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# The Relationship between Light Exposure and Fatigue and Mood in the Patient Undergoing Bone Marrow Transplant

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THE RELATIONSHIP BETWEEN LIGHT EXPOSURE AND FATIGUE AND MOOD

IN THE PATIENT UNDERGOING BONE MARROW TRANSPLANT


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| | |
|---|---|
| ALLO | Allogeniec bone marrow transplant |
| AUTO | Autologous bone marrow transplant |
| BC | Breast Cancer |
| BFS | Bidimensional Fatigue Scale |
| BL | Bright Light |
| BLT | Bright Light Therapy |
| BMT | Bone Marrow Transplant |
| BPI | Brief Pain Inventory |
| BSI | Brief Symptom Inventory |
| CCP | Chronic Cancer Pain |
| CDH | Chronic Daily Headache |
| CES-D | Center for Epidemiologic Studies Depression Scale |
| CLL | Chronic Lymphocytic Leukemia |
| CML | Chronic Myelogenous Leukemia |
| CRF | Cancer Related Fatigue |
| EPA | Environmental Protection Agency |
| GVHD | Graft Versus Host Disease |
| HADS | Hospital Anxiety & Depression Scale |
| HCT | Hematocrit |

| | |
|---|---|
| HGB | Hemaglobin HIV  Human Immunodeficiency Virus |
| HPA | Hypothalamus-Pituitary-Adrenal |
| HT | Height |
| IRB | Institutional Review Board for the Protection of Human Subjects |
| KPS | Karnofsky Performance Status |
| MBI | Modified Barthel Index |
| MDS | Myelodysplastic Syndrome |
| MFI | Multidimensional Fatigue Index |
| MFSI-SF | Multidimensional Fatigue Symptom Inventory – Short Form |
| MMSE | Mini-Mental State Examination |
| MOS SF-36 | Medical Outcomes Study – Short Form |
| MTD | Total Mood Disturbance |
| PBSC | Peripheral Blood Stem Cell |
| PBSCT | Peripheral Blood Stem Cell Transplant |
| PFS | Piper Fatigue Scale |
| PFS-R | Piper Fatigue Scale - Revised |
| PFS-SF | Piper Fatigue Scale – Short Form |
| POMS | Profile of Mood States |
| POMS-SF | Profile of Mood States – Short Form |
| PSQI | Pittsburgh Sleep Quality Index |
| SAD | Seasonal Affective Depression Disorder |
| TSES | Toronto Side Effect Scale |
| UPDRS | United Parkinson's Disease Scale |

| VAS | Visual Analog Scale |
| VOC | Volatile Organic Compounds |
| WBC | White Blood Cells |
| WT | Weight |

**ABSTRACT**

Exposure to light is known to produce changes within the human body. It has demonstrated ability to produce changes in the circadian rhythm and the sleep wake cycle and to change the production and secretion of melatonin and corticosteroids. The bulk of research is related to the use of bright light therapy (BLT) for certain depressive disorders. The literature does not provide a standard of care for BLT administration dose or schedule. This study intended to identify any relationship between natural and ambient light with a hospitalized patient's mood and/or fatigue level. Further it aimed to relate cumulative light levels with the hospitalized patient's activity. In essence, it was an investigation for potential correlation between light and the independent variables of activity, mood and fatigue. If a correlation was identified, there may be strength to pursue a trial utilizing BLT with a hospitalized patient population. Bone marrow transplant (BMT) patients were selected because of documented issues with mood disturbance and fatigue and because of the long hospital stay they experience during the transplant process. BMT participants were monitored at two time points, Day 0 to Day 2 and Day 9 to Day 11, for activity and completed tools to measure fatigue and mood. Monitoring devices captured light exposure and physical activity. Sample size was defined as 82 however 90 patients were enrolled. The study attrition rate was 33% yielding data for only 60 participants. In the study results, a correlation between light and the dependent variables of mood, fatigue and activity was not identified. There were correlations

identified between activity, mood and fatigue. The study demonstrated that activity could be a predictor of mood state and fatigue at D0-D2 and a predictor of mood state at D9-D11. These findings may be better understood in a study with higher participant retention.

**CHAPTER ONE**

**INTRODUCTION**

Nightingale said, "Little as we know about the way in which we are affected by form, by color and light, we do know this, that they have an actual physical affect" (Nightingale, 1859/1960, p. 34). Nightingale identified elements in the environment that promoted recovery. Elements such as light, color, sounds and surroundings continue to be studied in an effort to understand their impact on a patient's physical and mental wellbeing. As the patient interacts with the surrounding environment, that environment has the ability to produce negative or positive changes within the patient. While Nightingale did not fully understand the science behind patient and environment interactions, she believed that environment could have a dramatic effect on the patient.

There continues to be interest in creating healthcare spaces which maximize the patient's healing potential. Conceptually, the healing space may incorporate visual, tactile and auditory elements which produce positive mental and/or physical responses in the patient. A review of literature identifies components as positive distraction (including art, music and audiovisual), a connection to nature (such as exposure to the outside, plants, water and visual of nature) and exposure to natural or artificial light. Light as a physiological and psychological stimulus is the most validated element demonstrating varying levels of activity in its effect on the human body. Yet duration and intensity of

light exposure have not been studied within general inpatient populations and light as a therapy has only been investigated in a few patient populations.

Nightingale (1859) believed in the body's need for light without fully understanding how necessary it was for sustaining health. The usefulness and mystery of light's powers predates Ms. Nightingale by millennia. Ancient Egyptians utilized sunlight as a healing power (Cocilova, 1999). Even with a long history of interest in the power of light, we still know very little about its impact on the body's function.

**Light**

Scientists continue to explore how light enters the body. Current knowledge does not provide definitive information on how points of entry may influence light's ability to affect the body. Historically, the sole point of entry for light into the body was identified as the retina. This point of entry is associated with light's ability to stimulate the pineal gland and the hypothalamus (Tamminga, 2006). This activity causes chemical and hormonal changes while allowing light transmission to other parts of the body via neuronal pathways (Moore, Heller, Wurtman, & Axelrod, 1967). It is now also known that light can enter through the skin; research suggests that blood cells may serve to transport absorbed light through the body to be used in protein and collagen synthesis (Campbell & Murphy, 1998).

Light exposure changes the body's melatonin production (Lewy, Sack, & Singer, 1985) and causes changes in levels of norepinephrine, acetylcholine, cortisol, serotonin and dopamine (Morita & Tokura, 1996). Exposure to higher levels of light suppresses the body's production of melatonin (Lewy et al., 1985). An increase in adrenal gland

secretion of corticosteroids is also associated with light exposure (Leproult, Colecchia, L'Hermite-Baleriaux & Van Cauter, 2001). These chemical reactions promote the rationale for light's ability to impact fatigue, the sleep-wake cycle and the circadian rhythm; most likely these chemical reactions also create the relationship between light and mood state.

The human body requires light to manufacture vitamin D. Historically vitamin D deficiency was a product of poor diet and industrialization (Holick, 2008). While the United States has foods fortified with vitamin D such as milk, orange juice, breads and cereals, a natural dietary source of vitamin D is through oily fish. Even with many fortified foods, the labeling of exact content is not fail proof due to varied analytic methods for measurement and lack of standardization (Yetley, 2008). Achieving and maintaining adequate serum levels of 25 hydroxyvitamin D at an acceptable level (>40 nmol/L) is difficult for those living in the northern latitudes (Peppone, Huston, Reid, Rosier, Zakharia, et al, 2011).

Thomas and colleagues (1998) tested 290 patients admitted under a general medical service and found that 57% were < 40nmol/L and 27% were < 20nmol/L, the latter being a level that is considered severely vitamin D deficient. Tangpricha, Pearce, Chen & Holick (2002) found 30% of their sample of 142 healthy young adults in Boston to be considered vitamin D deficient at <40nmol/L when tested at the end of winter.

Short intervals of sunlight exposure can generate as much as 20,000 IU (Boyles, 2003) of vitamin D. But for populations living in the northern latitudes, substantial sun exposure would be required during the summer months to sustain adequate serum levels

throughout the winter months (Hanley & Davison, 2005; Mullin, Turnbull, Kines & Mullin, 2009). As researchers learn more about how critical vitamin D is to health and well being, there are significant connections being made between it and a protective effect against breast, colon and prostate cancers (Robsahm, Tretti, Dahlback, & Moan, 2004; Peppone et al., 2011). These findings are in addition to the established importance of vitamin D in bone and muscle health.

Low level interior light exposure coupled with society's knowledge of the sun exposure connection to skin cancer and acceleration of skin aging creates optimal conditions to produce a widespread deficiency in healthy light exposure. As the industrialization of manufacturing was believed to create a vitamin D deficiency in the early 1900's, today's epidemic of vitamin D deficiency may be the result of the combined effect of all of these conditions: longer periods in interior spaces and conscious avoidance of sun exposure whether due to fear of skin cancer or premature skin aging. Light is an essential element in a person's health and wellbeing. But beyond the requirement of light for adequate vitamin D levels, we are still learning about the role that light plays in other physiological systems.

In attempting to delineate exact mechanisms for light's ability to impact certain symptoms, one must consider a common organ which is stimulated by light. The hypothalamus is a portion of the brain which is connected to the nervous system as well as having indirect links to the endocrine system. It is a focal locus of control for such physiologic responses as fatigue, sleep and the circadian rhythm (Hauw, Hausser-Hauw, Girolami, Hasboun & Seilhean, 2011). While the biochemistry is not definitive, the use

of light in certain depressive disorders is also based on the ability of light to impact biochemical operants in the brain including the hypothalamus (Martensson, Petterson, Berlund & Ekselius, 2015). When focusing on the patient population that suffers from fatigue, mood disturbance and sleep-wake disruption, the patient undergoing peripheral blood stem cell transplant (PBSCT) is a prime example (Bevans, Mitchell, & Marden, 2008). To postulate that light could impact the patient undergoing PBSCT who is experiencing this triad of symptoms is not far reaching but appears to be a valid postulate worth investigation.

**Light as a therapy.** In its own basic unit, light is measured in units of candle lighting. One foot-candle describes the illumination of a surface by one candle placed one foot away from the object it intends to illuminate. The term, foot-candle, is rooted in the history of light measurement but the brightness of a light source in industry is measured in lux (Cocilovo, 1999). Lux, as a unit of measurement for the luminance of a light source is correlated with foot candle; one foot candle equals 10.764 lux. A person sitting out on a sunny, summer day is exposed to well over 2,000 lux, yet typical lighting provided in most interior public spaces ranges only from 300 to 500 lux or lower. Knowing the impact light has on biochemical functions in the body, lower light exposure may tend to have a negative impact on those functions.

Truly the focus of light as a therapy centers on the use of bright light therapy (BLT) and its application is very focused on seasonal affective disorder type depression (SAD), with emerging research on BLT application in neurological conditions such as dementia, Parkinson's Disease and Alzheimer's Disease (Ancoli-Israel, et al. 2003;

Hickman et al. 2007; Paus, Schmitz-Hubsch, Willner, Vogel, Klockgether & Abele, 2007). There is a void of research on the effect of natural and ambient light on the hospitalized patient. It can be assumed that light exposure to the inpatient environment is similar to what a person experiences in any interior space. Knowing that the intensity of light in interior spaces can be one-tenth of the exposure a person receives while outside on a sunny day, a prolonged hospitalization has the potential to seriously impact those physiological processes which are stimulated by exposure to light.

Light has shown an ability to effectively minimize fatigue, modulate mood states, enhance cognitive functioning and treat sleep-wake cycle disruption in select patient populations such as institutionalized Alzheimer's patients and elderly patients in residential settings as well as hospitalized psychiatric patients (Benedetti, Colomb, Barbini, Campori, & Smeraldi, 2001; Chong, 2013; Dowling, Graf, Hubbard & Luxenburg, 2007; Fetveit-Skjerve & Bjorvath, 2003; Hickman et al. 2007; Paus et al. 2007; Royer, Ballentine, Eslinger, Houser, Mistrick et al. 2012) . It may hold some promise as a treatment option in affecting cancer related fatigue, associated sleep disruption and mood distress. The use of light as a therapy has been applied to limited numbers of breast and esophageal cancer patient populations (Liu et al. 2005; Neikrug et al. 2012; Ono et al 2001). In order to investigate the use of BLT and relate these levels to selected outcomes, there must be some foundational work done to explain what light levels exist during the inpatient experiences. In baseline assessment of light levels, gaining knowledge about possible relations between light levels and common symptoms

experienced by the hospitalized cancer patient may be possible. Higher light levels should correlate with lower levels of fatigue and more positive mood states.

**Bone marrow transplant.** Bone marrow transplantation is a generalized heading for several procedures which intend to support or replace a person's own immune system. The immunity we possess is generated from the bone marrow. The transplant procedure includes acquiring the hematopoietic stem cells from bone marrow, peripheral blood, and umbilical cord blood (National Marrow Donor Program, 2016). The cells used in the transplant can be obtained from the patient intended for treatment (autologous) or from a related or a matched unrelated donor (allogeneic). Statistically there have been over 55,000 peripheral blood stem cell or marrow transplants in the U.S. since 2013 (National Marrow Donor Program, 2016). It remains a treatment with many risks and possibly high mortality dependent on the underlying disease and other patient characteristics.

Used primarily for the treatment of leukemias and lymphomas, bone marrow transplant is also being used for precursor conditions for hematologic malignancies, inherited blood and immune system disorders, certain autoimmune disorders and solid tumor cancers. Its application continues to grow as the science of tissue transplantation continues to develop. Due to potential life threatening toxicities associated with the procedure, stem cell or bone marrow transplant is typically performed in large academic medical center settings. The majority of transplant centers in the U.S. are part of the National Marrow Donor Program which is a non-profit, government supported registry that also promotes donorship to become part of the database to expand matching potential for patients.

The transplant process begins with finding an acceptable match for the patient if the condition being treated cannot use the patient's own peripheral blood stem cells (PBSC). In autologous transplant, the patient undergoes plasmapheresis to harvest cells. Once PBSCs are identified, the patient undergoes a therapy referred to as a conditioning regimen. This is typically a combination of cytotoxic medications which eliminate the malignant or abnormal cells as well as the bone marrow's ability to produce component cells for immunity. The treatment regimen may also involve radiation therapy. It is a very aggressive treatment regimen which renders the patient with minimal or no immunity potential. Along with a myriad of side effects, patients must remain protected from contact with any possible source of infection. The normal bacteria and viruses found routinely in the environment, which do not impact an individual with a functioning immune system could potentially infect and kill a patient with an incompetent immune system. The infusion of stem cells or bone marrow occurs at the completion of this regimen and the patient is monitored closely for 14 to 28 days while blood counts recover. During this period, patients are watched for complications which can include infection and acute graft versus host disease (GVHD). The time period following reinfusion presents a significant risk for morbidity and mortality. While the average length of hospital stay is 22 days, many patients may spend 100 days or more recovering from the treatment, awaiting cell engraftment (National Marrow Donor Program, 2016). The national average of patients alive at 1 year post bone marrow transplant lies around 50% but is dependent on the type of transplant, underlying malignancy and patient health

status prior to transplant (National Marrow Donor Program, 2016; Dartmouth-Hitchcock, 2007).

With the PBSCT, a patient can experience an inpatient stay that far exceeds inpatient stays of other patients receiving active cancer treatment. Because of the ablation of the patient's own bone marrow, infection is the greatest risk for the patient during the period post stem cell infusion prior to recovery of the bone marrow. The procedure requires reverse isolation/negative pressure rooms which limit exposure to friends and family. While many patients receiving autologous transplants are now able to receive much of their treatment on an outpatient basis, the allogeneic transplant carries more toxicities including graft versus host disease (GVHD) and a greater risk of mortality leading many of these patients to remain in the hospital for prolonged periods (Robin et al., 2009). GVHD is a condition where the transplanted cells launch an immune response against the patient and it can be an acute and/or chronic condition (Bevans, Mitchell & Marden, 2008). Because the patient must protect themselves from potential infection, many will remain inside rather than outside which will limit the level of light exposure to normal interior light levels of 300-500 lux. The consequence of this deprivation of moderate to high levels of light in this patient population has never been studied.

There are three symptoms that this patient population frequently experiences: fatigue, mood disturbance and sleep-wake disruption (Gaston-Johansson, Fall-Dickson, Bakos & Kennedy, 1999; Trask, Paterson, Riba, Brines, Griffith et al. 2002; So, Dodgson & Tai, 2003; Grulke, Bailer, Kachele & Bunjes, 2005; Hacker et al, 2006; Carlson, Smith, Russel, Fibich & Whittaker, 2006; Bevan et al.2008). Of interest, these symptoms

have been minimized or abated with light application in other patient populations. These patient populations include the elderly with and without neurologic decline or deficiency and patients with specific types of depressive conditions. These conditions and light's impact on them will be discussed in greater detail in the following chapter. Light levels have not been studied in the patient undergoing a PBSCT.

**Fatigue.** The toxicities of PBSCT as a treatment affetsaoct almost every physiologic system in the patient; however, one of the most common complaints in patients with any cancer diagnosis is that of fatigue. Fatigue associated with cancer and cancer treatment is a well-documented symptom, however its etiology has yet to be determined. There continue to be efforts toward defining characteristics that differentiate between general fatigue and cancer related fatigue (Stone & Minton, 2008). The most substantial qualifier is that cancer related fatigue is not directly related to exertion and does not abate with rest (Mock, Frangakis, Davidson, Ropke, et. al. 2005). Cancer related fatigue has been documented as beginning prior to treatment initiation, to exist during active treatment and to continue for months to years after treatment has been completed. Cancer related fatigue does not appear to discriminate between cancer cell types or treatment regimens. While there is emerging research on cancer related fatigue as a separate and distinct entity, the present research will focus on the general concept of fatigue and how it is experienced in the patient undergoing PBSCT for a malignancy.

Research investigating fatigue in PBSCT was often associated with the measurement of quality of life. Certainly fatigue is a symptom during and after the transplant process that impacts an individual's quality of life. Studies have shown that

fatigue is a predominant symptom not only during the first 100 days but may continue to affect the patient's functioning for a year post transplant (Winer. et. al., 1999, Watson. et.al., 2004; Bevans, Mitchell & Marden, 2008). Dependent on the study, moderate fatigue is reported in up to 60% of these patients at year one.

Within the current literature, there are several approaches being studied to decrease the fatigue associated with cancer treatment and post therapy. These include exercise including yoga (Banasik, Williams, Haberman, Blank, & Bendel, 2011; Taso, Lin, Lin, Chen, Huang, et al.2014), cognitive behavioral therapy (Berger, et al. 2009), and pharmacologic interventions (Yavuzsen, et al. 2009). The bulk of the research has been performed using exercise during and after treatment for cancer to mitigate fatigue.

Light exposure or BLT was only found in one study involving BMT patients (Redd, Valdimarsdottir, Wu, Winkel, Byrne et al. 2014) so there is very limited experience. Studies with breast cancer patients, fatigue and light exposure or BLT are found with greater frequency (Ancoli-Israel, Rissling, Neikrug, Trofimenko, Natarajan et al. 2012; Liu, et al. 2005; Redd et al. 2014)). In these research studies, a negative relationship was identified between the duration of light exposure and the patients' reports of fatigue.  Patients who were exposed to higher levels of natural light, ambient light or BLT reported lower fatigue scores. Sun and colleagues (2014) studied light exposure, fatigue, depression and sleep quality in cancer patients receiving outpatient chemotherapy. Calculating the number of minutes that patients received $\geq$ 1000 lux, researchers found patients who received greater light exposure over time reported better sleep quality, less fatigue and less depression ($r = -0.61$, $p < 0.001$; $r = -0.18$, $p = 0.03$; $r =$

-0.18, p – 0.02 respectively).  An additional study was found using BLT with post operative esophagectomy due to cancer (Ono, Taguchi, Kido, Fujino, & Doki, 2001); however this study centered on BLT reducing the amount of cognitive issues occurring in a postoperative ICU setting.

One hypothesis underlying the use of exercise to combat cancer related fatigue also has ties to the hypothalamus. In general, lack of activity and de-conditioning which often accompanies cancer treatment promotes fatigue; as treatment continues, fatigue also increases (Wilson, Jacobsen, & Fields, 2005). This can be perceived as a stressor to the mind-body homeostasis. One of the body's main neuroendocrine response to stress is activation of the hypothalamic-pituitary-adrenocortical axis, which results in the secretion of adrenal corticosteroids. Researchers have demonstrated chronic psychosocial stress leads to a dysregulation of the hypothalamus-pituitary-adrenal axis which predisposes the body to increased inflammation (Miller, Ancoli-Israel, Bower, Capuron, & Irwin, 2008). Inflammatory molecules can signal the brain and engender behavioral symptoms like fatigue (Dantzer, O'Connor, Freund, Johnson & Kelley, 2008; Miller, Ancoli-Israel, Bower, Capuron, & Irwin, 2008). As in the application of light, there is a trigger which promotes activity by the hypothalamus.

This hypothesis provides credible rationale given the knowledge that cancer related fatigue is not definitively connected to treatment initiation. Its etiology may be related to this hypothalamic stimulation and subsequent secretions by the pituitary and pineal glands. The stimulation of the inflammatory response would occur even prior to the actual diagnosing of the cancer. This could give reason for fatigue's presence before

treatment has been initiated. It could also be the reason why fatigue can remain with the patient long after the treatment has been completed. Ongoing inflammation at a subclinical level may be the etiology for the continued fatigue.

Yoga has been used to modulate the effects of fatigue with breast cancer survivors and patients receiving active treatment (Banasik et al. 2011; Bower, Greendale, Crosswell, Garet, Sternlich, et al. 2014; Danaher-Hacker, Ferrans, Verlen, Ravandi, van Besien et al, 2006; Taso, Lin, Lin, Cheng, Huang, et al. 2014). Yoga as an intervention is focused more on the mind body connection and not aerobic activity to combat fatigue. These studies typically are small and often times do not show clear direction in the findings. The available research suggests that motivated patients who stayed within the program requirements benefited (Danaher-Hacker et. al. 2006; Bower et al. 2014; Moadel, 2007; Taso et al. 2014). Success in some of these experiments may only translate to preventing the level of fatigue from increasing as treatment progresses versus providing an actual decline in fatigue. Taso and colleagues (2014) were able to show a reduction in fatigue with an eight week yoga program when compared to a control group which received standard care; this study did demonstrate any impact on depression or anxiety. Research performed by Bower and colleagues (2014) utilized yoga in breast cancer survivors and through a twelve week course identified reduced activity of a pro-inflammatory factor, increased activity of the anti-inflammatory glucocorticoid receptor, and changes in the soluble tumor necrosis factor receptor, a marker for TNF activity. This research demonstrated that there were significant differences in the plasma levels in biochemical elements in the body associated with yoga as an intervention. In other types

of cancers where primarily outpatient therapy is the course, attrition in exercise studies has been high (Andersen, Vinther, Poulsen & Mellemgaard, 2011; Wilson et. al. 2005).

There have been reported abnormalities in the circadian rhythm and cortisol levels in breast cancer investigations and this again suggests a link to dysregulation of the hypothalamus, the pineal and the pituitary glands (Sephton & Spiegel, 200; Stone, Schwartz, Smyth, Kirschbaum, Cohen et. al. 2001). The researchers do not propose the rationale for a connection between yoga or exercise and fatigue, however it is suggestive of a psychoneuroimmunology connection. This connection does promote the concept of mind-body collaboration but the associated biochemical activities are not well defined.

A longitudinal study investigating symptoms post BMT for multiple myeloma patients demonstrated that the most severe long term side effects such as fatigue and muscle weakness remained present in 35% of patients (Wang, Shi, Williams, Shah, Mendoza, et al, 2015). Inflammatory marker essays performed on the participants (N = 55) resulted in high symptom patients demonstrating a significantly elevated baseline tumor necrosis factor-alpha (p = 0.014). This type of ongoing research will hopefully lead to a clearer relationship between biochemical changes, inflammation and fatigue.

**Mood disturbance.** The transplant recipient has frequently undergone multiple failed treatments or relapses and may be receiving a PBSCT as a final treatment option. Even if the patient is receiving a transplant early in their diagnosis, mood disturbances are not uncommon and are documented in a variety of cancer conditions (Trask et al., 2002; Guelke, Larbig, Kachele & Bailer, 2008). Depression and other mood disturbances can present in this patient population before treatment begins and frequently transplant

programs have psychological support and treatment for this throughout the transplant experience. Many patients are placed on one or more antidepressants or antianxiety medications prior to, during and post transplant.

