CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY

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PROJECT #: 2012402

Version #: 3

STUDY TITLE: A PROSPECTIVE, RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED CLINICAL TRIAL EVALUATING THE USE OF PERIOPERATIVE INTRAVENOUS LIDOCAINE INFUSION TO DECREASE PAIN SCORES AND OPIOID CONSUMPTION AFTER ROBOTIC-ASSISTED PROSTATECTOMY AND ROBOTIC-ASSISTED PARTIAL NEPHRECTOMY

We invite you to take part in this research study. This consent form tells you why we are doing the study, what will happen if you join the study, and other important information about the study.

Please take as much time as you need to read this consent form. You can discuss it with your family, friends, or personal doctor. If there is anything you do not understand, please ask us to explain. Then you can decide if you want to take part in the study or not.

The Principle Investigator (also called the study doctor) is Dr. Katie Murray. The people working with Dr. Murray on this study are called the study team.

WHAT SHOULD I KNOW BEFORE I DECIDE WHETHER TO TAKE PART IN THIS STUDY?

- Research studies help us to learn new things and test new ideas about treating certain conditions/diseases.
- Taking part in a research study is voluntary. You decide if you want to take part, and you can stop taking part at any time. Your regular medical care at the University of Missouri Hospitals and Clinics will not be affected now or in the future if you decide you do not want to be in this study.
- We are doing this study because the use of continuous lidocaine infusions in patients undergoing robotic-assisted surgeries has not been well studied. We hope to learn how to better guide clinicians on the use of this treatment for robotic surgeries.
- We invite you to take part in this study because you are scheduled to have elective robotic urologic surgery at University Hospital in Columbia Missouri.

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ClinicalTrials.gov - NCT03824808

- About 46 people will take part in this study. All cases will be at the University of Missouri.
- If you take part in this study, all your study visits will occur at University Hospital. You will come for your scheduled surgery, be monitored by study staff during your hospital stay, and at your two-week clinic visit. You will be asked questions about your pain, surgical recovery, and satisfaction during these visits. We will explain these procedures in this form.
- If you join this study, you will not have to stop your planned surgical procedure or regular pain management treatment for as long as you are in the study.
- The total amount of time you could be in this study is about three weeks.
- Taking part in this study may or may not make your health better. We hope that the information we learn from this study will help in the future treatment of people who choose to have robot assisted urologic surgery. **There is no guarantee that taking part in this research will result in any improvement in your condition.**
- As with any research study, there are risks that we know about and there may be some we don't know about. We will explain these risks in this form.
- We will only include you in this study if you give us your permission first by signing this consent form.

WHY IS THIS STUDY BEING DONE?

Once a patient undergoes a robotic-assisted urological surgery it is necessary to control surgery-related pain. The purpose of this study is to determine if a continuous intravenous infusion of the medication lidocaine over the twenty-four-hour period following robotic-assisted urological surgeries will help to decrease postoperative pain.

Continuous infusions are performed using devices called infusion pumps. For this study, an infusion pump will be mounted on a pole located near your bed. The infusion will be started while you are asleep for your surgery and last for 24 hours.

This research is being done because the use of continuous lidocaine infusions in patients undergoing robotic-assisted urological surgeries has not been well studied. The benefit of continuous lidocaine infusions have been demonstrated to help patients' pain management in different surgeries.

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How Many People Will Take Part In The Study?

We plan to enroll 46 patients so that 40 people will take part in this study performed in University Hospital at the University of Missouri.

What Is Involved in the Study?

Whether or not you are in the study, you will receive the same medical care before, during and after your surgery. The type of medications used for the general anesthesia in this study will be the same in both groups and are the same medications used for general anesthesia for robotic-assisted urological surgery if you are not in the study. Your robotic-assisted urological surgery will be performed in the same manner that it would be done if you were not in the study.

If you are in the study, you will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance. It is like flipping a coin. Neither you nor the researcher will choose what group you will be in. You will have an equal chance of being placed in one of the groups, including a placebo. If you are in the placebo group you will not receive the study medication. Placebos are commonly used in studies involving medications

Intravenous lidocaine is currently approved for use in correction irregular heartbeats and it is commonly used as a numbing agent. It is still being investigated for use in the proposed manner in this study.

