CONSENT TO PARTICIPATE IN RESEARCH AND AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Sponsor / Study Title:	**The Metis Foundation / "Manual implantation of Full-Thickness Skin Microcolumns for 'Donor-Free' Skin Renewal"**
Principal Investigator: (Study Doctor)	**Rodney Chan, M.D., F.A.C.S., F.R.C.S.C.**
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KEY INFORMATION

You are invited to take part in a research study. This research study is studying a grafting technique using full-thickness skin microcolumns as a possible treatment for dermal regeneration. The Metis Foundation is sponsoring this research study.

1. This is a research study and your participation is voluntary.
2. The purpose of this research is to study a new method of skin grafting in which small punches of skin containing all layers of the skin are positioned onto a dressing and then placed onto an open wound.
3. The risks are very similar to those for the standard of care split-thickness skin grafting procedure. The complete list of risks / discomforts is listed later in this informed consent.
4. The length of time in this study is either the point of re-epithelization or a maximum of 6 months.
5. There may not be a direct benefit to you and there is no promise that your condition will get better.
6. There are alternative procedures/courses of treatment that you should know about; they include receiving the routine wound care or surgery your physician has prescribed for you.
7. You may be paid for your participation in this study.
8. The sponsor of this study, The Metis Foundation, is receiving funds through a grant from the Department of Defense.

This form is for use in a research study that may involve subjects who may or may not have the capacity to consent to take part in the study. When the subject cannot legally consent to take part, the pronouns "you" and "your" should be read as referring to the subject rather than the person (legally authorized representative) who is signing and dating this form for the subject. In

cases where the subject's representative gives consent, the subject should be informed about the study to the extent possible given his/her understanding. During the course of the study, if the subject regains the capacity to consent, informed consent will be obtained from the subject and the subject offered the ability to leave the study if desired.

Please read this form carefully. Take your time to ask the study doctor or study staff as many questions about the study as you would like. The study doctor or study staff can explain words or information that you do not understand. Reading this form and talking to the study doctor or study staff may help you decide whether to take part or not. If you decide to take part in this study, you must sign your name at the end of this form and date it.

INTRODUCTION

You are being asked to participate in a research study.

You are being invited to take part in this study because your doctor has identified you as having an open wound that needs a skin graft. This study is investigating whether a new technique of skin grafting can improve wound healing.

The use of this technique of skin grafting is investigational, meaning that it is not approved by the United States Food and Drug Administration (FDA).

This research study is a clinical trial. Clinical trials are designed to answer specific questions about drugs, vaccines, treatments, devices, or new ways to use known drugs, treatments, or devices.

Your participation in this research is voluntary. It is important that you read what is written below and ask the study doctor or designated study staff questions about anything you do not understand. You may want to talk with your family, friends, or others to help you decide if you want to be part of this study. You should understand the risks, benefits, and alternatives to joining this study. When you feel that your questions have been answered, you will be asked if you do or do not want to be part of the research. If you agree, you will be asked to sign and date this consent form. You will be given a copy of this form to keep.

WHY IS THIS RESEARCH BEING DONE?

The purpose of this research is to study a new method of skin grafting in which small punches of skin containing all layers of the skin are positioned within a wound dressing and then placed onto an open wound. This method of skin grafting may improve wound healing as compared to the standard of care split-thickness skin grafts. Split-thickness skin grafts do not take all layers of the skin and so do not include important skin elements that make skin functional such as hair follicles and sweat glands. Additionally, the donor site from which healthy skin is taken becomes a new, open wound. We hope that this new method will result in more functional skin once the injured area is healed and that the donor site with this new method will heal faster and result in less pain than the donor site needed for split-thickness skin grafts.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

Approximately 10 people with open wounds that require skin grafting will participate in this study.

HOW LONG WILL YOU BE IN THE STUDY?

You will be in the study for a maximum of 6 months. If your wound completely heals sooner than 6 months, you will be encouraged but not required to continue to participate in the study for the full 6 months.

Your participation in this study would include the initial skin grafting surgery, and then 4 weekly follow-up visits, a 6-week follow-up, and a 6-month follow-up.

