 Hypotheses:

1. It was hypothesized that the PCSA-weighted co-activation prediction models would better represent empirically measured co-activation compared to non-weighted co-activation prediction models.
2. It was hypothesized that the co-activation relationship determined for a subset of postures would be appropriately extrapolated to a unique subset of exertions.

Study 2 Main Findings:

Co-activation was defined for a healthy population during a subset of static IR and ER exertions:

- co-activation relationships were successfully defined for IR exertions ($r^2 = 0.70$)
- there was considerable unexplained variance in the co-activation relationships during ER exertions ($r^2 = 0.35$)
- humeral abduction and intensity were important factors in the prediction of co-activation

- there was no or minimal improvement in r^2 using PCSA-weighted co-activation ratios (r^2 = 0.62 and 0.42 for IR and ER exertions, respectively) suggesting low utility
- non-weighted co-activation relationship was successfully extrapolated to a novel set of IR exertions (r^2 = 0.76 and 0.40 for IR and ER exertions, respectively).

Study 3 Objectives:

1. Quantify the co-activation relationships of humeral internal and external rotators in breast cancer survivors
2. Compare survivor co-activation relationships with those of a healthy population

Study 3 Hypothesis:

It was hypothesized:

- muscle-activation patterns of the BCP will reveal survivors have a reduced internal/external humeral rotation co-activation ratio compared to healthy individuals during IR exertions (reflecting a decrease in pectoralis major activation).

Study 3 Main Findings:

Co-activation was defined for the BCP during a subset of static IR and ER exertions:

- co-activation relationships were successfully defined for IR exertions (r^2 = 0.77)
- co-activation relationships were successfully defined for ER exertions (r^2 = 0.77)
- Survivor co-activation relationships were very similar to healthy co-activation relationships, suggesting different muscle strategies were being employed to maintain glenohumeral stability.
    - humeral abduction and intensity continued to play important roles in co-activation
    - body mass affected the prediction of co-activation during ER exertions of the BCP
- co-activation ratios demonstrated the BCP had higher levels of rotator muscle activation during their respective rotation-type exertion

- Survivors demonstrated significant increases in activation of the pectoralis major muscles (up to +8.7%), compared to the healthy population, suggesting dysfunction may be more evident in more extreme ranges of motion when the moment arm is lengthened.

Study 4 Objectives:

1. Determine how muscle strategy is affected by specific muscle dysfunction (using an inverse-type simulation). Specifically, compare how closely SLAM muscle force predictions represent empirically measured survivor EMG during IR and ER exertions.
2. Determine if inclusion of survivor IR and ER exertion type co-activation constraints improve the physiological realism of the muscle force predictions (more closely represent the empirically recorded EMG).

Study 4 Hypotheses:

1. SLAM muscle force predictions will be more closely associated with empirically measured EMG activation levels during states of reduced pectoralis major capability. Specifically, correlations between EMG and muscle force predictions will be highest when the pectoralis major capability is set to 0.25, 0.50 and 0.75; and correlations will be lowest when capability is set to 0.0 or 1.0.
2. Inclusion of the co-activation constraint would result in the muscle force predictions more closely representing the empirically recorded muscle activation.

Study 4 Main Findings:

Specific muscle dysfunction of a breast cancer population was modeling using an optimization based muscle force prediction model, and predicted muscle forces were compared to experimentally measured muscle activation levels:

- the model consistently underestimated actual muscle force
- model predictions were influenced by muscle type, co-activation constraints, hand force and pectoralis major capability

- correlation analysis revealed the model was able to predict ER muscle group activity sufficiently ($r = 0.567$), while displaying lower prediction accuracy for IRs ($r = 0.347$)
- the model predicted EMG better during reduced (but not disabled) pectoralis major capability conditions, demonstrating the BCP did have some level of pectoralis major dysfunction
- model predictions more closely represented empirically measured EMG when BCP co-activation was included as a model constraint ($p<0.0001$), reinforcing the importance of inclusion of co-activation in biomechanical models
- model predictions were closer to actual measures during low intensity exertions ($p<0.0001$)

Section 8.2 Research contributions and significance

Previous to this body of work the physical capabilities and dysfunction of breast cancer survivors had not been rigorously documented, particularly for the upper extremity. This limits the effectiveness of treatments and strategies to improve BCP function and ability to return to work. The studies within this thesis provide further information about the capability and dysfunction of breast cancer survivors, which can be used to further the research, treatment and preventative strategies surrounding this population.

Study 1 Contributions and significance:

This investigation has produced the most comprehensive collection of 3D humerothoracic and scapulothoracic kinematics and electromyographic recordings for the BCP. Further, although strength and measures of quality of life and disability have been established before in this population, they have never been associated with the physical quantities (kinematics and EMG) as described in this current work. The results from this work have furthered the knowledge that is currently understood about survivor muscle activation, strength and kinematic patterns during a wide range of

tasks. Accurate documentation of physical capability and dysfunction is the first step towards developing targeted treatment and preventative strategies for this disabled population.

Study 2 Contributions and significance:

This is the first known attempt to quantify healthy co-activation at the shoulder. Co-activation was defined with confidence during internal rotation exertions, and was shown to extrapolate successfully to novel tasks. Accurate quantification of co-activation would be useful to researchers, aiding in the understanding of muscle functional changes with posture to meet stability demands, and would be useful to compare to patient populations in hopes of identifying dysfunction. Inclusion of co-activation into biomechanical models as constraints would improve physiological realism and may improve accuracy of muscle force predictions.

Study 3 Contributions and significance:

This is the first known attempt to quantify breast cancer survivor co-activation at the shoulder. Survivor co-activation was defined for both internal rotation and external rotation exertions, displaying high levels of explained variance, during a modest group of static tasks. The survivor co-activation relationships defined were incorporated into an optimization-based muscle force prediction model (Study 4). Further, these co-activation levels were compared with healthy co-activation relationships to provide insight into specific muscle strategies employed by the patient population. This study demonstrated that pectoral major activation was higher than that of a healthy population in postures mostly involving modest pectoralis major moment arms. This was an important finding as pectoralis major sternal activation was found to be reduced in survivors performing ROM, ADL and work tasks (from Study 1), suggesting that pectoralis major dysfunction is more evident as its moment arm is extended. Continued advancement of this knowledge could allow knowledge translation to clinicians to improve diagnostic capabilities, providing a more thorough understanding of what dysfunction is occurring and which muscles are affected, and may

promote the generation of evidence-based therapeutic preventative and treatment interventions to treat these identified dysfunctions.

Study 4 Contributions and significance:

This is the first known attempt to model specific muscle dysfunction of a breast cancer survivor population. Overall the model effectively estimated muscle activity in the ERs, and provided some insight into how IR and ER muscle strategy was affected by specific muscle dysfunction. The model predictions were more closely associated with EMG during reduced (but not dysfunctional) pectoralis major capability conditions, suggesting the survivors did have some level of pectoralis major dysfunction. Model predictions were more close to measured activation levels when survivor co-activation constraints were enforced. Advancements of this work will specifically contribute to the health of breast cancer survivors, by providing a conceptual understanding of what type and amount of muscle force decrements most affect functional outcomes. Additional works could include other patient populations, which could be useful in the return to work of injured populations by evaluating the capacity of workers and assessing this capacity in the context of workplace task demands.

Overall Thesis Contributions:

This thesis accomplished three major goals: Study 1 **defined capacity** of the BCP, Studies 2 and 3 **compared capacity** of the BCP with that of a healthy population, and Study 4 **predicted capacity** of the BCP. The main findings demonstrated that differences in ROM (altered kinematics), muscle activation (altered muscle strategies), and strength (reductions in force) were quantifiable on the affected cancer side in comparison with the contralateral limb. Despite modest absolute changes, the values were both statistically significant and clinically meaningful. Changes in kinematics aligned with synchronous changes in muscle activation, strength and ratings of perceived discomfort. Similar magnitudes of change have been reported in other injury populations, and have been linked to important biological alterations (Borstad & Szucs, 2012; Ebaugh, McClure, & Karduna, 2005; Ludewig & Cook, 2000; Lukasiewics, McClure, Michener, Pratt, & Sennett, 1999). Secondary changes were evident, showing that posterior shoulder muscles outside the primary field of surgery and radiation were affected, stressing the importance of their focus in rehabilitation in addition to that of the anterior chest wall muscles, and recommending consideration of the entire shoulder mechanism in treatment approaches. Co-activation of the BCP was very similar to that of the healthy population at the joint level, demonstrating the maintenance of joint stability, which was maintained through the adoption of alternative muscle strategies. Despite caution with generalization of the results, the BCP is encouraged to strengthen and enhance ROM for the posterior chest wall muscles, in addition to the regularly administered stretching, ROM and strengthening of muscles within the primary field of treatment and disturbance. This research has provided a breadth and depth of novel contributions to the field with respect to biomechanical quantification of capacity and disability of the BCP, and provides an important foundational base for many future biomechanical studies, which are essential to the development of effective preventative and treatment regimes. Improving the physical function of the BCP will have a positive impact on their level of independence, ability to work and support themselves, fulfill their required family responsibilities and in general improve their quality of life. This improvement will result in less reliance upon health and social assistance

programs, which will undoubtedly have profound economic and societal benefits in the nation and world-wide.

Section 8.3 Future directions

This study assessed BCP kinematics and muscle activity to an unprecedented extent during a wide variety of tasks, which made little data available for comparison. Some findings displayed considerable variability which was not surprising due to the variety of tasks performed and the diversity of the population under study. Future works should involve larger sample sizes which could allow for grouping of participants into treatment types. Future studies should also involve pre and post-surgical assessments to allow for baseline comparisons. Comparisons between healthy control groups, as well as within patients (unaffected vs. affected side comparisons) should continue as kinematic and muscle activation changes have been reported bilaterally in survivors. Exertions involving greater reach distances and lifting external loads should be of particular interest, as muscle dysfunction may be more evident in more muscularly demanding conditions.

Co-activation relationships in both healthy and survivor populations should continue to be examined in a wider range of tasks, intensities and demographic. The ability of these relationships to be extrapolated to novel tasks must be evaluated, as its successful integration into biomechanical modeling is dependent upon it. Future modeling attempts should investigate appropriate PCSA values for survivor populations, and should continue to enforce further-refined survivor co-activation constraints.

Furthering these research directions will undoubtedly enhance the knowledge and understanding of breast cancer capability and dysfunction, and will promote more targeted and effective treatment and preventative techniques that will enhance the ability, function and quality of life of these survivors – enabling them to lead functional and productive lives.

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Appendices

Appendix A: Standard operating procedures: intramuscular electromyography insertion into the rotator cuff muscles

Participant Preparation for Intramuscular Electrodes:

1.1 Prior to coming to the lab, each potential participant is asked at the time they volunteer if s/he has an allergy to latex or isopropyl alcohol. If s/he is allergic s/he is informed that s/he cannot participate in the study.

1.2 Prior to coming into the lab, each potential participant will be asked to fill out a self-report health screening checklist to assess past health problems as well as present health problems. Participants who report blood clotting disorders, HIV, Hepatitis B or C will not be able to participate in the study.

1.3 Participants are reminded to ask any questions whether they relate to the science or the procedure.

1.4 Prior to coming to the lab, participants will be advised that they will be asked to wear a sleeveless shirt during experimental set-up and testing. Male subjects may choose to go shirtless if that is their preference. The participant will lay prone on a clinical bench and the skin area over the muscle will be thoroughly cleaned with isopropyl alcohol.

1.5 Sterile single-use hypodermic needles of 3.5 inches or less and 27 gauge or smaller will be inserted through the skin into four muscles of the shoulder. This will feel similar to the prick of a needle that would be received at the doctor's office. The needle contains two very thin wires (44 gauge) of similar size to a strand of hair. The wires are bent at the end, so that once the needle is removed from the skin, the thin wires will remain in the muscle during testing. The wires extend by approximately 7 cm beyond the surface of the skin. It is unlikely that the participant will feel the presence of these wires within their muscle. After testing, these wires will be removed easily with a gentle tug. This removal will be painless because each wire is so pliable that the barb straightens out on traction and offers little, if any, palpable resistance (Basmajian, 1985). This wire will record the electrical activity of the muscle as the participant performs various movements. Four needles are inserted (one into each of four muscles), each needle containing two wires, so a total of eight fine wires will remain in the muscle during the testing (approximately 2 hours). Once the desired muscle contractions are completed, the fine wire will be removed from the muscle by pulling on the end of the wire that is lying outside the skin, the area will be cleaned with isopropyl alcohol, and a bandage will be placed over the area if required due to bleeding. The hypodermic needles will not be reused. After removal, hypodermic needles will be disposed of into a sharps container labelled biohazard waste.

1.6 The total depth into tissue will vary from participant to participant depending on the amount of subcutaneous fat present overlying the muscle. It is expected that the needles will be inserted approximately 1 cm into the supraspinatus, infraspinatus and teres minor. The needle for the subscapularis will be inserted approximately 3 cm deep.

1.7 The intramuscular electrode insertions will be carried out by Mrs. Rebecca Brookham, MSc, PhD Candidate. Mrs. Brookham is very familiar with the shoulder anatomy: she has 2 years of work experience working as a student Kinesiologist treating shoulder injuries and disorders, and has completed 4 years of academic research in shoulder biomechanics. Prior to intramuscular electrode

training on live participants, Mrs. Brookham observed Dr. Linda McLean from Queen's University insert approximately 50 intramuscular electrodes into the rotator cuff muscles during Mrs. Brookham's MSc thesis data collection (ORE 14008), and as well, Mrs. Brookham practiced inserting intramuscular electrodes into cadavers in the University of Waterloo anatomy lab. Mrs. Brookham then received training to insert intramuscular electrodes into the rotator cuff muscles on live male and female participants from Dr. McLean at Queen's University. Dr. McLean is an Associate Professor at Queen's University in the department of Rehabilitation Therapy and is an expert at inserting intramuscular electrodes. Dr. McLean has over eight years of experience and has performed numerous intramuscular insertions into the rotator cuff muscles, as well as into many other muscles. Dr. McLean has not once experienced any form of complication during or as a result of her needle insertions. Mrs. Brookham has inserted approximately 30 intramuscular insertions and is proficient at this skill.