In this study, one group will receive intravenous lidocaine and the other group will receive an intravenous normal saline as a placebo. Lidocaine is a numbing medication used for pain relief. Normal saline is a salt water solution. Both medication treatments are routinely used today. Neither you nor your doctor will know which drug you actually received until the end of the study. This "blinding" is usually used in clinical trials to get objective answers. In the case of unforeseen complications, on request your doctor will be told which medication you received.

<u>If you take part in this study, you will have the following tests and procedures</u>:

- There are no additional laboratory tests or medical scans if you take part in the study.

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- As part of the study, one group will receive the medication lidocaine and the other group will receive a placebo of normal saline.
- At the end of your surgery, you will leave the operating room with a blinded intravenous infusion providing either lidocaine or normal saline. This infusion will be started when you are asleep for your surgery and continue for twenty-four hours.
- We will visit you every day following your surgery until you are discharged from the hospital and ask you to rate your level of pain using a Visual Analog Scale (a four inch line on which you will mark your pain) and a scale of 1 (no pain) to 10 (worst imaginable pain). This will also occur at your 14 day follow-up visit. We will also record the amount of pain medication that you use each day.
- You will be monitored for side effects during your hospital stay.
- Your satisfaction with anesthesia will be evaluated using a questionnaire on the first day after surgery.

If you are not in the study, the drugs you will receive will be determined by your doctors as part of the standard of care. You may receive an intravenous lidocaine infusion regardless of participating in this study. This will be determined by your doctor.

The information we collect from you for this study will not be used or shared with other investigators for future research studies. This applies even if we remove all information that could identify you from the data.

HOW LONG WILL I BE IN THE STUDY?

You will be in this study from the time you sign the research informed consent form until your post-operative Urology Clinic visit.

The investigator and/or your doctor may decide to take you off this study if one of the study medications is not available, if your surgery is stopped before attempting to remove your cancer, or if the intravenous infusion fails for any reason.

You can stop participating at any time. Your decision to withdraw from the study will not affect in any way your medical care and/or benefits. If you decide to stop participating in the study, you are encouraged to discuss your decision with your doctor.

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WHAT ARE THE RISKS OF THE STUDY?

While on the study, you are at risk for the side effects described below. You should discuss these with the investigator and/or your doctor. There may also be other side effects that we cannot predict. You may receive other drugs to make side effects less severe and uncomfortable. Many side effects go away shortly after the drugs are stopped, but in some cases side effects can be serious or long-lasting or permanent.

All of the surgical procedures used are standard procedures and will be done whether you are in the study or not so they will not increase the risk. The medications that are used for general anesthesia in the study are the same as the medications used for anesthesia if you are not in the study. As such, there are no increased risks from the general anesthesia medication used or the procedures performed in the study.

We will be using one medication, lidocaine, and a placebo of normal saline. Both medications will be delivered by continuous intravenous infusion. Toxic levels of intravenous lidocaine are unlikely to be experienced following the dosage used in our protocol. The risks for both intravenous lidocaine and normal saline will be explained by our doctor.

Systemic reactions of the following types have been reported for intravenous lidocaine:

- Nervous System Disorders: respiratory depression (slow breathing) and arrest (stopped breathing); unconsciousness; convulsions (seizures); tremors (unintentional shaking); twitching; vomiting; blurred or double vision; drowsiness; dizziness; light-headedness; tinnitus (ringing in the ears); sensation of heat, cold or numbness; euphoria (feeling of intense happiness); apprehension (feeling that something bad will happen); agitation (anxiety and nervous excitement); confusion; paresthesia (burning or prickling sensation on body parts); dysarthria (damage to muscles used to produce speech).
- Cardiovascular System: cardiovascular arrest (stop in heart beat); bradycardia (slow heart rate) which may lead to cardiac arrest; hypotension (low blood pressure), Ventricular fibrillation (irregular heartbeat with quiver in the heart), Ventricular tachycardia (fast, abnormal heart rate), Ventricular arrhythmia (abnormal heartbeat), Asystole (stop in heart with no electrical activity).
- Gastrointestinal Disorders: Hypoesthesia oral (numbness in mouth), Nausea.

