The effect of an evidence-based management plan on upper limb and trunk lymphoedema, function and quality of life in breast cancer survivors. A series of N=1 studies.

Liesl Way

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Division of Physiotherapy
Department of Health and Rehabilitation Sciences
Faculty of Medicine and Health Sciences
Stellenbosch University

Supervisors:

Mrs Leoné Williams (MSc Physiotherapy SU)
Dr Dominique Leibbrandt (PhD Physiotherapy SU)

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Declaration

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Name: Liesl Way

Date: December 2022

Abstract

Introduction

Breast cancer-related lymphoedema is a chronic, degenerative disease for which there is no cure, and which requires lifelong monitoring and management. Breast cancer-related upper limb and trunk lymphoedema is a complication arising from damage and trauma to the regional lymphatic system sustained during breast cancer treatment. While upper limb BC is well documented in the literature, little is known about the occurrence of, and the risk factors and interventions for, truncal lymphoedema following breast cancer treatment. Breast cancer-related lymphoedema is an independent predictor for reduced quality of life and has a negative socio-economic and psycho-social impact on breast cancer survivors.

Objectives

The main aim of this study was to investigate the effect of an evidence-based multimodal management plan on upper limb and trunk lymphoedema, function and quality of life in breast cancer survivors with upper limb and trunk lymphoedema.

Methodology

A non-concurrent series of N=1 experimental baseline ($A_1B_1A_2B_2A_3$) design was utilised. Five participants who met the inclusion criteria, and gave informed consent, were included in the study. Baseline measurements were taken during the initial assessment to establish the presence and stage of lymphoedema, and these were repeated at the beginning and end of each phase of the study. Upper limb circumference was assessed using circumferential tape measurements which were converted to volume, in millilitres, using the truncated volume formula. The percentage tissue water content for the trunk was measured using the Moisture Meter D®. The function score was extracted from the function domain of the LYMQOL Quality of life was measured using the LYMQOL questionnaire. Two two-week intervention phases were administered, consisting of the following multimodal treatment techniques, namely: manual lymph drainage; compression therapy to the upper limb; skin care; exercise; deep breathing exercises; as well as adjunct low-level laser therapy and the application of Kinesio® tape to the trunk. Paired t-tests according to Satterthwaite's method were used to perform all data analysis. A p-value of ≤0.05 was considered statistically significant. Clinical significance was determined using the prescribed minimal detectable change (MDC) values for each specific outcome measure.

Results

The study participants (n=5) had a median age of 58 years (with a range of 47 to 64 years), a median body mass index (BMI) of 28.7kg/m^2, and presented with stage 0 or 1 upper limb, and stage 2 trunk lymphoedema.

The main finding of this study was a significant reduction in the volume of the affected upper limb for all participants between baseline and B_2 (p=0.01, mean 188 and 95% CI [55.7,287.8]. This significant reduction (p=0.02, mean 243.4 and 95%CI [4.6,334.3] was maintained at the 10-week follow-up assessment (A_3). A statistically significant reduction in the percentage tissue water content was found for the axilla region of the trunk from baseline to phase A_3. A clinically non-meaningful reduction in the percentage of tissue water content was demonstrated for the chest area from baseline to A_3; whereas the back region demonstrated a clinically meaningful increased percentage of tissue water content from baseline to A_3.

The results also showed a clinically meaningful improvement in function (0.82 points) for all participants, with a greater improvement for the youngest participant with the most recent diagnosis and medical management from phase B to A_3. Finally, the participants all experienced a statistically significant improvement in overall quality of life (p=0.005). The significant improvement of quality of life was noted from phase B_1 until the 10-week follow-up assessment phase (A_3) for the study participants.

Conclusion

The current study's findings showed that an evidence-based multimodal management plan has a significant, positive effect on reducing the volume of the affected upper limb, as well as the percentage of tissue water content in the axilla region of the trunk. Furthermore, a clinically meaningful improvement in function, and a statistically significant improvement in the quality of life, of five breast cancer survivors presenting with upper limb and trunk lymphoedema, was noted. Further studies are recommended to investigate the long-term maintenance of effects of the multimodal management plan, as well as to determine the effectiveness of the individual components of the multimodal management. The design and validation of a quality-of-life questionnaire for the trunk region, and a screening tool for lymphoedema risk factor identification, would be of value for further research and clinical use.

Opsomming

Inleiding

Borskanker verwante limfedeem is ‘n chroniese degeneratiewe siekte waarvoor daar tans geen geneesmiddel is nie en wat lewenslank gemonitor en behandel moet word. Limfedeem van die bolyf en boonste ledemate is ‘n komplikasie wat onstaan as borskanker behandeling die omliggende limfatiese stelsel beskadig. Borskanker verwante limfedeem van die boonste ledemate is goed verteenwoordig in die literatuur terwyl daar nog min inligting is oor die voorkoms, risiko-faktore en behandeling van bolyf limfedeem na borskankerbehandeling. Borskanker verwante limfedeem is ‘n onafhanklike voorspeller van laer lewenskwaliteit en het ‘n negatiewe sosio-ekonomiese en psigo-sosiale invloed op pasiënte wat borskanker gehad het.

Doelwitte

Die hoofdoel van hierdie studie was om die effek van ‘n bewysgebaseerde multimodale bestuursplan vir borskanker verwante boonste ledemaat en bolyf limfedeem op lewenskwaliteit en funksie te ondersoek.

Metodologie

‘n Nie-samelopende reeks van N=1 is as ‘n eksperimentele basislyn ($A_1B_1A_2B_2A_3$) gebruik. Vyf deelnemers, wat onderhewig was aan kwalifiserende kriteria, het deelgeneem aan die studie nadat hulle formele ingeligte toestemming gegee het. Basiese maatstawwe is bewerkstellig gedurende die aanvanklike ondersoek en is herhaal aan die begin en einde van elke fase. Die boonste ledemate se omtrek is gemeet met ‘n maatband en omgeskakel na volume in milliliter. Die persentasie weefselvloeistof van die bolyf is gemeet deur Moisture Meter D®. Die lewenskwaliteit en funksie punte is bepaal deur die LYMQOL vraelys. Twee twee-weeklikse ingrypingsfases van die multimodale bestuursplan is toegedien wat limfdreinasie, oefening, kompressie terapie, velsorg, asemhalingsoefeninge, laser terapie en Kinesio® verbande ingesluit het. Gepaarde t-toetse volgens Satterthwaite’s se metode is gebruik in die data analise. ‘n p-waarde van ≤0.05 is beskou as statisties beduidend. Kliniese betekenisvolle faktore is bepaal deur die voorgeskryfde minimale waarneembare verandering waardes vir elke spesifieke uitkomsmaatstaf.

Resultate

Die deelnemers (n=5) het ‘n gemiddelde ouderdom van 58 gehad (reikwydte van 47 tot 64 jaar) en ‘n gemiddelde liggaamsmassa-indeks (LMI) van 28.7kg/m^2 en is gediagnoseer met

fase 0 of 1 bolyf limfedeem. Die hoofbevinding van die studie was ‘n aansienlike vermindering in die volume van die boonste ledemate van alle deelnemers tussen basislyn en B_2 (p=0.01, mean 188 and 95% CI [55.7,287.8]. Hierdie beduidende vermindering (p=0.02, mean 243.4 and 95%CI [4.6,334.3] is onderhou van basislyn tot die opvolg assessering (A_3). Daar was ook ‘n beduidende vermindering in die weefselvloeistof in die okselstreek van die bolyf vanaf basislyn tot A_3. ‘n Nie-betekenisvolle persentasie vermindering van die bors weefselvloeistof is vertoon van basislyn tot fase A_3. Die rug het egter ‘n verhoogde persentasie weefselvloeistof vertoon, van basislyn tot fase A_3. Die resultate het ‘n klinies betekenisvolle verbetering van funksie vir al die deelnemers gewys (0.82 punte), met die grootste verbetering vir die jongste deelnemer wat onlangs gediagnoseer en behandel is van fase B tot A_3. Die deelnemers het almal ‘n aansienlike verbetering in lewenskwaliteit ervaar (p=0.005). Hierdie bevindiginge is gekry deur die uitslae van die begin van die studie (B_1) tot die einde van die finale opvolg-fase (A_3) te vergelyk wat 10 weke beloop het.

Slot

Die huidige studie se bevindiginge wys dat ‘n multimodale fisioterapie plan ‘n aansienlike positiewe effek het op volume vermindering van die boonste ledemate, asook ‘n aansienlike vermindering van die weefselvloeistof in die okselstreek van die bolyf. Verder het die bevindinge gewys dat die multimodale bestuursplan ‘n merkwaardige kliniese verbetering in funksie asook ‘n betekenisvolle verbetering in lewenskwaliteit vir borskanker pasiënte met boonste ledemaat en bolyf limfedeem kan bewerkstellig. Verdere studies word aanbeveel om beide langtermyn terapie nakoming en die effekte van die multimodale bestuursplan te ondersoek, asook om die doeltreffendheid van die individuele komponente van die bestuursplan te bepaal. Die ontwerp en geldigheidsbepaling van 'n lewenskwaliteit vraelys vir die bolyf, en ‘n siftingsinstrument vir limfedeem as risikofaktor, sal ook van waarde wees in toekomstige studies.

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List of Abbreviations

ALND	Axillary Lymph Node Dissection
AWS	Axillary Web Syndrome
BC	Breast Cancer
BCRL	Breast Cancer-Related Lymphoedema
BMI	Body Mass Index
CDT	Complete Decongestive Therapy
CLT	Certified Lymphoedema Therapist
DBE	Deep Breathing Exercise
KT	Kinesio® tape
LLLT	Low-Level Laser Therapy
LYMQOL	Lymphoedema quality of life questionnaire
MDC	Minimal detectable change
MLB	Multilayer Compression Bandaging
MLD	Manual Lymphatic Drainage
QOL	Quality of Life
SLNB	Sentinel Lymph Node Biopsy
TDC	Tissue Dielectric Constant

Glossary

Axillary Lymph Node Dissection

Lymphatic fluid from the upper limb and breast drains into the ipsilateral axillary lymph nodes which are situated in the armpit. In the presence of breast cancer, axillary lymph nodes are removed for histological examination to determine whether, and to what extent, the cancer has spread to these nodes.

Sentinel Lymph Node Biopsy

The sentinel lymph node is the first node within the axillary lymph node chain in the axillary basin. Sentinel lymph node biopsy is conducted using a dye to establish whether cancer has metastasised to the lymph node basin, and to stage the breast cancer.

Body Mass Index

This is a screening tool used to determine an individual's weight category for risk assessment for potential health-related problems. The individual's weight in kilograms is divided by the square of height in metres.

Multi-layer Compression Bandaging

The initial layer consists of a sleeve of stockinette to protect the skin, followed by cotton padding to ensure an even cylindrical form, and thus even compression to the upper limb. Foam padding is then applied to the limb and, finally, short stretch bandages are applied to facilitate compression of the lymphatic limb.

Manual Lymphatic Drainage

This is a specialised massage technique done by a certified lymphoedema therapist. Slow, gentle, repetitive skin-on-skin techniques are performed in the direction of the lymphatic flow to facilitate the uptake of the extracellular lymphatic fluid to the regional lymph nodes.

Multimodal Management Plan

This consists of evidence-based, complete decongestive therapy, including manual lymphatic drainage, compression therapy (multilayer bandaging and prescribed compression sleeves), exercise, deep breathing exercise, and skin care. Furthermore, the management plan for the current study included low-level laser therapy and the application of Kinesio® tape to the trunk (HPCSA 2022).

Chapter 1: Introduction

Breast cancer (BC) is the most common form of cancer affecting the female population worldwide (Torre et al., 2017), and it accounts for 25% of all known cancers. It has been reported that BC cases reached 2.3 million worldwide in 2020 (Sung et al., 2021). BC is the most common form of diagnosed cancer and second-most common cause of cancer deaths in sub-Saharan Africa (Joko-Fru et al., 2020). As most African countries lack National Cancer Registers, accurate information on the prevalence of BC is limited (Joko-Fru et al., 2020). It is projected that, by 2050, the burden of BC in sub-Saharan Africa (SSA) will double. The South African National Cancer Register, last updated in 2017, stated that BC was responsible for 23.11% of all female cancers in SA, with a total of 9624 new histologically diagnosed cases reported in South Africa in 2017. Medical advances and increased awareness of BC have resulted in early detection and diagnosis of this condition, thereby reducing mortality rates. The five-year survival rate following diagnosis has increased to 98% for stage 1 BC; 75% for stage 2; and 27% for stage 3 BC, in the United States of America (DeSantis et al., 2019). In comparison, the 3 year survival rate for early stage BC is 78% and for advanced BC (stages III-IV) is 40.3% in SSA (Joko-Fru et al., 2020).

The primary medical interventions for BC comprise surgery, systemic therapy (chemotherapy and endocrine therapy) and radiation therapy (Harbeck & Gnant, 2017; McDonald et al., 2016). BC may metastasise through the axillary lymph nodes, and any involvement of these nodes will necessitate either a sentinel lymph node biopsy (SLNB) or axillary lymph node dissection (ALND). These treatment interventions are known to result in complications such as local pain; scar tissue; axillary web syndrome; seroma; reduced function; swelling and lymphoedema (Ridner, 2013; Toyserkani et al., 2017; Yeung et al., 2015; Zomkowski et al., 2018). The most dreaded consequence of these interventions is breast cancer-related lymphoedema (BCRL) (Gebruers et al., 2017; Ohsumi & Shimozuma, 2013). BCRL occurs when the lymphatic system is dysregulated or compromised due to a traumatic event. This trauma may be as a result of breast-conserving surgery or mastectomy, ALND, SLNB, systemic therapy or radiation. The lymphatic system is rendered dysfunctional and a pathological state occurs (Ridner et al 2013). The consequence of this is the collection of a protein-rich fluid in the interstitium, which is referred to as lymphoedema (Grada & Phillips, 2017).

Due to the lack of a consistent definition for BCRL, diverse measurement tools, and the absence of a validated measurement tool for sub-clinical lymphoedema, there is no clear consensus in the literature regarding the incidence of BCRL (Kilbreath et al., 2016). It has been estimated that one-in-five BC survivors will develop BCRL, and the average incidence has been established at 16.6% (Di Sipio et al., 2013). The probability of individuals developing

BCRL is dependent on intrinsic, individual, modifiable and non-modifiable risk factors. The modifiable risk factors include a body mass index (BMI) of >30kg/m^2 (clinical obesity) and fluctuations of 5.45kg in body weight within any four-week period following breast cancer intervention. Timely identification of, and intervention for, the modifiable risk factors can improve or preserve quality of life for BC survivors and significantly reduce the incidence or severity of stage of BCRL (Gençay Can et al., 2019).

The lymphatic system plays a vital role in maintaining health and quality of life. This system is responsible for maintaining tissue homeostasis, immune surveillance and immune cell transportation; as well as the removal of cellular debris and the absorption of lipids from the intestinal system (Grada et al., 2020; Mortimer & Rockson, 2014). The lymphatic system has a unique architectural structure for optimal function. This structure permits the drainage of fluid from the interstitium into the circulatory system via the thoracic duct and right atrium of the heart. A dysregulated lymphatic system due to cancer interventions will result in cancer-related lymphoedema (Ridner, 2013). This can affect various body regions in cancer survivors, including the upper limb and the trunk (Koehler, Blaes, Haddad, Hunter, Hirsch, Ludewig et al., 2015).

Studies of upper limb lymphoedema are well represented in the literature (Medina-Rodríguez et al., 2019; Stuiver et al., 2015; Vignes et al., 2013). However, trunk oedema is an often undiagnosed, unrecognised and undertreated form of BCRL and can have a devastating effect on the quality of life of BC survivors (Jeffs, 2006). The true incidence of truncal oedema in BC survivors is largely unknown and rarely reported. Survivors of BC endure a lifetime risk of developing truncal oedema (Armer et al., 2003b). Telephonic interviews revealed the self-reported incidence of trunk swelling with the following prevalence: 10% affecting the back; 22% the armpit; 10% the anterior chest wall and breast tissue; and 14% the lateral chest wall (Bosompra et al., 2002). Jeffs et al. (2006) reported an incidence of 16% of truncal oedema in a study of 263 BC survivors in a clinical audit which was conducted at a lymphoedema clinic in London. Of the patients, 59% reported swelling within 12 months of cancer treatment and 35% within three months of either cancer surgery or radiation therapy (Jeffs, 2006).

As the survival rate for women with BC has increased, due to early detection and improved management, more survivors are likely to experience complications, such as upper limb and trunk lymphoedema, reduced function and compromised quality of life (Grada & Phillips, 2017b; Westby et al., 2016). BCRL is an independent predictor for decreased quality of life in BC survivors (Beaulac et al., 2002). Quality of life incorporates aspects of body image as well as physical, social and psychological well-being (Kalemikerakis et al., 2021; Kolodziejczyk & Pawlowski, 2019). Early screening of quality of life and function in BC survivors with

lymphoedema should form an integral part of the management of these patients. This would ensure timeous referral to healthcare specialists who can offer support and treatment to enhance the quality of life of these survivors.

BCRL requires specialised screening, prevention and management by trained and certified lymphoedema therapists (CLT). A significant lack of consensus regarding the efficacy of measurement tools for lymphoedema exists (Dylke et al., 2016). According to the literature, water displacement remains the gold standard for limb volume measurements. Perometry and bioimpedance spectroscopy (BIS) are also recognised as valid lymphoedema measurement tools, but these are expensive (Armer et al., 2013). It has been recommended that a circumferential tape measurement, which is subsequently converted to a limb volume measurement, is the best clinical practice measurement tool for limb lymphoedema (Devoogdt et al., 2010). However, the above measurement tools are impractical for measuring trunk lymphoedema due to the anatomical landscape of the trunk. The Moisture Meter D® has been validated as a reliable tool for the measurement of trunk lymphoedema as it can be used on any anatomical surface (Mayrovitz et al., 2008). Mayrovitz et al. conducted a study in America on 120 females diagnosed with unilateral BC in which it was suggested that measuring the tissue dielectric constant (percentage tissue water content) in the trunk region may provide useful measurement values for lymphoedema (Mayrovitz & Weingrad, 2018)

The first line of treatment for BCRL is a multimodal approach referred to as complete decongestive therapy (CDT) (Damstra et al., 2017), which includes manual lymph drainage (MLD); deep breathing exercises; multilayer compression bandaging (MCB); the prescription of compression garments; exercise and advice on skin care (Armer et al., 2013). This treatment is administered by a CLT and is accepted in the literature as the gold standard intervention for lymphoedema (Gebruers et al., 2017). Modalities such as low-level laser therapy (LLLT) (Smoot et al., 2015) and the application of Kinesio® tape have also been reported to be effective in reducing BCRL (Gatt et al., 2017), but are not routinely included in the multimodal treatment plan. Early intervention and patient education plays a vital role, as BCRL is a chronic, progressive, incurable disease and requires long-term management and surveillance in order to achieve successful treatment outcomes (Gençay Can et al., 2019).

A lack of consensus in the literature regarding multiple aspects of the diagnosis and treatment of BCRL has created a dearth of information guiding the management of this condition. This includes a lack of consensus on the most effective duration of the intensive phase of multimodal management, the debate on whether MLD is an effective modality within the multimodal context, the lack of high quality studies investigating the effectiveness of the

application of Kinesio® tape and the challenges that exist in assessing and compressing the trunk region.

BCRL presents as a complex condition, affecting both the physical and emotional well-being as well as overall quality of life of BC survivors. A multimodal approach to the management of this condition will address this multi-faceted presentation of BCRL which will result in both objective and patient-reported outcome measures. This study purposes to establish the baseline presentation of BCRL and the effects of a multimodal management plan on the upper limb volume, the percentage tissue water content of the trunk, and function and quality of life in BC survivors.

Chapter 2: Literature Review

2.1 Introduction

The aim of this literature review is to describe the baseline presentation of BC related upper limb and trunk lymphoedema and the evidence for implementing a multimodal management plan for this condition. The effect of various interventions on upper limb volume, percentage tissue water content of the trunk, function and quality of life will be presented. The current literature on key principles of assessment surrounding breast cancer-related lymphoedema and the management thereof will be described.

2.2 Breast Cancer

BC represents 24.5% of all cancers in females and 11.7% of all cancer cases worldwide, and is the most common form of cancer affecting the female population in 159 countries, including South Africa (Sung et al., 2021). According to the 2020 estimates by the International Agency for Research on Cancer, 2.3 million females were living with a diagnosis of BC in 2020, representing an incidence of one in four among females, worldwide (Sung et al., 2021). Medical advances, and an increased awareness of the importance of BC screening in women aged 40 years and over, who present with an average risk of developing BC, have resulted in earlier detection and management of this condition, which has resulted in reduced mortality rates (Oeffinger et al., 2015). The five-year survival rate following diagnosis has increased to 98% for stage 1 BC; 75% for stage 2; and 27% for stage 3 BC, in the United States of America (DeSantis et al., 2019). In contrast, the five-year survival rate for women with breast cancer in sub-Saharan Africa is less than 40%, accounting for the second highest cause of mortality from cancer in this region (Joko Fru et al., 2020). In South Africa, this five-year survival rate varies between 20% and 60% (Eastern Cape) due to the presentation of late stage (Stage 3 and 4) BC on diagnosis (Joko-Fru et al., 2020).

The South African National Cancer Register (SANCR), last updated in 2017, stated that BC was responsible for 23.11% of all female cancers in South Africa with a total of 9624 histologically confirmed new cases reported during 2017 (South African National Institute of Communicable Diseases, 2020). It is projected that, by 2050, the burden of BC in sub-Saharan Africa will have doubled.

2.3 Medical Management of Breast Cancer

The primary life-saving management of BC comprises surgery, systemic therapy such as endocrine therapy and chemotherapy, and radiation therapy (Harbeck & Gnant, 2017;

McDonald et al., 2016). Breast-conserving therapy has become the treatment of choice. Advances in surgical techniques and the successful prescription of systemic therapy, such as neoadjuvant endocrine therapy and chemotherapy, has made this possible (Haloua et al., 2013; Josephine, 2019; McDonald et al., 2016; Reinbolt et al., 2015). Neoadjuvant systemic therapy is administered prior to surgical intervention and adjuvant after surgical intervention. The administration of neoadjuvant endocrine therapy or chemotherapy plays a very important role in the multimodal medical treatment of BC. These interventions reduce the tumour size, which facilitates less invasive surgery and the avoidance of mastectomy surgery (Al-Hilli & Boughey, 2016; Harbeck & Gnant, 2017; Reinbolt et al., 2015; Vugts et al., 2016). Neoadjuvant or adjuvant endocrine therapy (e.g. Tamoxifen® or anthracyclines) is prescribed for a five-year period to women with BC. This reduces the recurrence of BC in the first nine years and reduces mortality by one third within the first fifteen years following diagnosis (Abrial et al., 2006). Adjuvant chemotherapy is administered in addition to surgical intervention to improve surgical success rates and reduce the incidence of recurrence of breast cancer (Fryback et al., 2006; McDonald et al., 2016; O'Toole et al., 2015).

BC can metastasise through the axillary lymph nodes and, depending on the involvement of these nodes, either a sentinel lymph node biopsy (SLNB) or axillary lymph node dissection (ALND) may be necessitated (Lucci et al., 2021; Tandra et al., 2019). Breast-conserving surgery and SLNB have led to a significant decrease in post-surgical complications, such as secondary upper limb or trunk lymphoedema (DiSipio et al., 2013).

Radiation therapy completes the triad of primary interventions for BC and is a vital and effective intervention for reducing mortality and increasing disease-free survival rates (Darby et al., 2011; Davidson et al., 2010; McCormick et al., 2015). Abe et al. (2005) reported that radiation therapy reduced the five-year local recurrence of cancer and fifteen-year mortality rates following diagnosis. In line with the breast-conserving approach to surgical management, radiation therapy is targeted to the axilla, supraclavicular and parasternal areas, with partial breast irradiation (Poortmans et al., 2015).

This triad of treatment interventions for BC, that is, surgery, systemic therapy (chemotherapy and endocrine) and radiation therapy, has resulted in both increased survival rates as well as an increased risk of potential complications. One such complication is breast cancer-related lymphoedema, which can have a detrimental effect on upper limb and trunk volume, function and quality of life of breast cancer survivors (Grada et al., 2020; Pusic et al., 2013).

2.4 Breast Cancer-related Lymphoedema (BCRL)

A common complication following the medical management of BC is the development of secondary upper limb or trunk lymphoedema (Gebruers et al., 2017; Ohsumi & Shimozuma, 2013). Lymphoedema is a chronic disease for which there is no medication or definitive cure (Grada et al., 2020). BC survivors are burdened with the perpetual and life-long prospect of experiencing breast cancer-related lymphoedema of the upper limb and trunk (Armer et al., 2003a; DiSipio et al., 2013; Hinrichs et al., 2004).

Despite reports on BCRL gaining momentum in the literature, a consistent and clear definition for this condition has yet to be established. Levenhagen et al. (2017) broadly described lymphoedema as being the retention of excess tissue fluid, consequential to a dysfunctional lymphatic system. Armer et al. (2010) referred to BCRL as a continuous swelling of the upper limb, resulting in either a 2cm, 200ml or 5-10% volume discrepancy between the affected and unaffected limbs. Lymphoedema resulting from BC interventions may present as abnormal swelling or an accumulation of protein-rich tissue fluid in the upper limb; breast; chest wall; thoracic wall; shoulder; back; lateral axilla and trunk (Armer et al., 2003a; DiSipio et al., 2013; Jeffs, 2006; Lawenda et al., 2009). This swelling can also present as fibroadipose tissue in more advanced stages in the lymphatic area (Dayan et al., 2018; Mayrovitz et al., 2009).

Despite the lack of a clear definition for lymphoedema, a clear and universal categorisation of staging of this condition exists in the literature (Society et al., 2016). According to the International Society of Lymphology (ISL), this is based on the skin condition, presence of pitting edema, fibrosis in the skin and limb volume difference. The staging of clinical lymphoedema according to the ISL is as follows (See Table 2.1):

Table 2.1: Staging of Lymphoedema (International Society of Lymphoedema)

Stage	Description	Limb Volume Differences
0 Subclinical	Subclinical swelling not apparent on clinical exam despite impaired lymph flow	5-10 %
1 Mild	Soft oedema that pits with no dermal fibrosis and subsides with limb elevation within twenty-four hours	10-20%
2. Moderate	Nonpitting lymphoedema that does not resolve with limb elevation, reflecting evolution of dermal fibrosis	20-40%
3. Severe	Lymphostatic elephantiasis with nonpitting oedema with fibrosis, skin changes of acanthosis and warty overgrowths and fat deposits	>40%

2.5 The Incidence of BCRL

It has been well established in the literature that all BC survivors are at risk of developing BCRL during their lifetimes (Armer et al., 2003a; Cormier et al., 2010; Paiva et al., 2013; Rockson, 2018). There is no clear consensus in the literature regarding the incidence of BCRL. This has been attributed to multiple factors: namely, the lack of a consistent definition for lymphoedema; the diversity of measurement tools available; the type of assessment methods used; and variations in the defined threshold of excess volume which confirms the presence of lymphoedema (DiSipio et al., 2013; Hayes et al., 2008). A lack of clarity regarding the relationship between time lapsed from surgery to the onset of BCRL has also influenced the reported incidence of this condition (DiSipio et al., 2013; Hayes et al., 2008).