In addition to being difficult on the body, the transplant process can be very frightening and overwhelming. The mainstay of treatment for these patients has been psychological therapy and medications. While BLT has been used in non-cancer patient populations with mood disturbances such as SAD and with a few neurological conditions, research on interaction between light and mood disturbances in the patient receiving PBSCT is limited. Occupational studies have shown worker attitudes about their work are positively correlated with higher exposure to natural light (Leather, Pyrgas, Beale & Lawrence, 1998). Because patients receiving PBSCT undergo a prolonged period of restriction from the outside, their exposure to natural light would be expected to decline during treatment and recovery. Increased exposure to natural and ambient light may not prove to resolve mood disturbances in this patient population, however it could be beneficial to establish relevancy for BLT use as an adjuvant treatment modality.

Psychological distress for the patient receiving transplant can frequently begin in the pre-transplant period. It is not only the magnitude of the treatment that can distress the patient, some patients find the isolation requirements overwhelming (Sasaki, et.al. 2000). Emotional distress and anxiety are issues that are addressed throughout the transplant process.

There are supporting studies linking a relationship between fatigue and psychological distress (Gaston-Johansson et al. 1999; Molassiotis, 1999). More research

has been performed with patients receiving allogeneic transplants as their recovery is typically filled with greater challenges than their autologous counterparts. Toxicities are more severe and isolation tends to be much more rigorous in allogeneic transplants.

As research has demonstrated that BLT effectively treats sleep-wake cycle disruption in select patient populations (Benedetti et al. 2001; Chong et al. 2013; Hickman et al. 2007), light therapy may hold some promise as a treatment option in the cancer related fatigue and associated sleep disruption. BLT has been beneficial in helping non-SAD patients with mood disturbances. Selecting patients receiving bone marrow transplantation will provide for the examination of light levels during a longer inpatient stay or a more intensive outpatient treatment regimen.

**Triad of symptoms and connection to light.** While it is accepted that stress on the body triggers a response from the hypothalamus-pituitary axis, the connection or interaction of light with this response has not been investigated. The ability of light to lessen fatigue, decrease depression, and/or enhance sleep-wake cycle may occur through alteration of the hypothalamic function. In fact, the one study performed by Liu and colleagues (2005) did find a significant negative relationship between fatigue and light. Jeste (et al., 2013) found BLT in breast cancer patients receiving treatment resulted in maintenance of quality of life scores and depression scores. Redd and colleagues (2014) study of post cancer treatment patients with CRF correlated BLT with decreased fatigue over time but excluded depression as a predictor in these patients. It is within this connection that interjects the question: what is light's relationship with these three vexing

symptoms of fatigue, mood disturbance, and poor sleep in this particular patient population?

**Significance to Nursing**

The goal for nursing has always been to improve the patient's outcome while enhancing the patient experience. As a science and a practice, nursing has continued to focus on the entire person rather than the sum of the parts. The domain of nursing is to provide interventions that are central to the patient's recovery while also coordinating with the medical interventions. Investigation of ambient and natural light as a non-invasive adjunct to patient treatment appears well within the scope of nursing practice and in fact could render an application that could be nurse driven to benefit patients.

The patient undergoing PBSCT is engaged in a fight for survival in many cases. Whether the transplant is an initial therapy or a salvage therapy, it is a difficult process with many side effects which can be lethal. The idea of something as benign as light to enhance the patient's experience and potentially impact their ability to withstand the hardships of therapy seems almost naïve but it is no more simplistic than Nightingale opening the windows to let fresh, clean air circulate in the nursing ward. It is not the belief that light can serve as a lifesaving therapy which will impact survival. But the application of light may provide a better patient experience as an intervention at no cost to the patient. The cost-benefit ratio could be astronomical if light's application can help the patient weather the treatment regimen by facilitating a better mental perspective and physical functioning,

**Purpose and Hypotheses**

The purpose of this study was to test the hypothesis that light levels have a relationship to the levels of fatigue and mood a patient experiences while undergoing a bone marrow transplant. In addition, it meant to establish baseline light levels during the transplant process that a patient is exposed to and determine the relationship that exists between light levels and the common complaints of fatigue, mood disturbance, and activity intolerance. The findings from this investigation are meant to identify if there are opportunities to employ the use of BLT with these patients during their prolonged hospital stay.

**Research Question**

What is the relationship between light levels and physical and psychological state in the patient undergoing a bone marrow transplant procedure?

**Aim 1.** Establish the relationship between, natural and ambient light exposure with fatigue and mood in the bone marrow transplant patient.

*Hypothesis 1.* There is a significant relationship between the level of light exposure and the patient's report of fatigue and mood.

**Aim 2.** Establish the relationship between the level of light exposure and a bone marrow transplant patient's physical activity during transplant hospitalization.

*Hypothesis 2.* There is a significant relationship between the level of light exposure and the patient's physical activity during transplant hospitalization.

**Aim 3.** Establish the relationship between the level of light exposure and fatigue at two time points in the bone marrow transplant process.

*Hypothesis 3.* There is a significant relationship between cumulative light exposure and the patient's perception of fatigue between pre-transplant and post-transplant day 11.

**Summary**

Light is part of the natural world and has been shown to interact with the human body. It has demonstrated benefit to specific patient populations in decreasing depressive symptoms and the regulation of sleep-wake cycles. Small studies are suggesting benefits to neurologic symptoms in Alzheimer's disease (Ancoli-Israel et al.2003), dementia (Graf et al. 2001; Hickman et al. 2007), and Parkinson's disease (Paus et al. 2007). While we know that light does affect the human body, the research on light as a therapy is limited for conditions such as cancer. The following chapter will provide foundational theoretical frameworks that support the concept of interaction between the human body and environmental light. The constructs found in Nightingale's (1859) early identification that the environment impacts the health- illness state in the human and Martha Rogers' Science of the Unitary Human Beings (Rogers, 1980) will be discussed. Chapter 2 will also iterate the state of knowledge regarding the interaction between light and the human body and any relationship between fatigue and mood distress and light in the patient undergoing PBSCT.

CHAPTER TWO

LITERATURE REVIEW

The study of light has relevance to the conceptual nursing model of Florence Nightingale (1859/1960). The study of light as an intervention also can be supported through the theory of Martha Rogers (1980): The Science of Unitary Human Beings. The concept of the human continuously interacting with their environment is central to understanding how light can impact change in the human. Central to these practice modes is the concern for human and environment interaction striving to regain healthful balance. This chapter will explore the use of these nursing theories as well as the supporting literature which provides practical application of light to benefit various patient populations

**Theoretical Frameworks**

**Florence Nightingale.** Nursing has always been concerned with creating an environment where the patient can recover and heal. The idea of the environment contributing or countering the patient's illness was part of Florence Nightingale's strategy in caring for the sick. Certainly in her work "Notes on Nursing: What it is and what it is not" (Nightingale, 1859/1960), she identified elements that were important in regaining health and well-being. These included clean air and water, efficient drainage, environmental cleanliness along with adequate ventilation and light (Nightingale, 1859/1960). She went beyond the basics to the esthetics when she promoted the use of light

and windows and the reduction of noise as environmental manipulations to aid in the

patient's recovery. Nightingale believed that a dark house was an unhealthy house and

that without sunlight, the mind and body degenerated (Nightingale, 1859/1960).

Nightingale was ahead of her time in her identification that oil based paint on

interior walls was sub-optimal due to the odor; this is still relevant today. Volatile organic

compounds (VOC) are a byproduct of certain paint types that can have atmospheric

photochemical reactions (EPA, 2010). VOCs can cause irritation to the eyes, nose and

throat; in its more potent phase, it can cause organ damage with continued exposure over

time. We see more paint companies producing low VOC paint to prevent what today is

termed "off gassing". Finally, Ms. Nightingale appreciated the value of pleasing interior

spaces saying "color and form means recovery" (Nightingale, 1859, p. 33). Only through

the use and application of light can one see or appreciate the color spectrum.

Nightingale wrote of being able to smell small pox growing in closed rooms or in

overcrowded nursing wards (Nightingale, 1859/1960). It was her belief that the

surrounding environment possessed a wealth of variables that intervened in the human

condition and those variables affected the success of nursing's interventions with the

patient (Robinson & Kish, 2001). Her approach focused on the physical spaces with less

emphasis on psychosocial interventions. Nightingale's concepts of the individual, the

environment, health/illness and nursing were all in play, interacting and affecting one

another (Gillette, 1996).

The relationship between fresh air and light with health are as central to

Nightingale's approach as that of cleanliness. Open windows in sick rooms meant fresh

air and light reached the patient. Those natural elements were important in Nightingale's approach to recovery but were less accessible in her environment. Conditions in the "healthcare environment" often impeded the patient's return to a healthy state. Sanitation was not generally addressed in public areas. Cities were often dark and dirty with only the wealthy being able to escape to the country.

Nightingale's worldview of nursing also delineated the roles of medicine and nursing with a great distinction. As medicine practiced from a framework of diagnosis and treatment, the nurse's goal and mission were to create an environment for the patient that would serve as an adjunct to the internal healing processes of the human body (Nightingale, 1859/1960; Tschirch, 1997). There was an overarching perspective that the body must be interacting with an environment that was conducive to healing.

Nightingale's framework for nursing included the concept of caring for the whole person – mind, body and spirit. The patient was not reducible to a diagnosis. This perspective is evident in more contemporary nursing theories and is a cornerstone for the practice of nursing. Martha Rogers carried this theme of patient and environment interaction to a refined framework for nursing practice. Rogers, similar to Nightingale, believed that nursing's charge was to promote health, using a consistent approach that did not include adaptation to illness.

**Roger's Science of Unitary Human Beings**

Nursing is typically not the designer of health care spaces yet nursing is charged with defining methods that positively impact the human health and wellness experience. As stated by Rogers (1970, p. 86) "nursing aims to assist people in achieving their

maximum health potential." This mission encompasses every location and condition associated with the patient because the person is central to everything that nursing does.

Similar to Nightingale's framework, Rogers' Science of Unitary Human Beings (Rogers, 1970) considers the whole person as continuously interacting with the environment and not as a diagnosis or an illness. Rogers' perspective encompasses the universe as multiple open systems with an importance on mutual processes between and among those systems. Change never ceases and supports continuous innovations and diversity (Lewandowski, 2004). The person and environment are energy fields that coexist. The concept of wholeness means that parts of the person cannot be addressed in isolation to describe or predict characteristics or responses; the whole cannot be reduced into parts. Rogers defines the person as "an irreducible, indivisible, pandimensional energy field identified by pattern and manifesting characteristics that are specific to the whole and cannot be predicted from the parts" (Rogers, 1992, p. 43). Each person is characterized by a particular wave pattern.

The basic concepts for Rogers' (1980) theory include the unitary human being, the environment and homeodynamic principles. Homeodynamic principles provide a way of perceiving unitary human beings. Each entity, whether human or environmental, has an energy field which varies in intensity, density and extent (Farren, 2009). There is openness between the human field and the environmental field with no boundaries and a constant exchange between the two. This describes a component of homeodynamics Rogers termed integrality (Biley, 1992). Resonancy, the second component of homeodynamics describes the directional changes occurring between the energy fields of

the person and the environment. Lastly, helicy describes the rhythmicity in life formation and the constant interaction between energy fields. Each of the energy fields has pattern which distinguishes it from another and gives identity to the field. Pan-dimensionality is a key concept of the theory-the human is multidimensional manifesting characteristics which are specific to that human as a whole (Rogers, 1970).

Rogers rejected the concept of adaptation to illness (Lewandowski, 2004). Illness is not seen as something external to the human therefore human change is not through adaptive measures (Malinski, 1994). Illness can be viewed as an internal stimulus which will induce the human to develop to an increasingly diverse pattern. This diverse pattern changes through mutual processes evolving to a higher frequency of wave patterns (Rogers, 1992). The focus has always been on the wholeness of the person and the rejection of causality (Wright, 2007). Rogers' perspective is essential to the present research in that she believed that her conceptual model would provide a platform for the human experiences that one cannot understand; there is still much mystery in how we are affected by our environment and conversely, how we impact our environment (Smith, 2007).

The theory posits that the person's energy field can change in its configuration. Rogers called this variation of energy fields 'patterning'. Patterning represents how the human and environment are able to interact which drives growth in the human energy field. (Bateson, 1979; Rogers, 1990). The goal is for the pattern to change and mobilize toward change. As the human field diversifies, change can occur more rapidly and within

the Rogerian perspective the more complex the field, the more rapid change can occur

(Rogers, 1980; Hastings-Tolsma, 2006).

Rogers viewed the patient evolving as an active participant in their health care.

Patients are challenged with an illness which they need to understand. If they are able to

understand the illness, they can also understand what they must do in order to affect the

outcome; hence the patient moves toward positive outcomes and mitigates the chance of

negative outcomes (Malinski, 2007). Since Rogers saw the patient as continually

interacting with their environment, they are able to embrace the knowledge of those

interactions. She also believed that non-medical interventions had a role to play, viewing

these as adjuvants which could again increase the probability toward positive outcomes.

This perspective is quite in line with the idea of light interaction impacting the person in a

positive way.

Walling (2006) applied Rogers' theory to the delivery of acupuncture for a patient

with chronic pain. Acupuncture is a method used to reduce the patient's pain through

manipulation of the environmental energy field. The application of acupuncture allows

for the manipulation of the environment energy field as it interacts with the patient's

energy field. Pathophysiologic processes can be seen as expressions of the life process in

the same manner as health. Disease can be utilized as information for the patient to

understand and get in touch with one's own pattern.

The environment is an energy field which continuously interacts with the human

energy field. It is inconceivable that the two energy fields are not always interacting.

While it is not always known whether the environment has a positive or negative

interaction with the human, a foundation of the theory is that there is interaction between the two. This perspective creates a rationale for why psychoneuroimmunology is plausible. It is through the mind's perception which connects to the individual's neurological, immunological and endocrine systems. This same relationship supports the idea that light has the ability to maneuver alterations in the human energy field. Just as Walling (2006) captured acupuncture operating external to the body (within the environmental energy field), yet impacting the human energy field, light should have the same ability. Lewandowski (2004) utilized Rogers' theory in the perspective of chronic pain interacting with the human energy field while the patient utilizes guided imagery under the same premise. The impact of pain is manifested in the mind-body-spirit interaction with the environment.

Acupuncture is an applied intervention and its application to alter the human experience may be viewed as similar to that of exposure to light. Both are external applications which can manipulate the internal body; both manipulate in ways which are not fully understood. The human energy field is continually interacting with the environmental energy field. Light is present in that environmental energy field and has the ability through that interaction to create change in the human energy field. The interaction has the ability to alter homeostasis in the human. The goal is always focused on enhancing the communication and interaction between the energy fields that exist with the human and the environment.

It is nursing's charge as well as its passion to explore methods which contribute to that achievement of wellness (Wright, 2007). From a Rogerian perspective, nursing must

form mutual care partnerships with patients while developing, advocating, and applying creative use of non-invasive modalities to assist the patient toward greater well-being (Malinski, 2007). The use of an innovative technique such as BLT is within that same vein. It can be part of nursing's professional domain and mission to use creative interventions to benefit patients (Malinski, 2007). The illness that a patient experiences may prevent the human energy field from evolving to a shorter wave and higher frequency pattern. The evolution to a more diverse patterning would manifest as a greater sense of well-being (Lewandowski, 2004). Utilization of Rogers' world view can only assist nursing's evolution as a science with the perpetual goal of extending and transforming our understanding of the patient and his/her environment (Malinski, 2008).

The concept of wellbeing is an intangible. However, none of us would deny its existence. Science has attempted to measure it using subjective tools. But within the perspective of Rogers, it may remain an intangible and something that is innately within the individual's energy field. We know it exists in the feelings we get when viewing a beautiful sunset or the distress we sense without knowing exactly what is wrong. It cannot be separated from the human and is a part of him/her. Rogers reminds us that the nurse is part of the experience; the observation of phenomena must include the observer while the observer also becomes part of the experience (Armstrong & Kelly, 1995). The Science of Unitary Human Beings can be applied to the current study of light interaction with the human. The following theoretical assumptions from Roger's (1980) theory are essential to laying the framework for the proposed study:

1. A human is a unified energy field which is more than the sum of its parts

2. A human and their environment continuously, simultaneously and mutually exchanging energy with each other

3. The human changes by way of patterning when light is integrated into the environmental energy field.

4. The patterning results in an exchange process which brings the human pattern to a higher and varied frequency.

5. The human energy field (person) is identified through pattern and frequency which can be impacted positively by changes in the environmental energy field such as light.

**Definitions**

**Unitary human being**. A four dimensional energy field that cannot be reduced or divided; it has characteristics that are part of the whole however the energy field can't be described by parts but only through the whole; one cannot summarize the parts to describe the whole (Rogers, 1970) .

**Environment.** An energy field which is identified by unique pattern and cannot be reduced to parts; it is an energy field that is integral with the human field (Rogers, 1970.

**Energy field.** A fundamental unit of both the living and non-living, it continuously varies in intensity, density and extent. The human and the environment are fields as energy fields which are irreducible wholes (Rogers, 1990)

**Openess.** Energy fields constantly exchange energy with one another without boundaries or barriers that would inhibit that flow of energy between fields (Rogers, 1970)

**Pattern.** It is the distinguishing characteristics of the energy field perceived as single waves; it is the abstraction that gives the field identity and uniqueness; pattern can change (Rogers, 1992)

**Pan dimensionality.** It is the domain the energy fields exist in and has no spatial or temporal attributes; parameters are arbitrary which humans use in language to describe events; the present is relative (Rogers, 1970)

**Resonancy.** The ordered arrangement of rhythm characterizing human and environmental fields; it undergoes continuous and dynamic change as the human and environmental fields interact (Rogers, 1990).

**Helicy.** The continuous, non-linear evolution of energy fields which are manifested by non-repeating rhythmicities (Rogers, 1990).

**Integrality.** Embodies the mutual and continuous relationship between human and environmental energy fields; there is a continuous re-patterning of these fields; the fields are one and integrated yet unique (Rogers, 1990).

This research will test the theory, Science of Unitary Human Beings (1970) in the relationship between the human and environment energy fields and patterning. Fatigue as a pattern in the energy field can serve as a disruption in the person-environmental field process. The energy field will continuously re-pattern in response to interaction with

internal and external waves. Pattern embodies the relationship between human and environment energy fields

It is within the framework of Rogers' (1980) theory that the human energy field may evolve through its continuous interaction with the environmental energy field. As it evolves, re-patterning occurs through this constant interaction. Healing is viewed as a rebalancing of the patterning. Light as a rhythmic wave of energy interacts with the human providing an opportunity for re-patterning of the human energy field. Light creates a change to the source of the energy imbalance, fatigue. In illness, multiple factors will cause a disruption and/or blocking of the pattern.

The Science of Unitary Beings theory (Rogers, 1980) places nursing in the role of effecting re-patterning aimed at promoting harmonious interaction between the fields. Nursing can employ interventions such as light, sound and colors to promote the harmonious interaction which in turn will impact the interaction between the human energy field and the environmental energy field. Patterning provides the energy field with its individual character, however it is not observable. The manifestation of patterning of the energy field is present in the change process. Changes occur within the interaction between the person and the environment (Rogers, 1970)

Within the theory, healing is viewed as the energy field's progress toward harmony within itself while illness is the blocking, disrupting and unbalancing of the movement toward harmony within the energy field (Rogers, 1970). Rogers postulated nursing interventions impact the energy field moving the human-environmental patterning to a higher frequency. With the application of light, the nurse becomes an

integral participant in altering the energy pattern of the patient. The nurse also lays the foundation for the patient to become an active participant through education. The patient has the knowledge to develop an expectation that light amount and duration of exposure may decrease the level of fatigue they perceive. Nursing can help patients become aware of their pattern within their own sense of well-being while encouraging the patient toward changing their own pattern through the use of choice, the freedom to act and become more aware of the interaction of self and environment (Rogers, 1970).

A person can experience fatigue as an energy field disturbance. In the present study, fatigue is viewed as a manifestation of the process of patterning. A patient's report of a reduction in fatigue indicates that there is a change in the patterning of the energy field toward a shorter wave, higher frequency and more diverse pattern – promoting harmony within the interactions between the two energy fields. Light may serve as a stimulus for change through re-patterning of the human energy field pushing it toward restoration of the balance and flow of this same energy field.

**Summary**

Nightingale (1859) and Rogers (1970) recognized the importance of the environment to the human experience. It has become a field of study for architecture in building therapeutic environments however there is much more research which needs to be performed in order to definitively draw conclusions. The environmental elements placed in a space should enhance the human experience. A variety of interior elements have been studied for their impact on people. The minimization of noise in the healthcare environment contributes in decreasing anxiety and facilitating rest (Pattison & Robertson,

1996). A portrait of nature or a water feature in the lobby of a hospital can enhance a patient's sense of comfort and pleasure with their surroundings (Ulrich, 1993; Kaplan & Kaplan, 1995). The focus for the current proposed research is that of light and its relationship to a patient's inpatient experience. As a component of the environmental energy field, it will be the goal to determine how the light components in the energy field interact with the patient. Is there an interaction that occurs between patient and environment energy fields as it relates to light exposure and the patient's perception of fatigue and/or mood?

**Light's Effect on the Human Subject**

**General effects of light.** The physiological effect of light is in the form of invisible wavelengths; it is believed that these light waves may have the ability to modify the immune response whether traveling through the skin or through the retina. Wavelengths of light can penetrate the epidermal and dermal layers of the skin and directly interact with circulating lymphocytes (Roberts, 2000). Lymphocytes are key players in the body's immune functions. It is also evident that the lymphocyte activity in the immune responses is impacted by circadian rhythm. Human circadian rhythm also has an explicit relationship to light.

Physiological research on phototransduction of light suggests that blood cells with photoreceptive abilities move through the body to support protein and collagen synthesis resulting in rapid regeneration of tissue (Campbell & Murphy, 1998). The research by Campbell and Murphy (1998) included fifteen subjects acting as their own controls. Subjects were exposed to dim light without their knowledge and during waking as well as

sleep times. Evidence suggested that endogenous phototransduction occurred with corresponding changes in melatonin production and core temperature. The connection between light therapy and tissue healing has been identified through a variety of wound treatment studies (Barolet & Boucher, 2010; Demidova-Rice, Salomatina, Yaroslavsky, Herman & Hamblin, 2007; Rennekampff, Busche, Knoblock & Tenenhaus, 2010). It is logical to posit that light could serve as a stimulus for cellular repair activities. In oriental medicine, light as a treatment modality is believed to move along the meridians, which serve as pathways for acupuncture and acupressure (Cocilova, 1999).

Stimulation of the pineal gland and hypothalamus by light is known to produce serotonin that can be converted to melatonin (Tamminga, 2006). The increase in adrenal gland secretion of corticosteroids is also associated with light exposure. A systematic review by Morgan & Rashid (2009) provided supportive information regarding the impact of light on neutrophil activity. Phototherapy with and without photosensitive pharmaceuticals has demonstrated a propensity to modulate immune responses. Autoimmune and skin disorders (e.g. psoriasis) respond positively to light therapy. These types of physiologic reactions support the theory that light has the ability to enter not only through the retinal receptors but also through the skin providing a direct line to the immune system (Roberts, 2000).

The first study to look at the side effects and/or toxicities associated with BLT was recently published. Botanov & Ilardi (2013) completed a placebo-controlled trial focusing on the side effects associated with BLT as there is a void in the research on the therapy's side effects and tolerability. Using healthy participants, the study had 2 groups.

The control group received light box exposure emitting 450 lux of red filtered light for 30 minutes compared to an experimental group who received unfiltered white light at 10,000 lux for 30 minutes once daily. The Toronto Side Effect Scale (TSES) was used to measure the occurrence of adverse treatment events on 17 items. Interestingly enough, of the 112 red light placebo participants and the 101 BLT participants, the side effects were statistically significant in the participant experience of eye strain and blurred vision. Analysis of variance (ANOVA) showed a significant main effect of time on eye strain, ($F(1, 211) = 32.36$, $p < .001$, d = .47), and blurred vision, ($F(1, 211) = 7.60$, $p = .006$, d = .19). Across both groups, the average post-treatment eye strain severity ($M = .4$, $SD = 1.0$) was greater than pre-treatment severity ($M = .1$, $SD = .5$) as was the average post-treatment blurred vision

**Light's effect on subjective response.** The creation of workspaces with sunlight exposure can increase worker satisfaction (Leather et al., 1998). In an evaluation of the work environment, researchers examined job satisfaction, well-being and a decreased intention to quit. The study, conducted in Southern Europe, involved 100 subjects in an office setting where all workspaces were well illuminated. While no bright light was directly administered to the workers, sunlight penetration of the work areas was measured by subjective assessment of the amount of floor area covered by sunlight. The workers' sunlight penetration assessment for their work area was directly and positively correlated with increased job satisfaction and general well-being. Intention to quit and anxious feelings were negatively correlated with sunlight exposure ($r = -.32$ and $-.36$, respectively, $p \leq .001$). Positive work attitudes were found to correlate with the size of

sunlight areas provided in the work place (r = +.25, p ≤ .01) as well as the natural

elements which were available to view via the window exposure (r = +.27, p ≤ .01).

