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Transcranial Continuous and Pulse Near-Infrared Light in Depression: a Placebo-Controlled Study (ELATED-3).

Study Sponsor
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Partners HealthCare System
Research Consent Form

Subject Identification

General Template
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Protocol Title: Transcranial Continuous and Pulse Near-Infrared Light in Depression: a Placebo-Controlled Study (ELATED-3).

Principal Investigator: Paolo Cassano M.D., Ph.D.

Site Principal Investigator:

Description of Subject Population: Adults with Major Depressive Disorder

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

Partners HealthCare System is made up of Partners hospitals, health care providers, and researchers. In the rest of this consent form, we refer to the Partners system simply as "Partners."

If you have any questions about the research or about this form, please ask us. Taking part in this research study is up to you. If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov,* as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Why is this research study being done?

The purpose of this study is to see if using Transcranial Light Therapy (TLT), also called near-infrared light, using the LiteCure® PhotoBioModulation-1000 (TPBM-1000) device, helps improve symptoms of major depressive disorder (MDD). TLT works by briefly delivering near-infrared (non-visible) light to the forehead. The light penetrates the brain and stimulates the cells' metabolism.

TLT has previously been evaluated in three large studies of people who have had a stroke. To date, TLT has been administered to over 550 people who have had a stroke. TLT has also been

used in 23 people with MDD who were taking part in three research studies. During this study, TLT was shown to relieve MDD symptoms without causing too many side effects. The LiteCure® TPBM-1000 device is not approved by the U.S. Food and Drug Administration. This means that its use in depression is experimental. This is the first use of the PhotoBioModulation-1000 Device in humans.

Remember, there is one TPBM-1000 device being used in this research study, and this device works in two modes: the active treatment mode and the sham treatment mode. The person operating the device has to push the same buttons for the device to turn on in both modes. The device acts the same way and produces the same sounds when it is in both modes. The only difference between the sham mode and the active mode is that the device produces transcranial light energy when it is in the active treatment mode and it does not produce transcranial light energy when it is in sham treatment mode. Because this light energy that the TPBM-1000 device produces when it is in the active treatment mode is invisible to the human eye, neither you nor any of the study staff involved in the actual TLT procedures during your study visits will be able to tell when you are receiving active treatment and when you are receiving sham treatment. Litecure, the company that makes the LiteCure® TPBM-1000 device, is lending the TPBM-1000 device to us. We are asking you to take part in this research study because you have major depressive disorder. About 50 people will take part in this research study at MGH.

How long will I take part in this research study?

It will take you about 13 weeks to complete this research study. During this time, we will ask you to make 25 study visits at Massachusetts General Hospital (MGH) (in Boston) for the TLT procedure and one visit for screening at MGH Depression Clinical and Research Program (DCRP).

What will happen in this research study?

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures. All visits will take place at the Depression Clinical and Research Program at MGH.

Screening Visit

The Screening Visit will take about 3 hours. During this visit, we will do some tests and procedures to see if you qualify to take part in this research study. The study doctor will review the results of these tests and procedures. If you don't qualify, the study doctor will tell you why. At this visit we will:

- Ask you about your medical and psychiatric history.
- Give you a physical exam, including height, weight, and vital signs (blood pressure, temperature, heart and breathing rates).
- Ask you for a urine sample. We will test your urine for certain drugs including illegal drugs. If your urine shows you have taken any of these drugs, you can't be in this study. The results of the urine drug test will not become part of your medical record. These test results will, however, remain part of your study record.
- Test your urine for pregnancy, if you are a female able to become pregnant. Pregnant women cannot take part in this research study.
- Draw 15-20cc (about a tablespoon) of blood to perform blood safety tests. The blood tests check basic function of vital organs and assure you are physically healthy enough to participate in the study.
- Give you some questionnaires to fill out about your general health and well-being, quality of life, mental health, emotional health, and mood.

Study Groups

If you qualify for the study after the Screening Visit, we will assign you by chance (like a coin toss) to receive the active treatment or sham treatment. Neither you nor the study doctor will know which study group you are in, but the study doctor can find out if it is absolutely necessary. You will have a **chance 1 in 3** of being assigned to **the active treatment**. You will have a **chance 2 in 3** of being assigned to **placebo or sham**.

