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BOSTON UNIVERSITY

SCHOOL OF MEDICINE

Thesis

WORKING THROUGH LYMPHEDEMA: EXPLORING WOMEN'S FUNCTIONAL WELL-BEING AND QUALITY OF LIFE

by

KATHERINE SCHULTZ

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Approved by

First Reader ____

Theresa A. Davies, Ph.D.
Director, M.S. in Oral Health Sciences Program
Adjunct Assistant Professor of Biochemistry

Second Reader ____

Alphonse Taghian, M.D., Ph.D.
Professor of Radiation Oncology, Harvard Medical School
Chief Breast Radiation Oncology
Massachusetts General Hospital

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WORKING THROUGH LYMPHEDEMA: EXPLORING WOMEN'S FUNCTIONAL WELL-BEING AND QUALITY OF LIFE

KATHERINE SCHULTZ

Boston University School of Medicine, 2013

Major Professor: Theresa A. Davies, Ph.D., Director, M.S. in Oral Health Sciences Program and Adjunct Assistant Professor of Biochemistry

ABSTRACT

Background: In order to best treat breast cancer related lymphedema it is important to realize that it is a progressive, and for some, a lifelong condition requiring surveillance. Breast cancer patients are educated to be aware of the signs of lymphedema, as are physicians. This is critical to capturing those patients most in need of treatment since there are less options and more comorbidities associated with more severe swelling. Impaired shoulder usage, loss of range of motion and discomfort associated with the swelling of lymphedema can severely impact a patient's lifestyle reducing their ability to work, be self sufficient and lowering their quality of life. Since 20% or more of patient's treated for breast cancer will go on to deal with lymphedema in the long term or transiently it is necessary to understand who is most affected and at what level of swelling it is necessary to treat this condition.

Methods: As a part of the lymphedema screening protocol at Massachusetts General Hospital we were able to analyze data on 138 women with newly

diagnosed breast cancer. They were followed for at least 18 months and measured at least 3 times using the perometer, which records their arm volume and compares it to baseline. At the same time they were asked to fill out the LEFT-BC questionnaire to assess their quality of life and answer relevant questions relating to arm usage.

This data was then used to analyze how each group separated by arm size, as either having no lymphedema, less than 10% but more than 5%, and those women with 10% or more relative volume change from baseline, might show trends in different survey responses. Six questions were analyzed at time points of 6, 12 and 18 months. The questions explored were: (1) I am able to work, (2) Because of my physical condition I have trouble meeting the needs of my family, (3) I feel sad, (4) I feel nervous, (5) I am losing hope in the fight against my illness, (6) I worry that my condition will get worse. This was then analyzed using a repeated measures analysis to see the trends or differences between these groups over time. Treatment and demographic information was also recorded and compared using chi-square tests to show that the groups were similar in composition.

Results: The group with the highest level of swelling, 10% or more, had the lowest scores for quality of life and functional well-being. They were less able to work and meet the needs of their family and generally showed more sadness than the other groups. The group with low level lymphedema, 5-10% was quite variable and showed some trends similar to the group with the most severe

lymphedema but were much less affected but these women were also very similar to the group with no swelling for certain responses.

Conclusions: For a condition like lymphedema there is much variability between patients and some women may be able to function with more swelling than another while others loose much of their arm function, and quality of life. The importance of looking at how each patient is uniquely affected will be the most useful tool in treating lymphedema. The study showed that arm swelling can possibly be a part of low functional well-being and quality of life relating to having lymphedema but more research needs to be done. Many researchers are looking for the causes of this condition but more needs to be done to see how low level swelling affects the patient physically, functionally, and emotionally. This would be beneficial to the patient, allowing them to tackle a problem before it is far beyond repair, and for healthcare providers to reduce costs and put resources where they are most needed.

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ABBREVIATIONS

ALND	Axillary Lymph Node Dissection
ASCO	American Society of Clinical Oncology
BC	Breast Cancer
BCRL	Breast Cancer Related Lymphedema
cSC	Cancer Stem Cells
CT	Chemotherapy
DASH	Disabilities of the Arm, Shoulder, and Hand
DCIS	Ductal Carcinoma *In Situ*
ER	Estrogen receptor
FACT-BC	Functional Assessment of Cancer Therapy- Breast
FWB	Functional Well-Being
HT	Hormone Therapy
LE	Lymphedema
LEFT-BC	Lymphedema Evaluation Following Treatment for Breast Cancer
LMR	Longitudinal Medical Record
MGH	Massachusetts General Hospital
PR	Progesterone receptor
QOL	Quality of life
RVC	Relative Volume Change
SEER	Surveillance Epidemiology and End Results

SLNB	Sentinel Lymph Node Biopsy
SX	Surgery
XRT	Radiation Therapy

INTRODUCTION

Breast Cancer

With as many as 226,870 women expected to be diagnosed with breast cancer (BC) in 2012 (SEER, 2011) it remains the most common diagnosis of nonskin cancer in women today (Davidson, 2007). BC, like other cancers, begins when a cell undergoes a mutation causing a malignant change where the cell cycle continues replicating unwanted cells in an unregulated fashion. According to Hanahan and Weinberg, there are six general traits that account for progression to malignant cancer (Figure 1).

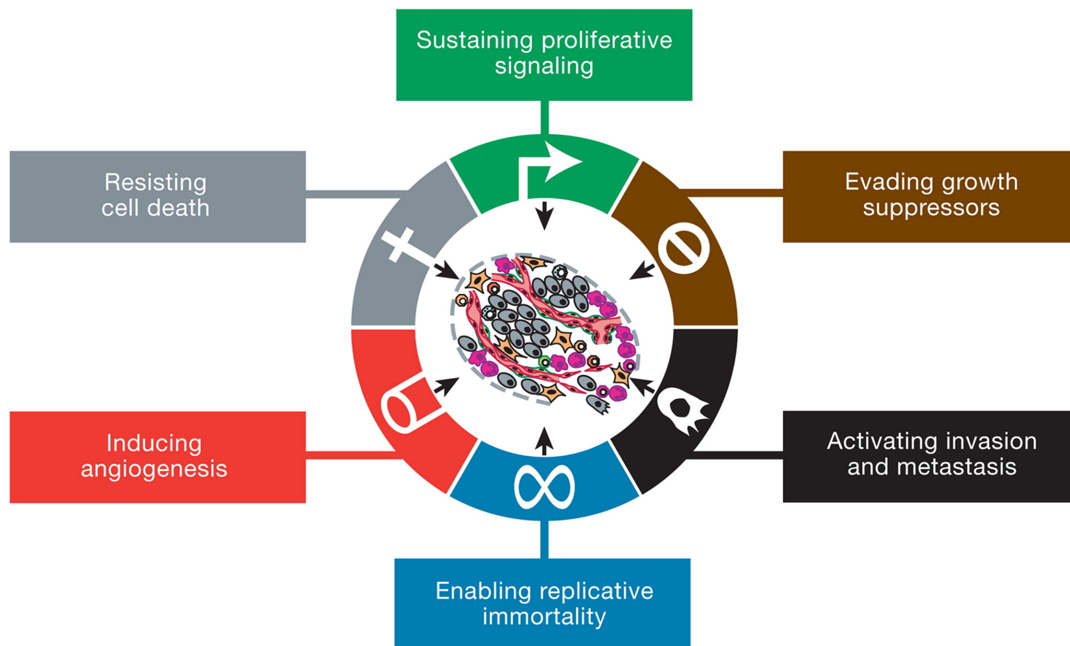

Figure 1: Acquired Capabilities of Cancer, from Hanahan and Weinberg (Cell, 2011). Control mechanisms function normally to produce healthy cells and organized tissues but mutations leading to unregulated cancer growth can be caused by one or more of the 6 pathways.

Breast cancer has distinct causes that lead to loss of cell control and the potential to progression to cancer. As women age their risk increases, also diet and alcohol use can be contributing factors, exposure to estrogen, reproductive history such as early menarche, late menopause, having children later in life or not having any pregnancies. Additionally, like many cancers, environmental exposures have all been shown to contribute to breast cancer (Davidson, 2007).

Specifically for BC, there seems to be two models regarding progression. Bombonati and Sgroi (2011) show that breast cancer may begin either sporadically, as a clonal growth from one cell that has undergone a mutation, or through cancer stem cells (cSC) where specific cells within the tumor dictate growth and progression. Both paths may play a role in the actual progression and research is ongoing to discover the specific pathways and turning points leading to pathogenesis. Understanding the pathways and the pathology of cancer is integral in treating it, as well as important in formulating targeted therapies.

Varied causes, in combination with a variety of cancer forms diagnosed, ranging from large invasive tumors to ductal carcinoma *in situ* (DCIS), suggests that this disease has a very heterogeneous nature both biologically and clinically. DCIS is known to be a precursor to invasive cancer, but previously only account for 5% of cancer diagnosis (Burstein, 2004) since it previously went unnoticed until seen on a mammogram. This has resulted in a two-fold increase in early-stage BC detection each year (Bleyer, 2012). Staging the disease based on tumor size and nodal involvement is critical in making choices regarding

treatment and management. Every individual's cancer cells can differ not only on the presence or absence of invasive qualities, but also by the different cellular markers unique to the tumor. Hormone positive cancers carry either or both estrogen and progesterone receptors (ER and PR). Another receptor common to BC tumors is the HER-2/neu receptor, which might reflect the aggressiveness of the tumor. This characteristic alone makes ER, PR, HER-2/neu positive cancers eligible for different targeted therapy approaches compared to a cancer that is triple negative for these receptors. The distinct features that a patient's cancer can present with will influence the way the disease spreads and what tools the physician is able to use to treat the cancer (Davidson, 2007).

Improved screening technology and more widespread mammography usage, have led to an increase in breast cancer diagnosis rates, a decrease in related mortality, as well as many more cases of early stage disease (Gøtzsche & Nielsen, 2011). Catching any disease at an early point usually tends to have the best-associated outcome; this is especially true of an invasive disease like some forms of breast cancer. The balancing act of not over-diagnosing patients while being able to decrease death rates from breast cancer is a topic still much debated; uncertainty about cancer progression and treatment outcomes leave many women who have early stage disease with the decision to act radically or conservatively and weigh the many risks of either choice usually based on the fear of recurrence (Morrow, 2007).

Treatments

After the initial breast cancer diagnosis is made and the staging is completed almost all patients will under go surgery. This ensures that the tumor will be removed by either a mastectomy, removal of the total breast tissue, or a lumpectomy, which conserves most of the breast tissue by removing only the tumor and a small margin of normal tissue. When the tumor is early stage there is the opportunity to individualize the surgical plan according to Hunt and Meric-Bernstam (2008); since both mastectomy and lumpectomy have similar results the decision can be patient driven for a multitude of reasons.

