Cover Page for Protocol, Statistical Plan and ICF

Official Title:	Bright Light Therapy to Improve Sleep Continuity Disturbances in Lung Cancer Survivors.
NCT number:	NCT02954809
Document Type:	Study Protocol
Date of the Document:	01/29/2017

PROTOCOL TITLE: Bright Light Therapy to Improve Sleep Continuity Disturbances in Lung Cancer Survivors.

INSTRUCTIONS: Complete Research Protocol (HRP-503)

- *Depending on the nature of what you are doing, some sections may not be applicable to your research. If so, you must provide the reason why the section is not applicable for the response. For example, most behavioral studies would answer all questions in section 30 with words to the effect of "drugs and medical devices are not used in this study."*
- *When you write a protocol, keep an electronic copy. You will need to modify this copy when making changes.*
- *Do not remove the italics instructions or headings.*
- *If you are pasting information from other documents be sure to use the "Merge Formatting" paste option so that the formatting of the response boxes is not lost. If information is presented outside of the response boxes, it will not be accepted.*
- *If this study involves multiple participant groups who participate in different research procedures, consent processes, etc., be certain to provide information in each applicable section for each participant group and clearly label each participant group within a section or subsection.*

PROTOCOL TITLE:

Bright Light Therapy to Improve Sleep Continuity Disturbances in Lung Cancer Survivors.

PRINCIPAL INVESTIGATOR:

Name Grace Dean

Department School of Nursing

Telephone Number (716) 829-3235

Email Address gdean@buffalo.edu

VERSION NUMBER:

DATE:01/29/2017

Include the date of submission or revision.

Grant Applicability:01/29/2017

Describe whether or not this protocol is funded by a grant or contract and if so, what portions of the grant this study covers.

This protocol has received an Oncology Nursing Society Foundation Grant in the amount of $25,000 for the years 2015-2017. The grant covers the entire study.

Table of Contents

1.0 Objectives

- Assess the effect of morning bright light versus dim light therapy (control) on fatigue and sleep continuity disturbance in lung cancer survivors.
- Predict efficacy to morning bright light therapy versus dim light therapy (control) on fatigue and sleep continuity disturbance in lung cancer survivors.
- Evaluate, in a preliminary way, the extent to which time from treatment (as a proxy iatrogenic effects), sleep homeostatic "de-prime" (mismatch between sleep opportunity and ability), and circadian factors (phase and amplitude) predict illness severity and treatment response.

1.1 Hypothesis

Hypothesis 1: Subjects in the Bright Light Treatment group will exhibit significant improvements as compared to Dim Light Treatment in fatigue, sleep and circadian activity rhythms.

Hypothesis 2: Subjects typed during baseline as having circadian dysrhythmia using actigraphy (circadian phase and amplitude abnormalities) will be significantly more likely to exhibit treatment responses.

2.0 Background

2.1 Describe the relevant prior experience and gaps in current knowledge.

Fatigue and sleep disturbance are common in cancer survivors (Berger et al., 2009; Roscoe et al., 2007; Pachman et al., 2012). Fatigue is reported in up to 97% of patients receiving cancer treatment and in 34% of cancer survivors (Goedendorp et al., 2013; Kapo et al., 2015). Sleep disturbance is reported in up to 88% of patients receiving cancer treatment and 56% of cancer survivors (Ancoli-Israel, 2009; Barsevick et al., 2010; Berger et al., 2009; Palesh et al., 2010). When compared to other patients diagnosed with cancer, patients with lung cancer have more than double the prevalence of fatigue and sleep disturbance (Davidson et al., 2002; Gooneratne et al., 2007).

The assessment of fatigue is common in cancer research. Less common is the evaluation of sleepiness and sleep disturbance. While related, these three phenomena may have distinct etiologic pathways and require (or best respond) to different treatment approaches. Fatigue refers to mental and physical weariness and exhaustion, where performance is compromised. Sleepiness is identical to fatigue with one critical difference: patients are also vulnerable to falling asleep at inappropriate times and places. Sleep disturbance is a generic term for all sleep complaints and disorders including sleep continuity disturbance (i.e., difficulty falling and staying asleep), respiratory disturbance during sleep (e.g., sleep apnea and nocturnal hypoxia/hypoxemia), and/or motor disturbances during sleep and parasomnias. For this study, sleep disturbance will specifically refer to sleep continuity disturbance (SCD) and respiratory disturbance (RD) during sleep.

The rather singular focus on cancer related fatigue and the assumption that this occurs with cancer treatment, suggests that fatigue should abate either with the response to, and discontinuation of, treatment. As noted above, this is largely true for fatigue (~60% reduction from treatment to survivorship) but less true for sleep disturbance (30% reduction from treatment to survivorship). In both cases significant, the survivorship prevalence is high and is comparable to, or exceeds, the population general population rates. The lack of resolution in both cases suggests that additional treatment is necessary, particular during survivorship. The question is "where and how to follow-up?" In the absence of mature data on sleepiness in cancer survivors, the higher prevalence rates of sleep disturbance suggests that this may be the best first therapeutic target. Given, a large literature on circadian rhythm disturbance in cancer patients and survivors (Golombek et al., 2013), this suggests that chronobiologic treatments in general, and Bright Light Treatment (BLT) in particular is an ideal option.

Preliminary testing of BLT has been conducted in a variety of cancer patients to improve cancer-related fatigue, but not in patients with lung cancer. Additionally, the efficacy of BLT on improving sleep continuity disturbances, daytime functioning and quality of life has not been assessed in lung cancer survivors. Accordingly, we proposed to conduct a preliminary study of the effects of BLT in patients who are lung cancer survivors.

2.2 Describe any relevant preliminary data.

The multidisciplinary team assembled for this project has conducted three studies that involved lung cancer survivors (ref). These studies established that lung cancer survivors (n=76) experienced middle insomnia (i.e. difficulty maintaining sleep) and determined that patients receiving

chemotherapy for lung cancer (n=50) had early (i.e. difficulty falling asleep) and middle (difficulty staying asleep) insomnia (Gooneratne, Dean et al. 2007, Dean, Finnell et al. 2010). Our most recent mixed method, longitudinal study with 4 measures over 6-months (n=29) found that 89% reported the occurrence of fatigue and 67% reported fatigue was persistent across treatment. In addition, poor sleepers (72%) had less activity, weaker rhythmicity and more phase delay compared to good sleepers before and during treatment for non-small cell lung cancer. Acrophase, where peak activity in a 24-hour period occurs, was significantly negatively related to FACT-L physical and functional subscales and total scores indicating later peak activity is related to poorer QOL. These findings support the occurrence of fatigue, sleep continuity disturbance and circadian activity rhythm disturbance in lung cancer survivors and support for the rationale for testing BLT.

2.3 Provide the scientific or scholarly background for, rationale for, and significance of the research based on the existing literature and how will it add to existing knowledge.

The guiding theory for this proposal is the Two-Process Model of Sleep Regulation, a leading theory of sleep regulation (Borbely 1982). It suggests that sleep occurs when the homeostatic drive to sleep (process S) approaches an upper threshold, and awakening from sleep occurs when process S reaches a lower threshold. The need to sleep increases the longer you are awake. The second process, process C, is a sinusoidal rhythm that fluctuates across the 24hour day and is driven by a clock-like mechanism in the brain (suprachiasmatic nucleii). The circadian system communicates time of day (light and dark cues from the retina) and thereby regulates the transition from wakefulness to sleep and the transition from sleep to wakefulness. For example, in an individual awake during the day and sleeping at night, the circadian process C is highest from 3am to 5am, when it is very difficult to overcome the need to sleep and is lowest from 4pm to 6pm, where sleep propensity is minimal. The circadian process C and the homeostatic process S both contribute to sleep consolidation. The interaction between these two processes forms the basis for a remarkably standardized period of sleep at night and a consolidated period of wakefulness throughout the day. However, mechanisms that oppose or enhance process S or process C can have a significant effect on the timing, duration and structure of sleep as well as daytime functioning.