Ulrich's (1984) findings suggested positive benefits to hospitalized patients given

access to natural light and elements of nature. In a review of 46 inpatient surgical records,

Ulrich (1984) found that the length of stay was different between patients admitted to a

surgical room with a window overlooking a landscaped area versus patients admitted to

rooms with windows overlooking an exterior brick wall. In this early study, Ulrich

demonstrated that patients assigned to the first room type had a significantly shorter

length of stay, used less pain medication while in the hospital and had a decreased

number of complaints. While this study was a retrospective chart review and had a small

sample size with surgical procedure variability in the sample, it was a significant early

attempt to quantify the inpatient's experience with light and exposure to the outside.

The amount of natural light entering a hospital room has been shown to influence

a patient's recovery from depression (Beauchemin & Hays, 1996). Patients requiring

inpatient treatment for major depressive disorders were admitted to a unit where all

rooms had windows. Researchers categorized patient rooms as either brightly lit or dim

based on the amount of sunlight the rooms received. Of the 174 admissions analyzed,

patients in the brightly lit rooms had an average of 2.6 days shorter length of stay (p =

0.05) than patients admitted to lower light level rooms. This suggested that the amount of

light in the room provided benefits to recovery time and could contribute to significant

cost savings of health care dollars. The researchers were not able to control for all of the

obvious patient differences such as psychiatric diagnoses, age and past psychiatric

history. An incidental yet significant finding was that male patients experienced shorter

length of stays than female patients regardless of the room illumination. The study was

replicated by Benedetti (et al. 2001) and colleagues five years later with similar findings.

Only one study was found that investigated a relationship between natural and

ambient light exposure and fatigue associated with chemotherapy (Liu, 2005). Fatigue is

a universally recognized side effect of cancer chemotherapy. Researchers recruited

female patients undergoing outpatient chemotherapy for breast cancer. The study did not

provide BLT but attempted to relate levels of fatigue to actual exposure to light. Patients

wore a wrist device which measured light exposure and activity. The light exposure

experienced by the patients was normally below 1000 lux, a level far below the amount

typically used in BLT. Even with these lower levels of light, the researchers found a

correlation between light exposure and the patient's report of general fatigue levels.

Using the Multidimensional Fatigue Symptom Inventory Short Form (MFSI-SF), there

was an inverse relationship found between fatigue and light levels for all patients. In the

first 2 weeks of each cycle, researchers found higher light exposure correlated with a

greater decline in subscales scores on the MFSI-SF. All subscale scores except for Vigor

are interpreted as the higher the score, the greater the fatigue. But for the Vigor subscale,

a higher score translates to less fatigue. The more light the patient was exposed to during

cycle 4, the higher the score on the Vigor subscale ($r=0.28$, $p=0.045$). A negative

correlation was seen in light exposure and the subscale, General ($r=-0.30$, $p=0.031$) as

well as in the overall MFSI-SF score ($r=-0.30$, $p=0.033$). The findings suggest, but cannot

confirm, a cause and effect relationship between fatigue and decreased light exposure.

Subscales of the measure individually supported this trend. There is a question of whether the light is actually decreasing the subject's perception of fatigue by improving the patient's mood or are patients spending less time in moderate to high light exposure because they are fatigued? Depressive moods, fatigue and loss of energy are frequent symptoms of patient receiving chemotherapy or radiation therapy for cancer.

The impact of natural or ambient light on the subjective and objective responses of the individual has not been extensively studied. The research on light used as a therapy centers on the application of bright light therapy (BLT). The application of this increased dosing of light exposure has been extensively studied in specific types of depression and neurologic conditions such as Parkinson's and Alzheimer's Diseases. It is fundamental to the present research to first develop foundational research that light does relate to fatigue before proceeding to study the use of BLT as a therapy for fatigue in the cancer patient population. However the research evidence related to BLT will be presented to provide a comprehensive view of light and how it relates to various states and symptoms.

**Bright light therapy.** Application of light correlates with bodily increases in rectal temperature and levels of urinary melatonin, particularly when the color and intensity of light is manipulated (Morita & Tokura, 1996). Patients were exposed to varying light color temperatures as measured in Kelvin (K). The Kelvin scale is a thermodynamic (absolute) temperature scale (New World Encyclopedia, 2010) which correlates to light color as well as temperature. For reference, 98 degrees Fahrenheit equals 309.82 Kelvin. Subjects had temperature monitoring and urinary melatonin measured. The use of a high color temperature light such as 6500 K suppressed normal

nocturnal temperature fall and suppressed the normal nocturnal production of melatonin as compared to lights of 3000 K.

The use of BLT in SAD and non-SAD depressed HIV positive patients demonstrated small alterations in the patients' T cell counts (Rosenthal, Brown, Oren, Galetto, Schwartz & Malley, 1994). In this cross-over design, subjects were exposed to 45 minutes of either white light or red light. The blood samples taken from the subjects demonstrated a small but significant increase in CD4 and CD8 cell counts in subjects who received the white light when compared to counts of patients receiving red light. The patients with a history of SAD demonstrated improved mood however this was not observed in the patients with a non-SAD depressive disorder.

The use of BLT is a well-established therapeutic intervention for those individuals who suffer from SAD (Lam, et al. 2006; Wileman, et al. 2001; Wirz-Justice, et al. 1996). However, research has revealed evidence that BLT benefits individuals with non-SAD type depression.

An early study looking at the effects of BLT on normal functioning elderly was completed by Fukuda and colleagues (1998). Subjects received 30 minutes of BLT at 6000 lux in the morning. Using a visual analog scale (VAS), the seven male subjects recorded their feelings in the morning and in the evening on seven criteria: alertness, mood, motivation, tension, fatigue, concentration and appetite. To create a control group, the same subjects were also instructed to sit without BLT for 30 minutes. All of the VAS parameters increased in the morning scoring with the BLT conditions and in the evening all VAS parameters declined ($p < 0.05$).

Research on the effects of BLT on healthy individuals (Group 1) as compared to sub-syndrome SAD individuals (Group 2) demonstrated that both groups could benefit from BLT (Partonen & Lonnqvist, 2000). This cross over design included four weeks of BLT (1 hour each day, 5 days per week) at 2500 lux alternated with four weeks of no therapy over a sixteen-week period. Researchers found benefits for both groups in subject reports of energy levels, sleep quality, physical activity, and socialization (r ranging from +.22 to +.18). Both groups reported higher levels of vitality at weeks 4 and 12 however Group 1 scored a little over 10% better. Both groups reported a significant reduction in depressive symptoms. Group 2 experienced slightly better improvement of subjective energy and quality of sleep as compared to Group 1. The significance of these findings implies that individuals without any evidence of tendencies toward SAD depression (Group 1) could benefit from BLT.

McEnany and Lee (2005) used BLT in outpatient treatment for depression in female patients. Subjects used a light visor worn by the treatment group that administered 10,000 lux of light for one hour in the morning. Research variables included depressive moods, fatigue and energy. With the treatment group of 16 women, the researchers found significant improvement in depressive moods demonstrating more than a 40% drop in the treatment group scores. The treatment group also experienced a dramatic increase in the measure of perceived energy (>40%) while the placebo group experienced a drop. Improved sleep was also significant in the treatment group with only a minimal change in the placebo group.

Light therapy is known to manipulate or modulate the circadian rhythms. This is the basis for research with SAD. It has also shown to be effective in alleviating delirium seen in the intensive care patient. Taguchi, Yano, and Kido (2007) studied intensive care patients who had undergone surgery for esophageal cancer. Post extubation, the patients were randomized to a control or treatment group. Eight patients were randomized to the study group and 7 to the control group. The treatment group received 5000 lux for two hours each morning while the control group received the normal amount of light in an intensive care patient room measured at 600 to 1000 lux. Only six patients could be evaluated in the treatment group. Five patients were evaluated in the control group. Sleep pattern and activities were evaluated as well as delirium. A 30 point confusion scale was completed by the nursing staff with higher scores indicating more normal functioning. There were no statistically significant differences between the groups when looking at activity or autonomic activities. However, there were significant differences in the delirium scores of the two groups. The control group displayed 24% more delirium than the study group ($p = 0.014$). In addition, the study group patients were able to begin ambulation 2 days earlier than the control group. Hallucinations and auditory hallucinations disappeared in the study group at the initial day of BLT.

Neikrug and associates (2012) utilized bright light therapy in women undergoing chemotherapy for breast cancer hypothesizing that women who received BLT would maintain a healthy sleep-wake cycle while a control group of breast cancer chemotherapy patients receiving dim red light would demonstrate a greater disruption in this circadian rhythms. Actigraphy was used to monitor circadian rhythm variables of sleep-wake and

activty in both groups. Mesor, the average value around which a variable oscillates, was used as one of the variables. If sample size is small or the rhythmic process has data points that are not equidistant, the mesor can produce an unbiased estimator of central tendency in the analysis of circadian rhythm research (Dictionary of circadian rhythm, 2015). The researchers demonstrated specific variables such as mesor and amplitude had significantly different changes between the two groups. The control group experienced a decline in mesor between baseline and cycle 4 treatment week (t=-2.67, p=.009) suggesting decreased activity of the circadian rhythms. The BLT group demonstrated a significant increase in mesor at cycle 4 recovery week (t=2.32, p=.02) indicating a more robust circadian rhythm. Similar changes were seen in the amplitude as well. The BLT group experienced significant increase in cycle 4 recovery week which would indicate stronger circadian rhythms (t = 2.31, p = .02) while the dim red light group had a decrease from baseline in cycle 4 treatment week (t = -2.67, p = .009) which would indicate decline in activity and/or stability of the circadian rhythm.

Patients undergoing a partial or complete esophagectomy frequently have a difficult post operative course often involving extended periods of intensive care which creates opportunities for sleep disruption and delirium. Ono and colleagues (2011) administered BLT to a study group (n = 10) while a control group (n = 12) received only natural and ambient light available in the intensive care setting. The study group was administered BLT for 2 hours in the morning on post op day 2-4. The measure of night activity was used as a proxy for sleeplessness. The amount of night activity for the intervention group (21.9 +/- 1.5 hours) was significantly lower than the control group

(24.1 +/- 3.2 hours) (p< 0.05). The study group demonstrated lower scores on the NEECHAM confusion scale used to measure delirium, however the analysis failed to show significance. The researchers postulated that the increased orientation seen in the study group may have been significant if a larger number of participants could have been accrued to the study.

Redd and colleagues (2014) performed a randomized study involving light exposure on 36 cancer survivors. Patients were breast or gynecologic cancer survivors who were either at least 3.5 years post stem cell transplant (SCT), or up to 3 years post chemotherapy or chemotherapy/radiation. Patients were randomized to BWL or DRL. Participants completed the FACIT-Fatigue tool at baseline, during the second week of the intervention, at the end of the fourth week of intervention and three weeks post completion. The FACIT-Fatigue required a score of </= 30 for clinically significant fatigue. Patients used either a light box that delivered bright sun like light at 110,000 to 120,000 lux (BWL, equal to natural sun light) or dim red light (DRL) that emitted < 50 lux. Patients received 30 minutes of light therapy every morning within 30 minutes of waking and this was continued for 4 weeks. Patients also completed the Brief Symptom Inventory-Depression score. Results showed a difference in baseline fatigue scores. There was a change in fatigue scores over time between the two groups with BWL having significantly less fatigue than DRL ($F(1,28) = 7.12$, $p = 0.0125$). Researchers found that depression was not a predictor of cancer related fatigue. At the end of the intervention all of the patients assigned to BWL had scores of > 30 on the FACIT-fatigue scale while 55% of DRL patients still showed significant fatigue scores.

**BLT in the Elderly**

Depression in the elderly occurs at similar rates as the general population. Elderly inpatients in the rehabilitative environment for stroke and spinal injury were treated with BLT (Tsai, Wong, Juang, and Tsai, 2004). The participants were not diagnosed with SAD. The average length of stay for the control group was 56.4 days and for the experimental group was 76 days. Participants were identified as having mild to moderate depressive moods but were not previously diagnosed or treated for depression. In addition, the subjects did not suffer from any significant cognitive dysfunction. The experimental group received 50 minutes of BLT (5000 lux) for 5 days and no treatment was provided to the control group. Using the Geriatric Depression Scale, scores of less than 10 are considered normal, 10 to 19 considered mild depression and scores greater than 19 indicate severe depression. Significant decreases in depressive moods were noted in the experimental group scoring 18 on the pre-test and 13.2 on the post test. The underlying co-morbidities between the groups were not a factor. The control group only experienced a 0.1 decrease between pre-test and post test scores. While only one study, these findings suggest benefit in the use of light therapy on rehabilitative patients who experience longer lengths of inpatient stays.

Numerous studies have investigated the effects of BLT in the elderly with cognitive dysfunction such as those with dementia (Hickman et al. 2007) and Alzheimer's disease (Ancoli-Israel et al. 2003). Many researchers have used BLT to treat depression while others have examined its impact on the activity-rest cycles, particularly in the institutionalized elderly. These studies may have implications for the BMT patient

as disruption of the circadian rhythm can occur in the BMT patient due to hospitalization or side effects from the treatment.

The assertion that BLT could benefit the cognitive functioning of dementia and Alzheimer's disease type dementia was supported in 2001 (Graf, et al. 2001). The effect of BLT (3000 lux) and dim light therapy (100 lux) on Mini-Mental State Examination (MMSE) scores was the focus in a small study involving institutionalized adults with dementia. The use of BLT was associated with a significant increase in subject MMSE scores. Every patient in the BLT group that was able to complete the MMSE pre and post BLT had an increase in score from 15.2 to 18.1 ($p = .0012$); a similar change was not found in the control group receiving dim light therapy. In 9 of 10 patients in the dim light group, only 3 patients had an increase in score. The remaining 6 either had similar or decreased scores. A component of the research was also the measurement of body temperature investigating its relationship with regulation of circadian rhythm. Body temperature changes seen were short lived which could possibly mean the effects of BLT might be short lived as well. Because a repeat measure of the MMSE was not performed posttest on day 10, this could not be validated. This research involved light administration between 5:00 and 7:00 pm for 10 days. The timing of the light administration was different from a majority of the reviewed research; other studies were careful to avoid evening hours for light administration. The researchers did not indicate their rationale for the timing of light administration.

A research team headed by Ancoli-Israel (et al. 2003) hypothesized that BLT could reduce evening agitation in Alzheimer's patients by manipulating the circadian

rhythm. The team observed that, patients who were awake during the night displayed agitation consistently throughout day and night without any observable period where there was no agitation. If the patient spent more time awake during the day, there were periods during the night and day that patients exhibited less agitation. The light levels institutionalized patients are exposed to are typically below 1000 lux. Ninety-two patients were enrolled in this study. Agitation was measured with two tools; one tool involved the caregiver rating the level of agitation over a prior 2-week period. A second tool was a behavioral rating scale completed by trained individuals with high level of inter-rater reliability evidence. Patients were randomly placed in one of three treatment groups to receive morning BLT, dim red light (placebo) and evening BLT. The physical agitation for the morning BLT was delayed during the treatment period when compared to baseline by 1.63 hours (p = 0.034). Of staff appraisals of patients, there were significant changes across all treatment groups. Staff rated declines in scores for physical agitation (10.4 to 9.6, p = 0.007), verbal agitation (11.3 to 10.0, p = 0.001) and total agitation (29.7 to 26.9, p = 0.0004) in all groups.

The research continues to be unclear on the exact prescription for BLT in the Alzheimer's disease patients. There may be specific criteria that researchers need to evaluate to further define where the therapy can be of greatest benefit. Schindler and colleagues (2002) published a report on five patients with Alzheimer's disease with and without delusions. Of the five patients, three were experiencing delusions. In these three patients, BLT was administered at 2500 lux for two hours daily. This treatment resulted in a slight improvement. One patient did not have delusions before, during or after the

BLT however one of the subjects experienced an increase in hallucinations and delusions. The researchers found that the level of disorientation increased with the BLT and the BLT had to be discontinued. The ability to make general assumptions on BLT therapy enhancing the Alzheimer's disease patient's orientation or agitation remains elusive. This research group emphasized that in the Alzheimer's disease patient population, BLT should not be continued in the face of any increase in agitation, delusions or hallucinations.

In the absence of depression, BLT was employed to successfully improve sleep in the institutionalized elderly (Fetveit et al. 2003). A small study (11 participants) with institutionalized elderly of varying degrees of dementia used BLT at levels of 6000-8000 lux for two hours in the morning. Researchers focused on sleep-wake disturbances such as number of awakenings, length of each awakening, waking after sleep onset and early morning awakening utilizing actigraphy monitors. Sleep efficiency improved in all patients by 13%; this translated into subjects falling asleep faster and experiencing less awakenings. Total time in bed decreased by about one-half hour while rising time remained unchanged. The patients experienced a decrease in sleep onset of 1 hour without an observed change in rising time. The researchers found a decrease in time spent on nocturnal waking by as much as 2 hours from pre-treatment to post treatment. As the BLT became more intense, greater improvement was found in the sleep-rest experience of the patient. The study participants had some dementia however the researchers did not provide a discussion of the level or severity of dementia.

Research on cognitively impaired institutionalized adults is challenging, as responses may need to be assessed by proxy. Hickman and colleagues utilized ambient bright light therapy with patients classified with varying degrees of dementia (Hickman, et al2007). The bright light levels were not as high as typically used (2533-2638 lux). Two study sites were used in different regions of the country. There were four light level interventions administered to the participants with each intervention lasting 3 weeks in length. The four interventions were: (A) 4 hours bright light in AM, (B) 4 hours bright light in PM, (C) all day bright light, and (D) standard lighting. Participants had multiple interventions over the course of the study. During each intervention, depressive symptoms would be measured. The researchers found mixed results with some subjects experiencing a negative response to the light. In general, females in the study experienced greater improvement in depressive symptoms with morning light versus standard light (p=.01) while their male counterparts experienced more depressive symptoms under morning bright light than with standard lighting (p=.007). Using the Cornell Scale for Depression in Dementia, researchers did not find many statistically significant differences between gender other than higher overall depressive symptoms in men than females regardless of study site. The use of bright ambient lighting challenged the researchers to create consistent light levels throughout the institution at a cost that would be prohibitive for most institutions. This was an extremely complex and probably very expensive study and while the findings were not impressive, it did demonstrate interesting gender differences with regard to the effect of light and generated questions about gender depressive responses to lighting conditions.

Dowling and colleagues (2007) studied the effects of light on neuropsychiatric behaviors in patients with Alzheimer's disease. Subjects were randomized to a control group or to one of two study groups. The control group received no BLT but experienced normal room light within the range of 150 to 200 lux. Within the study groups, each subject received either one hour of morning BLT or afternoon BLT. Researchers evaluated the subjects for changes in the presence, frequency, severity and disruptiveness of neuropsychiatric behaviors in nursing home patients. A larger score was interpreted as subjects having greater severity or frequency of problematic behavior. Statistically significant findings were seen in the behavior categories of agitation/aggression, depression/dysphoria, and aberrant motor behavior. Patients receiving BLT had lower severity and frequency scores, however the actual scoring changes were minimal. The researchers attributed the scoring as innate to the tool stating that the significance found did not translate in clinically meaningful results. Of note, this study relied heavily on staff interpretation of the subject's behavior which could interject greater variability in scoring. However a second study by Dowling, et al. (2008) investigated the sleep behaviors of a similar population melding light therapy with the addition of melatonin. Within the myriad of Alzheimer's disease, there is great disruption noted with the circadian regulation and one would expect some subject reaction to BLT. The inclusion of oral melatonin at a dose of 5mg to the trial provided a different approach than typically seen in the literature. Research is suggestive that melatonin is low in Alzheimer's patients. The control group received no interventions while the two experimental groups received BLT with melatonin (LM) versus placebo (LP). Actigraph wrist monitors were

used to monitor activity on all patients. The BLT was administered via light box with each subject in the experimental groups receiving on average 6204 lux. While no significant changes were seen in the night sleep time, there was a significant reduction in daytime sleep by 66 minutes. Subjects in the LM group demonstrated increased daytime activities and improvement of day/night sleep ratio. The LP group and control group experienced an increase in daytime sleep time ($p < .001$). The differences in responses were impressive with only one hour of BLT daily for this 10-week trial.

Research findings have suggested that the decline in melatonin production may be an important factor in the neurodegeneration seen with aging (Jenwitheesuk, Nopparat, Mukda, Wonchitrat, & Govitrapong, 2014). If true, then light therapy to manipulate natural melatonin production may be of use. Researchers proposed that bright light therapy (BLT) could have a positive effect on the symptoms of Parkinson's disease (Paus et al.2007). Subject selection provided for a control and placebo group with similar characteristics in stage of disease, physiological functioning and mental ability. Subjects received light box exposure for thirty minutes just after rising; the study group (N =18) received 7500 lux daily through light box and the placebo group (N =18) received a much smaller BLT dose. No significant changes were found in the placebo group. In the study group, researchers found a statistically significant increase in mood with a 25% decline in scores on the Beck Depression Inventory. Since none of the subjects had a diagnosis of depression, the change in the study group was attributed to the BLT. The United Parkinson's Disease Scale (UPDRS) was used to measure mentation, mood and behavior. The study group revealed an over 30% improvement in scores on the UPDRS. The BLT

produced a small improvement in the incidence of tremors and ADL function with slightly over 10% improved scores ($p < .05$ and $p < .01$ respectively). There were no significant findings in scores for rigidity and bradykinesis.

While the relationship between neuropsychiatric conditions in the elderly and BLT is far from conclusive, current research has provided the scientific community enough interest for further investigation. BLT is a low risk, non-invasive intervention which may provide higher quality of light and/or improved functioning for this particular patient population.

Researchers have investigated illumination levels experienced by nursing home patients (Schochat, Martin, Marler & Ancoli-Israel, 2000). Light levels were measured for a small group of 66 patients with dementia. The mean daytime light exposure was only 485 lux with almost 30 % of the subjects never being exposed to light over 1000 lux. Interior light levels typically are in the 400-500 lux range. In this research, light levels were negatively correlated with the number of awakenings at night ($r_S = -0.35$, $p = 0.004$); this finding was not impacted by the patient's level of dementia. Using Spearman rank correlation, time spent at lux greater than 1000 showed a tendency toward predicting fewer awakenings during the night ($r_S = -.21$, $p = 0.089$) but failed to reach statistical significance. In this patient population, severe dementia has typically been a predictor for increased sleep time and decreased wake time during the day. However in this study, the use of BLT was able to minimize the impact of the condition. Interestingly, the overall time spent in high illumination levels may be more important than short sessions at higher lux. There are research efforts ongoing to integrate the use of BLT in the

environment of the elderly to enhance cognitive function and minimize delirium (Chong, Chang, Kang, Han, Ding & Tan, 2011). BLT was built into a 5 bed unit specifically designed for geriatric patients with delirium. BLT of 2000-3000 lux was administered via ceiling lights from 6-10pm daily. The sample size of 228 patients was recruited from this unit over a 2 year time period. Functional status was measured via modified Barthel Index (MBI) with patients with hyperactive or mixed delirium subtypes showing improvement in scores ($p < 0.05$). The Delirium Rating Score at the sleep wake disturbance subscore showed significant improvements in all three delirium subtypes. Sleep improvements were primarily seen in hyperactive delirium patients: sleep time went from 6.4 hours to 7.7 hours ($p < 0.05$) with a decreased mean number of sleep bouts and awakening.

Based on the provided research, suffice to say there is a relationship between BLT and the inner workings of the human 'clock'. While the physiological or psychological reaction appears varied dependent on the patient population being investigated, there are human responses that occur related to the BLT. It is also important to note that light has a definitive relationship with the circadian rhythm. This relationship may be pivotal in understanding how light may produce changes in fatigue, as both the sleep-wake activity and fatigue are activities controlled by the hypothalamus. Low light levels of < 400 lux are similar to the light levels experienced by the BMT patients whether in hospital or home. There can be a suggestion of light's relationship with perception of fatigue however this has not been well explored in this cancer patient population.

**Fatigue**

Fatigue in general can be defined as a subjective experience encompassing weariness, tiredness or lack of energy (Dimeo, 2001). Fatigue occurs in all of us in the absence of disease but because of its pervasiveness in the cancer population, the term cancer related fatigue (CRF) has emerged. It is the most common symptom experienced by cancer patients (Cella, Peterman, Passik, Jacobsen, & Breitbart, 1998). While a universal complaint during treatment **(**Berger, 1998; Byar, Berger, Bakken & Cetak, 2006), it also remains an issue for many patients in the post treatment period at varied levels of intensity and duration. Fatigue has great impact on the patient's ability to tolerate any prescribed cancer treatment and can have a deleterious effect on the patient's ability to stay on course with treatments (Dodd, Miaskowki & Paul, 2001).