After six weeks of treatment, **if you were receiving the sham you would be reassigned by chance to receive the active treatment or sham** for the remaining six weeks. **You would have an equal chance of being assigned to either study group**. If you were originally assigned to the active treatment group you would continue receiving the active treatment for the rest of the study.

For the 12 weeks after the Screening Visit, you will have 2 study visits per week at MGH (with active or sham treatment sessions), starting with Visits 1 and 2 one week after the Screening Visit, through visits 23 and 24. Visit 25 will be a post-treatment visit, and will take place the week after visits 23 and 24.

Visit 1, 7, 13, 19

Visits 1, 7, 13, and 19 will each take approximately two and a half hours. At these visits, we will:

- Ask you to complete some questionnaires.

- Administer cognitive tests. These tests would last approximately 50 minutes – 1 hour. You will complete one or more voice tasks that will be recorded on a smartphone or tablet. You may be asked to read words, sentences or sequences of digits out loud or to speak about some topic for up to 3 minutes. During other tests, you will be exposed to different images on a computer screen. These photographs are meant to produce emotional response, but will not be very different from the images you might see on television news or in a movie. You may find some of the images you see during the computer task to be moderately frightening or unpleasant. If you find the images very upsetting, you can stop at any time.
- Have you meet with a study doctor to discuss how the study is going for you.
- Complete the TLT procedure. Remember that during this procedure some subjects will be receiving the active treatment and some will receive the sham treatment.

Visits 3, 5, 9, 11, 15, 17, 21, 23

The study visits will take about 1 hour. At these visits, we will:

- Ask you to fill out a form about any reactions or side effects you have had since your last visit.
- Have you meet with a study doctor to discuss how the study is going for you.
- Ask you to complete questionnaires on your depressive symptoms. You will complete some of the questionnaires by yourself and some with the study doctor.
- Complete the TLT procedure. Remember that during this procedure some subjects will be receiving the active treatment and some will receive the sham treatment.

Visits 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24

The study visits will take about 25 minutes. At these visits, we will:

- Complete the TLT procedure. Remember that during this procedure some subjects will be receiving the active treatment and some will receive the sham treatment.

Visit 25

This visit will take about 1 hour. At this visit, we will:

- Ask you to fill out a form about any reactions or side effects you have had since your last visit.
- Have you meet with a study doctor to discuss how the study was for you.
- Ask you to complete questionnaires on your depressive symptoms. You will complete some of the questionnaires by yourself and some with the study doctor.
  Administer cognitive tests. These tests would last approximately 50 minutes – 1 hour. You will complete one or more voice tasks that will be recorded on a smartphone or

tablet. You may be asked to read words, sentences or sequences of digits out loud or to speak about some topic for up to 3 minutes. During other tests, you will be exposed to different images on a computer screen. These photographs are meant to produce emotional response, but will not be very different from the images you might see on television news or in a movie. You may find some of the images you see during the computer task to be moderately frightening or unpleasant. If you find the images very upsetting, you can stop at any time.

Visit 1, Visit 13, and Visit 25

- On these visits, between 2-6mL (2-6 mL of blood is about 1 to 1 ½ teaspoons) of blood will be drawn to measure substances associated with inflammation.

The TLT procedure will take about 20 minutes. The TLT procedure will take place in a private examination room. Before we do the TLT procedure, we will examine your forehead for any possible skin lesions (for example, any cuts or signs of swelling). If you have any lesions on your forehead, you cannot have the TLT procedure.

During the TLT procedure, you will lie comfortably on an examination table. The study staff will be available during the entire TLT procedure (20 minutes). Because of the potential danger to the eyes, the procedure will be conducted in a safe environment by a member of the study staff who has been trained on the device. You will wear protective goggles or eye pads. The staff administering the treatment will be careful not to shine the light in or near your eyes
The actual Litecure (TPBM-1000) device is a small device, consisting of four light sources, each roughly the size of a quarter of a dollar coin. During active treatment, the device will be held on by a large adjustable band to allow reliable and comfortable positioning over the forehead. The device will deliver invisible light energy (TLT) through your skin and skull, into your brain. Both active and sham treatment procedures may leave your forehead feeling warm. After the treatment procedure is completed you will be asked to rest for five minutes. Your skin (at the forehead) will be inspected again before you leave the session.