In the context of cancer and cancer survivorship, the question is “are one or both of these processes” altered by the disease, its treatment, or by strategies adopted by patients to cope with and/or manage their fatigue and sleep disturbance. Homeostatic dysregulation may occur as a result curtailed time awake during the day and increased time in bed at night. The trigger for these behavioral changes (which de-prime sleep homeostasis) may be the patient’s sense of fatigue (which may occur with

the disease process or as a result of treatment) and signal to the patient that they need more sleep when what they are experiencing is fatigue and not sleepiness. The end result is a mismatch between sleep ability and sleep opportunity and that this results in sleep continuity disturbance, daytime sleepiness, and an exacerbation of extant daytime fatigue. Circadian dysregulation may also occur because of altered sleep wake schedules and/or to changes in how much and when the patient is exposed to bright light (Berger and Farr 1999, Berger, Farr et al. 2007, Ancoli-Israel, Rissling et al. 2012). Further, the circadian system may be dysregulated owing to intrinsic factors. Cancer, or its treatment, may directly alter core body temperature rhythms or amplitude, suppress, enhance or phase shift melatonin secretion, and/or fundamentally alter and dysregulate other neuroendocrine functions that have a circadian periodicity and influence fatigue, sleepiness, and sleep (Armaiz-Pena, Cole et al. 2013).

Most cancer research on fatigue (and to a lesser extent sleepiness and sleep disturbance) has focused on circadian dysregulation. To date it has been found that cancer patients exhibit circadian rhythm desynchronization of cortisol and melatonin (Dogliotti, Berruti et al. 1990, Dolberg, Hirschmann et al. 1998, Davis, Mirick et al. 2001), disrupted phase-delayed activity acrophase (Ancoli-Israel, Rissling et al. 2012, Berger, Hertzog et al. 2012), lower circadian quotient (Levin, Daehler et al. 2005, Berger, Hertzog et al. 2012) and that cancer survivors exhibit flattened biomarkers of circadian rhythms (Bower, Ganz et al. 2005, Bower 2006, Bower, Ganz et al. 2006, Bower 2007, Bower, Ganz et al. 2007). These data strongly suggest that circadian factors are associated with fatigue and sleep-wake disturbances (Levin, Daehler et al. 2005) and that chronobiologic interventions may be useful for the management of cancer related fatigue, sleepiness, and/or sleep disturbance (Ancoli-Israel, Rissling et al. 2012, Berger, Hertzog et al. 2012, Redd, Valdimarsdottir et al. 2014). Circadian rhythm disturbances are managed according to the specific type of disorder, but three common therapies are briefly discussed: Chronotherapy, Melatonin Therapy, and Bright Light Therapy.

Chronotherapy is a behavioral intervention to progressively re-align one's biologically based and preferred sleep phase with standard clock time (Eckerberg, Lowden et al. 2012). Melatonin Therapy entails the administration of exogenous melatonin (melatonin is also a neurohormone produced in the pineal gland) to exert chronobiotic effects (Burgess, Savic et al. 2003, Burgess and Fogg 2008, Burgess, Revell et al. 2008). That is, melatonin is used to produce phase shifts in the biological clock. These shifts, like those produce with chronotherapy, are used to re-align one's biologically based and preferred sleep phase with standard clock time. Bright Light Therapy uses an environmental cue to phase advance or phase delay circadian rhythms. Bright light therapy (BLT) has been shown to be effective in reducing sleep and circadian rhythm disturbances associated with a variety of disorders (e.g. jet lag, seasonal affective disorder, depression, delayed or advanced sleep phase and other sleep

disorders). Preliminary testing of BLT has been conducted in a variety of cancer patients to improve cancer-related fatigue, but not in patients with lung cancer. Additionally, the efficacy of BLT on improving sleep continuity disturbances, daytime functioning and quality of life has not been conducted with lung cancer survivors. Of the previously mentioned therapies, the proposed BLT delivered via eye mask may increase compliance, since the mask can be aimed directly at the eyes and treatment requires minimal effort. Light masks may be a more energy-efficient (through the use of only eight LEDs) and portable method, compared to traditional light boxes.

2.4 Include complete specific citations/references.

Ancoli-Israel, S., P. J. Moore and V. Jones (2001). "The relationship between fatigue and sleep in cancer patients: a review." Eur J Cancer Care (Engl) 10(4): 245-255.

Ancoli-Israel, S., M. Rissling, A. Neikrug, V. Trofimenko, L. Natarajan, B. A. Parker, S. Lawton, P. Desan and L. Liu (2012). "Light treatment prevents fatigue in women undergoing chemotherapy for breast cancer." Support Care Cancer 20(6): 1211-1219.

Armaiz-Pena, G. N., S. W. Cole, S. K. Lutgendorf and A. K. Sood (2013). "Neuroendocrine influences on cancer progression." Brain Behav Immun 30 Suppl: S19-25.

Berger, A. M. and L. Farr (1999). "The influence of daytime inactivity and nighttime restlessness on cancerrelated fatigue." Oncol Nurs Forum 26(10): 1663-1671.

Berger, A. M., L. A. Farr, B. R. Kuhn, P. Fischer and S. Agrawal (2007). "Values of sleep/wake, activity/rest, circadian rhythms, and fatigue prior to adjuvant breast cancer chemotherapy." J Pain Symptom Manage 33(4):398-409.

Berger, A. M., M. Hertzog, C. R. Geary, P. Fischer and L. Farr (2012). "Circadian rhythms, symptoms, physical functioning, and body mass index in breast cancer survivors." J Cancer Surviv 6(3): 305-314.

Berger, A. M., K. P. Parker, S. Young-McCaughan, G. A. Mallory, A. M. Barsevick, S. L. Beck, J. S. Carpenter, P. A. Carter, L. A. Farr, P. S. Hinds, K. A. Lee, C. Miaskowski, V. Mock, J. K. Payne and M. Hall (2005). "Sleep wake disturbances in people with cancer and their caregivers: state of the science." Oncol Nurs Forum 32(6): E98-126.

Berger AM, Kuhn BR, Farr L, et al. (2009). One-year outcomes of a behavioral therapy intervention trial on sleep quality and cancer-related fatigue. J Clin Oncol, 27: 6033-6040.

Borbely, A. A. (1982). "A two process model of sleep regulation." Hum Neurobiol 1(3): 195-204.

Bower, J. E. (2006). "Management of cancer-related fatigue." Clin Adv Hematol Oncol 4(11): 828-829. Bower, J. E. (2007). "Cancer-related fatigue: links with inflammation in cancer patients and survivors." Brain Behav Immun 21(7): 863-871.

Bower, J. E., P. A. Ganz, N. Aziz, R. Olmstead, M. R. Irwin and S. W. Cole (2007). "Inflammatory responses to psychological stress in fatigued breast cancer survivors: relationship to glucocorticoids." Brain Behav Immun 21(3): 251-258.

Bower, J. E., P. A. Ganz, K. A. Desmond, C. Bernaards, J. H. Rowland, B. E. Meyerowitz and T. R. Belin (2006).

"Fatigue in long-term breast carcinoma survivors: a longitudinal investigation." Cancer 106(4): 751-758. Bower, J. E., P. A. Ganz, S. S. Dickerson, L. Petersen, N. Aziz and J. L. Fahey (2005). "Diurnal cortisol rhythm and fatigue in breast cancer survivors." Psychoneuroendocrinology 30(1): 92-100.

Burgess, H. J. and L. F. Fogg (2008). "Individual differences in the amount and timing of salivary melatonin secretion." PLoS One 3(8): e3055.

Burgess, H. J., V. L. Revell and C. I. Eastman (2008). "A three pulse phase response curve to three milligrams of melatonin in humans." J Physiol 586(2): 639-647.