In a systematic review and meta-analysis conducted by DiSipio et al (2013), it was reported that one-in-five (21%) BC survivors would develop BCRL (DiSipio et al., 2013; Paskett et al 2012). This systematic review also reflected that 90% of all reported BCRL occurs in the first 24 months following breast cancer intervention, while the remaining 10% occurs years to decades later (DiSipio et al., 2013). The median onset of BCRL was reported to be between 14 and 18 months, post-surgery (Brunelle et al., 2015; DiSipio et al., 2013; Gebruers et al., 2015). One report states that the incidence of BCRL is between 5% and 50% (Sayegh et al., 2017). The mean incidence was established at 16.6%; ranging from 11.8% to 53% following surgery, with axillary lymph node dissection (ALND); and 0% to 15.8% after surgery with sentinel lymph node biopsy (SLNB) (DiSipio et al., 2013). The probability of developing BCRL after ALND is four times higher than with SLNB (Gebruers et al 2015, DiSipio et al 2013, Specht et al 2013). In a ten-year follow-up prospective observational study conducted by

Carolina et al. (2017), 29% of 964 BCRL cases of lymphoedema in the upper limb were identified through self-reported symptoms.

Trunk lymphoedema is an often undiagnosed, unrecognised and under-treated lymphoedema that can have a devastating effect on the quality of life of patients who present with it (Armer et al., 2003a; Warren et al., 2007). Just as with upper limb BCRL, survivors endure a lifelong risk of developing trunk oedema (Armer et al., 2003a; Jeffs, 2006). The true incidence of trunk oedema is largely unknown and rarely reported (Armer et al., 2003a; Fu et al., 2013). Verbelen et al. (2014) conducted a systematic review and reported the breast and trunk incidence of lymphoedema to be between 0% and 90.4%. Norman et al. (2009) reported an incidence of secondary upper quadrant lymphoedema of between 6% and 70%. Jeffs et al. (2006) reported an incidence of 13% of breast/chest oedema (34 out of 263 patients) in a London-based lymphoedema clinic. Bosompra et al. (2002) conducted telephonic interviews with 148 BC survivors to investigate the prevalence of trunk edema, based on self-reported symptoms. Out of the 148 BC survivors, 10% presented with self-reported symptoms affecting the back; 22% the armpit; 10% the anterior chest wall; 14% the breast tissue; and 14% the lateral chest wall (Bosompra et al., 2002).

This large variation in reported trunk lymphoedema in the literature can be ascribed to the type and extent of surgical intervention, the length of time for follow-up investigations, and the lack of a clear consensus on validated diagnostic tools and definition parameters for trunk oedema (Hidding et al., 2016; Stout Gergich et al., 2008; R. J. Tsai et al., 2009). To better understand breast cancer-related upper limb and trunk lymphoedema, a thorough knowledge of the anatomy and physiology of the lymphatic system is imperative.

2.6 Anatomical Considerations

The lymphatic system is a complex, unique system that plays an integral role in the human body in maintaining health and quality of life (Rockson, 2012). This system is gaining recognition and momentum in the literature, and with the advances that have been made using imaging techniques, the significance, complexity and function of the lymphatic pathways is better understood and acknowledged (Suami & Scaglioni, 2018). Despite advances in the diagnosis and management of a compromised lymphatic system, a medical cure for an impaired lymphatic system has yet to be identified (Lawenda et al., 2009; Rockson, 2008).

The lymphatics are responsible for regulating tissue homeostasis, for immune surveillance and immune cell transportation, and for the absorption of lipids from the intestinal system (Grada & Phillips, 2017b; Rockson & Rivera, 2008). Both superficial and deep lymphatic systems exist. The former is of great relevance to lymphoedema therapists (Lawenda et al.,

2009). This superficial lymphatic system is responsible for removing interstitial fluid and by-products from the skin and returning them to the intravascular circulation (Foldi & Foldi, (2012); Lawenda et al., 2009; Rockson, 2012).

The superficial lymphatic system comprises vessels and lymph nodes (Grada & Phillips, 2017b; Ridner, 2013). The vessels are strategically placed in a wide subcutaneous network to facilitate efficient drainage and transport of the interstitial fluid (a thin layer of fluid surrounding the cells in the body). Lymphatic vessels are made up of a single layer of unsealed overlapping endothelial cells (Suami & Scaglioni, 2018; Zawieja & Ph, 2009). Anchor filaments connect each cell to the surrounding tissues, promoting the opening and closing of these gaps in response to increased fluid in the interstitium and movement in the surrounding tissues (Zawieja & Ph, 2009). As the fluid volume in the interstitium increases, the anchor filaments are stretched, pull on the endothelial cells, and gaps open in the vessels (Wittlinger & Wittlinger, 2011Zawieja & Ph, 2009).

There is strong evidence in the literature that medical intervention for BC (including surgery, chemotherapy and radiation therapy) has a traumatic and detrimental effect on the local, superficial lymphatic system (Ridner, 2013; Suami & Scaglioni, 2018). The system becomes dysregulated and dysfunctional, and pathology occurs (Hinrichs et al., 2004; Kilbreath et al., 2016; Lawenda et al., 2009; Lucci et al., 2021). Lymphoedema occurs in the presence of an inadequate lymphatic system when filtration is normal, but the lymphatic transport system is compromised (Ridner, 2013). The protein-rich content in the interstitial fluid causes increased osmotic pressure, resulting in a backflow from the lymphatic collectors (Suami et al., 2019; Tsai et al., 2009), which pushes more fluid into the interstitium, causing chronic lymphoedema.

The lymphatic pathways of the upper limb, trunk and axilla are important considerations when analysing the local lymphatic pathology that surgical procedures and radiation therapy may cause in the presence of BC (Mayrovitz, 2009; Suami, 2020). The axilla houses between 20 and 40 lymph nodes (Kyriacou & Khan, 2020; Suami & Scaglioni, 2018). These lymph nodes receive drainage from 75% of the ipsilateral breast; upper back; chest; shoulder and antero-lateral abdominal wall. Drainage of the arm, trunk and breast are separate in the axilla region, but the lymphatic vessels are all anatomically connected (Mayrovitz et al., 2009). The life-saving medical interventions for BC may be responsible for disrupting an efficiently functioning lymphatic system (Tsai et al., 2009) that may create an environment for the development of upper limb or trunk BCRL.

2.7 Risk Factors for BCRL

The extent of surgery and the associated lymph node dissection has a significant influence on the risk of lymphoedema development (Kilbreath et al., 2016 DiSipio et al., 2013). The direct complications arising from surgical intervention include the following: localised scar tissue; post-surgical seroma formation; axillary web syndrome (AWS); infection; inflammation and pain (Ridner, 2013; Toyserkani et al., 2017; Yeung et al., 2015; Zomkowski et al., 2018). Localised scarring causes extrinsic disruption to the superficial lymphatic and vascular architecture, the surrounding musculature and soft tissue. A proliferation of post-surgical collagen tissue may result in permanent local fibrosis (Ghanta, Cuzzone, Torrisi et al., 2015). Local tissue fibrosis reduces the efficiency of the muscle pumping action which is a vital component of lymphatic fluid transportation.

A highly restrictive complication from both surgery and radiation is a condition known as axillary web syndrome (AWS) (Yeung et al., 2015). According to a systematic review conducted by Yeung et al. (2015), there is no clear consensus in the literature regarding the risk that AWS poses for lymphoedema development. O'Toole et al. (2013) confirmed, in a study of 308 patients with unilateral BC, that 31.5% developed AWS, and upper limb volume increased by 5% ($p<0.028$). This painful condition causes decreased shoulder range of motion, which further inhibits the local muscular pump efficiency (O'Toole, Miller et al., 2013; Yeung et al., 2015).

Post-surgical inflammation, together with protein-rich interstitial fluid stasis, may initiate a vicious cycle of inflammation and lymphoedema in women following BC treatment (Gillespie et al., 2018). It has been reported that the risk of lymphoedema is increased by 3.11 times in the presence of cellulitis (Ugur et al., 2013). Previous inflammation and infection was found to be a significant predictor for BCRL in a study conducted by Mak et al. (2008) in Hong Kong). The relationship between lymphoedema and cellulitis has been found to be interwoven and a vicious cycle of lymphoedema and cellulitis may ensue (Asdourian et al., 2016; Sayegh et al., 2017).

The presence of subclinical lymphoedema (stage 0), which is experienced as the subjective symptoms of tightness; heaviness; puffiness; tiredness and tenderness, was reported to increase the risk of BCRL developing at a later stage, following BC treatment intervention (Norman et al., 2009). Subclinical lymphoedema is defined as a limb volume difference of less than 10% (Damstra & Halk, 2017). A Turkish study, including 25 women with subclinical breast cancer-related lymphoedema, found that early detection and treatment of lymphoedema reduced the risk of developing more severe lymphoedema (Gençay Can et al., 2019).

Radiotherapy has been identified as an independent risk factor for the development of upper limb or trunk lymphoedema (Tsai et al., 2009; Ugur et al., 2013). In a systematic review, it was reported that radiation therapy increases the risk of BCRL five-fold (Allam et al., 2020). Ugur et al. (2013) conducted an analysis on 455 post-surgical BC patients and reported that radiotherapy increased the risk of lymphoedema by 1.83 times ($p<0.007$) (Ugur et al., 2013). Complications arising from radiation therapy may cause prolific degradation, and compromise the carrying capacity, of the local lymphatic system (Allam et al., 2020). These include the destruction of the lymphatic architecture; scar tissue; fibrosis; pain and reduced shoulder range of motion (Johansson et al., 2000). Fibrosis has been identified as an independent risk factor for BCRL (Avraham et al., 2010). These complications of BCRL and lymphoedema may result in upper limb dysfunction for breast cancer survivors. Lymph nodes are highly sensitive to irradiation, as they become depleted of lymphocytes, with fatty tissue changes occurring and fibrosis ensuing (Allam et al., 2020). The outcome of this process is a leakage of lymphatic fluid from the lymphatic vessels into the interstitium, with resultant lymphoedema. (Abe et al., 2005; Allam et al., 2020; Tsai et al., 2009)

Although there is no clear consensus in the literature that chemotherapy is a risk factor for BCRL, there is a pattern emerging that suggests that the destruction of the lymphatics by chemotherapy is possible and likely (Kim et al., 2016). A consequence of taxane-based chemotherapy is capillary leakage and fluid retention due to the resulting pathogenesis of the lymphatics. Kim et al. (2016) confirmed in their study, conducted in Korea, that adjuvant taxane-based chemotherapy increased the risk of BCRL in a cohort of 1073 patients who were followed up at 5.1 years. In contrast, Swaroop et al. (2015) found that, in a cohort of 1121 women with BC in America, at 18 months post- surgery, taxane-based chemotherapy was not a risk factor for BCRL.

In addition to these extrinsic risk factors, the prospect of BC survivors developing BCRL is also dependent on intrinsic, individual, modifiable and non-modifiable risk factors. An in-depth knowledge and understanding of these risk factors, as well as the process of identifying them timeously, is key to reducing the risk of developing BCRL of the trunk and upper limb (Michelotti et al., 2019). Modifiable risk factors can be managed and influenced through patient education, including self-monitoring and relevant lifestyle changes, thus reducing the risk of potential lymphoedema development. These risk factors include an increased body mass index (BMI) and regular fluctuations in body weight. A primary consideration is a high BMI score that indicates obesity (greater than 30kg/m^2). There is rich evidence in the literature that correlates pre-operative obesity with increased risk of BCRL occurrence (Mak et al., 2008; McLaughlin et al., 2008; O'Toole, Jammallo, Skolny et al., 2013; Tsai et al., 2009; Ugur et al., 2013). The increased presence of adipose tissue surrounding the lymphatic architecture will

compress and obstruct the lymphatic vessels, thus reducing the transport capacity (Zampell et al., 2012). Several studies have revealed that obesity triples the risk of BCRL development in BC survivors (Helyer et al., 2010; Jammallo et al., 2013). Equally important, individuals experiencing weight fluctuations of greater than 4.5kg within a four-week period following surgery (either gain or loss) have a higher probability of experiencing BCRL (Jammallo et al., 2013). Non-modifiable risk factors include age and genetics (Guliyeva et al., 2021).

According to a systematic review conducted in 2021, no clear consensus has been reached in the literature regarding the relationship between age and lymphoedema (Guliyeva et al., 2021). In a study conducted in the United States of America, 494 women completed a baseline interview regarding BCRL. It was found that a younger age at BC diagnosis (<55 years) was related to a two-fold risk of developing lymphoedema (Meeske et al., 2009). In contrast, a separate study revealed that the risk of developing lymphoedema increases in patients over the age of 50 years (Basta et al., 2016).

2.8 Quality of Life (QOL)

It is well documented that quality of life (QOL) is negatively influenced in BC survivors, especially those with BCRL (Beaulac et al., 2002; Ridner, Bonner et al., 2012; Ridner, Sinclair et al., 2012). A retrospective cohort study involving 151 breast cancer survivors, conducted by Beaulac et al. in 2002, revealed that BCRL is an independent predictor for decreased QOL in BC survivors. The women had undergone either breast-conserving surgery and radiation, or unilateral mastectomy without radiation. Almost 28% of these study participants were diagnosed with BCRL. The FACT-B quality of life questionnaire revealed that all the women experienced a diminished QOL (Beaulac et al., 2002). Breast cancer survivors with a higher BMI reported a diminished QOL ($p<.001$) compared to those with a normal/lower BMI (Beaulac et al., 2002). The physical, emotional and psychological aspects related to BCRL have been documented to include body image; financial burden; function; re-integration in the workplace; fear and stress; frustration; fatigue; anxiety and depression; pain; relationships; and psycho-social function (Beaulac et al., 2002; Pusic et al., 2013; Ridner, Sinclair et al., 2012; Smoot et al., 2010). A systematic review conducted in 2012 examined 39 published studies of health-related quality of life in BC survivors from countries including China, America, Korea and Turkey. Most of these studies reported diminished quality of life for breast cancer survivors in the domains of body image; physical function; psychological well-being and social adeptness (Pusic et al., 2013).

It is evident that one's perception of QOL is a complex, qualitative experience. Early intervention strategies and coping mechanisms should be implemented to preserve QOL in BC survivors (Pusic et al., 2013, Gençay Can et al., 2019). Patient education regarding the

potential deterioration of QOL following BC treatment is imperative, as education will equip these women to make informed decisions regarding treatment intervention options for BCRL (Gençay Can et al., 2019).

2.8.1 Function

Reduced physical function of the upper limb has been reported as a complication following BC management (Khan et al., 2012). BC surgery results in scar tissue as well as post-operative pain which may lead to shoulder stiffness and dysfunction. Poor posture as a result of pain and post-operative asymmetry following mastectomy surgery may also result in upper limb pain and dysfunction. Radiation therapy causes fibrosis of the soft tissue in the targeted area, especially of the local lymph nodes (sub and supraclavicular) and muscles of the anterior chest wall (Shaitelman et al., 2017). A potential complication following BC surgery and radiation is a condition called axillary web syndrome which is a painful condition caused by fibrosis and tight cords which may extend from the axilla, down the ipsilateral arm in the cubital fossa and into the wrist region. This condition may lead to reduced range of motion of the upper limb (especially shoulder flexion and abduction and elbow extension) (Luz et al., 2017).

The above complications may result in pain, weakness, challenges in the workplace and reduced ability to perform activities of daily living. This complication will require intensive treatment and rehabilitation in order for it to resolve (Luz et al., 2017). This may lead to financial burden, loss of income and reduced quality of life. The LYMQOL questionnaire assesses the physical function of the patient in questions 1,2 and 3. The questions relate specifically to activities of daily living including questions about occupation, housework, combing hair, dressing, writing, eating and cleaning teeth. The LYMQOL encompasses ability to work, look after the home and basic activities for hygiene. In addition, the questionnaire includes a section on leisure activities and social life, as well as patient independence (Keeley et al., 2010).

2.9 Measurement and Diagnosis of BCRL

The successful prevention and treatment of breast cancer-related trunk or upper limb lymphoedema relies on early screening and detection, as well as preliminary identification of risk factors (Gençay Can et al., 2019; Grada & Phillips, 2017a). Lymphoscintigraphy has been established as the gold standard choice of imaging for the measurement of lymphoedema (Pappalardo et al., 2021). The disadvantage of this imaging is the financial and time burden that is placed on the patient, as well as on the clinician. The choice of lymphoedema measurement instruments will be influenced by cost; practice setting; location; stage; and

importantly, the location of the lymphoedema. BC survivors are at risk of developing oedema in the upper limb and/or the trunk and breast region (Bosompra et al., 2002; Verbelen et al., 2014). As a consequence of the paucity of literature regarding trunk lymphoedema measurement and the contrast in anatomical architecture of the two regions, measurement techniques to assess the upper limb and trunk differ and cannot be standardised. The relevant measuring techniques for the upper limb and trunk will be presented separately.

2.9.1 Upper Limb Lymphoedema

Hidding et al. (2016) conducted a systematic review of 54 articles. These studies included a total of 1726 women from high income countries. These articles described various measurement tools for lymphoedema, such as water volumetry; circumferential tape measurements; perometry; bioimpedance spectroscopy; the Moisture Meter D® (percentage tissue water content); and tonometry. The authors recommended water volumetry and circumferential tape measurements as the best-practice measurement techniques for lymphoedema of the upper limb. The clinical studies were reviewed using Quality Assessment of Diagnostic Accuracy Studies-2 (QADAS-2) was performed and discussed by two independent researchers and only the studies that scored a low bias risk were included in the review. The data was synthesised using inter- and intra-rater intraclass correlation co-efficients (ICC_{inter} was .98 and ICC_{intra} was .99). Standard error of measurement was 0.7% (σ=0.8%) and was utilised to establish reliability for the upper limb measurement values. Devoogdt et al. (2010) conducted a study of 112 women with BCRL to determine the reliability and concurrent validity of tape measurements and water volumetry. The authors found a strong correlation (r > .80- .99) between the two measurement tools using intra- and inter-relator ICCs, as well as standard error of measurement parameters, for the upper limb. Water volumetry in a limb is calculated using circumferential tape measurements, taken at 4cm intervals, which are converted into a limb volume value using a unique truncated cone formula. This can be used to establish the presence of lymphoedema by comparing volume scores for affected and unaffected limbs (Devoogdt et al., 2010; Hidding et al., 2016).

The interpretation of the tape measurements for the confirmation and diagnosis of the presence of lymphoedema has been arbitrarily defined in the literature as either a 2cm increase in limb circumference, a 200ml increase in limb volume, or a 5-10% change in limb volume compared to the unaffected side (Ezzo et al., 2015, JMP Godoy et al., 2007). Once the presence of lymphoedema has been established, the condition may be staged, according to the International Society of Lymphology (ISL) (Society et al., 2016). Table 2.1 illustrates the staging of lymphoedema.

Self-reported symptoms have also been accepted as a defining strategy for experiencing early or subclinical lymphoedema of the upper limb, but not as a stand-alone diagnostic criterion. A

population-based prospective study in Philadelphia, USA, which included 631 BC survivors, found that self-reported symptoms are valuable in identifying early and subclinical signs of upper limb lymphoedema. A validated questionnaire (Memorial Symptom Assessment Scale) was utilised and the following symptoms were recognised as stand-alone clinically relevant/valuable in detecting subclinical upper limb lymphoedema: tightness; puffiness; pain; swelling; and tired thick, heavy skin of the upper limb (Norman et al., 2009).

2.9.2 Trunk Lymphoedema

One of the many challenges of detecting trunk oedema is the lack of validated diagnostic tools and criteria for accurate objective measurements of this area of the body. The use of tape measurements for the trunk is not recommended, as it is impossible to measure left and right sides separately for comparative values. Furthermore, it is impossible to obtain measurements for water displacement volumetry for the trunk region as this would necessitate immersing the torso in a container to measure the water displacement. The recommendations for measurement of the trunk are bioimpedance spectroscopy, tonometry and the Moisture Meter D® (Hidding et al., 2016; Mayrovitz, 2015). All these measurement tools have shown reliability and validity in trunk measurements (Hidding et al., 2016; Mayrovitz, 2015). However, these tools may not be accessible to many clinicians, as the cost may be prohibitive. Lack of access to the measurement tools for trunk oedema emphasises the challenge that many clinicians experience in successfully identifying trunk oedema in BC survivors.

There are few references in the literature to describe self-reported symptoms of trunk oedema, such as tenderness, changes in sensation, discomfort caused by underwear and poor sleeping habits (Hisano et al., 2021; Mayrovitz et al., 2009; Williams, 2006). It follows that, if self-reported symptoms have been validated as significant precursors in the subclinical stage of lymphoedema of the upper limb, then including self-reported symptoms in the assessment of trunk oedema may be vital. Where possible, it is important to correlate the subjective, self-reported symptoms of BC-related trunk oedema with reliable objective measurements (Fu et al., 2015).

2.10 Evidence-based Multimodal Management of BCRL

An evidence-based multimodal management plan is an essential component of the successful management of BCRL (Tzani et al., 2018). Historically, the first line of treatment for breast cancer-related lymphoedema has been complete decongestive therapy (CDT). This is a complex treatment process and consists of multimodal management, including manual lymphatic drainage (MLD); deep breathing exercises; multilayer compression bandaging (MCB); donning of compression garments; skin care; exercise prescription, and patient education (Damstra et al., 2017; Devoogdt et al., 2010; Lasinski et al., 2012). Gold standard

clinical practice guidelines have been set out by the Dutch Society of Dermatology (Damstra & Halk, 2017). Lasinski et al. (2012) conducted a systematic review which included 26 ‘moderately strong’ articles. The consensus among the authors was that CDT is an effective and safe approach in the treatment of lymphoedema, but the efficacy of the individual components remains unclear (Lasinski et al., 2012).

The management of BCRL consists of two phases of CDT intervention (Damstra et al., 2017; Lasinski et al., 2012). The initial reduction, or intensive, phase seeks to achieve maximum reduction of the lymphoedema volume (Damstra et al., 2017; Lasinski et al., 2012); and the long-term maintenance phase requires lifetime compliance from the patient (Damstra et al., 2017). The intensive phase is effective in accomplishing limb volume reduction due to the concentrated frequency of treatment sessions, as well as the application of multilayer compression bandaging and education of the patient regarding skin care, exercise and deep-breathing exercise (Damstra et al., 2017). There was little consensus amongst the authors regarding the most effective duration of the intensive phase. Vignes et al. (2006) referenced previous studies in which an intensive phase of between one and six weeks had been reported. In another study, it was reported that a two-week (five treatments per week) intensive phase is adequate to achieve the maximum reduction in limb volume (Vignes et al., 2011). More recently the authors reported that eleven days of intensive treatment is more effective for volume reduction than four days (Vignes et al., 2013).

The second phase, referred to as the maintenance phase, is aimed at maintaining the optimal limb volume reduction achieved during the intensive phase. The key interventions during this phase are the use of prescribed compression garments, exercise and efficient skin care (Ochalek et al., 2019; Vignes et al., 2007). The responsibility for lifelong surveillance and management of the lymphoedema is transferred to the patient (Damstra et al., 2017). The patient must be educated in skin care; exercise; deep breathing; compression therapy and self-MLD; and self-measurement of the upper limb (National Lymphoedema Network (2013); Gradalski et al., 2015; Damstra et al., 2017).

The LANA provides recommended standards for clinicians for certification to facilitate best practices for BCRL intervention (Sayegh et al., 2017). To participate in this training, attendees must be registered with their professional bodies, either as a physiotherapist, occupational therapist, or other medical professional. Training involves 135 hours of complete decongestive therapy training which includes coursework, including in-depth pathophysiology on lymphatic function, as well as theoretical and practical sessions on complete decongestive therapy. This includes skin care; MLD; multi-layer compression bandaging; measurement; and prescription of compression garments. Patient education for long-term self-management is also an integral

aspect of the training. To receive accreditation, the therapist must pass a theoretical and practical examination at the end of training (National Lymphatic Network 2013). McLaughlin et al. (2017), in a review on the management of BCRL, recommended that patients diagnosed with BCRL should be referred to a certified lymphoedema therapist (CLT) for management and treatment. Post-graduate training in CDT is not accessible and affordable to all healthcare providers or physiotherapists, although some of the treatment techniques are included in the undergraduate training of physiotherapists at national universities in South Africa (HPCSA 2022).

In comparison to the upper limb, there is a lack of evidence in the literature regarding the application of the gold standard multimodal management to the trunk region. All the relevant treatment interventions applicable to both upper limb and trunk lymphoedema, such as MLD; exercises; deep breathing exercises; low-level laser therapy; compression therapy; Kinesio® tape application, and skin care will be presented.

2.11 Multimodal Management Interventions for Upper Limb and Trunk Lymphoedema

2.11.1 Manual Lymphatic Drainage

Manual lymphatic Drainage (MLD) and central truncal clearance have been accepted as the cornerstone of successful reduction of both upper limb and trunk lymphoedema (N Mayrovitz et al., 2009). No studies have been conducted to investigate the efficacy of truncal or central clearance as precursors to MLD. However, this concept has been accepted widely by therapists, due to their understanding of the physiology of the lymphatic system (Mayrovitz et al., 2009). The application of MLD always follows the principle of regional lymph node pumping and clearing the trunk and proximal lymphatic regions. This sequencing promotes lymphatic flow from distal to proximal and encourages peristaltic contractions of the lymph vessels (Mayrovitz et al., 2009). In addition, MLD utilises watershed pathways and functional lymphatics to facilitate flow away from the congested dysfunctional lymphatics (Mayrovitz et al., 2009; Moseley et al., 2007; Suami, 2020) . Lymphoedema in the trunk is cleared first, in preparation for clearance of the upper limb lymphoedema. This is vital, as the trunk may act as a substitute region for lymphatic flow from the upper limb when the ipsilateral axillary nodes have been dissected or damaged (Mayrovitz et al., 2009, Suami, 2020). The principles of the application of MLD remain the same for the trunk, namely, that the clearance of the contralateral trunk will facilitate peristalsis of the lymphatic vessels and lymph contractility. This will assist in fluid transportation from the congested trunk region to the contralateral trunk and axilla (Mayrovitz et al., 2009, Suami, 2020).

