**UNIVERSITY OF CALIFORNIA, IRVINE**
**CONSENT TO ACT AS A HUMAN RESEARCH SUBJECT**

Micro/nanobubbles (MNBs) and Wound Therapy: A Pilot Study Involving a Novel Oxygen Delivery System for Treatment of Acute and Chronic Wounds

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**STUDY LOCATION(S):** UCI Douglas Hospital and Tower Building

**STUDY SPONSOR(S): None**

**SPONSOR MASTER PROTOCOL NUMBER: N/A**

**SUMMARY OF KEY INFORMATION:**

**The information provided in this box includes a brief yet complete summary of key information about the research, presented first as required by the federal regulations. Some sections that require additional information may be repeated later in this document.**

***Participation is Voluntary***
You are being asked to participate in a research study. Participation is completely voluntary. Please read the information below and ask questions about anything that you do not understand. A researcher listed above will be available to answer your questions.

***Study Purpose***
Oxygen delivery is one of the primary factors in wound healing. Micro/nanobubbles (MNBs) can be used to increase the oxygen dissolved in solution and increase oxygen delivery to a wound. The purpose of this research study is to determine if MNBs applied to a wound improve wound healing. MNBs are an investigational product that has not been previously used in humans or marketed treatment in the US. approved by the FDA. The safety and efficacy of this product is being evaluated in this study.

***Study Procedures***
We will assess the characteristics of your wound and take measurements before and after treatment. Depending on your wound type, you will be treated with MNBs in saline or saline solution only gauze which will be applied to your wound daily, or you will receive MNBs or saline solution in negative pressure wound therapy with instillation (NPWTi) which will be applied to your wound continuously throughout the day with the wound evaluated and sponge replaced every 3-5 days. This is consistent with the current standard of wound care with gauze or NPWTi. Tissue oxygenation using infrared technology and the wound healing will be measured and results collected for analysis.

***Expected Duration***
Participation will last approximately 2-4 weeks or the duration of your inpatient admission. If you are discharged from the hospital earlier than 2 weeks, the treatment will be discontinued and your results submitted for analysis.

***Risks of Participation***
Risks of participation include failure of the therapy to promote wound healing, need for continued wound care, poor wound healing, and unattractive scarring. Also, should there be a breach in confidentiality of your data, there is a slight risk that your private medical information could be shared with individuals who are not members of the study team.

***Benefits to Participants***
If you are in the group that receives MNB treatment and it proves to yield improved wound healing and a shorter healing period than the standard (usual) treatment, you may benefit from participating in the study, but this cannot be guaranteed.

***Benefits to Others or Society***
If outcomes are favorable, we will have heralded a new, inexpensive and portable solution for the oxygenation of wounds. The treatment method may be useful for reversal of acute skin ischemia, prevention of skin necrosis, and promote healing in chronic wounds. We hope that this novel solution will help in the treatment of future patients with wounds similar to yours.

***Alternative Procedures or Treatments***
If you decide not to participate, or if you withdraw from this study before it is completed, your other choices may include:
- Getting no treatment
- Getting standard treatment for your condition without being in a study (NPWT without instillation with MNBs, normal saline irrigation of wounds)
- Getting a different experimental treatment/taking part in another study.

**WHY IS THIS RESEARCH STUDY BEING DONE?**
The purpose of this research study is to find out if application of micro/nanobubbles (MNBs) to a wound can improve tissue oxygenation and potentially lead to improved healing. We also hope to find out whether applying MNBs in conjunction with negative pressure wound therapy with instillation (NPWTi), a procedure widely used to facilitate wound healing, will have improved wound healing.

**HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?**
Approximately 40 participants will take part in the research at UCI.

**AM I ELIGIBLE TO PARTICIPATE IN THIS STUDY?**
Please note this may not be a complete list of eligibility criteria. We have included a few examples of study criteria to help you better understand how your eligibility in the study will be determined; your study team will go through the study eligibility criteria with you to verify if you qualify for participation in this study.

***Inclusion Requirements***
You can participate in this study if you:
- are above the age of 18.
- have traumatic, surgical, or chronic wounds.
- have tissue injury related to radiation.
- have burn injuries.
- have ulcers or wounds due to lack of blood supply.