**Cancer related fatigue.** Cancer related fatigue can be defined as "a persistent subjective sense of tiredness related to cancer treatment that interferes with usual functioning" (National Comprehensive Cancer Network, 2011). It has been studied in a variety of cancer types, in progressive, metastatic disease as well as in adjuvant chemotherapy patients with no signs of disease and in patient populations prior to, during and after treatment. The difference between cancer related fatigue and fatigue the general population experiences is that rest does not alleviate the cancer related fatigue and it is not the result of physical activity (Yavuzsen, Davis, Ranganthan, et al. 2009). It does not appear that the fatigue experienced by patients during cancer treatment can be directly related to nutritional status (Beach, Siebeneck, Buderer & Ferner, 2006).

Researchers continue to investigate the components of cancer related fatigue because

of its prevalence in all cancer patient groups; depending on the study, its prevalence is stated anywhere from 25% to 99% in patients with cancer (Servaes, Verhagen, & Bleijenberg, 2002). The pathophysiologic etiology of it is still in question.

It is unclear whether cancer fatigue is a muscular phenomenon or whether it is more centrally generated through neuromuscular activities. Researchers hypothesized that fatigue during prolonged motor tasks in cancer patients would be more centrally located than in healthy controls (Yavuzsen et al, 2009). Subjects completed the Brief Fatigue Index to measure the patient's perception of the fatigue experience. Subjects (n= 29) had a variety of advanced cancers and were compared to 16 healthy controls. The research team measured maximum elbow flexion force using instrumentation. The instrument provided numeric readings of the patient's strength in sustaining elbow flexion against a constant pressure Patients with cancer fatigue had significantly less ability in elbow flexion force than healthy controls (186 $\pm$ 69 vs. 257 $\pm$ 77, p < 0.01). This finding suggested that patient with CRF had weaker muscles to sustain the elbow flexion than health controls. But the healthy controls experienced greater muscular fatigue after the sustained elbow flexion contractions than cancer fatigue patients (66% versus 46%, p < 0.05). This is suggestive of the hypothesis that cancer fatigue is not due to muscular fatigue.

While this research can provide differences in muscle potential between the cancer related fatigue patient and the healthy subject, the etiology of this multidimensional condition is far from understood. The literature is just beginning to delve deeper into a potential relationship between hypothalamic-pituitary-adrenal activity

(HPA) and cancer related fatigue. This relationship is of great interest to the present research for the mere fact that light also has a relationship with hypothalamic and pituitary activity.

**Cancer related fatigue and inflammation.** There is speculation on the role of the inflammatory process in the development of cancer related fatigue (CRF). In the pretreatment patient, CRF may develop due to a pro-inflammatory response to the disease process. During treatment, it is hypothesized the biochemical changes causing CRF development are generated by the treatment regimen (Prue et al 2010; Mills et al. 2005). It is difficult to conceive that this inflammatory response could also serve as a rationale for long term CRF in patients who have completed therapy months or years earlier. Work has also been performed on these inflammatory markers which may explain CRF's persistence or latent development (Collado-Hidalgo, Bower, Ganz, Cole & Irwin, 2006; Kruse & Strouse, 2015; Wang, Shi, Williams, Shah, Mendoza et al. 2015).

As early as 2001, research focused on identifying the relationship between chronic fatigue and the hypothalamus-pituitary-adrenal (HPA) functions (Cleare, Blair, Chambers, & Wessely, 2001). While the current proposed research will look for any connection between light and fatigue, it does not intend to provide further identification of biochemical changes due to this interaction. Suffice to say that the HPA connection and inflammation with fatigue is important to the present hypothesis, that light correlates with fatigue based on the same area of physiologic involvement.

Alexander, Minton, Andrews & Stone (2009) utilized defined criteria for establishing the presence of CRF in 208 breast cancer survivors who were out of

treatment between 9-11 months. They found that 60 (30%) women met the criteria for the diagnosis of CRF. A battery of tools was administered to the subjects measuring fatigue, quality of life, depression and work/social adjustment. In addition the researchers took blood specimens for hematologic and biochemical analysis and collected a 24 hour urine specimen for urinary cortisol. There were significant differences in the non-CRF and CRF groups on the Total BFS for fatigue (21.47 vs 54.07, $p<0.001$), and on the Total HADS score for depression (2.55 vs 5.58, ($p<0.001$); data showed greater levels of fatigue and depression in CRF subjects. There were no significant differences in urinary cortisol level between groups but there were some differences in the WBC counts and chemistry blood levels. Finding differences in the urinary cortisols could have contributed to the pro-inflammatory theory for CRF, but the study did not support the researcher's hypothesis.

Bower and colleagues (2011) examined fatigue and gene expression in support of the hypothesis that pro-inflammatory cytokines play a role in cancer related fatigue. This study was performed with breast cancer survivors who had persistent fatigue (n=11) and who did not have persistent fatigue (n=10). The researchers proposed that the fatigue group would have reduced activity in the glucocorticoid receptor which does not promote inhibition of NF-kB and other pro-inflammatory signaling pathways. The researchers found 437 transcript genes with greater than 30% difference in expression of leukocytes from the fatigue versus the non-fatigued subjects. The fatigued group had increased numbers of genes encoded with pro-inflammatory cytokines ($p< 0.001$) associated with increased activity of cytokines involved in immune and inflammatory response. A

reduced expression with response elements for glucocorticoids in the fatigue group was present (p<0.05). This was a very small study however it was able to show cellular differences between the fatigue breast cancer survivor and the non-fatigued breast cancer survivor.

CRF research has been studied predominantly in the breast cancer patient population. Studies have captured fatigue intensity during intercycle monitoring of adjuvant therapy (de Jong, Kester, Schouten, Abu-Saad & Courtens, 2006). Andrykowsky, Donovan, Laronga & Jacobsen (2010) utilized criteria for establishing the presence of CRF and assessing breast cancer (BC) patients at baseline, 6 months and 42 months post treatment. Comparisons were made between breast cancer survivors (n=304) and an equal number of healthy controls. Baseline measurement of fatigue in the BC group was comparable to prevalence at the 6-month mark post treatment (9.9% versus 9.2%). Of interest was that as high as 33% of the patients met the CRF criteria at all assessed time points. Finally, the off treatment CRF measure was 13.1 % in the BC group. This suggested that patients could experience delayed onset of CRF even in the absence of active treatment.

Fatigue in breast cancer has been widely studied more so than fatigue associated with any other cancer type. While breast cancer is not frequently treated with PBSCT, autologous transplant has been used as a treatment option for the patient population. Depending on the study, as many as 60% of breast cancer patients can suffer from moderate to high levels of fatigue for as long as one year after the transplant (Winer et.al. 1999). While allogeneic patients statistically have a more difficult recovery, both

autologous and allogeneic patients are plagued with fatigue as well as insomnia and negative mood (Watson et. al. 2004). In general, treatment related symptoms associated with transplant do not vary based on the primary cancer site or cell type.

Hoffman, Given, von Eye, Gift & Given (2007) examined the relationships between common symptoms experienced by newly diagnosed lung cancer patients who were within 56 days post chemotherapy. Not surprising, the researchers found that 97% of the patients stated that fatigue was the most significant symptom ($p = 0.05$) with pain coming in as second most significant at 68%.

CRF has been studied in patients with gynecological cancer, focusing on the fatigue during treatment as well as after the treatment has been completed (Prue, Allen, Gracey, Rankin, & Cramp, 2010). In a randomized trial, Prue and associates (2010) investigated the differences in severe fatigue between gynecological cancer patients (n=65) and healthy controls (n = 60). A key goal of the study was to determine any predictors for severe fatigue. Through the use of several tools with subscales for fatigue and symptom checklists, the findings suggested that symptoms may stem from both the disease as well as a post treatment changes. The fatigue experienced by the cancer group was significantly higher than healthy controls at all time points: before treatment, during treatment and after treatment ($p < 0.001$). At monthly time points, the fatigue experienced by the cancer group was ten times higher than the healthy group. Data collection continued monthly for 11 months. The psychological distress level was the only independent predictor of CRF ($p < 0.001$) during treatment and one of two predictors of fatigue after treatment ($p < 0.001$).

**Fatigue in the BMT patient.** For the patient undergoing cancer treatment via bone marrow or stem cell transplant, fatigue has often been studied as a component of quality of life. There are limited studies which focus on fatigue as a primary variable. However, the studies that are present suggest that it is a symptom prior to treatment, a symptom during treatment and can be a chronic symptom for years post- transplant. In addition, the majority of studies investigating the transplant experience look at the long term symptoms that effect the patient's quality of life rather than the time period pre-transplant to the first 100 days post transplant (Akaho et al. 2003; Andrykowski et al. 2005; Hayden et al. 2004).

Winer and colleagues (1999) found 60% of patients complained of moderate fatigue one year after receiving BMT for breast cancer. Those patients with less fatigue were found to have a significantly higher scores on the quality of life tool ($r = -0.61$, $p = 0.001$). Watson (et.al. 2004) found similar issues with fatigue when comparing quality of life issues between allogeneic and autologous transplants. In the total sample, the researchers found 79% of patients complaining of fatigue. A difference between the allogeneic and autologous fatigue complaints was not significant in patient percentages (87% versus 81% respectively). In another study, for patients receiving allogeneic hematopoietic stem cell transplant, the number one most prevalent and significant complaint at baseline was that of fatigue (Bevans et al. 2008). For these patients' first 100 days post-transplant, fatigue remained the first or second significant symptom in prevalence and distress at baseline, day 0 (at the day of PBSC infusion), day 30 and day 100.

Coleman and colleagues (2002) focused on patients undergoing very aggressive treatment for multiple myeloma utilizing stem cell transplant as one of the modalities. This chemotherapy regimen included induction with a variety of neoplastic medications, consolidation chemotherapy and tandem stem cell transplant. The patients were also on maintenance dosing of alpha interferon. The overall purpose was to control symptoms for patients and compare patients who successfully received outpatient transplant care versus patients who had unplanned admissions where they received the bulk of the therapy. Fatigue was measured by the patient stating the percent of usual energy they felt on a defined day prior to transplant, day of transplant and post transplant. All of the patients experienced an increase in fatigue but the patients who were successfully treated and managed as outpatients (n = 73) had less severity and intensity of fatigue than patients with unplanned hospitalization (80% versus 68%, p = 0.017). One could postulate multiple reasons, such as more fit patients would be the candidates to receive primarily outpatient treatments. Researchers could not clearly explain the underlying rationale for the differences.

Danaher-Hacker and colleagues (2006) completed a descriptive, exploratory study examining levels of fatigue in the immediate pre- and post-transplant periods, in addition to evaluating other variables. The goal was to identify any changes in fatigue, physical activity and sleep during the five days prior to and the five days after the infusion of stem cells post chemotherapy. Using a convenience sample (n = 20), the researchers utilized an Actiwatch in addition to a quality of life tool with three multi-item symptom scales for fatigue, pain, nausea and vomiting and single item questions about other physical side

effects such as sleep disturbances, appetite loss, dyspnea and gastrointestinal symptoms. This study mixed autologous and allogeneic transplant patients; this is an important nuance since the recovery can be vastly different between these two groups. A 10-point scale was used to subjectively measure the participant's perception of fatigue. Mild fatigue was reported prior to transplant by 75% of participants on day 1, by 83% of participants on day 2 and by 88% of participants on day 3. The researchers found a significant increase in fatigue levels in the immediate post-transplant period. The first day after transplant, 90% of patients reported moderate to severe fatigue. On the second day, 77% of participants reported moderate to severe fatigue and on the third day, 80% of participants reported moderate to severe fatigue. With successive days, there was a dramatic increase in the percentage of participants complaining of moderate to severe fatigue (90% of patients by day 5). At time one measurement, the mean fatigue score was 29.63 (pre-transplant) compared to mean fatigue score of 71.11 at time two (post transplant). Researchers also found that participants experienced a 58% decline in physical activity from day 0 to day 7. An obvious assumption would be that those two findings are directly related however the researchers did not provide any correlation.

Bevan's et al. (2008) research also focused on those early time periods with allogeneic transplant. Four data collection time points were identified including pre-transplant, day 0 (cell infusion), day 30 and day 100. Seventy-six transplant patients participated. Using a symptom distress scale, they found that 90% of the participants (n=60) rated fatigue as one of the most distressing symptoms and at day 100, 81% of the participants continued to rate it as highly distressing. Fatigue was the only recurring

distressing symptom in the latter three data collection times. With this research, the recovery from fatigue appears extremely slow in the post transplant experience so finding adjuvant interventions to minimize the magnitude and duration of the fatigue would be of great benefit in helping these patients return to a pre-transplant psychological and physiological status.

Fatigue is a universal complaint for the BMT patient during the conditioning regimen, the stem cell infusion, and can be a prolonged complaint in the long term post-transplant period. Fatigue is recognized for its subjective nature and significantly increases as physical activity decreases following the high dose chemotherapy and radiation (Danaher-Hacker, et al. 2006). While fatigue has been studied in the BMT population, studies differ in assessing its immediacy of onset post stem cell infusion. Multiple longitudinal studies have identified the chronicity of the symptom for years in some patients (Prue et al. 2010; Mills et al. 2005). There continue to be further opportunities to compare over time the type of fatigue experienced by these patients.

There have been suggestions that cancer related fatigue may have a relationship with the hypothalamus and the pituitary in addition to modulating the production and transport of a variety of white blood cells (Prue et al. 2010; Mills et al. 2005) While the immune stimulating properties of light have not been validated, the connection between how light interacts within the body and its connection to the hypothalamus and pituitary have been defined (Leproult et al. 2001). Baseline research first must make a connection between how the duration and intensity of light exposure may correlate with the patient's report of fatigue. Only one study was found that investigated any connection. Liu's

(2006) study with patients receiving adjuvant chemotherapy for breast cancer found a relationship between light exposure and reported fatigue.

Sleep disturbance is considered a common complaint of the cancer patient and it could be projected that it would increase during a patient's hospitalization. In addition, there is a feasible relationship between sleep disturbances and the occurrence of fatigue. Disruption of the sleep-wake cycle can contribute to the fatigue experienced by the cancer patient and sleep disruption occurs in the patient undergoing BMT (Rischer, Scherwath, Zander, Koch & Schulz-Kindermann, 2009). In this 2009 study, sleep assessments were performed prior to hospitalization, during the inpatient stay and up to 3 months post-transplant. Fifty transplant patients consented to participate however only 32 patients completed all assessments. Sleep assessments included the completion of the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al. 1989). At initial assessment, 32% of the 50 patients suffered sleeping difficulties. At the post-transplant assessment, 77.3% of the 32 patients reported an increase in sleep difficulties. For those patients that completed all assessments, a significant increase in sleep disturbances was seen between pre-admission and at 100 days post-transplant (p< 0.001).

**Mood Disturbance**

Depression, anxiety and distress are frequently present in the patient receiving a PBSCT. Similar to fatigue, mood disturbance can occur prior to the transplant and can persist long after the completion of the therapy. While some studies have attempted to connect survival with the patient's level of pre-transplant depression, this has not been conclusively determined to be the case (Grulke, Larbig, Kachele &Bailer, 2008). A study

performed by Jenks Ketterman & Altmaier (2008) with 86 BMT patients found that 29% of their patients were experiencing depressive symptoms pre-transplant and 27 % met criteria for clinical depression 1 year post transplant. The researchers utilized the CES-D (depression subscale) to measure levels of depression with a higher score indicating higher levels of depression. Scoring range on the CES-D is 0-60 with a score of >/= 16 considered a clinical level of depression. Their investigation demonstrated that pre-BMT depression was a predictor for depression 1 year post BMT. Similar to gender differences seen in fatigue studies, females scored higher for depression on the CES-D than males than males (11.80 versus 16.69 respectively, p=.025).

While many illnesses are associated with mood disturbances, the public's association with cancer is one of fear and sadness. Wang and associates (2007) investigated differences in mood and sleep comparing two patient groups with known pain issues. Chronic daily headache (CDH) patients (n=47) and chronic cancer patients (CCP) (n=47) were surveyed using a variety of measurement instruments. Participants with cancer had varying cell types with the largest number coming from patients with lung cancer (n=14). The Profile of Mood States tool (Shacham, 1983) was used as well as the Brief Pain Inventory (Wang, Mendosa, Gao & Cleeland, 1996) and the PSQI (Bussye et al., 1989). The CCP patient group had significantly more days per month where pain was present (28.13 days versus 24.45 days, p=0.03). Scoring for the BPI subscales was 0 to 10 with higher numbers equating to maximum negative impact to the patient. Subscale scores on the BPI demonstrated that CCP patients versus CDH patients perceived more disruption in performance of general activities (6.53 vs 5.21, p=0.03), walking (6.02 vs

4.00, p=0.001) and working (7.11 vs 4.66, p<0.001) respectively, due to pain. The only significant difference between the two patient groups on the POMS was on the Vigor subscale, with CCP patients perceiving less energy than CDH patients (p < 0.001). For the POMS-SF Fatigue subscale, there was a trend toward fatigue being a greater issue for the CCP versus CDH group however it did not reach the required level of significance.

Historically, the bulk of research examining the PBSCT experience has been through investigation of quality of life. But within those studies, fatigue and mood disturbances have been identified as variables which dramatically impact the patient's experience. Researchers still are in search of a uniform and consistent relationship between mood disturbances and fatigue in this patient population. Molassiotis (1999) examined the symptoms that hindered the patient during this treatment with 91 BMT survivors. Two groups were defined: survivors six months post transplant and survivors receiving maintenance therapy. Using three tools to measure symptoms, the researcher found that fatigue was highly correlated with anxiety (r = 0.52), depression (r = 0.59) and psychological symptom distress (r = 0.58) all at p < 0.001. This established mood disturbance measures as appropriate for the present study along with measures of fatigue. Again, the use of light has shown success in modulating mood disturbances in specific patient populations (Ancoli et al. 2003; Hickman et al. 2007; Paus et al. 2007).

Sasaki and colleagues (2000) investigated patients with leukemia (n = 39), receiving allogeneic transplants during their period of isolation. Sixteen patients (41%) scored higher on mental disorder criteria with predominant groups being female (p = 0.033) and patients receiving unrelated donor cells (p = 0.026). The research team

suggested that the period of isolation was instrumental in increasing the scores on mental disorder criteria. Trask's (et.al. 2002) study demonstrated that as high as 50% of the patients self reported emotional distress and anxiety ($p < 0.05$) with 20% of patients identifying depression as an issue. The 50 patients who participated were all candidates for allogeneic transplant so the data reflect the patients' emotional status prior to any conditioning regimen or PBSCT.

The issues of depression or mood disturbance can present throughout the continuum of care for bone marrow transplant patients. Prieto and colleagues (2002) investigated the frequency of mood disturbances prior to and during hospitalization for PBSCT, correlating the presence of mood disturbance with the length of stay for allogeneic ($n = 91$) and autologous transplants ($n = 129$). Participants were interviewed prior to hospitalization and weekly until discharge or death. Multiple tools were used to assess psychological adjustment disturbance, including the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983). The researchers found no significant difference between prevalence rates for mood, anxiety or psychological adjustment disorder between the two groups; 38.8% of autologous patients and 47.3% allogeneic patients experienced one of these conditions ($p = .26$). There was, however, an 8% increase in length of stay if the patient had a mood, anxiety or adjustment disorder ($p = .022$). Studies which focus on the psychological distress within the first month post transplant were found with less frequency than those focusing on the long term psychological wellbeing of this patient group.

Akaho and colleagues (2003) investigated psychological distress in the post transplant period in patients diagnosed with leukemia undergoing allogeneic bone marrow transplant. Of the 72 patients, there was a mix of those patients in their first remission, the first chronic phase, and later stages of the disease. The Profile of Mood States (POMS-SF) (Shacham, 1983) was completed by all patients one week prior to the start of the isolation period. Patients were interviewed at 2-3 weeks into the isolation period. The researchers abstracted anxiety, depression, anger, fatigue, and confusion data to combine these into one data grouping. Overall survival and disease free survival was significantly correlated with gender with female patients being three times as likely to survive when compared to the male participants (r=0.4-0.8, p=0.05).

There is a definitive need to have more research with a primary focus of mood disturbances in this patient population. It is most frequently addressed as a component of quality of life in the PBSCT patient. While the team lead by Schulz-Kindermann (et al. 2007) was investigating the relationship between quality of life and cognitive functioning in the transplant patient, they found no difference in the emotional or cognitive functioning prior to transplant and at day 100 post transplant (p = 0.159 and 0.804 respectively). As in many of the transplant studies, the sample size was small for patients who completed all study requirements (n = 19). The most distressing issue for the participants of this study was impaired physical functioning, not psychological distress. Another study performed the same year (Rusiewicz, DuHamel, Burkhalter, Ostroff, Winkel, et al. 2007) did focus on psychological distress of the PBSCT patient one year or longer post transplant. The Brief Symptom Inventory (BSI) (Derogatis, 1993) was used,

providing a global measure of psychological distress. Two of the nine BSI subscales directly relate to depression and anxiety. In the sample of 236 PBSCT patients, the researchers found that 23.7% (p < 0.05) of participants suffered from significant depressions and 22.5% (p < 0.05) from anxiety. Interestingly there were no significant differences in amount of psychological distress based on length of time post transplant. The researchers found that 43% of the participants reported clinically significant global psychological distress. The subscale Obsessive-Compulsive (trouble remembering, mind going blank) affected the highest number of participants (36.4%) and Somatization (pain, nausea, weakness) affected 31.4% of participants. While there has been no study to document the relationship, the authors of this study did discuss a hypothesis for future consideration. The existence of psychological distress could lead to a heightened self-report of cognitive symptoms.

Similar to the fatigue experience in PBSCT, mood disturbances can linger long after the transplant has been successfully completed. Depression was the focus of research for DeMarinis and colleagues (2009) involving patients 1 year post PBSCT. They investigated depression in 23 patients within that time frame and found explicit gender differences in the presence and treatment of depression. Women in the study had a significantly higher rate of depression (p=0.007) and were more likely to be receiving antidepressive therapy (p=0.02) at least 1 year post transplant.

Researchers seek methods to remedy the mood disturbances felt by this patient population. A unique but logical approach, using partner support to combat the distress, was the focus for Rini and colleagues' (2011) study. Like many of the available studies,

Rini focused on the 1- to 3-year post transplant period to investigate partner support as a predictor of stress in the patient. The study was also performed to see if the quantity of partner support or the effectiveness of the partner support would have the greatest impact on the patient. Participants (n = 230) completed tools to define the quantity of partner support and partner social support effectiveness. There was a negative association between partner support quantity and distress (r = -.09) however the correlation did not reach significance (p = .09). Partner social support effectiveness showed a statistically significant negative significant correlation with distress (r = -.49, p < .001). Participants who received more effective partner support reported significantly less distress than those who received less effective partner support. There were interesting predictors of post-transplant distress revealed in this study. Unmatched allogeneic transplant was associated with greater distress than autologous or matched allogeneic transplants (p = .03). Female participants experienced more distress than male counterparts (p = .004) and participants with greater than a high school education reported less distress than those with a high school education or less (p = .01).

In the review of studies investigating the impact of mood disturbances on the transplant recipient, it is almost uniform to find studies with small sample sizes, a variety of transplant types and mixed cell types for the primary cancer diagnosis. In a review performed by Moser and colleagues (2009), only 22 prospective reports were found containing at least 20 participants in a 5-year span which addressed the physical, psychological and social aspects of quality of life for the transplant patient. There appears to be great opportunity to study the frequency of mood disturbances in the patient

population, particularly in the immediate post transplant period, and to investigate interventions beyond drug therapy to assist patients in supporting their emotional stability.

**Relation between fatigue and mood disturbance.** BMT patient research has demonstrated a relationship between two of the variables in this study, fatigue and mood disturbance. In a relatively early study investigating relations of symptoms in the transplant population, Gaston-Johansson et al. 1999) surveyed patients with breast cancer undergoing BMT. The study demonstrated a significant correlation between fatigue and mood with these 127 patients ($r = 0.58$, $p < 0.001$). Molassiotis (1999) also studied correlations between the symptoms experienced by patients at least 6 months post transplant. In the participants ($n = 91$), he found that lack of energy was correlated with depression ($r = 0.59$, $p < 0.001$), psychological distress ($r = 0.52$, $p < 0.001$) and depressed mood ($r = 0.45$, $p < 0.001$).

El-Banna and colleagues (2004) studied these two variables in patients with lymphoma undergoing bone marrow transplant. As with many of the studies, the sample size was small with 27 participants. This study also utilized the PFS-R instrument (Piper et.al., 1998) to measure fatigue levels but used The Center for Epidemiologic Studies-Depression Scale (Radloff, 1977) to measure depression rather the broader concept of mood disturbance. This study found that the fatigue scores, total and subscale, and depression scores were highest at day 7 post transplant (all $p < 0.05$). Spearmen correlation between depression and all fatigue scores ranged from 0.851 to 0.929 ($p = 0.001$ and 0.009, respectively).

**Summary**

Nightingale (1859) utilized controllable variables in the environment to facilitate

healing. She promoted light, color and cleanliness to enhance the patient's recuperation.

