Effects of Bright Light on Co-occurring Cancer-related Symptoms in Breast Cancer Survivors

NCT03304587

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Statistical Analysis Plan

May 1, 2022

Statistical Analysis Plan

The data analysis of **Aim 1** will be descriptive in nature. To assess the feasibility of the proposed study protocol, the numbers of subjects contacted and screened, the proportion of eligible subjects from those contacted, the proportion of those successfully recruited from the pool of eligible subjects, the proportion retained of those recruited, completeness of the data collected, ease of using each measure, and adverse effects (if there are any) will be described using summary statistics. Adherence to treatment will be assessed by measuring timing of visor cap usage. Adherence to outcome reporting will be evaluated by estimating completion rates of scheduled PSG recordings, core body temperature measures, and self-report forms at both time periods. The proportion and the reason for missing data on each outcome will also be assessed.

The objective of **Aim 2** is to assess the effects of bright light on the 4 symptoms (sleep disturbance, fatigue, depression, cognitive dysfunction) and quality of life. Nocturnal sleep patterns will be measured objectively and subjectively. Objective sleep patterns will be monitored in a sleep laboratory by all-night PSG before and after the light intervention. The endpoints for sleep patterns (the sleep continuity measures include sleep onset latency, arousals, wake after sleep onset, and sleep efficiency) will be derived from scoring the PSG record by a polysomnographer blind to intervention assignment. Subjective endpoints for sleep patterns (sleep onset latency, sleep disturbance, and sleep efficiency) will be self-reported by participants before and after the light intervention. For each endpoint, the between-group difference will be compared using two-way ANOVA for repeated measurement data and to account for potential correlation among multiple measurements taken from the same individual. Important covariates such as ambient light and the level of stress (as measured by PSS) will be adjusted if necessary. Fatigue, depression, cognition, and quality of life will be subjectively and objectively assessed before and after the light intervention. Between-group differences in those subjective measurements will be compared using two-way ANOVA.

The objective of **Aim 3** is to assess the effects of bright light on circadian rhythms. Circadian rhythm will be measured by nocturnal core body temperature before and after the light intervention. The phase shift of the nocturnal core body temperature will be calculated by the timing of the peak and trough of the temperature curve. To take full advantage of the availability of intensive data from continuous sleep-time core body temperature measurement, the difference in circadian rhythms between groups will also be compared using functional data analysis (FDA), a collection of emerging techniques about the analysis of information on curves or functions. Unlike the conventional methods such as ANOVA that only focus on the differences at a few fixed time points, FDA provides information about curves, surfaces, or anything else varying over a continuum. Specifically, after a proper registration or alignment of the temperature curves from each individual, FDA will allow us not only to compare the overall circadian rhythms between groups, but also correlate the curves with other measured data such as symptom scores from Aim 2. Such a curve-based analysis will allow us to compare not only the magnitude (peak and trough) but also the shift in the circadian cycle.

Mediation analysis will also be performed to better understand the possible mechanism of bright light intervention on the 4 symptoms. Specifically, functional principal component analysis (FPCA) will first be applied to core body temperature during pre- and post-treatment periods separately to identify distinct patterns of circadian rhythms. The causal-step approach outlined in the classic work of mediation analysis will then be used to estimate the direct and indirect treatment effects and to quantify the potential mediating effects of circadian rhythms. Due to relatively small sample size, the interest will focus more on the estimation and precision of mediating effects rather than significance testing.