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Self-Reported Stress Perception in Breast Cancer Patients Treated with Integrative Metal Color Light Therapy: The LUCIA Study Protocol

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Abstract

Introduction: Many breast cancer patients benefit from appropriate oncological therapies, but they also experience side effects or ongoing restrictions that significantly impact their health-related quality of life. Non-Pharmaceutical interventions (NPIs) such as physical exercise, movement, art therapy, yoga or mindfulness-based stress reduction can help reduce distress and pain while supporting resilience strategies. Metal Colored Light (MCL) therapy, an integrative art therapy utilizing metal-colored glasses, has previously been used to alleviate symptoms, improve quality of life, and support coping strategies. The LUCIA study aims, for the first time, to systematically investigate whether the self-reported perception of stress can be influenced in breast cancer patients through a series of MCL sessions.

Methods and Analysis: The LUCIA-study will enroll 60 breast cancer patients treated with MCL therapy, consisting of nine individual MCL sessions per patient over a six-week period. The primary outcome is the analysis of self-reported stress perception in breast cancer patients using the National Comprehensive Cancer Network (NCCN) Distress Thermometer.

Secondary endpoints include the assessment of internal coherence using the Internal Coherence Scale (ICS), and the assessment of health-related quality of life using the European Organization for Research and Treatment of Cancer Questionnaire C30 (EORTC-QLQ-C30). Longitudinal changes in symptom burden will be assessed, and multivariate analyses performed.

Ethics and disseminations: The present study is approved by the ethics committee of the Medical Association Berlin within the Network Oncology with the reference number Eth-27/10. The results will be presented at scientific conferences and published.

Trial registration number: The study was registered at the German Register for Clinical Trials under DRKS00013335 on 27/11/2017

Keywords
Metal color light therapy; Integrative oncology; Breast cancer patients; Art therapy; Self-reported stress perception

Strengths and limitations of this study

- First systematic investigation of the impact of MCL therapy on stress perception in breast cancer patients, offering new insights into its potential as a supportive care strategy
- Self-reported stress perception of each participant in this study will be evaluated before (T0) and after Metal Colored Light (MCL) therapy (T1)
- Changes in self-reported distress level, internal coherence and health-related quality of life will be monitored and assessed three months (T2) and six months (T3) after T0
- Prospective study design ensuring systematic evaluation of all participants
- Potential biases and confounding factors can be limited through the use of adjusted analyses
- There is no formal control or placebo group, and no blinding has been implemented

Introduction

A growing number of individuals are living with cancer or have survived it [1]. Advances in early detection and increasingly effective oncology therapies have significantly improved survival rates. However, ensuring the well-being of cancer survivors remains a crucial research focus, as many patients experience long-term health challenges. The majority of breast cancer patients suffer from persistent impairments after completing their primary therapy. Oncology therapies are often associated with long-term side effects that significantly impact distress levels and health-related quality of life, persisting for years after treatment [2]. Both, the tumor itself and oncological therapies interfere with various metabolic pathways and hormonal regulatory circuits. This may contribute to a variety of impairments such as chronic pain, cognitive dysfunction, and severe fatigue, commonly referred to as cancer-related fatigue [3,4].

Experience with breast cancer treatment programs highlight the importance of physical activity and conscious emotional management in strengthening physical fitness and mental well-being [5,6]. Meditation and yoga in particular have been shown to be effective, while music therapy has shown benefits in reducing anxiety and stress [7]. Additionally, dance-based therapy, including Tango Argentino, has shown to alleviate cancer-related fatigue among breast cancer survivors [8]. Art therapy is widely

recognized as a mental health intervention aimed at improving or restoring psychological well-being [9]. Research on adult women suggests that art therapy may effectively alleviate symptoms of depression and anxiety [10]. A systematic review further supports the potential of art therapy in helping breast cancer patients manage anxiety, depression, and fatigue [11].

Low level light therapy, also known as photo-biomodulation therapy, has been utilized for over four decades as a non-invasive treatment option to promote wound healing and reduce inflammation, edema, and pain [12]. This light therapy employs non-ionizing light sources, such as laser diodes in the visible and near-infrared spectrum. It has gained attention as a supportive intervention for managing breast cancer-related lymphedema, improving shoulder mobility, and alleviating pain [13]. A meta-analysis of five randomized controlled trials, involving 231 participants with Parkinson's disease, evaluated the efficacy and safety of light therapy using active light sources [14].