In order to make sure there are no residual tumor cells involving the axillary lymph nodes, the surgeon will map the sentinel nodes and determine if a less invasive sentinel lymph node biopsy (SLNB) can be performed. On the other hand, if tumor cells are extensively present within the nodes, the more thorough axillary lymph node dissection can be done (ALND). After surgery is confirmed to have removed all the cancer, then chemotherapy (CT) is begun if indicated or radiation therapy (XRT) dependent upon their case and pathology. Both of these therapies target the potential few remaining cancer cells. The majority of patients who chose lumpectomy will need to follow surgery with radiation to the breast, however, for patients treated by mastectomy, only the ones with positive axillary lymph nodes would need radiation to the chest wall and possible other high risk areas. Both groups will have less than a 10% recurrence rate after completing XRT (Davidson, 2007).

Long-term control requires hormone therapy (HT) lasting, in some cases, at least 5 years. Commonly this treatment consists of tamoxifen for estrogen receptor (ER) positive cancers or aromatase inhibitors for postmenopausal women only to control high levels of estrogen in the body. Herceptin, a monoclonal antibody drug, interacts with the HER-2/neu receptor and offers women with this tumor characteristic another treatment tool to create a personalized care plan. Additionally supportive care is offered to many patients ranging from peer support groups to social workers who can refer a patient for help coping with their disease and treatment (Davidson, 2007).

Choices

Following the diagnosis of breast cancer the patient is faced with numerous decisions and treatment choices that must be made in a relatively short amount of time. Many patients want to be a part of their decision process and find that this participation in their treatment planning brings higher satisfaction later if they are involved in the shared decision making process (Hillyer G.C. et al., 2012). However, it becomes difficult when, there is no definitively correct choice to make, a challenge that many breast cancer patients face. In these situations the doctors' opinions become more important and relying on guidelines for clinical practice can simplify a difficult process (Katz and Morrow, 2012). The American Society of Clinical Oncology (ASCO) continually updates oncologists about current practice guidelines or suggestions for treating

BC (ASCO, 2013). Some guidelines, such as the decision to omit ALND for early stage breast cancers when the less invasive SLNB is acceptable for disease-free surgery can have major implications for the patient's survivorship and quality of life (QOL) (Lyman et al., 2005).

Another aspect of the decision making process is the emerging area of genetic counseling. Patients can opt to have genetic testing done to learn if their cancer carries certain mutations known to change BC recurrence rates. If the patient has a family history with high incidence of cancer, especially in young patients, they may test for BRCA1 and 2 mutations, which are common in BC, and for BART which looks for large rearrangements in that gene (Shannon et al., 2011). The benefit of this knowledge is that it is useful in planning prophylactic measures that can reduce the patient's long-term risk. Kurian et al. (2012) have created an online tool to show patients and physicians the specific impact to outcomes associated with each possible option they are about to make.

Choosing a treatment plan also involves looking specifically at the biology of the tumor to generate the most well tailored therapy. Patients who are ER positive and node negative are also able to utilize the predictive 21-gene recurrence score assay (OncoType Dx) to find out their sensitivity to chemotherapy and risk of recurrence. Unfortunately, those who receive intermediate score results and who are faced with making a decision to undergo chemotherapy or not, may have added distress leading to a decreased QOL (Sulayman, 2012).

Choosing a path for treatment requires weighing options, being well informed, and preparing for what is to come. Some common side effects of BC therapy may include the following: arm morbidities such as lymphedema, local pain, stiffness, weakness, neuropathy, and inflammation (Hayes, 2012).

Lymphedema

One of the most difficult complications of BC treatment is lymphedema (LE), which can become a life long problem beginning soon after the initial treatment course has ended (Hunt, Askew and Cormier, 2009). LE is caused when lymph, a protein rich fluid, overwhelms transportation within the lymphatic system in that area causing swelling as seen in Figure 2 (Cemal, 2011). For BC patients this is most notable commonly caused by ALND but many cases are complicated by other disease, treatment and patient-related causes (Van der Veen, 2004). Other contributors can be axillary radiation, which causes fibrosis, or extensive positive axillary lymph nodes, both of which will block normal lymph drainage and can lead to LE (Brennan, 1996; Kilbreath, 2011).

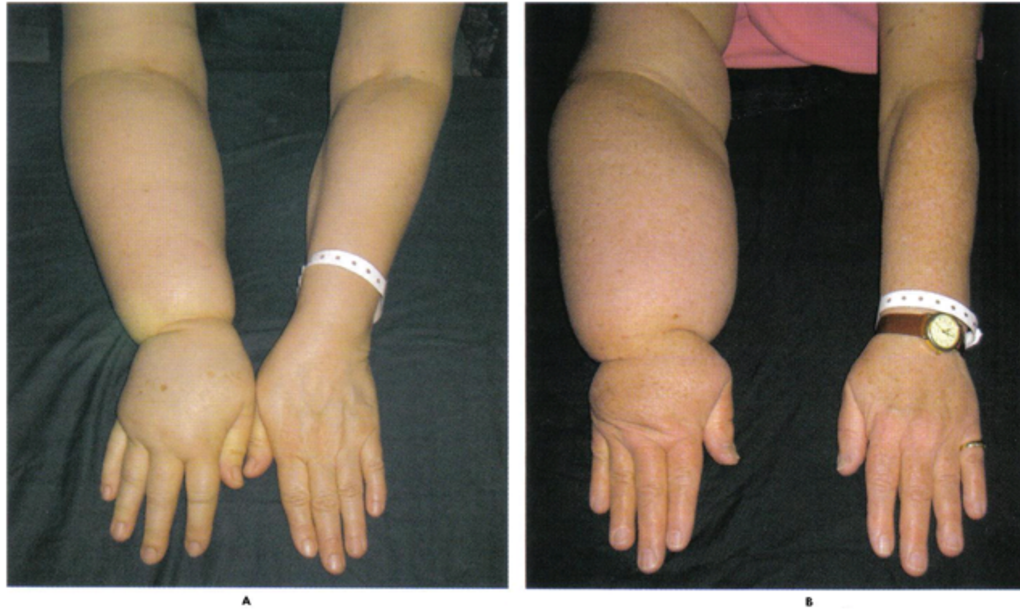

Figure 2: Lymphedema in two patients, from Women's Health & Education Center (2011). This image depicts the size difference between a normal and affected arm.

Many clinicians and researchers are still struggling to determine why some women will develop breast cancer related lymphedema (BCRL) and others with matched treatment plans will not and further research is ongoing (Paskett, 2012). Furthermore, the incidence of LE is so poorly documented that it is unclear how many women are affected at all. A Meta analysis by Erickson (2011) of 10 previous LE studies reported various rates from 0% to 56% after two years. The consensus seems to suggest an incidence somewhere between 20-30%.

Beyond inconsistencies in overall reported incidences there still remains much variation in methods for detecting LE. Widely used methods, include circumferential tape measurement and water displacement (Figure 3); both

methods are able to distinguish the presence of LE but lack consistency and repeatability (Taylor, 2006; Hunt, Askew and Cormier, 2009). Furthermore, the range of confirmed LE depends on clinical cutoffs that seem somewhat arbitrary; many women with even low or no clinical lymphedema who are experiencing symptoms may disagree with a 10% volume change from baseline as being the definition of lymphedema. Armer et al. found that a 10% volume change from baseline was a conservative cutoff point and may not include all cases of self-reported or clinically relevant LE (Armer and Stewart, 2005; Paskett, 2012). BCRL may also be difficult to detect using this method since some patients initially have arms of different sizes and it is difficult to limit all sizes of women to the basic diagnostic tools such as 2 cm differences. To be able to effectively diagnose and treat these patients' LE, there needs to be a way to identify LE as it progresses, and not only as it hits a peak value, since it is not a static condition (Ancukiewicz et al., 2012). Utilizing prospective screening allows for longitudinal data to be collected from their preoperative state through recovery, which can show temporal changes.

Figure 3: **Using water displacement measurement**, from Johansson, 2010. Water displacement is one technique used for measuring BCRL in some clinics.

One way to meet this need is to use electro-optical perometry to visualize arm volume changes (Ward, 2009). In a large-scale study of practice guidelines perometry is recommended as a more suitable measurement tool as compared to circumference methods (Harris, 2012). The Perometer is used to measure arm volumes and finds percent difference between the contralateral and ipsilateral arms. The accurate and reliable arm volume measures obtained via perometry are best qualified using the relative volume change (RVC) equation: RVC = $(A_2U_1)/(U_2A_1) - 1$, where A_1, A_2 are volumes on the side of the treatment at two different time points, and U_1, U_2 are volumes on the opposite side (Figure 4) (Ancukiewicz et al., 2011). This formula accounts for any normal asymmetry between the arms, utilizes the unaffected arm as a control, and allows for the

quantification of relative arm volume changes over time, from baseline through postoperative treatment.

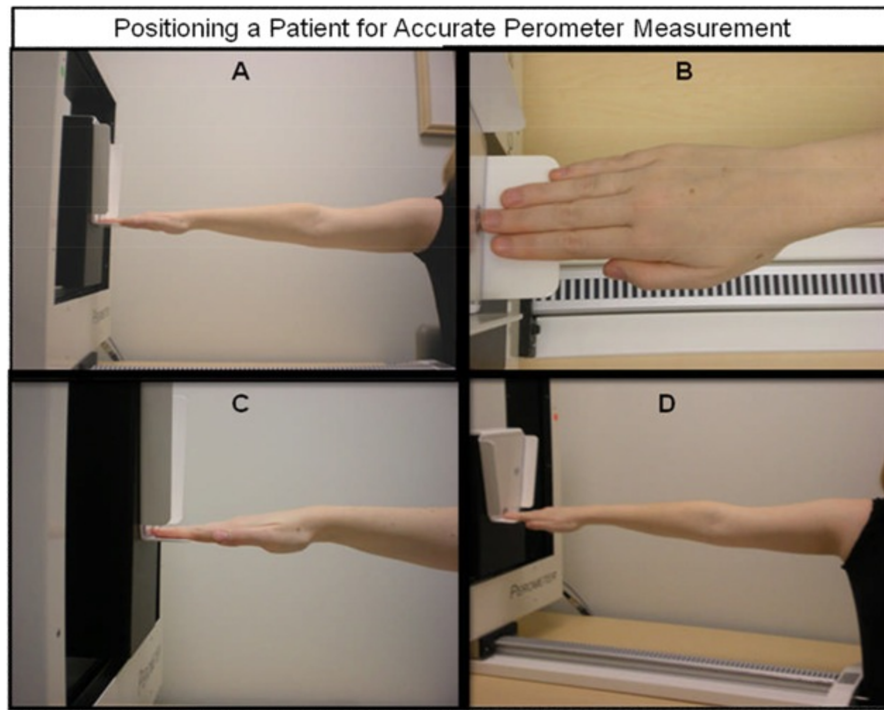

Figure 4: Depiction of the Perometer in use at the MGH, from Ancukiewicz et al. (International Journal of Radiation Oncology Biology Physics, 2011). The suggested arm placement for use of the Perometer is shown to ensure accurate and repeatable methods.

