Informed Consent Form for Participation in a Research Study

Study Title: **The Effect of Topical TRanexamic Acid vs. placebo on Acute Postoperative Pain following Distal Radius Fracture Fixation: A Randomized Controlled Trial - The TRADR Study**

Principal Investigator:
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Funder: Canadian Orthopedic Association Legacy Grant, Arthrex WeCan Grant

Emergency Contact Number (24 hours / 7 days a week): 416-603-5839 - Ask for Dr. Paul.

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*Please note that communication via e-mail is not absolutely secure. Thus, please do not communicate personal sensitive information via e-mail.

INTRODUCTION
You are being invited to participate in a research clinical trial. You are invited to participate in this clinical trial because you are awaiting operative treatment for your wrist fracture. This consent form provides you with information to help you make an informed choice. Please read this document carefully and ask any questions you may have. All your questions should be answered to your satisfaction before you decide whether to participate in this research study. You may find it helpful to discuss it with your friends and family.

The study staff will tell you about the study timelines for making your decision. Taking part in this study is voluntary. You have the option to not participate at all or you may choose to leave the study at any time. Whatever you choose, it will not affect the usual medical care that you receive outside the study include standard pain medications and care as usual.

IS THERE A CONFLICT OF INTEREST?
The study doctors, Dr. Paul and Dr. Chan are receiving financial payment from Canadian Orthopedic Association to cover the cost of conducting this study. Both have an interest in completing this study. Their interests should not influence your decision to participate in this study.

WHAT IS THE BACKGROUND INFORMATION FOR THIS STUDY?

Wrist Fractures are frequently encountered injuries and are often treated with surgery. Surgical repair is associated with good long term functional outcomes, but it can also result in significant pain afterwards. The standard treatment for post-operative pain is pain-relieving medications, including Tylenol, vitamin C (which may help with nerve pain), and Celebrex (an anti inflammatory, if it can be tolerated by the patient). You may receive stronger opioid medication for higher levels of pain - either Hydromorphone, oxycodone, or tramadol. This is based on what may be best or most familiar for you. Opioids can help with post-surgery pain, but they come with serious problems like the risk of getting addicted or taking too much, which can be harmful. Because of these reasons, healthcare providers are always looking to find ways to use fewer opioids while still making sure pain is treated after surgery.

Tranexemic acid (TXA) is a drug that is approved in Canada for the treatment and prevention of surgical bleeding and swelling. TXA has been shown to reduce pain after spine and shoulder procedures when given topically (applied directly on the affected place). This is why TXA may also help with pain after wrist surgery and may therefore reduce the need for strong painkillers and prevent extra visits to the doctor.

Although TXA is an approved drug, the way it is being used in this study has not been approved by Health Canada.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to find out whether the use of topical TXA into the surgical wound will result in less post-operative pain, less pain killer use, and better post-operative use of the wrist in people undergoing surgery for a wrist fracture compared to not using topical TXA.

To do this, some of the participants in this study will get topical TXA and others will receive a placebo (a substance that looks like the study drug but does not have any active or medicinal ingredients). A placebo is given in this study to reduce the chances of believing that a disease is getting better because one is receiving a new drug. Really, we don't know if the new drug or no drug with standard treatment is better than the other so we are doing this study to try and find that out.

WHAT OTHER CHOICES ARE THERE?

You do not have to take part in this study in order to receive treatment or care. Your decision to enroll in this study will not affect your current or future care.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

It is anticipated that about 90 people will take part in this study from Toronto Western hospital, UHN. This study should take 18 months to complete and the results should be known in about two years.

WHAT WILL HAPPEN DURING THIS STUDY?

ASSIGNMENT TO A GROUP

If you decide to participate then you will be "randomized" into one of the groups described below. Randomization means that you are put into a group by chance (like flipping a coin). There is no way to predict which group you will be assigned to. You will have an equal chance of being placed in either group. Neither you, the study staff, nor the study doctors can choose what group you will be in.

- Participants in group 1 will receive a solution of TXA in addition to the standard care.
- Participants in group 2 will receive a solution of placebo (saline) in addition to the standard care.