Although strong principles for the application of MLD exist, the effectiveness thereof as a stand-alone modality is still debated (Ezzo et al., 2015). A Cochrane systematic review, by Ezzo et al. in 2015, confirmed that MLD is a safe and well-tolerated technique by BC survivors (Ezzo et al., 2015). Furthermore, in a meta-analysis conducted by Liao et al. in 2013, it was found that, compared with the application of skin care, exercise and compression, additional MLD did not achieve a significant reduction in limb volume (Liao et al., 2013). The pooled results of the systematic review by Ezzo et al. (2015) substantiated the results of Liao et al (2013). A systematic review that was conducted in 2021 also concluded that further research is needed to ascertain the efficacy of MLD as a stand-alone intervention in the management of BCRL (Thompson et al., 2021).

The inconsistencies regarding MLD in the literature suggest that its inclusion in the treatment of upper limb lymphoedema may be beneficial for mild to moderate lymphoedema and superfluous in more severe presentations of lymphoedema (Ezzo et al., 2015). If this modality were to be excluded, treatment would become more financially accessible to BC survivors (Gradalski et al., 2015). However, the time spent with the patient during the application of MLD in the intensive phase, creates opportunity for patient and family counselling (Damstra et al., 2017). MLD has also been shown to improve quality of life in BC patients who present with upper limb lymphoedema (Lasinski et al., 2012).

Management of the trunk lymphoedema without the use of MLD would present a challenge to therapists. This is due to a number of reasons, such as the anatomical location of the trunk, which presents a challenge for self-management, such as the application of self-MLD and Kinesio® tape (Mayrovitz, 2009). The architecture and location of the trunk also present a challenge in the application of compression bandaging during the intensive treatment phase (Mayrovitz, 2009). The omission of MLD for lymphoedema management would place severe limitations on the available treatment modalities for the trunk region (Mayrovitz, 2009).

2.11.2 Compression Therapy

Compression therapy is gaining momentum in the literature as a key component in CDT. More evidence is becoming available to indicate that multilayer compression bandaging should be applied as the first line of treatment intervention to reduce limb volume (Dayes et al., 2013; Malicka et al., 2014; Zasadzka et al., 2018). It has been noted that the application of multilayer compression bandages prevents the progression of lymphoedema, even in the subclinical phase or Stage 0 of lymphoedema (Smykla et al., 2013; Zasadzka et al., 2018). As part of the gold standard for the multimodal management of BCRL, the application of multilayer short-stretch bandages is the most effective method of compression in the intensive reduction phase of treatment (Smykla et al., 2013; Zasadzka et al., 2018). Dayes et al., (2013), and McNeely,

(2004), reported that compression bandaging reduced upper limb volume, regardless of whether MLD was applied (Dayes et al., 2013). Multilayer compression bandaging is applied using padding and short-stretch bandages, which have a low resting, and high working, pressure. The bandages reduce ultrafiltration into the interstitium and the high working pressure encourages an efficient pumping action adjacent to the lymphatics. This drives the lymphatic fluid through the whole lymphatic system effectively, facilitating effective decongestion of the lymphatic areas (Cheville et al., 2003; Mayrovitz, 2009).

The application of compression bandages requires the specialised skill of a certified lymphoedema therapist and is applied with a high-pressure gradient distally, which gradually decreases proximally (Lasinski et al., 2012). The compression bandages will undergo up to 30% pressure loss as upper limb volume reduction is achieved (Damstra & Partsch, 2009). Frequent re-application of the bandages during the day is thus indicated for optimal efficacy of this modality. This would present a challenge to the level of patient compliance, as self-application is complex and time consuming (Wigg & Lee, 2014).

Once optimum upper limb volume reduction is achieved in the intensive phase of multimodal management, compression garments should be prescribed to be worn daily during the maintenance phase to maintain this volume reduction (Rogan et al., 2016). The compression is graded in mm/Hg according to individual patient needs; and the optimal pressure required to influence volume reduction in the upper limb is the equivalent of 20-30mm/Hg (Damstra & Partsch, 2009). The application of compression garments results in reduced limb volume and maintenance of the reduced volume, as well as improved quality of life (Huang et al., 2013; Ochalek et al., 2019; Rogan et al., 2016). According to the Clinical Practice Guidelines from the American Cancer Society, pressure garments should be worn from morning to night, during daily activities, and removed at bedtime (Harris et al., 2012; Kligman et al., 2004). Vignes et al. (2007) conducted a large cohort prospective study and the results showed a 61% risk reduction for volume increase of 10%, compared with patients who did not wear a compression garment. This study substantiated the importance of long-term compression therapy to maintain the volume reduction achieved during the intensive phase of therapy.

Compression therapy presents one of the largest challenges in the management of trunk oedema following breast cancer intervention (Lasinski et al., 2012). Due to the anatomical location and asymmetrical architecture of the trunk following BC surgery, compliance with the scientific principles of compression bandaging, such as graded compression from distal to proximal, is not feasible (Lasinski et al., 2012). Ridner et al. (2010) reported a reduction in trunk lymphoedema following the use of a pneumatic compression device. Compression interventions in the maintenance phase of treatment for the trunk, such as pneumatic

compression pumps, are available for BC survivors. However, the cost of these devices may be prohibitive in middle- to low-income countries, such as South Africa (Mayrovitz, 2009).

2.11.3 Deep Breathing Exercises

Deep breathing exercises have been included by numerous authors in the multimodal management protocol for BCRL (Jeffs & Wiseman, 2013; McClure et al., 2010; Tsai et al., 2009; Vignes et al., 2013). Moseley et al. (2005) and Gautam et al. (2011) reported that a home maintenance programme, including deep-breathing exercises, resulted in a significant reduction of upper limb volume; improvement in quality of life; and decreased symptoms of pain, tightness, pins and needles, and heaviness, in the affected upper limb (Gautam et al., 2011;. Moseley et al., 2005). It has been postulated that deep breathing improves lymphatic flow due to the decrease in intrathoracic pressure during inspiration (Moseley et al., 2005). The pressure changes in the abdomen that result from deep breathing decrease hyperfiltration and facilitate the drainage of the lymphatic system (Baines KNS et al., 2021; Wittlinger D, Wittlinger H.,2010, Moseley et al., 2005).

2.11.4 Exercise

Exercise facilitates physical and psychological well-being and optimal QOL among breast cancer survivors (Schmitz et al., 2010). It has been included in the clinical practice guidelines for the gold standard multimodal management of lymphoedema, as well as in the Dutch guidelines for lymphoedema management (National Lymphoedema Network. Position Statement of the National Lymphoedema Network, Damstra et al., 2017). Exercise increases the muscle pump action which stimulates lymphatic transport and improves physical endurance (Ridner, 2013). A sedentary lifestyle may lead to obesity, which is a well-documented risk factor for the development of breast cancer-related lymphoedema (Jammallo et al., 2013). Much controversy has existed regarding the safety and advantage/efficacy of exercise for BCRL. It has emerged, in a systematic review by Kwan et al. (2011), that aerobic, strength and resistance training are safe as individual components and do not exacerbate or cause BCRL. The review found that a controlled and supervised exercise programme (in terms of prescription of resistance and repetitions) is an integral component of intervention and may reduce lymphoedema (Kwan et al., 2011). The American College of Sports Medicine (ACSM) has found that exercise has multiple benefits for patients with BCRL. These benefits include improved flexibility and muscle strength; decreased fatigue and anxiety; improved body image; and reduced risk of secondary cancer development (Schmitz et al., 2010). Authors have not reached a consensus regarding the use of compression garments on the lymphatic upper limb during exercise (Kwan et al., 2011). Guidelines have recommended that exercise be conducted with a prescribed pressure garment in situ. This is in accordance with

the position statement of the National Lymphoedema Network (National Lymphoedema Network, 2011).

2.11.5 Skin Care

A key component in the successful long-term management of BCRL is patient education regarding good precautionary skin care habits which maintain skin integrity (British Lymphology Society, 2010; Harris et al., 2012; Rockson, 2018). The structure and integrity of the skin may change in the presence of lymphoedema. This includes degradation, infection and cellulitis. Skin should be kept clean and well moisturised to prevent cracking and roughening, which could lead to bacterial infection (Asdourian et al., 2016; Damstra et al., 2017). It has been recommended that drawing of blood, blood pressure monitoring and injections on the affected side should be avoided (Asdourian et al., 2016). However, there is no definitive data in the literature to support these guidelines (Asdourian et al., 2016). Comprehensive patient education regarding all aspects of lymphoedema care is imperative for the long-term management of BCRL (Asdourian et al., 2016; Bland & Kosir, 2019; Damstra et al., 2017).

2.11.6 Low-level Laser Therapy

CDT can be time-consuming, so it is pertinent to investigate the efficacy of less labour-intensive adjunct treatment modalities for BCRL. Low Level laser Therapy (LLLT) is one such modality. The most common laser wavelength utilised in a systematic review conducted in 2012 was 904nm (Omar et al., 2012). It has potential efficacy in the treatment of BCRL, due to its ability to facilitate lymphangiogenesis and lymphatic flow; stimulate lymphatic motricity; and prevent tissue fibrosis, which is known to disrupt lymphatic function (Kaviani et al., 2006; Kozanoglu et al., 2009).

In a meta-analysis conducted by Baxter et al. in 2017, moderate-strength evidence suggested that the use of LLLT for breast cancer-related lymphoedema was more effective than ‘sham’, or no, LLLT at short-term follow-up; but was no more effective than other modalities (Baxter et al., 2017). A two-component cross-over study that was carried out by Cariarti in 2003 showed a significant reduction in mean limb volume in breast cancer patients with lymphoedema following a two-cycle exposure to LLLT, as compared to a sham/control group. At two to three months, 31% of the participants had a >200ml reduction in limb volume ($p=0.01$), compared to 4% in the sham/control group (Ahmed Omar et al., 2011). Evidence in the literature supports the use of LLLT, using one-to-two joules per fibrotic or swollen point as an adjunct to the multimodal approach in the treatment of upper limb lymphoedema (Omar et al., 2012).

2.11.7 Kinesio® tape

To overcome challenges in the application of compression bandaging to the trunk area, the use of Kinesio® tape has been implemented as an adjunct to the gold standard multimodal management in the management of upper limb and trunk oedema (Gatt et al., 2017). The physiological benefits of Kinesio® tape have been reported to include an increase in subcutaneous lymph drainage, decreased tissue fluid congestion, and augmented blood and lymphatic circulation (Pekyavaş et al., 2014; Tsai et al., 2009). In addition, Kinesio® tape normalises muscle tension, which decreases pain and improves the motility of lymphatic fluid through the lymphatic vessels. The lack of literature addressing the effectiveness of Kinesio® tape in the management of lymphoedema is unfortunate. This may be due to the lack of availability studies with a control group. Kinesio® tape has the potential to address the aforementioned challenge of trunk compression due to the ability to apply it to asymmetrical and non-cylindrical surface areas (Finnerty et al., 2010). A meta-analysis was conducted by Gatt et al. in 2017, to determine the effectiveness and safety of Kinesio® tape application in lymphoedema management of the upper limb. The authors suggested that Kinesio® tape should be utilised when compression bandages cannot be applied; for example, on the trunk (Gatt et al., 2017). A randomised, controlled study conducted by Pekyavas et al. (2014) showed that the combination of multimodal management and Kinesio® tape may result in improved reduction of upper limb and trunk lymphoedema (Pekyavaş et al., 2014).

2.12 Conclusion

In conclusion, it has been well established in the literature that a multimodal approach to the treatment of BCRL by a certified lymphoedema therapists is essential. BCRL is a degenerative and incurable condition and early detection and management may prevent the progression of this condition. BCRL has a negative impact on the quality of life and function in BC survivors and may result in anxiety, depression, reduced ability to complete activities of daily living and may lead to psycho-social dysfunction. More research is needed in the South African context regarding the screening and diagnosis of BCRL as well as referrals and access to certified lymphoedema therapists. Transport issues, communication/language barriers, shortage of certified lymphoedema therapists as well as a lack of equipment in rural areas and public hospitals create a challenge to both BC patients and therapists. BCRL places a financial burden on the patient as treatment is ongoing and compression garments are expensive.

There is a need for knowledge to be extended to all healthcare professionals working with BC patients to ensure patients' timeous access to the multimodal approach to intervention and management of BCRL.

The aim of this study is to investigate the effects of a multimodal management plan on upper limb and trunk BCRL, function and quality of life in a South African setting. It is apparent from the literature that a multimodal approach to BCRL management reduces limb volume, improves function and enhances quality of life. Should these results be achieved in the South African context, it would be imperative to ensure that this multimodal approach to treatment be made available and accessible to all BC survivors in South Africa.

Chapter 3: Methodology

3.1 Aim of the Study

The main aim of this study was to investigate the effect of multimodal management on upper limb and trunk lymphoedema, and self-reported function relating to daily activities and quality of life, in breast cancer survivors. The specific objectives were:

- to determine the effect of multimodal management on upper limb and trunk lymphoedema on women after breast cancer management;
- to describe the effect of multimodal management in improving self-reported function relating to daily activities in women following breast cancer treatment; and
- to describe the effect of multimodal management interventions on quality of life in women following breast cancer treatment.

3.2 Study Design

A non-concurrent series of N = 1 experimental baseline ($A_1B_1A_2B_2A_3$) study design was utilised. The sequence of phases $B_1A_2B_2$ were randomised to strengthen the internal validity of the study. Three participants were randomly allocated to the $A_1B_1A_2B_2A_3$ and two to the $A_1B_1B_2A_2A_3$ group. This design enabled a participant-oriented approach to the study and the effects of the multimodal management plan could be evaluated for each individual participant. Multiple outcome measurements could be evaluated, and randomisation of the intervention phases could be implemented to assess the efficiency of the intervention phase duration.

Table 3.1: Participant Randomisation

PARTICIPANT	01	02	03	04	05
GROUP 1 A1B1A2B2A3	X			X	X
GROUP 2 A1B1B2A2A3		X	X		

A1=washout phase; B1=intervention phase; A2=withdrawal phase; B2=intervention phase; A3=withdrawal phase

3.3 Study Setting

The experimental study was conducted at a private, outpatient physiotherapy practice in a private, 290-bed, hospital in Westville, Durban, KwaZulu-Natal, South Africa. The main

researcher is a qualified physiotherapist with 30 years of experience, registered with the HPCSA. She is the owner of a private physiotherapy practice and has been a certified lymphoedema therapist for six years, with a special interest in the management of breast cancer-related upper limb and trunk lymphoedema.

3.4 Study Population

The population for this study consisted of adult female breast cancer survivors who had undergone either a mastectomy or breast-conserving surgery, and who presented with breast cancer-related upper limb and/or trunk lymphoedema. Participants should have completed their chemotherapy and radiation treatment at least six weeks prior to the commencement of the study, as these interventions may have influenced the participants' response to the treatment interventions (DiSipio et al., 2013; Norman et al., 2009).

3.5 Study Sample Size

A pragmatic approach to the selection of a sample was taken. Six out of ten potential participants were included in this study following a screening process. One participant withdrew from the study prematurely during Phase B_2 as a result of concerns over the Covid-19 pandemic.

3.6 Inclusion and Exclusion Criteria

3.6.1 Inclusion Criteria

Participants who met the following criteria were considered for inclusion:

- female breast cancer survivors who had undergone a single or bilateral mastectomy and presented with either upper limb or trunk lymphoedema, or both concurrently
- female breast cancer survivors who had undergone breast-conserving surgery and who presented with either upper limb or trunk lymphoedema, or both concurrently
- adult female breast cancer survivors who were eighteen years and older

3.6.2 Exclusion Criteria

The following exclusion criteria applied:

- participants who had active, untreated cellulitis. Concurrent acute cellulitis is a contra-indication to compression and exercise therapy (British Lymphology Society, 2010; Szuba et al., 2002)

- participants who were currently receiving radiation therapy, as radiation therapy is a well-known independent risk factor for the development of lymphoedema (DiSipio et al., 2013)
- participants who were currently receiving chemotherapy, as taxane-based chemotherapy has been identified as a risk factor for lymphoedema occurrence (Norman et al., 2009)
- participants who had a body mass index (BMI) greater than 30kg/m2. This body mass index score indicates clinical obesity, which presents a triple-fold risk of developing breast cancer-related lymphoedema (Helyer et al., 2010; O'Toole et al., 2013; Jammallo et al., 2013)
- participants who had experienced weight fluctuations of greater than 4.5kg per month since diagnosis of BC, as this is a risk factor for the development of breast cancer-related lymphoedema (O'Toole, Jammallo, Miller, et al., 2013)
- participants who presented with axillary web syndrome. Although there is no clear consensus in the literature, tissue dielectric constant values have indicated that axillary web syndrome is a potential risk factor for both arm and trunk lymphoedema development following breast cancer surgery (Koehler, Blaes, Haddad, Hunter, Hirsch & Ludewig, 2015).
- participants who had a history of post-surgical seroma. Although no consensus exists in the literature, this condition is considered to be a risk factor for breast cancer-related lymphoedema (Wang et al., 2016).
- participants who presented with unmanaged chronic cardiac failure, as compression bandaging is contra-indicated with this condition (British Lymphology Society, 2010)
- participants who had acute thrombosis in the upper limb, as this condition is contra-indicated for compression therapy (British Lymphology Society, 2010)
- participants who developed allergic contact dermatitis during the patch test which was conducted during Phase A_1, as this could predispose them to the development of cellulitis, which contraindicates compression and exercise therapy (British Lymphology Society, 2010)

3.7 Recruitment and Sampling

Convenience sampling was used. A letter was sent via email to the medical and surgical oncologists in the Durban Metropole area, informing them of this research study, and requesting referrals of potential study participants (Appendix 1). This was followed up with a reminder telephone call after one week. As physiotherapists are first-line practitioners, participants were sought from patients independently seeking physiotherapy intervention for breast cancer-related upper limb and trunk lymphoedema. Recruitment of potential

participants also took place through the placing of advertisements on Facebook and Whatsapp lymphoedema support groups (Appendix 2) and other relevant social media sites. All the study participants were ultimately recruited from the social media advertisements.

3.8 Screening

Potential participants received a screening form via email, detailing the exclusion criteria (Appendix 3). This was filled in and returned via email. If the potential participant was found to be eligible for the study, the participant was then invited to participate in the study (Appendix 4) and scheduled for an initial consultation. Informed consent was provided (Appendix 7) and a demographic information form (Appendix 5) was filled in during this consultation. A subjective and physical assessment (Appendix 6) of each study participant was conducted using an assessment form. Body mass index was calculated by using the formula kg/m^2 once weight and height had been measured for each participant. Each participant was invited by the receptionist to select one sealed opaque envelope out of a possible two. Each envelope contained one of two random versions of the study phases. The participants were allocated to a specific study randomisation according to their envelope selection. Each participant scheduled all their physiotherapy treatment sessions for the duration of the study to suit themselves. Directly after the first consultation and measurement session, a small test patch of Kinesio® tape was applied by the researcher to the anterior chest in the trunk region on each participant. The patch was to remain on the skin for 48 hours or be removed according to specific instructions as soon as an allergic reaction became apparent. Each participant was requested to read and sign an informed consent form (Appendix 8) before the patch test was conducted and each received clear instructions regarding skin observation and removal of the Kinesio® tape. Patch testing is the gold standard diagnostic test for the exclusion of allergic contact dermatitis (Wolf et al., 2013).

3.9 Informed Consent

Each potential participant was verbally informed by the physiotherapist of the study objectives and study procedure before commencement of the initial consultation. The selected participants were required to read and complete a letter of informed consent (Appendix 7) which detailed the exact nature and purpose of the study. The participants were also required to read and sign a letter of consent for access to medical records (Appendix 9) and for consent for medical photographs (Appendix 10) to be taken.

3.10 Multimodal Management Plan

A multimodal management plan was utilised for each study participant. The management for the upper limb lymphoedema included MLD, compression therapy and LLLT. The trunk lymphoedema was managed with MLD, LLLT and Kinesio® tape. The participants were also instructed in skin care, a home exercise programme and deep breathing exercises.

3.11 Study Tools and Outcome Measurements

The following outcome measurements were used to assess upper limb lymphoedema, truncal lymphoedema, function and quality of life

- Upper limb lymphoedema was measured using arm circumferential tape measurements (Appendix 25) which were converted to a limb volume value using the truncated cone formula (Taylor et al., 2006).
- Trunk lymphoedema was measured using a Moisture Meter D®, which measures the tissue dielectric constant (percentage tissue water content) value in the oedematous tissue (Appendix 26).
- Quality of life was measured using the LYMQOL questionnaire (Keeley et al., 2010) (Appendix 11).
- Function was measured by extracting the results from the function domain of the LYMQOL questionnaire (Keeley et al., 2010).

The outcome measurements were recorded on the participant score sheets and body charts (Appendices 24 and 25) during each phase. Each outcome measurement was compared, as the percentage difference between the baseline and individual phases of the study.

3.11.1 Trunk Percentage Tissue Water Content using the Moisture Meter D®

The moisture meter D® (Delfin Technologies, Kuopo, Finland) was the tool used to measure the percentage of trunk tissue water content in the study participants. This tool was sponsored for the duration of this study by Haddenham Healthcare, United Kingdom. The moisture meter D® (Delfin technologies, Kuopo, Finland) is a non-invasive, quantitative, measurement tool for local skin tissue water content. The scanner depth is between 2.0mm and 2.5mm and measures the percentage water content of the dermis and epidermis. It is suitable for detecting tissue water content in any anatomical location or surface and is, therefore, a valuable measurement tool for trunk lymphoedema. High frequency and low power (300MHz) electromagnetic energy is transmitted to the skin via a probe, which behaves as a co-axial transmission line (Alanen et al., 1999). The portion of the wave that is reflected is proportional

to the amount of free water in the skin tissue (Alanen et al., 1999; Mayrovitz, 2007). This value is known as the tissue dielectric constant (TDC). Pure water has a TDC value of 78.5; air has a value of 1 (Nuutinen et al 2004., Alanen et al., 1999). A TDC ratio between the affected side (lymphoedema) and non-affected side can be calculated by simply dividing the value of the affected side by the value of the unaffected side (Alanen et al., 1999). It has been suggested that a TDC ratio of 1.2 or higher indicates the presence of clinical lymphoedema. The moisture meter D® was used in the present study to evaluate the effect of a multimodal management plan on the percentage tissue water content in the trunk (H. N. Mayrovitz & Weingrad, 2018). Short-term intra-rater reliability has been established in the lower limb for the Moisture Meter D®, with an intraclass correlation co-efficient (ICC) of 0.996, with a 95% confidence interval of 0.965 – 1.000. The inter-rater reliability has an ICC of 0.997, with a 95% confidence interval of 0.988 to 0.999 (Mayrovitz et al., 2009). Long-term intra-rater reliability has been established with an ICC of 0.9 and a 95% confidence interval of 0.835-0.946. (Mayrovitz et al., 2009). The researcher carried out all the measurements for the duration of the study.

Validity of the Moisture Meter D® was established with strong correlations between TDC ratios, arm volume (r = 0.69) and segmental volume measurements (r = 77). A strong relationship between interarm TDC ratios and the number of lymph nodes removed was demonstrated, with R = 0.55. (Mayrovitz, Brown-Cross et al., 2009).

According to Mayrovitz et al. (2009), the minimum detectable change or difference in values for the tissue dielectric constant ratios, which can be interpreted as being real, has a value of between 5.3% and 8%. This was calculated at the 95% confidence level. This statistical analysis was done in the study conducted by Mayrovitz et al. (2019) and using the SPSS version 16.

3.11.2 Circumferential Tape Measurements of the Upper Limb

A gold standard for the measurement of upper limb lymphoedema has not been established (Horbal et al., 2019). The most practical measurement tool for limb lymphoedema in a clinical setting is a non-stretch, flexible tape measure. To establish consistency in successive measurements in the present study, the following protocol was applied from a study conducted by Devoogdt et al. in 2010:

- The wrist crease was marked as the starting point of the upper limb measurements.
- Thereafter measurements were taken at 4cm intervals (Devoogdt et al., 2010). All measurement points were marked with a kohl marker. These points were freshly demarcated at the commencement of each consultation.
- The participant was in a supine position. Once all the measurements were recorded, the limb volume was calculated using an excel limb volume calculator as follows:

$$V = L \times \frac{(C_1^2 + C_1C_2 + C_2^2)}{12\pi}$$

where the truncated volume formula is as follows:

L = distance between consecutive measurements

C_1 and C_2 = successive circumferential measurement in cm

V = volume between 2 successive circumferential measurements.

- Total limb volume = the sum of consecutive volume measurements in the limb.
- A comparison was made with the contralateral limb and the lymphoedema was classified or staged according to the International Society of Lymphology, 2016. (Refer to Table 2.1.)

An intraclass correlation co-efficient (ICC_{intra}) of .99 (95% CI=.99) and an interclass correlation co-efficient (ICC_{inter}) of .98 (95% CI=.98) were demonstrated in pooled data in three studies (Deltombe et al., 2007; Devoodg et al., 2010; Gjorup et al., 2010). The weighted mean standard error of measurement (SEM) was 2.8%. This indicates an excellent reliability score for circumferential tape measurements.

Concurrent validity using water volume displacement as a comparison was established to be between .80 and .99. The convergent validity of 4cm versus 10 cm measurement distances was established to be .87 (Hidding et al., 2016).

The smallest real difference in limb volume, which represents clinically relevant changes, is considered to be 3.5% in the intra-rater measurements (N. Devoogdt et al., 2010)
Circumferential tape measurement is considered to be a reliable and valid assessment tool for the measurement of upper limb lymphoedema.

3.11.3 Lymphoedema Quality of Life Questionnaire

The Lymphoedema Quality of Life Questionnaire (LYMQOL) was developed by healthcare professionals in conjunction with lymphoedema patients (Keeley et al., 2010). An arm-specific LYMQOL lymphoedema questionnaire was developed by Dr Vaughan Keeley. The questionnaire has four domains: symptoms, appearance, function and mood. Scores for each domain were evaluated. The scoring system is the same in each domain: not at all =1; a little =2; quite a bit =3; a lot =4. The lower the score for these domains, the better the quality of life. The total score for each domain is calculated by dividing the total score by the number of questions. The overall quality of life score was obtained separately using a vernacular method of scoring on a scale of 1 to 10. A score of one represented a poor quality of life and ten, excellent quality of life.

Permission to use the LYMQOL questionnaire was granted by Dr Vaughan Keeley, the developer of the questionnaire (Appendix 12). The participants were required to complete a hard copy of the LYMQOL questionnaire directly following the treatment session, without the assistance of the researcher.

The face validity of the LYMQOL was previously confirmed during testing by Dr Vaughan Keeley and it was described as being clear, easy to complete and not too long (Keeley et al., 2010). The criterion validity showed good correlation for all the domains when compared with the EORTC QLQ-C30 (European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire). For function, the ICC was 0.686, and the correlation co-efficient 0.689. In the symptom domain, the ICC was 0.643 and the correlation co-efficient 0.688. The mood domain had a correlation co-efficient of 0.860 and an ICC value of 0.868 (Keeley et al., 2010). The overall quality of life scores had a correlation co-efficient of 0.937 and ICC of 0.941. Internal validity was confirmed for all four domains and Cronbach's alpha is > 0.8. Cronbach's alpha for each domain for internal consistency was as follows: the function domain was 0.882; the appearance domain 0.832; symptoms 0.851; and for mood 0.867 (Keeley et al., 2010).