1.8 Researcher Preparation The researcher will wear latex gloves at all times during insertion procedures. Used gloves will be discarded in the garbage and new latex gloves will be used for each participant.

1.9 Skin Preparation All skin in the area surrounding the insertion sites will be cleansed with isopropyl alcohol. Sufficient time (approximately 30 s to 2 min depending on room temperature, humidity and participant skin temperature) will be given for the isopropyl alcohol to dry (confirmed visually) before needles are inserted. Allowing the isopropyl alcohol to dry will allow for sterilization to occur and will prevent isopropyl alcohol to be leaked into the insertion site which could cause potential tissue irritation.

1.10 Biohazard Material Disposal Once the needles are removed from the skin, they will not be recapped. Used needles will be put directly into a biohazard material sharps container.

1.11 Fine Wire Removal Fine wires will be removed with a quick tug out of the skin in the direction opposite to that in which the needle was inserted. These wires will be thrown in the garbage since any small amounts of blood that may be present on these wires will dry quickly and since the wires are flexible and not sharp, there is no risk of anyone being punctured by them. Disposal of these wires in the garbage would be similar to throwing out a bloodied adhesive bandage.

1.12 General Insertion Techniques The participant should relax the muscle of interest (muscle in which the needle will be inserted), as flexing the muscle could result in potential discomfort during insertion. The skin in the area over the insertion site will be pulled taut so that the needle can easily and quickly puncture the skin. Once the needle has punctured the skin, the needle should progress slowly to the final destination within the muscle. Several pauses can be taken at increments of a few millimetres at a time before the needle is progressed further. Slow and paused insertion procedures will decrease discomfort to the participant (Daube & Rubin, 2009).

The needle should avoid contact with bone (scapula). If the wire were to hit the bone, this could cause discomfort to the participant (periosteum pain) and the wires could become lodged in the bone and would not record any signal from the muscle of interest. If the needle were to contact to the bone, the needle and wires will be removed, and a new needle will be inserted. Visual and auditory electromyography cues will guide insertions.

If participant experiences any burning, tingling or pain (indicating the needle has hit a nerve) the needle will be immediately removed, and can be re-inserted into a slightly different area.

1.13 Auditory and Visual Guidance during Insertions During needle insertion, the researcher will feel different levels of resistance as the needle passes through the skin, subcutaneous fat, fascia connective tissues and muscle. Before insertion, the electromyographic recordings will appear and sound very noisy (large random spikes and sound like static). If equipment permits auditory recording, insertional activity will be heard ("swish") and seen as a burst of activation as the needle is first inserted into the muscle: this activity is the electrical response of the muscle to the mechanical damage produced by the movement of the needle (Daube & Rubin, 2009). After the needle has first punctured the muscle and is progressing into it, a contraction of that muscle will result in contraction activity that will be heard ("swish") and seen (distinct motor units which appear as large obvious spikes, as seen in Figure 1 and 2). Using the visual-auditory electromyographic guidance during insertion, the depth and location of the needle can be adjusted to proper positioning, and reduce the likelihood of improper placements, and re-insertions. Proper insertion can then be further verified by:

i) Contraction of the muscle of interest: Expect large amplitude of electromyographic activity.

ii) Contraction of surrounding nearby muscle (where the needle could mistakenly be inserted): expect very limited activation.

Figure 1: Visual Guidance during Intramuscular Insertion

Figure 2: Visual Guidance during Intramuscular Insertion: The appearance of motor units

1.14 Specific Insertion Placements The insertion placement procedures for supraspinatus, infraspinatus and teres minor are taken from guidelines outlined in *Anatomic localization for needle electromyography*, 2nd Ed., Steve R Geiringer (1999). The insertion placement procedures for subscapularis are taken from guidelines outlined by Nemeth et al (1990).

Supraspinatus (similar to Geiringer, 1999)

Participant Position: Prone with arm relaxed at side.

Localization: Landmark spine of scapulae, and lay finger along spine. Insert needle 2 fingerbreadths superior to spine, at medial one-third of scapular spine (approximately 2 cm from edge of medial border). Insert needle parallel to skin in direction towards the finger which overlays the spine. Direct needle towards suprascapular fossa to ensure bone is beneath insertion (this will avoid risk of pneumothorax). Needle will pass through middle trapezius before inserting in supraspinatus.

Test: Have participant abduct against resistance with arm at side. Expect audio-visual EMG confirmation.

Figures 3 and 4 demonstrate landmarking techniques for supraspinatus intramuscular electrode insertion.

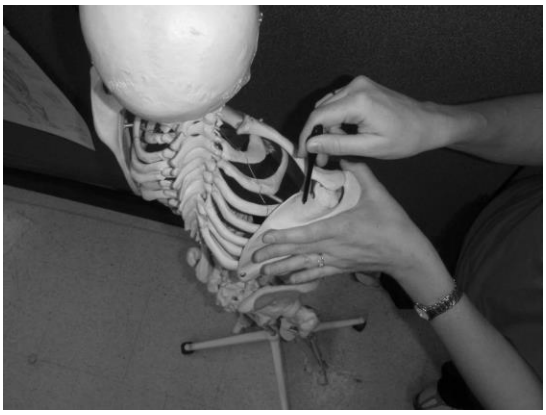

Figure 3 Landmarking technique for supraspinatus insertion on skeletal model

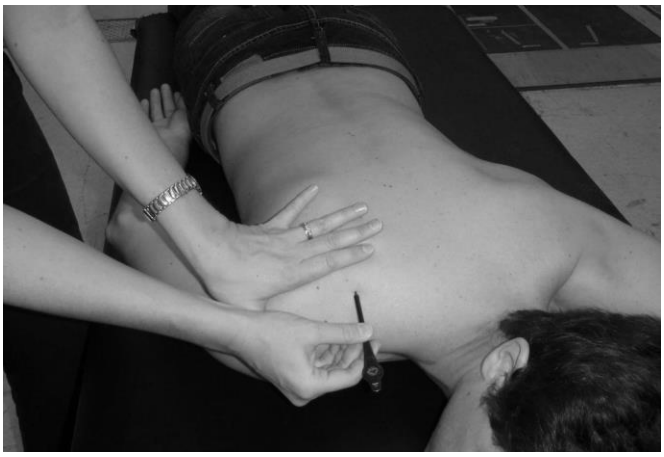

Figure 4 Landmarking technique for supraspinatus insertion

Infraspinatus **(similar to Geiringer, 1999)**

Participant Position: Prone with arm relaxed at side.

Localization: Landmark scapular spine, medial and lateral borders and find centre of infraspinatus fossa (halfway between scapular spine and inferior angle, midway between lateral and medial borders). Insert needle into centre of infraspinatus fossa. Needle will pass through middle trapezius before reaching infraspinatus.

Test: Confirm with scapular retraction the needle is not in middle trapezius (expect little EMG activation). Confirm with external rotation (while arm is at side), that needle is in infraspinatus (expect large EMG activation).

Figures 5 – 7 demonstrate landmarking techniques and insertion for infraspinatus intramuscular electrode insertion.

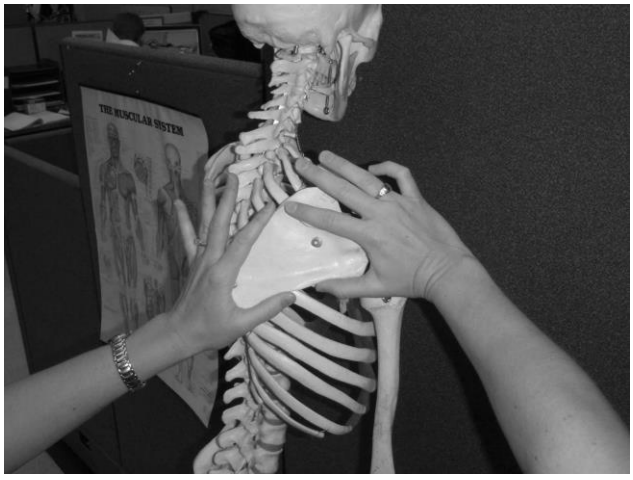

Figure 5 Landmarking technique for infraspinatus insertion on skeletal model

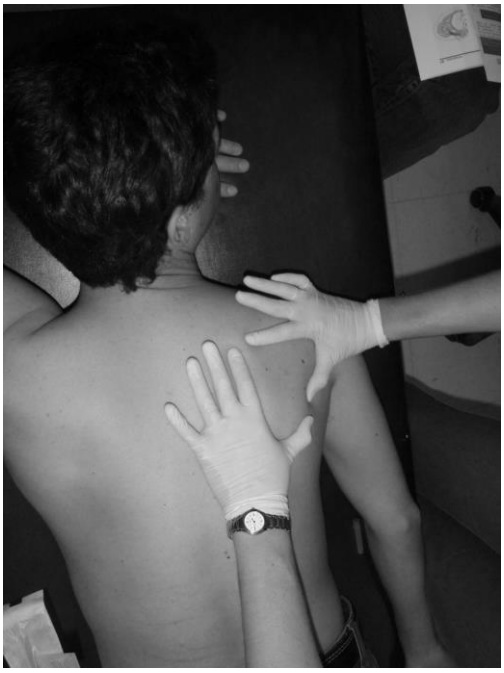

Figure 6 Landmarking technique for infraspinatus insertion

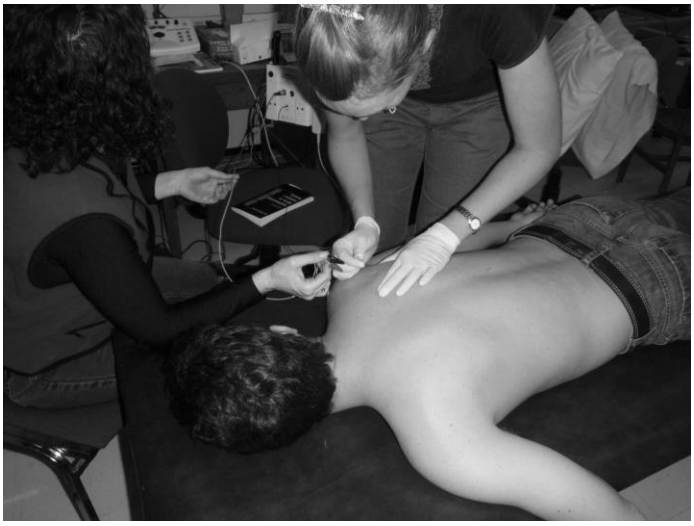

Figure 7 Insertion of intramuscular electrode into infraspinatus

Teres Minor **(similar to Geiringer, 1999)**

Participant Position: Prone with arm relaxed at side.

Localization: Landmark midpoint between acromion and inferior angle on lateral border of scapulae. Trace ribcage and ensure that at this midpoint, the ribcage is not underneath the scapulae – this will ensure the needle is not inserted through the ribcage. Palpate the lateral border and insert the needle immediately lateral to the border at this midpoint (should be at similar height on the scapulae as the infraspinatus insertion).

Test: Expect large EMG activation when participant externally rotates arm at side.

Figure 8 – 10 demonstrate landmarking techniques and insertion for teres minor intramuscular electrode insertion.

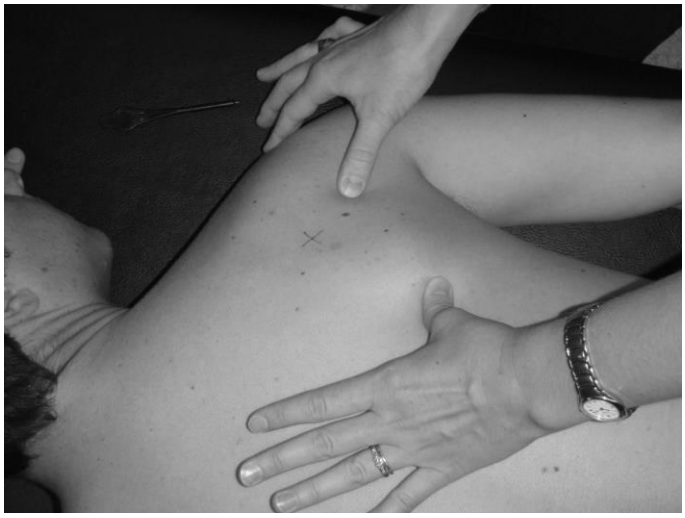

Figure 8 Landmarking the midpoint between the inferior angle and acromion for the teres minor insertion site