WHAT WILL HAPPEN DURING THIS RESEARCH?

If you agree to participate in this research, you will be asked to do the following things:

The study doctor will first assess the open wound that needs skin grafting. He/she will also determine the appropriate location for the donor site. The donor site is the area from which healthy skin is taken, and then this healthy skin is placed on the injured area to help it heal.

You will then be taken to the operating room where the procedure will occur. You will be given anesthesia and the injured area and donor site area will be cleaned. Small columns of healthy skin from the donor site will be taken and placed into a dressing that has been cut to fit the shape of your wound. The dressing will then be placed on the injured wound and the wound will be covered with additional dressings.

After the grafting surgery, you will be asked to follow up once a week for 30 days, at 6-weeks and at 6-months after the surgery. Visits may occur in the hospital if you are an inpatient, or as an outpatient in the clinic if you have been discharged.

To be completed prior to study treatment:

- Screening, including a medical history review
- Physical exam, including vital signs
- Digital photography (This photography is required; if you do not want your photograph taken for research purposes, you cannot participate in this study.)

To be completed at each assessment follow-up visit:

- Vital signs and wound assessments
- Digital photography
- SilhouetteStar® camera photograph (Optional) (this will help us determine the rate of healing of the wound)
- Patient and Observer Scar Assessment Scale (questionnaire)

Each appointment will last approximately 30-60 minutes.

Things to remember while participating in the study:

- Do not remove the dressing from the wound unless directed by the study staff
- If you have any concerns about the wound, please contact the study staff prior to making any changes
- Inform the study staff of any changes in your medical history, pregnancy status, etc.

WHAT ARE THE POTENTIAL RISKS AND DISCOMFORTS FROM BEING IN THIS RESEARCH?

Risks of the investigational skin grafting procedure

These risks are very similar to those for the standard of care split-thickness skin grafting procedure. Some of those risks may include the following:

- Inability to Heal: Skin grafts require an adequate blood supply to survive. If the area of injury does not have a good blood supply because of the injury or another underlying disease, the injured area may not be able to support the skin graft. In this case, the skin graft might not survive. In other cases, the injured area is simply too large or the injury too significant to allow the skin graft to heal and close the wound. More-involved reconstructive surgical procedures may be necessary.
- Skin Sensation: Diminished (or loss) of skin sensation at either the donor or treated sites may occur and not resolve completely following this procedure. Because of this, these areas are at higher risk for injury as a result of excessive heat, cold, or physical force if sensation does not entirely return. Attention to these areas to avoid injury and prevent complications is crucial.
- Skin Contour Irregularities: Skin contour irregularities can occur at either the donor or treated sites. These may improve with time or require additional surgery.
- Delayed Healing: Wound disruption or delayed wound healing is possible at either the donor or treated sites. Some areas may experience such delayed healing that part of the graft does not survive, requiring additional dressing changes, procedures, or surgery. **Smokers have a greater risk of skin loss and wound healing complications.**
- Skin Discoloration / Swelling: Swelling and bruising can be normal immediately after surgery. However, this should resolve with time. Both the donor and treated sites are at risk for changes in color during the healing process. These areas can become either darker or lighter than the surrounding skin. These changes can be permanent.
- Skin Sensitivity: Itching is common after skin grafting at both the donor and treated sites. Graft abrasion may occur due to scratching. These areas may also have heightened sensitivity to hot or cold temperatures. This usually resolves over time but can be permanent.
- Inability to Restore Function: In some cases, skin grafts are not able to restore the normal functions of intact skin. Additional treatment and surgery may be necessary.
- Buried Surgical Staples / Sutures: Staples and sutures are initially used to hold the skin graft in place. As the graft heals, skin may begin to cover the staples and sutures, burying them within the wound. They may spontaneously poke through the skin, become visible, or produce irritation that requires removal. Additional surgery may be required to remove the buried staples or sutures.

- Lack of Graft Durability: Skin grafts may not have the same padding and durability of normal, undamaged skin. Because of this, the treated area is at higher risk of abrasion and injury as compared to intact skin even after healing.