This is a double-blind study, which means that neither you, the study doctors, the study staff, nor your usual health care providers will know which group you are in. Your group assignment can be identified if medically necessary. When you finish your participation in the study and would like to know what study group you were in, let the study team know. Please note that you may not be able to get this information until the entire study is completed.

WHAT IS THE STUDY INTERVENTION?

- Group 1 (Experimental intervention): Standard intervention for wrist fracture fixation surgery plus experimental intervention of topical TXA.

  If you are randomized to this group, you will receive a solution of TXA. During the surgery, the solution will be poured into your surgical wound after the fracture is fixed but before wound closure.

- Group 2 (Non-Experimental Intervention): Standard intervention and placebo

  If you are randomized to this group, you will receive solution of placebo (saline). During the surgery, the solution will be poured into your surgical wound after the fracture is fixed but before wound closure.

The TXA or placebo solution will be applied to the wound once during the surgery for a duration of five minutes. Subsequently, the solution will be sucked out. Following this, a standard dressing and plaster splint will be applied to the incision.

WHAT ARE THE STUDY PROCEDURES?

There will be 4 study visits during your participation in this study.

- Visit 1 will be for the screening and collecting baseline information and will take one hour.
- Visit 2 will be a phone call at 24 to 72 hours after surgery and will take 15 to 20 minutes.

- Visit 3 and 4 will take place at Toronto Western Hospital and each visit will take 15 to 30 minutes.

All study visits will be timed so as to be a part of your typical standard of care visits.
The study doctor and his/her study team will look at your medical chart and collect only the information they need for the study.

Experimental Procedures
The following procedures will only be done for participants on this study:

Questionnaires
You will be provided with two questionnaires before you begin the study, day 1 to 7 after surgery, and then at two and six weeks after surgery. The purpose of the questionnaire is to understand your baseline pain intensity and then to know how the study intervention and illness affects your level of pain and function. Each questionnaire will take about 10 to 15 minutes to complete.

The information you provide is for research purposes only. Some of the questions are personal. You can choose not to answer questions if you wish. Even though you may have provided information on a questionnaire, these responses will not be reviewed by your health care team - if you wish them to know this information please bring it to their attention.

Participant Diaries
You will be asked to keep a pain diary, recording the intensity of your pain, any painkiller usage (e.g., opioids), and instances where you need to visit the emergency room or be seen by your doctor due to pain or other issues related to your surgery. Please record the level of pain and the dose of pain killers taken every day. You will be asked to return the diary to this centre.

WHAT ARE THE RESPONSIBILITIES OF STUDY PARTICIPANTS?
If you choose to participate in this study, you will be expected to:

- Tell the study doctor about your current medical conditions
- Tell the study doctor if you are, or plan on being, pregnant before or immediately after the surgery
- Tell the study doctor about all prescription and non-prescription medications especially contraceptives, hormone replacement therapy, and anticoagulant treatments and supplements, including vitamins and herbals, and check with the study doctor before starting, stopping or changing any of these. This is for your safety as these may interact with the intervention you receive on this study.
- Tell the study doctor if you are thinking about participating in another research study
- Return any diaries and questionnaires that you take home to complete during the day 1 to 7 post-op

HOW LONG WILL PARTICIPANTS BE IN THE STUDY?

You will be asked to come back to the hospital at 2 and 6 weeks after the surgery as part of your standard visit. You may be seen more often if the study doctor determines that this is necessary.

CAN PARTICIPANTS CHOOSE TO LEAVE THE STUDY?

You can choose to end your participation in this research (called withdrawal) at any time without having to provide a reason. If you choose to withdraw from the study, you are encouraged to contact the study doctor or study staff. You may be asked questions about your experience with the study intervention and to have physical examinations considered necessary to safely stop your study involvement.

If you decide to leave the study, you can ask that the information that was collected about you not be used for the study. Let the study doctor know if you choose this. Information that was recorded before you withdrew will still be used by the researchers for the purposes of the study, but no information will be collected after you withdraw from the study.

CAN PARTICIPATION IN THIS STUDY END EARLY?