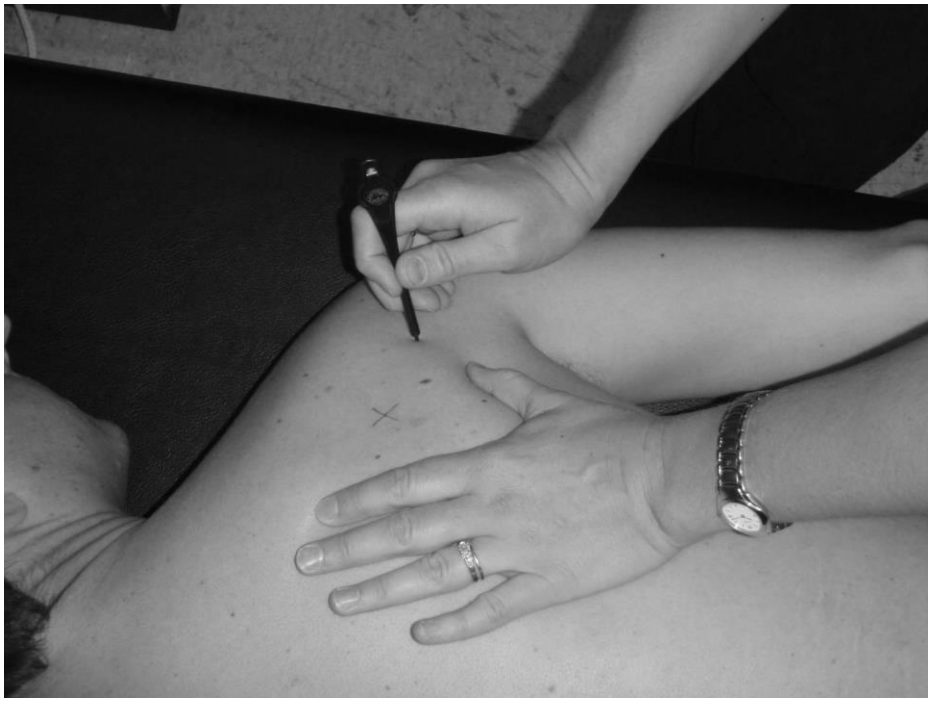

Figure 9 Direction of needle for teres minor insertion

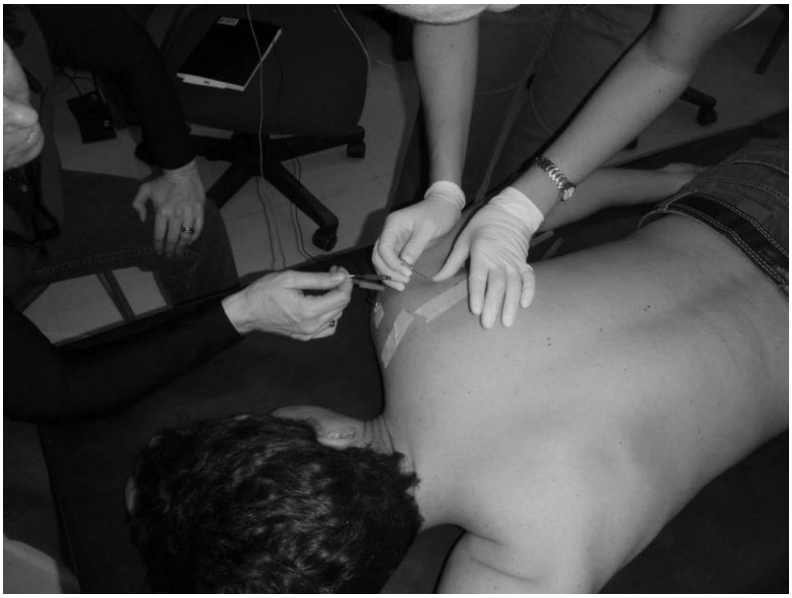

Figure 10 Insertion of teres minor intramuscular electrode

Subscapularis

Subscapularis Axilla Insertion – preferred technique (similar to Nemeth et al., 1990)**:**

Patient Position: Sitting, with arm abducted 90°, elbow flexed 90° and humerus internally rotated. Have an assistant hold the participants' arm and protract the scapula.

Localization: Palpate the inferior angle and lateral border of scapulae. Find midpoint between acromion and inferior angle of scapulae. Researcher will support the scapulae with the palm of their hand, and will indent the skin anterior to scapulae (grabbing the lateral border) at this midpoint. Insert the needle posteriorly into the direction of the subscapular fossa. Since this insertion site is slightly below the axilla, there is minimal risk of complications including pneumothorax, brachial plexus or arterial injury (Nemeth et al., 1990). Ensuring the needle is pointing posteriorly and directed towards the subscapular fossa and in a direction away from the rib cage will ensure there is no risk of pneumothorax.

Test: Expect large EMG activation in internal rotation.

Figures 11 and 12 demonstrate landmarking techniques used for insertion of the subscapularis intramuscular electrode through the axilla.

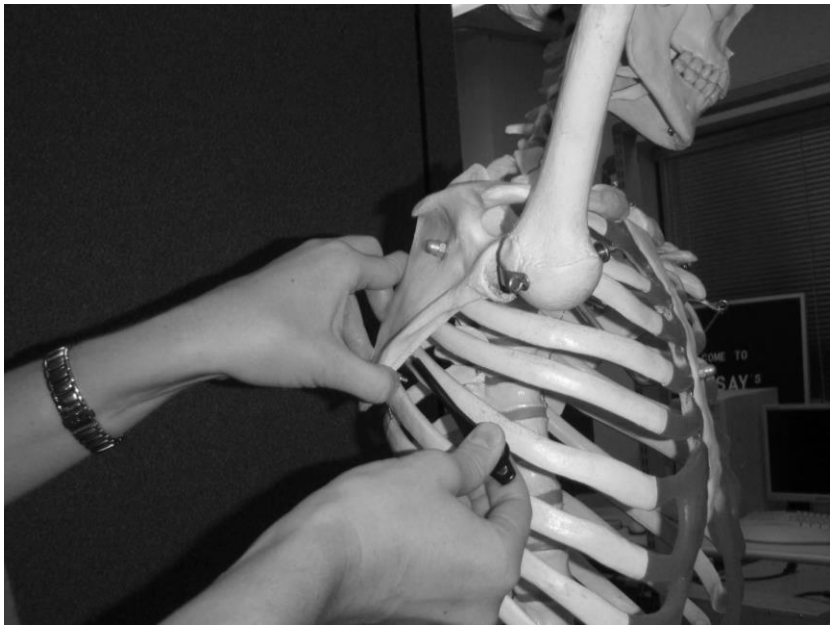

Figure 11 Landmarking techniques of the subscapularis intramuscular electrode through the axilla on a skeletal model

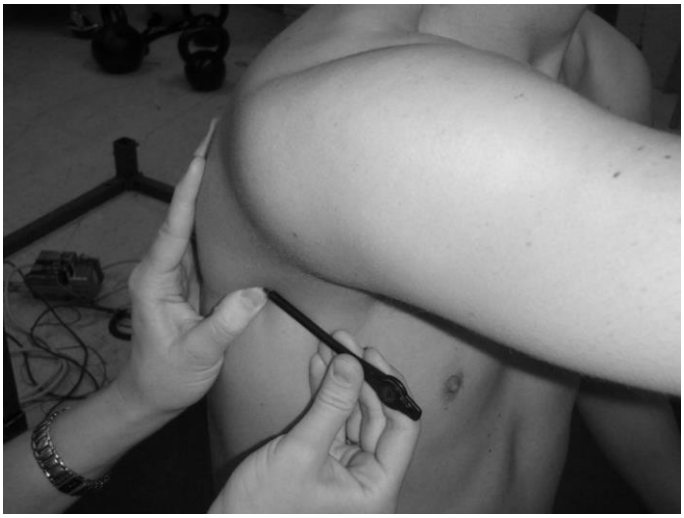

Figure 12 Landmarking techniques of the subscapularis intramuscular electrode through the axilla

<u>Subscapularis Medial Border Insertion</u> – used if participant has limited range of scapular protraction **(similar to Kadaba et al., 1992)**

Participant Position: Sitting, with the hand behind the back (approximately level of L5), causing the scapula to wing.

Localization: Landmark inferior angle and move superiorly up the medial border approximately 3 finger breadths. Insert the needle horizontally in the direction towards the anterior portion of the scapula (subscapular fossa). The needle will pass through the middle trapezius, rhomboids and possibly the serratus anterior (Decker 2003) before entering the subscapularis. Steer the needle in a direction opposite to (away from) the ribcage. If the needle is not pointing enough towards the subscapular fossa, the needle will continue laterally in the scapular retractors, and not enter the subscapularis.

Test: Expect large EMG activation with internal rotation. Should see very limited activation during scapular retraction.

Figures 13 and 14 demonstrate landmarking techniques used for insertion of the subscapularis intramuscular electrode through the medial border of the scapula.

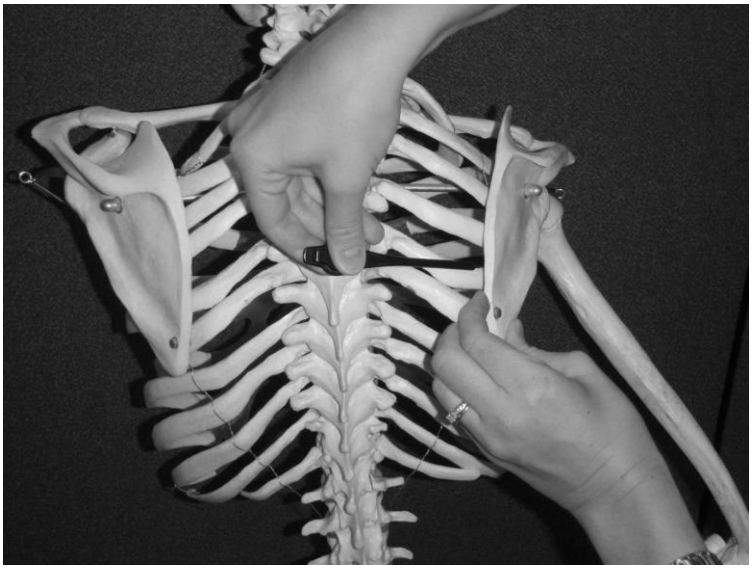

Figure 13 Landmarking techniques of the subscapularis intramuscular electrode through the medial border of the scapula on a skeletal model

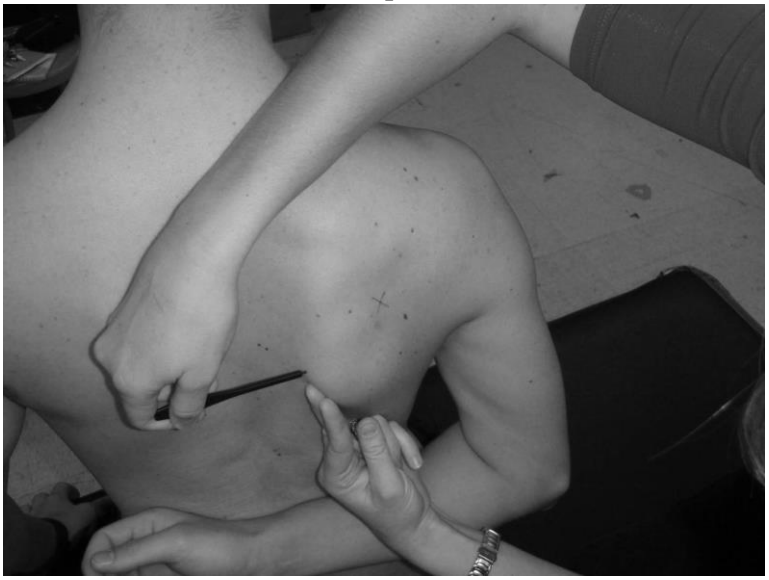

Figure 14 Landmarking techniques of the subscapularis intramuscular electrode through the medial border of the scapula

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1.15 Protocol Immediately following insertions Firm pressure will be applied to reduce any risk of bleeding and/or bruising. The ends of the fine wires will be looped and taped down to the skin before the participant moves from insertion positioning.

References:

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Kadaba, M.P., Cole, A., Wootten, M.E., McCann, P., Reid, M., Mulford, G., April, E. & Bigliani, L. (1992). Intramuscular wire electromyography of the subscapularis. *Journal of Orthopaedic Research*, *10*, 394-397.

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Appendix B: Brief demographic & medical history questionnaire

Age:_____
Height:_____
Weight:_____
Upper Arm Length:_____
Lower Arm Length:_____
Affected (cancer) side (right or left): _____
Dominant Hand (right or left): _____
Grip strength (right hand): _____
Grip strength (left hand): _____

Treatment Information:

1) Approximate date of breast cancer diagnosis:
   _____

2) Did you have surgery?
   YES / NO

   a. If yes, what type of surgery? Check all that apply:
      i. Radical Mastectomy_____
      ii. Lumpectomy_____
      iii. Axial Node Dissection
         1. Sentinel Node Dissection_____
         2. Full Node Dissection_____
         3. Number of nodes removed_____

   b. Approximate date of most recent surgery:
      _____

3) What type of adjuvant therapy did you receive? Please check all that apply:
   a. Hormone Replacement Therapy_____
      i. Ongoing? YES / NO
      ii. Date completed:_____
   b. Chemotherapy_____
   c. Radiation Treatment_____
   d. Other (please specify):_____

Daily Living Information

1) Are you currently working?
   YES / NO

a. Full- time of Part-time?_____

2) Do you exercise regularly? YES / NO
   a. How many days per week?_____

3) Do you have any difficulty in completing daily tasks? YES / NO
   a. If yes, please list what tasks you have trouble doing (e.g., reach overhead, lifting):
      _____
      _____
      ____

4) Do you often feel tightness in the chest or shoulder of your affected arm? YES / NO
   a. If yes:
      i. Does this occur at a certain time of day or after a certain activity (i.e., morning, night, after exercise)?
         _____
         __
      ii. Does anything help ease the tightness (i.e., certain exercises, medications)?
         _____
         __
      iii. Do you experience the following in the chest/shoulder/arm of affected side?
         1. Pain_____
         2. Swelling_____
         3. Decreased range of motion_____
         4. Weakness_____
         5. Cording_____
         6. Numbness_____
         7. Other? Please describe.

5) Have you had any shoulder or arm injuries un-related to your cancer treatments? (example: rotator cuff tear years ago?) Please describe.