In some cases, LE has been shown to be a transient condition. Lack of evidence makes it difficult to determine if the patient will ultimately be affected in the long-term as rates of development are widely unknown. Wondering if they may need clinical management, such using a compression sleeve or physical therapy, or if the condition will resolve on its own are some of the questions patients are left facing. Hayes et al. (2008) found that up to 60% of cases were

managed without treatment and resolved within 3 months while the rest went on to be long term and chronic LE. This means that women not only face the struggles of coping with their initial BC treatment, but that soon afterwards, they must face the reality of their potential risk for developing LE, as most self reported cases of lymphedema are known to occur in the first year after treatment (Gärtner, 2010). The unknown aspect of how long the problem will last, if it will require further physical therapy, and if a compression sleeve must be worn at all times adds to the uncertainty and fear associated with LE.

Functional Well-Being and Quality of Life

LE and other post-treatment complications cause long-term consequences on survivors' function and QOL. Overall, the presence of BCRL can be a continual source of anxiety and worry for women as it persists and reminds her of the earlier cancer fears. It can make functioning normally difficult and requires understanding of the emotional issues as well as the physical problems that may include treatment or physical therapy (Maguire, 1999).

Recently, due to awareness, more patients are identifying LE as it affects their function and is noticeable to them but remains below the threshold of 10% volume change. This encourages the idea that self-reporting functional problems may be an accurate and important part of diagnosing and treating the many women dealing with low level BCRL (Pain, 2003).

According to Dorval et al, it was shown that women treated for BC, compared to matched controls, were more likely to have arm morbidities and self-reported lower QOL for some time (Dorval, 1998). Arm morbidities including tightness, swelling, numbness and pain can affect both function and obviously also influence QOL as any hindrance to using one's arm means a decrease from full potential. Even after many years, women who undergo ALND are more likely to have these limitations to function. When looking longitudinally at this data, Land et al. found that some of these arm problems seem to dissipate in some women while others continue to experience them after one year and onward (Land, 2010).

Functional well-being (FWB) is a problem for many women treated for BC with nearly one quarter of women attesting to it affecting their work and regular activities. For those with severe functional impairment, it has been shown to be as high as nearly 50% (Kopec, 2012). Stamatakos et al. (2011) reviewed much of the BCRL literature and found that it is common for women to experience pain, swelling, and heaviness in the affected limb, among other issues that restricts them from working and also accomplishing household chores. Additionally, patients face body image issues, anxiety and depression, which add to their psychosocial distress; some even require psychiatric services to address these issues.

Implications for Survivorship

With more women affected each year, and improved clinical management for the disease, there is now an ever growing population of BC survivors. As of 2009, it was estimated that there are 2,747459 women living with a history of breast cancer (SEER, 2012). Being a cancer survivor, according to the National Cancer Institute, begins at diagnosis and continues on for the entirety of the patient's life (NCI, 2013). These women face many challenges long after their diagnosis and immediate treatment. BC is known to be a slow growing disease and therefore the waiting game can be a powerful part of a survivor's life; waiting to see if there will be a recurrence can be as much of a struggle as dealing with the complications after treatment has ended (Waldrop, 2011).

SPECIFIC AIMS

In this paper, the importance of breast cancer survivors' long-term functional well-being and present and future QOL as related to LE development will be explored. The goal of the current study is to determine how differing levels of LE affect functional well-being and QOL over the course of 18 months after initial treatment. Those with higher level LE are expected to be the most severely affected as is generally found to be true compared to controls. This study will also seek to evaluate how women with lower level LE are affected compared to women without LE.

METHODS

Study Design

This observational study followed the protocol set forth under the clinical trial "Prospective Analysis of Symptoms and Lymphedema in Patients Following Treatment for Breast Cancer" at the Massachusetts General Hospital (MGH), Boston (Clinicaltrials.gov: NCT01521741). The objective of this study is to investigate the patient's long-term functional well-being and QOL changes relating to LE in a cohort of BC patients.

The Perometer was used to measure patients' arm volumes according to the methods outlined in the protocol. This allowed for a preoperative baseline measurement, and after surgery, CT and XRT and then follow up measurements every 3-8 months. In conjunction with each perometer measurement, patients completed a questionnaire regarding symptoms, function and QOL. This questionnaire is a condensed form of the combined Lymphedema and Breast Cancer Questionnaire (LBCQ), the Disabilities of the Arm, Shoulder and Hand (DASH), and the Functional Assessment of Cancer Therapy- Breast (FACT-B) validated surveys; it is referred to as the Lymphedema Evaluation Following Treatment for Breast Cancer (LEFT-BC). The LEFT-BC survey was administered each time the patient came in for a perometer measurement and was either to be completed during the visit using a tablet which uploads the data directly to a database, or later mailed in as a paper copy.

Participants

The study was open to all newly diagnosed patients who received a baseline arm volume measurement by perometry, and completed the LEFT-BC questionnaire, at baseline, prior to surgery. The eligibility criteria for inclusion in this study were: (i) must have newly diagnosed BC which is pathologically confirmed as cancer or carcinoma *in situ*, (ii) must be without previous history of breast cancer OR lymphedema, (iii) the patient must be a female, age 18 years or older, and (iv) must be without known metastatic disease and no prior surgery or radiation to the head, neck, or upper thoracic region, (v) must have a baseline measurement, (v) must have at least 18 months of follow-up. Additionally, since the measurements are taken at the Gillette Center for Breast Cancer at the MGH any patient who was not able to return for treatment and follow-up at MGH was excluded from the study. All patients treated at MGH for BC who meet the trial criteria were eligible, and those who chose to enter were enrolled in the study to be screened using both the perometer and the LEFT-BC survey.

In order to properly investigate FWB long-term it was decided that patients must have over one year of measurements in order to look beyond initial treatment related complications which are usually completed by 6 months after diagnosis (Hayes et al., 2008). Thus, participants were required to have at least 18 months of follow-up after their initial breast cancer diagnosis. This criterion yielded a cohort of 138 patients (N=138). Eighteen months was deemed suitable since many women have LE within their first year post treatment, and by 18

months 30% have developed symptoms so the majority of cases would be captured in this cohort (Hayes et al., 2008).

Data Collection and Process

The patients' survey data was either retrieved from the tablet database or from the paper survey database. Their answers to certain questions pertaining to FWB and QOL were then combined in Excel. The questions used to assess FWB were: (1) I am able to work, (2) Because of my physical condition I have trouble meeting the needs of my family, (3) I feel sad, (4) I feel nervous, (5) I am losing hope in the fight against my illness, (6) I worry that my condition will get worse.

Relevant information about the patient's treatment for BC was also included in the analysis in order to investigate the impact of specific treatments for breast cancer on their long-term FWB. Table 1 displays the treatment-related information included in the analysis. This information was obtained from the Partner's Health Care Longitudinal Medical Record system (LMR). Information regarding patient demographics was also found in the same manner and this included the following: age at diagnosis, handedness, marital status, number of children, and employment type (Table 1).

Table 1: Therapy-Related Information

Treatment/Category	*Specific information included*
Cancer	Type: in situ or invasive Pathologic stage Grade
Surgery *	Type: lumpectomy or mastectomy Nodal sx: SLNB or ALND Number of nodes removed Number of positive nodes
Chemotherapy *	Type: neoadjuvant before or adjuvant after sx Regime and dosing Number of cycles Duration of treatment
Radiation *	Dose Fields, area of directed treatment Fractions Energy level

*(Surgery, chemotherapy, and radiation also include no treatment as an option)

Information regarding patient demographics was also found in the same manner and this included: age, age at diagnosis, handedness, marital status, children, and employment.

Data Analysis

The cohort of N=138 patients was then separated by their LE status using the RVC value generated using the perometer data. Those patients who experienced an RVC of 10% and above were separated into group 1 (N=10), those with an RVC at any time in the recorded 18 months of 5% up to 10% were group 2 (N=35), and those with no previous events of an RVC above 5% were group 3 (N=93). This allowed for three groups to be compared so that differences

between those with no lymphedema and those at differing levels of LE could be discerned.

The LEFT-BC survey allows for patients to chose from five possible choices: (0) Not at all, (1) A little bit, (2) Somewhat, (3) Quite a bit, (4) Very much and for those who marked that they did not want to answer a question, or if the result was left blank, it was scored as unknown (U) The survey is easily filled out by hand or using a tablet device and responses are marked as seen in Figure 5.

	Not at all	A little bit	Somewhat	Quite a bit	Very much	Do not wish to answer
I am able to work					✔	
Because of my physical condition, I have trouble meeting the needs of my family		✔				
I feel sad			✔			
I feel nervous			✔			
I am losing hope in the fight against my illness	✔					
I worry that my condition will get worse			✔			

Figure 5: Example of Responses in the LEFT-BC Questionnaire: This shows the questions patients complete in the LEFT-BC survey and an example of how it would be marked by the patient.

A repeated measures model was chosen to compare between groups and within each group over time points of 6, 12 and 18 months. For each question used from the survey a separate analysis was done to see what specifically was contributing, if any, to a change in self-reported FWB and QOL relating to their

having LE or not. The data was analyzed using SPSS version 20 with the variables set as scale variables; output tables and graphs were generated using this program as well (IBM SPSS 20, 2013).

RESULTS

Qualitative Results

Aspects regarding patient demographics were looked at to explore similarities or differences between groups; these are shown in Tables 2 and 3.