What are the risks and possible discomforts from being in this research study?

Potential Side Effects from the TLT Procedure

Common Side effects

Insomnia, restless sleep, erratic sleep, early morning awakenings
Irritability
Seeing vivid colors

Less Common Side Effects

None

Rare Side Effects

Based on human clinical trial experiences to date, each adverse event listed below has been reported by less than 1% of the more than 1,000 randomized subjects as having a relationship with either a similar device or the procedure in the active and/or sham control groups:

1. Abdominal bloating
2. Amnesia
3. Reddening of the skin at the application site
4. Skin peeling and chafing at the application site
5. Application Site Pain
6. Application Site Reactions such as warming sensations and thermal pain
7. Abnormal taste
8. Decreased heart rate
9. Hair Growth Abnormal
10. Blood may clot at the location of a previous stroke in the brain causing the brain to become oxygen deprived. This oxygen deprivation may cause cell damage or death, and swelling or bleeding in the brain.
11. Insomnia
12. Nausea
13. Neck Pain
14. "Out-of-body" experiences
15. Itchy Skin
16. Rash
17. Skin Laceration
18. Skin Lesion
19. Skin burn if the device is not used as intended
20. Vivid dreams
21. Vomiting
22. Word finding difficulties

Other Potential Side Effects

- Worsening of depression and increased suicidality (possible but not reported)
- Manic switches — this is when a person switches from depression to mania. One way to think about mania is as the opposite of depression. Signs of mania include:

unusually high or positive mood, unusually high levels of energy, a decreased need for sleep, and racing thoughts.

- In a study of stroke victims in Germany, a patient experienced a worsening of his stroke-related symptoms after TLT treatment.
- Risk of Bruising and venipuncture might result in accidental bruising at the sight of blood drawing on the forearms.

Risks in Pregnancy and Breastfeeding

The effect of TLT on an embryo or fetus (developing baby still in the womb) is unknown and may be harmful. Because of unknown risks, women cannot take part in this study if they are:

- Pregnant
- Trying to become pregnant
- Breastfeeding

If you are a menopausal woman and have not had a menstrual period for the past 12 months or more, you will not need to have a pregnancy test. Also, you will not need to have a pregnancy test if you have had a hysterectomy (surgical removal of your uterus and/or ovaries). All other female subjects must have a negative pregnancy test at the Screening Visit before starting the study procedures.

If you are sexually active and able to become pregnant, you must agree to use two of the birth control methods listed below. You must use birth control for the length of the study and for 30 days following any study procedures.
Acceptable birth control methods for use in this study are:

- Hormonal methods, such as birth control pills, patches, injections, vaginal ring, or implants
- Barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- Intrauterine device (IUD)
- Abstinence (no sex)

If you miss a period, or think you might be pregnant during the study, you must tell the study doctor immediately. If you become pregnant, you must stop taking part in the study.

In Case of Worsening Depression

TLT is experimental and therefore may not be effective for depression. In such a case, there is a risk that your depression could get worse while you are taking part in the study. In addition,

some of the subjects will not receive TLT until the second part of the study. These subjects will have a delay of any possible benefits and their depression symptoms may get worse.

If you feel your depression is getting worse or if you have any thoughts of hurting or killing yourself, you should page one of the study doctors immediately. You can page Dr. Cassano, 24 hours a day, 7 days a week, by calling the MGH page operator at (617)-726-2066 and asking to have one of the doctors paged.

What are the possible benefits from being in this research study?

You may not receive any direct benefit from taking part in this study. This study may possibly provide relief of depressive symptoms to some subjects.

The study may also benefit other people in the future with major depressive disorder by increasing our understanding of TLT treatment for depression.

What other treatments or procedures are available for my condition?

You do not have to take part in this research study to be treated for your depression. There are other treatments available for your depression. These include a variety of antidepressant medications such as:

- fluoxetine (Prozac®)
- paroxetine (Paxil®)
- buproprion (Wellbutrin®)

Psychotherapies (talk therapies) are also available, as well as cognitive-behavioral therapy (CBT), which involves behavior, thinking, and memory.
Talk with the study doctor if you have any questions about any of these treatments or therapies.