The study doctor may stop your participation in the study early and without your consent if you are no longer eligible for it. For example, this may occur if you have complications from your surgery. If you are removed from this study, the study doctor will discuss the reasons with you and plans will be made for your continued care outside of the study.

WHAT ARE THE RISKS OR HARMS OF PARTICIPATING IN THIS STUDY?

You may experience side effects from participating in this study. Some side effects are known and are listed below, but there may be other side effects that are not expected. You should discuss these with the study doctor. The study doctor will watch you closely to see if you have side effects. If you experience a serious side effect and need immediate treatment and are unable to return to the clinic/hospital, please call 911 or go to the nearest emergency room. Then the study doctor should be contacted as soon as possible.

Risks and side effects related to **topical TXA** administration are very **rare** (1 – 4%): In 100 people receiving study drug, between 1 and 4 may have:

- Eye Disorders: temporary impaired vision, blurred vision or color vision impairment (chromatopsia)
- Nervous System Disorders: dizziness and seizures.
- There is no known case of over dosage of Tranexamic Acid in humans. Symptoms may be nausea, diarrhea, dizziness, headache, convulsions, vomiting orthostatic symptoms and hypotension.
- Blood clots in your veins

The risks are temporary and reversible. There is no risk associated with washing the joint with

saline.

An experimental topical TXA is being added to the standard treatment for the condition you have. This combination may change the side effects or the effectiveness of the standard treatment. This may mean that you experience more side effects than you would with the standard treatment alone. It may also mean that the standard treatment does not work as expected.

It is possible that other drugs (prescription and non-prescription drugs), vitamins, or herbals can interact with the study intervention. This can result in either the intervention not working as expected or result in severe side effects. Please check with the study team if the study drug may interfere with your medications and consult with the study team before taking any new medications.

Phone call follow-up
You may become uncomfortable while discussing your experiences. You may refuse to answer questions or ask to end the call at any time if you experience any discomfort.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?
You may or may not benefit from receiving TXA. You will not benefit from the placebo used in this study. We hope the information learned from this study will also help other people with distal radius fracture in the future.

HOW WILL PARTICIPANT INFORMATION BE KEPT CONFIDENTIAL?
If you decide to participate in this study, the study doctors and study staff will only collect the information they need for this study. Your data will be shared as described in this consent form and/or as required by law and/or applicable research regulations. Records identifying you at this centre will be kept confidential and, to the extent permitted by applicable laws, will not be disclosed or made publicly available.

Authorized representatives of the following organization may come to the hospital or be given remote access to an electronic portal (via Internet) to look at your original (identifiable) medical/clinical study records at the site where these records are held, to check that the information collected for the study is correct and follows proper laws and guidelines. When using the electronic portal, we will share your medical record number using a secure method, so that your records are included as part of their review.

- Representatives of the University Health Network including the UHN Research Ethics Board, who oversees the ethical conduct of this study at UHN

These individuals have completed privacy training and signed confidentiality agreements and/or are required by law to keep your information confidential.

Whether on-site or remotely, UHN makes all efforts to ensure that your information is shared in a way that is secure and private (encrypted). However, any electronic communication carries some risk of third parties gaining unauthorized access to information.

Studies involving humans sometimes collect information on race and ethnicity as well as other characteristics of individuals because these characteristics may influence how people respond to different interventions. Providing information on your race or ethnic origin is voluntary.

In addition to the data that will be collected for this study, the researchers will also be collecting the following personal health information: your name, address, date of birth, new or existing medical records, including a description of treatment performed for fractures (ie. splinting / casting / reductions), description of the mechanism of injury, and medical comorbidities relevant to surgery. These additional data are being collected to help researchers better understand common trends between your condition and other health problems.

If the results of this study are published, your identity will remain confidential. It is expected that the information collected during this study will be used in analyses and will be published/ presented to the scientific community at meetings and in journals. Even though the likelihood that someone may identify you from the study data is very small, it can never be completely eliminated. The study doctor will keep any personal health information about you in a secure and confidential location for 10 years. Your participation in this study will also be recorded in your medical record at this hospital. This is for clinical safety purposes.