Table 2: Treatment-related information: Surgery and other treatment variables are shown for the whole cohort and for each subgroup

Treatment information	Group 1 N=10	Group 2 N=35	Group 3 N=93	Average N=138
Median age at dx-	55	57.9	55.3	55.97
Range- (36-79)				
Surgery type-				
Lumpectomy	7 (70%)	27 (77.1%)	68 (73.1%)	102 (74%)
Mastectomy	3 (30%)	8 (22.9%)	25 (26.9%)	36 (26%)
Tumor type-				
DCIS	0	3 (8.6%)	8 (8.6%)	11 (8%)
Invasive	10 (100%)	32 (91.4%)	85 (91.4%)	127 (92%)
Type of node surgery-				
None	0	1 (2.9%)	5 (5.4%)	6 (4.3%)
SLNB	2 (20%)	27 (77.1%)	67 (72%)	96 (69.5%)
ALND	8 (80%)	7 (20%)	21 (22.6%)	36 (26.2%)
Number nodes removed-				
None	0	1 (2.9%)	5 (5.4%)	6 (4.3%)
Less than 5	2 (20%)	25 (71.4%)	62 (66.7%)	89 (64.5%)
5 or more	8 (80%)	9 (25.7%)	26 (27.9%)	43 (31.2%)
Neoadjuvant CT-	0	2 (5.7%)	3 (3.2%)	5 (3.6%)
Adjuvant CT-	6 (60%)	13 (37.1%)	36 (38.7%)	55 (39.8%)
Radiotherapy-	9 (90%)	31 (88.6%)	72 (77.4%)	112 (81%)

Table 3: Demographics information: Marital status, children and work environment percentages are included for the whole cohort and for each subgroup

Demographics	Group 1 N=10	Group 2 N=35	Group 3 N=93*	Average N=138
Marital status				
Married/partner	8 (80%)	24 (68.6%)	69 (74.3%)	101 (73.2%)
Divorced	0	2 (5.7%)	13 (13.9%)	15 (10.9%)
Single	1 (10%)	5 (14.3%)	6 (6.4%)	12 (8.7%)
Widowed	1 (10%)	4 (11.4%)	5 (5.4%)	10 (7.2%)
Children				
None	3 (30%)	9 (25.7%)	16 (18%)	31 (22.4%)
1-2	6 (60%)	17 (48.6%)	43 (48.3%)	66 (47.9%)
3 or more	1 (10%)	9 (25.7%)	30 (33.7%)	40 (29.6%)
Work environment				
Active	3 (30%)	8 (22.9%)	22 (23.7%)	33 (23.9%)
Home	4 (40%)	12 (34.3%)	35 (37.6%)	51 (37%)

*For group 3: 4 patients have no accurate data regarding children so N=89.

Even with uneven group size, all share very similar compositions; the exception being group 1 which is so small it may not be close to the average for certain criteria which are correlated to their having BCRL such as nodal surgery. One specific difference within type of nodal surgery shows that participants in group 1 underwent far more ALND than SLNB, whereas participants in groups 2 and 3 underwent predominantly more SLNB. Group 1 also received more chemotherapy than the other groups possibly since none of those cases were DCIS, while groups 2 and 3 had 8.6% DCIS.

Patient demographics were also very comparable overall. Additionally, work environment characteristics were also very similar meaning that comparisons between groups relating to this and FWB will accurately show

differences without interactions of these confounding the results. When a chi-square test was done to test for a difference between the three groups regarding work environment ($X^2 = 1.600$, df =2) there was no significance. Similarly for working at home ($X^2 = 0.449$, df =2) there was no difference across groups.

Functional Well-Being

The three groups, separated by different LE status, all show similar trends for the questions on the LEFT-BC survey regarding FWB and work such as; (Q1) I am able to work, and (Q2) Because of my physical condition I have trouble meeting the needs of my family. All three groups over time showed an improvement in their self reported feelings about their ability to work, as time is the only significant variable with a p-value < 0.0001 (Table 4). Those with more significant LE (≥10%) had lower mean scores at each time point compared to the other groups. The opposite trend is shown between group 2 and 3 there is the opposite trend seen. For question 1, higher scores show a greater ability to work and for question 2 lower scores show that their FWB was less affected; this difference is based on the wording of the questions.

Table 4: Mean Scores for Questions 1 and 2: (1) I am able to work and (2) Because of my physical condition I have trouble meeting the needs of my family

Group	Mos	Q1 Mean	Q2 Mean
1	6	2.800	.900
	12	3.600	.400
	18	3.500	.500
2	6	3.364	.471
	12	3.697	.176
	18	3.697	.147
3	6	3.299	.345
	12	3.609	.250
	18	3.552	.155

The within subjects repeated measures results for question 1 shows that the interaction of time is significant (p-value < 0.0001, F= 12.912) but for the interaction of time by groups it is not significant (p= 0.409, F=0.998) when sphericity of the data is assumed, which it can be by SPSS with significance of p < 0.0001 (Figure 6).

Within subjects for question 2 the interaction of time is significant (p-value < 0.0001, F= 9.184) but for the interaction of time by groups it is not significant (p= 0.286, F= 1.260) (Figure 7).

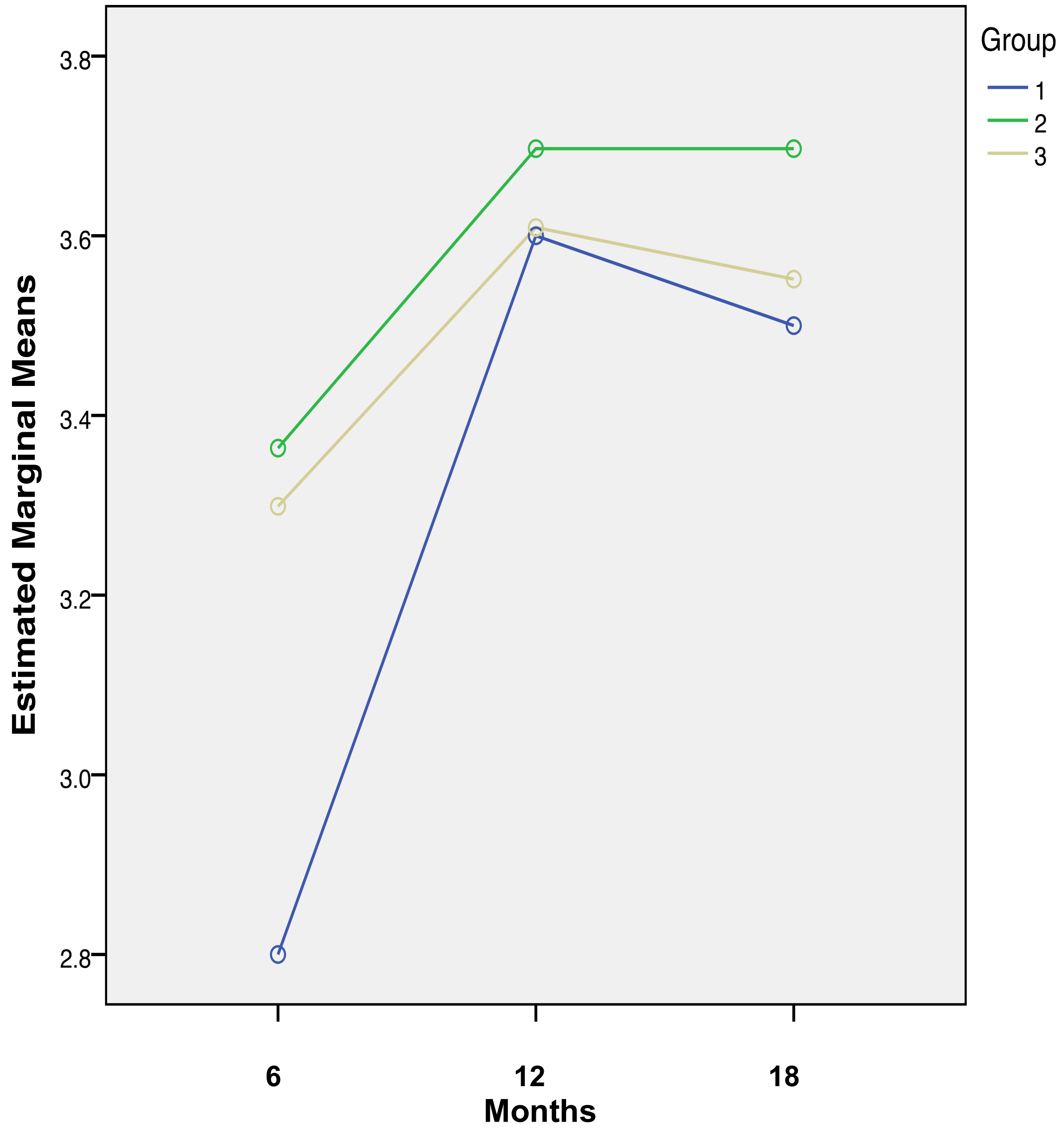

Figure 6: Change in "I am able to work" responses over time: (Group 1: ≥ 10%, Group 2: 5% to 10%, and Group 3: less than 5%) those with the most significant LE in group 1, had the lowest initial scores regarding their ability to work, while the other two groups showed similar trends over time but with group 2 having the best responses.