Burgess, H. J., N. Savic, T. Sletten, G. Roach, S. S. Gilbert and D. Dawson (2003). "The relationship between the dim light melatonin onset and sleep on a regular schedule in young healthy adults." Behav Sleep Med 1(2): 102114.

Cella, D. (1998). "Factors influencing quality of life in cancer patients: anemia and fatigue." Semin Oncol 25(3 Suppl 7): 43-46.

Cella, D., J. S. Lai and A. Stone (2011). "Self-reported fatigue: one dimension or more? Lessons from the Functional Assessment of Chronic Illness Therapy--Fatigue (FACIT-F) questionnaire." Support Care Cancer 19(9): 1441-1450.

Cleveland, W. S. (1994). Visualizing Data. Summit, NJ, Hobart Press.

Corbett, M. A. (2013). "A potential aid to circadian adaptation: re-timer." Aviat Space Environ Med 84(10): 11131114.

Davidson JR, MacLean AW, Brundage MD, Schulze K. (2002). Sleep disturbances in cancer patients. Soc Sci Med, 54(9):1309-21.

Davis, S., D. K. Mirick and R. G. Stevens (2001). "Night shift work, light at night, and risk of breast cancer." J Natl Cancer Inst 93(20): 1557-1562.

Dean, G. E., D. S. Finnell, M. Scribner, Y. J. Wang, L. M. Steinbrenner and N. S. Gooneratne (2010). "Sleep in Lung Cancer: The Role of Anxiety, Alcohol and Tobacco." Journal of Addictions Nursing 21: 130-138. 2

Dogliotti, L., A. Berruti, T. Buniva, M. Torta, A. Bottini, M. Tampellini, M. Terzolo, R. Faggiuolo and A. Angeli (1990). "Melatonin and human cancer." J Steroid Biochem Mol Biol 37(6): 983-987.

Dolberg, O. T., S. Hirschmann and L. Grunhaus (1998). "Melatonin for the treatment of sleep disturbances in major depressive disorder." Am J Psychiatry 155(8): 1119-1121.

Eckerberg, B., A. Lowden, R. Nagai and T. Akerstedt (2012). "Melatonin treatment effects on adolescent students' sleep timing and sleepiness in a placebo-controlled crossover study." Chronobiol Int 29(9): 1239-1248.
Golombek, D. A., L. P. Casiraghi, P. V. Agostino, N. Paladino, J. M. Duhart, S. A. Plano and J. J. Chiesa (2013). "The times they're a-changing: effects of circadian desynchronization on physiology and disease." J Physiol Paris 107(4): 310-322.

Goedendorp MM, Gielissen MF, Verhagen CA, Bleijenberg G. (2013). Development of fatigue in cancer survivorship: a prospective follow-up study from diagnosis into the year after treatment. J Pain Symptom Manage, 45(2):213-22.

Gooneratne, N. S., G. E. Dean, A. E. Rogers, J. E. Nkwuo, J. C. Coyne and L. R. Kaiser (2007). "Sleep and quality of life in long-term lung cancer survivors." Lung Cancer 58(3): 403-410.

Hoffman, A. J., B. A. Given, A. von Eye, A. G. Gift and C. W. Given (2007). "Relationships among pain, fatigue, insomnia, and gender in persons with lung cancer." Oncol Nurs Forum 34(4): 785-792.

Horne, J. A. and O. Ostberg (1976). "A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms." Int J Chronobiol 4(2): 97-110.

Johns, M. W. (1991). "A new method for measuring daytime sleepiness: the Epworth sleepiness scale." Sleep 14(6): 540-545.

Kapo, Jennifer M. MD, Akgun, Kathleen M. MD, MS. (2015). Integrating palliative care into the care of patients with advanced lung cancer. Cancer Journal, 21(5):434-439.

Levin, R. D., M. A. Daehler, J. F. Grutsch, J. Quiton, C. G. Lis, C. Peterson, D. Gupta, K. Watson, D. Layer, S. HuffAdams, B. Desai, P. Sharma, M. Wallam, M. Delioukina, P. Ball, M. Bryant, M. Ashford, D.

Copeland, M. Ohmori, P. A. Wood and W. J. Hrushesky (2005). "Circadian function in patients with advanced non-small-cell lung cancer." Br J Cancer 93(11): 1202-1208.

Liu, L., M. R. Marler, B. A. Parker, V. Jones, S. Johnson, M. Cohen-Zion, L. Fiorentino, G. R. Sadler and S. AncoliIsrael (2005). "The relationship between fatigue and light exposure during chemotherapy." Support Care Cancer.

McCullagh, P. and J. A. Nelder (1989). Generalized linear models. London, UK, Chapman & Hall.

Nishiura, M., A. Tamura, H. Nagai and E. Matsushima (2014). "Assessment of sleep disturbance in lung cancer patients: Relationship between sleep disturbance and pain, fatigue, quality of life, and psychological distress." Palliat Support Care: 1-7.

Pachman DR, Barton DL, Swetz KM, Loprinzi CL. (2012). Troublesome symptoms in cancer survivors: fatigue, insomnia, neuropathy, and pain. J Clin Oncol. 20;30(30):3687-96.

Palesh OG, Roscoe J, Mustian KM, et al. (2010). Prevalence, demographics, and psychological associations of sleep disruption in patients with cancer: University of Rochester Cancer Center-Community Clinical Oncology Program. J Clin Oncol, 28: 292-298.

Redd, W. H., H. Valdimarsdottir, L. M. Wu, G. Winkel, E. E. Byrne, M. A. Beltre, E. S. Liebman, T. Erazo, J. A. Hayes, L. Isola, E. Scigliano, Y. Meschian, S. Lutgendorf and S. Ancoli-Israel (2014). "Systematic light exposure in the treatment of cancer-related fatigue: a preliminary study." Psychooncology.

Roscoe J, Kaufman ME, Matteson-Rusby SE, et al. (2007). Cancer-related fatigue and sleep disorders. Oncologist, 12: 35-42.

3.0 Inclusion and Exclusion Criteria

3.1 Describe the criteria that define who will be included or excluded in your final study sample.

Fifty-two lung cancer survivors with sleep continuity disturbance will be recruited over 2 years. Eligibility criteria include the following: age >21, stage I-III, non-small cell lung cancer, ≥6weeks and ≤3years post-surgical resection who are medically and psychiatrically stable. Subjects must be able to give consent. An NCI-designated comprehensive cancer center with a well-established thoracic surgery practice will be the recruitment site. A collaborative recruitment arrangement in the past has resulted in successful recruitment goal achievement.

3.2 Describe how individuals will be screened for eligibility.

The PI or research assistant (RA) will screen all eligible participants for sleep apnea using the ApneaLink device. Participants who screen positive for sleep apnea will receive 2 printed reports of the ApneaLink results: one for themselves and a copy for their provider, who will be advised to refer the participant for further sleep evaluation. Following a negative screen for sleep apnea, participants will be evaluated for sleep continuity disturbance through the use of Insomnia Severity Index, Epworth Sleepiness Scale and 14-day sleep diaries. Participants will also be screened for circadian activity rhythm disturbance with 14-day actigraphy and Morningness-Eveningness Questionnaire. A folder will be provided with each of the pretreatment instruments to complete and an actigraph to wear 24/7 at home. Following completion of pretreatment measures, participants will be randomized using a random number assignment to either red-yellow (control dim light) versus blue-green (experimental bright light) directed light therapy. Participants will be trained on how to wear the directed light therapy for 60-minutes within 30-minutes upon awakening for 1-week (Redd et al., 2014).

3.3 Indicate specifically whether you will include or exclude each of the following special populations: (You may not include members of these populations as subjects in your research unless you indicate this in your inclusion criteria.)

- *Adults unable to consent*
- *Individuals who are not yet adults (infants, children, teenagers)*
- *Pregnant women*
- *Prisoners*

These populations will not be included in the study.