Reliability was established in the lower limb lymphoedema LYMQOL questionnaire by using the test-retest method. Reliability was found to be adequate (greater than or equal to 0.8) or good (greater than or equal to 0.9) for each of the domains in the LYMQOL (Keeley et al., 2010). Scores from the initial patient responses were compared with the scores after one week and one month. There were no significant score differences for LYMQOL (arm) after one week and one month. Responsiveness was assessed using Pearson's correlation coefficient (Keeley et al., 2010).

The minimal detectable change for each domain in the LYMQOL questionnaire is as follows: function 0.64 points; appearance 0.4 points; symptoms 0.53 points; and mood 0.81 points. The minimum detectable change for the overall quality of life score is 1.96 points. These values were established in a cross-cultural adaptation and validation study for Italian women (Monticone et al., 2021). The LYMQOL questionnaire does not address midline or trunk oedema. However, this study is concerned with the effect of upper limb lymphoedema on quality of life and function, which is addressed in the LYMQOL. The LYMQOL is a valid and reliable measurement tool for investigating the quality of life and function of women who have breast cancer-related lymphoedema of the upper limb.

3.11.4 Function

The results from the function domain of the LYMQOL questionnaire (Q1,Q2,Q3) were extracted and the function was represented by these scores. The validity and reliability of the LYMQOL questionnaire has been described in 3.11.3.

3.12 Study Procedures

3.12.1 Commencement of the Study

The study commenced according to a specific protocol which followed predetermined sequencing of phases. (Refer to Figure 3.1)

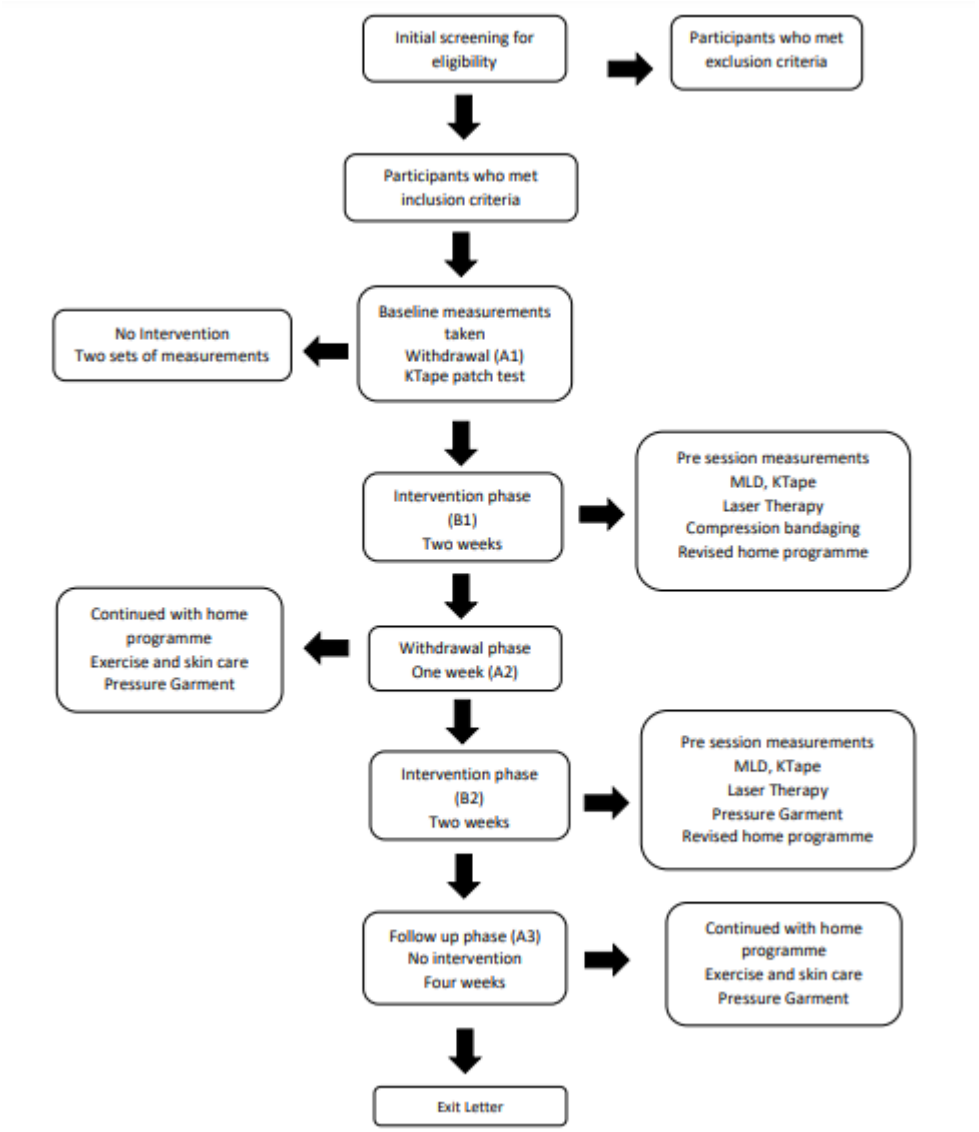


Figure 3.1: Flow Chart for Study

Note: Randomisation of phases: Group1 ($A_1B_1A_2B_2A_3$) and Group 2 ($A_1B_1B_2A_2A_3$)

3.12.2 Phase A_1: Baseline measurement and washout phase

Phase A_1 was the baseline measurement phase in which no intervention was included. This phase lasted one week with the aim to minimise the effects of previous interventions. One participant had been wearing a prescribed compression sleeve which she doffed for the washout phase A_1. None of the remaining participants were currently receiving lymphoedema

treatment. One baseline measurement assessment for each measurement outcome was carried out at the commencement of this phase. A short washout phase was preferred, due to the fact that lymphoedema is a chronic irreversible, progressive and distressing condition Foldi M, Foldi E (2012);Tandra et al., 2019a). Early intervention is imperative for the successful management of this condition (Grada et al., 2020, Lacomba et al., 2010). Any undue delay in the commencement of a treatment intervention may result in a faster progression in the severity of the stage of lymphoedema, which may reduce the efficacy of intervention (Stuiver MM et al., 2015).

Baseline measurements for the percentage tissue water content, using the Moisture Meter D®, for the trunk were taken and recorded on a measurement chart (Appendix 25). These measurements were recorded at the initial consultation during Phase A_1. To achieve consistency in subsequent measurements using the Moisture Meter D®, the following protocol applied:

- Participants were required to have a ten-minute acclimatisation rest period prior to the commencement of measurement.
- The participants were advised to not apply any cream to the area being measured.
- The participant was measured in a supine position, head supported with pillows and arms resting on the plinth in a neutral position. The participant's torso was covered with a towel to ensure privacy.
- Room temperature and participant positioning remained constant for each measurement procedure.
- The participant was undressed. No bra was worn for the application of the Moisture Meter D® to the trunk region. Privacy was ensured by having the window blinds closed and the treatment cubicle closed with a 'Do not disturb' sign clearly displayed. A gown was available for the participant to use. Only the researcher had access to the treatment area.

Circumferential tape measurements of the upper limb were taken to detect the presence of lymphoedema at the beginning of phase A_1, one week before the participants entered the initial treatment phase (phase B_1). The participants remained in the supine position following the Moisture Meter D® trunk measurements for the recording of the circumferential tape measurements. The measurements were recorded on a measurement chart (Appendix 24) during the initial consultation during phase A_1. The quality of life questionnaire (LYMQOL) (Appendix 11) was filled out once by each participant at the beginning of Phase A_1, during the initial consultation.

3.12.3 Phase B_1: Intervention measurement phase

Phase B_1 was the intervention phase, comprising the multimodal management plan. This period lasted two weeks and consisted of six treatment sessions, each lasting 75 minutes, on alternate days, excluding weekends. A shortened intensive treatment phase has proven to be effective in lymphoedema reduction and enhancing the quality of life in patients (Vignes et al., 2011; Yamamoto et al., 2008). Circumferential tape measurements of the upper limb, as well as the percentage tissue water content of the trunk using the Moisture Meter D®, were recorded on each participant's measurement chart at the commencement of each of the six individual treatment sessions over the two-week period during phase B_1. The interventions for the trunk included manual lymphatic drainage (MLD) (Tzani et al., 2018); low-level laser therapy (LLLT) (Baxter et al., 2018; Smoot et al., 2015); and Kinesio® tape application (See figure 3.4 (Gatt et al., 2017). Upper limb interventions consisted of MLD, LLLT, and 24-hour donning of multilayer compression bandaging (See figure 3.2) (Gebruers et al., 2017; Tzani et al., 2018). Skin care education, upper limb washing and multilayer compression bandage re-application were done following each consultation by the principal researcher. The incorrect application of multi-layer compression bandaging could exacerbate the lymphoedema or render the compression useless (Tzani et al., 2018). A prescribed daily home programme of upper limb and trunk exercises; a fifteen minute walking programme; skin care (Appendix 16) and deep breathing exercises were given to all participants (Appendix 17) (Armer et al., 2013; Gebruers et al., 2017b; Tzani et al., 2018). Participants were required to fill out a daily skin care and exercise compliance diary (Appendix 18). Immediately following this intervention phase, or once maximum reduction had been achieved and reached a plateau, each participant was fitted with a prescribed Class 2 compression garment, and a gauntlet or glove in the presence of hand or finger swelling.

The quality of life questionnaire (LYMQOL) was filled in twice at the research venue by each participant; at the commencement and again at the end of the intervention phase (B_1).

Figure 3.1
Individual components multilayer bandaging

Figure 3.2
Multilayer compression bandages

Participant consent was obtained to include this photograph

3.12.4 Phase A_2: Withdrawal measurement phase

All interventions were withdrawn for a one-week period following the initial multimodal management phase (Phase B_1) in the $A_1B_1A_2B_2A_3$ group. All intervention was withdrawn for a one-week period following the second measurement intervention phase (Phase B_2) in the $A_1B_1B_2A_2A_3$ group. The participants were required to continue with the home exercise programme and to wear a prescribed Class 2 compression garment during the day. The percentage tissue water content of the trunk (Moisture Meter D®), circumferential upper limb tape measurements, and quality of life (LYMQOL) were recorded on one occasion at the end of this phase and commencement of the next phase.

3.12.5 Phase B_2: Intervention measurement phase

Phase B_2 was the second intervention measurement phase comprising the multimodal management plan applied during Phase B_1. The same protocol and time frame as in phase B_1 was followed, with the exception of the application of multilayer compression bandaging to the upper limb. The rationale behind the exclusion of the multilayer compression bandaging was based on the reduction of the participants' limb volumes and these reductions having reached a plateau. Furthermore, the participants were wearing the prescribed compression garments (See Figure 3.3) daily, which served the same purpose as the multilayer compression bandaging.

Figure 3.3

Class 2 Compression sleeve in situ

Participant consent was obtained to include this photograph

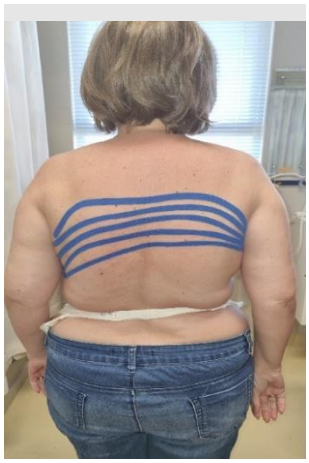


Figure 3.4

Kinesio® tape on trunk during intervention

Participant consent was obtained to include this photograph

3.12.6 Phase A_3: Washout and follow-up phase

Phase A_3 was the final four-week follow-up phase. This phase followed intervention phase B_2 in the $A_1B_1A_2B_2A_3$ group and intervention phase A_2 in the $A_1B_1B_2A_2A_3$ group. All intervention was withdrawn during this phase. The participant was required to continue with the prescribed home exercise programme (Appendix 17) and to wear the prescribed pressure garment during the day, as well maintain a compliance diary. At the end of this phase, final outcome measurements were recorded on each participant's chart. The final measurements included the percentage tissue water content of the trunk (Moisture Meter D©), circumferential tape measurements of the upper limb, and the LYMQOL questionnaire. In addition, the participants completed a hard copy exit questionnaire (Appendix 15) at the end of this phase.

3.13 Exit Questionnaire

The questionnaire (Appendix15) was developed by the researcher and required each participant to confirm that treatment had been received, as well as to confirm their compliance with the prescribed exercise programme, skin care and application of the compression garment. The participants completed a hard copy of the exit questionnaire at the final measurement appointment.

3.14 Data Management

Each participant was assigned a study-specific code which was linked to the research project code. Access to the data computer was restricted and the computer was password protected. A daily data backup was performed and stored on a password-protected external hard drive which was locked away in a safe at a different venue. The computer was stored in a secure location when not in use. Respondent-specific information, such as signed consent forms and data collection, was coded, marked and stored in a file in a locked cabinet. The researcher captured the information on a study-specific excel spreadsheet. A separate spreadsheet for each major outcome was created for data management purposes. All the study data will be kept and stored in a safe at the PI's domicile for at least five years as per SU guidelines. A copy of this data will be submitted to the Physiotherapy Department for safe-keeping and record purposes for five years following the completion of this study.

3.15 Data Analysis

The program RStudio version 1.4.1717 was used to perform all data analyses. The principal investigator was in consultation with a biostatistician (Dr Merga Feyasa) from the Division of Epidemiology and Biostatistics SU, to assist with the statistical analysis and interpretation of results where needed. A p-value of $p \leq 0.05$ was considered significant, and 95% confidence intervals (CI) were reported. Clinical significance was established using MDC values.

Participant-specific and group results were analysed. Demographic information was analysed descriptively and presented in tables. Individual results for upper limb volume, percentage trunk tissue water content and quality of life were analysed descriptively using measurements of central tendency (means and standard errors). The upper limb volume (derived from circumferential tape measurements using the truncated cone formula) was compared between each phase. Statistical significance and the minimum detectable change (MDC) were used to report on upper limb volume outcomes. The smallest real difference representing a clinically meaningful change in limb volume for the participants was considered 3.5% (Devoogdt et al., 2010).The differences in upper limb volume were calculated, based on the participant's initial volume at baseline and between the study intervention phases. The group limb volume results were determined using statistical analysis represented by a p-value.

The percentage tissue water content of the trunk for the group were compared between each phase using paired t-test. For the trunk, percentage tissue water content results were reported in three respective areas, namely chest, axilla and back. The minimum detectable change (MDC) representing a clinically meaningful change is between 5.3% and 8.0% (Mayrovitz et

al., 2019). The differences in percentage tissue water content of each region of the trunk were calculated based on the participant's initial percentage tissue water content at baseline and between the study intervention phases.

Overall quality of life was measured using the LYMQOL questionnaire. The overall quality of life score was obtained separately from each domain using a verbal method of scoring on a scale of 1 to 10. An improvement in the overall quality of life is demonstrated with an increasing score (maximum score 10). The minimum detectable change indicating a clinically meaningful change is 1.96 points (Monticone et al., 2021).
For each participant, the quality of life scores for each individual were compared between every intervention session using MDC values. Quality of life and the function domain for each individual and for the group was compared between each phase: namely A_1, phase B_1, phase B_2, phase A_2, phase B_2 and phase A_3.
Function was measured by extracting the values for the function domain from the LYMQOL questionnaire. A decrease in score represented an improvement in the function domain. A minimal detectable change of 0.64 points represents a clinically meaningful change in the function domain (Monticone et al., 2021).

For the group results for the outcomes of quality of life, percentage tissue water content and limb volume, a paired t-test was applied to establish differences between baseline and post-intervention phases, as the data was normally distributed. Individual results were determined using MDC values.

3.16 Ethical Considerations

Ethical approval for this study was obtained from Stellenbosch University Health Research Ethics Committee (SU HREC) (S20/11/329).
The rights of the participants were observed at all times during this study. Prior to the commencement of the study, each participant was informed that their voluntary participation would exclude any pressure or coercion by the researcher. The right to opt in or out of the study could be exercised at any given time with no negative consequences or repercussions. All the study participants were provided with informed consent and were required to provide written consent once the procedures, benefits and risks of the study had been presented verbally and in writing. The participants were offered an opportunity to ask questions to ensure their full understanding of the study. The name of the institution, department and supervisors were provided in the event

that additional information was required by the participant. The participants were assured of confidentiality and their right to privacy. The treatment area was private, with only the researcher having access, and the participant was always covered with a towel. All respondent-specific information, as well as all the outcome measurements, were anonymised and coded and stored on a password-protected device; and a backup disc and signed forms were stored at a separate location in a locked safe.

The participants were informed of the purpose and benefits, as well as any potential social, psychological or physical risks, related to their participation in the study. Insurance was granted through Stellenbosch University (Appendix 14) in the event that participants required assistance and referral to specialists due to any potential risks occurring during the study.

The participants gave signed, informed consent for the use of photographs for the purpose of this study, with the understanding that all photographs would exclude the face or distinguishing characteristics of the participant.

Chapter 4: Results

The following chapter introduces the five participants and details the initial findings regarding their characteristics and the medical management of their breast cancer. The results of this study are discussed systematically and provide information on the effects of the multimodal management plan for lymphoedema, using predetermined outcome measurements. Upper limb volumes are presented first (circumferential tape measurements converted to a limb volume score using a limb volume calculator). Trunk percentage tissue water content measurements are then presented. The trunk measurements include three regions (chest, axilla and back). A presentation of the function outcome then follows. The final outcome measurement presented is the quality of life (LYMQOL questionnaire).

4.1 Participant Characteristics

This section contains a brief description of each of the five study participants, as well as their history of breast cancer and stage of lymphoedema at initial assessment. Further information on the study participants can be found in Table 4.1.

Participant 01 was a 49-year-old female who was diagnosed with Stage 3 right breast cancer at the age of 44 (Refer to Table 4.1). She underwent breast-conserving surgery and a sentinel lymph node biopsy (13 nodes removed), followed by a mastectomy one week later. On initial assessment, Stage 1 lymphoedema of the upper limb and Stage 2 of the trunk was detected. See Table 4.2 for the baseline limb volume and trunk percentage tissue water measurements, compared to the contralateral regions.

Participant 02 was a 47-year-old female who was diagnosed with Stage 2 left breast cancer at the age of 46 (Refer to Table 4.1). She underwent a mastectomy and axillary lymph node dissection (seven nodes removed). She presented with Stage 1 lymphoedema of the upper limb and Stage 2 trunk lymphoedema on her initial assessment. See Table 4.2 for the baseline limb volume and trunk percentage tissue water measurements, compared to the contralateral regions.

Participant 03 was a 58-year-old female who was diagnosed with Stage 3c right breast cancer at the age of 56 (Refer to Table 4.1). She underwent a mastectomy and axillary lymph node dissection in which 15 lymph nodes were removed. Stage 0 lymphoedema of her upper limb and Stage 2 trunk lymphoedema were detected on initial assessment. See Table 4.2 for the baseline limb volume and trunk percentage tissue water measurements, compared to the contralateral regions.

Participant 04 was a 64-year-old female who was diagnosed with Stage 2a left breast cancer at the age of 59 (Refer to Table 4.1). She underwent a mastectomy and complete axillary lymph node dissection (all nodes were removed). On initial assessment she presented with Stage 0 upper limb and Stage 2 trunk lymphoedema. See Table 4.2 for the baseline limb volume and percentage trunk tissue water measurements, compared to the contralateral regions.

Participant 05 was a 60-year-old female who was diagnosed with Stage 2a right breast cancer at the age of 53 (Refer to Table 4.1). She underwent breast-conserving surgery and a sentinel lymph node biopsy with the removal of six axillary nodes. Stage 0 upper limb and Stage 2 trunk lymphoedema were detected at the initial assessment. See Table 4.2 for the baseline limb volume and trunk percentage tissue water measurements, compared to the contralateral regions.

Table 4.1: Participant Descriptions

PARTICIPANT	01	02	03	04	05
RACE	White	White	White	White	Indian
AGE	49	47	58	64	60
DOMINANT SIDE	Right	Right	Left	Right	Right
MARITAL STATUS	Married	Married	Married	Married	Married
OCCUPATION	Bookkeeper	Nail Technician	Retired school - teacher	Retired Bank Manager	Housewife
AFFECTED BREAST	Right	Left	Right	Left	Right
AGE AT DIAGNOSIS	44	46	56	59	53
SURGERY	Mastectomy	Mastectomy	Mastectomy	Mastectomy	Lumpectomy
CHEMOTHERAPY	Adjuvant	Adjuvant	Adjuvant	Adjuvant	Adjuvant
RADIATION	Adjuvant	Adjuvant	Adjuvant	Adjuvant	Adjuvant
ENDOCRINE THERAPY	Herseptin	Herseptin	Herseptin	Herseptin	Tamoxifen
CELLULITIS EPISODES	3	3	2	None	3
BMI (kg/m^2)	29.7	29.9	28.7	25	24.3

Table 4.2 Upper Limb volume difference and percentage tissue water content of the trunk at Initial assessment.

PARTICIPANT	UPPER LIMB VOLUME DIFFERENCE#	BACK ^ Difference in % tissue water content	AXILLA^ Difference in % tissue water content	CHEST^ Difference in % tissue water content
01	10.6%	15.5%	26.1%	19.5%
02	12.4%	10.3%	2.9%	15.5%
03	6%	16.3%	20.4%	21.7%
04	7%	9.5%	18.7%	5.7%
05	9%	18.1%	16.6%	14.6%

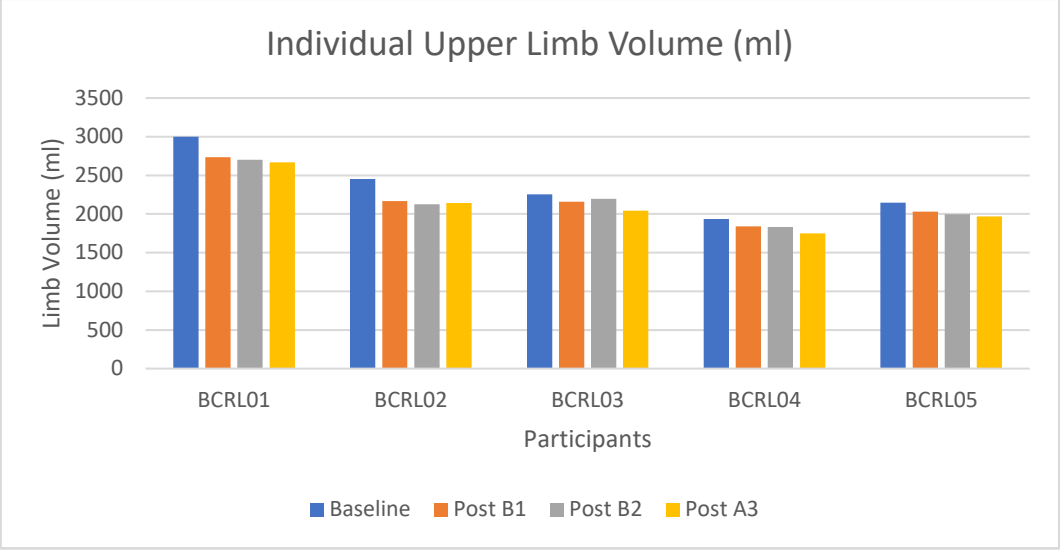
 # represented as a percentage difference^ baseline percentage tissue water content difference represented as a percentage/

4.2 Upper Limb Volume

4.2.1 Upper Limb Volume: Results for Individual Participants

Each participant was subjected to a randomized sequence. Refer to Table 3.1

All five participants demonstrated a decrease in upper limb volume, individually, across the phases, denoting a positive outcome and reduction in lymphoedema (see Figure 4.2). Participant 01 demonstrated a clinically meaningful reduction in limb volume of 8.8% from phase A_1 to post phase B_1; 1.2% from phase B_1 to post phase B_2; 1.1% from phase B_2 to post phase A_3; and overall, a clinically meaningful reduction of 11.1% from baseline phase to post phase A_3. Participant 02 experienced a clinically meaningful reduction in limb volume from baseline to post phase B_1 of 11.5%; B_1 to post phase B_2 of 1.9%; and 0.7% from B_1 to post B_2 phase. A clinically meaningful overall reduction of 12.6% was found from baseline to phase A_3,. Participant 03 experienced a clinically meaningful reduction in upper limb volume from baseline to post phase B_1 of 4.3%; from phase B_1 to post phase B_2 of 1.8%; and a clinically meaningful reduction from phase B_2 to post phase A_3 of 6.7%. A clinically meaningful overall reduction of 9.2% was noted from baseline to post phase A_3. Participant 04 presented with a clinically meaningful reduction in upper limb volume from baseline to phase B_1 of 5.0%; an increase of 0.5% from phase B_1 to post phase B_2; and a clinically meaningful reduction of 4.4% from phase B_2 to post phase A_3. A clinically meaningful overall reduction of 9.7% was noted from baseline to post phase A_3. Participant 05 experienced a clinically meaningful reduction in limb volume of 5.5% from baseline to post phase B_1; A clinically meaningful reduction of 4.4% and 8.3% was noted for phase B_2 to post phase A_3; and overall from baseline to post phase A_3, respectively.



BCRL 01=participant 01, BCRL 02=participant 02, BCRL 03=participant 03, BCRL 04=participant 04, BCRL 05=participant 05

Figure 4.1: Individual Upper Limb Volume Scores (ml)

4.2.2 Upper Limb Volume: Group Results

Similar to the individual results, the whole group demonstrated a trend of decreasing upper limb volumes across the phases from baseline to post phase A_3, with a statistically significant finding and p-value of p=0.001, mean of 243.4 and 95% CI [155,331]. Clinically meaningful mean volume reductions, of 7.02% (baseline to post phase B_1), and 10.2% (baseline to post phase A_3), were measured for the group as a whole (Figure 4.2).