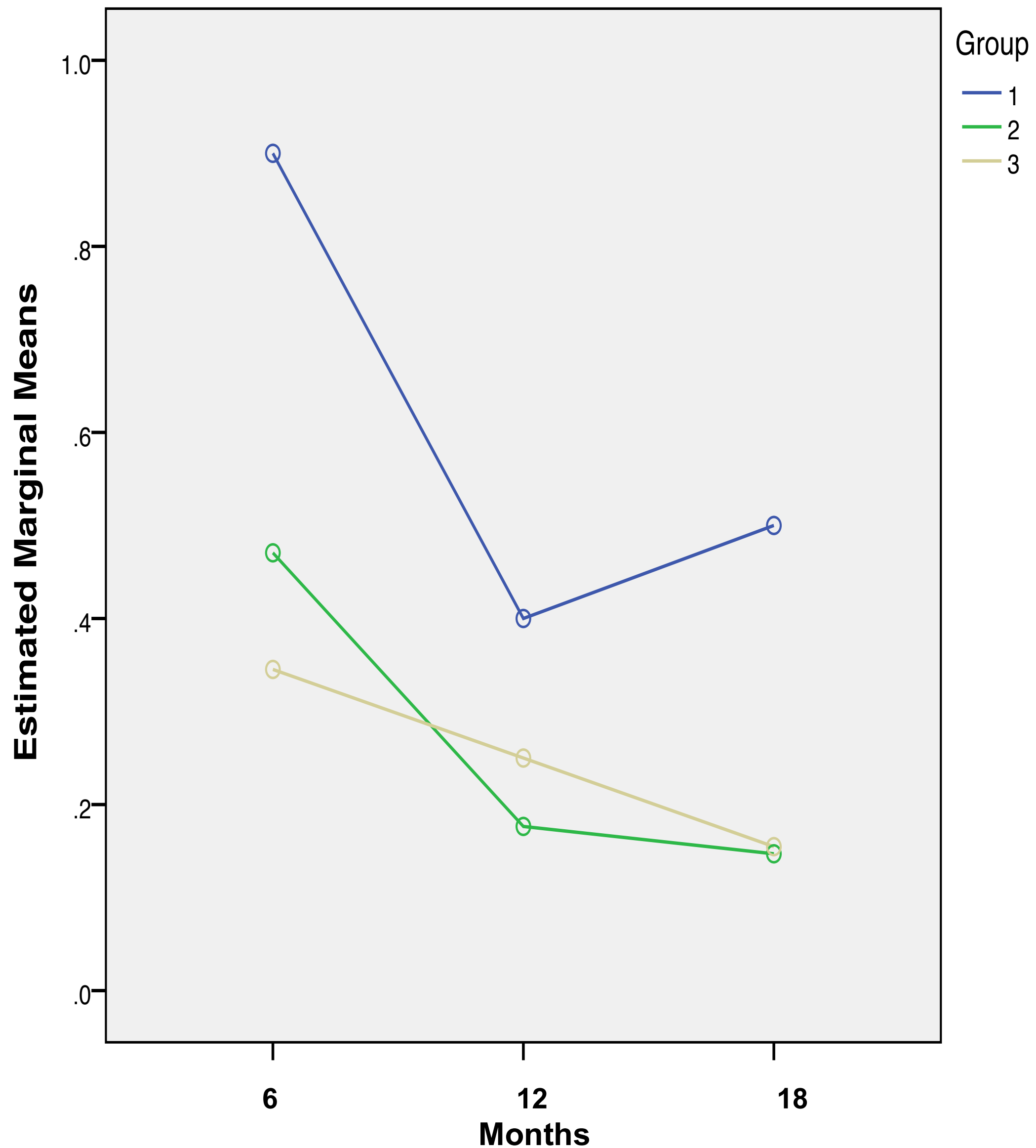

Figure 7: Change in "Because of my physical condition I have trouble meeting the needs of my family" responses over time: This graph shows that those with 10% LE in group 1 seemed to be most affected when it comes to meeting the needs of their families while groups 2 and 3 have overall lower mean scores that those patients in group 1.

Present Emotions

To assess QOL at each time point the questions (Q3) I feel sad, and (Q4) I feel nervous were included in separate analyses with values shown in Table 5.

Table 5: Mean Scores for Questions 3 and 4: (3) I feel sad, and (4) I feel nervous

Group	Mos	Q3 Mean	Q4 Mean
1	6	1.111	.889
	12	1.111	1.000
	18	1.333	1.111
2	6	.571	.743
	12	.514	.629
	18	.486	.514
3	6	.977	1.227
	12	.828	1.011
	18	.770	1.000

Emotional well-being and QOL scores for all groups were low, showing none of the groups had significant negative responses during the 18 months following treatment. As some groups decreased their level of sadness and other increased it shows time is not a contributing factor (p= 0.774, F= 0.256). There was no interaction between groups seen for either Question 3 (p= 0.543, F= 0.775) or Question 4 (p= 0.512, F= 0.822) (Figure 8).

The same trends were seen in responses to Question 4 over time and also showed that time was not significant (p= 0.702, F= 0.354). Group 2 had the overall lowest scores and both group 2 and 3 showed improvement over time while group 1 reported higher scores for sadness and nervousness (Figure 9).

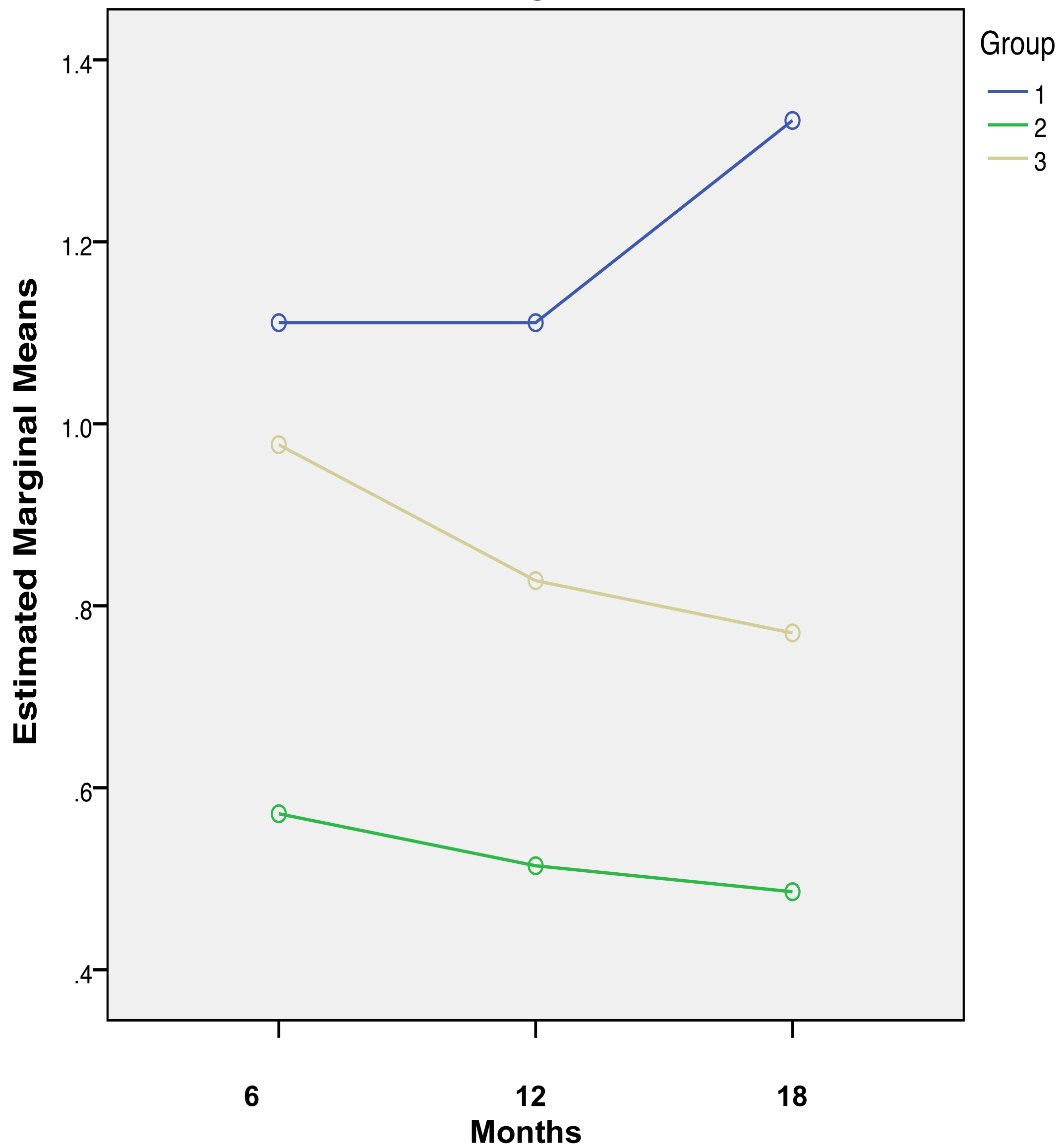

Figure 8: Changes in "sadness" over time: From the plot for question 3, group 2 had the overall lowest scores; they decreased over time showing less sadness as time went on. Those in group 3 also showed less sadness overtime. Group 1 responded in an opposite trend showing more sadness over time, and were the highest scorers showing an overall higher level of sadness than the other two groups.

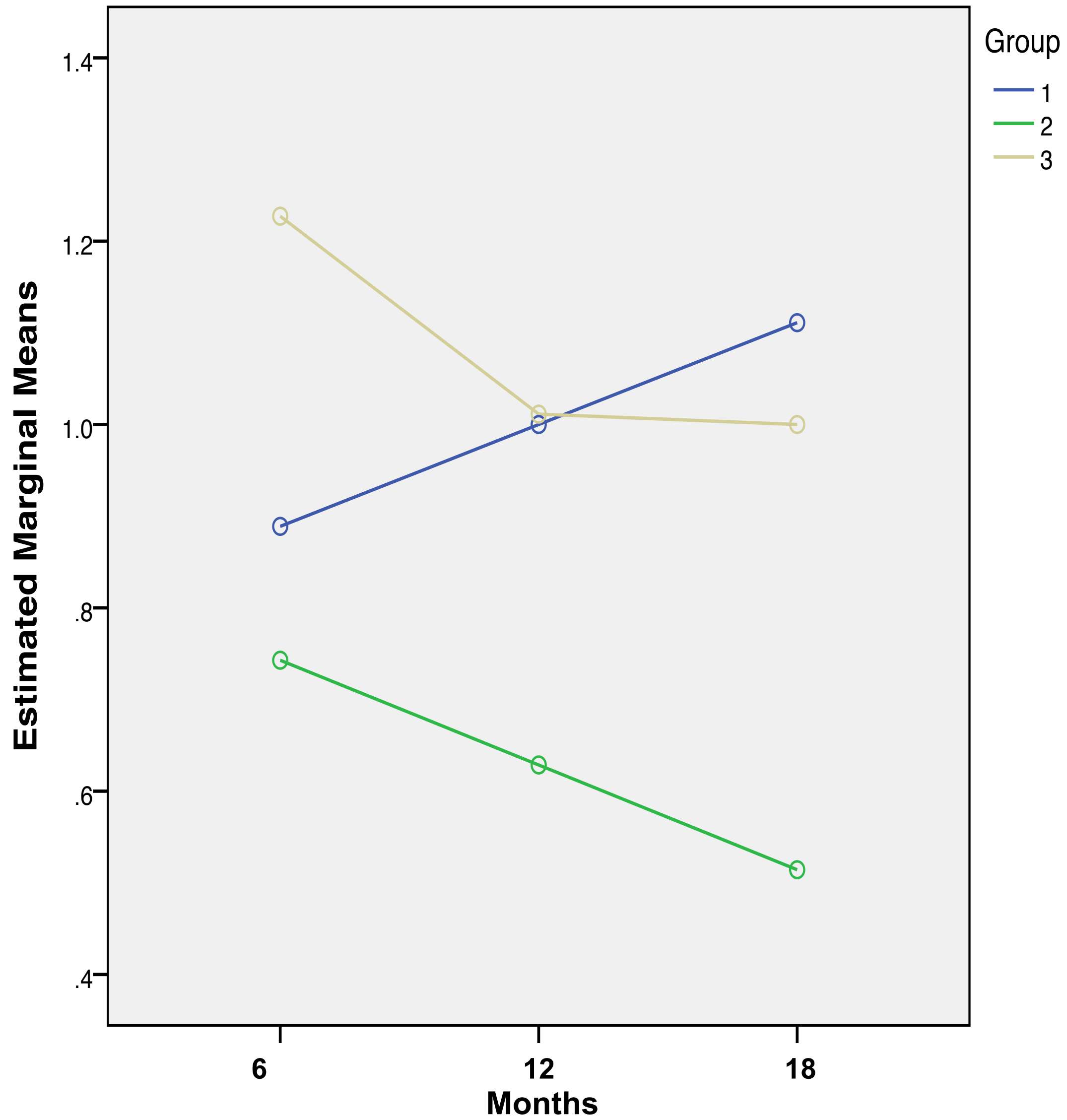

Figure 9: Changes in “nervousness” over time: Group 2 had the lowest scores overall and experienced a decrease in nervousness overtime. The women in group 3 had the highest scores initially but decreased longitudinally. As time went on, those in group one gradually increased their level of nervousness and ended at 18 months with the highest scores of the three groups.