Research Information in Shared Clinical Records

If you participate in this study, information about you from this research project may be stored in your hospital file and in the UHN computer system. The UHN shares the patient information stored on its computers with other hospitals and health care providers in Ontario so they can access the information if it is needed for your clinical care. The study team can tell you what information about you will be stored electronically and may be shared outside of the UHN. If you have any concerns about this, or have any questions, please contact the UHN Privacy Office at 416-340-4800, x6937 (or by email at privacy@uhn.ca).

Phone call follow-up:

During the phone call, participants will be encouraged to refrain from using names. If names or other identifying information is shared during the call, it will not be included in the written records. The audio recordings will be stored in a secure location and viewed only by members of the research team. The recordings will be kept until they have been transcribed (turned into written records), and then they will be destroyed.

WILL FAMILY DOCTORS/HEALTH CARE PROVIDERS KNOW WHO IS PARTICIPATING IN THIS STUDY?

Your family doctor/health care provider will not be informed by the study team that you are taking part in the study. You can choose to let your family doctor/health care provider know, if you like.

Will information about this study be available?

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.

Study results will be shared with you if/when they become available after the entire study is completed. It is expected that this may take a number of years. The results will be shared with you based on your preferred communication method indicated in UHN's medical record system. Please talk to your study doctor if you have any questions about the results.

WHAT IS THE COST TO PARTICIPANTS?

Participation in this study will not involve any additional costs to you or your private health care insurance.

ARE STUDY PARTICIPANTS PAID TO BE IN THIS STUDY?

You will not be paid for taking part in this study.

WHAT WILL HAPPEN IF PARTICIPANT IS INJURED DURING THE STUDY?

In the case of research-related side effects or injury, medical care will be provided by your doctor.

WHAT ARE THE RIGHTS OF PARTICIPANTS IN A RESEARCH STUDY?

You will be told, in a timely manner, about new information that may be relevant to your willingness to stay in this study. Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.

By signing this form, you do not give up any of your legal rights against the study doctor, sponsor or involved institutions for compensation, nor does this form relieve the study doctor, sponsor or their agents of their legal and professional responsibilities.

WHOM DO PARTICIPANTS CONTACT FOR QUESTIONS?

If you have questions about taking part in this study, or if you suffer a research-related injury, you can talk to your study doctor, or the doctor who is in charge of the study at this institution. That person is:

Dr. Ryan Paul (416) 603-5839

If you have questions about your rights as a participant or about ethical issues related to this study, call the Chair of the University Health Network Research Ethics Board (UHN REB) or the Research Ethics office number at 416-581-7849. The REB is a group of people who oversee the ethical conduct of research studies. The UHN REB is not involved in the study at all. Everything that you discuss will be kept confidential.

You will be given a copy of this signed and dated consent form prior to participating in this study. A copy of the consent form that you sign to enter the study may be included in your health record/hospital chart.

TITLE: **The Effect of Topical TRanexamic Acid (TXA) vs. placebo on Acute Postoperative Pain following Distal Radius Fracture Fixation: A Randomized Controlled Trial - The TRADR Study**

CONSENT

- All of my questions have been answered
- I allow access to medical records and related personal health information as explained in this consent form
- I do not give up any legal rights by signing this consent form,
- I agree to take part in this study.

_____	_____	_____
Signature of Participant/	PRINTED NAME	Date
_____	_____	_____
Signature of Person Conducting the Consent Discussion	PRINTED NAME & ROLE	Date

The following attestation must be provided if the participant is unable to read or requires an oral translation:
If the participant is assisted during the consent process, please check the relevant box and complete the signature space below:

☐ The person signing below acted as an interpreter, and attests that the study as set out in the consent form was accurately sight translated and/or interpreted, and that interpretation was provided on questions, responses and additional discussion arising from this process.

_____	_____	_____
PRINT NAME of Interpreter	Signature	Date

_____
Language

☐ The consent form was read to the participant. The person signing below attests that the study as set out in this form was accurately explained to the participant, and any questions have been answered.

_____	_____	_____
PRINT NAME of witness	Signature	Date

_____

Relationship to Participant