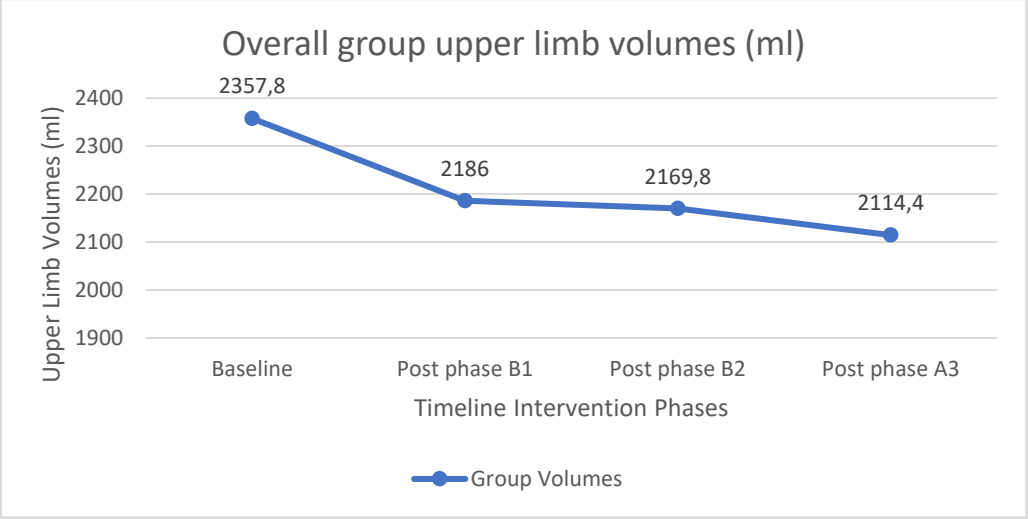


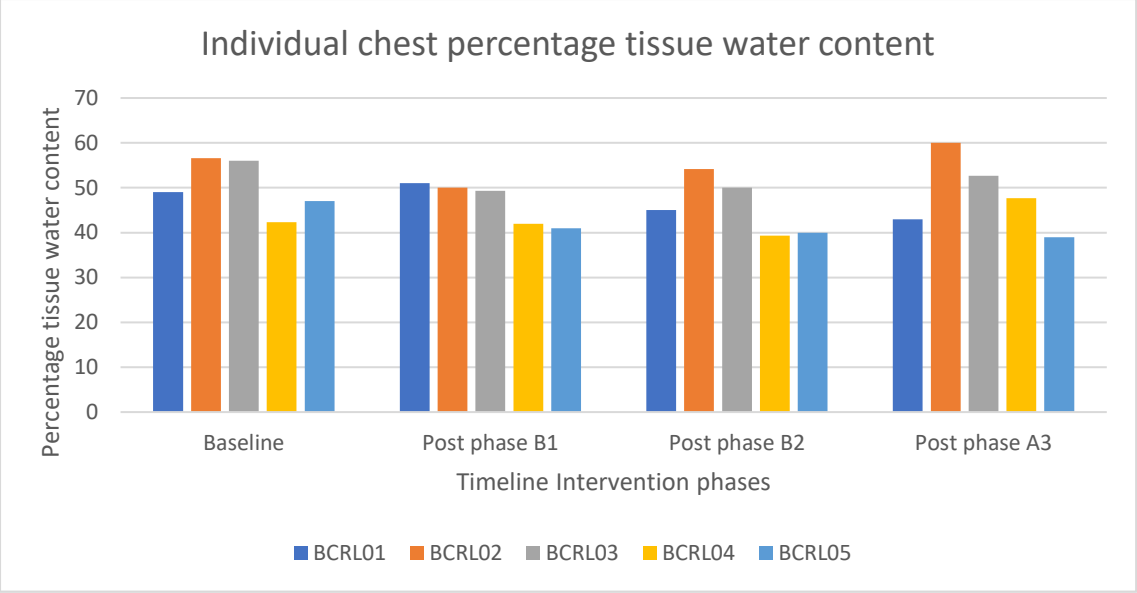
Figure 4.2: Group Upper Limb Volume Scores (ml)

4.3 Percentage Trunk Tissue Water Content

4.4 Percentage Chest Tissue Water Content

4.4.1 Percentage Chest Tissue Water Content: Results for Individual Participants

A clinically meaningful decrease in tissue water content of 11.7% and 12.1% was found for participant 01 from phase B_1 to post phase B_2 and from baseline to post phase A_3, respectively. A non-clinically meaningful reduction of 4.4% was noted from phase B_2 and post phase A_3 for this participant, as well as an increase of 4% from baseline to post phase B_1. Participant 02 demonstrated a clinically meaningful decrease in tissue water content of 11.6% from baseline to post phase B_1 and a clinically meaningful increase of 8.4%, 10.7% and 7.5% between the phases B_1 to B_2, B_2 to A_3 and from baseline to post phase A_3, respectively. Participant 03 experienced a clinically meaningful reduction in tissue water content from baseline to post phase B_1 of 11.9% and a clinically non-meaningful reduction of 5.1% from baseline to post phase A_3. Increases of 1.4% and 5.4% were noted for participant 03 from phase B_1 to B_2 and phase B_2 to post phase A_3. Participant 04 experienced a clinically meaningful reduction of 6.4% from phase B_1 to post phase B_2 and a clinically meaningful increase of 21.3% from phase B_2 to post phase A_3, as well as a clinically meaningful increase of 12.8% from baseline to post phase A_3. An increase of 0.7% was found between the baseline and post phase B_1. Participant 05 was the only participant to experience a reduction of tissue water content of the chest across all the study phases. Clinically meaningful reductions of 12.7% and 7.8% were found from baseline to post phase B_1 and baseline to post phase A_3, respectively. Non-clinically meaningful reductions of 2.4% and 2.5% were noted between baseline and post phase B_2 and phase B_2 to post A_3, respectively, for Participant 05.



BCRL 01=participant 01, BCRL 02=participant 02, BCRL 03=participant 03, BCRL 04=participant 04, BCRL 05=participant 05

Figure 4.3: Individual Chest Percentage Tissue Water Content

4.4.2 Percentage Chest Tissue Water Content: Group Results

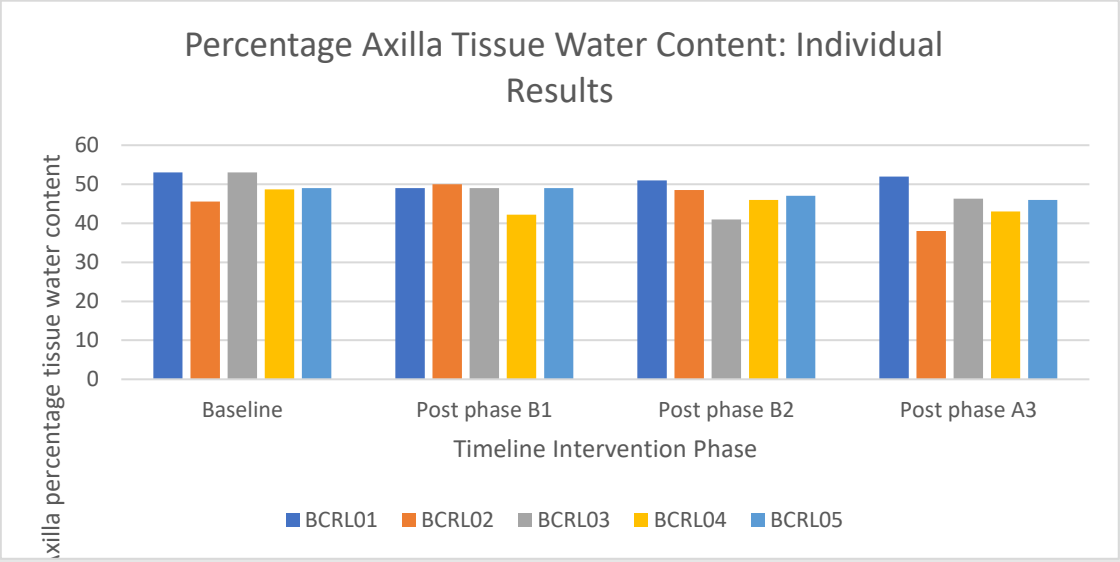
The whole group demonstrated a statistically significant decrease in percentage tissue water content from baseline to post Phase B_2 (p=0.006) mean 4.48 with a 95% CI [2.04,6.91]. A clinically meaningful mean decrease of 6.58% from baseline to post phase B_1, and 10.7% from B_1 to post phase B_2 was measured for the whole group. A clinically meaningful mean increase of 6.1% in the percentage tissue water content for the chest area from phase B_2 to post phase A_3 was detected. As a whole, the group demonstrated a non-clinically meaningful mean decrease in percentage tissue water content of 3.3% from baseline to post phase A_3 (Appendix 19).

4.5 Percentage Axilla Tissue Water Content

4.5.1 Percentage Axilla Tissue Water Content: Results for Individual Participants:

All the participants demonstrated a clinically meaningful decrease in the percentage tissue water content scores, and thus lymphoedema, in the axilla region from baseline to post phase A_3, with the exception of participant 01. Participant 01 demonstrated a clinically meaningful reduction of 7.5% from baseline to post phase B_1 and a non-clinically meaningful decrease in percentage tissue water content of 1.5% from baseline to post phase A_3. Clinically meaningful decreases of 23% and 16.6% and were demonstrated by participant 02 from phase B_2 to post

phase A_3 and from baseline to post phase A_3, respectively. This participant experienced a clinically meaningful increase of 9.6% in tissue water content from baseline to post phase B_1. Participant 03 demonstrated clinically meaningful reduction in percentage tissue water content of the axilla of 7.5%, 15% and 12.6% from phase baseline to post phase B_1, B_1 to post phase B_2 and baseline to post phase A_3 respectively. A clinically meaningful increase in tissue water content of 12.9% was noted from phase B_2 to post phase A_3 for this participant. Participant 04 demonstrated clinically meaningful reductions of 13.5%, 6.5% and 11.7% from baseline to post phase B_1, B_2 to post phase A_3 and baseline to post phase A_3, respectively. A clinically meaningful increase of 9% was noted for this participant, from phase B_1 to post phase B_2. Participant 05 demonstrated a clinically meaningful reduction of 6.1% from baseline to post phase A_3; and a non-clinically meaningful decrease of 4% and 2% from phase B_1 to post phase B_2 and from phase B_2 to post phase A_3, respectively. No change was noted from baseline to post phase B_1 for participant 05.



BCRL 01=participant 01, BCRL 02=participant 02, BCRL 03=participant 03, BCRL 04=participant 04, BCRL 05=participant 05

Figure 4.4: Percentage Axilla Tissue Water Content: Individual Results

4.5.2 Percentage Axilla Tissue Water Content: Group Results

The whole group demonstrated a statistically significant reduction in the percentage tissue water content of the axilla from baseline to post phase A_3 with a p-value =0.01, mean of 4.8 and 95% CI [1.4,8.1]. A clinically meaningful mean reduction of 9.7% for the whole group was measured between baseline and post phase A_3. This was followed by 3.78% (baseline to B_1), 3.32% (phase B_2 to A_3) and 1.84% (phase B_1 to B2), which were all non-meaningful results (Appendix 20).

4.6 Percentage Back Tissue Water Content

4.6.1 Percentage Back Tissue Water Content: Results for Individual Participants

Participants 01, 03, 04 and 05 each demonstrated an increase in percentage tissue water content for the back of 1.9%, 5.8% (clinically meaningful), 2.1% and 0.2%, respectively; thus, an increase in lymphoedema from baseline to post phase A_3. A decrease in tissue water content of 3.1% from baseline to post phase A_3, which was not clinically meaningful, was demonstrated by Participant 02. Participant 05 demonstrated a clinically meaningful decrease in tissue water content of 7.6% from baseline to phase B_1 and a non-clinically meaningful decrease in tissue water content of 4.1% from phase B_1 to B_2. A clinically meaningful increase in tissue water content of 11.9% from phase B_2 to post phase A_3 was measured for participant 05 (Appendix 22).

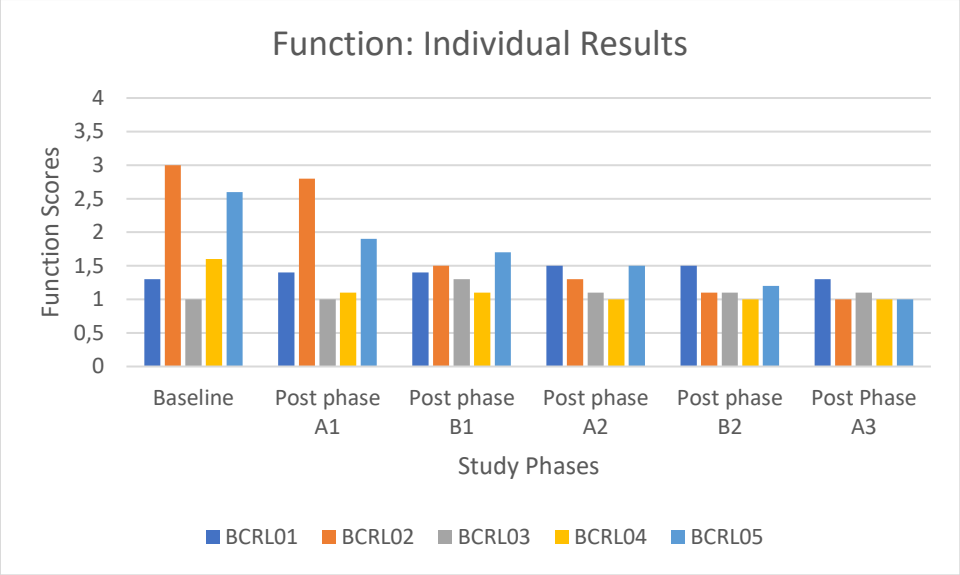
4.6.2 Percentage Back Tissue Water Content: Group Results

The whole group demonstrated a mean increase in the percentage tissue water content of 3.3% (clinically non-meaningful) and 17.9% (clinically meaningful) from phase B_1 to phase B_2 and phase B_2 to post phase A_3, respectively. A total clinically meaningful increase of 6.9% from baseline to post phase A_3 for the back was found, which indicated an overall increase in lymphoedema in this region of the trunk (Appendix 21).

4.7 Function

4.7.1 Function: Results for Individual Participants

Clinically meaningful improvements of 2.0 points and 1.6 points (representing a decreasing score) in the function domain from baseline to post phase A_3 were measured for participants 02 and 05, respectively. A clinically meaningful decrease of 1.5 points was found for participant 02 from baseline to post phase B_1. Participant 01 had no change in the function score from baseline to post phase A_3. Participant 03 demonstrated an increased score of 0.1 and a decline in function (not clinically meaningful) when comparing baseline to post phase A_3. Participant 04 had an improved score of 0.6 points in function from baseline to post A_3, but this was not clinically meaningful (Figure 4.5).



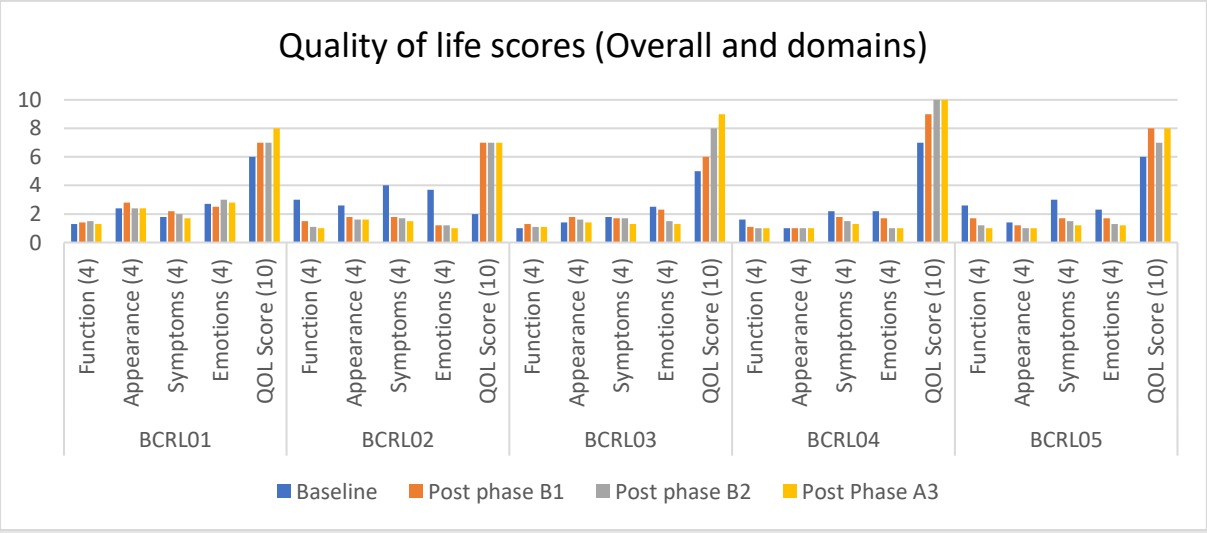
BCRL 01=participant 01, BCRL 02=participant 02, BCRL 03=participant 03, BCRL 04=participant 04, BCRL 05=participant 05

Figure 4.5: Function Scores: Individual Results

4.7.2 Function: Group Results

As a whole, the group demonstrated a clinically meaningful mean improvement of 0.82 points for function across the study phases from baseline to post phase A_3. A non-clinically meaningful mean improvement in function of 0.54 points was demonstrated from baseline to post phase B_1 for the group as a whole.

4.8 Quality of Life



BCRL 01=participant 01, BCRL 02=participant 02, BCRL 03=participant 03, BCRL 04=participant 04, BCRL 05=participant 05

Figure 4.6: Quality of Life and Domain Scores

4.8.1 Quality of Life: Results for Individual Participants

A clinically meaningful improvement in quality of life was measured for each participant from baseline to post phase A_3 (Figure 4.6). An improvement in scores of 2, 5, 4, 3 and 2 points were found for participants 01, 02, 03, 04 and 05, respectively. A clinically meaningful improvement in quality of life of 5, 2 and 2 points from baseline to post phase B_1 was demonstrated by participants 02, 04 and 05, respectively. A clinically meaningful improvement in quality of life of 2 points from phase B_1 to post phase B_2 was found for participant 03.

Table 4.4: Inter-phase Quality of Life Scores (out of 10)

The quality of life scores for each individual participant were recorded after each study phase followed by the change in these scores between each study phase. (Refer to Table 4.4)

Participant	Baseline	Post phase B1	Changes B-B1	Post phase B2	Changes B1-B2	Post phase A3	Changes B2-A3	Changes B-A3
01	6	7	1	7	same	8	1	2*
02	2	7	5*	7	same	7	same	5*
03	5	6	1	8	2*	9	1	4*
04	7	9	2*	10	1	10	Same	3*
05	6	8	2*	7	-1	8	1	2*

*B=baseline/ *clinically meaningful (minimal detectable change=1.96 points)*

4.8.2 Quality of Life: Group Results

A statistically significant finding (p=0.005) and 95% CI [4.8,1.5] . was demonstrated in the mean overall quality of life scores for all the study participants across the study phases, from baseline to post phase A_3. All the participants demonstrated a statistically significant improvement in the overall quality of life scores from baseline to post intervention phase B_1 (p=0.04), from baseline to post intervention phase B_2 (p=0.02), and from baseline to post phase A_3 (p=0.005) (Appendix 23).

Chapter 5: Discussion

This study sought to describe the effect of a multimodal management plan on upper limb and trunk breast cancer-related lymphoedema, function and quality of life in breast cancer survivors. This condition has a multi-faceted presentation. Therefore, numerous outcome measurements were adopted to achieve the objectives of this study. The study provided additional insight into the relationship between upper limb and trunk lymphoedema, function and quality of life in five female breast cancer survivors.

5.1 Study population

A comparison of participant characteristics was made between the current study and a study conducted by Vignes et al. (2013) in France. Although a few of the participant characteristics were similar, the participant characteristics for the two study populations differed. A comparison between the current study and the 2013 study by Vignes et al. was made due to the similarity in the multimodal management and the number of treatments that were administered. Twelve treatments were administered in the current study and eleven in the study conducted by Vignes et al. in 2013. Although the participant demographics differed, upper limb volume reduction was experienced by the participants in both studies. The sample population in the current study consisted of five female participants aged between 47 and 64 years, with a median age of 58 years. The study conducted by Vignes et al. (2013) in France included female patients with BCRL with a median age of 64 years. The participants in the current study were diagnosed with BC ranging from Stage 2 to Stage 3a; with time from diagnosis of lymphoedema ranging from one to six years, with a median of five years post diagnosis. Vignes et al. (2013) reported a median of two years and four months post lymphoedema diagnosis. In the present study, four of the five participants (80%) had undergone a mastectomy and one had breast-conserving surgery. Vignes et al. reported that 42% of participants in their study had undergone mastectomy surgery. All the participants in the current study underwent axillary lymph node dissection (ALND), with between six and all lymph nodes dissected. The study conducted by Vignes et al. (2013) matched this, as 100% of the participants had undergone ALND. They presented with either Stage 0 or Stage 1 upper limb, and Stage 2 trunk, lymphoedema, two on the dominant side and three on the non-dominant side.

Three participants in this study were retired, while the remaining two had returned to work following the surgical, radiation and chemotherapy interventions. All the participants in the current study had received endocrine therapy, whilst 54% of the participants in Vignes et al. (2013) study had received endocrine therapy. The median body mass index in the current

study was 28.7kg/m^2, compared to 27.4kg/m^2 in the Vignes (2013) study. Despite the lack of similarity between each study's participants, the results from the study by Vignes et al supported the findings of the current study which demonstrated a reduction in upper limb volume following multimodal intervention by trained certified lymphoedema therapists.

5.2 Main findings

5.2.1 Upper Limb Volume

The whole group demonstrated a statistically significant reduction (p=0.001) in upper limb volumes across the study phases, which was maintained at phase A3, four weeks after the final treatment phase (B_2). The presentation of early-stage non-fibrotic upper limb lymphoedema which was established with the pitting test (stage 0 and stage 1) in all the participants may have contributed to the positive response to the multimodal management plan. Multimodal management in the early stage of BCRL has been shown to reduce the risk of the development of fibrotic lymphoedema and to be effective in limb volume reduction (Gençay Can et al., 2019). It is suggested that the central truncal clearance applied in this study as a precursor to upper limb MLD may have contributed to this significant upper limb volume reduction (Mayrovitz et al., 2009). This outcome is supported in the literature, which states that central lymph vessel clearance promotes lymphatic flow from distal to proximal due to increased peristalsis of the lymphatic vessels (Mayrovitz et al., 2009).

The combination of the multimodal management plan interventions, including MLD, may have played a pivotal role in the positive outcome of upper limb volume reduction. Two separate systematic reviews conducted by Ezzo et al., in 2015, and Thompson et al., in 2021, as well as a study conducted by Huang et al. (2013), reported that MLD alone is not effective in reducing lymphoedema, but may be effective in combination with the multimodal management plan. This conclusion is as a result of a lack of high quality studies, the variety of study designs, lack of control groups and conflicting results between the studies (Thompson et al., 2021).

In the current study, as part of the multimodal management plan, MLD was administered in conjunction with multilayer compression bandaging during the first two-week intervention phase (B_1). The application of the compression bandaging following the MLD reduces ultrafiltration of lymphatic fluid into the interstitium, which could have contributed to the statistically significant results that were found. The literature supports the fact that multilayer compression bandaging is more effective in reducing limb volumes during the initial intensive treatment than a compression garment (Badger et al., 2000, King et al., 2012). MLD is utilised to empty functional lymph nodes, to reduce tissue and lymph fluid fibrosis, and to facilitate the

uptake of lymphatic fluid into the lymphatic vessels. Compression therapy (both multilayer bandaging and compression garments) reduces the ultrafiltration of lymphatic fluid into the interstitium and enhances the muscle pump effect, thereby promoting the uptake of lymphatic fluid into the lymphatic system and enhancing the effects of the MLD (Dayes et al., 2013). Therefore, the literature supports the results of this study, in which a statistically significant upper limb volume reduction was achieved following the application of multilayer compression bandaging and MLD during the initial two-week intervention phase.

In the current study, once optimal reduction had been achieved during the initial two-week intervention phase, the multilayer bandages were replaced by a prescribed Class 2 compression sleeve which the participants had to wear during the day for the duration of the second two-week intervention phase (B_2) and phase A_3. The application of compression garments following multilayer compression bandaging facilitates the maintenance of the initial volume reduction achieved during the intensive phase of intervention (Badger et al., 2000). The treatment approach used in the current study is based on clinical practice guidelines that recommend the use of compression bandages during the initial lymphoedema reduction phase and a compression garment once optimal reduction has been achieved. (Damstra & Halk, 2017). This may have contributed to the overall upper limb volume reduction and maintenance achieved for the participants in this study.

All the participants reported compliance with the prescribed exercise programme in their compliance diaries and this may have contributed to the overall reduction in upper limb volume. This is in agreement with the literature which reports that exercise has a positive effect in reducing BCRL (Reike et al., 2018). The upper limb exercise component may have resulted in an efficient muscle pumping action surrounding the lymphatic architecture, resulting in improved transportation of lymphatic fluid through the lymphatic system (Ridner, 2013).

The application of LLLT was used as part of the multimodal management plan for the upper limb lymph nodes and vessels in the oedematous regions. This may also have contributed to the reduced volume of the limb as the LLLT may have stimulated a more efficient transportation of the lymphatic fluid within the lymphatic system. The use of LLLT as part of a multimodal intervention plan is supported by findings in the literature that LLLT stimulates lymphangiogenesis and lymph motricity, thereby facilitating movement of the lymphatic fluid through the lymphatic vessels and nodes. (Kaviani et al., 2006; Kozanoglu et al., 2009).

5.2.2 Trunk Lymphoedema

The percentage tissue water content was measured in three separate regions of the trunk: namely, the back, chest and axilla regions. A mean increase in tissue water content of 3.58% was found for the whole group in the ipsilateral back region from the baseline to post phase A3, a total of ten weeks post baseline. For this study population, the back region presented with the lowest total baseline percentage tissue water content but was the only assessed area with an increase in tissue water content for the group as a whole, from baseline to post phase A_3 (Bozkurt et al., 2017). This unexpected finding could be due to backflow of lymphatic fluid from the affected limb, axilla and chest to the upper ipsilateral back region. This rationale is supported in the literature by Suami et al. (2018), who identified the concept of dermal backflow in the presence of a disrupted and dysfunctional lymphatic system in breast cancer patients who had undergone axillary lymph node dissection (Suami et al., 2019; Suami & Scaglioni, 2018).

A further contributing factor to the increased tissue water content in the back region could be that the entire posterior thoracic wall and scapular region drain into a single group of ipsilateral subscapular lymph nodes (Kyriacou & Khan, 2020; Suami & Scaglioni, 2018). This may have further influenced the increased back tissue water content in the presence of an already compromised lymphatic system. In addition, it is possible that the use of ill-fitting and incorrect, non-prescribed bras, unsuitable for post-breast cancer surgery, may have resulted in a tourniquet effect near the subscapular nodes, creating focussed compression in this area, and contributing to the localised dermal backflow. This concept of a localised tourniquet effect contributing to the risk of the development of lymphoedema in any area of the body is supported in the literature (Asdourian et al., 2016).

The location and architecture of the back region may have made it challenging for self-management using manual lymphatic drainage, Kinesio® tape and compression of this region, all of which are considered pivotal interventions in managing BCRL during the maintenance phase (Gatt et al., 2017; Mayrovitz, 2009; Mayrovitz et al., 2009). Participants 01 and 03 were diagnosed with Stage 3 breast cancer and both underwent mastectomy surgery with the dissection of 13 and 15 axillary nodes, respectively. The stage of disease, as well as the excessive lymph node removal, could explain why a marked increase in tissue water content in the back region was observed in these participants. There is evidence to suggest that the combination of mastectomy surgery and dissection of at least 50% of axillary lymph nodes may increase the tissue water content, as extensive lymph node dissection has been identified as a risk factor for a dysfunctional lymphatic system (Kilbreath et al., 2016).