Can I still get medical care within Partners if I don't take part in this research study, or if I stop taking part?

Yes. Your decision won't change the medical care you get within Partners now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should I do if I want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will I be paid to take part in this research study?

We will pay you $300 if you complete the study. You will be compensated $12.50 per treatment visit, for a total of $300 if all twenty four treatment visits are completed. Compensation will be provided after Weeks 2 ($50), 4 ($50), 6 ($50), and 8 ($50), 10 ($50) and 12 ($50), with $12.50 subtracted for each treatment visit missed.
We will also validate for parking if you park in one of our three hospital garages (Fruit, Parkman, or Yawkey).

What will I have to pay for if I take part in this research study?

Study funds will pay for certain study-related items and services. We may bill your health insurer for, among other things, routine items and services you would have received even if you did not take part in the research. You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care. If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff. If necessary, we will arrange for you to speak with someone in Patient Financial Services about these costs.
The transcranial light therapy treatment will be provided at no cost. In addition, study funds will pay for your study visits and any tests or procedures listed in this consent form as they are being done only for this research.
Costs for any ongoing our routine care you would receive apart from this study will be billed to you or to your insurance company in the usual way.

What happens if I am injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you

may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the next section of this consent form.

If I have questions or concerns about this research study, whom can I call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Paolo Cassano, MD, PhD is the person in charge of this research study. You can call him at (617) 723-9622, Monday through Friday from 9:00 am to 5:00 pm. After hours, you can call the MGH page operator 24 hours a day, at 617-726-2066, and ask for Dr. Cassano to be paged. You can also call the Research Coordinator, Benjamin Campbell, at 617-724-0586 Monday through Friday from 9:00 am to 5:00 pm with questions about this research study.

If you have questions about the scheduling of appointments or study visits, please call the Research Coordinator, Benjamin Campbell at 617-724-0586 during the hours noted above.

If you want to speak with someone **not** directly involved in this research study, please contact the Partners Human Research Committee office. You can call them at 857-282-1900.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research

Also, if you feel pressured to take part in this research study, or to continue with it, they want to know and can help.

If I take part in this research study, how will you protect my privacy?

During this research, identifiable information about your health will be collected. In the rest of this section, we refer to this information simply as "health information." In general, under federal law, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so.

In this study, we may collect health information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable health information and why they may need to do so:

- Partners research staff involved in this study
- The sponsor(s) of this study, and the people or groups it hires to help perform this research
- Other researchers and medical centers that are part of this study and their ethics boards
- A group that oversees the data (study information) and safety of this research
- Non-research staff within Partners who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- The Partners ethics board that oversees the research and the Partners research quality improvement programs.
- People from organizations that provide independent accreditation and oversight of hospitals and research
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- Federal and state agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health, and other US or foreign government bodies that oversee or review research)
- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)
- Other:

Some people or groups who get your health information might not have to follow the same privacy rules that we follow and might use or share your health information without your permission in ways that are not described in this form. For example, we understand that the

sponsor of this study may use your health information to perform additional research on various products or conditions, to obtain regulatory approval of its products, to propose new products, and to oversee and improve its products' performance. We share your health information only when we must, and we ask anyone who receives it from us to take measures to protect your privacy. The sponsor has agreed that it will not contact you without your permission and will not use or share your information for any mailing or marketing list. However, once your information is shared outside Partners, we cannot control all the ways that others use or share it and cannot promise that it will remain private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health information.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifying information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others.

You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.

- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my health information to be used and shared as described above.

Subject	Date	Time (optional)

Email security
The Partners standard is to send email securely. This requires you to initially set up and activate an account with a password. You can then use the password to access secure emails sent to you from Partners HealthCare. If you prefer, we can send you "unencrypted" email that is not secure and could result in the unauthorized use or disclosure of your information. If you want to receive communications by unencrypted email despite these risks, Partners HealthCare will not be held responsible.

Your preference to receive unencrypted email will apply to emails sent to you from research staff in this study ONLY.

Please select one of the following options:
I consent to receive unencrypted emails (please use your initials to indicate your response):
Yes:_____No: _____

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

Study Doctor or Person Obtaining Consent	Date	Time (optional)

Consent Form Version: 2.0