There may be other risks that are unknown.

Risks of General Anesthesia

You may be placed under general anesthesia for this procedure. You will be asked to sign a separate consent form for this; this is done to make sure you fully understand the risks of the anesthesia. Since you need skin grafting, whether by the investigational method performed in this research study or by the standard of care split-thickness skin graft procedure, you will likely need general anesthesia either way. The following are risks of general anesthesia:

- Nausea / Vomiting
- Temporary inability to empty your bladder (urinate)
- Hoarseness
- Mouth or throat pain
- Injury to mouth or teeth
- Awareness under anesthesia
- Injury to blood vessels
- Allergic reaction to anesthetic
- Problems breathing
- Excessive bleeding
- Changes in blood pressure and heart function
- Constipation
- Blood Clot
- Fever and chills

Occur rarely:

- Heart attack
- Pneumonia (lung infection)
- Kidney Failure
- Stroke
- Death

Risks of Local Anesthesia

You may be given local anesthesia for this procedure. You will be asked to sign a separate consent form for this; this is done to make sure you fully understand the risks of the anesthesia. Since you need skin grafting, whether by the investigational method performed in this research study or by the standard of care split-thickness skin graft procedure, you would likely receive local anesthesia either way. The following are risks of local anesthesia:

- Allergic reaction to anesthetic
- Nerve damage
- Numbness or tingling in the area of anesthesia
- Swelling, bruising, or soreness at the injection site
- A blood-filled swelling called hematoma at the injection site
- Temporary rapid heartbeat

WHAT ARE THE POSSIBLE BENEFITS FROM BEING IN THIS RESEARCH?

It is possible that this investigational skin grafting method could improve healing of your open wound, but it is also possible that you may not receive any direct benefit from this study. We hope that the information learned from this study will benefit other people with open wounds like yours in the future. We also hope that this information will help guide treatment for soldiers who suffer burn injuries on the battlefield. Your participation may help investigators plan better treatment for people with your condition.

WHAT ALTERNATIVE OPTIONS TO PARTICIPATION ARE AVAILABLE TO ME?

If you do not wish to take part in the research study, your study doctor will discuss other options with you, including their benefits and risks. These options may include:

- Being treated with the standard of care treatment, likely split-thickness skin graft, for your open wound
- Taking part in other investigational studies, if they are available

Talk to your study doctor about each of these choices before you decide if you will take part in this study. If you decide not to take part, withdraw your participation after starting the study, or are taken off the study, the study doctor will discuss other options with you.

COMPENSATION FOR PARTICIPATION

You will be compensated up to $175.00 total, $25.00 per completed study visit.

You will receive compensation when you complete the study. If you do not complete the study, for any reason, you will be paid for each study visit you do complete.

If you are affiliated with the Department of Defense and on duty, you will not be compensated for your participation in this study, as it is prohibited by federal regulations.

If you have any questions regarding your compensation for participation, please contact the study staff.

WILL I HAVE TO PAY FOR ANYTHING IF I TAKE PART IN THIS RESEARCH?

You and/or your medical insurance company will be responsible for the cost of the non-study related medical care you receive as a result of your open wound. You will be responsible for the costs of travel to and from the study clinic for follow-up visits.

If your study doctor requires you to stay overnight in the hospital as a result of a study-related issue, you or your insurance company will not be responsible for the cost.

If you are required to stay in the hospital overnight due to non-study related issues, you or your insurance company may be responsible for the cost.

Medical care costs for non-study related issues will be at your expense and/or your insurance company's expense.

IN CASE OF STUDY-RELATED INJURY

If a "research-related injury" results from your participation in this research study, medical treatment will be provided at no cost to you and paid by The Metis Foundation, sponsor of the study. A "research-related injury" means an injury caused by the product or procedures required by the research that you would not have experienced if you had not participated in the research study. The sponsor will cover the cost of reasonable and necessary medical treatment for a research-related injury. You, or your medical insurance, will be responsible for other medical expenses resulting from your medical condition.