The science behind the interaction between light and color on an individual has not yet

been defined in the 21st century. Nightingale used anything within her control to provide

an improved outcome for those receiving care. And it is for this reason she embodies

what nursing has always been. The goal of nursing has always been to improve the

patient experience while improving patient outcomes, whether in the 19th or 21st

centuries.

Roger's (1980) abstraction of the human interaction with their environment

funnels momentum into just how critical nursing is in the patient's recovery. The idea

that environment can constantly impact, change and modify the human experience is

pivotal to the idea that light can impact symptomatology. Walling's (2006) use of

acupuncture as an example of the environment changing the internal functioning of the

human provides one with a concise picture of Rogers' vision. In emerging research in

psychoneuroimmunology, the Rogerian viewpoint of patient and environment interaction

appears more logical and plausible.

Fatigue and mood disturbances are frequent symptoms experienced by patients

prior to, during and after PBSCT (Andrykowski et al. 2005; Bevans et al. 2008; Carlson

et al. 2006; Coleman et al. 2002). These are internal experiences that patients identify yet

their etiology can only be assumed to originate from the cancer or the treatment applied

to cure it. The application of light as an environmental element in interaction with human

biochemical processes is plausible but not fully defined or understood. There is evidence that light plays a part in a multitude of biochemical changes that occur within the inner workings of physiology. Light as a therapy has a very limited body of knowledge in the cancer patient population, so the connection between light, fatigue, and mood disturbances in this population is still a question. The measurement of natural and ambient light exposed to the patient during the treatment phase of PBSCT has not been performed.

Nursing defines interventions which make differences in not only the patient's experience, but the patient's outcome. The research on the impact of light on the PBSCT experience is non-existent, yet there appears to be supportive research to apply it to this patient population. The vast majority of patients undergoing PBSCT are not in the position to have multiple options for treatment. Nursing may have the opportunity to provide supportive interventions which could make the patient feel better and perform better in the post transplant process. While the use of light as a therapy may not provide a curative intervention to treat symptoms of fatigue and mood disturbances, it may be used as an adjunct along with other interventions such as exercise or cognitive behavioral therapy to aid the patient toward a better outcome.

The following chapter will discuss the design of the study and the measurement instruments used. It will discuss the sample characteristics and the analysis for the findings.

# CHAPTER THREE

## METHODS

This chapter will describe the methods used in this study. A review of the study purpose and research aims and hypotheses are provided. The study design, sampling methods, sample characteristics and sample size are discussed. Variables, details of measurement instruments, data collection and management, data analysis and ethical considerations are also included.

**Study Purpose and Aims**

The purpose of this study was to examine the relationship between light exposure during the immediate post-bone marrow transplant experience, activity levels post transplant and the perception of fatigue and mood. Light levels had not been studied in the bone marrow transplant patient nor had the associations between light and fatigue and mood been explored. Patients undergoing BMT served as the sample population since they have prolonged inpatient stays and most have moderate to severe fatigue (Molassiotis, 1999).

Martha Rogers' (1980) Science of Unitary Human Beings theory provided the foundational constructs and framework for the study of light exposure and a patient's symptoms. The use of light as the independent variable is identified as a component of the larger environmental energy field. Between the environment and the human energy

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field interaction, light served as a stimulus for pattern change occurring in the human energy field.

**Study Design**

This study was descriptive and exploratory, using measures at time points during the transplant process to determine the relationship between natural and ambient light exposure to the patient experience during and following the bone marrow transplant. Since the relations between the selected variables have not been defined, this study acted as a precursor to investigating light as an intervention within the stated patient population.

Measurement tools for fatigue and mood provided a way of evaluating the relationship between the variables. Instruments for fatigue and mood state were completed by participants at three time points: prior to admission, Day 2 of post transplant and Day 11 post transplant. Light levels in the patient environment were measured at two time points using a wrist light meter with memory. The light levels were measured for a maximum of 48 hours at each time point. The patient's activities during study participation were recorded by using a wrist worn activity monitor with memory (Philips Respironex, 2013). This device was used to count steps taken during two 48 hour periods. The two data collection time points for light and activity were measured at Day 0-2 of transplant and Day 9-11 of transplant.

**Study Site**

The research was conducted at Loyola University Medical Center located in Maywood, IL. It is a teaching, tertiary care, level 1 trauma center with an active bone

marrow transplantation program. The hospital is licensed for 569 acute care beds with 27

bone marrow transplant beds (15 inpatient, 12 outpatient). Between 2009 and 2013,

Loyola has performed 581 adult bone marrow transplants (BMTinfonet, 2015). It is one

of the largest bone marrow transplant programs in Illinois (National Marrow Donor

Program, 2016).

**Sample**

Participants approached for participation in this study had all been approved for

bone marrow transplantation for a hematologic non-solid tumor malignancy. As part of

the preparation for transplant, these individuals received full physiological work ups

which included assessment of neurological, cardiac and renal function. It is for these

reasons that participant co-morbidity was not addressed as exclusion criteria. All patients

received the transplant procedure and the majority of their care at either the Cardinal

Bernardin Cancer Center or the Bone Marrow Transplant Unit at Foster G. McGaw

Hospital, both at Loyola University Medical Center. Patients receiving autologous or

allogeneic bone marrow or stem cell transplant were invited to participate.

**Inclusion criteria.** Participants invited to participate in the study were between

the ages of 18 and 75 and able to understand, read, write and speak English. Participants

between the ages of 18 and 75 were considered eligible. The participants had to be

accepted to receive a bone marrow or stem cell transplant for treatment of leukemia,

lymphoma, malignant myeloma, and precursor conditions to these. Finally, the

participants were expected to receive pre-transplant care and the first 100 days post

transplant care at Loyola University Medical Center and/or the Cardinal Bernardin Cancer Center in Maywood Illinois.

Participants were required to have normal mental status and capacity to understand. They were alert, oriented and able to maintain attention and eye contact during interview. Speech was assessed to be clear and understandable. Patients had an intact memory and were able to comply with the study related interviews

**Exclusion criteria.** Participants receiving a stem cell or bone marrow transplant for solid tumor malignancies or autoimmune diseases as the underlying condition were not eligible to participate. Participants who had received a prior transplant for any condition were not approached to participate. It was believed that patients naïve to the transplant process would provide more information from the transplant experience and would not be influenced by a prior transplant experience. Screening for transplant entails survey of physiologic functions so no subject co-morbidities were addressed in the exclusion criteria. Presence of co-morbidities such as a low ejection fraction or significant renal insufficiency could preclude patients from undergoing a bone marrow transplant.

**Sample size estimation.** According to Browner, Newman, Cummings, and Hulley (2001), using a significance level of 0.05 for a two sided hypothesis, a medium effect size of .30 and a power of .80, a sample size of 85 was projected. An additional method for determination of sample size required for the current study included power analysis for the hypotheses (Browner et al. 2001). All of the hypotheses assumed that the threshold for rejection of the null hypothesis was to be a p value of .05 using a two-tailed

test. Further, the desired level of statistical power was .80, a level that is generally viewed as acceptable for exploratory research (Browner et al. 2001). Estimates of effect size in the power analysis were based on prior research on the relationship between light exposure and the dependent variables in the present study. Computations of statistical power were based on the G-Power 3 software package (Faul, Erdfelder, Lang & Buchner, 2007). This software package enabled the investigator to enter specific effect sizes based on prior research on the relationships under study.

To test hypothesis 1, the bivariate correlations between light levels and measures of fatigue and mood were examined. Prior research suggested that light levels have a correlation of approximately 0.3 with these outcomes (Liu, 2005; Partonen & Lonnqvist, 2000). Using this estimate of the effect size (r = 0.3), a sample size of 82 was needed to attain a power level of .80. For hypothesis 2, bivariate correlations between light levels and physical activity were computed. While prior studies of the effects of light do not provide an estimate of effect size specifically for activity, the effect sizes noted earlier in Chapter 2 for other dependent variables tend to range around .30. Using this figure as an estimate of the effect of light on activity, a sample size of 82 was needed to attain a power level of .80 for hypothesis 2. To test hypothesis 3, a multiple regression procedure was utilized, in which levels of fatigue at defined time points post transplant were regressed onto two predictor variables: pre-transplant fatigue and cumulative light exposure. If we assume that the effect size for cumulative light exposure is approximately as large as the bivariate association between light exposure and fatigue at one time point (r = .3), then a sample size of 82 cases would be needed to attain a power level of .80. In

order to provide adequate statistical power for testing all three hypotheses, a sample of 82 was needed. Given the reality of a combined mortality rate between autologous and allogeneic transplants and attrition, additional patients were enrolled. The ending study sample size was defined as 90.

**Recruitment.** It was anticipated that the prospective participants would be identified primarily by the BMT Coordinator scheduling process. Physicians in the Section of Hematology and Oncology at Loyola University Medical Center agreed to allow their patients to be approached for study participation. The preparation for the transplant admission was tracked by the BMT coordinators; this schedule was shared with the investigator on a weekly basis. All participants and their primary care givers were required to attend a 4-hour class to prepare the patient for the transplant as well as to prepare the primary care givers to handle outpatient care and needs. Once the patient was on the schedule for either class attendance, line placement or plasmapheresis, the investigator met them and an explanation of the study was provided. A copy of the consent was provided to any participants who indicated interest in participating in this study. The participant could sign at the first meeting with the investigator or the patient could sign at a later date but signature was required prior to admission for transplant. As the trial went on, accrual was slow. With the approval of Cancer Center Administration and the Cancer Research Office, the BMT Research RN also began introducing the study to prospective participants as she was discussing other studies that the participant might wish to participate. The BMT Research RN would meet with all transplant patients prior to hospitalization to educate them on research trials for which they were eligible for.

Approximately 6 months into the trial with accrual continuing to be slow, the investigator was also invited to present the trial to all patients attending the BMT Patient & Caregivers Class. At that time a copy of the consent was provided to all BMT patients. Either the investigator or the BMT Research RN would follow up with patients regarding their signed consent and willingness to participate. This approached assisted in connecting the investigator to the prospective participants however accrual continued to be slow.

**Variables**

**Independent variable.** Light was the independent variable within this research. Conceptually, light was defined as "a form of energy that makes it possible to see things; the brightness produced by the sun, by fire or by a lamp" (Merriam-Webster, 2015). An operational definition for light was an electromagnetic radiation that is visible and perceivable by the normal human eye made up of colors between red and violet in varying frequencies and wavelengths (FreeDictionary, 2015). The measurement of light was accomplished through the use of the wrist worn device. This wrist worn meter was programmed to take light readings at defined intervals with a memory capable of holding multiple days of data. Light was described in terms of lux for intensity. Light exposure was derived from artificial interior devices (ambient light) or from natural sunlight coming in through doors or windows within the hospital.

Light exposure was measured by Philips Actiwatch 2 meter (Philips Respironex, 2013). It is designed in the style of a wrist watch and can take continual light readings at defined time intervals. Both ambient and natural sun light were captured. Light exposure

was measured for 48 hours: Day 0 (date of actual transplant) to Day 2 and Day 9 to Day 11 post transplant. Light was reported as one cumulative number in lux for each measurement period.

**Dependent variables.** The defined dependent variables for the study were fatigue, mood, and activity. Fatigue was conceptually defined as a subjective experience encompassing weariness, tiredness or lack of energy (Dimeo, 2001). Operationally, fatigue was defined in the scores on the 22 item Piper Fatigue Scale-Revised (PFS-R) (Piper et al. 1998).

Within this cancer patient population, research is also being performed to define "cancer related fatigue" (CRF) with the development of specific criteria which would differentiate it from fatigue associated with other illnesses. CRF is described as persistent subjective sense of tiredness related to cancer treatment, it is based on the patient's perception and it interferes with the person's normal functioning (Piper & Cella, 2008). This work on CRF is evolving in the literature and is not universally measured with a specific tool. For this reason, fatigue was addressed as a variable that is present within the defined subject population.

The second dependent variable was that of mood. Conceptually, mood was defined as the emotional state of an individual's mind (FreeDictionary, 2011) and was reflective of how the person was experiencing the feeling at a particular point in time. Mood may have many feelings and the feelings can be transient. Psychological distress may also be considered as a synonym for mood. Operationally, mood was defined by the scores on the Profile of Mood States-Short Form (POMS-SF) (Shacham, 1983).

The third dependent variable was physical activity. Conceptually, physical activity was defined as the independent movement of the body performed by the individual. Operationally, physical activity was measured in quantity of steps taken using a Philips Respironex Actical (Philips Respironex, 2013) which will be detailed in the next section.

**Measurement Instruments**

**Light.** In the original plan for this research, light was to be measured using a digital lux/footcandle meter which was advertised to measure up to 100,000 lux. The ExTech Model LX-1108 distributed by D.A.S. Distribution, Inc. located in East Granby, CT was marketed as having data logging capability and computer interface. It was programmed to take light readings every 30 minutes for a 48-hour period and was used on the first two patients enrolled in the study. At the end of the 48-hour period, the instrument only provided intermittent readings and not a sustained data log. After working with the company, this equipment was abandoned. A protocol amendment was submitted to use the Actiwatch 2 light meter.

For the remainder of the study, light exposure was measured using a digital lux meter which measures up to 100,000 lux. Actiwatch 2 was used as the light measurement with data logging capability and computer interface. This model had a built in clock with date and time stamp and data storage recording intervals from 1 second to 60 minutes based on programming. It is distributed by Philips, Inc. located in East Granby, CT. The Actiwatch 2 is manufactured by Philips Respironex using a silicon photodiode light sensor. The device is re-chargeable with a battery life of up to 30 days set at 1 minute

intervals. The light measurement is provided in lux with an illumination range of 5-100,000 lux. The device has an accuracy of 10% at 3000 lux. It is marketed as having moisture protection with water resistance at 1 meter for 30 minutes. It is resistant to dust, water, heat, perspiration and cold. It works with Windows 2000 operating systems and was set to take light readings every minute for a 48-hour interval. Participants were instructed to wear the meter on the wrist for the defined time interval. Wrist devices were disinfected with antibacterial wipes and actual bands were removed and sterilized between patients. This device has been tested in multiple settings validating its reliability in the measurement of lux exposure (Long, Palermo, & Manees, 2008; Osse, Joke, Tulan, Hengeveld & Bogers, 2008; Wener, Luciano, Guyer & Jenni, 2008).

The Actiwatch 2 was placed on the participant's wrist on Day 0 and removed on Day 2 accounting for 48 hours of light measurement. The Actiwatch 2 was placed on the participant's wrist on Day 9 and removed 48 hours later on Day 11. Participants were instructed to keep the wrist band fully exposed for maximum accuracy in light measurement.

**Fatigue.** The Revised Piper Fatigue Scale (PFS-R), developed by Piper, Dibble, Dodd, Weiss, Slaughter et al (1998) was used to measure fatigue. The instrument consists of 22 items, asking the subject about their current state of fatigue in the last 1 to 2 days. It was derived from the original Piper Fatigue Scale (PFS) (Piper, Lindsey, Dodd, Ferketich, Paul et al. 1989) which has 42 items. The original and revised tools have been used primarily with breast cancer patients (Demiralp, Oflaz, & Komurcu, 2010); however, these tools have also used with other oncology patient populations (Alt, Gore,

Montagnini, & Ng, 2011; Battaglini et al. 2009; Berger, 1998; Berger, Grem, Visovsky, Marunda & Yurkovich, 2010; Berger & Higginbotham, 2000; El Banna, 2004; Gaston-Johansson et al. 1999; Piper et al., 1998; Schneider & Hood, 2007). While its use in non-oncology conditions is limited, it has been used in female patients with benign breast disease (Andrykowski, Curran, & igLhtner, 1998) and care providers of cancer patients (Gaston-Johansson et al. 2004). It has been translated and validated in multiple languages including Portuguese (dos Santos, Mota, & Pimenta, 2009; Lamino, Mota, & Pimenta, 2011), Italian (Giacalone et al, 2010; Annunziata et al., 2010), Chinese (Liu & Yuan, 2011), Greek (Lavdaniti, Patiraki, Dafni, Katapoki, Papthanosoglou & Sotiropoulou, 2006), and Swedish (Ostlund, Gustavvsson & Furst, 2007) among others.

The tool has one overall score and 4 subscales scores: behavioral/mood (6 items), sensory (5 items), affective (5 items), and mental/cognition (6 items). The behavioral/mood subscale relates to the severity, distress and degree of disruption that fatigue has on the subjects' activities of daily living. The sensory subscale relates to the subjective physical symptoms of fatigue. The affective subscale focuses on the emotional attributes the subject assigns to the fatigue experience. Lastly, the mental/cognition subscale addresses the mental and mood states of the subject (Clark, 2006). Items are scored in a Likert type scale format from 0 being no distress or none to 10 being a great deal or significant distress.

Subscale mean scores are calculated by summing the individual items related to that subscale and dividing the number of items in the subscale/total scale to be consistent with the 0-10 scaling. Mild symptoms are defined as 0-3.99, 4-6.99 for moderate

symptoms and severe as 7-10. The tool takes about 2-5 minutes to complete. Adult cancer patients have found the tool easy to use (Berger et al. 2009).

In Piper's original study, content and face validity of the PFS were determined through analysis by an expert panel as well as through an extensive literature search (Piper et al. 1989). In the revised tool, three of the original dimensions were retained and a cognitive/mental dimension was added (Piper et al. 1998). Similar to the original PFS, the PFS-R measures the multidimensional fatigue experience. Convergent validity has been established with the Fatigue Symptom Checklist (r = 0.55) (Whitehead, 2009). It has been correlated with the Symptom Experience Report (SER) subscales: SER-Weak (r = .66) and SER-Tired (r = .75) (Andrykowski, Brady & Hunt, 1993). An exploratory factor analysis found strong support for construct validity in the behavioral/severity and affective meaning subscales (Clark et al., 2006). Concurrent validity between the PFS-R and POMS-SF Fatigue subscale was established with an r = 0.53 to 0.65 (Giacolone, et al. 2010). The tool has convergent and discriminate validity with the POMS-SF (Piper et al. 1998). Criterion validity has been established between the PFS-R and Multidimensional Fatigue Index (MFI) (Smets, Garssen, Bonke, & DeHaes, 1995) with correlations between MFI-general fatigue subscale and MFI-physical fatigue with the four PFS-R subscales respectively (r = 0.62-0.84; r = 0 .56-0.81). Dagnelie and colleagues (2006) also found criterion validity between the PFS-R Total and the MFI Subscale General Fatigue (Pearson's correlation of 0.84; p < 0.01). Construct validity was evaluated between the MFI and PFS-R in breast and lung cancer patients.

Piper and colleagues (1998) tested the reliability of the PFS-R with 382 breast

cancer survivors achieving excellent Cronbach's alphas for the total score and the four

subscales from .92 to .95: sensory = .959, affective = .954, cognitive/mood = .926,

behavioral/severity = .920 and total = .966. Factor analysis was performed to determine

items to be kept. The standardized alpha for the entire PFS-R is 0.97. Test-retest

reliability was performed with a .98 correlation (So et. al. 2005) and Pearson's correlation

coefficients of 0.63 and .91 between subscales (Giacalone et al. 2010). Internal

consistency of the PFS-R in a variety of cancer patient populations has been established

with Cronbach's alphas of .85 to .97 (Piper et al. 1998; Gledhill, Rodary, Mahe & Laizet,

2002; Gaston-Johannson et al. 1999; Schneider & Hood, 2007).

The PFS-R has been widely used in evaluating fatigue in breast cancer patients

prior to chemotherapy, during treatment and post treatment with good Cronbach's alpha

scores of .92 to .95 (Berger & Higginbotham, 2000; Andrykowski, Curran & Lightner,

1998). It has been able to detect significantly different levels of fatigue with only a 7-

point difference in mean scores ($p<0.05$) (Andrykowski, Curran & Lightner, 1998). Total

fatigue scores correlate with three of the PFS-R subscales ($r \geq .87$). The tool has been

used with bone marrow transplant patients and their caregivers with Cronbach's alphas of

.83-.90 (El-Banna, Berger, Farr, Foxall, Friesth, et al. 2004; Gaston-Johannson et al.

1999; Gaston-Johansson et al. 2004).

The PFS-R was completed by the participant at three time points. A baseline

measure was taken prior to the participant's admission into the hospital for the transplant

procedure. The participant completed the PFS-R at Day 2 and again on Day 11 at the time the wrist monitors, the Actical and the Actiwatch 2 were removed.

**Mood Disturbance**

The Profile of Mood States short form (POMS-SF) (Shacham, 1983) was used to measure the mood state of the participants. It was derived from the original Profile of Mood States (POMS) created by McNair, Lorr & Droppelman (1971). It is important to note that there are several shortened versions of the POMS from the original 65 item format. Shacham (1983) developed a 37 item version of the POMS-SF which utilizes five of the original mood states: tension-anxiety, depression-dejection, vigor-activity, fatigue-inertia and anger-hostility. The sixth mood state on the tool is confusion-bewilderment. The POMS-SF has been used extensively in the cancer patient population (Tfijsburg, Van Knippenberg & Rijpma, 1992) as well as with healthy subjects and subjects with a variety of conditions.

Using the same Likert type scale as POMS, subjects completing the POMS-SF can select from 0 (none or not at all) up to 4 (the most or maximum). The maximum score for any one mood state is 4 as questions in each subscore are added and then divided by the number of items for that mood state. The higher the score, the more negative the mood state. The composite score of the tool is termed the Total Mood Disturbance (TMD) and is calculated by adding the individual scores for Tension, Depression, Anxiety, Fatigue and Confusion subscales and subtracting the Vigor subscale score. The maximum TMD score is 16.

In developing the shortened version, Shacham (1983) eliminated 2 to 7 items from each subscale without decreasing the internal consistency. In the process, the Confusion subscale and Tension subscale saw improved internal consistency coefficients. The tool was validated with 83 participants with a cancer diagnosis however the management of these patients was focused on pain management rather than disease treatment. The correlations in the subscales between the original POMS and the POMS-SF were all high, (r > .95) with the TMD of .99. There was no factor analysis in the original work performed by Shacham (1983).

Curran and colleagues (1995) tested psychometric properties of the POMS-SF as compared with the original POMS. Four of the six patient participant groups included BMT survivors (n=210), BMT candidates (n= 85), breast cancer patients (n=46) and a healthy group of subjects (n= 76). Of most interest to the current study, BMT candidates and BMT survivors demonstrated a high internal consistency in the scores and TMD of the POMS-SF and POMS. In fact, it was felt that the POMS-SF had stronger internal consistency than the original tool. The BMT candidate TMD score correlated well with all subscale scores between the POMS and POMS-SF (r ≥ 0.78). In the BMT survivor group, correlation between TMD score and subscale scores was also high (r ≥ 0.80) between the two tools.

Baker (et al., 2002) evaluated the internal consistency and validity of the POMS-SF with 428 cancer patients awaiting bone marrow transplantation. The Cronbach's alpha ranged from .78 to .91 for the six subscales and overall TMD score. This study also included a confirmatory factor analysis which supported the six factor interpretation of

the POMS items to the POMS-SF. Convergent and discriminant validity was shown through correlations made between POMS-SF and other tools. The CES-D correlated with both the POMS-SF TMD and the POMS-SF-Depression subscale at .63 and .63 (p<0.001). The researchers projected a positive correlation between the POMS-SF -Vigor and the Bradburn positive affective scale (Bradburn & Caplovitz, 1965). This was validated with an r = .53 (p < 0.001). In the same light, the POMS-SF fatigue subscale would not be expected to correlate with the Bradburn positive affective scale. This was consistent with the weak, negative relationship found between these two tools (r = -0.17, p < 0.001).

Baker, et al. (2002) assessed convergent and discriminant validity of the POMS-SF subscales as related with other measures of psychological distress. He proposed that the Depression subscale of the POMS-SF would correlate highest with the CES-D, which it did with an r = 0.63. The researchers also expected that Fatigue and Vigor subscales would correlate highest with two measure of physical functioning – the MOS Physical Functioning Scale (Aaronson et al. 1965) and the self-rated Karnofsky Performance Status (KPS) scale (Karnofsky & Burchemal, 1949). This was also confirmed with the Vigor subscale having the highest correlation with these two instruments (Vigor and MOS, r = .42; Vigor and KPS, r = .39). He also proposed that the Fatigue subscale would have the least correlation with the MOS and KPS scale which it did (Fatigue and MOS, r = -.42; fatigue and KPS, r = -.40) (p < 0.001). While the tool has been used widely with breast cancer patients (Von Ah et al. 2008), it has also been used in patients with gynecological cancer (Gould, Brown & Bramwell, 2010), prostate cancer (Bailey,

Mishel, Belyea, Stewart, & Mohler, 2004), and mixed tumor types (Cunningham, Edmonds, Phillips, Soots, Hedley et al. 2000; Silver-Aylaian & Cohen, 2001).