Appendix C: Functional Assessment of Cancer Therapy Questionnaire

FACT-B (Version 3)

Below is a list of statements that other people with your illness have said are important. By circling one number per line, please indicate how true each statement has been for you *during the past 7 days.*

PHYSICAL WELL-BEING	not at all	a little bit	some-what	quite a bit	very much
1. I have a lack of energy	0	1	2	3	4
2. I have nausea	0	1	2	3	4
3. Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
4. I have pain	0	1	2	3	4
5. I am bothered by side effects of treatment	0	1	2	3	4
6. I feel ill	0	1	2	3	4
7. I am forced to spend time in bed	0	1	2	3	4

8. Looking at the above 7 questions, how much would you say your PHYSICAL WELL-BEING affects your quality of life? (circle one number)

0 1 2 3 4 5 6 7 8 9 10

Not at all — Very much so

SOCIAL/FAMILY WELL-BEING	not at all	a little bit	some-what	quite a bit	very much
9. I feel distant from my friends	0	1	2	3	4
10. I get emotional support from my family	0	1	2	3	4
11. I get support from my friends and neighbors	0	1	2	3	4
12. My family has accepted my illness	0	1	2	3	4
13. Family communication about my illness is poor	0	1	2	3	4
14. I feel close to my partner (or the person who is my main support)	0	1	2	3	4
15. Have you been sexually active during the past year? No ___ Yes ___ If yes: I am satisfied with my sex life	0	1	2	3	4

16. Looking at the above 7 questions, how much would you say your SOCIAL/FAMILY WELL-BEING affects your quality of life? (circle one number)

0 1 2 3 4 5 6 7 8 9 10

Not at all — Very much so

RELATIONSHIP WITH DOCTOR	not at all	a little bit	some-what	quite a bit	very much
17. I have confidence in my doctor(s)	0	1	2	3	4
18. My doctor is available to answer my questions	0	1	2	3	4

19. Looking at the above 2 questions, how much would you say your RELATIONSHIP WITH THE DOCTOR affects your quality of life? (circle one number)

0 1 2 3 4 5 6 7 8 9 10

Not at all — Very much so

EMOTIONAL WELL-BEING	not at all	a little bit	some-what	quite a bit	very much
20. I feel sad	0	1	2	3	4
21. I am proud of how I'm coping with my illness	0	1	2	3	4
22. I am losing hope in the fight against my illness	0	1	2	3	4
23. I feel nervous	0	1	2	3	4
24. I worry about dying	0	1	2	3	4
25. I worry that my condition will get worse	0	1	2	3	4

26. Looking at the above 6 questions, how much would you say your EMOTIONAL WELL-BEING affects your quality of life? (circle one number)

0 1 2 3 4 5 6 7 8 9 10

Not at all — Very much so

FUNCTIONAL WELL-BEING	not at all	a little bit	some-what	quite a bit	very much
27. I am able to work (include work in home)	0	1	2	3	4
28. My work (include work in home) is fulfilling	0	1	2	3	4
29. I am able to enjoy life	0	1	2	3	4
30. I have accepted my illness	0	1	2	3	4
31. I am sleeping well	0	1	2	3	4
32. I am enjoying the things I usually do for fun	0	1	2	3	4
33. I am content with the quality of my life right now	0	1	2	3	4

34. Looking at the above 7 questions, how much would you say your FUNCTIONAL WELL-BEING affects your quality of life? (circle one number)

0 1 2 3 4 5 6 7 8 9 10

Not at all — Very much so

Appendix D: QuickDASH (Disability of Arm, Shoulder and Hand Questionnaire)

QuickDASH

Please rate your ability to do the following activities in the last week by circling the number below the appropriate response.

	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	UNABLE
1. Open a tight or new jar.	1	2	3	4	5
2. Do heavy household chores (e.g., wash walls, floors).	1	2	3	4	5
3. Carry a shopping bag or briefcase.	1	2	3	4	5
4. Wash your back.	1	2	3	4	5
5. Use a knife to cut food.	1	2	3	4	5
6. Recreational activities in which you take some force or impact through your arm, shoulder or hand (e.g., golf, hammering, tennis, etc.).	1	2	3	4	5

	NOT AT ALL	SLIGHTLY	MODERATELY	QUITE A BIT	EXTREMELY
7. During the past week, *to what extent* has your arm, shoulder or hand problem interfered with your normal social activities with family, friends, neighbours or groups?	1	2	3	4	5

	NOT LIMITED AT ALL	SLIGHTLY LIMITED	MODERATELY LIMITED	VERY LIMITED	UNABLE
8. During the past week, were you limited in your work or other regular daily activities as a result of your arm, shoulder or hand problem?	1	2	3	4	5

Please rate the severity of the following symptoms in the last week. *(circle number)*	NONE	MILD	MODERATE	SEVERE	EXTREME
9. Arm, shoulder or hand pain.	1	2	3	4	5
10. Tingling (pins and needles) in your arm, shoulder or hand.	1	2	3	4	5

	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	SO MUCH DIFFICULTY THAT I CAN'T SLEEP
11. During the past week, how much difficulty have you had sleeping because of the pain in your arm, shoulder or hand? *(circle number)*	1	2	3	4	5

*Quick*DASH DISABILITY/SYMPTOM SCORE = $\left(\left[\frac{\text{(sum of n responses)}}{n}\right] - 1\right) \times 25$, where n is equal to the number of completed responses.

A *Quick*DASH score may not be calculated if there is greater than 1 missing item.

Appendix E: Surface electrode placement instructions

Surface Electrodes	**Placement Location**
Pectoralis Major (clavicular)	*Electrode Placement:* Between sternoclavicular joint and the caracoidus process, 2 cm below the clavicle (on an angle down and laterally). *Test Contraction:* While sitting, flex elbow and shoulder to 90º, horizontally adduct & flex shoulder. Resist (from above) proximal to elbow joint in a downward and outward direction.
Pectoralis Major (sternal)	*Electrode Placement:* 6 cm above the nipple. *Test Contraction:* Subject lies supine. Shoulder is horizontally abducted to 30º with elbow flexed to 90º. Resist horizontal adduction of shoulder.
Latissimus Dorsi	*Electrode Placement:* 6 cm below the inferior angle of the scapula. *Test Contraction:* Sit with shoulder abducted to 90º and elbow flexed to 90º. Adduct shoulder against resistance.
Posterior Deltoid	*Electrode Placement:* 2 cm below lateral border of scapular spine, oblique angle toward arm (parallel to muscle fibers). *Test Contraction:* Subject is prone with head turned to right side. Resist shoulder extension when shoulder is abducted to 90º, elbow flexed to 90º and thumb points up to ceiling.
Upper Trapezius	*Electrode Placement:* 2/3 on the line between the trigonum spinae and the 8th thoracic vertebrae, 4 cm from muscle edge, at approximately a 55° oblique angle. *Test Contraction:* Subject is prone with head turned to right side. Resist shoulder abduction at 90º with elbow extended, thumb down to floor.
Serratus Anterior	*Electrode Placement*: anterior midaxillary region over 5th and 6th rib, anterior to latissimus dorsi and placed vertically.* *Test Contraction:* Forward punch (resisted) at 90° shoulder abduction and 105° horizontal abduction.*
Infraspinatus	*Electrode Placement*: Parallel to spine of scapulae, approximately 4 cm below, over the infrascapular fossa. *Test Contraction:* Subject is lying on left side. Arm is at side with elbow bent to 90°. External rotation of the arm is resisted.
Supraspinatus	*Electrode Placement:* Midpoint and 2 finger-breadths superior to scapular spine* *Test Contraction:* Subject is lying of left side. Shoulder is abducted to 5° with elbow extended (thumb forward). Abduction is resisted.

Similar to Daniels & Worthingham (1986); Cram & Kasman (1998)
*similar to Hintermeister et al. (1998)
Note: Neck held neutral (looking straight ahead) in all conditions unless otherwise indicated.

Appendix F: Mean total muscle effort and integrated EMG for BCP in Study 1

Table 40 Mean TME and iEMG values for unaffected and affected sides of all tasks in Study 1 (Affected side = shaded cells)