It is important for you to follow your study doctor's instructions, including notifying your study doctor as soon as you are able to about any complications or injuries that you experience.

There are no plans to pay you for any other injury- or illness-related costs, such as lost wages.

If you receive Medicare benefits, the Sponsor is required by law to report payments made to you for treatment, complications, and injuries that arise from this study. Information that you are taking part in the study, medical treatments received, Medicare claims, and other personal information about you such as your name, social security number, and date of birth will be provided to the Centers of Medicare and Medicaid Services and its agents and/or contractors for this purpose.

Please be aware that some insurance plans may not pay for research-related injuries or overnight observation. You should contact your insurance company for more information.

By signing and dating this document, you will not lose any of your legal rights or release anyone involved in the research from responsibility for mistakes.

HOW WILL YOU PROTECT MY PRIVACY AND THE CONFIDENTIALITY OF RECORDS ABOUT ME?

The study doctor will keep records of your participation in the research. To protect your privacy, any of your research-related records including photographs and objective and subjective measurements will be labeled or "coded" with an assigned study ID number that will not include your name or social security number. The study doctor will keep the link between your study ID number and your research records in a locked records room. The study doctor and study staff are the only people who will be able to match your study ID number with any of your personal identifying information. However, absolute confidentiality cannot be guaranteed.

When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity to others.

To help protect your privacy in the photographs, identifying features such as eyes, mouth, or tattoos will be redacted. If photographs of you will be used for educational purposes, your identity will be protected or disguised. Photographs published will include the wound only.

Authorized representatives of the following groups may need to review your research and/or medical records as part of their responsibilities to protect research subjects:

- The sponsor or persons working on behalf of the sponsor
- Advarra IRB
- The United States Food and Drug Administration (FDA)
- Human Research Protections Office or other offices charged with oversight of human research
- The Department of Defense (DoD)

FUTURE RESEARCH

No human specimens will be stored for future research.

Identifiers might be removed from your identifiable private information collected during this study, which could then be used for future research studies or distributed to another investigator for future research studies without additional informed consent.

No genetic testing will be performed on your specimens, and the specimens themselves will not be stored.

COMMERCIAL PROFIT

Your specimens collected during this study may be used for commercial profit (even if identifiers are removed) and you will **not** share in this profit.

CLINICALLY RELEVANT RESULTS

Research results that are clinically relevant, including individual research results, **will be disclosed to you**.

WHAT IF I DECIDE NOT TO PARTICIPATE IN THIS RESEARCH?

Your participation in this research is voluntary. You may decline to participate now, or stop taking part in this research at any time, without any penalty or loss of benefits to which you are entitled. Deciding not to participate now or withdrawing at a later time will not harm, or in any way affect, your medical care.

WHAT COULD END MY INVOLVEMENT IN THE RESEARCH?

The study doctor may withdraw you from participating in this research if circumstances arise which warrant doing so including but not limited to the following:

- Your study doctor is concerned about your health
- The side effects of the study treatment are too dangerous for you
- New information shows the study treatment will not work or is not safe for you
- You do not follow the study doctor's instructions
- The study is closed for safety, administrative, or other reasons

The study doctor will make the decision and let you know if it is not possible for you to continue. Your taking part in the study may be stopped without your consent if it is determined by the study doctor that remaining in the study might be dangerous or harmful to you.

WHAT IF ANY NEW INFORMATION IS FOUND OUT?

During the course of the research, the study doctor will tell you of any new findings that might cause you to change your mind about continuing in the study. If new information is provided to you, the study doctor will obtain your consent to continue participating in this study.

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns, or complaints about the study, such as:

- Whom to contact in the case of a research-related injury or illness;
- Payment or compensation for being in the study, if any;
- Your responsibilities as a research subject;
- Eligibility to participate in the study;
- The study doctor's or study site's decision to withdraw you from participation;
- Results of tests and/or procedures;

Please contact the study doctor at the telephone number listed on the first page of this consent document.

If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, contact:

- By mail:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00071475.