***Exclusion Requirements***
You cannot participate in this study if you:
- have infected wounds.
- have wounds with exposed vital structures such as nerves, arteries, and/or veins.
- have wounds associated with malignancy.

**HOW LONG WILL THE STUDY GO ON?**
You will be treated with MNBs or with MNBs combined with NPWTi for a maximum of 4 weeks or until you are no longer an inpatient at UCI Health. After you have completed the treatment, researchers will ask you to visit the office for at least two (2) follow-up exams.

**WHAT PROCEDURES ARE INVOLVED WITH THIS STUDY?**
***Before you can participate in the main part of the study...***
You will need to have "screening" exams, tests or procedures. The screening process helps the researchers decide if you meet the study requirements listed below. The screening procedures includes:
- a medical record screening in which the study team will review their UCI patients' records and abstract data directly from those records.
- wound evaluation to determine the characteristics of your wound and make sure there is no active infection, exposed important structures, or associated malignancy.

***During the main part of the study...***
If the screening exams, tests and/or procedures show that you can continue to be in the study, and you choose to take part, then you will have the following procedures and tests done. The main study tests and procedures include…
*1.* Pre-treatment oxygen assessment - Near Infrared Spectroscopy Imaging (NIRS) will be used to assess tissue oxygenation prior to MNB or MNB/NPWTi application. This will provide a baseline wound oxygen measurement.

*2.* The MNB or saline solution will be used as a wet to dry wound care dressings with twice daily scheduled dressing changes for one month or until you are discharged from the hospital.
Or
NPWTi with MNB or saline solution will be applied to the wound with standard instillation settings and wound VAC dressing changes every 5 days for one month or until you are discharged from the hospital. You have 50% chance to receive the investigational product MNB or the saline solution which is the standard or care.

*3.* NIRS will be used to assess tissue oxygenation with each dressing change and wound measured
*4.* Photographs will be taken with each dressing change to assess wound healing progress.

**Summary table for study procedures**

| 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|
| Wound assessment | Pre-treatment NIRS oxygen assessment, wound measurement, and photographs | Application of MNB gauze dressing or MNB/ NPWTi | NIRS oxygen assessment, wound measurement, and photographs with dressing changes | Post-treatment oxygen assessment, wound measurement, and photographs |

***After you complete the main part of the study…***
You will have a follow-up appointment with your physician and final post-treatment oxygen assessment, wound measurement, and photographs will be obtained.

**RETURN OF RESULTS**
You will not be provided any clinically relevant information that may pertain to your health. You will not be provided with the photographs or results of the study as all results will be de-identified prior to collection and analysis.

**WHAT ARE THE POSSIBLE SIDE EFFECTS OR RISKS RELATED TO THE STUDY?**
You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, researchers don't know all the side effects that may happen. Side effects may be mild or very serious.

You should talk to the research team about any side effects you experience while taking part in the study. There may be risks related to the research that we don't know about yet. However, you will be informed of any additional risks to which you may be exposed, and any changes that are made to the study, as a result of any newly-identified risks.

**Unlikely**

- -Poor wound healing, < 1% - Same risk as irrigation of wounds with normal saline.
- -Scarring < 1% - Same risk as irrigation of wounds with normal saline.

**Less Likely, but serious**

- -Infection <1% - equal to the risk of irrigating wounds with saline alone. In fact, irrigation reduces the risk of infection.

**Randomization:** You will be assigned to a study group by chance (like a coin flip) rather than by a medical decision made by the researchers. The treatment you receive may prove to be less effective or to have more side effects than the other study group, or than standard treatments available for your condition.

**Unknown risks:**
There may be risks related to the research that we don't know about yet. However, you will be informed of any additional risks to which you may be exposed, and any changes that are made to the study, as a result of any newly-identified risks.

## WILL I BE PAID FOR TAKING PART IN THIS STUDY?

***Compensation***
You will not be compensated for your participation in this research study.

***Reimbursement***
You will not be reimbursed for any out of pocket expenses, such as parking or transportation fees.

## WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?
There is no cost to you or your insurer/third party payer for participation in this study. However there may be out-of-pocket expenses such as transportation fees for your follow-up appointment.

## WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?
It is important that you promptly tell the researchers if you believe that you have been injured because of taking part in this study. You can tell the researcher in person or call him/her at the number listed at the top of this form.

If you are injured as a result of being in this study, UCI will provide necessary medical treatment. The costs of the treatment may be covered by the University of California or billed to you or your insurer just like other medical costs, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about this, you may call UCI Human Research Protections (949) 824-6068 or (949) 824-2125 or by e-mail at IRB@research.uci.edu

## WHAT HAPPENS IF I WANT TO STOP TAKING PART IN THIS STUDY?
You are free to withdraw from this study at any time. **If you decide to withdraw from this study, you should notify the research team immediately**. The research team may also end your participation in this study if you do not follow instructions, miss scheduled visits, the study sponsor decides to stop the study or your safety and welfare are at risk.

If you experience any of the side effects listed above, if your health worsens, or if you are injured during the research, you may need to be withdrawn from the study, even if you would like to continue. The research team will make this decision and let you know if it is not possible for you to continue. The decision may be made to protect your safety and welfare, or because the research plan does not allow people who develop certain conditions to continue to participate.

If you withdraw or are removed from the study, the researcher may ask you to return for a final close-out visit or evaluation.

If you elect to withdraw or are withdrawn from this FDA-regulated research study, the data collected from your participation in this study must remain in the trial database in order for the study to be scientifically valid.

## HOW WILL INFORMATION ABOUT ME AND MY PARTICIPATION BE KEPT?
***Subject Identifiable Data***
**Subject Identifiable Data**
Identifiable information collected about you will be removed and replaced with a code. A list linking the code and your identifiable information will be kept separate from the research data. The personal identifiers retained will be your medical record number only to use if necessary to access your medical record during screening, data collection, and scheduling your follow-up appointment.

**Data Storage**
Research data will be stored electronically on a secure network in an encrypted file with password protection.

**Data Retention**
In accordance with UC Office of the President policy, information will be retained for 10 years after the end of the calendar year in which the research is completed, unless otherwise specified in the award agreement. In addition, this research involves the investigation of FDA regulated products. As such, information will be retained for two years after an approved marketing application. If approval is not received, the information will be kept for 2 years after the investigation is discontinued and the FDA is notified per FDA sponsor requirements.

**WHO WILL HAVE ACCESS TO MY STUDY DATA?**
The research team, authorized UCI personnel and regulatory entities such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP), may have access to your study records to protect your safety and welfare.

While the research team will make every effort to keep your personal information confidential, it is possible that an unauthorized person might see it. We cannot guarantee total privacy.

***Future Research Use***
Researchers will use your wound oxygenation, measurements, and photographs to conduct this study. Once the study is done using your information, we may share them with other researchers so they can use them for other studies in the future. We will not share your name or any other private identifiable information that would let the researchers know who you are. We will not ask you for additional permission to share this de-identified information.

> **ClinicalTrials.gov**
> ClinicalTrials.gov is a Web site that provides information about clinical trials. 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.

***Medical Care***
If you agree to participate in this research study, a signed copy of this consent document and the privacy authorization form may be filed in your electronic medical record (EMR) and your study participation may be added to your EMR. This information will be used for your care and treatment and for healthcare operations, which may include billing and payment.

**ARE THERE OTHER ISSUES TO CONSIDER IN DECIDING WHETHER TO PARTICIPATE IN THIS STUDY?**

***Investigator Financial Conflict of Interest***
No one on the study team has a disclosable financial interest related to this research project.

**Future Contact**
The study team would like your permission to contact you for future research. Please initial your level of permission below:

_____ Yes, UCI researchers may contact me in the future to ask me to take part in other research studies.

_____ No, UCI researchers may **not** contact me in the future to ask me to take part in other research studies.

**WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?**
If you have any comments, concerns, or questions regarding the conduct of this research, please contact the research team listed at the top of this form.