The POMS-SF was completed by the participant at three time points. A baseline measure was taken prior to the participant's admission into the hospital for the transplant procedure. The participant completed the POMS-SF at Day 2 and again on Day 11 at the time the wrist monitors, the Actical and the Actiwatch were removed.

**Activity.** In the original protocol, activity was going to be documented through a self-reported diary kept by each participant. When the search for a new light meter ensued, it was decided that activity would also be measured by a device as well. The Actical activity monitor, manufactured by Philips Respironex, Inc., was used to measure activity. It is a 1" x 1.5" titanium accelerometer which can be worn at waist, wrist or ankle. For the purposes of this study, the device was worn at the wrist, preferably on the arm not used to push intravenous pole while up. It uses a CR 2025 lithium coin battery and has a 32mb memory (Philips Respironex, 2013). The maximum recording time is dependent on the programming but expected to be </= 12 days. It is advertised as waterproof at 1 meter for 30 minutes. The device was programmed to measure number of steps for a 48-hour period. It syncs with Windows 7 operating system when linked with an ActicReader interface device and a computer.

The Actical was placed on the participant's wrist on Day 0 and removed on Day 2 accounting for 48 hours of activity measurement. The Actical was placed on the participant's wrist on Day 9 and removed 48 hours later on Day 11. Participants were

instructed to push their IV pole with the opposite hand from the Actical placement for better measurement of steps via arm movement.

**Additional data.** The medical record of the patient was accessed for data retrieval. Specific physiologic data were extracted from the medical record for the three data collection times. This information included age, gender, type of transplant, type of underlying malignancy, date of original diagnosis, height, weight, ethnicity, KPS and hematology laboratory results. These data were collected for additional correlational investigation. The complete blood count and the KPS may provide additional information about the participant's activity tolerance. In addition, the KPS has established correlation with the POMS-SF Vigor and Fatigue subscales.

## Research Procedures

After the approval by the dissertation committee, the research proposal was submitted to the Loyola University Medical Center IRB for review and approval. Participants were required to sign the IRB approved informed consent and were provided with a copy. The participants were educated on the requirements for participation, which emphasized that participation could end at any time, upon their decision, without any consequence to their care and treatment.

After the protocol had been approved by the designated IRBs, meetings were held with nursing staff, BMT Nurse Practitioners and Hematologist to discuss eligibility requirements and critical elements of protocol. Potential participants were identified by the BMT Coordinators responsible for scheduling all critical elements of the patient's pre transplant work up. The majority of potential participants were met during the Patient &

Caregiver Class held at the Cardinal Bernadin Cancer Center. All transplant patients and their caregivers were required by the transplant program to attend this 3-hour educational session to prepare them for the post discharge period.

If the participant was interested in participation, the informed consent document was reviewed, including a description of the study, the risks and benefits, confidentiality issues and a statement indicating that participants could withdraw from participating in the study at any time with no consequence. Once the potential participants were screened and confirmed to meet eligibility criteria, the informed consent process was completed.

All information obtained from the participant or their respective medical record was secured by the investigator with only the study roster and the participant's signed informed consent containing the name and medical record number. All other documents used for data collection were de-identified.

**Data Collection and Management**

Participants were identified on study related documents using first and last initials and a unique identification number. One master study roster matching participant name and identification number was kept in a locked and secured location. Participants completed measurement tools, PFS-R and POMS-SF, prior to admission, on Day 2 and Day 11. During Day 0-2 and Day 9-11 post transplant, light levels and activity were monitored for 48 hours. Participants were instructed to wear the Actical activity monitor and the Actiwatch 2 monitor continuously on their wrist for the 48 hour period but were requested to remove both devices when taking the twice daily tub bath. For the Actical monitor, participants were requested to push the IV pole with the opposite hand in order

to gain better accuracy. For the Actiwatch, participants were requested to keep the wrist monitor uncovered by clothing to gain the maximum recording of light exposure. Contact with the participants took place in the Cardinal Bernardin Cancer Center and the Loyola University Medical Center.

At each time point during the participant's post transplant, the instruments were administered for completion and immediately retrieved. Data were collected using patient completed questionnaires and downloading data from the Actical activity monitor and the Actiwatch 2 light monitor. Data downloaded from the two meters was done for 48 hour periods during Day 0-2 and Day 9-11 post transplant. The rationale for this data collection at two time points was to document changes in light levels and activities as the patient began bone marrow engraftment.

All study related documents were coded with the participant number were locked in a file cabinet of the investigator.

**Data Entry, Cleaning, and Analysis**

Data were entered into and analyzed using SAS Statistical Software ®. All data entry were doubled checked for accuracy by an independent reviewer at each data entry point. Random review of data with verification of computer entered measures was performed throughout the data collection period to ensure accuracy. Data analysis for Aim 1and Aim 2 included using Pearson Product Moment Correlation and regression analysis with an alpha of 0.05. Cross sectional correlations between light levels and measures of the dependent variables were conducted at each of the following measurement points: prior to admission, Day 0-2 post-transplant and Day 9-11 post

transplant. Data analysis for Aim 3 and testing of Hypothesis 3 was performed using multiple regression analysis at an alpha of .05.

**Considerations**

 **Risk benefit ratio to participants.** The BMT patient had no interventions imposed as a result of their participation in this study. The only identifiable risk to the patient was the disclosure of personal protected health information. This risk was mitigated through document control including locking all study related material in locked cabinets in the home of the investigator. This risk was also mitigated by linking medical record data with only the assigned patient code. Participants were informed that they could end their participation at any point during the study. Any data that were collected from the participant's medical record were recorded only once on study forms with only the participant's initials and the three-digit participant study number. There were no direct benefits for participation to the subject. A higher level benefit was the contribution to the body of knowledge regarding the transplant experience.

 **Ethical considerations.** The study was submitted to the Loyola University Medical Center IRB for review and approval to ensure that elements for protection of human subjects were present. Participants were fully informed of the specifics of the research prior to signing the IRB approved informed consent document. Participants also verbalized the understanding that withdrawal from participation could occur at any time point during the study without consequences or impact to the course of treatment.

**Summary**

In this chapter, study related procedures were described including protocol approval, study procedural requirements, patient accrual process and data collection/control. In chapter 4, the results of this study are presented.

# CHAPTER FOUR

## RESULTS

The purpose of this study was to test the hypotheses that light levels have a relationship to the levels of fatigue and mood a patient experiences while undergoing a bone marrow transplant. A secondary purpose was to investigate any relationship between light level exposure and physical activity. In addition, it meant to determine the relationship between cumulative light levels and fatigue. The aims of the study were as follows: (1) to establish the relationship between natural and ambient light exposure and a bone marrow transplant patient's level of fatigue and mood state during hospitalization, (2) to establish the relationship between the level of light exposure and a bone marrow transplant patient's physical activity during transplant hospitalization, and (3) to establish the relationship between the cumulative level of light exposure with fatigue in a patient during the bone marrow transplant process.

### Recruitment Information

Ninety patients were consented and enrolled in this study (See Figure 1 for enrollment diagram). Participants were only consented if they met study criteria. Of the 90 participants, 4 participants were initially excluded due to withdrawal of consent (n=2, 2%) or failure to provide baseline information at the beginning of the study (n=2, 2%). Eighty-six participants (95%) completed the baseline measures. After the baseline measurement period, 4 participants (4.65%) withdrew consent and 4 participants (4.65%).

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were too ill to continue. When participants stated they did not wish to continue, it was primarily due to them feeling unwell. For participants that were assessed as too ill to continue, it was due to change in condition which prevented them from participating. Changes in condition included decreased level of consciousness or endotracheal intubation. After the baseline measures had been collected, 2 participants (2.32%) expired prior to getting to transplant. Since the participants were severely immunocompromised, any symptoms of illness by the investigator would prohibit her from seeing the participants for monitor application or completion of measurement tools. This occurred once prior to the Light Time 1 measurement period (n=1, 1.16%).

For Light Time 1 measurement, 74 (82.2%) participants were included. Prior to Light Time 2 measurements, 6 participants (8.1%) were discharged home prior to Day 9, 5 participants (6.75%) declined to continue participation, 1 participant (1.35%) was too ill to continue, and 1 participant's data was not retrieved due to investigator illness (n=1, 1.35%). There were only 61 (67.7%) participants available for Light Time 2 measurement period. One participant (1.35%) experienced cardiopulmonary arrest during this measurement period so data were incomplete. This meant that complete study data were only retrieved for 60 of the 90 consented participants or 66.6%.
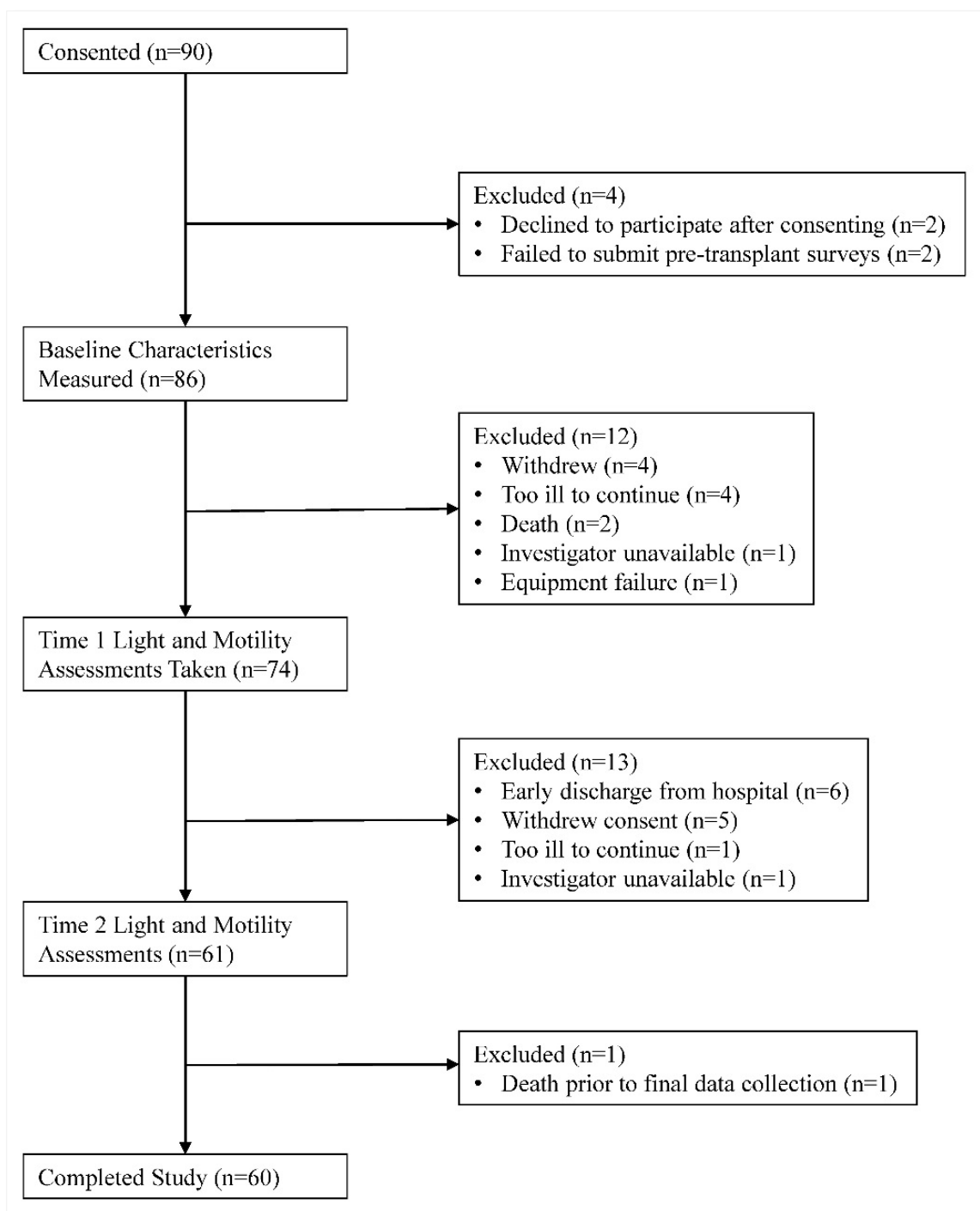
Figure 1. CONSORT 2010 Flow Diagram.

**Missing Data**

Missing data were most frequently due to the participant not feeling well enough to complete the instruments or not inclined to wear wrist devices. If completed by the participant, the POMS-SF and PSF-R were checked for completeness prior to leaving the patient. Missing items were addressed verbally with the participant at that time. There were limited issues with incomplete instruments as the investigator addressed missing items with participants at time of retrieval. Missing data also resulted from malfunction of monitoring devices or misuse by the participant. At the beginning of the trial, different devices were employed. After the first two participants were enrolled, it was identified that the light monitoring equipment was not performing as advertised so equipment was changed out to the present equipment identified in the study. Two participants failed to remove the wrist devices for the twice daily tub baths. This resulted in the failure of the devices to adequately record data. These monitors were sent to the manufacturer but data were not able to be retrieved. If the participant did not feel well enough or so inclined to participate in the Day 0-2 activities, they were asked if they could be re-approached for the Day 9-11 activities. Hence some participants might not have completed Day 2 measures but did complete Day 11 measures. Participants were well aware that they could withdraw at any time. For the most part, a participant's refusal to continue in the trial was directly related to how unwell they felt when the investigator visited them in hospital to place the wrist meters on or to have the participant complete the tools (n=9, 10%). There were participants that experienced a change in condition which prevented them from carrying out all study requirements (n=5, 5.5%). There were 3 (3.33%)

participants that expired during some portion of their participation in the trial. Six participants (n=6, 6.6%) were discharged home prior to the Light Time 2 measurements. Equipment failure with one participant (1.11%) prevented completion of all measurement points. Because participants were immunocompromised, investigator illness prevented a portion of data collection on 2 participants. As per the protocol, no drop outs were replaced with new participants.

**Characteristics of Overall Sample**

The majority of the sample was male (n=62, 68.8%), Caucasian (n=78, 86.6%) and over age 60 (n=29, 44.3%). Demographics of the participants are provided on Table 1. The sample of participants was not diverse as only four African Americans and eight Latinos were enrolled (4.4% and 8.8% respectfully). The majority of the participants (n=70, 79.5%) were receiving a transplant for either multiple myeloma, lymphoma or AML. Multiple myeloma made up the largest group of participants by disease type (n=29, 32.9%). The second most frequently diagnosis was that of lymphoma (n=24, 27.3%) followed by AML (n=17, 19.3%).

Autologous transplants are treatment options for multiple myeloma and lymphomas while allogeneic/cord blood transplants are treatment choices for the leukemias. Because of this, autologous transplants were planned for 54 (61.4%) of the participants while 34 participants (38.6%) were receiving allogeneic or cord blood transplants.

Table 1. Participant Demographics

|  | *N* | % |
|---|---|---|
| Gender | *N* (Total = 90) | |
|    Male | 62 | 68.8 |
|    Female | 28 | 31.1 |
| | | |
| Age | *N* (Total = 88) | |
|    18-40 years | 15 | 17.0 |
|    41-60 years | 34 | 38.7 |
|    >60 years | 39 | 44.3 |
| | | |
| Race | *N* (Total = 90) | |
|    Caucasian | 78 | 86.6 |
|    Hispanic | 8 | 8.8 |
|    African-American | 4 | 4.4 |
| | | |
| Diagnosis | *N* (Total = 88) | |
|    Multiple Myeloma | 29 | 32.9 |
|    Lymphoma | 24 | 27.3 |
|    Acute Myelogenous Leukemia | 17 | 19.3 |
|    Acute Lymphocytic Leukemia | 5 | 5.7 |
|    Chronic Myelogenous Leukemia | 5 | 5.7 |
|    Chronic Lymphocytic Leukemia | 4 | 4.5 |
|    Myelodysplastic Syndrome | 2 | 2.3 |
|    Other | 2 | 2.3 |
| | | |
| Transplant Type | *N* (Total = 88) | |
|    Autologous | 54 | 61.4 |
|    Allogeneic | 29 | 31.8 |
|    Allogeneic Sibling | 3 | 3.4 |
|    Cord Blood | 2 | 2.3 |

KPS attempts to define the level of function the BMT patient has. This is most frequently assessed by the Hematologist or their mid-level provider. In this study, consistent data capture of the KPS was prevented by lack of documentation in the medical record. For baseline KPS measures, it was only found in the documentation for 78 participants (86%). For Light Time 1 and Light Time 2 measures it was found in the documentation for 50 (67.56%) and 43 (70.49%) participants respectively. The mean for

KPS (82.6, S.D.9.7) at baseline was slightly higher than the mean KPS for Light Time 1

(74.8, S.D.6.6) and Light Time 2 (74.2, S.D. 8.2) measurements. A KPS of 80% differs

from 70% in the level of effort the patient must exert to continue with activities of daily

living. While a patient with a KPS of 70% would be able to care for his/her individual

needs, it would be difficult for the patient to carry on with normal pre-illness activity or

work. With a KPS score of 80%, the patient would be able to maintain normal activities

but with much greater effort exerted. KPS data can be seen in Table 2.

Table 2. KPS Status Score

|  |  | KPS |
| --- | --- | --- |
| Baseline (n = 78) | *M* (*SD*) | 82.6 (9.7) |
|  | Min | 60 |
|  | Max | 100 |
| Time 1 (n = 50) | *M* (*SD*) | 74.8 (6.6) |
|  | Min | 50 |
|  | Max | 100 |
| Time 2 (n =4 3) | *M* (*SD*) | 74.2 (8.2) |
|  | Min | 60 |
|  | Max | 90 |

Biomarkers retrieved during the study included completed blood count results.

These data were retrieved because of the relationship between activity tolerance and

anemia. As the hemoglobin and hematocrit decrease, the person's ability to tolerate

activity declines, and subsequent fatigue can be experienced. As expected, baseline

results were mostly within normal range and as the participant received pre-transplant

chemotherapy, those numbers fell. The most dramatic shift in the results is that of the

WBC which was well below normal at Time 1 measurements but demonstrated a level of

recovery by Time 2 measurements. The participant's blood product transfusion experience was not part of the data collection. The changes or lack of significant changes may be reflective of transfusion support provided between the data collection tines. These results can be seen in Table 3.

Table 3. Biomarkers

|  |  | HGB(13.5-17.5g/dL) | HCT(36-50%) | WBC(3.5-10.5K/MCL) |
|---|---|---|---|---|
| Baseline | $n$ | 86 | 85 | 86 |
|  | $M$ ($SD$) | 11.1 (1.8) | 32.6 (6.2) | 11.1 (16.9) |
|  | Min | 6.4 | 11 | 0.6 |
|  | Max | 14.3 | 43.9 | 83.5 |
| Time 1 | $n$ | 74 | 74 | 74 |
|  | $M$ ($SD$) | 9.8 (1.3) | 28.6 (4) | 1.4 (1.4) |
|  | Min | 7.4 | 20.8 | 0.1 |
|  | Max | 13.9 | 41 | 7 |
| Time 2 | $n$ | 60 | 60 | 60 |
|  | $M$ ($SD$) | 9.2 (1) | 26.5 (3.1) | 3.1 (2.9) |
|  | Min | 5.3 | 14.2 | 0.1 |
|  | Max | 12.9 | 36.1 | 11.8 |

The light measures were recorded from Day 0 (day of transplant) until Day 2 comprising 48 hours of data. This is identified as Light Time 1. The second collection period was from Day 9 until Day 11for 48 hours and this is identified as Light Time 2. The data for cumulative light exposure is displayed in Table 4. Light Time 1 lux was smaller than Light Time 2 with greater variation in the maximum and minimum values.

It would be expected that participants who performed more activity outside of the hospital room would receive a greater amount of light exposure by virtue of the brighter lighting in the halls than in the interior of the inpatient room. There were significant correlations between all three light measures. Light measures taken at Light Time 1 were

moderately correlated with Light Time 2 (r=.32, p=0.02. These can be seen in further

detail in Table 5.

Table 4. Light Exposure

|  |  | Lux (in thousands) |
| --- | --- | --- |
| Time 1 ($n = 67$) | $M$ ($SD$) | 113.39[a] (95.17) |
| Day 0-Day 2 | Min | 9.15 |
|  | Max | 428.71 |
| Time 2 ($n = 56$) | $M$ ($SD$) | 127.28* (130.76) |
| Day 9-Day 11 | Min | 6.57 |
|  | Max | 628.32 |

[a] Mean for total light exposure for 48-hour period

Table 5. Light Exposure Time 1 and Time 2

|  |  | Light Time 1 | Light Time 2 | Light Total |
| --- | --- | --- | --- | --- |
| Light | $r$ | 1 | 0.32 | 0.78 |
| Time 1 | $p$ |  | 0.02 | <.0001 |
|  | $n$ | 66 | 51 | 51 |
| Light | $r$ | 0.32 | 1 | 0.85 |
| Time 2 | $p$ | 0.02 |  | <.0001 |
|  | $n$ | 51 | 55 | 51 |

In the POMS-SF Total scores, the lowest mean was seen at baseline measures

(2.41, S.D.3.65) indicating the least amount of negative mood at the beginning of the

transplant. At Time 1 measure, the POMS-SF Total was at its highest (4.13, S.D. 3.74).

These numbers were not indicative of a negative mood state as the POMS-SF Total

maximum score is 16.

The Tension-Anxiety Subscale mean was lowest at Time 2 (0.85, SD 0.85). The

Tension-Anxiety Subscale mean for Baseline and Time 1 measurement periods were the

same at 1.11 (SD=0.97 and 0.85 respectively). One could assume that anxiety would be highest at the beginning of the transplant process, with so many unknowns about patient response to treatment.

The Depression-Dejection Subscale mean was lowest at Baseline (0.52, SD=0.73). The mean for this subscale at measurement point Time 1 was the highest (0.66, SD=0.73). There was only 0.06 difference between the means at Time 1 and Time 2 measurement point (Time 2: 0.60, SD=0.76). It could be anticipated that the longer the patient was hospitalized, the greater the depression would be however the data show a minimal difference in scores between the two time periods.

The Anger-Hostility Subscales was lowest at Baseline (0.49, SD=0.76). Means for Time 1 and Time 2 measurement points were the same at 0.52 (SD=0.70 and 0.69 respectively).

The Vigor Subscale was lowest at Time 1 measurement point (1.19, SD=0.78) and highest at Baseline (1.57, SD=0.97). This would mirror the escalation of fatigue as the patient moves through the transplant process. There is a slight increase in the mean at Time 2 measurement when the blood counts should be increasing as the bone marrow engrafts resulting in improved activity tolerance.

The Fatigue-Inertia Subscale has the lowest mean at Baseline measurement time point (1.32, SD=1.05). Fatigue appears to increase at Time 1 measurement (2.04, SD=1.05) to its highest measurement of the three time points. This would correspond to the measurement taken closest to the date of the actual transplant. At Time 2 measurement, there is a small decrease in the fatigue mean (1.84, SD=1.23)

Finally, the Confusion-Bewilderment Subscale has the lowest mean occurring at Time 2 (0.67, SD=0.82). There is very little difference between the means obtained at Baseline and Time 1 measurement (0.72, SD=0.72 and 0.73, SD=0.75 respectively). One might expect an increase in this subscale at Time 2 as the patient is preparing for impending discharge, which involves a lot of planning and information exchange. The data do not follow this assumption as there is very little numerical difference among scores at the three time points. Table 6 displays all the POMS-SF Total and Subscale scores.

The PFS-R Total mean was lowest at Baseline (3.58, SD=1.99) and was highest at Time 1 measurement period (4.19, SD=1.79). Each PFS-R Subscale has a maximum score of 10. Mild to moderate fatigue would score between 0 and 6.99. All of the PFS-R Total and Subscale mean scores fell into the mild (0-3.99) to moderate (4.0-6.99) fatigue range. None of the mean scores on the PFS-R Total Score or subscales at any of the three measurement time points reached the level of severe fatigue. The vast majority of the means saddled closely between the upper limits of mild and lower limits of moderate distress as it related to fatigue.

The Behavioral-Severity Subscale had the lowest mean at the Baseline measurement period (3.35, SD=2.83) and the highest mean occurred at Time 1 measurement period (4.08, SD=2.47). This subscale measures the patient's perception of degree to which the fatigue is disrupting their ability to perform activities of daily living. The scoring does reflect the expectation that fatigue is greatest surrounding the transplant.