3.4 Indicate whether you will include non-English speaking individuals. Provide justification if you will exclude non-English speaking individuals.
(In order to meet one of the primary ethical principles of equitable selection of subjects, non-English speaking individuals may not be routinely excluded from research. In cases where the research is of therapeutic intent or is designed to investigate areas that would necessarily require certain populations who may not speak English, the researcher is required to make efforts to recruit and include non-English speaking individuals. However, there are studies in which it would be reasonable to limit subjects to those who speak English: e.g., pilot studies, small unfunded studies with validated instruments not available in other languages, numerous questionnaires, and some non-therapeutic studies which offer no direct benefit.)

Non-English speakers will not be included in the study because this is a pilot study.

4.0 Study-Wide Number of Subjects (Multisite/Multicenter Only)

4.1 If this is a multicenter study, indicate the total number of subjects to be accrued across all sites.

This is not a multicenter study.

5.0 Study-Wide Recruitment Methods (Multisite/Multicenter Only)

If this is a multicenter study and subjects will be recruited by methods not under the control of the local site (e.g., call centers, national advertisements) describe those methods. Local recruitment methods are described later in the protocol.

5.1 Describe when, where, and how potential subjects will be recruited.

Response: NA

5.2 Describe the methods that will be used to identify potential subjects.

Response: NA

5.3 Describe materials that will be used to recruit subjects. (Attach copies of these documents with the application. For advertisements, attach the final copy of printed advertisements. When advertisements are taped for broadcast, attach the final audio/video tape. You may submit the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording, provided the IRB reviews the final audio/video tape.)

Response: NA

6.0 Multi-Site Research (Multisite/Multicenter Only)

6.1 If this is a multi-site study where you are the lead investigator, describe the processes to ensure communication among sites, such as:

- *All sites have the most current version of the protocol, consent document, and HIPAA authorization.*
- *All required approvals have been obtained at each site (including approval by the site's IRB of record).*
- *All modifications have been communicated to sites, and approved (including approval by the site's IRB of record) before the modification is implemented.*
- *All engaged participating sites will safeguard data as required by local information security policies.*
- *All local site investigators conduct the study appropriately.*

- *All non-compliance with the study protocol or applicable requirements will reported in accordance with local policy.*

Response: NA

6.2 Describe the method for communicating to engaged participating sites:

- *Problems.*
- *Interim results.*
- *The closure of a study*

Response: NA

7.0 Study Timelines

7.1 Describe the duration of an individual subject's participation in the study.

Subjects will be expected to participate for approximately 10 weeks during which ApneaLink screening, completion of pre-intervention data collection, 1 week for intervention, and completion of post-intervention data collection will occur.

7.2 Describe the duration anticipated to enroll all study subjects.

Approximately 18 months.

7.3 Describe the estimated date for the investigators to complete this study (complete primary analyses)

December, 2017.

8.0 Study Endpoints

8.1 Describe the primary and secondary study endpoints.

The primary endpoint is whether subjects have a significant improvement in self-reported fatigue, sleep and circadian rhythms with the bright light intervention as compared to the dim light intervention. The secondary endpoint is to determine whether pre-treatment subjects with circadian dysrhythmia (circadian phase and amplitude abnormalities) will be significantly more likely to exhibit treatment responses than those who were not identified as having circadian dysrhythmia.

8.2 Describe any primary or secondary safety endpoints.

Response: It is expected that some patients with stage I-III NSCLC may experience periods of low oxygenation during sleep that may be identified during screening with the ApneaLink. We added a letter of referral to give to patients who may wish to alert their Providers about this finding.

9.0 Procedures Involved

9.1 Describe and explain the study design.

This pilot study will include 52 lung cancer survivors using a 2X2 mixed model with Pre-Post assessments in two groups. Twenty-six participants will be randomized to red yellow directed light (control) and 26 participants will receive blue green (experimental) directed light therapy. The light source (Re-Timer) will be worn for 60-minutes every morning within 30-minutes upon awakening for 1-week. Participants will receive a weekly telephone call to ensure adherence to treatment plan and screen for safety/adverse events.

9.2 Provide a description of all research procedures being performed and when they are performed, including procedures being performed to monitor subjects for safety or minimize risks.

Screening for inclusion criteria includes a YES response to the following questions:

Are at least 21 years of age?

Do you have a diagnosis of non-small cell lung cancer stage I, II or III?

Have you had your lung cancer surgically removed at least 6 weeks ago, but not longer than 3 years ago?

Screening for exclusion criteria includes a NO response to the following questions:

Do you have any unmanaged medical or psychiatric diagnoses?

Are you currently pregnant?

Do you have a diagnosis of epilepsy?

Following informed consent, in order to rule-out sleep apnea as a confounder and assess for respiratory disturbance, all eligible participants will be screened for sleep apnea and hypoxia using the portable ApneaLink device for one night. Following a negative screen for sleep apnea, demographics, diagnoses, treatments, comorbidities, etc. will be recorded using the Demographics and Treatment Survey. Fatigue will be measured using the Functional Assessment of Chronic Illness Therapy Fatigue (FACIT) (Cella, Lai et al. 2011). Sleep continuity disturbance will be determined by Insomnia Severity Index (Bastien et al., 2001), 14-day sleep diary and the Epworth Sleepiness Scale (Johns 1991). Circadian activity rhythm disturbance will be assessed using the 14-day actigraph (Ambulatory Monitoring, Inc, Ardsley, NY) and Morningness-Eveningness Horne-Ostberg/Questionnaire (MEQ) (Horne and Ostberg 1976). Surveys and actigrahy will be performed at baseline and again after treatment ends. Expectation for treatment effectiveness will be assessed with the investigator developed Expectation Questionnaire before and

after treatment. Treatment adherence and safety will be evaluated by self-report start/end time on sleep diaries and with weekly telephone/text reminders.

9.3 Describe procedures performed to lessen the probability or magnitude of risks.

Weekly telephone calls will be negotiated and utilized to identify Adverse Events and adherence, in addition to self-report adherence on sleep diaries.

9.4 Describe all drugs and devices used in the research and the purpose of their use, and their regulatory approval status.

Response:

- **Direct Light Therapy** - Re-Timer is a directed light device, worn like a pair of glasses that produces a 100% UV-free red-yellow (dim light-control) or blue-green (bright light-experimental), which may improve sleep and reset circadian rhythms. Regulatory status: classified as a wellness device (no FDA classification as medical device)
- **ApneaLink** – ApneaLink is a compact, lightweight, portable device used for overnight screening for sleep apnea, providing information about respiratory effort, pulse, oxygen saturation, nasal flow and snoring. Regulatory status: approved (FDA)
- **Actigraphy (Ambulatory Monitoring, Inc., Ardsley, NY)** – is a wrist worn device that uses a piezoelectric sensor that generates a signal based on movement. The analog signal is then digitalized and for each 1-minute epoch an activity count is calculated and stored. Software application allow for objective sleep-wake patterns (total sleep time, sleep latency, wake after sleep onset, number of awakenings, sleep efficiency) and circadian activity rhythm assessment (mesor, amplitude, acrophase, etc.). Regulatory status: approved (FDA)

9.5 Describe the source records that will be used to collect data about subjects. (Attach all surveys, scripts, and data collection forms.)

- **Demographics and Treatment Survey:** A general demographics questionnaire used to assess personal (age, gender), lifestyle (smoking history and current use of tobacco, stimulants, and alcohol), disease (stage and type of lung cancer) and treatment (schedule, type and dose of chemotherapy, other medications used and side effects) factors.
- **Functional Assessment of Chronic Illness Therapy Fatigue (FACIT) (Cella, Lai et al. 2011)** – The FACIT Measurement System is a part of a collection of quality of life questionnaires targeted to the management of chronic illness. FACIT has 13-items with a 5-point Likert scale with well established validity and reliability to assess fatigue.