Findings suggest that light therapy significantly enhances both motor and non-motor function, including improvements in depression and sleep disturbances [14]. However, the precise mechanisms underlying these effects remain unclear. Researchers hypothesize that light absorption by endogenous chromophores may trigger physiological changes [15]. Light exposure plays a crucial role in regulating the melatonin metabolism, which governs the sleep-wake rhythm and circadian rhythm [16]. Unlike artificial light therapy, MCL therapy utilizes only natural daylight, filtered through metal-colored glasses [17]. It was hypothesized, that MCL may stimulate the metabolic activity and promote mental and psychological balance, thereby reducing stress, emotional strain and difficulties associated with managing illness [17]. The study seeks to determine whether MCL therapy can modulate stress perception. Additionally, it aims to identify specific stress-related impairments that may be alleviated through this intervention.

Methods

This report follows the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines for the minimum content of a clinical trial protocol [18].

Study setting

This study is conducted by the Research Institute Havelhöhe (Forschungsinstitut Havelhöhe, FIH) at the hospital Gemeinschaftskrankenhaus Havelhöhe in Berlin (GKHB) within the Network Oncology (NO) [19]. The study participants are recruited at the primary care facility of the German Cancer Society – certified Breast Cancer Centre at the GKHB.

Eligibility criteria for participants

Participants eligible for inclusion in the study must meet the following criteria:

- signed written informed consent and
- age ≥ 18 years and
- non-metastatic breast cancer
- diagnosis of breast cancer 6 to 36 months before enrollment

Patients will be excluded when they meet one of the following exclusion criteria:

- no signed written informed consent

- pregnancy or breastfeeding
- concurrent participation in other clinical trials
- receiving concurrent chemotherapy or radiation therapy
- linguistic, medical, psychiatric, cognitive or other conditions that may compromise the patient's ability to understand the patient information, comply with the study protocol or complete the study.

Who will take informed consent?

It is the responsibility of the study physician to provide sufficient verbal and written information on the study's purpose and procedures, information on data protection procedures, possible advantages and disadvantages of participation, and on the option for the patient to withdraw from the study at any time and without any given reason and to take informed consent. Written informed consent will be obtained from all participants prior study enrolment.

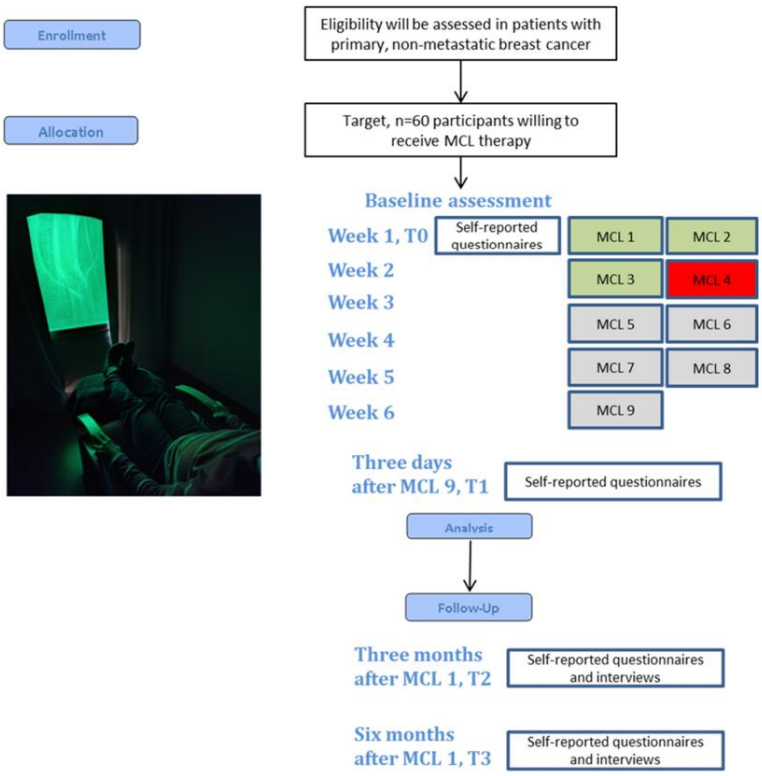

Figure 1: Flow chart and timeline of the LUCIA study MCL, metal color light; T0, baseline, day 0, day of first MCL.