Test	TME		PecMaj Clav iEMG		PecMaj Stern iEMG		PostDelt iEMG		LatDorsi iEMG		SerrAnt iEMG		UpTrap iEMG		SupraS iEMG		InfraS iEMG	
	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD
1	3.2E+06	2.E+06	2.3E+05	2.E+05	2.7E+05	2.E+05	2.3E+05	1.E+05	4.2E+05	3.E+05	6.4E+05	3.E+05	4.4E+05	3.E+05	5.3E+05	4.E+05	4.5E+05	7.E+05
1	3.2E+06	2.E+06	2.1E+05	1.E+05	2.3E+05	2.E+05	2.7E+05	2.E+05	4.1E+05	4.E+05	6.8E+05	5.E+05	4.4E+05	2.E+05	5.4E+05	3.E+05	3.4E+05	3.E+05
2	3.0E+06	2.E+06	1.8E+05	1.E+05	2.8E+05	2.E+05	5.1E+05	2.E+05	7.5E+05	1.E+06	3.4E+05	3.E+05	2.4E+05	2.E+05	4.3E+05	3.E+05	3.6E+05	4.E+05
2	3.0E+06	2.E+06	1.6E+05	1.E+05	2.4E+05	2.E+05	6.2E+05	5.E+05	6.3E+05	6.E+05	3.6E+05	4.E+05	2.7E+05	2.E+05	5.5E+05	3.E+05	3.3E+05	3.E+05
3	3.1E+06	2.E+06	1.9E+05	1.E+05	2.6E+05	2.E+05	2.7E+05	2.E+05	3.9E+05	3.E+05	5.4E+05	3.E+05	4.5E+05	2.E+05	5.8E+05	5.E+05	4.7E+05	7.E+05
3	3.4E+06	2.E+06	1.9E+05	1.E+05	2.3E+05	2.E+05	3.4E+05	2.E+05	4.1E+05	4.E+05	6.5E+05	6.E+05	5.3E+05	3.E+05	6.7E+05	4.E+05	3.9E+05	3.E+05
4	2.2E+06	1.E+06	1.1E+05	7.E+04	2.2E+05	2.E+05	1.5E+05	8.E+04	3.3E+05	3.E+05	3.0E+05	2.E+05	2.1E+05	2.E+05	4.1E+05	4.E+05	4.8E+05	3.E+05
4	2.4E+06	1.E+06	1.1E+05	9.E+04	1.9E+05	2.E+05	1.8E+05	1.E+05	3.4E+05	3.E+05	3.5E+05	3.E+05	2.7E+05	2.E+05	4.5E+05	3.E+05	4.6E+05	3.E+05
5	2.1E+06	1.E+06	1.3E+05	8.E+04	2.4E+05	2.E+05	2.5E+05	1.E+05	2.7E+05	2.E+05	2.7E+05	2.E+05	2.4E+05	2.E+05	4.1E+05	3.E+05	2.8E+05	3.E+05
5	2.2E+06	1.E+06	1.3E+05	9.E+04	2.1E+05	2.E+05	3.1E+05	3.E+05	2.6E+05	2.E+05	3.1E+05	3.E+05	2.8E+05	2.E+05	4.8E+05	3.E+05	2.7E+05	3.E+05
6	3.2E+06	1.E+06	2.3E+05	2.E+05	2.8E+05	2.E+05	2.4E+05	1.E+05	4.0E+05	3.E+05	6.2E+05	3.E+05	4.8E+05	2.E+05	5.8E+05	4.E+05	4.8E+05	7.E+05
6	3.3E+06	1.E+06	2.2E+05	1.E+05	2.4E+05	2.E+05	3.0E+05	2.E+05	4.1E+05	3.E+05	7.0E+05	6.E+05	5.3E+05	3.E+05	6.4E+05	4.E+05	3.9E+05	3.E+05
7	9.3E+05	7.E+05	5.9E+04	5.E+04	2.0E+05	2.E+05	4.1E+04	4.E+04	2.5E+05	2.E+05	1.6E+05	1.E+05	6.1E+04	7.E+04	7.3E+04	8.E+04	1.1E+05	2.E+05
7	9.7E+05	8.E+05	7.6E+04	1.E+05	1.7E+05	2.E+05	5.0E+04	6.E+04	2.5E+05	2.E+05	1.7E+05	2.E+05	7.8E+04	1.E+05	9.7E+04	1.E+05	8.5E+04	9.E+04
8	2.0E+06	1.E+06	2.2E+05	2.E+05	3.1E+05	2.E+05	7.5E+04	6.E+04	3.7E+05	3.E+05	4.6E+05	3.E+05	1.8E+05	2.E+05	1.9E+05	2.E+05	2.1E+05	2.E+05
8	2.1E+06	1.E+06	2.3E+05	2.E+05	2.7E+05	2.E+05	1.0E+05	1.E+05	3.6E+05	3.E+05	4.9E+05	4.E+05	1.9E+05	1.E+05	2.1E+05	2.E+05	2.0E+05	1.E+05
9	2.6E+06	2.E+06	1.4E+05	9.E+04	2.4E+05	2.E+05	1.3E+05	1.E+05	7.2E+05	7.E+05	2.9E+05	2.E+05	4.1E+05	3.E+05	4.4E+05	2.E+05	3.0E+05	4.E+05
9	2.8E+06	2.E+06	1.5E+05	1.E+05	2.1E+05	2.E+05	1.7E+05	2.E+05	6.9E+05	6.E+05	3.1E+05	2.E+05	5.0E+05	5.E+05	5.4E+05	4.E+05	2.6E+05	3.E+05
10	4.1E+06	1.E+06	5.3E+05	3.E+05	3.8E+05	2.E+05	2.3E+05	1.E+05	4.1E+05	3.E+05	6.3E+05	3.E+05	5.4E+05	3.E+05	6.4E+05	4.E+05	7.2E+05	8.E+05
10	4.1E+06	1.E+06	5.3E+05	3.E+05	3.4E+05	2.E+05	2.8E+05	1.E+05	4.5E+05	4.E+05	7.2E+05	4.E+05	5.6E+05	2.E+05	6.9E+05	3.E+05	5.3E+05	3.E+05
11	3.2E+06	1.E+06	3.3E+05	2.E+05	3.1E+05	2.E+05	1.3E+05	9.E+04	4.2E+05	3.E+05	5.3E+05	3.E+05	4.5E+05	3.E+05	5.0E+05	5.E+05	5.5E+05	5.E+05
11	3.2E+06	2.E+06	3.3E+05	2.E+05	2.7E+05	2.E+05	1.7E+05	1.E+05	4.2E+05	3.E+05	5.9E+05	4.E+05	4.7E+05	3.E+05	5.0E+05	4.E+05	4.6E+05	3.E+05
12	3.2E+06	1.E+06	6.2E+05	3.E+05	6.2E+05	4.E+05	9.3E+04	7.E+04	3.8E+05	3.E+05	5.7E+05	3.E+05	4.3E+05	3.E+05	3.2E+05	3.E+05	2.6E+05	3.E+05
12	3.4E+06	2.E+06	6.5E+05	3.E+05	5.6E+05	4.E+05	1.1E+05	8.E+04	3.8E+05	3.E+05	6.3E+05	5.E+05	4.5E+05	3.E+05	3.7E+05	3.E+05	2.5E+05	2.E+05
13	2.9E+06	2.E+06	2.6E+05	2.E+05	3.6E+05	3.E+05	3.6E+05	2.E+05	7.5E+05	8.E+05	3.6E+05	3.E+05	2.1E+05	2.E+05	3.3E+05	3.E+05	3.8E+05	3.E+05
13	3.2E+06	2.E+06	2.4E+05	1.E+05	3.3E+05	3.E+05	4.1E+05	3.E+05	8.0E+05	8.E+05	3.7E+05	3.E+05	2.5E+05	2.E+05	3.8E+05	2.E+05	4.2E+05	3.E+05
14	2.1E+06	1.E+06	3.6E+05	2.E+05	3.6E+05	2.E+05	6.7E+04	5.E+04	3.1E+05	3.E+05	3.4E+05	2.E+05	2.5E+05	2.E+05	2.3E+05	2.E+05	1.8E+05	2.E+05
14	2.1E+06	1.E+06	3.8E+05	2.E+05	3.1E+05	2.E+05	9.0E+04	9.E+04	3.0E+05	2.E+05	3.8E+05	3.E+05	2.6E+05	2.E+05	2.3E+05	2.E+05	1.9E+05	1.E+05
15	1.8E+06	1.E+06	1.9E+05	1.E+05	2.2E+05	2.E+05	6.4E+04	4.E+04	2.8E+05	2.E+05	2.6E+05	2.E+05	2.5E+05	2.E+05	2.7E+05	2.E+05	2.4E+05	2.E+05
15	1.9E+06	1.E+06	2.1E+05	1.E+05	1.8E+05	1.E+05	8.8E+04	9.E+04	2.8E+05	2.E+05	3.2E+05	3.E+05	2.8E+05	2.E+05	3.1E+05	3.E+05	2.1E+05	2.E+05
16	2.1E+06	1.E+06	1.6E+05	1.E+05	2.7E+05	2.E+05	2.6E+05	1.E+05	4.8E+05	5.E+05	2.5E+05	2.E+05	1.9E+05	1.E+05	2.9E+05	2.E+05	2.7E+05	2.E+05
16	2.3E+06	1.E+06	1.6E+05	9.E+04	2.4E+05	2.E+05	3.4E+05	3.E+05	4.6E+05	4.E+05	2.7E+05	2.E+05	2.2E+05	2.E+05	3.5E+05	2.E+05	2.9E+05	3.E+05
17	2.5E+06	2.E+06	2.1E+05	1.E+05	3.2E+05	3.E+05	3.3E+05	2.E+05	5.4E+05	6.E+05	2.9E+05	2.E+05	2.2E+05	2.E+05	3.2E+05	3.E+05	3.1E+05	3.E+05
17	2.7E+06	2.E+06	1.9E+05	1.E+05	2.9E+05	2.E+05	4.0E+05	4.E+05	5.1E+05	5.E+05	3.0E+05	2.E+05	2.6E+05	2.E+05	3.8E+05	3.E+05	3.4E+05	3.E+05
18	2.7E+06	1.E+06	2.3E+05	2.E+05	2.5E+05	2.E+05	1.8E+05	2.E+05	3.3E+05	3.E+05	5.5E+05	4.E+05	4.0E+05	2.E+05	4.4E+05	3.E+05	3.8E+05	5.E+05
18	2.9E+06	2.E+06	2.4E+05	2.E+05	2.2E+05	2.E+05	2.0E+05	1.E+05	3.7E+05	3.E+05	6.1E+05	6.E+05	4.4E+05	3.E+05	5.5E+05	4.E+05	3.0E+05	2.E+05
19	3.5E+06	2.E+06	3.9E+05	3.E+05	3.1E+05	2.E+05	1.9E+05	1.E+05	3.9E+05	3.E+05	6.6E+05	4.E+05	4.9E+05	3.E+05	5.7E+05	4.E+05	5.7E+05	7.E+05
19	3.8E+06	2.E+06	3.8E+05	2.E+05	2.6E+05	2.E+05	2.4E+05	2.E+05	4.2E+05	3.E+05	8.0E+05	8.E+05	5.7E+05	3.E+05	6.7E+05	4.E+05	4.9E+05	3.E+05
20	2.4E+06	1.E+06	2.2E+05	2.E+05	2.5E+05	2.E+05	1.3E+05	9.E+04	3.0E+05	3.E+05	4.5E+05	3.E+05	3.3E+05	2.E+05	3.9E+05	3.E+05	3.4E+05	5.E+05
20	2.5E+06	1.E+06	2.4E+05	2.E+05	2.2E+05	2.E+05	1.6E+05	1.E+05	3.4E+05	2.E+05	5.3E+05	6.E+05	3.6E+05	2.E+05	4.3E+05	3.E+05	2.7E+05	2.E+05
21	3.3E+06	2.E+06	4.0E+05	3.E+05	3.0E+05	2.E+05	1.6E+05	1.E+05	3.6E+05	3.E+05	6.1E+05	4.E+05	4.4E+05	2.E+05	5.1E+05	3.E+05	5.3E+05	7.E+05
21	3.3E+06	2.E+06	3.9E+05	2.E+05	2.5E+05	2.E+05	2.0E+05	2.E+05	4.0E+05	3.E+05	7.3E+05	9.E+05	4.9E+05	3.E+05	5.6E+05	4.E+05	4.4E+05	3.E+05
22	2.3E+06	1.E+06	1.2E+05	8.E+04	2.3E+05	2.E+05	2.3E+05	1.E+05	3.0E+05	3.E+05	2.8E+05	2.E+05	3.7E+05	2.E+05	4.9E+05	4.E+05	3.6E+05	6.E+05
22	2.6E+06	1.E+06	1.5E+05	1.E+05	1.9E+05	2.E+05	2.9E+05	2.E+05	3.0E+05	2.E+05	3.5E+05	4.E+05	4.2E+05	2.E+05	5.7E+05	3.E+05	2.8E+05	3.E+05
23	3.3E+06	2.E+06	2.9E+05	2.E+05	2.7E+05	2.E+05	2.8E+05	1.E+05	3.6E+05	3.E+05	4.2E+05	3.E+05	5.3E+05	3.E+05	6.5E+05	5.E+05	5.7E+05	7.E+05
23	3.5E+06	2.E+06	3.0E+05	2.E+05	2.4E+05	2.E+05	3.2E+05	2.E+05	3.8E+05	3.E+05	5.1E+05	4.E+05	5.7E+05	3.E+05	7.5E+05	4.E+05	4.5E+05	3.E+05
24	2.3E+06	1.E+06	3.1E+05	2.E+05	2.9E+05	2.E+05	9.9E+04	5.E+04	4.7E+05	4.E+05	3.6E+05	2.E+05	2.3E+05	2.E+05	2.7E+05	2.E+05	3.1E+05	3.E+05
24	2.4E+06	1.E+06	3.0E+05	2.E+05	2.4E+05	2.E+05	1.3E+05	1.E+05	4.6E+05	4.E+05	4.0E+05	3.E+05	2.7E+05	2.E+05	3.2E+05	2.E+05	3.2E+05	2.E+05

Appendix G: Euler Rotational transformational matrices for scapulothoracic and humerothoracic rotations

Scapulothoracic

$$R_{y\gamma} = \begin{pmatrix} \cos(\gamma_1) & 0 & \sin(\gamma_1) \\ 0 & 1 & 0 \\ -\sin(\gamma_1) & 0 & \cos(\gamma_1) \end{pmatrix} \quad R_{x\beta} = \begin{pmatrix} 1 & 0 & 0 \\ 0 & \cos(\beta) & -\sin(\beta) \\ 0 & \sin(\beta) & \cos(\beta) \end{pmatrix} \quad R_{z\alpha} = \begin{pmatrix} \cos(\alpha) & -\sin(\alpha) & 0 \\ \sin(\alpha) & \cos(\alpha) & 0 \\ 0 & 0 & 1 \end{pmatrix}$$

$$R_{01} = \begin{pmatrix} \cos(\alpha) & -\sin(\alpha) & 0 \\ \sin(\alpha) & \cos(\alpha) & 0 \\ 0 & 0 & 1 \end{pmatrix} \cdot \begin{pmatrix} 1 & 0 & 0 \\ 0 & \cos(\beta) & -\sin(\beta) \\ 0 & \sin(\beta) & \cos(\beta) \end{pmatrix} \cdot \begin{pmatrix} \cos(\gamma_1) & 0 & \sin(\gamma_1) \\ 0 & 1 & 0 \\ -\sin(\gamma_1) & 0 & \cos(\gamma_1) \end{pmatrix}$$

$$R_{01} = \begin{pmatrix} \cos(\gamma_1)\cdot\cos(\alpha) - \sin(\gamma_1)\cdot\sin(\beta)\cdot\sin(\alpha) & -\cos(\beta)\cdot\sin(\alpha) & \sin(\gamma_1)\cdot\cos(\alpha) + \cos(\gamma_1)\cdot\sin(\beta)\cdot\sin(\alpha) \\ \cos(\gamma_1)\cdot\sin(\alpha) + \sin(\gamma_1)\cdot\cos(\alpha)\cdot\sin(\beta) & \cos(\beta)\cdot\cos(\alpha) & \sin(\gamma_1)\cdot\sin(\alpha) - \cos(\gamma_1)\cdot\cos(\alpha)\cdot\sin(\beta) \\ -\sin(\gamma_1)\cdot\cos(\beta) & \sin(\beta) & \cos(\gamma_1)\cdot\cos(\beta) \end{pmatrix}$$

Humerothoracic

$$R_{y\gamma} = \begin{pmatrix} \cos(\gamma_1) & 0 & \sin(\gamma_1) \\ 0 & 1 & 0 \\ -\sin(\gamma_1) & 0 & \cos(\gamma_1) \end{pmatrix} \quad R_{x\beta} = \begin{pmatrix} 1 & 0 & 0 \\ 0 & \cos(\beta) & -\sin(\beta) \\ 0 & \sin(\beta) & \cos(\beta) \end{pmatrix} \quad R_{y\gamma_1 2} = \begin{pmatrix} \cos(\gamma_{12}) & 0 & \sin(\gamma_{12}) \\ 0 & 1 & 0 \\ -\sin(\gamma_{12}) & 0 & \cos(\gamma_{12}) \end{pmatrix}$$

$$R_{01} = \begin{pmatrix} \cos(\gamma_{12}) & 0 & \sin(\gamma_{12}) \\ 0 & 1 & 0 \\ -\sin(\gamma_{12}) & 0 & \cos(\gamma_{12}) \end{pmatrix} \cdot \begin{pmatrix} 1 & 0 & 0 \\ 0 & \cos(\beta) & -\sin(\beta) \\ 0 & \sin(\beta) & \cos(\beta) \end{pmatrix} \cdot \begin{pmatrix} \cos(\gamma_1) & 0 & \sin(\gamma_1) \\ 0 & 1 & 0 \\ -\sin(\gamma_1) & 0 & \cos(\gamma_1) \end{pmatrix}$$

$$R_{01} = \begin{pmatrix} \cos(\gamma_1)\cdot\cos(\gamma_{12}) - \sin(\gamma_1)\cdot\cos(\beta)\cdot\sin(\gamma_{12}) & \sin(\beta)\cdot\sin(\gamma_{12}) & \sin(\gamma_1)\cdot\cos(\gamma_{12}) + \cos(\gamma_1)\cdot\cos(\beta)\cdot\sin(\gamma_{12}) \\ \sin(\gamma_1)\cdot\sin(\beta) & \cos(\beta) & -\cos(\gamma_1)\cdot\sin(\beta) \\ -\cos(\gamma_1)\cdot\sin(\gamma_{12}) - \sin(\gamma_1)\cdot\cos(\beta)\cdot\cos(\gamma_{12}) & \sin(\beta)\cdot\cos(\gamma_{12}) & \cos(\gamma_1)\cdot\cos(\beta)\cdot\cos(\gamma_{12}) - \sin(\gamma_1)\cdot\sin(\gamma_{12}) \end{pmatrix}$$

Appendix H: Scapulothoracic and humerothoracic angles for all tests in Study 1

Table 41 Mean scapulothoracic (ST) beta angles for all subjects for each test. Angles (°) shown include ROM angles (max – min), maximum and minimum achieved angles. Upward rotation is described as a positive value, and downward rotation is denoted as a negative value. Unaffected and affected [shaded cells] sides are shown.