- **Insomnia Severity Index (ISI) (Bastien et al., 2001) –** is a self-report psychometrically sound instrument used to measure perceived insomnia severity.
- **Sleep diary** – is a self-report instrument to prospectively assess an individual's sleep.
- **Functional Assessment of Cancer Therapy-Lung Scale (Butt, Z., et al.,2005)** FACT-L is a widely used quality of life instrument in lung cancer clinical trials and provides validated clinically meaningful score changes.
- **Epworth Sleepiness Scale (Johns 1991)** – is a self-reported questionnaire assessing trait daytime sleepiness that relies on retrospective reports of dozing behavior in various hypothetical situations to establish an assessment of a patient's global level of sleepiness.
- **Morningness-Eveningness Horne-Ostberg/Questionnaire (MEQ) (Horne and Ostberg 1976)** – is a self-reported questionnaire used to determine individual differences in morningness and eveningness-the degree to which respondents are active and alert at certain times of the day. Results of this questionnaire inform circadian typology.
- **Treatment Expectation (investigator developed) self-report survey to determine treatment expectations for treatment effectiveness before and after treatment**.
- **Pittsburgh Sleep Quality Index (Buysee et al., 1991),** a 19-item, self-report questionnaire assesses sleep quality and quantity. The PSQI assesses a range of sleep disturbances including: insomnia, sleep apnea and limb movement disorders, as well as daytime consequences of sleep.
- **Snellen Visual Acuity chart –** Assess visual acuity before and after the interventions.
- **Brief Fatigue Inventory (Mendoza, 1999) –** BFI is a valid and reliable measure of clinically significant fatigue, assessing fatigue severity, and impact of fatigue on daily functioning.
- **Hospital Depression and Anxiety Scale (Zigmond & Snaith, 1983).** HADS is valid and reliable self-assessment of depression and anxiety for inpatients and outpatients.

9.6 What data will be collected including long-term follow-up.

Response: Quantitative data on demographics, disease and treatment; screening for sleep apnea; self-report data on sleep, fatigue and quality of life; movement data used for objective sleep-wake data; treatment adherence and treatment expectations.

9.7 For HUD uses provide a description of the device, a summary of how you propose to use the device, including a description of any

screening procedures, the HUD procedure, and any patient follow-up visits, tests or procedures.

N/A

10.0 Data and Specimen Banking

10.1 If data or specimens will be banked for future use, describe where the data/specimens will be stored, how long they will be stored, how the data/specimens will be accessed, and who will have access to the data/specimens.

N/A

10.2 List the data to be stored or associated with each specimen.

N/A

10.3 Describe the procedures to release data or specimens, including: the process to request a release, approvals required for release, who can obtain data or specimens, and the data to be provided with specimens.

Response: N/A

11.0 Data Management

11.1 Describe the data analysis plan, including any statistical procedures.

Hypothesis testing will be conducted using 2x2 ANOVAs for the first specific aim, with Logistic Regressions for the second specific aim (predicting treatment response and non-response) and with Linear and Logistic Regressions for the third specific aim (predicting illness severity and treatment response).

11.2 Provide a power analysis.

Response:

The primary outcome for sleep is the sleep efficiency score. Previous research has indicated that persons with satisfactory sleep have a sleep efficiency score exceeding 85, whereas persons reporting unsatisfactory sleep have a score at most 70, with both groups reporting a standard deviation of approximately 15. The estimated effect size from this study

is 1. The goal of this study is to improve sleep efficiency from an unsatisfactory level to a satisfactory level. Using a large effect size of .08 with a one-tailed significance of .025 and power of 80%, the required sample size for the two-group comparison is 26 per group for a total sample of 52.

11.3 Describe the steps that will be taken secure the data (e.g., training, authorization of access, password protection, encryption, physical controls, certificates of confidentiality, and separation of identifiers and data) during storage, use, and transmission.

All members of the research team have completed CITI training on ways to protect subject's data throughout the research process. Following informed consent, each participant will be assigned a unique numeric identifier. Consents will be stored in a locked file cabinet in a locked office in the School of Nursing. Data will be de-identified before being coded, entered, stored securely, backed up regularly, and analyzed using the SPSS software at the University at Buffalo School of Nursing in room 301B Wende Hall, 3435 Main Street, Buffalo, NY 14214. To ensure safety in data management and data analysis, data entry will be performed on a protected computer, secured by the University at Buffalo Standards for Securing Regulated Private Data and the New York State Information Security Breach Notification Act with access limited by UBIT safety policies to data management, including: secure server and computer, base encryption, UBIT password and name account verification and daily electronic secure back up. Data destruction will be manually performed in accordance with the applicable institutional schedule at the end of its life cycle.

11.4 Describe any procedures that will be used for quality control of collected data.

All data is initially checked by the PI for completeness and incomplete data is reviewed with participant to ensure incomplete answers were addressed. All data that is coded and entered will be independently verified by at least one other research team member, with monthly random checks performed by the PI. Data analysis will begin with an assessment of means, standard deviations, frequencies and confidence intervals to identify any outliers. Outlier data will be reviewed with statistician on data management.

11.5 Describe how data and specimens will be handled study-wide:

Response: Data will be de-identified by assigning a unique subject number to each consented participant's data file. De-identified data will be abstracted from the electronic medical record and recorded on the Demographics and Treatment Survey after each eligible participant is

consented. De-identified data will be tranferred to an SPSS file and stored on a password protected computer in a locked office in Wende Hall at the University at Buffalo School of Nursing within 24 hours. Demographics and Treatment Survey data will be stored in a locked file cabinet in room 301B Wende Hall. The PI, Research Assistant and co-investigators will have will have access to the SPSS de-identified data files.

11.6 What information will be included in that data or associated with the specimens?

Response: Demographics, lifestyle data, lung cancer treatment history, current medications, sleep, fatigue and quality of life survey results, sleep apnea and oxygen saturation data and circadian activity rhythm data.

11.7 Where and how data or specimens will be stored?

Response: Data will be stored securely and backed up regularly at the University at Buffalo School of Nursing in room 301B Wende Hall, 3435 Main Street, Buffalo, NY 14214. To ensure data safety, data entry will be performed on a protected computer, secured by the University at Buffalo Standards for Securing Regulated Private Data and the New York State Information Security Breach Notification Act with access limited by UBIT safety policies to data management, including: secure server and computer, base encryption, UBIT password and name account verification and daily electronic secure back up.

11.8 How long the data or specimens will be stored?

Data will be stored for a minimum of three years and data destruction will be manually performed in accordance with the applicable institutional schedule at the end of its life cycle. Each team member will access the data following the University at Buffalo Standards for Securing Regulated Private Data as mentioned above.

11.9 Who will have access to the data or specimens?

Members of the research team who have completed the required SUNY Buffalo CITI training will have access to data with UB secure access generated by UBIT password via authorized UB computers at University at Buffalo School of Nursing.

11.10 Who is responsible for receipt or transmission of the data or specimens?

The principal investigator and research assistant will be responsible for receipt of the data from participants. Once data is de-identified, data coders will code, enter, verify and analyze the data under the direction of the PI. This study will not use specimens.

11.11How data and specimens will be transported?

Response: De-identified survey data will be transported by the PI in a briefcase.

12.0 Provisions to Monitor the Data and Ensure the Safety of Subjects

12.1 Describe the plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe.

The PI will be responsible for ensuring data integrity and safety monitoring for human subjects and communicating any negative outcomes or any serious events to the IRBs and other offices/agencies. Because of the minimal to low risk associated with this protocol, the data safety and monitoring plan (DSMP) for this project involves close monitoring by the principal investigator (PI) and a safety officer, an Nurse Practitioner in the School of Nursing. The data safety monitoring team will ensure participant safety, ensure the validity and integrity of the data, monitor study progress, and make recommendations regarding appropriate protocol and operational changes which may have substantial effects upon the ultimate interpretation of the study. They will also be responsible for promptly report any serious adverse events to the Institutional Review Boards (IRB) at Roswell Park Cancer Institute, the VA Western New York Health Systems (VA WNYHS) and the University at Buffalo

Weekly reviews of participant accrual will be conducted by the PI during weekly research meetings. If participant accrual and/or retention drop below what is required for successful completion of this study, the PI will alert the statistician and strategies will be developed to overcome the identified problems. Records from subjects recruited during that week will also be scrutinized to insure that all participants are eligible for participation in the study. The PI and members of the research team will be monitoring developments in the literature and results of related studies that may have an impact on the safety of participants or on the ethics for the research study. Additionally, Michael Perlis, PhD, a sleep research expert and consultant, will serve as a resource for new findings in the field and to assist with this clinical trial.