Interventions

Intervention description

The MCL therapy sessions take place in a darkened room, with the only daylight passing through the MCL panels. The patient is seated approximately one meter away from the MCL panel (Figure 1).

Each MCL session begins with a preparatory discussion lasting 10-15 minutes between the patient and therapist before viewing the panel. The viewing typically lasts 5-10 minutes, during which the patient remains silent. Afterwards, the therapist covers the MCL panel and leaves the room, while the patient rests in the darkened room for 20-minute, seated in the chair. A course of MCL therapy consists of nine MCL sessions over a period of five to seven weeks per patient (Figure 1). Patients will be asked to complete self-report questionnaires prior to the first MCL. Patients will be asked self-report questionnaires prior to the first MCL session (T0) and three days after the ninth treatment (T1). Three different MCL panels will be used in this study: an iron-green panel, a gold-red panel, and a manganese-purple panel, each approximately one meter in height and 65 centimeters in width (Figure 2).

Figure 2: Metal Colored Light panels, iron-green gold-red, manganes-purple.

The intervention consists of a standardized component and an open section. The first three sessions are conducted using the iron-green panel, the fourth with the gold-red panel, and the remaining sessions are determined individually at the discretion of the therapist (Figure 1). Participants will be interviewed and surveyed at three months (T2) and six months (T3) following the MCL treatment.

Criteria for discontinuing or modifying allocated interventions

Participants are encouraged to report any discomfort or issues. If a participant misses a therapy session, she will be contacted by phone, asked about her well-being, and options will be explored regarding whether and how to continue or discontinue the MCL therapy.

Strategies to improve adherence to interventions and complete follow-up

At the start of each MCL therapy session, participants are asked about their experience with the previous session. Their feedback and preferences are also discussed. The number of sessions each attended by each participant will be recorded, and participants will receive a phone call reminder to complete and return self-reported questionnaires. For the follow-up surveys, participants will be contacted by postal mail, with stamped return envelopes enclosed, and followed-up with personal.

Relevant concomitant care permitted or prohibited during the trial

Concomitant medications, including nutritional supplements, vitamins, and natural remedies, will be recorded in the case report form. Standard routine care and medication for endocrine treatment should be maintained and will not affect the eligibility of patients to participate in the study. Concomitant physical activities will also be documented and should be continued. This will not affect the eligibility of study participation.

Outcomes

The primary endpoint is the patient's self-reported distress, measured using the German version of the National Comprehensive Cancer Network (NCCN) Distress Thermometer [20] before and after nine MCL sessions. Participants will rate their distress experienced over the past week on an 11-point scale, ranging from 0 ("No distress") to 10 ("Extreme distress"). The Distress Thermometer is supplemented with a symptom checklist covering practical, emotional, or physical issues such as fatigue, pain, nausea, sleep disturbances, or breathing problems. Symptoms identified will be evaluated alongside the distress level but are not part of the primary endpoint. Secondary endpoints include self-reported internal coherence, measured with the Internal Coherence Scale (ICS) [21], and self-reported quality of life, assessed using the European Organization for Research and Treatment of Cancer Questionnaire C30 (EORTC-QLQ-C30) [22]. Calculations will be performed as outlined in the ICS and the EORTC-QLQ-C30 manuals. The ICS is a brief, highly reliable, and valid self-report questionnaire consisting of two subscales: one with eight items (Inner Coherence and Resilience) and a second subscale (Thermo Coherence) with two items [21]. The EORTC scores range from 0 to 100, with higher scores representing a better self-reportedlevel in the functioning in the various dimensions, but also a higher degree of symptom burden. Baseline data on diagnosis, such as histology, tumor classification, and previous treatments, will be collected from the clinical interview at study inclusion and participants' medical records.

All participants will be asked to complete the questionnaires at baseline (T0) and post-treatment (T1). Figure 1). The same self-reported questionnaires will be used to monitor changes at follow-up assessments (T2 and T3). The courses of stress perception and quality of life in participants of the LUCIA-study will be compared with those of other breast cancer patients from the network oncology [23], matched for age, breast cancer type, and oncological treatment.

Implementation

All patients who give their written consent to participate and fulfil the inclusion criteria will be enrolled in this study and will be documented by the investigator. Patient data will be handled in accordance with the General Data Protection Regulation (GDPR). All data from the participants will be kept confidential before, during, and after the trial and will be securely stored at the study site, with restricted access. The study design and participant timeline is depicted in (Figure 1).