	ST Beta ROM Angle (max-min)		ST Beta Max Angle (upward rot'n [+])		ST Beta Min Angle (downward rot'n [-])		ST Beta Angle ROM (max-min)		ST Beta Max Angle (upward rot'n [+])		ST Beta Min Angle (downward rot'n [-])	
Test	Mean	SD±	Mean	SD±	Mean	SD±	Mean	SD±	Mean	SD±	Mean	SD±
1	58.0	16.5	48.6	22.3	-9.4	15.0	55.8	14.7	48.2	18.7	-7.6	10.9
2	10.3	5.8	-1.3	12.2	-11.6	11.4	9.4	4.7	1.9	16.7	-7.5	16.2
3	57.0	19.0	48.9	22.6	-8.1	13.9	56.3	15.2	50.4	17.9	-6.0	11.9
4	12.1	6.8	8.9	12.5	-3.2	11.7	11.4	5.8	10.9	14.9	-0.5	14.0
5	6.1	3.5	1.4	12.6	-4.8	12.1	6.1	3.4	3.5	17.2	-2.6	16.6
6	56.6	18.4	48.7	21.6	-7.9	14.3	54.8	15.3	48.8	18.9	-6.0	12.5
7	1.6	2.6	-4.1	11.0	-5.6	11.2	1.5	2.9	-0.9	13.6	-2.4	13.8
8	17.2	7.3	11.2	13.8	-6.0	12.6	16.8	6.8	15.2	14.5	-1.5	13.4
9	13.7	5.2	8.1	11.8	-5.6	12.2	13.1	7.2	10.3	16.0	-2.8	14.6
10	5.7	2.8	0.7	10.9	-5.0	10.8	5.3	2.4	3.2	13.8	-2.1	14.0
11	41.1	14.7	36.9	18.1	-4.1	13.7	39.3	13.2	36.3	17.6	-3.1	13.2
12	31.2	9.8	26.2	15.9	-4.9	13.3	31.3	14.0	29.1	13.6	-2.3	15.0
13	15.9	6.8	-0.5	13.9	-16.4	13.8	15.4	4.9	2.9	16.2	-12.5	15.8
14	17.7	6.6	14.4	13.9	-3.2	11.7	17.7	7.6	16.2	13.6	-1.5	14.4
15	15.8	8.7	10.8	14.8	-5.0	13.4	14.6	8.6	11.5	16.4	-3.2	15.3
16	12.0	4.6	-0.3	10.1	-12.4	10.5	12.1	3.6	2.1	15.9	-10.1	15.6
17	15.3	6.3	0.6	11.7	-14.7	11.9	14.0	4.6	2.6	17.4	-11.4	16.9
18	38.8	11.3	33.5	18.4	-5.3	14.5	39.4	12.1	35.7	14.7	-3.8	14.8
19	36.7	12.9	31.3	18.1	-5.4	13.8	37.4	13.0	33.9	14.7	-3.5	14.7
20	33.8	10.2	29.2	14.2	-4.6	10.0	33.4	9.7	30.2	14.9	-3.2	13.3
21	33.1	12.7	28.0	14.1	-5.1	10.8	31.5	10.5	28.2	16.1	-3.3	14.7
22	30.9	10.7	24.7	16.8	-6.1	13.4	27.6	7.7	24.9	15.6	-2.8	15.1
23	24.5	10.0	19.9	15.8	-4.6	13.5	23.2	8.1	21.5	14.4	-1.7	14.1
24	15.1	5.6	5.0	12.3	-10.1	13.0	17.4	12.6	10.6	15.9	-6.8	15.4

Table 42 Mean scapulothoracic (ST) alpha angles for all subjects during each test. Angles (°) shown include ROM angles (max – min), maximum and minimum achieved angles. Anterior tilt is described as a positive value, and posterior tilt is denoted as a negative value. Unaffected and affected [shaded cells] sides are shown.

	ST Alpha ROM Angle (max - min)		ST Alpha Max Angle (Anterior Tilt [+])		ST Alpha Min Angle (Posterior tilt [-])		ST Alpha ROM Angle (max - min)		ST Alpha Max Angle (Anterior Tilt [+])		ST Alpha Min Angle (Posterior tilt [-])	
Test	Mean	SD±	Mean	SD±	Mean	SD±	Mean	SD±	Mean	SD±	Mean	SD±
1	30.8	27.1	22.0	20.3	-8.8	23.1	27.6	26.5	19.7	28.1	-7.9	27.3
2	15.8	11.0	22.9	22.2	7.2	21.3	17.4	19.0	23.3	24.3	5.9	22.8
3	28.9	31.8	22.6	21.2	-6.3	25.7	23.9	25.7	19.5	27.8	-4.4	28.8
4	5.4	2.9	11.8	19.8	6.3	19.7	6.1	5.8	10.5	21.2	4.4	22.9
5	6.3	4.7	13.6	21.2	7.3	20.5	7.5	8.7	13.4	20.6	5.9	22.0
6	28.4	27.8	21.9	20.4	-6.5	24.9	23.6	25.1	18.4	29.2	-5.3	28.1
7	1.4	3.0	9.1	19.7	7.7	19.5	1.2	2.1	8.3	20.9	7.1	21.5
8	11.3	8.0	15.4	21.4	4.1	20.6	9.2	5.8	13.3	21.6	4.1	21.4
9	12.8	5.5	18.7	19.0	5.9	20.5	17.1	27.5	18.9	23.2	1.8	28.2
10	3.7	1.5	8.6	17.5	4.9	17.4	3.6	2.8	8.1	21.0	4.6	21.2
11	17.6	13.7	17.4	16.4	-0.2	17.0	19.0	17.7	16.8	22.3	-2.2	24.9
12	18.4	11.0	22.3	19.5	3.9	18.9	20.8	18.2	20.3	23.5	-0.5	24.9
13	16.1	8.7	21.7	22.0	5.6	22.2	17.3	12.7	22.7	24.6	5.3	21.1
14	10.4	6.3	15.2	19.5	4.8	17.2	11.2	7.3	13.1	20.5	1.9	21.3
15	7.7	7.7	12.2	17.9	4.5	19.6	8.4	11.3	11.4	20.6	3.1	23.0
16	16.1	10.0	21.2	20.0	5.1	21.2	16.9	12.1	23.0	24.2	6.1	20.6
17	15.3	5.6	21.3	22.1	6.0	20.6	18.8	18.9	24.8	26.6	6.0	21.2
18	14.6	11.4	17.2	17.6	2.6	16.8	19.5	22.3	16.5	21.9	-2.9	29.5
19	14.0	12.2	16.4	17.8	2.4	16.6	18.7	22.2	15.3	21.1	-3.4	28.3
20	13.5	10.4	16.4	17.8	2.8	16.3	14.9	15.0	13.7	21.0	-1.2	25.8
21	15.5	13.8	17.6	18.3	2.1	15.1	16.1	15.0	14.7	21.0	-1.5	24.2
22	14.2	14.8	18.3	18.8	4.1	17.3	14.3	14.8	15.9	20.8	1.6	25.7
23	11.0	7.4	14.5	17.2	3.6	16.8	12.6	12.4	13.1	21.3	0.5	24.3
24	17.1	6.8	21.1	23.7	3.9	22.9	19.2	12.9	22.9	23.2	3.7	21.4

Table 43 Mean scapulothoracic (ST) gamma angles for all subjects during each test. Angles (°) shown include ROM angles (max – min), maximum and minimum achieved angles. Retraction is described as a positive value, and protraction is denoted as a negative value. Unaffected and affected [shaded cells] sides are shown.

	ST Gamma ROM Angles (max - min)		ST Gamma Max Angles (Retraction [+])		ST Gamma Min Angles (Protraction [-])		ST Gamma ROM Angles (max - min)		ST Gamma Max Angles (Retraction [+])		ST Gamma Min Angles (Protraction [-])	
Test	Mean	SD±	Mean	SD±	Mean	SD±	Mean	SD±	Mean	SD±	Mean	SD±
1	31.4	30.7	-16.9	33.1	-48.4	19.8	23.1	22.1	-19.3	33.0	-42.4	26.2
2	14.4	6.6	-22.7	13.8	-37.1	14.0	17.3	28.8	-19.3	26.0	-36.6	20.9
3	26.2	25.5	-17.5	29.3	-43.8	21.2	21.0	19.4	-17.7	31.4	-38.8	27.0
4	9.2	4.7	-26.6	16.9	-35.8	16.0	8.9	6.4	-22.5	27.1	-31.4	22.9
5	6.1	6.2	-31.1	15.6	-37.2	13.9	6.0	8.3	-27.0	24.6	-33.0	19.3
6	24.8	20.9	-20.7	28.0	-45.5	20.3	20.9	19.0	-20.0	31.1	-40.9	27.9
7	1.8	3.3	-35.2	15.9	-37.0	15.9	1.4	2.4	-33.7	19.2	-35.1	19.2
8	19.2	6.9	-32.7	20.1	-51.9	19.8	17.1	7.0	-32.7	22.9	-49.9	21.5
9	26.4	9.7	-12.8	16.1	-39.2	14.7	25.0	9.6	-9.9	23.1	-34.9	19.8
10	3.9	2.2	-37.8	13.9	-41.7	13.7	3.9	3.0	-34.7	20.9	-38.6	19.8
11	19.9	12.1	-27.7	22.0	-47.6	16.7	20.7	14.9	-24.3	29.6	-45.0	22.5
12	27.4	10.7	-33.0	20.8	-60.4	23.2	29.6	24.6	-30.3	29.6	-60.0	25.0
13	12.1	16.4	-28.8	16.7	-40.9	17.3	11.7	12.7	-28.1	19.4	-39.8	15.6
14	15.5	5.5	-36.9	16.6	-52.4	17.7	16.2	7.3	-33.3	21.1	-49.4	21.7
15	6.2	5.5	-35.2	16.3	-41.4	17.2	7.4	10.0	-29.9	25.3	-37.3	20.8
16	11.0	7.0	-30.9	13.1	-41.9	12.2	12.2	12.1	-27.6	20.2	-39.8	16.7
17	9.6	4.3	-31.3	15.6	-40.8	15.1	12.8	19.5	-27.1	22.3	-39.9	17.4
18	16.9	8.5	-33.5	19.8	-50.4	18.2	17.6	13.1	-27.5	31.7	-45.1	23.2
19	16.2	11.1	-34.4	20.9	-50.6	17.6	15.1	13.1	-30.8	28.7	-45.9	21.4
20	16.8	7.6	-33.9	17.4	-50.7	16.7	15.1	10.0	-31.7	26.1	-46.8	21.2
21	21.1	27.2	-32.3	24.3	-53.4	17.1	16.2	17.3	-30.0	28.1	-46.1	21.6
22	19.2	13.2	-21.3	20.6	-40.5	12.9	19.0	16.6	-18.2	32.4	-37.2	20.7
23	20.0	10.6	-22.2	17.6	-42.2	13.5	19.4	12.6	-19.9	28.5	-39.3	19.4
24	22.2	7.7	-32.1	19.4	-54.3	16.0	24.9	11.2	-30.5	20.8	-55.4	15.3

Table 44 Mean humerothoracic (HT) beta angles for all subjects during each test. Angles (°) shown include ROM angles (max – min), maximum and minimum achieved angles. Elevation is described as a positive value. Unaffected and affected [shaded cells] sides are shown.

	HT Beta ROM Angle (max - min)		HT Beta Max Angle (Elevation [+])		HT Beta Min (Elevation [+])		HT Beta ROM Angle (max - min)		HT Beta Max Angle (Elevation [+])		HT Beta Min (Elevation [+])	
Test	Mean	SD±	Mean	SD±	Mean	SD±	Mean	SD±	Mean	SD±	Mean	SD±
1	79.7	23.2	115.1	25.3	35.4	14.3	83.9	28.2	114.5	24.7	30.6	15.5
2	27.0	15.1	62.5	13.3	35.5	13.8	28.9	17.1	59.1	17.3	30.2	14.7
3	76.0	23.1	110.5	25.5	34.4	17.1	78.5	24.5	107.0	24.8	28.5	17.0
4	11.3	11.5	55.7	10.7	44.4	11.9	6.9	5.0	48.0	14.0	41.1	14.1
5	13.6	10.8	62.0	11.6	48.4	11.4	10.5	7.1	53.1	14.4	42.7	13.1
6	76.4	23.5	111.8	24.4	35.4	15.3	77.2	23.4	107.1	28.7	29.9	18.2
7	1.7	4.0	43.8	13.2	42.2	12.2	1.1	2.1	39.1	13.4	38.0	13.5
8	24.3	18.6	63.6	17.4	39.4	13.0	19.6	13.9	57.1	15.9	37.5	13.2
9	11.6	7.2	50.6	11.8	39.0	11.8	9.6	7.1	43.9	11.5	34.3	14.2
10	10.8	7.9	52.4	11.2	41.6	11.0	9.7	6.7	50.9	15.4	41.2	15.7
11	55.9	18.9	92.7	18.8	36.8	16.8	60.3	22.5	95.8	24.6	35.5	17.9
12	56.8	25.0	93.4	19.4	36.6	17.2	62.8	31.3	95.4	28.5	32.6	16.3
13	22.0	11.4	63.0	11.9	41.0	10.7	18.9	10.8	57.1	11.7	38.2	14.1
14	34.5	18.4	73.0	22.7	38.4	15.6	45.6	31.1	77.4	29.6	31.7	17.1
15	24.7	14.2	62.0	14.8	37.2	16.6	28.0	18.6	62.7	23.2	34.6	17.2
16	21.6	12.3	62.5	12.9	40.9	10.3	18.7	10.4	56.1	11.6	37.4	14.2
17	23.8	13.6	65.3	13.1	41.5	9.7	18.5	11.2	56.5	12.1	38.0	15.0
18	66.2	16.9	100.2	19.0	34.0	16.2	74.5	25.2	108.0	24.6	33.4	20.8
19	62.0	19.3	96.5	18.7	34.4	18.8	65.9	24.8	101.0	27.6	35.2	19.1
20	65.5	18.4	99.7	19.0	34.2	16.2	73.4	21.6	104.5	24.7	31.1	18.6
21	60.4	19.3	96.2	22.4	35.8	19.5	61.2	23.4	95.8	26.3	34.6	21.3
22	35.6	15.0	70.7	20.5	35.1	13.4	36.9	18.7	69.8	23.2	32.9	18.7
23	31.4	16.3	66.1	18.0	34.8	13.7	36.5	16.3	68.9	20.8	32.5	16.1
24	42.5	20.2	74.3	21.9	31.8	13.8	45.3	16.7	77.5	21.0	32.2	12.1

Table 45 Mean humerothoracic (HT) gamma angles for all subjects during each test. Angles (°) shown include ROM angles (max – min), maximum and minimum achieved angles. Plane of elevation is described as 0° at abduction and -90° in forward flexion. Unaffected and affected [shaded cells] sides are shown.