12.2 Describe what data are reviewed, including safety data, untoward events, and efficacy data.

Data review includes eligibility, referral for sleep apnea, referral for low oxygen during sleep, completion of data collection instruments, adherence to intervention, number of follow up phone calls accepted, and outcome measures of efficacy: fatigue, sleep and circadian activity rhythms. Daytime sleepiness will also be evaluated daily, but monitored weekly.

12.3 Describe how the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with participants).

Daytime sleepiness may be hazardous for patients at risk for falling asleep while driving, for example. This is a safety question that is monitored

daily and assessed weekly by telephone with the participant. It is also assessed at baseline and end of study with the Epworth Sleepiness Scale.

12.4 Describe the frequency of data collection, including when safety data collection starts.

Data collection will occur during and immediately following the screening process, and will continue throughout the intervention period (1-week), concluding with the post intervention data collection period (2-weeks). Data collection will be conducted approximately weekly, to include a safety question. The daytime sleepiness question is important to determine if participants are at risk for harm.

12.5 Describe who will review the data.

The PI will review the data for completeness, accuracy and safety. A second team member will code, enter, and then verify the data with a third member of the research team.

12.6 Describe the frequency or periodicity of review of cumulative data.

Cumulative data will be reviewed monthly by the PI. Data coding and entry errors will be identified and corrected.

12.7 Describe the statistical tests for analyzing the safety data to determine whether harm is occurring.

If a participant scores >10 on the Epworth Sleepiness Scale or scores a 3 or higher on the daily sleepiness scale, we will discuss this result with the participant to determine if they are at risk for harm and monitor the patient more frequently.

12.8 Describe any conditions that trigger an immediate suspension of the research.

Response: We do not anticipate any condition that would trigger an immediate suspension of the research.

13.0 Withdrawal of Subjects

13.1 Describe anticipated circumstances under which subjects will be withdrawn from the research without their consent.

Subjects will be withdrawn from the research without their consent if they are unable to complete their responsibilities listed on the consent form or if they falsify responses.

13.2 Describe any procedures for orderly termination.

The participants that require early termination from the study will receive a telephone call alerting them to the termination and thanking them for their participation. If participants are not available via telephone, a letter notifying them of their termination will be mailed to their home address.

13.3 Describe procedures that will be followed when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection.

Response: It is conceivable that some participants may decide not to fully participate, for example, not wear the light therapy (i.e. Re-Timers), but complete survey and actigraph data. Their data is still valuable. Data collection would continue and participants would receive appropriate compensation.

14.0 Risks to Subjects

14.1 List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related to the subjects' participation in the research. Include as may be useful for the IRB's consideration, a description of the probability, magnitude, duration, and reversibility of the risks. Consider physical, psychological, social, legal, and economic risks.

The *known risks associated with this study include the possibility that participants may become upset thinking about some of the questions or topics in this study. If this occurs, the participant should notify the research assistant and will then be provided with an appropriate referral for assistance. The skin on the participant's wrist may become irritated by wearing the actigraph. If this occurs, the participant will be advised to remove the actigraph, apply a thin layer of Eurcerin lotion to the affected area and wear the actigraph on the opposite wrist.*

14.2 If applicable, indicate which procedures may have risks to the subjects that are currently unforeseeable.

Response: N/A

14.3 If applicable, indicate which procedures may have risks to an embryo or fetus should the subject be or become pregnant.

Response: N/A

14.4 If applicable, describe risks to others who are not subjects.

Response: N/A

15.0 Potential Benefits to Subjects

15.1 Describe the potential benefits that individual subjects may experience from taking part in the research. Include as may be useful for the IRB's consideration, the probability, magnitude, and duration of the potential benefits.

Response: Preliminary testing of the efficacy of light therapy has demonstrated an improvement in sleep continuity disturbances, daytime

functioning and quality of life in a variety of cancer survivors. Participants may benefit with a better sleep quality and overall quality of life. Furthermore, this light therapy device (i.e. Re-Timer) may be a more energy-efficient (through the use of LEDs) and convenient (portable method), compared to traditional light boxes.

15.2 Indicate if there is no direct benefit. Do not include benefits to society or others.

Response: Some participants may not achieve any benefit from this therapy.

16.0 Vulnerable Populations

16.1 If the research involves individuals who are vulnerable to coercion or undue influence, describe additional safeguards included to protect their rights and welfare.

- *If the research involves pregnant women, review "CHECKLIST: Pregnant Women (HRP-412)" to ensure that you have provided sufficient information.*
- *If the research involves neonates of uncertain viability or non-viable neonates, review "CHECKLIST: Neonates (HRP-413)" or "HRP-414 – CHECKLIST: Neonates of Uncertain Viability (HRP-414)" to ensure that you have provided sufficient information.*
- *If the research involves prisoners, review "CHECKLIST: Prisoners (HRP-415)" to ensure that you have provided sufficient information.*
- *If the research involves persons who have not attained the legal age for consent to treatments or procedures involved in the research ("children"), review the "CHECKLIST: Children (HRP-416)" to ensure that you have provided sufficient information.*
- *If the research involves cognitively impaired adults, review "CHECKLIST: Cognitively Impaired Adults (HRP-417)" to ensure that you have provided sufficient information.*
- *Consider if other specifically targeted populations such as students, employees of a specific firm or educationally/economically disadvantaged persons are vulnerable to coercion or undue influence. The checklists listed above for other populations should be used as a guide to ensure that you have provided sufficient information.*

N/A

17.0 Community-Based Participatory Research

17.1 Describe involvement of the community in the design and conduct of the research.

Response: N/A

Note: "Community-based Participatory Research" is a collaborative approach to research that equitably involves all partners in the research process and recognizes the unique strengths that each brings. Community-based Participatory Research begins with a research topic of importance to the community, has the aim of combining knowledge with action and achieving social change to improve health outcomes and eliminate health disparities.

18.0 Sharing of Results with Subjects

18.1 Describe whether or not results (study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) will be shared with subjects or others (e.g., the subject's primary care physicians) and if so, describe how it will be shared.

Response: Sleep apnea and nighttime oxygenation results will be reported to participants and, if abnormal, to the participant's primary provider if we receive permission from the participant to do so.

19.0 Setting

19.1 Describe the sites or locations where your research team will conduct the research.

Response: Roswell Park Cancer Institute, VA WNYHS and Cancer Care of Western New York will be the sites used to conduct the research.

19.2 Identify where your research team will identify and recruit potential subjects.

Response: The research team will identify and recruit potential subjects in the thoracic clinics at Roswell Park Cancer Institute, VA WNYHS and Western New York oncology offices and community centers that provide service to patients with lung cancer.

19.3 Identify where research procedures will be performed.

Response: Research procedures will be conducted in the thoracic clinics at Roswell Park Cancer Institute, VA WNYHS and Western New York oncology offices and community centers that provide service to patients with lung cancer.

19.4 Describe the composition and involvement of any community advisory board.

Response: N/A

19.5 For research conducted outside of the organization and its affiliates describe:

- *Site-specific regulations or customs affecting the research for research outside the organization.*
- *Local scientific and ethical review structure outside the organization.*

Response: N/A

20.0 Resources Available

20.1 Describe the qualifications (e.g., training, experience, oversight) of you and your staff as required to perform their role. When applicable describe their knowledge of the local study sites, culture, and society. Provide enough information to convince the IRB that you have qualified staff for the proposed research. Note- If you specify a person by name, a change to that person will require prior approval by the IRB. If you specify people by role (e.g., coordinator, research assistant, co-investigator, or pharmacist), a change to that person will not usually require prior approval by the IRB, provided that person meets the qualifications described to fulfill their roles.