Sample size

The expected longitudinal differences between the means of the outcomes assessed will be estimated based on our previously published breast cancer studies [24, 25]. For sample size calculation, assuming a power of 90%, a significance level of 5% and a small to medium effect size ($d > 0.2$), a total of 50 patients would be required to detect a statistically significant treatment effect, according to Schoenfeld et al. [26].

Considering a dropout rate of 20%, 60 patients need to be recruited for this study.

Recruitment

Female breast cancer patients who have been treated at the GKH Breast Cancer Center are contacted and invited to participate in this study. A clinical interview is scheduled for eligible and interested patients. After obtaining written informed consent questionnaires, will be provided to the participants.

Statistical methods

All statistical analyses will be performed using Excel 2010 (Microsoft, USA) and the software R (RVersion 4.0.5) [27]. Baseline data will be summarized using descriptive statistics. Continuous variables will be described as means with standard deviation, median with interquartile range (IQR); categorical variables summarized as frequencies and percentages. Student´s t-tests will be applied, to detect group and longitudinal differences, p-values < 0.05 are considered to be significant. For characterization of group differences, Pearson's Chi-squared tests with Yates' continuity correction will be performed. To identify influencing factors and to address potential sources of bias and potential confounders, adjusted multivariable linear regression analyses will be performed. In order to yield reliable model results, stepwise regression selections will be performed and models with high adjusted R^2 will be chosen.

According to Cohen's interpretation [28] R^2 values between 13% to 25% indicate medium and R^2 values 26% or above indicate high effect sizes. In addition to statistical significance, we will report descriptive statistics and effect size estimates. Multilevel modeling can be used for subgroup analyses and to account for confounding variables. Confounding variables (age, body mass index, tumor stage, hormonal status, endocrine treatment, concomitant medication, and the respective outcome values at baseline) will be considered. Furthermore, adjusted multivariable linear regression analyses will be performed, to address potential confounders and influencing factors. Subgroup analyses will be performed regarding possible confounders such as concurrent endocrine treatment and concomitant medications for symptom relief.

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data

Patients who are unable to participate in the MCL treatment or withdraw consent will be excluded and not replaced. If individual sessions are missed, this will be noted, but the surveys will proceed as planned. For the evaluation of questionnaires, we will follow the EORTC-QLQ-C30 scoring manual for calculation and handling of missing data. Imputation will not be used when reporting outcome data. Both per-protocol and intention-to treat analyses will be performed. An interim analysis will be conducted after 20 participants have received the MCL treatment.

Adverse event reporting and harms

During each MCL therapy session information on the occurrence of adverse events is regularly retrieved and documented. Adverse events related to the MCL treatment during the six weeks will be recorded by the coordinating investigator.

Patient and public involvement

Patients are involved in the selection of MCL panels after third MCL therapy session (patient decision making). Participants in the study will be involved in the focus of the development of research questions, and their suggestions and objections will be taken into account.

Dissemination plans

The study results will be presented in conferences and symposia and submitted for publication in relevant peer-reviewed medical journals. Parts from this study will also be included in a doctoral thesis.

Discussion

MCL therapy is a novel integrative approach that combines principles of light therapy and art therapy, using metal-infused colored glass and natural daylight instead of artificial light sources. Unlike other non-pharmaceutical interventions (NPIs) such as mindfulness or movement-based therapies, MCL requires no active participation yet may still influence emotional and physiological stress responses. In this study project, the effects of metal color light therapy on the perception of stress and the well-being of breast cancer patients will be evaluated. The expected therapeutic effects of MCL can unfold on many levels. These effects may range from relaxation and mood enhancement through warmth, deeper breathing, and specific organ-related responses, to support in coping with illness and/or biographical crises. Bright light therapy has been shown to be effective in the treatment of depression and circadian rhythm disorder, such as delayed or advanced sleep phase syndromes [29]. However, scientific, systematic investigations and studies on the application of light therapy in people with or after cancer are still scarce [13,12].