A 24-hour number is also listed on the top of this form to report any health concerns or unanticipated problems you may experience after normal hours or on weekends.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any suggestions, problems or concerns you may have about the study, please contact the UCI Institutional Review Board by phone, (949) 824-6068 or (949) 824-2125, by e-mail at IRB@research.uci.edu or at 160 Aldrich Hall, Irvine, CA 92697.

**What is an IRB?** An Institutional Review Board (IRB) is a committee made up of scientists and non-scientists. The IRB's role is to protect the rights and welfare of human subjects involved in research. The IRB also assures that the research complies with applicable regulations, laws, and institutional policies.

**HOW DO I AGREE TO PARTICIPATE IN THIS STUDY?**

You should not sign and date this consent form until all of your questions about this study have been answered by a member of the research team listed at the top of this form. You will be given a copy of this signed and dated consent form, and the attached "Experimental Subject's Bill of Rights" to keep. **Participation in this study is voluntary.** You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your future relationship with UCI or your quality of care at the UCI Medical Center.

If, during the course of this study, significant new information becomes available that may relate to your willingness to continue to participate, this information will be provided to you by the research team listed at the top of the form.

Your signature below indicates you have read the information in this consent form and have had a chance to ask any questions you have about this study.

**Note: If the research described in this form involves your protected health information (PHI), you will be asked to sign separate UC HIPAA Research Authorization form for the use of your PHI.**

***I agree to participate in the study.***

_____ _____

**Subject Signature** **Date**

_____

**Printed Name of Subject**

_____ _____

**Signature of Person Obtaining Informed Consent** **Date**

*(For research that is greater than minimal risk, this individual must be listed on Page 1 of this consent)*

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**Printed Name of Person Obtaining Informed Consent**

***A witness signature is required on this consent form only if: (Researchers: check which one applies)***

**IMPORTANT! If no witness signature is required, this witness signature section of the consent form may be left blank.**

☐ Consent is obtained from the subject via the Short Form process, as approved by the IRB.
☐ The subject has decision-making capacity, but cannot read, write, talk or is blind.
☐ The subject's guardian/legally authorized representative (LAR) cannot read, write, talk or is blind.
☐ The IRB specifically mandated a witness signature for this study (e.g., high risk and/or invasive research procedures).

**For the witness:**
I confirm that the information in this consent form was accurately explained to and understood by the subject or legally authorized representative and that informed consent was given freely.

_____ _____
**Witness Signature** **Date**

Note: The witness must be impartial (i.e. not a member of the subject's family, not a member of the study team).

_____
**Printed Name of Witness**

**UNIVERSITY OF CALIFORNIA, IRVINE**
**Experimental Subject's Bill of Rights**

**The rights listed below are the right of every individual asked to participate in a research study. You have the right:**

1. To be told about the nature and purpose of the study.

2. To be told about the procedures to be followed in the research study, and whether any of the drugs, devices, or procedures is different from what would be used in standard practice.

3. To receive a description of any side effects, discomforts, or risks that you can reasonably expect to occur during the study.

4. To be told of any benefits that you may reasonably expect from the participation in the study, if applicable.

5. To receive a description of any alternative procedures, drugs, or devices that might be helpful, and their risks and benefits compared to the proposed procedures, drugs or devices.

6. To be told of what sort of medical treatment, if any, will be available if any complications should arise.

7. To be given a chance to ask any questions concerning the research study both before agreeing to participate and at any time during the course of the study.

8. To refuse to participate in the research study. Participation is voluntary. You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your right to receive the care you would receive if you were not in the experiment.

9. To receive a copy of the signed and dated written consent form and a copy of this form.

10. To be given the opportunity to freely decide whether or not to consent to the research study without any force, coercion, or undue influence.

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If you have any concerns or questions regarding the research study you should contact the research team listed at the top of the consent form.

If you are unable to reach a member of the research team and have general questions, or you have concerns or complaints about the research study, research team, or questions about your rights as a research subject, please contact the UCI's Human Research Protections unit in the Office of Research by calling (949) 824-6068 or (949) 824-2125 Monday – Friday, 8 am – 5 pm; or by e-mail at IRB@research.uci.edu; or by writing us at 160 Aldrich Hall, Irvine, CA 92697.