	HT Gamma ROM Angles (max - min)		HT Gamma Max Angles (-90=flex; 0=abduct)		HT Gamma Min Angles (-90=flex; 0=abduct)		HT Gamma ROM Angles (max - min)		HT Gamma Max Angles (-90=flex; 0=abduct)		HT Gamma Min Angles (-90=flex; 0=abduct)	
Test	Mean	SD±	Mean	SD±	Mean	SD±	Mean	SD±	Mean	SD±	Mean	SD±
1	46.4	32.0	-13.7	32.3	-60.1	25.9	35.0	22.2	-19.1	31.4	-54.1	23.6
2	35.2	21.8	50.2	22.5	15.0	34.3	36.1	27.8	52.9	26.3	16.8	38.2
3	37.2	27.6	-8.2	18.8	-45.3	19.3	30.3	23.0	-8.2	23.7	-38.5	21.1
4	15.5	13.2	-9.4	20.1	-24.9	20.2	11.8	10.6	-13.3	20.0	-25.1	20.5
5	17.8	17.5	-7.6	27.2	-25.4	23.7	14.1	11.9	-8.4	20.7	-22.5	20.7
6	37.4	23.7	-12.1	20.3	-49.4	18.8	27.5	19.3	-16.9	18.8	-44.4	18.2
7	2.6	3.8	-28.9	18.2	-31.5	18.6	2.7	6.4	-33.1	20.8	-35.8	22.1
8	31.1	25.1	-25.3	19.0	-56.4	31.0	20.9	17.4	-30.1	19.8	-51.0	19.1
9	35.7	25.1	-2.1	29.8	-37.8	19.6	33.7	33.1	-5.8	32.1	-39.5	20.2
10	11.6	9.4	-28.1	17.1	-39.6	18.4	9.4	6.2	-34.0	18.6	-43.4	18.3
11	36.0	29.1	-24.1	19.7	-60.0	30.3	29.4	22.8	-29.4	20.9	-58.8	25.4
12	52.9	37.6	-32.0	32.9	-84.9	33.8	39.3	30.0	-39.6	30.1	-78.9	30.0
13	41.1	29.1	41.2	23.1	0.1	32.0	43.0	37.6	35.7	22.6	-7.3	35.3
14	43.0	31.3	-27.6	20.2	-70.6	30.6	34.0	28.0	-32.6	23.2	-66.6	23.7
15	16.8	12.0	-28.2	17.1	-45.0	19.4	14.6	10.7	-31.9	21.9	-46.5	22.3
16	41.9	28.1	38.9	24.4	-3.0	34.8	40.9	28.3	32.9	20.9	-8.0	34.6
17	40.7	28.7	37.0	22.9	-3.7	35.5	38.9	29.7	31.5	20.8	-7.3	35.1
18	31.7	20.7	-29.3	31.8	-61.0	27.0	31.2	26.9	-30.4	26.5	-61.6	23.6
19	32.7	23.7	-30.4	28.4	-63.1	26.4	28.7	27.5	-32.4	29.2	-61.1	24.4
20	35.0	20.9	-29.8	27.2	-64.8	25.8	29.9	24.4	-30.6	28.2	-60.5	21.6
21	33.0	20.9	-30.8	29.0	-63.8	26.6	26.2	18.7	-34.9	25.6	-61.1	22.4
22	28.6	19.5	-9.2	18.5	-37.8	20.4	30.6	24.8	-10.2	21.1	-40.9	23.6
23	32.5	19.5	-10.0	19.0	-42.4	20.7	33.0	24.7	-11.8	20.9	-44.8	22.6
24	55.3	33.7	-15.3	27.4	-70.6	26.0	50.1	32.9	-16.5	26.6	-66.6	18.4

Table 46 Mean humerothoracic (HT) gamma2 angles for all subjects during each test. Angles (°) shown include ROM angles (max – min), maximum and minimum achieved angles. External rotation is described as positive values and internal rotation is denoted as negative values. Unaffected and affected [shaded cells] sides are shown.

	HT Gamma2 ROM Angles (max - min)		HT Gamma2 Max Angles (ER [+])		HT Gamma2 Min Angles (IR [-])		HT Gamma2 ROM Angles (max - min)		HT Gamma2 Max Angles (ER [+])		HT Gamma2 Min Angles (IR [-])	
Test	Mean	SD±	Mean	SD±	Mean	SD±	Mean	SD±	Mean	SD±	Mean	SD±
1	40.2	31.3	-2.6	35.5	-42.8	25.5	35.8	30.9	-7.7	39.8	-43.5	24.7
2	34.4	28.7	-13.3	36.5	-47.7	36.3	37.7	26.8	-5.2	42.8	-42.9	39.4
3	38.0	31.5	3.9	42.3	-34.1	29.3	37.6	36.2	-5.1	44.3	-42.7	24.5
4	22.1	16.7	24.9	28.2	2.8	26.5	26.0	22.1	24.7	30.1	-1.3	33.6
5	38.6	28.5	-1.9	25.3	-40.5	29.4	42.2	29.2	-6.7	30.2	-48.9	33.0
6	39.9	34.2	3.5	38.6	-36.4	25.9	37.0	37.7	-3.2	44.0	-40.2	25.5
7	3.8	7.1	1.8	30.2	-2.0	30.4	6.6	15.0	-5.7	35.1	-12.4	37.0
8	41.1	26.7	3.8	32.0	-37.3	35.6	57.8	38.3	4.7	35.6	-53.1	49.4
9	38.3	30.3	17.3	30.4	-21.0	29.3	52.4	29.5	24.5	34.6	-27.9	37.3
10	17.0	12.4	2.5	30.8	-14.6	30.7	16.7	12.6	0.7	34.4	-16.0	30.7
11	47.1	44.4	-3.2	40.0	-50.2	35.4	46.0	45.7	-3.2	45.7	-49.2	25.2
12	68.0	52.7	-5.0	40.6	-73.0	39.3	62.3	48.2	-4.7	43.9	-67.0	25.2
13	80.2	58.5	9.0	31.7	-71.2	46.3	96.0	56.8	4.8	39.3	-91.2	40.9
14	55.8	36.3	-14.6	30.5	-70.3	34.3	52.2	44.2	-16.6	38.3	-68.8	36.8
15	25.6	21.4	2.0	36.8	-23.6	26.9	29.1	28.2	-10.0	40.7	-39.1	28.8
16	74.7	53.5	6.1	33.0	-68.6	41.8	91.7	56.5	9.3	42.7	-82.4	36.3
17	77.8	54.1	6.0	32.5	-71.8	41.3	95.9	55.3	7.7	39.4	-88.3	37.9
18	37.2	31.0	0.7	40.7	-36.5	31.1	43.4	40.6	-4.5	46.8	-47.8	24.3
19	40.8	32.3	3.5	40.9	-37.4	26.6	41.2	36.3	-4.8	46.1	-46.0	22.6
20	40.4	33.5	3.2	41.7	-37.3	28.9	42.2	36.8	-4.5	46.6	-46.7	22.4
21	37.3	32.7	0.4	39.9	-36.9	27.2	37.3	36.6	-11.5	44.4	-48.8	22.2
22	26.3	22.7	3.3	38.8	-23.0	31.6	28.9	29.2	-1.8	38.8	-30.7	27.2
23	26.9	25.2	6.7	41.6	-20.2	31.0	32.9	33.3	1.3	43.3	-31.6	29.9
24	93.0	41.3	44.0	42.5	-49.0	48.4	108.4	61.8	29.2	54.9	-79.2	52.9

Appendix I: Mean activation and standard deviation of healthy participants in Study 2

Table 47 Mean activation (%MVC) of healthy participants during Study 2 exertions, including wire and surface supraspinatus (SupraW/S) and infraspinatus (infraW/S), surface pectoralis major sternal/clavicular, posterior deltoid and latissimus dorsi.

Test	SupraW	InfraW	SubscapW	PecStern	PecClav	PostDelt	Lats	SupraS	InfraS
1	14.3	20.7	7.1	2.0	1.8	4.7	4.3	15.7	16.1
2	22.0	16.3	3.4	2.3	2.1	7.7	3.4	22.2	11.5
3	23.5	16.2	4.5	3.2	3.2	6.7	5.1	23.1	15.2
4	12.0	15.0	8.3	2.2	2.4	4.0	4.9	13.2	18.0
5	20.3	16.9	3.8	2.4	2.2	7.7	3.3	21.3	12.9
6	20.5	17.5	4.0	3.0	3.0	7.4	5.2	21.5	12.3
7	15.0	20.9	11.9	2.8	2.3	4.5	5.4	18.5	20.1
8	21.1	19.5	5.3	3.1	2.4	7.3	3.6	24.3	18.6
9	27.6	16.9	5.7	3.6	4.4	8.7	5.4	25.5	21.2
10	25.3	40.1	10.0	3.3	3.4	10.9	8.6	30.8	39.1
11	33.6	26.9	6.8	3.2	2.9	14.1	4.6	33.7	19.9
12	31.8	28.8	6.8	4.4	5.8	12.3	8.0	31.5	26.6
13	24.1	31.6	17.2	5.2	5.0	9.1	9.5	26.1	32.6
14	34.3	25.5	5.7	3.2	3.1	17.7	5.1	34.4	21.7
15	29.6	24.1	5.1	3.9	4.1	12.2	7.3	29.4	21.4
16	30.6	39.2	12.1	3.6	3.5	11.4	10.5	35.4	46.6
17	31.4	31.0	9.1	4.1	5.8	13.8	5.8	36.0	34.3
18	34.9	27.3	9.3	4.7	5.2	17.0	8.9	36.5	34.4
19	38.3	58.9	15.5	4.9	5.1	23.4	18.5	45.1	61.8
20	45.5	41.8	11.6	4.5	4.2	25.0	8.1	49.7	31.2
21	43.7	46.8	11.4	6.2	7.8	20.8	11.1	42.5	42.9
22	37.5	55.0	24.4	4.6	5.0	21.9	13.7	43.2	61.3
23	40.1	40.6	10.4	4.4	4.6	25.0	6.9	44.5	30.2
24	44.6	40.2	7.4	5.5	7.7	19.5	8.9	40.9	29.2
25	42.2	62.2	20.6	5.1	5.3	21.7	25.7	49.2	63.0
26	55.4	44.9	15.3	5.3	4.8	28.9	10.3	61.4	50.4
27	62.2	55.1	12.5	7.5	8.8	32.3	18.9	54.5	64.1
28	4.9	2.3	21.4	15.9	10.0	1.0	6.2	3.3	4.0
29	8.0	3.2	5.8	7.4	6.9	2.5	3.6	8.6	3.2
30	15.9	3.3	7.2	4.6	4.2	4.9	5.4	16.3	4.5
31	5.1	3.7	23.9	12.1	8.4	1.6	6.7	3.5	5.3
32	7.9	3.0	6.0	8.3	6.9	2.5	2.7	8.8	3.5
33	12.7	2.7	6.7	6.0	4.4	4.8	4.5	13.5	4.7
34	5.5	2.3	11.7	13.9	8.9	0.9	6.5	4.8	3.7
35	9.9	3.0	4.4	6.8	6.6	2.5	3.1	9.5	2.9
36	11.7	3.2	6.4	5.1	5.8	4.2	4.5	13.1	4.7
37	6.1	3.3	41.7	34.9	21.8	2.0	13.7	4.6	8.6
38	8.6	4.4	9.8	18.5	16.9	3.3	4.5	10.6	6.7
39	16.6	5.0	25.1	9.5	7.1	8.5	12.7	18.1	7.2
40	6.9	4.1	42.3	29.4	18.3	3.2	18.3	5.9	11.9
41	9.1	4.5	12.2	20.0	15.3	3.5	5.2	11.2	7.4
42	18.9	4.8	14.2	12.6	10.3	7.6	9.6	18.1	8.5
43	6.1	2.9	33.8	25.7	17.7	2.0	13.3	5.3	7.5
44	10.5	3.5	13.6	16.2	14.1	4.5	10.5	11.5	5.7
45	18.6	7.6	13.6	13.8	14.9	7.4	10.2	20.8	8.9
46	8.8	4.8	60.3	52.1	37.2	3.5	20.8	9.4	13.3
47	10.9	5.2	35.6	29.0	21.6	8.1	16.0	15.8	10.7
48	27.8	7.5	51.2	15.7	16.0	16.3	25.7	30.9	13.7
49	8.7	5.9	74.1	58.9	32.8	5.9	29.3	9.7	17.3
50	10.1	5.2	20.8	34.3	25.8	5.9	10.7	14.9	11.6
51	25.7	6.9	25.5	17.1	16.8	12.0	16.9	28.7	12.5
52	8.1	3.8	59.4	44.6	33.1	3.3	21.9	9.6	9.8
53	11.0	5.9	27.9	23.9	19.6	6.5	13.9	16.6	8.3
54	23.0	5.9	40.6	17.9	17.7	11.9	21.5	26.0	10.4
55	9.3	10.7	4.4	1.7	1.9	2.1	3.4	9.7	8.5
56	19.9	30.2	10.0	2.9	2.7	7.5	5.9	22.1	26.1
57	32.0	52.4	21.4	4.2	4.2	16.8	11.4	39.0	48.6
58	4.5	2.5	16.3	8.4	6.5	0.7	3.2	3.1	1.9
59	5.2	2.8	31.6	24.3	15.8	1.4	9.5	4.3	6.4
60	7.3	3.4	51.7	39.9	30.2	2.7	16.1	7.6	11.0
61	14.6	10.7	3.2	2.0	1.8	5.3	3.2	17.3	8.7
62	26.4	22.1	10.2	3.0	2.6	12.6	6.1	29.6	15.0
63	39.7	36.3	9.4	3.9	3.7	22.7	7.0	44.6	29.1
64	8.6	3.9	2.9	4.3	4.4	2.6	2.0	8.8	2.6
65	9.0	4.4	12.4	11.9	10.8	3.8	6.1	10.3	4.9
66	9.7	4.1	19.9	22.9	19.0	4.3	7.3	12.8	8.0
67	17.2	13.4	3.1	2.5	2.3	5.4	4.7	18.8	10.9
68	27.3	25.9	6.0	3.7	3.8	10.2	6.5	28.1	21.5
69	34.1	35.7	9.9	5.1	7.3	16.3	9.7	36.4	34.6
70	12.0	2.8	2.2	2.6	2.7	3.4	3.0	13.4	3.4
71	16.4	3.5	14.7	7.5	5.3	6.6	8.4	15.9	5.8
72	26.0	7.0	33.9	12.6	13.9	12.1	19.8	25.8	11.5
73	9.9	6.7	61.5	75.0	54.1	4.9	26.8	12.9	18.9
74	52.3	78.5	33.1	7.1	8.2	39.6	31.9	65.2	82.3
75	17.4	3.2	4.4	2.7	3.8	4.4	4.4	17.2	5.3
76	17.3	4.8	7.5	4.1	5.1	5.9	5.4	18.8	5.3
77	26.3	4.2	7.8	6.7	9.9	7.2	6.7	23.0	6.5
78	31.8	5.7	13.9	9.4	10.8	10.3	12.6	28.7	8.4
79	30.1	11.0	5.6	3.2	4.0	5.9	4.9	25.8	13.0
80	26.8	15.0	6.1	3.7	4.6	7.9	6.1	26.2	16.2
81	31.2	18.3	7.0	4.3	4.5	10.1	7.7	30.5	21.5
82	42.2	19.3	8.4	5.4	8.3	16.1	9.6	40.0	25.0

Table 48 Standard Deviation of Mean EMG of Healthy Participants during Study 2 Exertions, including wire and surface supraspinatus (SupraW/S) and infraspinatus (infraW/S), surface pectoralis major sternal/clavicular, posterior deltoid and latissimus dorsi.