Response: The PI completed a 2-year fellowship in Sleep and Respiratory Neurobiology at the University of Pennsylvania in 2006 and has conducted a variety of funded sleep studies at RPCI. The PI has collaborated with medical oncology for the past 5 years and thoracic surgery for the past year at RPCI and the VA WNYHS. The research team includes School of Nursing faculty who are sleep experts serving as co-investigators (Dickerson and Jungquist), a graduate nursing student learning to become a sleep scientist (Carleara Ferreira da Rosa Silva), two consultants (Perlis and Wright) who are experts in insomnia treatment and light therapy to improve circadian rhythms and a collaborating thoracic surgeon (Dexter). The PI has been looking for a project to collaborate with Dr. Shah at Cancer Care of Western New York.

Describe other resources available to conduct the research: For example, as appropriate:

20.2 Justify the feasibility of recruiting the required number of suitable subjects within the agreed recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit?

Roswell Park Cancer Institute admits approximately 700 new patients with lung cancer annually. More than 400 of those 700 patients have stage I-III disease. Fifty lung cancer survivors with sleep continuity disturbance will

be recruited over 2 years. Not all lung cancer survivors have sleep continuity disturbance, but in our current sleep study, we were able to recruit 20 lung cancer survivors with insomnia within 6 months at Roswell Park Cancer Institute. Retention rate of study participants is anticipated to be 80% based on our previous experience. Oversampling will result in the desired target sample size at this rate. At the time of enrollment in the study, three forms of contact information will be obtained, email address, telephone number, and address for delivery of the data collection instruments and return mailers. In addition, an alternate contact person will be obtained to help decrease loss to follow up due to the length of the study.

20.3 Describe the time that you will devote to conducting and completing the research.

Response: 20% of the PI's research time, 10% of the Co-I's time and the RA will work 10 hours/week on this study.

20.4 Describe your facilities.

Response: Recruitment Site: Roswell Park Cancer Institute (RPCI) was founded in 1898 is America's first cancer center and holds the National Cancer Institute designation of "comprehensive cancer center." RPCI has 133 hospital beds and 12 multidisciplinary clinics and is the only comprehensive cancer center of Western New York area. As a member of the prestigious National Comprehensive Cancer Network, RPCI has played a vital part in setting clinical guidelines for the care of Oncology patients. RPCI plays a pivotal part in cancer research with several ongoing funded research projects.

The thoracic clinic provides state of the art comprehensive multidisciplinary care to approximately 700 patients with lung cancer annually. The presence of several specialties -pulmonary medicine, medical oncology and thoracic surgery along with the undiagnosed clinic in a single location with additional support from nearby radiation oncology clinics and interventional radiation ensures excellent patient care and satisfaction. The patients with lung masses and suspected lung cancer are promptly seen by the pulmonary clinic or the undiagnosed clinic and scheduled for diagnostic biopsy procedures. Several multidisciplinary meetings are conducted each week to make complicated management decisions for the patients.

The VA WNYHS provides care to approximately 100 newly diagnosed veterans with lung cancer annually.

Research Offices: The University at Buffalo School of Nursing (SON) is located in Wende Hall, a newly renovated historic building on the South Campus, is in close proximity to the four other Health Sciences Schools of Medicine, Dentistry, Pharmacy, and Public Health and Health Related

Professions. As a SON situated in a research intensive university, creation, translation, and transmission of knowledge is an expectation of faculty in support of the University mission. Excellence in teaching and service to the university, the community and the profession are also expectations in support of the mission and goals of the University and SON. A variety of offices, classrooms, and conference rooms are available for faculty. There are two videoconferencing rooms in the SON to accommodate a recently funded distance education PhD grant as well as other videoconferencing facilities located in the Health Sciences Library. The PI has 10 wrist-actigraphs (Octogonal Sleep Watch 2.0) and ActionW software (Version 2.0) purchased from Ambulatory Monitoring, Ardsley, NY, to use in this study.

20.5 Describe the availability of medical or psychological resources that subjects might need as a result of an anticipated consequences of the human research.

Response: Roswell Park Cancer Institute, VA WNYHS and Western New York oncology offices and community centers that provide service to patients with lung cancer have dedicated social workers and a psychologist assigned to ambulatory clinics.

20.6 Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions.

Response: When we begin a new study, we take turns reading the research protocol out loud during a team meeting to ensure each member of the team has read the protocol and understands it. Team members are encouraged to ask questions about the research protocol during the meeting. We each perform the research procedures that we ask research participants to engage in to increase our understanding of the procedures/process and ensure the data collection instruments collect the information that we require.

21.0 Prior Approvals

21.1 Describe any approvals that will be obtained prior to commencing the research. (E.g., school, external site. funding agency, laboratory, radiation safety, or biosafety approval.)

Response: This study is funded by the Oncology Nursing Society Foundation. Before releasing the funding, University @ Buffalo's IRB approval is needed.

22.0 Recruitment Methods

22.1 Describe when, where, and how potential subjects will be recruited.

The Principal Investigator will screen medical records for eligibility criteria. Potential participants will be approached face to face and after

signed informed consent will be randomly assigned to control and experimental group.

22.2 Describe the source of subjects.

Response: All participants at Roswell Park Cancer Institute, VA WNYHS and Western New York oncology offices and community centers that provide service to patients with lung cancer meeting the eligibility criteria.

22.3 Describe the methods that will be used to identify potential subjects.

Potential participants will be screened for eligibility criteria by reviewing electronic medical records for eligibility in the thoracic clinics at Roswell Park Cancer Institute, VA WNYHS and Western New York oncology offices and community centers that provide service to patients with lung cancer.

22.4 Describe materials that will be used to recruit subjects. (Attach copies of these documents with the application. For advertisements, attach the final copy of printed advertisements. When advertisements are taped for broadcast, attach the final audio/video tape. You may submit the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording, provided the IRB reviews the final audio/video tape.)

Response: An IRB-approved recruitment flyer will be used.

22.5 Describe the amount and timing of any payments to subjects.

Response: A total of $50 will be paid to participants that complete data collection. After completing baseline data participants will receive $25 and after completing f/u data collection participants will receive another $25.

23.0 Local Number of Subjects

23.1 Indicate the total number of subjects to be accrued locally.

Response: 50

23.2 If applicable, distinguish between the number of subjects who are expected to be enrolled and screened, and the number of subjects needed to complete the research procedures (i.e., numbers of subjects excluding screen failures.)

Response: 50 recruited and 40 to complete. We anticipate approximately 80% retention from previous research on this patient population.

24.0 Confidentiality

Describe the local procedures for maintenance of confidentiality.

24.1 Where and how data or specimens will be stored locally?

De-identified data will be coded, entered, store securely, backed up regularly, and analyzed using the SPSS software at the University at Buffalo School of Nursing phone number 716-829-3235 at Room 301B Wende Hall, at 3435 Main Street, Buffalo, NY 14214. To ensure safety in data management and data analysis, data entry will be performed in a protected computer, secured by the University at Buffalo Standards for Securing Regulated Private Data and the New York State Information Security Breach Notification Act with access limited by UBIT safety policies to data management, including: locked server and computer, base encryption, UBIT password and name account verification, daily electronic secure back up and locked store.

24.2 How long the data or specimens will be stored locally?

Response: 3 years.

24.3 Who will have access to the data or specimens locally?

Response: Research team members.

24.4 Who is responsible for receipt or transmission of the data or specimens locally?

The principal investigator and research assistant will be responsible for receipt of the data.

24.5 How data and specimens will be transported locally?

Response: The PI will transport the surveys from Roswell Park Cancer Institute, VA WNYHS and Western New York oncology offices and community centers that provide service to patients with lung cancer to UB School of Nursing in a briefcase.