Participant 05 experienced the biggest increase in back tissue water content from phase B_2 to post phase A_3. This could be attributed to the fact that she had the longest time (seven years) in the study population since her breast conserving surgery. This, in combination with stage 2 trunk lymphoedema, may have resulted in increased fibrosis in her back region, which may have had a limited response to the self-maintenance phase of four weeks in which no physiotherapy intervention was given. The literature has identified that fibrosis and adipose tissue respond poorly to the multimodal management plan (Vignes et al., 2006), and that self-management of the trunk, including the application of Kinesio® tape, self MLD and compression, present a challenge (Vignes et al., 2007). Participant 05 also achieved the highest total reduction in the study population in tissue water content of the back between the preceding two phases A_1-B_1 (7.6%) and B_1-B_2 (4.1%). This marked reduction in back tissue water content may be as a result of the intensive multimodal management that was administered by the therapist during these phases. According to a systematic review conducted by Lasinski (2012), complete decongestive therapy, which includes MLD; compression therapy; deep breathing exercise; skin care and exercise is effective in managing the various stages of BCRL (Lasinski et al., 2012). The less invasive breast-conserving surgery the patient underwent, as well as having the fewest axillary nodes dissected of all the participants in the study group, may also have played a role in this outcome (Kilbreath et al., 2016).

The sole participant to achieve a reduction in back tissue water content from baseline to post phase A_3 was participant 02, the youngest participant at age 47. This finding is in contrast to the literature which reports that patients under the age of 55 years present with a two-fold risk of BCRL development of the upper limb (Meeske et al., 2009). No mention is made of the risk of trunk lymphoedema in this study. Participant 02 had the shortest time from breast cancer surgery (one year) in the current study and presented with less fibrosis, which may have affected her positive response to the multimodal management plan (Gençay Can et al., 2019). A clinical trial conducted by Lacomba et al. in 2010 revealed that early multimodal intervention, up to a year post surgery, could prevent the development of secondary lymphoedema following surgery (Lacomba et al., 2010), which supports the findings in the current study.

In contrast to the back region, each participant and the group as a whole experienced a reduction in percentage tissue water content of the axilla region. The axilla region had the highest baseline presentation of percentage tissue water content, but also the highest total reduction of percentage tissue water content in the trunk from baseline to post phase A_3. The axilla region drains directly into the nearby ipsilateral axilla and clavicular lymph nodes (Kyriacou & Khan, 2020). This proximity, as well as the absence of soft tissue fibrosis in the

axilla, could have resulted in the improved drainage of the axilla region (Gençay Can et al., 2019).

It is interesting to note that participants 02 and 03, who were randomly allocated to the study phase sequence of $A_1B_1B_2A_2A_3$, achieved the highest reduction in the axilla region from baseline to post A_3 of 16.6% and 12.6%, respectively. The four consecutive weeks of application of the multimodal management plan may have contributed to this reduction of tissue water content. The main aim of the initial intensive phase of physiotherapy intervention is lymphoedema reduction. The benefit to the patient is that the treatment and bandaging are administered frequently by a trained therapist, resulting in the correct technique and 24-hour compression therapy. The multilayer bandaging enhances lymphatic drainage and reduces ultrafiltration, mobilises the lymphatic fluid and reduces fibrosis (Yüksel et al., 2016). This statement is supported by the findings in the literature, that a multimodal management plan administered frequently during the initial or intensive treatment phase is more effective than infrequent or erratic intervention for BCRL (Damstra et al., 2017). A systematic review of the evidence for CDT reported that the greatest initial reduction of limb volume takes place in the first five consecutive days of the initial intensive multimodal management (Lasinski et al., 2012).

The highest reduction of percentage tissue water content of the axilla was recorded for participant 02. This reduction may be due to this participant's low baseline percentage tissue water content of the axilla and early stage 1 lymphoedema, where fibrosis and adipose tissue are absent (this was established using the pitting oedema test). Findings in the literature show that early stage BCRL responds well to the multimodal management plan and support the findings of the current study (Gençay Can et al., 2019; Stout Gergich et al., 2008).

Participant 01 presented with the highest baseline water content difference between the axilla and the unaffected side, yet experienced the lowest percentage tissue water content reduction from baseline to post the four-week maintenance phase. This participant's high number of dissected lymph nodes (Di Sipio et al.,2013), and a high body mass index of 29.7kg/m^2 (Jamallo et al., 2013), may have contributed to this finding.

A non-meaningful mean reduction of tissue water content of 3.3% in the chest region was experienced for the group as a whole. All the participants presented with anterior chest wall scar tissue and fibrosis, which may be as a result of the surgical scar and localised radiation therapy (Ugur et al., 2013), and may have contributed to the lack of a meaningful reduction in tissue water content of the chest region. The literature supports the negative impact of both breast surgery and localised radiation therapy on the lymphatic system, and their contribution to the risk of the development of BCRL (Ghanta et al., 2015, Ugur et al., 2013).

The application of Kinesio® tape, as part of the multimodal management plan, may have contributed to the reduction of tissue water content in the chest region. This is supported by the literature which reports that Kinesio® tape improves lymphatic drainage and motility of the lymphatic fluid through the lymph vessels (Pekyavaş et al., 2014) and that the application of Kinesio® tape in the absence of compression bandaging yet as part of a multimodal intervention programme is effective for the management of lymphoedema (Gatt et al., 2017).

Despite receiving four consecutive weeks of multimodal management, both participants 02 and 03 (randomly allocated to the $A_1B_1B_2A_2A_3$ group) experienced increases in the tissue water content of the chest during the intervention phases B_1 and B_2. Both these study participants presented with stage 2 fibrotic lymphoedema of the chest region. This further reduces the efficiency of the local lymphatic system and the muscle pumping action. Fibrosis in the chest region may have contributed to these participants' limited response to the multimodal management plan of the study (Avraham et al., 2013). This finding contradicts the literature, which has found that an intensive, daily, multimodal management plan effectively results in the reduction of BCRL (Damstra et al., 2017). Another possible factor that could have influenced these participants' results is the high baseline body mass index scores which present a direct risk of BCRL (Jammallo et al., 2013).

5.2.3 Function

Function was measured by extracting data from the function domain on the LYMQOL questionnaire (Keeley et al., 2010). The whole group demonstrated a baseline impairment in function (mean score of 1.9). The whole group demonstrated a clinically meaningful improvement in function from baseline to post phase A_3. It is postulated that this positive outcome may have been influenced by the commencement of an upper limb exercise programme from phase B_1 through to post phase A_3. The exercise programme included daily active range-of-motion and pendulum exercises which addressed shoulder flexion; extension; abduction; internal and external rotation; as well as scapula protraction; retraction; elevation; depression; and upward and downward rotation. In addition, concentric light resistance (1kg) exercises for the glenohumeral muscles, including the deltoid; supraspinatus; infraspinatus; subscapular; biceps and triceps were prescribed. The strengthening exercise regime also addressed the scapulothoracic muscles, namely rhomboid major and minor, and teres major and minor.

The exercise programme that was implemented in the current study was adapted from a complex exercise routine that was utilised in a study conducted by Park et al. (2017). The exercise programme may have contributed to an improvement in glenohumeral and scapula

range of motion and muscle strength which would have had a direct positive impact on the functioning of the participants. Previous studies have reported that a prescribed shoulder exercise programme results in improved function by improving flexibility and strength in the shoulder region (Schmitz, 2010 Smoot et al., 2010; Harris et al., 2012; Park, 2017;). Stretches for scar and fibrotic tissue in the ipsilateral chest and axilla region were performed every day, which may have contributed to the improvement in upper limb mobility and function. This is supported in the literature, which recommends that prescribed exercise may reduce tissue fibrosis and adhesions following breast cancer management (Moseley et al., 2005).

The youngest participant (02) experienced the greatest improvement in function from baseline to post phase A_3, and this finding was clinically meaningful. She presented with a baseline upper limb volume discrepancy of greater than 10% on her non-dominant, surgical side, which, according to the literature, will have a negative impact on function (Park et al., 2021). The participant experienced the greatest reduction in the group in upper limb lymphoedema over the study period from baseline to post phase A_3. It is suggested that the statistically significant upper limb volume reduction achieved may have contributed to the improved upper limb mobility and function, as the presence of BCRL has a negative impact on function (Anbari et al., 2021). The literature reports that exercise enhances protein uptake from the interstitium and lymph circulation (Ahmed et al., 2006), as well as the musculoskeletal contractions and microcirculation (Cho et al., 2016), which facilitates lymph uptake. In addition, the compression therapy was administered to her affected, non-dominant side, which may suggest that it did not interfere with, or restrict, her work. The participant had returned to work as a self-employed nail technician. The literature reports that returning to work presents one of the greatest challenges to BC survivors due to decreased upper limb mobility and function, and the time needed off work for lymphoedema treatment for patients presenting with BCRL (Sun et al., 2020). The challenges facing BC patients on returning to work have been reported in the literature to be unrealistic expectations by the employer of pre-cancer work performance; decreased physical health relating to reduced ability to perform optimally; and financial stress (Kennedy & Sciences, 2007). Relationships with colleagues and superiors present a challenge to re-integration in the workplace (Sun et al., 2020).

Participant 02 transitioned back into her work environment successfully and this could have been due to her being self-employed; and due to the nature of her work, which did not challenge her non-dominant upper limb restrictions. Participant 02 presented with the shortest time since BC diagnosis. It is also suggested that, due to this fact, the consequences of radiation therapy and fibrosis were limited, resulting in an optimal response to the early commencement of a localised exercise programme and improvement in upper limb function

(Gençay Can et al., 2019). It is postulated that the participant may not have developed mal-adaptive postural and movement patterns in the year following her diagnosis, with a resultant positive improvement in function.

Participant 05 also experienced a clinically meaningful improvement in function from baseline to post phase A_3. This participant is a housewife who continued with household chores after BC surgery and presented at baseline with the lowest BMI in the study group. This suggests that she continued to lead a functionally active lifestyle which, in combination with the prescribed exercise programme, resulted in her enhanced function (Gençay Can et al., 2019; Moseley et al., 2005).

5.2.4 Quality of Life

The overall quality of life scores in the current study were measured using the LYMQOL questionnaire (Keeley et al,. 2010), which was designed for measuring quality of life in the presence of limb lymphoedema. The whole study population presented with a decrease in QOL at baseline with a mean score of 5.2. The entire study population experienced a statistically significant improvement in overall quality of life across the phases from baseline to post phase A3 ($p=0.005$) (group average) and more importantly a clinically meaningful improvement in their experience of quality of life.

In the current study the group experienced the greatest, mean clinically meaningful improvement in quality of life between baseline and post the initial two-week intervention phase B_1. The group experienced the next biggest improvement in quality of life between the second intervention phase and post phase A_3. In addition, a group mean 2-point improvement in overall quality of life was experienced from intervention phase B_1 to post intervention phase B_2. The application of the multimodal management plan during these phases may have contributed to the improvement in quality of life for the participants. The literature supports this finding, where it is reported that the use of MLD and compression, as components in multimodal management, resulted in improved quality of life because the participants experienced limb volume reduction, were educated on lifestyle and self-management, and were empowered to make informed decisions regarding the lymphoedema (Bland et al., 2019; Temur et al 2019, Pinto et al., 2011).

The holistic multimodal management used in the current study involved physical treatment modalities, exercise prescription and emotional support, as well as a participant education programme. Each participant received a hard copy manual detailing appropriate skin care; avoidance of infection and injury; self-lymphatic massage; avoidance of blood pressure cuffs and blood draws from the affected limb; as well as protection of the limb from overheating and

constriction. In addition, self-monitoring of the limb circumference and subjective symptoms was taught. Two previous studies (Bland et al 2019; Gencay-Can et al. 2019) supported this approach as they found that an early, structured teaching programme empowered patients to make informed decisions regarding the management and prevention of lymphoedema, which contributed to an improved overall quality of life. In another qualitative study conducted by Anbari in 2021, it was recommended that early education regarding self-management would improve quality of life in patients with BCRL.

Participant 02 was the only participant to experience a clinically meaningful improvement in the appearance domain from baseline to post phase A_3. This participant had the shortest timeframe since diagnosis and experienced the greatest limb volume reduction from baseline to post phase A_3 in the current study. These factors may have contributed to the participant's improvement in the appearance domain of the LYMQOL questionnaire. This is supported in the literature in a study which confirmed that the early implementation of multimodal management following medical management improves patients' quality of life by improving body image; reducing pain; improving self-esteem; and reducing anxiety associated with finances and disease progression (Kalemikerakis et al., 2021).

In this study, participants were given a prescribed exercise programme which included deep breathing exercises; shoulder range of motion and strength exercises; aerobic exercise; and upper limb stretching, which may have contributed to the significant improvement in overall quality of life. It has been reported in the literature that a prescribed exercise routine improves the quality of life in patients with BCRL (Pinto et al., 2011). A meta-analysis was conducted at the Breast Cancer Research Centre in Iran in which one qualitative and 81 quantitative studies on the quality of life in breast cancer survivors were found to be eligible for inclusion in this review of the literature between 2008 and 2018. The meta-analysis confirmed that physical activity and exercise contributed to an improvement in quality of life in BC survivors (Mokhatri-Hesari & Montazeri, 2020). The importance of optimal limb function is essential for good quality of life, as this will have a positive influence on independence, appearance and emotional well-being, as well as a smooth transition back to work for breast cancer survivors.

The study participants presented with similar subjective symptoms in the lymphatic regions of the upper limb and trunk to those reported in the literature. These symptoms typically included pain; numbness; pins and needles; weakness and heaviness. In addition, fatigue; anxiety; difficulties in sleeping; irritability and depression were described by the participants. According to the findings in the literature, BCRL has a detrimental effect on quality of life in the body image, physical, psychological and social domains; resulting in anxiety, fatigue, frustration,

fear and pain (Pusic et al., 2014; Pinto et al., 2011). However, there was a dearth of qualitative reviews on BCRL and quality of life in the literature. Abari et al. (2021) conducted a qualitative analysis over a period of seven years on the relationship between BCRL and quality of life among 97 women with newly diagnosed BCRL in the Midwestern region of America. The average age of the study population was 53 years, compared to an average age of 55.6 years in the current study. It was reported that a decreased quality of life was related to pain, fatigue and inactivity for this study population. These factors, once positively addressed, will enhance quality of life in the presence of breast cancer-related lymphoedema, which is aligned to the results of the current study.

Quality of life is an intangible, qualitative and subjective outcome and is dependent on each individual's perception of their physical, emotional and psychological well-being in relation to the environment in which they exist. Lymphoedema is a chronic and progressive disease for which there is no cure. This emphasises the importance of effective multimodal management which focusses on enhancing quality of life in women with BCRL. The improvement in quality of life experienced by the participants in the current study would have facilitated good emotional health, leading to feelings of happiness, satisfaction, acceptance and self-confidence, and improved self-worth within the framework of their daily lives. This would have contributed to higher functional competence and independence, as well as a sense of value within the home, work and social environments of each participant.

Chapter 6: Conclusion

Following the series of five n=1 studies, the application of the multimodal management plan was effective in, statistically significantly, reducing breast cancer-related lymphoedema in the upper limb for all the study participants, and in facilitating a statistically significant improvement in quality of life. Furthermore, the participants experienced a statistically significant reduction in the breast cancer-related lymphoedema in the axilla region of the trunk from the baseline to post maintenance phase, ten weeks in total. A non-significant reduction in chest lymphoedema and a clinically meaningful reduction in percentage tissue water of chest from phase B to B_1 and B_1 to B_2 was noted. A clinically meaningful reduction in percentage tissue water content of the axilla and improvement in function was achieved for all the study participants across the study phases.

The multimodal management approach to breast cancer-related lymphoedema was effective in achieving the above outcomes in this study. The absence of fibrotic changes in the upper limb and axilla regions found in the current study suggested that timeous multimodal management for lymphoedema in the early stages (stage 0 and stage 1) is imperative for the successful prevention and management of BCRL. Consistent improvement in the quality of life scores for each participant were achieved directly, following both two-week intervention phases during the study. This suggests that, in addition to the frequent multimodal management received during these phases, the support, encouragement and education received during the sessions empowered the participants to remain compliant with the treatment and home programme, to make informed decisions, and to confidently self-manage their lymphoedema. This is evident in the positive outcomes experienced following the four-week self-maintenance phase which concluded the study.

6.1 Clinical implications

Due to the chronic and progressive nature of BCRL, the implementation of a pre- and post-operative lymphoedema screening tool would alert both clinicians and patients to the potential risk factors for developing BCRL. In the current study, all the potential study participants were referred from breast cancer survivor support groups. No referrals were received from medical practitioners, surgeons or oncologists. This could either indicate a lack of continuity in the identification of BCRL in the multi-disciplinary team, a possible lack of knowledge or the role of other team members and/ or poor communication among team members. BCRL presents as a complex condition affecting both physical and emotional aspects as well as having a negative impact on quality of life. Clinicians are encouraged to apply the multimodal approach to management, as this addresses each of these impairments and facilitates both objective

and patient reported improvement in both physical and emotional well-being. A multidisciplinary team-based approach to lymphoedema assessment and management is strongly recommended. This education should extend to all healthcare workers, such as nurses; physiotherapists; surgeons; general practitioners; and oncologists involved with treating breast cancer survivors. Knowledge about the early signs and symptoms of breast cancer-related upper limb and trunk lymphoedema, deteriorating quality of life and function, and reduced upper limb motion and strength, should be imparted to the healthcare professionals. Better informed and educated health care professionals would facilitate the timeous management of BCRL and counselling of patients.

Healthcare professionals, including physiotherapists who are not certified in lymphoedema management, should be encouraged to refer BC patients to a certified lymphoedema therapist early, as management of this condition is specialised. This will allow these patients to receive adequate early management. However, where a certified lymphoedema therapist is not available, physiotherapists are encouraged to continue with the management of these patients, focusing on those aspects which fall within their scope of practice, such as education on exercise and skin care; deep breathing exercises; relaxation techniques; laser and Kinesio® tape application (HPCSA, 2022). Patient education from the time of BC diagnosis is imperative in order to empower BC survivors with the knowledge and skills to prevent the progression of lymphoedema and to seek the correct medical treatment and support early on in their diagnosis. The establishment of lymphoedema support groups, both in the private and public sector, with a trained lymphoedema therapist in attendance, would offer support and advice to patients with breast cancer-related lymphoedema, with the goal of reducing the burden of lymphoedema in BC survivors.

6.2 Study Strengths and Limitations

The present study possesses various strengths. To the author's knowledge, this is the first n=1 study investigating the effect of multimodal management on BCRL, function and quality of life in breast cancer survivors in South Africa. This study design allowed for a pragmatic approach that improved the clinical appropriateness of the intervention. The n=1 study design allowed for the implementation of participant-specific treatment protocols and the administration of multiple individual treatment sessions. The design facilitated individual participant feedback and involvement and multiple outcomes could be measured. All the participants attended every measurement and treatment session and compliance with the intervention protocol was good. Only one participant left the study, due to her concerns related to the Covid-19 pandemic.

The present study also had some limitations that should be acknowledged. The limited variety of ethnicity of the study population was not a true representation of the South African population and the study sample was small. Therefore, the results cannot be generalised to the South African context. The study population included only breast cancer survivors with lymphoedema in a private healthcare setting. This was not an accurate reflection of the South African population, where the majority of the population are dependent on accessing health care services through the public healthcare system. The treatment protocol adopted for this study demanded a significant amount of travel and treatment time from the participants, which would also have been restrictive due to financial cost and missed time from work.

In addition, the study design did not provide evidence of the effectiveness of individual treatment interventions, as a multimodal approach was used. The outcome measurements were dependent on each individual's response to the multimodal management. The study design included two washout phases during which the participants did not receive any treatment intervention. This may have negatively influenced the measurement outcomes, as lymphoedema is a chronic and progressive disease, if left untreated.

The current study measured outcomes immediately post-intervention and did not include a long-term follow-up phase beyond four weeks after completion of the final treatment phase (phase B_2). A longer-term follow-up of the study participants, up to one year post completion of the treatment phase, would have provided further evidence of the effect of the multimodal management plan on the long-term reduction and maintenance of breast cancer-related upper limb and trunk lymphoedema, quality of life and function. Another challenge was the lack of a validated quality of life questionnaire for the trunk, and this presented a limitation in the current study. Lymphoedema of the trunk presents differently to that of the upper limb, and diagnosis thereof relied heavily on subjective symptom reporting by the study participants. The main researcher was solely responsible for assessing all study participants and implementing the management interventions. This could have increased the risk of researcher and measurement bias.

6.3 Recommendations for future research

More research on BCRL in the South African context and, in particular, in the public sector, is needed. A larger study population with diverse ethnicity and socio-economic status would facilitate generalisation of the study outcomes to the South African population. Future research should include longitudinal study designs to monitor compliance and long-term outcomes of the multimodal management plan. In addition, randomised controlled trials with larger sample sizes are needed to establish the effect of the individual intervention components included in the multimodal management approach in the current study. The use of a trunk compression

vest in future studies of this nature would provide the key component of compression from the basket of care for the trunk region. This would facilitate a more accurate evaluation of the effectiveness of multimodal management on trunk lymphoedema. It is recommended that future research should include the design and validation of a quality of life questionnaire for the trunk, as well as the design and validation of a screening tool for upper limb and trunk lymphoedema to be utilised directly post-operatively for the identification of risk factors and subclinical BCRL.

In future research, it would also be useful to include expert clinical feedback from clinicians specialising in managing BCRL, and to include this in the development of education programmes in both private and public settings, for the early identification and management of BCRL.

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List of Appendices

Appendix 1: Letter to attending specialists

Dear

I am currently conducting research in part fulfilment of a Masters in physiotherapy at Stellenbosch University. I am a certified Lymphoedema Therapist (ILWTI, LTA). The title of my study is:
The effect of evidence-based management intervention on upper limb and trunk oedema, function and quality of life in breast cancer survivors. A series of N=1 study.
The study will take place in the following five phases:

1. Washout phase (1week)
2. Intervention Phase (2 weeks)
3. Withdrawal Phase (1 week)
4. Intervention Phase (2 weeks)
5. Medium-term follow-up phase (4 weeks)

I have applied for clearance from the Health research Ethics Committee (HREC) at Stellenbosch University to conduct this study (Study Number: S20/11/329). The study participants will be screened to confirm their eligibility for inclusion in the study. Those that are eligible will receive detailed information on the study objectives, phases and interventions and will be requested to sign an informed consent form.

The objective assessment will include circumferential tape measurements and the tissue dielectric constant will be measured by the validated Moisture Meter D. The patients will be required to fill in the LYMQOL Quality of Life Questionnaire at this time. The evidence-based interventions will consist of manual lymphatic drainage, laser therapy, Kinesio® tape and multi-layer compression bandaging. The patients will receive a prescribed home exercise programme, and details on daily skin care and risk reduction. Once limb and trunk reduction are achieved the participant will be expected to wear a prescribed pressure garment to maintain treatment results.

The study will take place between March 2021 and July 2021 and I would like to request that you would consider referring patients who have had either a mastectomy or breast conserving surgery and present with breast cancer related lymphoedema (clinical or subclinical) to me for screening for eligibility for inclusion in the study. Those who are not eligible for inclusion will still have the option to receive evidence-based interventions and management for their lymphoedema.
If you are prepared to assist me, please kindly email confirmation and I will be in further contact with you in the near future.

Thank you in advance.

Yours sincerely

Liesl Way B.Sc. Physio (US) Lymphoedema Therapist (ILWTI, LTA)

Appendix 2: Advertisement on Facebook and Whatsapp support groups

I am currently conducting research in part fulfilment for a Masters in Physiotherapy through Stellenbosch university and my topic of interest is Breast Cancer related Lymphoedema. Having trained as a Lymphoedema Therapist, I understand how life changing proper management of this condition can be. I have ethical approval and am recruiting participants in the Durban Metropole who struggle with the above condition. Comprehensive Gold Standard treatment will be administered at no cost if the participants meet the criteria for my study. Please contact me if you or someone you know suffers with breast cancer related lymphoedema Email: lieslwaylw@gmail.com

Appendix 3: Participant screening tool

Participant ID…… Date: ……

PATIENT SCREENING TOOL (please tick the relevant box)		
	YES	NO
Have you had a mastectomy or breast conserving surgery for breast cancer?		
Have you had chemotherapy treatment?		
Did your chemotherapy treatment finish prior to the last six weeks?		
Have you had radiation therapy?		
Was your radiation therapy completed prior to the last six weeks?		
Do you currently have untreated cellulitis?		
Do you have axillary web syndrome?		
Do you have a BMI above 30kg/m^2		
Have you had weight fluctuations of greater than 4.5kg in the last month?		
Do you have a seroma near the scar site?		
Do you experience swelling or tightness of your arm?		
Do you experience swelling or heaviness in your trunk?		
Do you experience numbness in your arm?		
Do you experience numbness in your trunk?		
Do you have pain/tenderness in your arm?		
Do you have pain/tenderness in your trunk?		
Have you had a breast implant?		

OBJECTIVE MEASUREMENTS

According to circumferential tape measurements is arm lymphoedema detected?		
According to the percentage water content in the trunk and arm, is lymphoedema detected in the trunk and arm?		

Appendix 4: Letter of invitation to participate in the study

STUDY TITLE: The effect of an evidence-based management plan on upper limb and trunk lymphoedema, function and quality of life in breast cancer survivors. A series N=1 studies.

Reference Number: S20/11/329
Principal Investigator (PI): Liesl Way

Address: Division of Physiotherapy, Medical School
Stellenbosch University
Francie Van Zijl Drive, Tygerberg, 7505
Cape Town, South Africa

Contact Number: 084 2650999

Dear ……..

You are invited to participate in the above study which will be conducted in Westville, Kwa-Zulu Natal. The study forms part of the requirements for a Masters degree in Physiotherapy. You will be screened on your initial visit to confirm your eligibility for this study. You will be required to fill in a form with your personal details, as well as a form with “Yes” or “No” answers detailing your experience of your lymphoedema. A comprehensive assessment of your lymphoedema will then be conducted by the researcher. Prior to this screening process, the Informed Consent Form will be made available for you to read in full and an opportunity given for you to clarify any questions you may have regarding the study. If you meet all the inclusion criteria you will receive further information regarding the details of the study. If you do not meet the inclusion criteria for this study, you will still have the option to receive evidence-based treatment interventions and management for your lymphoedema. You will have the option of receiving this treatment from the researcher outside the parameters of this study, or you will be referred to an alternative lymphoedema therapist for the proper management and care for your condition.

The study involves five different phases which will take place over 10 weeks. You will be required to attend all your consultations and follow a basic prescribed daily home programme. You will be reimbursed for all travel costs and you will not be charged for the treatment interventions that you receive as a part of this research.