Table 6. POMS-SF Total and Subscale Scores

| | | POMS-SF total | Tension-anxiety | Depression-dejection | Anger-hostility | Vigor | Fatigue-inertia | Confusion-bewilderment |
|---|---|---|---|---|---|---|---|---|
| Baseline (n=85) | *M* (*SD*) | 2.41 (3.63) | 1.11 (0.97) | 0.52 (0.73) | 0.49 (0.76) | 1.57 (0.97) | 1.32 (1.05) | 0.72 (0.72) |
| | Min | -3.06 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Max | 12.48 | 3.33 | 2.88 | 3.28 | 4.00 | 3.60 | 3.80 |
| Time 1 (n=73) | *M* (*SD*) | 3.92 (3.58) | 1.11 (0.85) | 0.66 (0.73) | 0.52 (0.70) | 1.19 (0.78) | 2.04 (1.05) | 0.73 (0.75) |
| | Min | -2.57 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Max | 12.88 | 3.50 | 2.75 | 3.33 | 3.17 | 4.00 | 3.60 |
| Time 2 (n=60) | *M* (*SD*) | 3.39 (4.02) | 0.85 (0.85) | 0.60 (0.76) | 0.52 (0.69) | 1.21 (1.00) | 1.84 (1.23) | 0.67 (0.82) |
| | Min | -3.60 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Max | 15.74 | 3.50 | 3.13 | 2.86 | 4.00 | 4.00 | 3.60 |

*Note.* Time 1= Day 0-Day 2; Time 2 = Day 9-Day 11.

The Affective Meaning Subscale had the lowest mean occurring at Baseline (3.48, SD=2.48) and the highest mean at Time 2 measurement (4.12, SD=2.63). This scale reflects the emotional attributes that the patient assigns to the fatigue experience. Certainly the Time 2 measurement point would be at the point where discharge planning is very active and this may reflect the patient's emotional concerns about the fatigue they feel.

The Sensory Subscale had its lowest mean at Baseline (4.28, SD=2.40) and its highest mean at Time 1 (5.05, SD 2.17). This subscale reflects the subjective physical symptoms of the fatigue the patient perceives. One would expect that the highest mean would be associated more closely to the transplant date which is consistent with Time 1 measurement period. The mean at Time 1 for this subscale was the highest mean on this tool. PFS-R Total and subscale scores can be found in Table 7.

Table 7. PFS-R Total and Subscale Scores

| | | PFS-R Total | Behavioral Severity | Affective Meaning | Sensory | Cognitive Mood |
|---|---|---|---|---|---|---|
| Baseline (*n* = 84) | *M* (*SD*) | 3.58 (1.99) | 3.35 (2.83) | 3.48 (2.48) | 4.28 (2.40) | 3.20 (1.99) |
| | Min | 0 | 0 | 0 | 0 | 0 |
| | Max | 7.68 | 8.83 | 8.40 | 8.20 | 9.00 |
| Time 1 (*n* = 73) | *M* (*SD*) | 4.19 (1.79) | 4.08 (2.47) | 3.82 (2.18) | 5.05 (2.17) | 3.80 (1.98) |
| | Min | 0 | 0 | 0 | 0 | 0 |
| | Max | 9.00 | 9.33 | 8.80 | 9.40 | 9.50 |
| Time 2 (*n* = 60) | *M* (*SD*) | 4.13 (2.13) | 3.82 (2.58) | 4.12 (2.63) | 4.82 (2.49) | 3.88 (2.18) |
| | Min | 0 | 0 | 0 | 0 | 0 |
| | Max | 8.59 | 9.66 | 8.80 | 9.20 | 9.33 |

*Note.* Time 1= Day 0-Day 2; Time 2 = Day 9-Day 11.

**Data analysis for aim 1.** Aim 1 focused on demonstrating a relationship between light exposure and mood and fatigue scores. There were no Light Measures at baseline. The analysis for correlation also included KPS to evaluate whether there was any significant correlation between it and the other tools. Light Time 1 measure significantly correlated with Light Time 2. There was no correlation seen between Light Time 1 and POMS-SF Total Time 1 (r=0.08, p=0.54), PFS-R Total Time 1 (r=0.07, p=0.54) or KPS Time 1 (r=-0.14, p=0.34). There were no correlations seen between Light Time 2 and POMS-SF Time 2 (r=0.05, p=0.72), PFS-R Time 2 (r=0.04, p=0.75) or KPS Time 2 (r=0.11, p=0.51). These results are displayed in Table 8.

There were no correlations found between any of the Light Measures Time 1 and any of the Subscale score for the POM-SF Time 1, PFS-R Time 1 or for the KPS completed on Day 2 of transplant. These data are shown in Table 9. There were no correlations found between Light Measure Time 2 and any of the Subscale score for the POM-SF Time 1, PFS-R Time 2 or for the KPS completed on Day 11 of transplant. These data are shown in Table 10.

**Data analysis for aim 2.** Aim 2 for this study was to investigate the relationship if any between light exposure and physical activity in the bone marrow transplant patient. The assessment of physical activity was made by measurement of the number of steps the participant took during the 48 hour periods of Day 0 to Day 2 (Steps Time 1) and Day 9 to Day 11 (Steps Time 2). The step data can be found in Table 11 and steps have been calculated in the thousands. The means between Time 1 and Time 2 measurements were very similar, as were the minimum and maximum readings.

Table 8. Light Correlation with POMS-SF Total, PFS-R Total and KPS

| | | Light Time 1 | Light Time 2 | Time1 | | | Time 2 | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | POMS Total | PFS Total | KPS | POMS Total | PFS Total | KPS |
| Light | *r* | | 0.33 | 0.08 | 0.07 | -0.14 | | | |
| Time | *p* | | 0.02 | 0.54 | 0.54 | 0.35 | | | |
| 1 | *n* | | 52 | 67 | 67 | 47 | | | |
| Light | *r* | 0.32 | | | | | 0.05 | 0.04 | 0.11 |
| Time | *p* | 0.01 | | | | | 0.725 | 0.75 | 0.51 |
| 2 | *n* | 52 | | | | | 55 | 55 | 38 |

*Note.* Time 1= Day 0-Day 2; Time 2 = Day 9-Day 11.

Table 9. Light Correlations with POMS-SF & PFS-R Subscales at Time 1

| | | POMS-SF Subscales – Time 1 | | | | | | PFS Subscales – Time 1 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Tension-Anxiety | Depression-Dejection | Anger-Hostility | Vigor-Activity | Fatigue-Inertia | Confusion-Bewilderment | Behavioral Severity | Affective Meaning | Sensory | Cognitive Mood |
| Light | *r* | -0.05 | 0.11 | 0.12 | -0.06 | 0.05 | 0.08 | 0.06 | -0.02 | -0.05 | 0.14 |
| Time 1 | *p* | 0.68 | 0.36 | 0.35 | 0.65 | 0.70 | 0.52 | 0.64 | 0.89 | 0.69 | 0.24 |
| | *n* | 67 | 67 | 67 | 67 | 67 | 67 | 67 | 67 | 67 | 67 |

*Note.* Light Time 1 = Day 0-Day 2.

Table 10. Light Correlations with POM-SF & PFS-R Subscales at Time 2

| | | POMS-SF subscales – Time 2 | | | | | | PFS-R subscales – Time 2 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Tension-Anxiety | Depression-dejection | Anger-hostility | Vigor-activity | Fatigue-inertia | Confusion-bewilderment | Behavioral severity | Affective meaning | Sensory | Cognitive mood |
| Light | *r* | 0.043 | -0.025 | 0.04 | 0.05 | -0.07 | 0.05 | -0.005 | 0.05 | -0.03 | 0.09 |
| Time 2 | *p* | 0.75 | 0.85 | 0.77 | 0.69 | 0.60 | 0.71 | 0.97 | 0.70 | 0.81 | 0.53 |
| | *n* | 55 | 55 | 55 | 55 | 55 | 55 | 55 | 55 | 55 | 55 |

*Note.* Light Time 2 = Day 9-Day 11.

Table 11. Steps Data

|  |  | Steps (in thousands) |
|---|---|---|
| Time 1 ($n = 69$) | $M$ ($SD$) | 8.45 (4.17)[a] |
|  | Min | 1.44 |
|  | Max | 16.90 |
| Time 2 ($n = 57$) | $M$ ($SD$) | 7.26 (3.78)[a] |
|  | Min | 1.36 |
|  | Max | 15.16 |

[a] Cumulative steps for 48 hour period

Physical activity, as measured through number of steps taken, was not shown to be correlated with levels of light exposure. Of note, there were significant fewer participants for step calculations between Steps Time 1 (n=69) and Steps Time 2 (n=57). This was due to participants dropping out of the study and to the couple of documented equipment failures. These data can be seen in Table 12. A correlation was seen however between Steps Time 1 and Steps Time 2. The number of steps taken during the first measurement period was statistically significant to the number of steps the participant took during the second measurement period (r = 0.50, p < 0.0001).

Table 12. Correlation between Light and Steps

|  |  | Steps Time 1 | Steps Time 2 |
|---|---|---|---|
| Light Time 1 | $r$ | -0.12 |  |
|  | $p$ | 0.31 |  |
|  | $n$ | 67 |  |
| Light Time 2 | $r$ |  | -0.00046 |
|  | $p$ |  | 0.99740 |
|  | $n$ |  | 55 |

**Aim 3 data analysis.** The third aim of this study was to establish the relationship between the level of light exposure and fatigue levels during the in hospital bone marrow transplant experience.

The regression analysis for this aim is displayed in Table 13. Parameters for all biomarkers at Time 2 (Age, Height, Baseline Weight, Gender, Diagnosis and Transplant type) were added to the model and assessed for fit through stepwise backwards selection. All parameters except for baseline PFS-R (and including Total Light) were forced out of the model. Baseline PFS-R was shown to have a strong relationship to PSF-R at Time 2 (Estimate =0.72, SE = 0.12, P = 0.0001). At this time there is not enough evidence to draw an association between fatigue at 11 days post-transplant, light, and these other factors.

Table 13. Fatigue at Time 2, with Baseline Fatigue and Light Exposure as Covariates Regression

|  | Parameter Estimate (*SE*) | *T* | *p* | Variance inflation |
|---|---|---|---|---|
| Intercept | 1.042(0.52) | 2.01 | 0.05 | 0.00 |
| Light (in thousands) | 0.00136(0.00130) | 1.05 | 0.30 | 1.08 |
| Baseline PFS-R | 0.72(0.12) | 6.15 | 0.0001 | 1.08 |

*Note. n* = 49.

**Post hoc data analysis.** The question of whether activity and light would be significant predictors of mood, at time 1, was explored. A regression model using POM-SF Total Time 1 with Light Time 1 and Steps Time 1 demonstrated that at Time 1, light

was not show to have a significant effect on POMS-SF, while steps was a significant

predictor of total mood (p = 0.005). These results can be seen in Table 14.

Table 14. Coefficients with Light 1 and Steps 1 and Mood at Time 1

| Model | Unstandardized coefficients | | Standardized coefficients | | |
|---|---|---|---|---|---|
| | B | SE | β | t | Sig |
| 1 Constant | 6.47 | 1.14 | | 5.690 | .000 |
| Steps_1 | 0.000 | 0.000 | -.34 | -2.910 | .005 |
| Light_1 | 1.237E-6 | 0.000 | .03 | 0.282 | .780 |

*Note*. Dependent Variable: Mood, Time 1.

Similarly, the question of whether activity and light were predictors of fatigue, at

time 1, was explored. A regression model using PFS Total Time 1, with Light Time 1 and

Steps Time 1 demonstrated that at time 1, light was not show to have a significant effect

on PFS Total Time 1 while, similar to the results for mood, the number of steps was a

significant predictor of fatigue (p = 0.010). Patients who engaged in more activity had

lower levels of fatigue. These results can be seen in Table 15.

Table 15. Coefficients with Light 1 and Steps 1 and Fatigue, Time 1

| Model | Unstandardized coefficients | | Standardized coefficients | | |
|---|---|---|---|---|---|
| | B | SE | β | t | Sig |
| 1 Constant | 5.38 | .55 | | 9.71 | .000 |
| Steps_1 | 0.000 | .00 | -.34 | -2.84 | .010 |
| Light_1 | 5.99E-7 | .00 | .03 | 0.28 | .780 |

*Note*. Dependent Variable: Total Fatigue, Time 1.

Similar to the results for time 1, a regression model for mood at Time 2

demonstrated that light did not have a significant effect on POMS-SF Time 2, while steps

continued to be a predictor of mood (p = 0.030). These results are shown in Table 16.

Table 16. Coefficients with Light 2 and Steps 2 and Mood, Time 2

| Model | Unstandardized coefficients | | Standardized coefficients | | |
|---|---|---|---|---|---|
| | B | SE | β | t | Sig |
| 1 Constant | 6.0 | 1.27 | | 4.70 | .000 |
| Steps_2 | 0.00 | 0.00 | -.30 | -2.27 | .030 |
| Light_2 | -1.923E-6 | 0.00 | .06 | -0.47 | .640 |

*Note*. Dependent Variable: Mood, Time 2.

Finally, similar to the results for Time 1, a regression model using Total fatigue at Time 2, with the independent variables of Light at Time 2 and Steps at Time 2 demonstrated that light was not shown to have a significant effect on total fatigue at Time 2, and steps was no longer a significant predictor of total fatigue ($p = 0.14$). These results can be seen in Table 17.

Table 17. Coefficients with Light 2 and Steps 2 and PFS TFS 2

| Model | Unstandardized coefficients | | Standardized coefficients | | |
|---|---|---|---|---|---|
| | B | SE | β | t | Sig |
| 1 Constant | 4.89 | .71 | | 6.85 | .000 |
| Steps_2 | 0.00 | .00 | 2.20 | -1.48 | .140 |
| Light_2 | 7.051E-6 | .00 | 0.04 | 0.31 | .760 |

*Note*. Dependent Variable: PFS_TFS, Time 2.

Further exploratory analyses were undertaken with the subscales of the POMS and PFS, with no change in the pattern of findings. These findings should be viewed with caution. Considering the number of analyses completed and the possibility of an inflated Type I error rate, light was not a significant predictor of any dimensions of fatigue or mood.

In summary, the sample was predominantly male, Caucasian and was receiving a BMT for multiple myeloma, lymphoma or AML. The KPS showed minimal change at the three assessment time points and did not have any correlation to light exposure. Scores on the PFS-R demonstrated predominantly moderate fatigue levels. There were no correlations found between Light and measures for fatigue, mood or activity. In post hoc analysis, there were identified correlations between steps and mood at Time 1 and 2 and steps and fatigue at Time 1. The following chapter will discuss the findings from this study, the implications for nursing science and thoughts on future research directions.

# CHAPTER FIVE

## DISCUSSION

The purpose of this exploratory study was to determine whether there is a relationship between natural and ambient light exposure and the hospitalized bone marrow transplant patient's perceived state of mood and fatigue. A second aim was to evaluate the relationship between the bone marrow transplant patient's exposure to light and the patient's physical activity at two time points during the hospitalization. The aims of this research were achieved, however the findings were not of the magnitude expected. While the relationship between light exposure and the dependent variables of mood, fatigue and activity was not exposed, a relationship between activity, mood and fatigue was identified in the data. Regardless, the findings do provide valuable information for current knowledge and future studies. In this chapter, the overall characteristics of the sample will be discussed in addition to the study's aims and the summary of findings. The limitations of this study, the implications for the profession of nursing and recommendations for future research are also provided.

**Characteristics of the Overall Sample**

As previously discussed in the results chapter, the majority of the sample were male, Caucasian and age 60 and over. The sample lacked substantial diversity with only eight Latinos, four African Americans and 28 females participating in the study. The site of the study is a suburban area, which is very racially diverse however it would not

appear that the patient population being served reflects this. The availability of Hispanic participants was larger, however a language barrier prevented enrollment with some patients not possessing a level of English proficiency which would allow them to understand the verbal explanation of the study or the reading and comprehension of the consent document. In addition, there were no interpreters available to interact with the investigator in attempting to recruit this subset of patients. With the lack of diversity in the sample, it is unknown whether the results could have been different with a more diverse sample.

A multiple myeloma diagnosis constituted a third of the participants for the study (n = 29, 32.9%) with lymphomas and leukemia representing the remainder of the participants with one exception of myelodysplastic syndrome. Multiple myeloma is typically a malignancy seen in older populations while lymphomas and leukemias affect all age groups.  The present treatment approach for multiple myeloma begins with chemotherapy as the initial treatment. This treatment has the opportunity to keep the disease "at bay" for multiple years. Bone marrow transplant is not the initial treatment approach for multiple myeloma but will be considered when the patient demonstrates progression after multiple regimens.

Lymphomas and leukemias both have multiple sub-categories with cell types reacting differently in the disease trajectory and resilience against treatment response. Both of these malignancies contain subcategories where treatment with chemotherapy plus or minus radiation can be effective in disease remission; however, both have subcategories of very aggressive disease courses requiring chemotherapy, radiation and

ultimately bone marrow transplantation.  The variability in the underlying diagnosis and disease/treatment histories for the participants in the study created a sample that may lack satisfactory and significant homogeneity. That being said, examining for any correlations within the variables by diagnosis type did not yield any further information.

Autologous transplant was used in over 60% of the participants. The post transplant trajectory can be different for autologous versus allogeneic transplants. Since the cells providing the allogeneic transplant are not coming from the patient, this type of transplant may encounter more GVHD which can dramatically change the post transplant recovery. Post hoc testing for correlations between the variables delineated by the type of transplant did not yield any significant findings. Given a larger sample size, differences may have been found between malignancy types, treatment histories, and type of transplant.

There was an intentional rationale for not collecting demographic data involving occupation, median income, or family information. The transplant process is a long one so most of these participants would not be actively employed; occupation and income were judged as not relevant to the study aims. All the participants had to have some type of family or friend support in order to complete the post discharge transplant requirement so collecting family information was not deemed relevant.

In planning this research, a power analysis projected the need to enroll 82 patients. With the investigator's estimate of a 10% attrition rate, the sample size was increased to 90 patients. In reality, the study experienced more than a 30% attrition rate yielding a final sample size of 60 patients with completed measures. Many of the studies

discussed in the second chapter of this paper had very small sample sizes yet they demonstrated statistical significance in their findings. Sixty participants should have provided sufficient numbers to reveal any associations, however, this was not seen in the results.

The significant number of patients who withdrew from the study due to feeling unwell may have provided more extreme values in the measures had they continued to participate. If the patients that remained in the study were more 'healthy' than those who declined to continue, it could be expected that they had lower mood disturbance and/or fatigue. Those patients who withdrew from the study may have contributed much different data had they continued. Those who felt well enough to continue may have had a more positive mood, less fatigue and/or greater activity. There is no way to know how different the findings would have been had the attrition rate truly been only 10%. A study with a much larger sample size may provide more insight.

This investigator was acutely aware of the difficult treatment regimens these patients undergo. With substantial mortality rates associated with BMT, the treatments and resulting BMT can tax the participant in almost every aspect of their lives. At any time, if the patient stated they did not feel up to participating in that data collection point, their decision was accepted immediately. If there was a future data collection point, the patient would be asked if they could be approached for that activity. Having worked in clinical trials for many years, the value of the participant's consent along with their ability to retract that consent at any time was forefront in the investigator's mind. This

could have impacted the attrition rate; however, even a captive audience should have the ability to leave at any time.

**Discussion of Aims**

**Discussion of aim 1.** The primary goal for this study was to determine whether there is a relationship between light and a BMT patient's perceived mood state and fatigue level. The literature reviewed in preparation for this study indicated that mild fatigue level scores would be present in both autologous and allogeneic patients at the beginning of the transplant process. For example, previous findings demonstrated by Day 5 post transplant, 90% of the patients would score themselves with moderate to severe fatigue (Danaher-Hacker et al. 2006). Another study found a high correlation between fatigue scores and those of anxiety and depression during the transplant process (Molassiotis, 1999). Findings from this present study demonstrated fairly stable fatigue levels over time from Day 0 to Day 11. There were no dramatic shifts observed in the means for the PFS-R or POMS-SF Totals or subscales at any of the measurement points. All measures on these two instruments indicated that patients in this study were in the upper limit of mild symptoms to the middle limits for moderate symptoms. This study's findings were not consistent with present literature. As stated earlier, patients who completed the trial could have constituted the healthier patient group when compared to those who withdrew.

The lack of findings in any correlation between light exposure, fatigue and mood at Time 1 or Time 2 was disappointing, particularly because it does not appear to be in line with previous studies. While a 30% drop out rate may be indicted as a possible case

for the lack of correlation, it is unknown whether a larger sample size would have revealed different results.

In the self-administered tools, there were instances when the tools were only partially completed by the patient. In these cases, if the patient was still in the hospital, the investigator would work with the subject in completing the instrument. There were instances where the patient was discharged prior to day 11 and prior to the investigator meeting with the patient. Failure to have the entire tool completed may have impacted study findings. In addition, having the investigator assist the patient with the completion of the tool may have affected the way the patient responded to the questions.

It was frequently noted that patients who were obviously experiencing a tremendous amount of fatigue ranked themselves "lively" or "active" when completing the PFS-R. Patients may have been projecting how they would like to feel rather than giving a score that truly reflected the amount of distress the fatigue was causing them. While the majority of the patients were not on any anti-depressant medications, there were medications which may have affected the patient response on the instrument. Narcotics and anti-anxiety medications could make the patient feel tired which would predispose them to completing the instrument with more or less fatigue or mood change. It is again important to note that studies discussed in Chapter 2 had much greater fatigue and mood distress in transplant patients than seen in this present study.

Nightingale (1859/1960) spoke of sunlight as being beneficial to patient recovery in a time of limited availability of ambient lighting devices. Within this study design, there was no differentiation in the type of light the patient received. Not being able to

quantify the level of natural lighting versus artificial lighting the patients received may have assisted in further explanations for the measured variables.

Finally, data on light levels had to be impacted by how the device was worn by the patient. While patients were coached to keep the wrist wearing the device outside of bed linens and robes, compliance with this was frequently found an issue. Finding the patients ambulating in the hall with robes on or resting in their bed under linens, the wrist device was frequently found to be covered. This would definitely impact the devices ability to correctly record light levels. In addition, patients would be removing the devices for twice daily tub baths. The duration of time the device was off of the patient was not captured. This time interval could vary greatly between patients; some patients admitted forgetting to re-apply the wrist device in a timely fashion after bathing. Because it was impossible for the investigator to be present all the time to address this with participants, this could not be controlled for and could definitely impact the light exposure data. Possibly placing the light meter on the intravenous pole for the 48 hours would have provided more accurate data.

**Discussion of aim 2.** The second aim of the study was to establish a relationship between the light level exposures and the physical activity of the patient. The mean for Step Time 1 was higher than Step Time 2 mean however these two measures were moderately correlated with one another (.50, $p = <.0001$). This could mean that activity between the 2 time points did have a relationship and patients were consistent with their activity between those time intervals. This finding was unexpected considering patients receiving the transplant on Day 0 typically have very little activity on that day. For that

reason, one could assume that Step Time 2 measure would be higher. It also would be

impossible to project how the attrition rate between these two measurement points

impacted the statistics. Other than this correlation, this study did not find any relations

between light exposure and the steps taken for either Time 1 or Time 2 measurement

periods.

The KPS score mean for Time 1 measure was very similar to Time 2 measure.

Theoretically, a decline in the patient's KPS score could be associated with the patient's

activity. There was an identified problem with the measurement of this variable because

its documentation by physicians in the medical record was inconsistent. Even though

KPS is not an activity scale but addresses functional performance, a correlation between

KPS and Light Time 1 and 2 was performed. No correlation found between the KPS

measures and these 2 light measurement periods.

Similar to the discussion of Aim #1 regarding light meter placement, there was an

issue with how the activity monitor was worn by the participant. While the measurement

by the Actical was not impacted by robes or bed sheets, the data from it may have been

impacted similar to the Actiwtach in the length of time the device was off of the patient

during the twice daily tub baths. It is not known exact time intervals when activity may

not have been recorded during that 48 hours period. While both devices are water

resistant, they were not water proof so full submersion for a short length of time would

render them non-functional. As it were, at least one patient forgot to remove the devices

during a bath causing the devices to stop working. The devices were returned to the

manufacturer who unsuccessfully attempted data retrieval and the devices were deemed permanently inoperable.

Patients were coached to apply the Actical on the same wrist throughout the 48 hour time period and were asked to push their IV pole with the hand opposite from the wrist of the Actical placement. It was felt that the free swinging of the arm would facilitate more accurate activity measure. But patients were frequently found ambulating without being compliant of this request. With all the interventions the patient is experiencing, their inability to remember instructions is not surprising. Alternatively, the placement of the Actical could have been around the patient's waist or on the patient's ankle. These locations were not selected for two reasons. Waist placement was avoided because it was felt that the device might be easily lost with changing gowns frequently due to the twice daily tub baths. Ankle placement was not possible for all patients due frequent lower leg and feet swelling. A majority of the participants experienced this side effect, making ankle placement not consistently possible for all patients.

While the light exposure means for Day 0-2 and Day 9-11 were not grossly different, the Time 2 mean was slightly higher (113.39 lux versus 127.28 lux respectively). This could be expected. As the transplant engrafts, the blood counts slowly rise. Given this increase in hemoglobin and hematocrit, increased activity tolerance would be expected as the patient progresses post transplant. There was a correlation between Light Time 1 and Light Time 2; the amount of light exposure at Time 1 could be a predictor of light exposure for Time 2. However logic would say that greater light exposure occurs in the hallway and the hallway is associated with patient activity.