Future Fears

The questions that address future fears and QOL were: (Q5) I am losing hope in the fight against my illness and (Q6) I worry that my condition will get worse (Table 6).

Table 6: Mean Scores for Questions 5 and 6: (5) I am losing hope in the fight against my illness, and (6) I worry that my condition will get worse

Group	Mos	Q5 Mean	Q6 Mean
1	6	.111	1.300
	12	.111	1.100
	18	.111	1.200
2	6	.000	.909
	12	.114	1.152
	18	.114	1.182
3	6	.045	1.128
	12	.034	1.023
	18	.023	.977

For question 5 there is no significance for time (p = 0.685) or between groups (p = 0.265). All three groups had similar, low level scores close to 0, representing little to no loss of hope in their fight (Figure 10).

The results for question 6 shows that group 1 had the highest overall scores at all time points. Within subjects analysis for question 6, showed that time is not significant (p = 0.954, F= 0.047) and for the interaction of time across groups is also not significant (p= 0.061, F= 2.283) for this question (Figure 11).

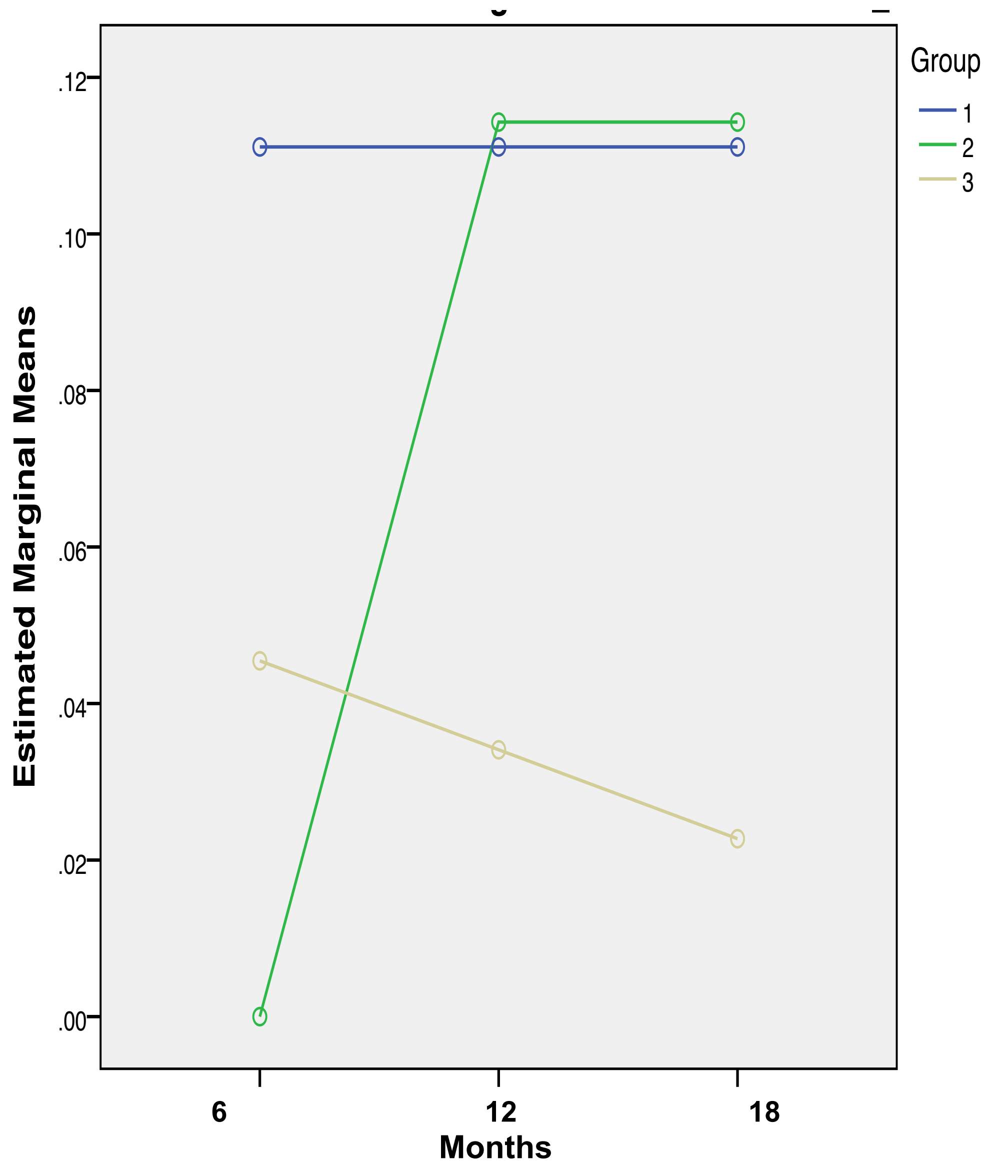

Figure 10: Change in "I am losing hope in the fight against my illness" responses over time: The most affected and the least affected groups are separated the most showing a difference in responses. More women in group 3 showed more hope, and had overall lower scores, and this decreased over time. The group 1 women had slightly higher scores showing an increase in responses of losing hope in the fight against their disease, and this remained constant during the whole duration. This is not seen in group 2, however. These women jump from the lowest scores to the highest within the first year and remain higher than even those in group 1.

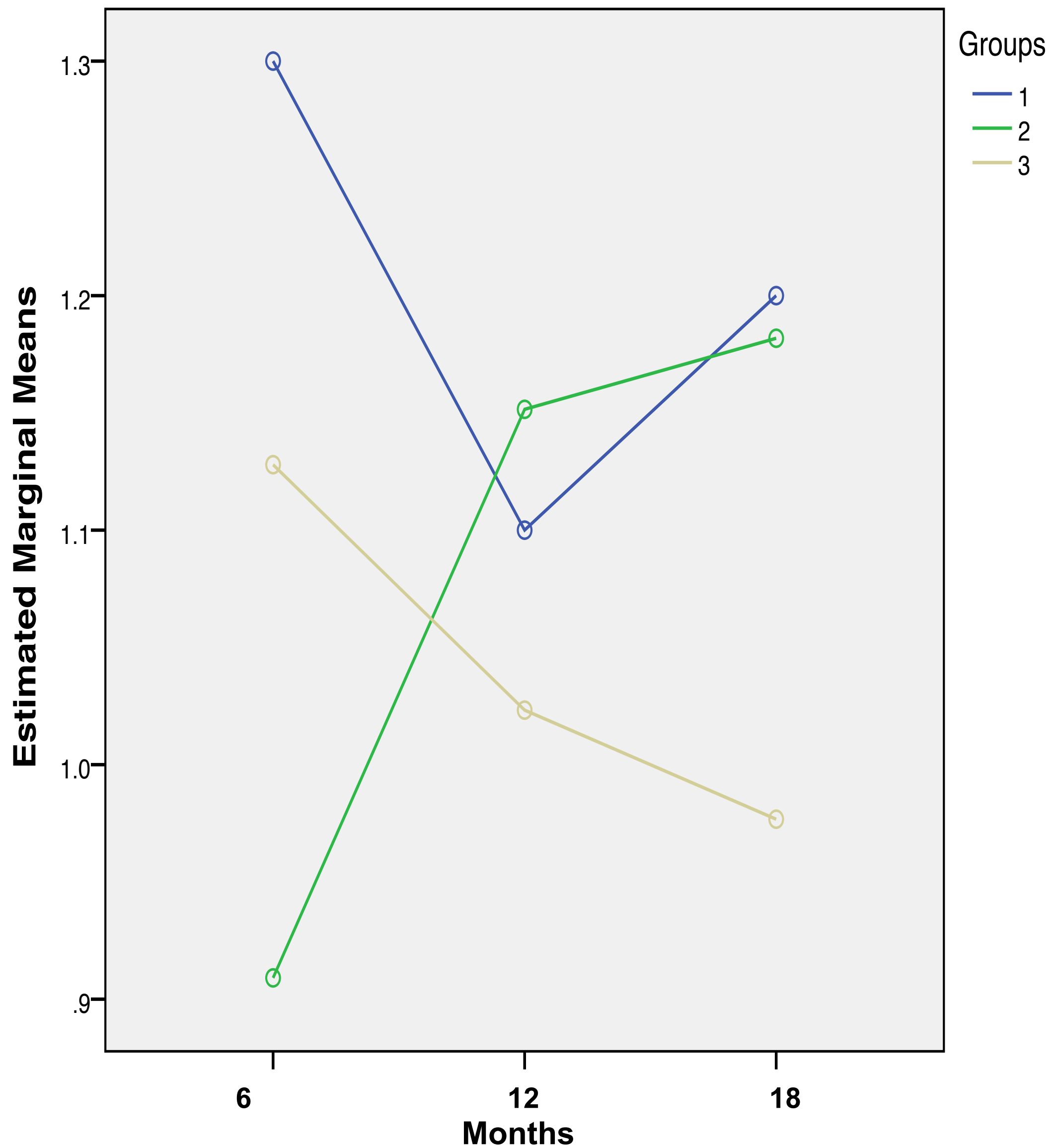

Figure 11: Changes in "I worry that my condition will get worse" responses over time: Across all three groups there are other aspects affecting their answers as no trends are really seen regarding their level of worry over time. Group 1 has an initial decrease and then a gradual recurrence of worry at 18 months. Group 2 women show increased worry about their condition over time while group 3 shows a decreasing trend towards worry at one year and 18 months after baseline. Again, group 2 begins with the lowest scores but drastically increases to the highest score at one year above both other groups.