Participation in this research is completely voluntary and you may withdraw at any time. Your medical records will remain anonymous at all times. Your participation in the research will be of great importance in raising awareness of the need to identify and treat arm and trunk lymphoedema in women following breast cancer treatment, and how it affects the quality of life of those who have it. The results of this study will be used to bring awareness to breast cancer survivors, health professionals and specialists in this field.

If you are willing to be screened for potential participation in this study, please indicate by signing below.

Signature…….
Date……

Thank you for your time.

Yours sincerely

Liesl Way
B.Sc Physio (Stell)
Lymphoedema Therapist

Appendix 5: Patient demographics form

Participant ID											
Address					Suburb			Code			
								Date of Birth			
Contact Details	Home Phone				Work Phone			Cell Phone			
Email address											
Title		**Marital Status**			**Race**			**Preferred Contact**			
Doctor		Married			White			Email			
Mr		Single			Black			Cell Phone			
Mrs		Divorced			Indian			Work Phone			
Miss		Separated			Coloured			Home Phone			
Master		Widowed			Asian			SMS			
Other		Life Partner									
Size of family		2-4 members			5-6 members			6-8 members			
Referred by:	GP		Specialist		Self		Other				
Referring doctor /specialist											
Employment Status											
Self employed		Employed		Unemployed		Medically Boarded		Sick leave			
Position Held/Occupation											

Appendix 6: Subjective and objective assessment form

Participant ID	
AGE	
DOMINANCE (L/R)	
SPORT/HOBBIES	
REFERRING DOCTOR	

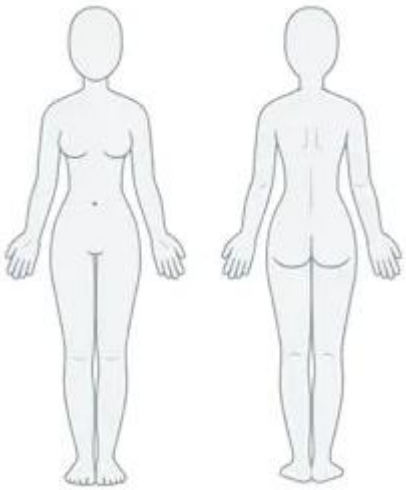
HISTORY OF CONDITION	
Previous Cancer	
CURRENT CANCER	
Stage of Cancer	
Date of Diagnosis	
Date of Surgery	
Chemotherapy (start/end dates)	
Radiation (start/end dates)	

SPECIAL HEALTH QUESTIONS (tick = yes, cross = no)			
Diabetes		Previous Cellulitis	
Smoking		Renal function	
Peripheral Arterial Disease		Blood Pressure	
Deep Vein Thrombosis		Previous Cancer	
Chronic Heart Failure		Allergies	
BMI>30kg/m^2		Weight fluctuation > 4.5kg in a month	

BREAST CANCER CHARACTERISTICS AND TREATMENT (Y or N)			
Age at diagnosis		Chemotherapy	
Left or Right Breast		Radiation therapy	
Mastectomy		Anti-estrogen drugs	
Breast Conserving Surgery		Breast reconstruction	
ALND		Previous Seroma	
SNB		Axillary Web Syndrome	

MEDICATION (tick=yes, cross=no, include the name of the drug)			
Antibiotics		HRT	
Anti-emetics		Steroids	
Pain Meds		Anti-coagulants	
Diuretics		Other	

SUBJECTIVE SYMPTOMS (tick=yes, cross=no) See body chart			
Tightness		Tenderness	
Heaviness		Pain	
Swelling		Numbness	
Pins and Needles		Weakness	



FRONT BACK

SKIN CONDITION	
SURGICAL SCARS	
SCAR TISSUE	
SKIN TEXTURE	
SKIN COLOUR	
SENSATION	
(hot/cold; light touch)	
STEMMER SIGN	
RADIAL PULSE	
PITTING EDEMA	STAGE 0 1+ 2+ 3+ 4+
CAPILLARY REFILL	
REBOUND TIME	

ARM FUNCTION (range of motion)					
SHOULDER		ELBOW		WRIST	
Abduction		Flexion		Flexion	
Flexion		Extension		Extension	
Lat Rot		Supination		Radial Dev	
Med Rot		Pronation		Ulnar Dev	
HBB					

LYMPHOEDEMA STAGING				
Stage 0	Stage 1	Stage 2	Stage 2+	Stage 3

Appendix 7: Participant information leaflet and consent form

Title of Research Project:

The effect of an evidence-based management plan on upper limb and trunk lymphoedema, function and quality of life in breast cancer survivors. A series of N=1 studies.

Reference Number: S20/11/329

Principal Investigator (PI): Liesl Way

Study Supervisors: Mrs Leone Williams Senior Lecturer, Division of Physiotherapy
Dr Dominique Leibbrandt

Address: Division of Physiotherapy, Medical School
Stellenbosch University
Francie Van Zijl Drive, Tygerberg, 7505
Cape Town, South Africa

Contact Number: 084 2650999

You are being invited to participate in a research project in partial fulfillment of a Masters degree in Physiotherapy. The details of this project will be presented to you in this form, please take time to read all the information thoroughly. You are encouraged to ask questions if there is anything regarding the study that you do not understand. It is vital that you are satisfied and clearly understand what the research and your participation therein entails. Your participation is voluntary, and you may decline to participate. If you decline, you will not be negatively affected in any way. You are also at liberty to withdraw from the study at any point, even if you agree to participate initially.
This study has been approved by the Health Research Ethics Committee at Stellenbosch University and will be conducted according to the ethical guidelines and principles of the International Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

What Is The Research Study About?
The aim of this study is to describe the effect of specific treatment techniques on your trunk and arm lymphoedema, function and quality of life. The treatment intervention will include the accepted Gold Standard techniques of manual lymphatic drainage, compression therapy, exercises, deep breathing and skin care, as well as laser therapy. The study will also investigate the effect of this treatment both immediately after a series of treatment and four weeks after the treatment is terminated. The study will take place at a private Physiotherapy practice, Liesl Way Physiotherapists, at Life Westville Hospital, Westville, KwaZulu-Natal.

What Will The Study Entail?
The study will take place in four phases as follows:

1. During the initial one week phase the lymphoedema of your arm and trunk will be measured on two different occasions using a non-invasive lymph Moisture Meter and

a flexible tape measure. These measurement sessions will take 30 minutes to complete. This is not painful or uncomfortable in any way. These measurements will be recorded on a score sheet which will be locked in a secure location. You will be required to fill out a questionnaire regarding your quality of life on your first visit.

2. The following phase will take place over two weeks and you will receive six individual treatments for your arm and trunk swelling. Each treatment session will take 75 minutes. At the commencement and end of this phase you will be required to fill out the questionnaire for a second and third time. The trunk and arm measurements will be repeated before each treatment session and recorded on your sheet. Treatment will consist of manual lymphatic drainage massage, laser therapy to your trunk and manual lymphatic drainage, laser therapy and multilayer bandaging to your arm. Skin care and a daily home exercise programme will be prescribed and demonstrated and you will receive an information leaflet to take home.
3. The next phase of the study will take place over one week and all individual treatment will be withdrawn. You will be expected to continue with your daily home management programme and wear your compression garment during the day. The measurements of your arm and trunk will be repeated at the end of this one- week period. You will be asked to fill out the quality of life questionnaire at the end of the week.
4. The final phase of the study will record the outcome of the treatment intervention after four weeks. You will be expected to continue with your exercise regime and wear your compression garment during the day. Final measurements of the trunk and arm will be recorded at the end of this phase and you will be requested to fill out the quality of life questionnaire once again. Finally you will requested to fill out an exit questionnaire.

Why Have You Been Invited To Participate?

You have been invited to participate because you have had either a mastectomy or breast conserving surgery following your diagnosis of breast cancer (Stage 1 -3) and have completed your treatment interventions (chemotherapy and radiation therapy) prior to the past 6 weeks. As a result of this life saving treatment intervention, you have developed lymphoedema of your arm and/ or truncal region. Further to this, you fit all the criteria for inclusion in this study.

What Will Your Responsibilities Be?

You will be required to attend all the physiotherapy appointments, to comply with your prescribed home exercise programme and fill in the quality of life questionnaire on five different occasions.

Will You Benefit From Taking Part In This Research?

Your lymphoedema will be accurately assessed and explained in detail, and you will receive comprehensive and evidence-based treatment for your condition, free of charge. The treatment outcomes will be monitored regularly throughout the study. You will also receive counselling regarding potential risk factors for your lymphoedema as well as a custom designed exercise and self-management programme.

Are There Any Risks Involved In Taking Part In This Research?

Your participation in this study should not present any risk to yourself. In the unlikely event that you have an adverse reaction to any of the treatment interventions, you will be referred to your GP or referring specialist for further investigation and intervention. Even though it is unlikely that you will have an adverse reaction, Stellenbosch University will provide comprehensive no-fault insurance and will pay for any medical costs that may be incurred as a result of your participation in the research. You will not need to prove that the researcher was at fault.

There are no obvious physical risks to your participation in this research. However, due to the sensitive nature of the topic of the subject matter (the development of trunk and arm lymphoedema following breast cancer treatment), you may experience emotions that you were unaware of and that are upsetting to you. Should you feel distressed during or after the initial interview, please speak to the researcher. I will refer you to an appropriate health care provider as soon as possible to assist you.

If You Do Not Agree To Take Part, What Alternatives Do You Have?
If you do not wish to take part in this study or feel the need to withdraw at any stage, free assessment and treatment of your condition will not be available. However, the same level of care will be available at normal practice rates from the current practice Participation is completely voluntary.

Who Will Have Access To Your Medical Records?
The information collected will be coded and anonymised and treated as confidential. If it is used in a publication or thesis, your identity will remain anonymous. Only the researcher will have access to this information.

Will You Be Charged For The Assessment And Treatment Interventions Given During This Study?
No, you will not be charged for the assessment and subsequent treatment interventions that you receive. You will be remunerated for all your travel costs to and from your appointments, at the current AA rate. This will amount to all the travel costs incurred by you to attend every session at Westville Hospital.

Is There Anything Else That You Should Know Or Do?
You can contact the Health Research Ethics Committee on 021 9389207 if you have any concerns or complaints that have not been adequately addressed by your study investigator. A copy of this information and consent form for your own records will be provided.

Declaration by participant
By signing below, I ……. agree to take part in a research study entitled: **The effect of an evidence-based management plan on upper limb and trunk lymphoedema, function and quality of life in breast cancer survivors. A series of N=1 studies**.

I declare that:

- I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is voluntary and I have not been pressurised to participate.
- I may choose to leave the study at any time and will not be penalised or prejudiced in any way.
- I may be asked to leave the study before it is finished, if the study researcher feels it is in my best interests, or if I do not follow the study plan, as agreed to.

- I understand that by agreeing to participate in this study, I allow the PI to access my medical records pertaining to my breast cancer and that all information will be treated confidentially.

Signed at (place) …….. on (date) ……..202….

Signature of participant
……

Signature of Witness
Signed at ..... on (date).....202.....

Name :..... Signature .....

Declaration by investigator

I ……. declare that:

- I have explained the information in this document to ……..
- I have encouraged her to ask questions and allocated adequate time to answer them.
- I am satisfied that she has a complete understanding of all aspects of the research, as discussed above.

Signed at …….. on……..……..202….

Signature of investigator

…….

Appendix 8: Kinesio® tape patch test consent form

Description:
Kinesio® tape is a recognized and effective treatment intervention for the management of lymphoedema. In order for this intervention to be effective, the taping system is applied to the lymphatic area (In this study, your trunk) and should be worn for 24 hours a day. The tape is latex free and has an acrylic adhesive. It can be worn for 24 hours a day and is waterproof. The tape will be removed and new tape reapplied when necessary during your intervention phase.

Purpose:
The tape acts as a pump, stimulating the lymphatic flow and reducing muscle tension. This facilitates increased blood and lymphatic flow, decreases pain and increases motility of the lymphatic fluid through the lymphatic vessels. The tape application will form an important part of your treatment intervention for your lymphoedema.

Guidelines for the patch test:

1. The patch test will be conducted to check for skin irritation or allergies.
2. A small piece of ktape will be applied to your trunk area and should be worn for 48 hours.
3. Monitor it closely for the first 12-24 hours. If any irritation is noted (redness, itching, rash) please remove the tape immediately. You may remove it after 48 hours if no irritation is noted.

How to remove the tape:

1. Loosen one end of the tape and begin slowly peeling the skin away from the tape as you press down on the skin. DO NOT PULL THE TAPE OFF THE SKIN QUICKLY. If tape is not removing easily, place a thin layer of baby oil, vegetable oil or tape remover over the tape and let it soak in for 15 minutes.
2. After removal use a lotion to hydrate the skin and relieve any irritation.

I declare that:

- I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this procedure is voluntary and I have not been pressurised to participate.

Signed at (place) …….. on (date) ……..202….

Signature of participant

……

Declaration by investigator

I …… declare that:

- I have explained the information in this document to ……..
- I have encouraged her to ask questions and allocated adequate time to answer them.
- I am satisfied that she has a complete understanding of all aspects of this procedure, as discussed above.

Signed at ……..…… on……..202….

Signature of investigator

…….

Appendix 9: Consent for medical records

STUDY TITLE: The effect of an evidence-based management plan on upper limb and trunk lymphoedema, function and quality of life in breast cancer survivors. A series of N=1 studies.

Reference Number:
Principal Investigator (PI): Liesl Way

Address: Division of Physiotherapy, Medical School
Stellenbosch University
Francie Van Zijl Drive, Tygerberg, 7505
Cape Town, South Africa
Contact Number: 084 2650999

Patient name: ……..
Date…….....

I …… hereby give consent for Liesl Way to gain access to all my Medical Records pertaining to my diagnosis and treatment for breast cancer. The access is granted for the sole purpose of this research and I understand that the information shall be anonymized, remain confidential and locked away in a safe location in my patient file or stored on a flash drive in a safe. No-one else shall have access to this information.

The following information may be released:

- Results of the test imaging
- Results of breast biopsy
- Surgical Procedures and any post-operative complications
- Node excision technique and number of nodes removed
- Chemotherapy intervention
- Radiation intervention
- Hormonal treatment
- Previous lymphoedema treatment interventions
- Follow up imaging and testing

I understand that I may withdraw this consent, in writing, at any time and that it will not negatively impact my treatment and management.

Signed at …….
On…….....

Signature…….....
Witness…….

Appendix 10: Consent for medical photographs

STUDY TITLE: The effect of an evidence-based management plan on upper limb and trunk lymphoedema, function and quality of life in breast cancer survivors. A series of N=1 studies.

Reference Number:
Principal Investigator (PI): Liesl Way

Address: Division of Physiotherapy, Medical School
Stellenbosch University
Francie Van Zijl Drive, Tygerberg, 7505
Cape Town, South Africa

Contact Number: 084 2650999

Patient name: ……. Date: ……..

I consent for medical photographs to be made of my upper limb and truncal region only, with no inclusion of my head or face by the researcher Liesl Way only. I understand that the information may be used in my medical record for submission for this research project only, or for publication in medical journals as I have designated below. I understand that the photographs will not be taken or stored on a cell phone device. The photographs will not be used on any social media platforms including Facebook, Whatsapp, Instagram or any other platform. By consenting to these medical photographs, I understand that I will not receive payment from any party. Refusal to consent to photographs will in no way effect the medical care I will receive. If I have any queries or wish to withdraw my consent in the future I may contact: Mrs Liesl Way 084 2650999 or email lieslwaylw@gmail.com.

I understand that should I withdraw my consent for photographs, all photography will be destroyed and deleted in my presence.

By signing this form below I confirm that this consent form has been explained to me in terms which I understand.

1. I consent for these photographs to be used in medical publications. I understand that the image may be seen by members of the general public, in addition to medical researchers that regularly use these publications in their professional education. Although these photographs will be used without identifying information such as my name or my face, I understand that it is possible that someone may recognize me. I also agree for my image to be used for submission for this Masters research study and to be used for my medical record.
   The photographs will be stored on an external hard drive in a safe locked location which will only be accessed by the researcher. The photograph will be stored and indexed according to the code given to my medical records, and will not be stored with my name.

   Signature ……
   Witness……...

2. I agree for my image to be shown, for submission for this Masters research AND to be used for my medical record AND medical publication.

   Signature……
   Witness……

3. I agree to the use of my image for submission for this Masters research study ONLY

   Signature…… Witness……

4. I agree to the use of my image for submission for this Masters research AND for use for my medical records.

   Signature…….. Witness……..

5. I agree to the use of my image for submission for this Masters research AND for publication in a medical journal.

   Signature…… Witness……

Appendix 11: LYMQOL questionnaire

LYMQOL ARM

Lymphoedema Quality of Life Tool

This questionnaire has been designed and validated for patients with chronic oedema/ lymphoedema of one or both arms to measure quality of life.

Please tick the box that best describes how you feel about each of the questions.

Participant ID…….. **Date:** ……

(Q1) How much does your swollen arm affect the following daily activities?

If any of the items are not applicable to you, please write N/A in the relevant answer box(es).	**Not at all**	**A little**	**Quite a bit**	**A lot**
a) occupation				
b) housework				
c) combing hair				
d) dressing				
e) writing				
f) eating				
g) washing				
h) cleaning teeth				

(Q2) How much does it affect your leisure activities/ social life?				

Please give examples of this .....

(Q3) How much do you have to depend on other people?				

	Not at all	A little	Quite a bit	A lot
(Q4) How much do you feel the swelling affects your appearance?				
(Q5) How much difficulty do you have finding clothes to fit?				
(Q6) How much difficulty do you have finding clothes you would like to wear?				
(Q7) Does the swelling affect how you feel about yourself?				
(Q8) Does it affect your relationships with other people?				

	Not at all	A little	Quite a bit	A lot
(Q9) Does your lymphoedema cause you pain?				

(Q10) Do you have any numbness in your swollen arm?				
(Q11) Do you have any feelings of "pins & needles" or tingling in your swollen arm?				
(Q12) Does your swollen arm feel weak?				
(Q13) Does your swollen arm feel heavy?				
(Q14) Do you feel tired?				

In the past week….	Not at all	A little	Quite a bit	A lot
(Q15) Have you had trouble sleeping?				
(Q16) Have you had difficulty concentrating on things, e.g. reading?				
(Q17) Have you felt tense?				
(Q18) Have you felt worried?				
(Q19) Have you felt irritable?				

(Q20) Have you felt depressed?				

(Q21) Overall, how would you rate your quality of life at present?

Please mark your score on the following scale:

0 1 2 3 4 5 6 7 8 9 10

poor **excellent**

Thank you for completing this form.

If you have any comments or queries about it, please discuss these with Mrs. Liesl Way

Dr V L Keeley, Consultant

Questions 15 to 20 have been reproduced with permission from the EORTC.

These questions are only a part of the QLQ-C30 Questionnaire.

Appendix 12: Permission to use LYMQOL questionnaire

Derby Hospitals NHS
NHS Foundation Trust

Dr V.L. Keeley

DERBY LYMPHOEDEMA SERVICE

M&G Level 3,

Royal Derby Hospital,

Uttoxeter Rd, Derby. DE22 3NE

Tel: 01332 783075

e-mail: vaughan.keeley@nhs.net

Dear Colleague,

LYMQOL has been developed to assess the impact of lymphoedema/ chronic oedema of the arm(s) or leg(s) on the quality of life of patients. It can also be used to monitor the impact of treatment. It has been validated and presented at lymphoedema conferences a further formal publication is in preparation.

- V L Keeley, D Veigas, S Crooks, J Locke, H Forrow. The development of a condition-specific quality of life measure for lymphoedema (LYMQOL). European Journal of Lymphology 2004; 12(41) Sp: 36
- British Lymphology Society Annual Conference (2005).
  The validation of a condition-specific quality of life tool for lymphoedema (LYMQOL).
- International Society of Lymphology Conference (2005) Salvador, Brazil.
  The validation of a condition-specific quality of life tool for lymphoedema (LYMQOL).
- Keeley V et.al (2010) A quality of life measure for limb lymphoedema (LYMQOL) Journal of Lymphoedema, 5 (1) p26-37

You are welcome to use LYMQOL, but we would be grateful if you would let us know if you plan to use it and feed back your experiences. We ask you to complete your contact details and intended use on the slip below and return it to us. We would then send you updated versions and results of any further studies we undertake.
There are separate arm and leg questionnaires, Appendix 1 & 2. Scoring is as follows:
Arm: The score for individual responses are provided in the scoring copy of the questionnaire (Appendix 3). If the item is not scored and left blank or the recorded response is not applicable this is scored with a 0.
Domain totals are calculated by adding the individual scores and dividing the total by the number of questions answered. (If >50% of questions per domain are not answered this cannot be calculated and =0).
The four domains and their corresponding questions are: Function 1 (a-h), 2, 3.
Appearance 4,5,6,7,8.
Symptoms 9,10,11,12,13,14

Emotion 15,16,17,18,19,20.

Overall quality of life (Q21) is scored as the value marked by the patient, between 0-10.

Leg: The score for the individual responses are provided in the scoring copy of the questionnaire (Appendix 4). If the item is not scored and left blank or the recorded response is not applicable this is scored with a 0.

Domain totals are calculated by adding the individual scores and dividing the total by the number of questions answered. (If >50% of questions per domain are not answered this cannot be calculated and =0).

The four domains and their corresponding questions are: Function 1 (a-f), 2,3
Appearance 4,5,6,7,8,9,10
Symptoms 11,12,13,14,15
Emotion 16,17,18,19,20,21.

Overall quality of life (Q22) is scored as the value marked by the patient, between 0-10.

If you have any further questions, please contact us at the address above or contact Katie Riches, research nurse on (01332) 787931 or Katie.riches@nhs.net

Yours Sincerely,

V. L. Keeley

Dr V.L Keeley
Consultant in Palliative Medicine.

LYMQOL Registration of Intended Use:

Name: LIESL WAY **Title: MRS**

Work Address: SUITE 100, LIFE WESTVILLE HOSPITAL, WESTVILLE KZN

SOUTH AFRICA

Contact Number: 084 2650999

Email Address: lieslwaylw@gmail.com

Intended use: Research Project

Details: (Please include information about the patient group (age, diagnosis), numbers of patients, number of times LYMQOL will be completed by each patient etc.)

Patient Group: females following breast cancer intervention with trunk and arm lymphoedema

Number of patients: 5 (series of N = 1 study)

Each participant will fill in the arm LYMQOL 5 times

LYMQOL will be used as an outcome measure for Gold Standard treatment interventions

---

Please send me revised versions of LYMQOL: **Yes** ☐ **No** ☐

Please send me the references of future publications: **Yes** ☐ **No** ☐

Thank you for taking the time to complete this form.

Appendix 13: LYMQOL scoring system

LYMQOL ARM-*Scoring System*

Lymphoedema Quality of Life Tool

The score for the individual responses are given below. If the item is not scored and left blank or not applicable this is scored with a 0.
Domain totals are calculated by adding the individual scores and dividing the total by the number of questions answered. (If >50% of questions per domain are not answered this cannot be calculated and =0).
The four domains and their corresponding questions are: Function 1 (a-h), 2,3
Appearance 4,5,6,7,8 Symptoms 9,10,11,12,13,14 and Emotion 15,16,17,18,19,20.
Overall quality of life (Q21) is scored as the value marked by the patient, between 0-10.

(Q1)How much does your swollen arm affect the following daily activities?
If any of the items are not applicable to you, please write N/A in the relevant answer box(es).

	Not at all	A little	Quite a bit	A lot
a) occupation	1	2	3	4
b) housework	1	2	3	4
c) combing hair	1	2	3	4
d) dressing	1	2	3	4
e) writing	1	2	3	4
f) eating	1	2	3	4
g) washing	1	2	3	4
h) cleaning teeth	1	2	3	4

(Q2) How much does it affect your leisure activities/ social life?	1	2	3	4

Please give examples of this .....

(Q3) How much do you have to depend on other people?	1	2	3	4

	Not at all	A little	Quite a bit	A lot
(Q4) How much do you feel the swelling affects your appearance?	1	2	3	4
(Q5) How much difficulty do you have finding clothes to fit?	1	2	3	4
(Q6) How much difficulty do you have finding clothes you would like to wear?	1	2	3	4
(Q7) Does the swelling affect how you feel about yourself?	1	2	3	4
(Q8) Does it affect your relationships with other people?	1	2	3	4

	Not at all	A little	Quite a bit	A lot
(Q9) Does your lymphoedema cause you pain?	1	2	3	4

(Q10) Do you have any numbness in your swollen arm?	1	2	3	4
(Q11) Do you have any feelings of "pins & needles" or tingling in your swollen arm?	1	2	3	4
(Q12) Does your swollen arm feel weak?	1	2	3	4
(Q13) Does your swollen arm feel heavy?	1	2	3	4
(Q14) Do you feel tired?	1	2	3	4

In the past week….	Not at all	A little	Quite a bit	A lot
(Q15) Have you had trouble sleeping?	1	2	3	4
(Q16) Have you had difficulty concentrating on things, e.g. reading?	1	2	3	4
(Q17) Have you felt tense?	1	2	3	4
(Q18) Have you felt worried?	1	2	3	4

(Q19) Have you felt irritable?	1	2	3	4
(Q20) Have you felt depressed?	1	2	3	4

(Q21) Overall, how would you rate your quality of life at present?

Please mark your score on the following scale:

0 1 2 3 4 5 6 7 8 9 10

poor **excellent**

Thank you for completing this form.

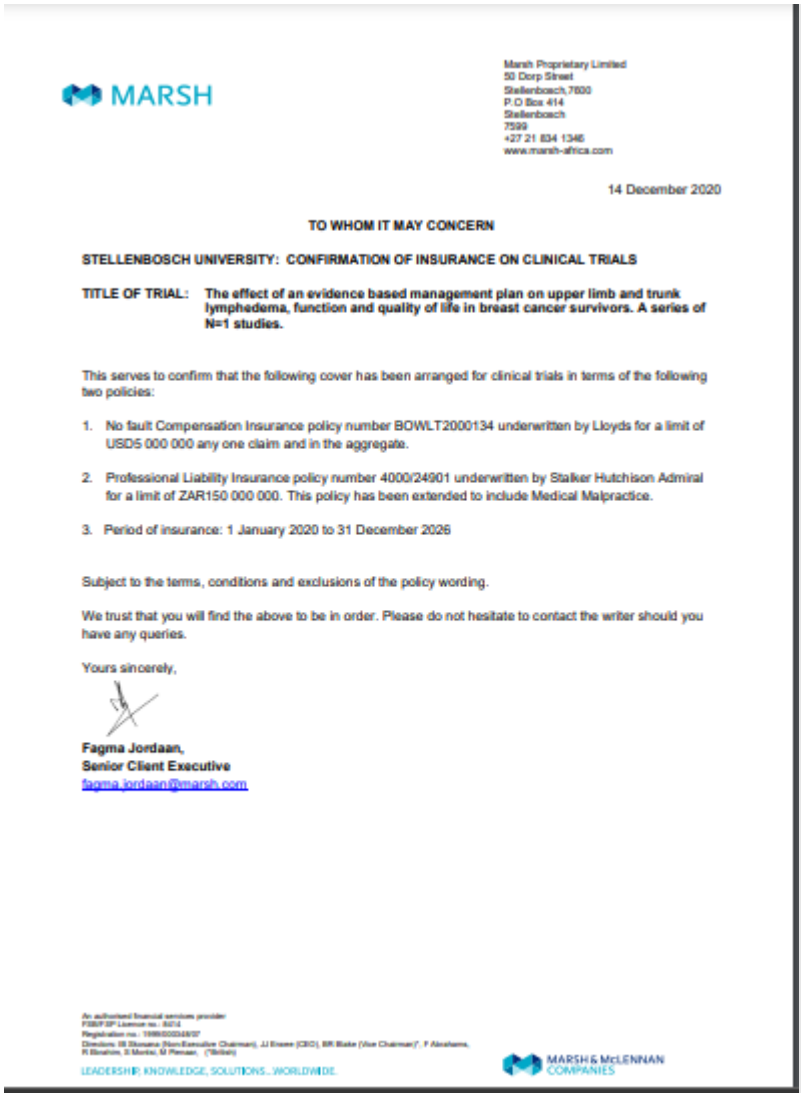
If you have any comments or queries about it, please discuss these with ……..