However, this logic was not held by the statistics. Light exposure did not have any correlation of step data at either one of the time intervals.

**Discussion of aim 3.** For the third aim, the study intended to determine whether there was a relationship between light exposure and fatigue. A regression model utilized PFS-R at baseline plus total measure of light plus any error equaling PFS-R Time 2. The cumulative measure of light was not found to be significant to the remainder of the model. The model shows that for every increase in the baseline of PFS-R, there was an increase of 0.7 in the scoring of PFS-R Total Time 2. This was not supported by the model. Similar to the discussion of aim #1, it is unknown whether a larger sample size would have provided different findings.

**Discussion of post hoc analysis**. While light exposure was not significantly associated with mood, fatigue or activity, the post hoc analysis demonstrated that steps might be the primary predictor for mood and fatigue for this patient population during the transplant hospitalization period. This is an important finding which demonstrates the benefit for these patients to push themselves toward greater activity during the acute transplant phase. The patient's ability to gain an improved mood state alone is a reason to get the patient up and walking outside of their hospital room.

**Study Limitations**

This study was exploratory and utilized a convenience sample. This design was appropriate for examining any relations between the variables, absent any intervention. The study did not have adequate ethnic or racial diversity and was hindered by not having Spanish literature, consent and interpreters available for recruitment. While the study site

was located in a racially diverse suburb, opening up the study as a multi-institutional study may have provided a better participant pool. Providing translated materials and interpreters would definitely have impacted recruitment for Hispanic patients.

As discussed previously, the participants of this study had multiple types of malignancies. The differences in disease characteristics, duration of illness, prior treatment regimens, type of transplant and time to transplant create a participant pool that may not have been similar enough. The disease details may be worthy of a secondary analysis looking for relationship of variables in subcategories. The only elements which were evaluated statistically were those of diagnosis and transplant time; this analysis did not support any relevant findings.

While the power analysis performed pre-study determined patient accrual of 82 as adequate, the attrition rate within the 90 participants was 30%. This rate is definitely impacted by the nature of the underlying cancer diagnosis and the severity of the treatment. Participants who initially seemed enthusiastic in participating prior to hospitalization had no way of anticipating how unwell they may feel once admitted and treatment is initiated. Increasing accrual would be appropriate given this experience with attrition in this patient population.

The question of an underpowered study should be considered. A post hoc power analysis uses the observed, rather than the predicted correlation. In planning the study, an estimate of effect size, along with a planned alpha level of .05 for hypothesis testing, and a power of .80 were used. After the study, in post-hoc power analyses, all results obtained were underpowered, based on the effect sizes obtained. An adequately powered study

should have included a larger number of patients to achieve a higher percentage of complete data sets. The central problem with doing a post hoc power analysis is that it implies a conclusion that if the study had encountered the full number of necessary patients with completed data sets, a difference would have been found. However, in reality, one can never know what the additional patient data sets would look like. Either way, the conclusion is the same; the study was impacted by significant participant attrition with a smaller than anticipated effect size. As noted earlier in this discussion, it can not be projected how different the data would have looked had the attrition rate been lower and more of the patients who felt unwell had chosen to continue.

A limitation to the study may be the lack of control regarding the wearing of the data collection devices. It has already been discussed that the taking of devices on and off as well as not wearing the devices appropriately may have impacted the data obtained in this study.  Had the investigator been on site more, possibly better control may have been achieved in how the devices were worn.

Using paper instruments to measure variables can be challenging. For the patient who does not feel well, the instrument may not be completed, the patient 'circles anything' to complete it, or they select responses based on how they would like to feel rather than their current state. Interventions may impact the patient responses such as medications being administered or blood transfusion causing distress. That being said, it is an accepted way of collecting patient feelings; it just may be more challenging with a patient population as sick as the BMT patient.

**Implications for Nursing**

Nursing has always been interested in how the patient interacts and adapts to the environment, in sickness and in health. As a profession, Nursing has been ready and willing to investigate non-medical interventions in the endeavor to help a patient recover to a pre-illness state. Nightingale (1859/1960) was on the forefront of understanding that some elements in the environment were harmful to the patient, while recognizing that some truly made a difference in recovery. She recognized light and fresh air as beneficial to patients at a time when light was scarce and air was foul. While this research was not able to identify the exact correlations, there are a plethora of research that has done just that. Nursing needs to continue this endeavor because these elements of the environment are interventions that we can educate our patients on, help our patients apply, and monitor patient for their response.

Roger's (1970) Science of Unitary Human Beings uses the same idea, however ramps it up to true theoretical status. But the underlying concepts and interactions are under the same perspective as Nightingale (1859). From all we know at the present, we can say with certainty, the person is continually interacting with their environment. Whether it is light coming in the window or pollution coming from the air, the human is interacting with this. We know that environmental elements cause illness and that light can facilitate healing. We also know that through this interaction, the person changes in some way. Within Rogers' theory, light is part of the environmental energy field that the patient's energy field interacts with on a continual basis. The underlying disease process of cancer as well as the BMT treatment process are internal stimuli that impact the

patient's energy field. Those internal stimuli should be able to change the patient's patterning just as the interaction between patient and environmental light can induce changes.

This study did not demonstrate that higher light exposure could decrease fatigue, make the mood better or help the patient's activity increase. But because of the work in psychoneuroimmunology and circadian rhythms, we know that there is a connection between the physiologic functioning of the body and mind with that of light. We also know that inflammation associated with cancer diagnosis and treatment is associated with biochemical functions in the body. The significant finding in the correlation of number of steps with mood state and fatigue does support that interacting with our environment (through activity) may be a predictor for mood state and fatigue levels. The underpinning of this idea again supports Roger's model.

While we know the runners attain a boost in mood with running, we are just beginning to examine what activity can do for the person fighting against a serious disease. BMT patients are aware of the activity requirements which are part of the treatment plan. In our education of these patients, we need to help them make that connection. The benefits of activity are not only to prevent pulmonary complications associated with bedrest; the activity is going to make them feel better.

A nurse is continually educating people toward achieving better states of health and wellness. Certainly the research on how the body interacts with the environment is one that nursing should be sharing. But as an active participant, the patient needs to understand the disease as a stimulus so they can understand what they must do to impact

the outcome of the treatment process. Consistent with Rogers (1970), allowing the patient to participate in this research may have assisted them in addressing the changes that were evolving within themselves. The patient could attempt to receive the maximum amount of light and perform the maximum amount of activity in an attempt to increase the amount and type of patterning as they respond to their illness. This approach of maximum light and activity would be an area for further study. Nursing has the ability to work with patients undergoing BMT coaching them toward higher activity and maximum light exposure as an intervention in the plan of care. This is within the scope of nursing practice.

BLT can be viewed as a non-invasive intervention that has a positive effect on certain patient populations. As a non-invasive intervention, it should be within the realm of nursing to use it with patients who may benefit from it. The negative side effects are minimal. Commercially available bright light lamps are available without a prescription. The problem does still exist that we do not have a standard of care for the time of day for delivery, the frequency and the dosing of how much BLT is needed for any particular patient. This is why BLT should be an intervention that nursing is excited about investigating in more diverse patient populations. While this research may not illuminate the exact mechanisms of its benefit for the patient, BLT holds a promise in improving patient lives and experiences.

**Suggestions for Future Research**

Certainly more research needs to be done on patient response to light exposure and BL therapy. Much is still unknown in how and why it works for certain patient

populations such as those with neurodegenerative disease. BLT has a potential role of interacting with the body at a cellular level making biological and pathophysiological changes that are not understood.  Designing a study which would include the application of different BLT dosages and different treatment times and time intervals might be a good starting point. The literature does not provide enough scientific evidence on any of these criteria. This type of study would add much to the body of knowledge on BLT.

As we continue to understand more about psychoneuroimmunology, the idea that light has an effect on that system is accepted.  If the patient has lost their immune system through the BMT process, is the pathway for beneficial effects of light on the body somehow disrupted?  Light exposure may not 'work' in the patient who has lost a critical part of that psychoneuroimmunology system. Possibly looking at a patient with a similar hospital stay without an immune aberration compared to the hospitalized BMT patient would better illuminate that question.

In summary, this exploratory study did not achieve its original aims.  However, it demonstrates that there is much more investigation that needs to be completed to truly understand the relationship of light and other factors in the transplant patient. The findings may inspire others to perform more research on light application to this patient population. The information shared here will benefit the next researcher interested in pursuing the idea that light may be a good intervention for the hospitalized BMT patient.

**APPENDIX A**

**INFORMED CONSENT**

IRB NUMBER: 204782101712
LOYOLA UNIVERSITY CHICAGO
HEALTH SCIENCES DIVISION
MAYWOOD, ILLINOIS

INFORMED CONSENT

**Participant's Name**: _____
**Medical Record Number**: _____

**Title of Study:** The Relationship between Light Exposure and Fatigue and Mood in the Patient Undergoing Bone Marrow Transplant

# THE APPROVAL FOR THIS PROJECT EXPIRES ON 07/24/2015.
**Participant Information**

    **Principles concerning research**. You are being asked to take part in a research study. It is important that you read and understand the principles that apply to all individuals who agree to participate in the research project described below:

1. Taking part in the research is entirely voluntary.

2. You will not benefit from taking part in the research but the knowledge obtained may help others.

3. You may withdraw from the study at any time without anyone objecting and without penalty or loss of any benefits to which you are otherwise entitled.

    The purpose of the research, how it is to be done and what your part in the research will be is described below. Also described are the risks, inconveniences, discomfort and other important information, which you need to make a decision about whether or not you wish to participate. You are urged to discuss any questions you have about this research with the staff members.

    **Purpose of research**. You are being asked to participate in this study because you are undergoing a bone marrow transplant.

    The purpose of this study is to investigate the relationship between light exposure and the perception of fatigue and mood during the bone marrow transplant procedure. This research will also evaluate levels of physical activity and sleep/wake intervals in relationship to light exposure.

This research is for a doctoral dissertation, a graduate school project being done by Kim Anderson-Drevs.

    Approximately 90 people will participate in this research.

**Description and explanation of procedures**. If you agree to participate in the study, you will be asked to sign this informed consent document once the study has been explained to you. Prior to hospitalization or prior to your chemotherapy starting, you will be asked to complete two surveys providing information about your fatigue and your mood. On Day 0 of your transplant, you will be asked to wear a small light meter and activity monitor on your wrist which measure the amount of light you receive, your sleep and your activity over a 48 hour period. At the end of the 48 hour period, you will be asked to complete the 2 surveys regarding fatigue and mood again. This process will be repeated at Day 9 of your transplant; wearing the wrist band for 48 hours and completing the 2 surveys at the end of the 48 hour period.

**Risk/discomforts**. There no treatment component in this study. It is not anticipated that participation will result in any risk or discomfort.

**Benefits.** You will not benefit from participating in this study.

**Alternative.** You do not have to participate in this research project to receive care and treatment at Loyola University Medical Center.

**Financial information.** There is no cost associated with your participation in this study. Neither you nor your insurance provider will be billed for any procedures that are performed exclusively for this research study. Those procedures that are being performed for research purposes only include the completion of surveys and monitoring light and activity with devices.

**Research related injury**. In the event that you are injured as a result of participating in this research project, your doctor will take the necessary steps to treat the problem. There are no funds available from Loyola University Medical Center to pay for the cost of care of the problem. You will be financially responsible for the cost of care of any problems.

**Information collected and what will happen to it.** In order to meet the goals of the research study, we will collect information on you, your survey results and how you do. The information will be collected by Kim Anderson-Drevs. In this collection, we will learn about the relationship between light levels and a patient's perception of fatigue and mood during hospitalization.

The information we will collect includes:

__X__ DEMOGRAPHIC INFORMATION (E.G. NAME, ADDRESS, PHONE NUMBER, MEDICAL RECORD NUMBER

__X___ MEDICAL RECORDS (INCLUDING BUT NOT LIMITED TO, HISTORY AND PHYSICAL EXAM NOTES, PROGRESS NOTES, CONSULTATION REPORTS, LABORATORY TEST RESULTS AND/OR OPERATIVE REPORTS)

We will collect information about you for as long as you are in the study which is considered up to 16 days after your transplant.

The results of is research study may be published in a journal for the purposes of advancing nursing knowledge. You will not be identified by name or by other identifying information in any publication or report about this research.

**Withdrawal of consent**. Your consent to use and disclose your medical information for this research study is completely voluntary. You can withdraw your consent for LUMC to use and disclose your information and your consent to participate in this study at any time without affecting your ability to receive care and treatment at LUMC unrelated to the research study. Withdrawal means that all study procedures and follow up will stop.

If you withdraw from the study, we will ask that you sign the form attached to this consent and send it to:

Kim Anderson-Drevs
1408 W. Taylor Street
#401
Chicago, IL 60607
(708) 212-5558

Your withdrawal from the study will not have any effect on any actions by LUMC taken before the attached form is received.
Your study doctor and the Institutional Review Board, regulatory authorities or the principle investigator may terminate the study at any time with or without your consent.
Your doctor may choose to take you out of the study.

CONSENT
I have fully explained to _____ the nature and purpose of the above described procedures and any risks that are involved in its performance. I have answered and will answer all questions to the best of my ability. If you have any questions about this study, you should contact Kim Anderson-Drevs at (708) 212-5558 or Lee Schmidt, PhD, chairman of the dissertation committee at (708) 216-3573.

_____  _____
Signature Date

If you ever feel that you have been injured by participating in this study or if you have any questions concerning your rights as a research participant, you may contact either Kenneth Micetich, MD, Chair of the Institutional Review Board for the Protection of Human Subjects-Loyola University Chicago Health Science Division at 708-216-2633 or Elaine Fluder, MSN, Director of the Human Research Subject Protection Program at 708-216-4608.

Although you have the right to revoke this authorization, you accept that such revocation will not apply to any uses and disclosures of your information that are described in the Loyola University Health System Notice of Privacy or otherwise allowable under any Federal or State laws.

You will receive a signed copy of this informed consent document.

You have been fully informed of the above described research program with its possible benefits and risks. Your signature below indicates that you are willing to participate in this research study and agree to use and disclosure of information about you as described above. You do not give up any of your legal rights by signing this consent document.

_____   _____

Signature: Participant Date

_____   _____

Signature: Witness Date

**PROJECT TITLE: The Relationship between Light Exposure and Fatigue and Mood in the Patient Undergoing Bone Marrow Transplant**

**REVOCATION OF AUTHORIZATION
TO RELEASE PROTECTED HEALTH INFORMATION (PHI)**

I, _____, hereby revoke my consent to participate in the research, The Relationship Between Light Exposure and Fatigue and Mood in the Patient Undergoing Bone Marrow Transplant at Loyola University Medical Center (LUMC). I also revoke my consent to release information I provided to LUMC that allowed LUMC to use and disclose my medical information to the principle investigator listed as outlined on the consent form, which I signed on _____. I understand that this revocation does not apply to any action LUMC has taken in reliance on the consent I signed earlier.


_____  _____
Signature: Participant Date


Please return this form to:

Kim Anderson-Drevs
1408 W. Taylor Street
#401
Chicago, IL 60607

**APPENDIX B**

**PIPER FATIGUE SCALE-REVISED**

## THE PIPER FATIGUE SCALE

**Patient ID no._____**

Directions: For each of the following questions, circle the number which best describes the fatigue you are experiencing now. Please make every effort to answer each question to the best of your ability.

1. How long have you been feeling fatigued
   a. _____ minutes
   b. _____ hours
   c. _____ days
   d. _____ weeks
   e. _____ months
   f. _____ other (please describe): _____

2. To what degree is the fatigue you are feeling causing you distress?

No distress                                                      A great deal of stress
0      1      2      3      4      5      6      7      8      9      10

3. To what degree is the fatigue you are feeling interfering with your ability to complete your work or school activities?

None                                                                  A great deal
0      1      2      3      4      5      6      7      8      9      10

4. To what degree is the fatigue you are feeling interfering with your ability to visit or socialize with your friends?

None                                                                  A great deal
0      1      2      3      4      5      6      7      8      9      10

5. To what degree is the fatigue you are feeling interfering with your ability to engage in sexual activity?

None                                                                  A great deal
0      1      2      3      4      5      6      7      8      9      10

6. Overall, how much is the fatigue which you are experiencing now interfering with your ability to engage in the kind of activities you enjoy doing?

None                                                                  A great deal
0      1      2      3      4      5      6      7      8      9      10

7.  How would you describe the degree of intensity or severity of the fatigue which you
    are experiencing **now**?

Mild                                                                          Severe
   0     1     2     3     4     5     6     7     8     9    10

**To what degree would you describe the fatigue which you are experiencing now as
being:**

8.
Pleasant                                                                    Unpleasant
   0     1     2     3     4     5     6     7     8     9    10

9.
Agreeable                                                                   Disagreeable
   0     1     2     3     4     5     6     7     8     9    10

10.
Protective                                                                  Destructive
   0     1     2     3     4     5     6     7     8     9    10

11.
Positive                                                                    Negative
   0     1     2     3     4     5     6     7     8     9    10

12.
Normal                                                                      Abnormal
   0     1     2     3     4     5     6     7     8     9    10

**To what degree are now feeling?**

13.
Strong                                                                      Weak
   0     1     2     3     4     5     6     7     8     9    10

14.
Awake                                                                       Alert
   0     1     2     3     4     5     6     7     8     9    10

15.
Lively                                                                      Listless
   0     1     2     3     4     5     6     7     8     9    10

16.
Refreshed                                                                                    Tired
  0        1        2        3        4        5        6        7        8        9        10

17.
Energetic                                                                              Unenergetic
  0        1        2        3        4        5        6        7        8        9        10

18.
Patient                                                                                  Impatient
  0        1        2        3        4        5        6        7        8        9        10

19.
Relaxed                                                                                    Intense
  0        1        2        3        4        5        6        7        8        9        10

20.
Exhilarated                                                                             Depressed
  0        1        2        3        4        5        6        7        8        9        10

21.
Able to concentrate                                                        Unable to concentrate
  0        1        2        3        4        5        6        7        8        9        10

22.
Able to remember                                                             Unable to remember
  0        1        2        3        4        5        6        7        8        9        10

23.
Able to think clearly                                                         Unable to think clearly
  0        1        2        3        4        5        6        7        8        9        10

24. Overall, what do you believe is most directly contributing to or causing your fatigue?

25. Overall, the best thing you have found to relieve your fatigue is:

26. Is there anything else you would like to add that would describe your fatigue better to us?

27. Have you experienced any other symptoms this week?
No _____
Yes _____   Please describe:

## Piper Fatigue Scale-Revised Scoring and Survey Results

1. The PFS-R in its current form is composed of 22 numerically scaled, "0" to "10" items that measure four dimensions of subjective fatigue: Behavioral/severity (6 items #2-7); affective meaning (5 items: #8-12); sensory (5 items: #13-17; and cognitive/mood (6 items: #18-23). These 22 items are used to calculate the four sub-scale/dimensional scores and the total fatigue scores.

2. Five additional items (#13 and #24-27) are not used to calculate subscale or total fatigue scores but are recommended to be kept on the scale as these items furnish rich, qualitative data. Item #1, in particular gives a categorical way in which to assess the duration of the respondent's fatigue.

3. To score the PFS-R, add the items contained on each specific subscale together and divide by the number of items on that subscale. This will give you a subscale score that remains on the same "0" to "10" numeric scale. Should you have missing item data, and the respondent has answered at least 75%-80% of the remaining items on that particular subscale, calculate the subscale mean score based on the number of items answered, and substitute that mean value for the missing item score (mean-item substitution).

4. Recalculate the subscale score. To calculate the total fatigue score, add the 22 items scores together and divide by 22 in order to keep the score on the same numeric "0" to "10" scale.


Severity Codes:
    0       NONE
    1-3 MILD
    4-6 MODERATE
    7-10 SEVERE

**APPENDIX C**

**PROFILES OF MOOD STATES-SHORT FORM**

Below is a list of words that describe feelings people have. Please read each one carefully. Then circle ONE answer to the right, which best describes HOW YOU HAVE BEEN FEELING DURING THE **PAST 24 HOURS**.

**The numbers refer to these phrases:**
**0= not at all**
**1= a little**
**2 = moderately**
**3 = moderate**
**4 = extremely**

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. | Tense | 0 | 1 | 2 | 3 | 4 | 20. | Discouraged | 0 | 1 | 2 | 3 | 4 |
| 2. | Angry | 0 | 1 | 2 | 3 | 4 | 21. | Resentful | 0 | 1 | 2 | 3 | 4 |
| 3. | Worn out | 0 | 1 | 2 | 3 | 4 | 22. | Nervous | 0 | 1 | 2 | 3 | 4 |
| 4. | Unhappy | 0 | 1 | 2 | 3 | 4 | 23. | Miserable | 0 | 1 | 2 | 3 | 4 |
| 5. | Lively | 0 | 1 | 2 | 3 | 4 | 24. | Cheerful | 0 | 1 | 2 | 3 | 4 |
| 6. | Confused | 0 | 1 | 2 | 3 | 4 | 25. | Bitter | 0 | 1 | 2 | 3 | 4 |
| 7. | Peeved | 0 | 1 | 2 | 3 | 4 | 26. | Exhausted | 0 | 1 | 2 | 3 | 4 |
| 8. | Sad | 0 | 1 | 2 | 3 | 4 | 27. | Anxious | 0 | 1 | 2 | 3 | 4 |
| 9. | Active | 0 | 1 | 2 | 3 | 4 | 28. | Helpless | 0 | 1 | 2 | 3 | 4 |
| 10. | On edge | 0 | 1 | 2 | 3 | 4 | 29. | Weary | 0 | 1 | 2 | 3 | 4 |
| 11. | Grouchy | 0 | 1 | 2 | 3 | 4 | 30. | Bewildered | 0 | 1 | 2 | 3 | 4 |
| 12. | Blue | 0 | 1 | 2 | 3 | 4 | 31. | Furious | 0 | 1 | 2 | 3 | 4 |
| 13. | Energetic | 0 | 1 | 2 | 3 | 4 | 32. | Full of pep | 0 | 1 | 2 | 3 | 4 |
| 14. | Hopeless | 0 | 1 | 2 | 3 | 4 | 33. | Worthless | 0 | 1 | 2 | 3 | 4 |
| 15. | Uneasy | 0 | 1 | 2 | 3 | 4 | 34. | Forgetful | 0 | 1 | 2 | 3 | 4 |
| 16. | Restless | 0 | 1 | 2 | 3 | 4 | 35. | Vigorous | 0 | 1 | 2 | 3 | 4 |
| 17. | Unable to concentrate | 0 | 1 | 2 | 3 | 4 | 36. | Uncertain about things | 0 | 1 | 2 | 3 | 4 |
| 18. | Fatigued | 0 | 1 | 2 | 3 | 4 | 37. | Bushed | 0 | 1 | 2 | 3 | 4 |
| 19. | Annoyed | 0 | 1 | 2 | 3 | 4 | | | | | | | |

1.

**Scoring Instructions for the POMS-SF**

Items by subscale
Tension-Anxiety: 1, 10, 15, 16, 22. 27
Depression-Dejection: 4, 8, 12, 14, 20, 23, 28, 33
Anger-Hostility: 2, 7, 11, 19, 21, 25, 31
Vigor-Activity: 5, 9, 13, 24, 32, 35
Fatigue-Inertia: 3, 18, 26, 29, 37
Confusion-Bewilderment: 6, 17, 30, 36, 34

Likert scores for each item in the subscale are added and divided by the number of items in the subscale. This renders a sub-scale score. For the Total Mood Score (TMD), all sub-scale scores are added together with the exception of the Vigor-Activity score which is subtracted from the total.

**APPENDIX D**

**KARNOFSKY PERFORMANCE STATUS SCALE**

| KARNOFSKY PERFORMANCE STATUS SCALE | | |
|---|---|---|
| Able to carry on normal activity and to work, no special care needed | 100 | Normal; no complaints; no evidence of disease |
| | 90 | Able to carry on normal activity; minor signs or symptoms of disease |
| | 80 | Normal activity with efforts; some signs or symptoms of disease |
| Unable to work; able to live at home and care for most personal needs; varying amount of assistance may be needed | 70 | Cares for self; unable to carry on normal activity or to do active work |
| | 60 | Requires occasional assistance, but is able to care for most of personal needs |
| | 50 | Requires considerable assistance and frequent medical care |
| Unable to care for self; requires equivalent of institutional or hospital care; diseases may be progressing rapidly | 40 | Disabled; requires special care and assistance |
| | 30 | Severely disabled; hospital admission is indicated although death is not imminent |
| | 20 | Very sick; hospital admission necessary; active supportive treatment necessary |
| | 10 | Moribund; fatal processes progressing rapidly |
| | 0 | Dead |

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The dissertation is therefore accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy.


_____          _____
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