DISCUSSION

Functional Well-Being

As expected those women with 10% RVC showed overall more of an effect of their condition resulting in limitations in ability to work and difficulty meeting the needs of their families. Having LE, therefore, may impact FWB especially for those with significant swelling although further investigation is needed.

Both groups with LE show significant improvements in FWB from the beginning of their treatment to the first 12 months, but show much less of an increase out to the 18 month data point. This is not seen in the group without LE possibly since they are steadily improving over time due to the usual time course for recovery from BC therapy and treatment. Possibly the patients with LE see less improvement from 1 year to 18 months out due to the lingering complications of their LE which can affect their FWB even once regular healing and adjuvant treatments have ended. Those women experiencing some effects of LE and the lingering fear and distress that accompany the condition (Waldrop, 2011) may feel less able to work and believe that they are still affected in meeting the needs of their families due to their BCRL.

The inconsistent trends seen in groups 2 and 3 might suggest that other factors are at play. The effects of specific surgeries and treatments may have been confounding variables especially in questions regarding their ability to work

and FWB. Many women experience fatigue, loss of energy (Rosedale, 2010) and cardiac toxicity (Khouri, 2012) after breast cancer treatment especially due to chemotherapy use. Over time the changes seen may have been caused by this interaction as well as due to the LE. According to Ganz et al. (2011) it is known that QOL usually does significantly improve in the year following breast cancer treatment, regardless of the type or severity of the treatment. Those with more severe and persistent symptoms tend to be those who did receive chemotherapy. Conversely, according to a review of the literature by Lee et al. (2008) it was concluded that radiation was not a precipitator of arm problems although it did cause some problems with shoulder function, and it also was not a cause for lowered QOL.

Taking this into account, it seems that the low level LE group and the group unaffected by LE show similar results for reasons relating to their initial treatment, radiation, and chemotherapy as well as their LE status. It would be good to see where these patients chart later on, if their LE resolves and how these things affect their condition and FWB.

Present Emotions

Over time, those with low levels of LE and no LE have less sadness and nervousness over time. Women in group 1, however, have more of both of these negative emotions over time. It is possible that their long lasting condition negatively impacts their day-to-day QOL by causing them more distress and

sadness than other groups. Those women with low level LE had the lowest scores of all groups for both sadness and nervousness. This may have been due to the fact that it was a small group, whereas, group 3 is much larger and any outliers may have more of an effect. It is important to note that on average none of the three groups had more than an average of “somewhat” sadness or nervousness.

Emotions can vary so much over time and since these data points are just one-day snapshots, therefore, they do not represent all of these likely changes over time. Also sadness and nervousness are impermanent emotions not only related to only LE but a range of other stressors both health-related and personal. Up to one-third of BC patients are so affected by their condition that it leads to depression, anxiety disorders, or adjustment problems (Maguire, 1999).

Future Fears

The question, “I am losing hope in the fight against my illness” had the lowest overall scores among groups of all the questions analyzed. Initially, it was not thought that this would be so polarizing. The community here at MGH is a critical part of their confidence since compassionate care and positivity can bring a lot of calm to worried patients. The strong community of all BC survivors also plays a role in their refusal to quit or lose hope. According to Documet et al. (2012), women with BC defined survivorship not only as being in a cancer free state after treatment, but as a part of their outlook on life. They believed in

helping others on their journey through cancer, being a source of strength for others, and helping find positivity in setbacks and adversity. For all of the groups, the low scores reflected this positivity in outlooks. Group 2 was the only group to have a higher perceived loss of hope, but since it was a small sample it may also be due to by small sample size. However, it may also show some correlation between developing LE and an impact on future fears. Group 1 had slightly higher scores than the other groups and remained unchanged overtime suggesting that their BCRL may be tied to this loss of hope.

Fear of the future, of recurrence, and fears for one's family are found to be issues that affect all women with breast cancer (Waldrop, 2011). This was seen slightly in this cohort as well, although overall the scores were low but still correlated with time. As the recovery process reached into the second year both groups affected with LE had significant jumps in worrying if their condition would get worse. This later time trend is not seen for group 3 as they become less and less worried over time as their treatments end and recovery stabilizes. The lymphedema patients are not following this trend possibly due to the daily reminder of LE. Group 2 with the low level of LE showed even worse scores than those with 10% RVC at one year. This dramatic difference may show the impact of developing LE, at any level, has on worry.

Many breast cancer survivors experience higher distress, and lower QOL during their treatment and for years to come. This implication carries over to the family members and can create additional concerns for the patient about their

and their family's future (Waldrop, 2011). The cycle of worry leads many patients to withhold these concerns from their physicians while they confirm their poor outlook themselves, thus reinforcing this negative psychological coping (Maguire, 1999).

Limitations

From our data it is clear that the LEFT-BC survey as a whole is quite helpful in assessing the patient's QOL relating to lymphedema at that point in time. However, each question separately only targets a specific emotion or aspect of life. Therefore the answers may be related to how they feel that day regardless of their condition in the month before, and if their condition is affecting their mood or function that day. What is seen may also be just a snapshot rather than the actual complexities of the condition over time, so more frequent data points could be used for those patients during an episode of LE or those already with clinical BCRL.

Macefield et al. (2013) found that patient-reported outcomes in arm morbidity may be more valuable than clinical cancer outcomes since they are able to show how different aspects of treatment affect arm morbidity and QOL in the short term. This means that the data gathered here can reflect how these women's recoveries changed overtime and developed into a life of survivorship where improvement in all aspects of FWB and QOL is the main goal.

Selection bias accounts for some of the limitation of this study. All baseline new breast cancer patients are approached to be involved in the screening but some are unable to return to the MGH, may chose to not come to the perometer room to be measured, or fail to return their questionnaires. Additionally, those with ALND and more severe cases may be a higher proportion of patients screened since they are more at risk for developing LE, thus more closely followed and willing to participate more frequently.

Future Studies

Lymphedema diagnosis and management needs to become more uniform to better serve the patient and the healthcare field overall. Hayes et al. recommend that immediate prospective surveillance of patients may be beneficial since it notifies the patient while they are in the hospital setting and can still receive treatment, and it may help target minorities and women in lower socioeconomic groups. They also showed that it is feasible in a breast clinic setting already (Hayes, 2012).

From a healthcare perspective, lymphedema causes a serious increase in post-treatment spending according to Shih et al. who found an additional 2 years cost of BCRL ranging between $14,00-$23,000 for all related medical expenses (Shih, 2009). Screening may be a tool to decrease this as early detection leads to a substantial decrease in cost from over $3,000 to treat one individual to only $600 (Stout, 2012). This is one area where a complication of BC treatment that is

well understood by both patient and physician can be managed and not only left to chance. While developing BCRL is still uncertain in each patient this begins to bring some management to a confusing and complicated world for breast cancer survivors.

Exercise after breast cancer treatment may be another way to help improve function without causing arm morbidity or being harmful to QOL as seen in the RESTORE trial (Anderson, 2012). This may present a way to improve patients health and decrease LE problems all with less healthcare spending.

CONCLUSION

In conclusion, the impact of developing LE, at any level, on a woman recovering from breast cancer cannot be overlooked as it affects more that 20% of all patients. It affects their functional well-being, their emotional well-being, their QOL and fears for the future. Lymphedema education has enabled women to understand the changes associated with the progression of the condition so that they can become an active part of their treatment. Self reported LE could be found as a slight volume change and should be evaluated and managed. The patients seen here with 10% or more RVC are usually the most severely affected when it comes to function and QOL, but it is important to not forget that those with lower levels of LE, whether measured using perometry, measuring tape, or by self report may also be personally affected even if not clinically classified as having LE. Diagnosing a condition that progresses and changes over time requires the ability to accommodate the need when it is found. Those requiring treatment and management at all levels deserve attention; the emphasis on returning all patients back to full function and restoring a high QOL should remain the goal overall regardless of numbers.

REFERENCES

Ancukiewicz, M., Miller, C. L., Skolny, M. N., O'Toole, J., Warren, L. E., Jammallo, L. S., … Taghian, A. G. (2012). Comparison of relative versus absolute arm size change as criteria for quantifying breast cancer-related lymphedema: the flaws in current studies and need for universal methodology. *Breast Cancer Research and Treatment*, *135*(1), 145–152.

Ancukiewicz, M., Russell, T. A., Otoole, J., Specht, M., Singer, M., Kelada, A., … Taghian, A. G. (2011). Standardized Method for Quantification of Developing Lymphedema in Patients Treated for Breast Cancer. *International Journal of Radiation Oncology Biology Physics*, *79*(5), 1436–1443.

Anderson, R. T., Kimmick, G. G., McCoy, T. P., Hopkins, J., Levine, E., Miller, G., Mihalko, S. L. (2012). A randomized trial of exercise on well-being and function following breast cancer surgery: the RESTORE trial. *Journal of cancer survivorship: research and practice*, *6*(2), 172–181.

Armer, J. M., & Stewart, B. R. (2005). A Comparison of Four Diagnostic Criteria for Lymphedema in a Post-Breast Cancer Population. *Lymphatic Research and Biology*, *3*(4), 208–217.

American Society of Clinical Oncology (ASCO) n.d. Retrieved on March 20, 2013 from http://www.asco.org/guidelines/breast-cancer

Bleyer, A., & Welch, H. G. (2012). Effect of Three Decades of Screening Mammography on Breast-Cancer Incidence. *New England Journal of Medicine*, *367*(21), 1998–2005.

Bombonati, A., & Sgroi, D. C. (2011). The molecular pathology of breast cancer progression. *The Journal of Pathology*, *223*(2), 308–318.

Brennan, M. J., DePompolo, R. W., & Garden, F. H. (1996). Focused review: Postmastectomy lymphedema. *Archives of Physical Medicine and Rehabilitation*, *77*(3), S74–S80.

Burstein, H. J., Polyak, K., Wong, J. S., Lester, S. C., & Kaelin, C. M. (2004). Ductal Carcinoma in Situ of the Breast. *New England Journal of Medicine*, *350*(14), 1430–1441.

Cemal, Y., Pusic, A., & Mehrara, B. J. (2011). Preventative Measures for Lymphedema: Separating Fact from Fiction. *Journal of the American College of Surgeons*, *213*(4), 543–551.