25.0 Provisions to Protect the Privacy Interests of Subjects

25.1 Describe the steps that will be taken to protect subjects' privacy interests. "Privacy interest" refers to a person's desire to place limits on whom they interact or whom they provide personal information.

All reasonable efforts will be used to protect the confidentiality of the participants' protected health information. Identifiable data is immediately de-identified and de-identified data is stored separately from identifiable data. The results of this research will be published. However, we will keep participants' names and other identifying information confidential.

25.2 Describe what steps you will take to make the subjects feel at ease with the research situation in terms of the questions being asked and the procedures being performed. "At ease" does not refer to physical discomfort, but the sense of intrusiveness a subject might experience in response to questions, examinations, and procedures.

Response: To ensure participants feel at ease with the research situation in terms of the questions being asked and the procedures being performed, the PI or RA will conduct the informed consent process in a private room with the participant and family member(s) (participant's discretion) in attendance. PI/RA will provide a schema of the procedures and examples of the surveys and equipment used in the study in an unhurried manner to allow the participant time to absorb and process the information and allow for questions and answers about their participation.

25.3 Indicate how the research team is permitted to access any sources of information about the subjects.

Response: A HIPAA Partial Waiver has been requested to access the electronic medical record in order to determine participant eligibility.

26.0 Compensation for Research-Related Injury

26.1 If the research involves more than Minimal Risk to subjects, describe the available compensation in the event of research related injury.

Response: N/A

26.2 Provide a copy of contract language, if any, relevant to compensation for research-related injury.

Response: N/A

27.0 Economic Burden to Subjects

27.1 Describe any costs that subjects may be responsible for because of participation in the research.

Subjects will have no cost related to their participation in this research.

28.0 Consent Process

28.1 Indicate whether you will be obtaining consent

Written informed consent will be obtained at the recruitment.

28.2 Describe where the consent process take place

Consent process will take place in the thoracic clinics at Roswell Park Cancer Institute, VA WNYHS and Cancer Care of Western New York.

28.3 Describe any waiting period available between informing the prospective subject and obtaining the consent.

Response: Participants may sign consent within 30-minutes of learning about the study, but may take as long as they need before signing the consent.

28.4 Describe any process to ensure ongoing consent.

Response: At each contact with participants, the PI/RA will routinely remind them of their volunteer status and ability to withdraw from participation at any time.

28.5 Describe whether you will be following "SOP: Informed Consent Process for Research (HRP-090)." If not, describe:

- *The role of the individuals listed in the application as being involved in the consent process.*
- *The time that will be devoted to the consent discussion.*
- *Steps that will be taken to minimize the possibility of coercion or undue influence.*
- *Steps that will be taken to ensure the subjects' understanding.*

Response: This study will follow SOP: Informed Consent Process for Research (HRP-090).

Non-English Speaking Subjects

28.6 Indicate what language(s) other than English are likely to be spoken/understood by your prospective study population or their legally authorized representatives.

Non – English speaking participants will not be included in this study.

28.7 If subjects who do not speak English will be enrolled, describe the process to ensure that the oral and written information provided to those subjects will be in that language. Indicate the language that will be used by those obtaining consent.

Response: N/A

Waiver or Alteration of Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception)

28.8 Review the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" to ensure you have provided sufficient information for the IRB to make these determinations. Provide any additional information necessary here:

Response: N/A

28.9 If the research involves a waiver the consent process for planned emergency research, please review the "CHECKLIST: Waiver of Consent for Emergency Research (HRP-419)" to ensure you have provided sufficient information for the IRB to make these determinations. Provide any additional information necessary here:

Response: N/A

Subjects who are not yet adults (infants, children, teenagers)

28.10Describe the criteria that will be used to determine whether a prospective subject has not attained the legal age for consent to treatments or procedures involved in the research under the applicable law of the jurisdiction in which the research will be conducted. (E.g., individuals under the age of 18 years.) For research conducted in NY state, review "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "children."

Response: Age will be determined from the electronic medical record.

28.11For research conducted outside of NY state, provide information that describes which persons have not attained the legal age for consent to treatments or procedures involved the research, under the applicable law of the jurisdiction in which research will be conducted. One method of obtaining this information is to have a legal counsel or authority review your protocol along the definition of "children" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."

Response: N/A

28.12Describe whether parental permission will be obtained from:

- *Both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.*
- *One parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.*

Response: N/A

28.13Describe whether permission will be obtained from individuals other than parents, and if so, who will be allowed to provide permission. Describe the process used to determine these individuals' authority to consent to each child's general medical care.

Response: N/A

28.14Indicate whether assent will be obtained from all, some, or none of the children. If assent will be obtained from some children, indicate which children will be required to assent.

Response: N/A

28.15When assent of children is obtained describe whether and how it will be documented.

Response: N/A

Cognitively Impaired Adults

28.16Describe the process to determine whether an individual is capable of consent. The IRB sometimes allows the person obtaining assent to document assent on the consent document and does not automatically require assent documents to be used.

Response: Eligible participants will be monitored during the screening and consent process for indications that they understand.

Adults Unable to Consent

When a person is not capable of consent due to cognitive impairment, a legally authorized representative should be used to provide consent and, where possible, assent of the individual should also be solicited.

28.17List the individuals from whom permission will be obtained in order of priority. (e.g., durable power of attorney for health care, court appointed guardian for health care decisions, spouse, and adult child.) For research conducted in NY state, review "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "legally authorized representative." The list in the consent template signature section corresponds to the priority list for NYS.

Response: N/A

28.18For research conducted outside of NY state, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the procedure(s) involved in this research. One method of obtaining this information is to have a legal counsel or authority review your protocol along the definition of "legally authorized representative" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."

Response: N/A

28.19Describe the process for assent of the subjects. Indicate whether:

- *Assent will be required of all, some, or none of the subjects. If some, indicated, which subjects will be required to assent and which will not.*
- *If assent will not be obtained from some or all subjects, an explanation of why not.*
- *Describe whether assent of the subjects will be documented and the process to document assent. The IRB allows the person obtaining assent to document assent on the consent document and does not routinely require assent documents and does not routinely require subjects to sign assent documents.*

Response: Signed informed consent is required of all participants for this study.

28.20For HUD uses provide a description of how the patient will be informed of the potential risks and benefits of the HUD and any procedures associated with its use.

Response: N/A

29.0 Process to Document Consent in Writing

If your research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context, the IRB will generally waive the requirement to obtain written documentation of consent.

(If you will document consent in writing, attach a consent document. If you will obtain consent, but not document consent in writing, attach a consent script. Review "CHECKLIST: Waiver of Written Documentation of Consent (HRP-411)" to ensure that you have provided sufficient information. You may use "TEMPLATE CONSENT DOCUMENT (HRP-502)"to create the consent document or script.)

29.1 Describe whether you will be following "SOP: Written Documentation of Consent (HRP-091)." If not, describe whether and how consent of the subject will be obtained including whether or not it will be documented in writing.

Response: This study will require SOP: Written Documentation of Consent (HRP-091).

30.0 Drugs or Devices

30.1 If the research involves drugs or device, describe your plans to store, handle, and administer those drugs or devices so that they will be used only on subjects and be used only by authorized investigators.

Response: The device used in this research study is already available commercially.

If the drug is investigational (has an IND) or the device has an IDE or a claim of abbreviated IDE (non-significant risk device), include the following information:

30.2 Identify the holder of the IND/IDE/Abbreviated IDE.

Response: N/A

30.3 Explain procedures followed to comply with FDA sponsor requirements for the following:

	Applicable to:		
FDA Regulation	***IND Studies***	***IDE studies***	***Abbreviated IDE studies***
21 CFR 11	***X***	***X***	
21 CFR 54	***X***	***X***	
21 CFR 210	***X***		
21 CFR 211	***X***		
21 CFR 312	***X***		
21 CFR 812		***X***	***X***
21 CFR 820		***X***	

Response: N/A