Test	SupraW	InfraW	SubscapW	PecStern	PecClav	PostDelt	Lats	SupraS	InfraS
1	10.5	13.8	8.1	1.0	2.2	2.0	4.0	8.8	7.2
2	13.3	12.0	2.8	1.4	2.5	2.8	1.9	7.9	4.9
3	11.5	7.2	4.5	1.7	3.7	4.9	3.1	7.7	10.1
4	7.1	8.6	13.5	1.2	2.2	2.2	6.5	6.4	11.7
5	10.7	11.3	5.2	1.4	2.4	4.2	2.2	9.4	8.7
6	9.9	10.3	4.0	1.4	3.4	5.7	3.4	8.2	7.2
7	8.8	10.9	18.8	2.8	2.1	2.5	6.1	8.4	15.1
8	7.3	13.0	6.7	2.4	2.9	4.6	1.7	10.0	12.1
9	22.1	8.3	7.3	1.8	6.2	5.8	2.9	11.8	16.0
10	14.0	26.3	10.4	1.6	3.1	5.8	6.2	14.4	28.0
11	22.2	11.6	8.7	1.6	3.1	6.0	2.8	12.9	9.2
12	15.1	15.9	6.2	1.9	5.6	9.1	5.7	9.4	22.2
13	18.3	21.3	18.5	8.8	4.3	4.4	9.9	17.5	18.6
14	26.1	21.5	6.0	1.8	3.7	12.1	3.1	10.3	11.8
15	13.9	12.9	5.3	1.7	4.6	10.7	5.2	9.8	14.9
16	20.3	23.0	14.7	1.5	3.5	4.7	6.8	13.4	39.9
17	17.3	16.2	12.6	1.9	9.9	15.0	3.6	13.6	25.6
18	19.0	14.8	11.5	2.0	5.9	15.0	5.2	22.5	32.2
19	21.1	28.8	11.4	2.3	4.8	15.0	15.8	13.4	28.4
20	25.7	29.3	12.7	2.2	4.4	13.2	5.5	18.3	17.6
21	24.4	32.5	9.8	2.4	10.0	16.9	8.1	18.7	39.8
22	29.6	36.3	23.1	2.6	4.6	11.4	11.2	28.9	41.0
23	29.9	29.0	12.9	2.3	4.5	15.1	4.5	18.4	12.1
24	21.3	27.7	6.6	2.9	7.7	11.2	5.9	12.8	17.5
25	22.7	32.3	20.8	2.4	5.0	13.0	30.2	21.5	37.3
26	32.5	24.7	23.5	2.5	4.8	22.1	7.7	25.1	44.7
27	32.8	35.4	11.5	3.2	11.2	21.5	14.9	28.2	53.9
28	6.4	3.2	21.3	10.4	5.7	0.4	7.1	2.9	3.1
29	6.2	4.5	11.6	3.0	4.9	0.8	7.1	4.4	1.8
30	9.3	4.5	9.7	2.9	4.9	2.5	4.8	7.9	2.3
31	5.6	5.3	13.3	6.3	6.1	0.9	4.9	2.6	4.0
32	5.9	3.8	7.7	4.1	4.6	1.0	2.0	4.9	2.2
33	6.1	3.1	11.2	4.1	4.4	2.4	3.0	5.6	2.9
34	5.7	2.6	11.8	7.4	5.0	0.6	6.7	3.4	2.8
35	7.8	4.2	5.8	3.0	4.6	1.5	3.5	5.7	1.6
36	7.0	3.1	11.1	3.1	4.4	2.3	3.0	5.6	2.8
37	6.4	3.7	41.6	20.2	12.1	1.0	18.4	3.2	6.5
38	7.0	5.2	9.4	11.1	10.3	2.1	4.1	7.5	4.7
39	9.0	6.0	26.1	6.8	7.0	5.9	9.8	9.0	5.7
40	7.5	3.8	38.5	18.1	12.0	1.7	28.2	4.9	10.6
41	8.7	5.4	17.9	14.2	10.1	1.9	7.5	7.3	6.3
42	11.5	6.1	11.9	11.1	10.0	5.9	5.4	8.3	6.6
43	6.6	3.4	18.3	18.4	10.9	1.2	9.6	3.7	6.4
44	7.6	3.2	15.8	10.1	10.4	1.8	15.0	6.8	2.4
45	10.9	8.6	13.2	11.5	12.5	4.1	9.2	9.0	5.4
46	9.0	5.4	26.5	28.1	23.4	2.2	15.4	7.8	7.9
47	8.8	5.8	33.6	16.6	13.6	6.9	27.0	9.5	6.7
48	16.0	9.5	39.3	9.9	18.9	9.4	17.4	15.0	9.1
49	8.0	5.6	59.9	47.2	18.1	3.1	27.1	6.8	14.9
50	8.6	5.6	21.7	28.7	15.5	3.9	11.0	10.9	7.1
51	14.0	9.5	17.2	12.1	14.7	8.7	14.7	15.8	6.6
52	9.1	4.0	54.5	29.0	21.6	1.5	21.6	9.3	6.6
53	8.6	9.1	23.7	12.6	12.7	3.1	11.4	16.0	5.2
54	21.0	6.9	50.6	13.7	17.0	9.7	22.6	14.7	6.4
55	7.3	5.4	4.1	1.0	2.0	1.0	2.8	5.7	5.2
56	14.4	20.8	12.6	1.5	2.7	3.4	4.7	11.2	13.3
57	21.0	30.0	25.7	2.1	3.9	11.2	8.7	19.5	29.8
58	5.9	3.8	25.0	4.0	4.0	0.5	2.3	3.0	1.1
59	6.1	3.1	23.4	16.8	10.8	0.8	12.4	3.2	4.9
60	7.8	3.7	35.9	16.2	14.8	1.1	14.1	5.6	7.7
61	6.7	4.3	3.2	1.2	2.2	2.9	2.6	8.0	4.3
62	12.6	17.3	19.0	1.6	3.0	8.2	9.7	9.3	7.3
63	21.6	26.4	13.1	1.9	3.6	13.9	7.1	17.9	16.7
64	6.9	4.0	3.4	2.5	3.6	1.7	1.2	4.6	1.6
65	6.9	5.5	18.1	6.5	7.1	1.9	9.2	5.1	3.7
66	8.8	4.3	23.3	13.5	13.1	2.0	8.3	8.6	5.1
67	7.5	10.2	2.8	1.2	2.7	3.7	3.0	6.5	6.5
68	15.1	16.7	5.5	1.4	4.2	7.9	3.9	10.4	16.2
69	20.5	18.3	10.6	2.5	6.6	12.4	6.6	11.7	24.2
70	5.2	3.1	2.2	1.3	3.3	1.7	2.0	5.2	2.0
71	11.1	3.5	15.1	5.5	5.4	4.0	7.1	8.6	4.1
72	19.1	7.8	29.2	11.2	18.3	7.6	16.5	15.3	7.8
73	8.3	8.7	48.4	25.7	22.9	2.4	25.3	7.7	13.6
74	23.7	41.9	35.1	3.3	7.3	20.5	23.8	27.5	27.4
75	13.7	2.6	8.7	1.3	4.6	2.6	3.3	9.0	3.3
76	11.4	6.3	9.4	2.6	4.5	5.0	3.5	10.6	2.6
77	25.3	5.7	9.5	4.7	10.3	6.6	5.9	16.4	4.0
78	24.5	6.4	18.3	7.8	10.7	9.1	11.8	13.9	4.8
79	27.5	7.3	8.0	1.7	6.9	3.2	3.0	14.9	10.0
80	17.5	10.4	8.4	1.8	7.6	5.5	3.7	11.6	9.9
81	22.2	19.6	8.3	2.5	6.1	8.1	5.1	13.1	17.9
82	29.3	16.3	8.6	3.0	12.9	14.0	6.4	18.8	20.2

Appendix J: Mean muscle activation of BCP during Study 3

Table 49 Mean muscle activation and standard deviation of breast cancer population during Study 3 exertions.

Test	Pec Maj Clav		Pec Maj Stern		Post Delt		Lat Dorsi		Supra Surface		Infra Surface		Supra Wire		Infra Wire		Subscap Wire	
	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD
1	13.4	11.6	15.5	12.3	2.6	2.1	14.8	13.6	7.2	6.6	4.6	3.4	13.4	7.3	15.5	2.6	2.6	23.9
2	18.5	11.9	23.0	13.0	3.3	2.3	19.0	14.8	6.5	6.7	6.4	4.2	18.5	7.4	23.0	2.8	3.3	19.7
3	25.2	16.5	32.0	18.9	4.1	3.0	24.6	18.8	6.7	7.3	8.8	6.7	25.2	8.0	32.0	3.1	4.1	27.8
4	32.8	23.8	40.5	24.3	4.9	3.0	30.3	21.2	7.3	7.7	11.6	11.4	32.8	9.1	40.5	3.8	4.9	32.8
5	41.7	27.3	55.0	33.7	6.8	4.4	38.0	27.0	8.8	10.2	14.7	15.3	41.7	15.3	55.0	6.0	6.8	32.2
6	52.3	34.2	66.9	38.6	9.1	5.6	49.3	39.0	10.8	16.8	18.6	16.0	52.3	15.2	66.9	5.7	9.1	50.4
7	5.3	4.3	10.2	8.7	6.4	6.1	15.9	12.8	12.4	7.5	11.6	6.1	5.3	8.6	10.2	6.6	6.4	19.2
8	5.6	4.7	10.4	8.9	8.6	5.4	17.9	14.1	15.3	8.9	17.0	7.8	5.6	10.5	10.4	10.3	8.6	20.2
9	6.4	4.9	11.0	9.3	13.6	11.6	21.7	22.4	18.7	9.9	24.4	10.6	6.4	12.8	11.0	14.3	13.6	21.3
10	7.4	5.3	11.6	9.2	19.0	14.6	26.3	23.2	25.1	16.2	30.7	13.9	7.4	17.5	11.6	17.3	19.0	23.3
11	8.3	6.1	13.0	10.0	25.0	19.4	27.7	20.7	31.0	17.5	40.4	18.4	8.3	22.7	13.0	19.6	25.0	35.9
12	9.7	6.5	13.4	9.6	33.8	20.4	36.1	20.4	41.3	19.7	51.5	22.8	9.7	23.4	13.4	25.1	33.8	42.2
13	9.7	7.0	14.4	10.7	6.6	3.7	14.1	10.8	13.1	9.4	6.7	5.2	9.7	8.0	14.4	2.5	6.6	12.3
14	17.5	11.8	22.8	14.6	10.3	4.5	27.3	18.6	11.8	9.1	11.1	9.2	17.5	7.5	22.8	3.3	10.3	38.4
15	5.6	4.6	10.9	9.4	13.1	9.2	17.2	14.0	28.6	14.6	20.8	10.0	5.6	14.8	10.9	13.2	13.1	13.5
16	7.9	6.4	12.7	12.0	22.9	11.8	24.3	21.6	40.1	17.9	34.5	14.6	7.9	23.3	12.7	26.0	22.9	44.4
17	8.4	7.1	14.4	11.6	16.9	9.1	20.1	12.1	22.3	14.7	12.2	10.9	8.4	27.6	14.4	15.1	16.9	27.1
18	9.9	7.9	13.7	12.7	21.4	11.3	23.6	16.9	45.8	25.8	32.1	20.7	9.9	32.7	13.7	17.4	21.4	26.6
19	42.1	27.0	56.2	35.6	6.8	4.1	37.3	31.3	8.5	7.2	17.5	21.5	42.1	10.0	56.2	4.7	6.8	40.3
20	11.3	7.1	14.7	10.6	35.4	17.6	37.5	30.6	43.7	22.5	55.6	25.3	11.3	39.2	14.7	24.8	35.4	41.4
21	21.5	16.8	32.6	31.0	3.9	3.6	25.4	29.2	7.3	8.1	8.3	7.9	21.5	9.1	32.6	2.5	3.9	29.1
22	6.4	6.2	11.6	11.2	17.1	15.5	25.0	29.0	26.7	28.7	29.8	25.0	6.4	19.5	11.6	9.7	17.1	25.3