The effects of light therapy on fatigue and sleep disturbances in breast cancer survivors have been explored in a controlled trial, with preliminary results already published [30]. MCL therapy can be used for people with chronic diseases affecting the intestines, respiratory and cardiovascular systems, as well as cancer and states of exhaustion [17]. In oncology, MCL therapy is thought to offer symptomatic relief for respiratory problems, pain, exhaustion, depression and other stress-related conditions. Furthermore, outpatient MCL therapy can provide a supportive service for coping with and overcoming cancer [17]. Assessing the distress experienced by breast cancer patients after their primary standard care, as undertaken in this study, may help determine which stress symptoms can be influenced by MCL therapy.

The purpose of this study is to determine whether MCL therapy is an appropriate therapeutic approach for improving well-being and reducing stress in breast cancer patients. While this study provides valuable insights into MCL therapy, the lack of a control group and blinding are recognized limitations. Future research should address these by incorporating a randomized controlled design with appropriate control conditions, such as sham light exposure or standard care, to isolate the specific effects of MCL therapy. Additionally, implementing blinded outcome assessments and integrating objective physiological measures will strengthen the reliability of findings. A larger, multicenter study could further enhance generalizability and reduce potential biases.

This study is the first systematic investigation of the impact of MCL therapy on stress perception in breast cancer patients, offering new insights into its potential as a supportive care strategy. To generate

hypotheses for follow-up studies, qualitative evaluations regarding the perceived experiences and feelings of the MCL participants should be considered in the future.

Trial Status

The current protocol version is 1.0, dated from 10. August 2023. The trial is ongoing and currently enrolling. The first participant was enrolled on 06 September 2023 and recruitment is expected to be completed in the 2nd quarter of 2025 with the follow-up completed by the end of 2025.

Declarations

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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We would like to thank Friedlinde Meyer for her supportive discussions regarding the establishment of the MCL therapy and the design of the study. Friedlinde Meier was deeply committed to Metal Color Light therapy. She helped to initiate and accompanied this study with all her strength. Unfortunately she passed away on May 6, 2024. We thank her from the bottom of our hearts. We would also like to thank Irena Cop and all the other members of the medical staff at the Havelhöhe Hospital for their support in this work.

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Ethics approval and consent to participate

This study complies with the principles laid down in the Declaration of Helsinki and has beenapproved by the Ethics Committee of the Berlin Medical Association (Ethik-Kommission der Ärztekammer Berlin) under the number Eth-27/10 and Amendment 7 on February 2, 2023. This trial was registered at the German Clinical Trials Register (Trial registration number DRKS00013335 on27/11/2017. Written informed consent will be obtained from all participants prior to study enrollment. All substantial protocol deviations or modifications will be communicated to the Ethics Committee and German Clinical Trials Register.

Availability of data and materials

Any material required to support the protocol can be supplied on reasonable request.

Consent for publication

Model consent forms will be provided on request.

Author statement

SLO conceived the study, initiated the study design, developed the methodology, was responsible for data curation, formal analysis, validation, visualization, wrote the first draft of the manuscript and reviewed it. JG conceived the study, initiated the study design, developed the methodology, was responsible for validation, writing, reviewing, and recruitment of participants. MG conceived the study, initiated the study design, developed the methodology, was responsible for validation, visualization, writing, reviewing and implemented the MCL protocol. GG conceived the study, initiated the study design, developed the methodology, and was responsible for validation, visualization, writing, reviewing, and recruitment of participants. LF conceived the study, initiated the study design, developed the methodology, and was responsible for validation, visualization, writing, reviewing, and recruitment of participants. SJ conceived the study, initiated the study design, developed the methodology, and was responsible for validation, writing and reviewing. FS is the principal investigator of the study, he conceived the study, initiated the study design, developed the methodology, and was responsible for funding acquisition, validation, visualization, writing, reviewing and project administration. AT is the scientific coordinator of the study, she conceived the study, initiated the study design, developed the methodology, was responsible for data curation, formal analysis, validation, visualization, writing, and reviewing. All authors commented on drafts of the manuscript and read and approved the final manuscript.

Competing interests

JG reports grant from Roche, Siemens, mte, and Celgene (travel and speaker honoraria) outside submitted work. FS reports grant from Helixor Heilmittel GmbH (travel costs and honoraria for speaking), grants from AstraZeneca (travel costs and honoraria for speaking), grants from Abnoba GmbH, outside the submitted work. The other authors have declared that no competing interests exist. No payment was received for any other aspects of the submitted work. There are no patents, products in development or marketed products to declare. There are no other relationships/conditions/circumstances that present a potential conflict of interest

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