Dr V L Keeley, Consultant

Questions 15 to 20 have been reproduced with permission from the EORTC.

These questions are only a part of the QLQ-C30 Questionnaire.

Appendix 14: US insurance



MARSH

Marsh Proprietary Limited
50 Dorp Street
Stellenbosch,7600
P.O Box 414
Stellenbosch
7599
+27 21 834 1346
www.marsh-africa.com

14 December 2020

TO WHOM IT MAY CONCERN

STELLENBOSCH UNIVERSITY: CONFIRMATION OF INSURANCE ON CLINICAL TRIALS

TITLE OF TRIAL: **The effect of an evidence based management plan on upper limb and trunk lymphedema, function and quality of life in breast cancer survivors. A series of N=1 studies.**

This serves to confirm that the following cover has been arranged for clinical trials in terms of the following two policies:

1. No fault Compensation Insurance policy number BOWLT2000134 underwritten by Lloyds for a limit of USD5 000 000 any one claim and in the aggregate.
2. Professional Liability Insurance policy number 4000/24901 underwritten by Stalker Hutchison Admiral for a limit of ZAR150 000 000. This policy has been extended to include Medical Malpractice.
3. Period of insurance: 1 January 2020 to 31 December 2026

Subject to the terms, conditions and exclusions of the policy wording.

We trust that you will find the above to be in order. Please do not hesitate to contact the writer should you have any queries.

Yours sincerely,

Fagma Jordaan,
Senior Client Executive
fagma.jordaan@marsh.com

Appendix 15: Exit questionnaire

Participant ID : .....

Dear Participant

Thank you for agreeing to participate in this research study. The results will be utilized to assist and guide Lymphoedema Therapists in the future with regards to the management of other patients who develop Breast Cancer Related Lymphoedema.

Please would you take 5 minutes to complete the final questionnaire for this study. I value your time and participation.

Thank you very much.

Liesl Way

Please tick the appropriate box:

	YES	NO
1. Did you receive your information brochure?		
2. Did you receive an exercise brochure?		
3. Did the researcher explain your exercises adequately?		
4. Did the researcher explain your skin care routine adequately?		
5. Did you fill in your diary every day?		
6. Did you do your exercises every day?		
7. Did you follow a good skin care routine every day?		
8. Did you wear your bandages as required?		
9. Are you wearing your compression sleeve every day?		
10. Did you attend all your treatment sessions?		
11. Are you satisfied with the outcome of your treatment?		
12. Did you find it possible to comply with all the treatment and advice?		

Additional Comments:

_____
_____
_____
_____
_____
_____
_____

Appendix 16: Participant information brochure

WHAT IS LYMPHOEDEMA?

Lymphoedema is an abnormal swelling caused by a collection of lymphatic fluid in the tissues below the skin. This condition can occur in the arms, chest or trunk following breast cancer treatment and can present immediately after surgery or years after initial cancer treatment. It occurs when the lymphatic system is damaged due to the removal of lymph nodes during surgery, or as a result of radiation treatment.

HOW DO I KNOW IF I HAVE LYMPHOEDEMA?

You may notice some or all of these signs and symptoms in the affected area:

- A feeling of heaviness or fullness
- Pins and needles
- Discomfort or aching
- Painless or painful swelling
- Tightness in the skin
- Tight fitting clothing or jewellery in one specific area
- Longstanding swelling causes the skin tissue to become thickened and hardened.

CAN THIS CONDITION BE TREATED?

Lymphoedema is a chronic condition, which means there will always be a tendency for the affected area to swell. Specialised treatment is aimed at reducing the swelling and teaching you to self- manage the condition. With early diagnosis and correct treatment, you can enjoy a productive life with minimal impact on your lifestyle and quality of life.

WHAT IS THE RECOMMENDED TREATMENT?

Your treatment should be performed by a specially trained lymphoedema therapist. The treatment is known as Complete Decongestive Therapy (CDT) and consists of the following:

- Manual Lymphatic Drainage Therapy (MLD)
- Multi-layered Lymphoedema Bandaging
- Meticulous skin care
- Compression garments
- Exercise and self-massage.

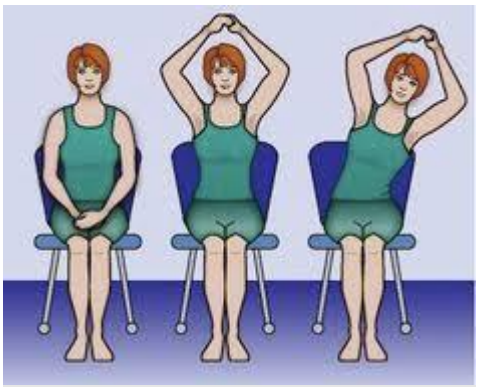
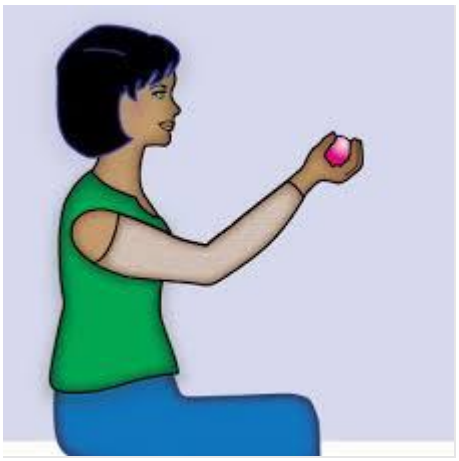
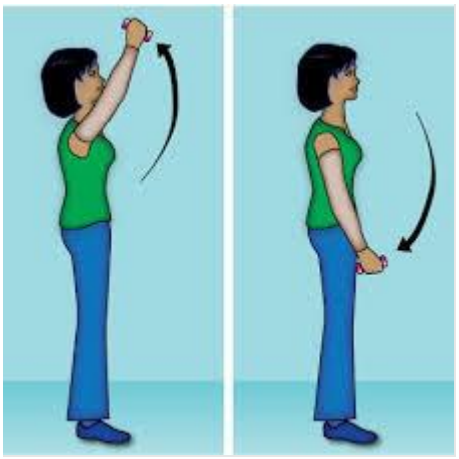
HOW CAN I REDUCE THE RISK OF DEVELOPING LYMPHOEDEMA?

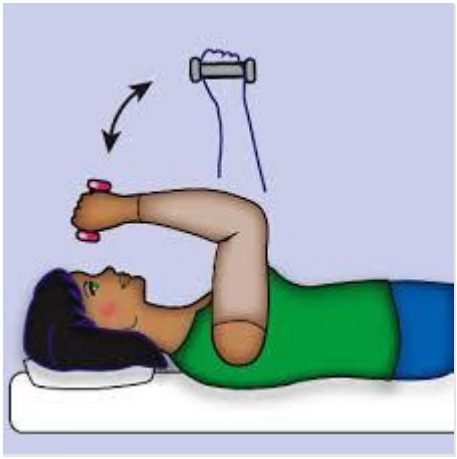
There are many things you can do to ensure you reduce your risk of developing lymphoedema.

ACTIVITY / LIFESTYLE • Gradually Build up the duration and intensity of your activity or exercise • Take frequent rest periods during activity to allow for limb recovery. • Maintain optimal weight, try to avoid weight fluctuations of greater than 4.5kg per month. • Monitor your lymphoedema during and after activity for any change in size, shape, tissue texture, soreness, heaviness or firmness. • Support your arm and trunk with a prescribed compression garment for strenuous activity Such as weight training.	**EXTREMES OF TEMPERATURE** • Avoid exposure to extreme cold e.g. ice treatment as this can be associated with rebound swelling or chapping of skin. • Avoid prolonged exposure to heat (greater than 15 minutes) especially hot tubs and saunas. • Avoid placing your limb in water temperatures above 39^{o} Celsius.
SKIN CARE – AVOID GETTING CELLULITIS • Keep your skin clean and dry. • Apply a non-petroleum based moisturiser daily to prevent chapping of your skin. • Pay attention to your nail care; do not cut your cuticles. • Use care with razors to avoid nicks and skin irritation. • Where possible, avoid punctures such as injections and blood draws. • Wear gloves while doing activities that may cause skin injury e.g. gardening, using chemicals and detergents. • If scratches or punctures to the skin occur, wash with soap and water, apply antibiotics and observe for redness. • Protect exposed skin with sunscreen or insect repellent. • IF A RASH, REDNESS, ITCHINESS, FEVER OR FLU-LIKE SYMPTOMS OCCUR CONTACT YOUR PHYSICIAN FOR TREATMENT FOR POSSIBLE CELLULITIS.	**COMPRESSION GARMENTS** • These should be well fitting and prescribed by a trained therapist. • Consider wearing a well-fitting compression garment for air travel. • It is advisable to wear a well-fitting night garment and a compression sleeve during the day. • Garments should be replaced every 6 months to ensure good outcomes.

The above recommendations form part of the National Lymphoedema Network (NLN) Risk Reduction practices. http://www.lymphnet.org

Appendix 17: Patient exercise brochure

	• Sit straight up and comfortably in a chair, feet resting on the floor. • Raise arms above your head, whilst taking in a deep breath. • Bend your trunk over to the side whilst exhaling. • Return to your staring position. • Repeat to the other side. • Repeat the entire exercise 10 times.
	• Remain seated comfortably. • Take hold of a soft stress ball in your hand, keeping your hand in your lap. • Gently bend your elbow halfway, then raise your arm to shoulder height. • Squeeze and release the ball slowly 5 times. • Lower your hand into your lap. • Repeat the exercise 10 times. • Remember to keep breathing!
	• Stand comfortably with your feet apart. • Hold a 1kg weight in your hand. • Gently raise the straight arm above your head and lower again. • Repeat the exercise 10 times. • Remember to breathe.

	• Stand comfortably with your feet apart. • Hold a 1 kg weight in your hands. • Raise your arms gently to above your head. • Lower back to your sides. • Repeat this exercise 10 times. • Remember to breathe.
	• Lie comfortably on your back with your knees bent. • Arms at your side. • Hold a 1kg weight in your hand. • Gently raise your arm to shoulder height whilst bending your elbow. • Keep your shoulder in this position and gently straighten and bend your elbow 10 times. • Lower your arm to your side. • Remember to breathe.
	• Lie comfortably on your back with your knees bent. • Hold 1 kg weights in your hands, with your arms out at 90 degrees. • Gently raise your arms up to your midline until the weights touch. • Lower your arms to the starting position. • Repeat the exercise 10 times. • Remember to breathe.

IMPORTANT:

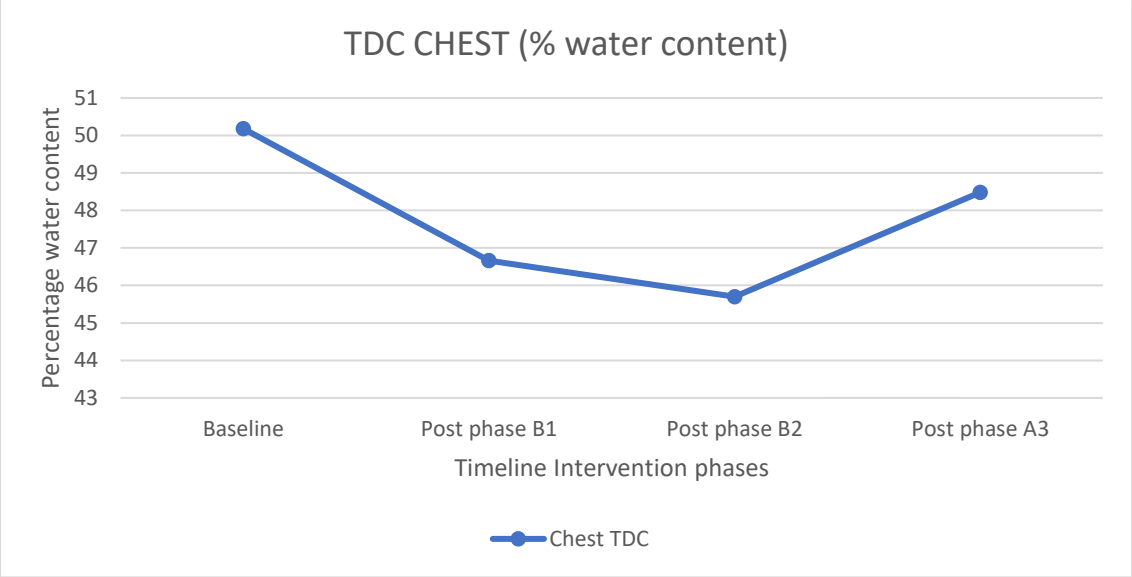
Always exercise in a cool environment.
Wear loose comfortable clothing.
Wear your compression garment whilst exercising.
Keep your exercises rhythmical, do not rush them.
Continue with deep breathing (x5) after each exercise set.
Walk at an even consistent pace for 15 minutes per day.
Use your stress ball to empty your axilla lymph nodes after each set of exercises.

Appendix 18: Compliance diary

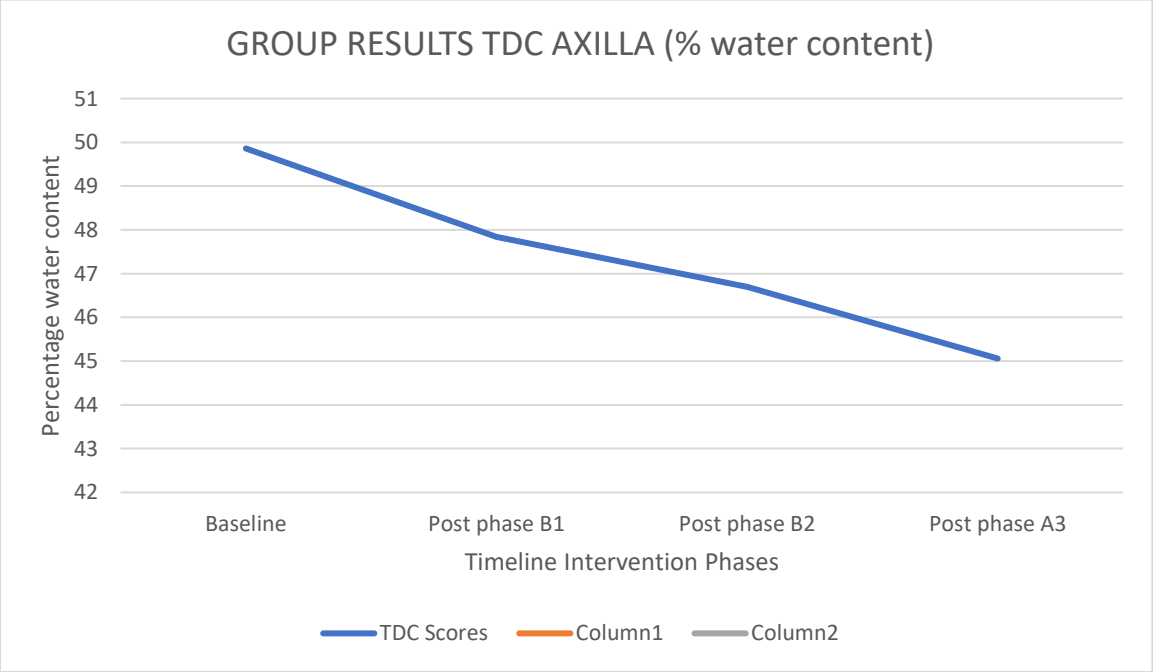
In order for you to have the best possible treatment outcome, it is important to keep up good daily habits regarding your skin care and exercise regime. This diary will assist you in keeping an accurate record of your progress at home. You will receive hard copies for each day. Please fill it in on a daily basis and bring it to your sessions so that together, we can ensure that you achieve good treatment results. Thank you.

SKIN CARE	Dates:						
Did you moisturise?							
Did you use sunblock?							
Did you check for insect bites or open wounds?							
Did you check for redness, heat or swelling?							
Did you cut your nails?							
Did you use insect repellent?							
EXERCISES							
Did you exercise today?							
Were you motivated to exercise?							
Did you breathe correctly?							
Did your arm feel tight/heavy afterwards?							
Did your trunk feel tight/heavy afterwards?							
Did you complete all the exercises?							
Did you prime your lymph nodes?							
COMPRESSION BANDAGING							
Is your bandaging/compression comfortable?							
Is the bandaging/compression chaffing you?							
Does your arm feel restricted with movement?							
Does the bandage feel secure?							
Has the bandage moved at all?							

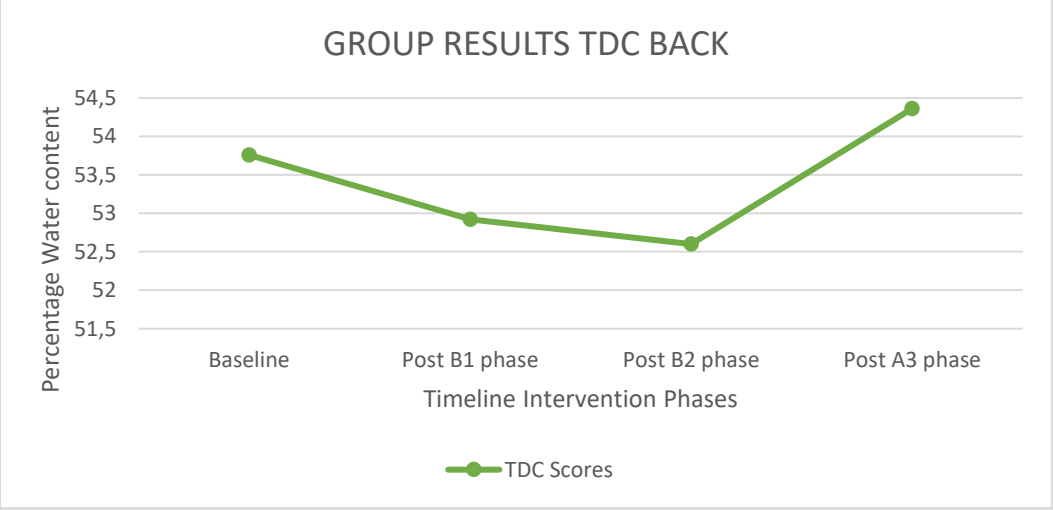
Appendix 19: Graph percentage tissue water chest: whole group



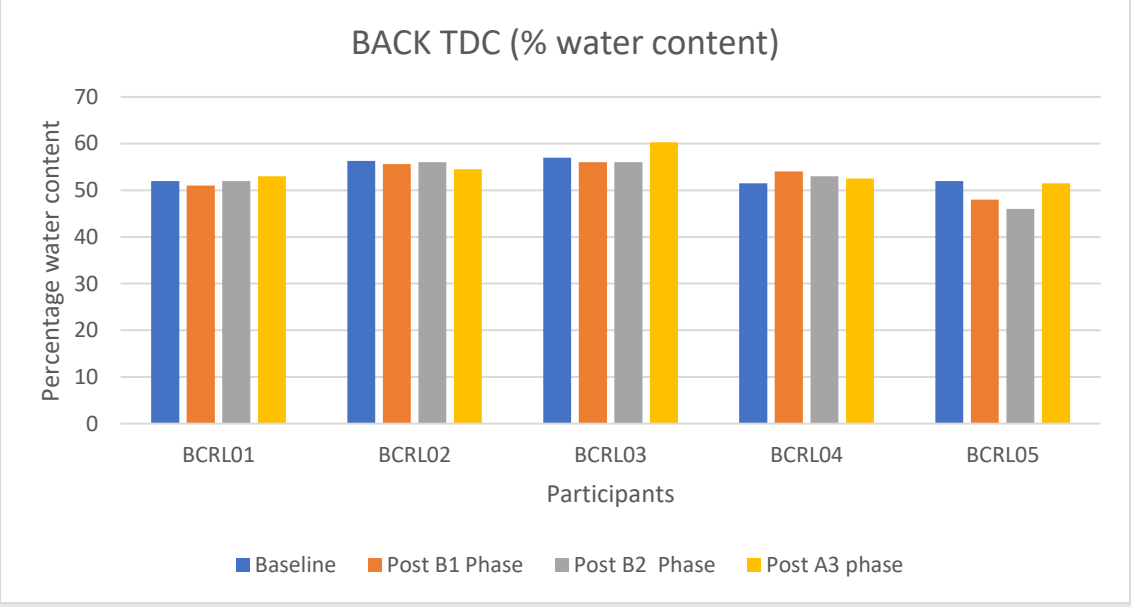
Appendix 20: Graph percentage tissue water content axilla: whole group



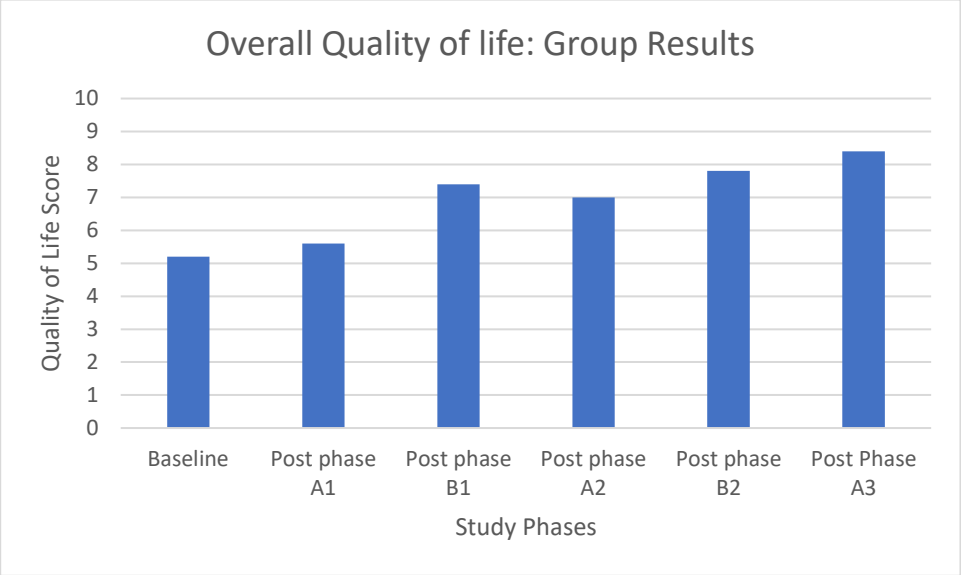
Appendix 21: Percentage tissue water content back: whole group



Appendix 22: Percentage tissue water content back: individual results



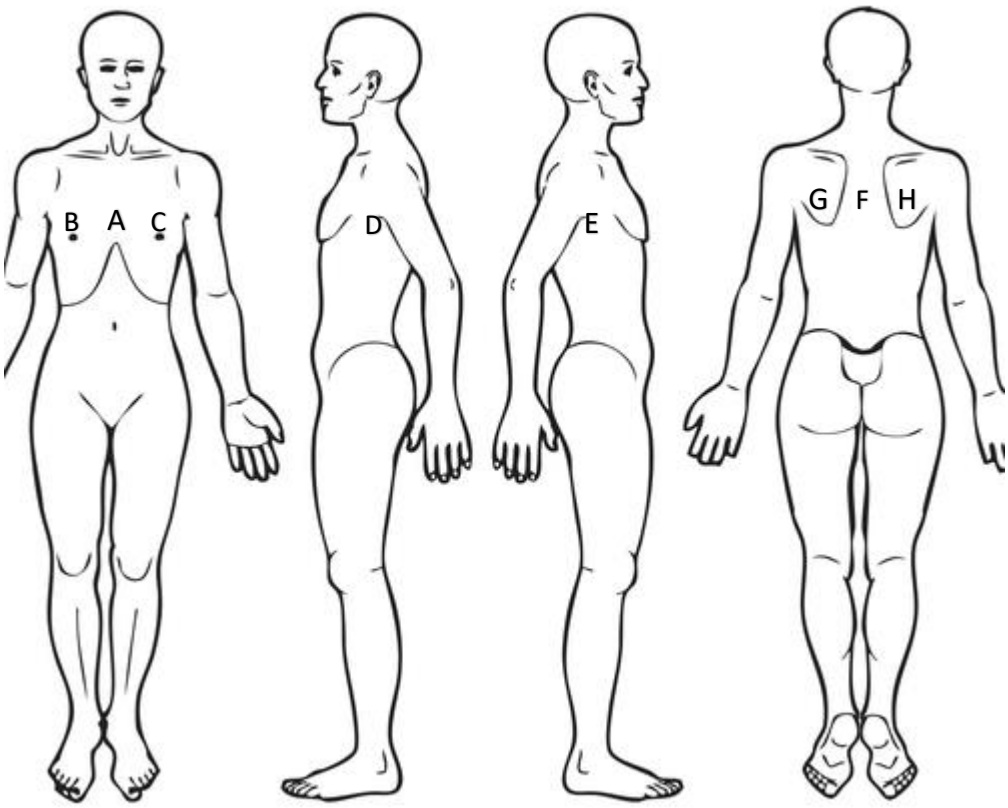
Appendix 23: Graph quality of life



Appendix 24: Tape measurement chart

DATE					
		cm	cm	cm	cm
		RIGHT	LEFT	RIGHT	LEFT
HAND	MCP				
	Web Space				
0cm	Wrist				
A	Cm				
B	Cm				
C	Cm				
D	Cm				
E	Cm				
F	Cm				
G	Cm				
H	Cm				
I	Cm				
J	Cm				
K	Cm				
L	Cm				
M	Cm				
N	Cm				
O	Cm				
P	Cm				
Q	Cm				
R	Cm				
S	Cm				
Volume	ml				

Appendix 25: TDC (percentage tissue water content) measurements trunk



KEY TO TDC MEASUREMENT POINTS OF THE TRUNK:

A: Mid-sternum at T4 level
B: Midway between A and E
C: Midway between A and D
D: Mid-axillary line T4 level
E: Mid-axillary line T4 level
F: Spinous process T4
G: Midway between D and F
H: Midway between F and E