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

If you decide to be in this study, the study doctor and study staff will use and share health data about you to conduct the study. Health data may include:

- Your name.
- Address.
- Phone number.
- Date of birth.
- Medical history.
- Information from your study visits, including all test results.

Health data may come from your study records or from existing records kept by your doctor or other health care workers.

For this study, the study staff may share health data about you with authorized users. Authorized users may include:

- Representatives of The Metis Foundation.
- Representatives of Advarra IRB (an Institutional Review Board that reviews this study).
- The Food and Drug Administration (FDA) and other US federal and state agencies.
- The Department of Defense (DoD) or other governmental agencies.
- Outside individuals and companies, such as laboratories and data storage companies, that work with the researchers and sponsor and need to access your information to conduct this study.

Your health data will be used to conduct and oversee the research, including, for instance:

- To see if the study treatment works and is safe.
- To compare the study treatment to other treatments.
- For other research activities related to the study treatment.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law and could possibly be used or disclosed in ways other than those listed here.

Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner.

You may revoke (take back) your permission to use and share health data about you at any time by writing to the study doctor at the address listed on the first page of this form. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you decide not to sign and date this form, you will not be able to take part in the study.

STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use, and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing and dating this form.

_____
Printed Name of Subject

_____ _____
Signature of Subject Date

_____ _____
Signature of Legally Authorized Representative Date

_____
Authority of Legally Authorized Representative to act on behalf of Subject

WITNESS SIGNATURE FOR SUBJECTS WHO CANNOT READ

The study subject has indicated that he/she is unable to read. The consent document has been read to the subject by a member of the study staff, discussed with the subject by a member of the study staff, and the subject has been given an opportunity to ask questions of the study staff.

_____
Printed Name of Impartial Witness

_____ _____
Signature of Impartial Witness Date

SIGNATURE OF RESEARCH SUBJECT

I have read the information provided above. I have been given an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing and dating this consent document.

_____
Printed Name of Subject

_____ _____
Signature of Subject Date

_____ _____
Signature of Legally Authorized Representative Date

_____
Authority of Legally Authorized Representative to act on behalf of Subject

WITNESS SIGNATURE FOR SUBJECTS WHO CANNOT READ

The study subject has indicated that he/she is unable to read. The consent document has been read to the subject by a member of the study staff, discussed with the subject by a member of the study staff, and the subject has been given an opportunity to ask questions of the study staff.

_____
Printed Name of Impartial Witness

_____ _____
Signature of Impartial Witness Date

SIGNATURE OF PERSON OBTAINING CONSENT

My signature certifies that the subject signed and dated this consent form in my presence as his/her voluntary act and deed.

_____
Printed Name of Person Obtaining Consent

_____ _____
Signature of Person Obtaining Consent Date

PHOTO RELEASE FORM

You give the company paying for this research study the right to use, copy, and give out the pictures taken of your surgical incision. The purpose for taking the photos is to document the healing.

Your pictures may be used for publications or presentations describing this research.

We will try to hide your identity. Your name will not be on the pictures. You have the right to review your pictures and cancel this Photo Release Form.

Statement of Consent:

I have read this release and understand its meaning. I understand I do need to sign and date this Photo Release Form in order to be in the study. You will receive a signed, dated copy of this consent form to keep.

_____
Printed Name of Subject

_____
Signature of Subject Date

_____ _____
Signature of Legally Authorized Representative Date

_____
Authority of Legally Authorized Representative to act on behalf of Subject

WITNESS SIGNATURE FOR SUBJECTS WHO CANNOT READ

The study subject has indicated that he/she is unable to read. The consent document has been read to the subject by a member of the study staff, discussed with the subject by a member of the study staff, and the subject has been given an opportunity to ask questions of the study staff.

_____
Printed Name of Impartial Witness

_____ _____
Signature of Impartial Witness Date

SIGNATURE OF PERSON OBTAINING PHOTOGRAPHY CONSENT

My signature certifies that the subject signed and dated this consent form in my presence as his/her voluntary act and deed.

_____

Printed Name of Person Explaining Photo Release Form

_____

Signature of Person Explaining Photo Release Form Date