Davidson, N. E., (2007). Breast Cancer. *Oncology*. American College of Physicians' Medicine, 1-16. Available from, http://acpmedicine.com.ezproxy.bu.edu/acpmedicine/institutional/instSearchReader.action?bookId=ACP&chapId=1183&partId=part13.50&type=chapID&start=0&heading=chapter&from=Chapter&hitStart=0

Documet, P. I., Trauth, J. M., Key, M., Flatt, J., & Jernigan, J. (2012). Breast cancer survivors' perception of survivorship. *Oncology nursing forum*, *39*(3), 309–315.

Dorval, M., Maunsell, E., Deschênes, L., Brisson, J., & Mâsse, B. (1998). Long-term quality of life after breast cancer: comparison of 8-year survivors with population controls. *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*, *16*(2), 487–494.

Erickson, V. S., Pearson, M. L., Ganz, P. A., Adams, J., & Kahn, K. L. (2001). Arm Edema in Breast Cancer Patients. *Journal of the National Cancer Institute*, *93*(2), 96–111.

Ganz, P. A., Kwan, L., Stanton, A. L., Bower, J. E., & Belin, T. R. (2011). Physical and psychosocial recovery in the year after primary treatment of breast cancer. *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*, *29*(9), 1101–1109.

Gärtner, R., Jensen, M.-B., Kronborg, L., Ewertz, M., Kehlet, H., & Kroman, N. (2010). Self-reported arm-lymphedema and functional impairment after breast cancer treatment – A nationwide study of prevalence and associated factors. *The Breast*, *19*(6), 506–515.

Gøtzsche, P. C., & Nielsen, M. (2011). Screening for breast cancer with mammography (Review). In *Cochrane Database of Systematic Reviews*. John Wiley & Sons, Ltd.

Hanahan, D., & Weinberg, R. A. (2011). Hallmarks of Cancer: The Next Generation. *Cell*, *144*(5), 646–674.

Harris, S. R., Schmitz, K. H., Campbell, K. L., & McNeely, M. L. (2012). Clinical practice guidelines for breast cancer rehabilitation: syntheses of guideline recommendations and qualitative appraisals. *Cancer*, *118*(8), 2312–2324.

Hayes, S. C., Janda, M., Cornish, B., Battistutta, D., & Newman, B. (2008). Lymphedema after breast cancer: incidence, risk factors, and effect on upper body function. *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*, *26*(21), 3536–3542.

Hayes, S. C., Johansson, K., Stout, N. L., Prosnitz, R., Armer, J. M., Gabram, S., & Schmitz, K. H. (2012). Upper-body morbidity after breast cancer. *Cancer*, *118*(S8), 2237–2249.

Hillyer, G. C., Hershman, D. L., Kushi, L. H., Lamerato, L., Ambrosone, C. B., Bovbjerg, D. H., Neugut, A. I. (2012). A survey of breast cancer physicians regarding patient involvement in breast cancer treatment decisions. *The Breast*.

Hunt, K. K., Askew, R., & Cormier, J. N. (2009). Measuring lymphedema in patients with breast cancer: go with the flow? *Breast Cancer Research and Treatment*, *117*(3), 559–560.

Hunt, K. K., & Meric-Bernstam, F. (2008). Surgical Options for Breast Cancer. *Breast Cancer 2nd edition* (pp. 197–234). Springer New York.

IBM SPSS Statistics version 20. Available through ftp://public.dhe.ibm.com/software/analytics/spss/documentation/statistics/20.0/en/client/Manuals/IBM_SPSS_Statistics_Brief_Guide.pdf

Johansson, K., & Branje, E. (2010). Arm lymphoedema in a cohort of breast cancer survivors 10 years after diagnosis. *Acta Oncologica,* 49(2), 166-173.

Katz SJ, Morrow, M. (2012). The challenge of individualizing treatments for patients with breast cancer. *Journal of the American Medical Association*, *307*(13), 1379–1380.

Kilbreath, S. L. (2011). Breast Cancer. In B.-B. Lee, J. Bergan, & S. G. Rockson (Eds.), *Lymphedema* (pp. 501–505). London: Springer London.

Khouri, M. G., Douglas, P. S., Mackey, J. R., Martin, M., Scott, J. M., Scherrer-Crosbie, M., & Jones, L. W. (2012). Cancer Therapy–Induced Cardiac

Toxicity in Early Breast Cancer Addressing the Unresolved Issues. *Circulation*, *126*(23), 2749–2763.

Kopec, J. A., Colangelo, L. H., Land, S. R., Julian, T. B., Brown, A. M., Anderson, S. J., Ganz, P. A. (2012). Relationship Between Arm Morbidity and Patient-Reported Outcomes Following Surgery in Women with Node-Negative Breast Cancer: NSABP Protocol B-32. *The Journal of Supportive Oncology*.

Kurian, A. W., Munoz, D. F., Rust, P., Schackmann, E. A., Smith, M., Clarke, L., Plevritis, S. K. (2012). Online Tool to Guide Decisions for BRCA1/2 Mutation Carriers. *Journal of Clinical Oncology*, *30*(5), 497–506.

Land, S. R., Kopec, J. A., Julian, T. B., Brown, A. M., Anderson, S. J., Krag, D. N., Ganz, P. A. (2010). Patient-Reported Outcomes in Sentinel Node–Negative Adjuvant Breast Cancer Patients Receiving Sentinel-Node Biopsy or Axillary Dissection: National Surgical Adjuvant Breast and Bowel Project Phase III Protocol B-32. *Journal of Clinical Oncology*, *28*(25), 3929–3936.

Lee, T. S., Kilbreath, S. L., Refshauge, K. M., Herbert, R. D., & Beith, J. M. (2008). Prognosis of the upper limb following surgery and radiation for breast cancer. *Breast Cancer Research and Treatment*, *110*(1), 19–37.

Lyman, G. H., Giuliano, A. E., Somerfield, M. R., Benson, A. B., 3rd, Bodurka, D. C., Burstein, H. J., Winer, E. P. (2005). American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*, *23*(30), 7703–7720.

Macefield, R. C., Avery, K. N. L., & Blazeby, J. M. (2013). Integration of clinical and patient-reported outcomes in surgical oncology. *British Journal of Surgery*, *100*(1), 28–37.

Maguire, P. (1999). Late adverse psychological sequelae of breast cancer and its treatment. *European journal of surgical oncology: the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology*, *25*(3), 317–320.

Morrow, M., & O'Sullivan, M. J. (2007). The dilemma of DCIS. *The Breast*, *16*, 59–62.

National Cancer Institute (NCI) (2012). DCCPS: OCS. Retrieved from http://cancercontrol.cancer.gov/ocs/prevalence/definitions.html

Oncotype DX Breast Cancer Assay. Retrieved on March 15, 2013 from http://www.oncotypedx.com/

Pain, S., Vowler, S., & Purushotham, A. (2003). Is physical function a more appropriate measure than volume excess in the assessment of breast cancer-related lymphoedema (BCRL)? *European Journal of Cancer*, *39*(15), 2168–2172.

Paskett, E. D., Dean, J. A., Oliveri, J. M., & Harrop, J. P. (2012). Cancer-Related Lymphedema Risk Factors, Diagnosis, Treatment, and Impact: A Review. *Journal of Clinical Oncology*, *30*(30), 3726–3733.

Rosedale M., & Fu, M. R. (2010). Confronting the Unexpected: Temporal, Situational, and Attributive Dimensions of Distressing Symptom Experience for Breast Cancer Survivors. *Oncology Nursing Forum*, *37*(1), E28–E33.

Surveillance Epidemiology and End Results (SEER) Retrieved on March 20, 2013 from http://seer.cancer.gov/statfacts/html/breast.html

Shannon, K. M., Rodgers, L. H., Chan-Smutko, G., Patel, D., Gabree, M., & Ryan, P. D. (2011). Which individuals undergoing BRAC Analysis need BART testing? *Cancer Genetics*, *204*(8), 416–422.

Shih, Y.-C. T., Xu, Y., Cormier, J. N., Giordano, S., Ridner, S. H., Buchholz, T. A., Elting, L. S. (2009). Incidence, Treatment Costs, and Complications of Lymphedema After Breast Cancer Among Women of Working Age: A 2-Year Follow-Up Study. *Journal of Clinical Oncology*, *27*(12), 2007–2014.

Stamatakos, M., Michael, S., Stefanaki, C., Charikleia, S., Kontzoglou, K., & Konstantinos, K. (2011). Lymphedema and breast cancer: a review of the literature. *Breast cancer (Tokyo, Japan)*, *18*(3), 174–180.

Stout, N. L., Pfalzer, L. A., Springer, B., Levy, E., McGarvey, C. L., Danoff, J. V., Soballe, P. W. (2012). Breast Cancer–Related Lymphedema: Comparing Direct Costs of a Prospective Surveillance Model and a Traditional Model of Care. *Physical Therapy*, *92*(1), 152–163.

Sulayman, N., Spellman, E., Graves, K. D., Peshkin, B. N., Isaacs, C., Schwartz,

M. D., & O'Neill, S. C. (2012). Psychosocial and Quality of Life in Women Receiving the 21-Gene Recurrence Score Assay: The Impact of Decision Style in Women with Intermediate RS. *Journal of Cancer Epidemiology*, *2012*, 1–8.

Taylor, R., Jayasinghe, U. W., Koelmeyer, L., Ung, O., & Boyages, J. (2006). Reliability and Validity of Arm Volume Measurements for Assessment of Lymphedema. *Physical Therapy*, *86*(2), 205–214.

Van der Veen, P., De Voogdt, N., Lievens, P., Duquet, W., Lamote, J., & Sacre, R. (2004). Lymphedema development following breast cancer surgery with full axillary resection. *Lymphology*, *37*(4), 206–208.

Waldrop, D. P., O'Connor, T. L., & Trabold, N. (2011). "Waiting for the other shoe to drop:" distress and coping during and after treatment for breast cancer. *Journal of psychosocial oncology*, *29*(4), 450–473.

Ward, L. C., Czerniec, S., & Kilbreath, S. L. (2009). Operational Equivalence of Bioimpedance Indices and Perometry for the Assessment of Unilateral Arm Lymphedema. *Lymphatic Research and Biology*, *7*(2), 81–85.

Women's Health & Education Center. (2011). Breast Cancer Surgical Treatment Complications & Lymphedema. *Gynecological Oncology.* Retrieved from http://www.womenshealthsection.com/content/gyno/gyno005.php3

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