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- Hematologic Effects: methemoglobinemia (blood disorder with low oxygen delivered to cells)
- Psychiatric Disorders: Disorientation (confusion)
- Allergic reactions, including anaphylactic (serious, life-threatening) reactions, may occur but are infrequent. There have been no reports of cross sensitivity (reaction to a drug) between lidocaine hydrochloride and procainamide or quinidine (both drugs used to treat abnormal heart rhythms).

Reactions which may occur because of the solution or the technique of administration of Normal Saline:

- Fever (temporary increase in body temperature)
- Infection at the site of injection
- Venous thrombosis (blood clot) or phlebitis (vein inflammation) extending from the site of injection
- Extravasation (leakage of intravenously infused fluid into tissue around site of infusion)
- Hypervolemia (fluid overload in blood)

In clinical trials where you and the investigator do not know what drugs you are given, there will be a mechanism to discover which treatment you are receiving if your condition worsens. Research personnel will disclose which medication you receive on your physician request.

For the reasons stated above the investigator will observe you closely while giving the treatment described and, if you have any worrisome symptoms or symptoms that theinvestigator or her associates have described to you, notify the investigator immediately. Dr. Murray can be reached by telephone at 573-884-2384 / 573-884-8768 / 573-884-4057. For more information about risks and side effects, ask the investigator or contact Kate Muzzey, RN, BSN (Urology Nurse Navigator) at 573-884-2384.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct medical benefit to you. You may expect to benefit from taking part in this research to the extent that you are contributing to medical knowledge. We hope the information learned from this study will benefit other patients who are having robotic-assisted urologic surgery in the future.

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There is no guarantee that taking part in this research will result in any improvement in your condition. However, the information gained in this study may be used to improve the care of adults who need robotic-assisted urologic surgery in the future.

WHAT OTHER OPTIONS ARE THERE?

Instead of being in this study, you have these options:

An alternative is to not participate in this research study. You can have your robotic-assisted urologic surgery performed with general anesthesia.

You may receive an intravenous lidocaine infusion even if you do not take part in this study.

Please discuss these and other options with the investigator and your doctor.

WHAT ABOUT CONFIDENTIALITY?

A copy of this consent will be placed in the medical record. Anyone accessing your record will be able to view the document and see that you have agreed to participate in the study. Medical information produced by this study will become part of your hospital medical record. Information that does not become part of your medical record will be stored in the investigator's file and identified by a code number only. The code key connecting your name to specific information about you will be kept in a separate, secure location. Information contained in your records may not be given to anyone unaffiliated with the University Hospital in a form that could identify you without your written consent, except as required by law. If the investigator conducting this study is not your primary, or regular doctor, the investigator must obtain your permission before contacting your regular doctor for information about your past medical history or to inform them that you are in this trial.

It is possible that your medical and/or research record, including sensitive information and/or identifying information, may be inspected and/or copied by the study sponsor (and/or its agent), the Food and Drug Administration (FDA), federal or state government agencies, or hospital accrediting agencies, in the course of carrying out their duties. If your record is inspected or copied by the study sponsor (and/or its

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agents), or by any of these agencies, the University Hospital will use reasonable efforts to protect your privacy and the confidentiality of your medical information.

The results of this study may be published in a medical book or journal or used for teaching purposes. However, your name or other identifying information will not be used in any publication or teaching materials without your specific permission.

WHAT ARE THE COSTS?

There is no cost to you for the study drug itself. However, you will be paying for the normal cost of your routine medical care. Any procedure related solely to research that would not otherwise be necessary will be explained. Your doctor will discuss these with you.

In addition, the use of other medications to help control side effects could result in added costs that may or may not be covered by your medical insurance.

You will not be charged for the questionnaires that are part of this research study. You or your insurance company will, however, be charged for any other portion of your care that is considered standard care.

You or your insurance company will be charged for continuing medical care and/or hospitalization.

A social worker and financial counselor are available to discuss medical/financial concerns with you such as insurance coverage. Please let the study staff know if you would like to visit with these individuals and they will arrange an appointment.

WILL I BE PAID FOR PARTICIPATING IN THE STUDY?

You will receive no payment for taking part in this study.

WHAT IF I AM INJURED?

It is not the policy of the University of Missouri to compensate human subjects in the event the research results in injury. The University of Missouri, in fulfilling its public responsibility, has provided medical, professional and general liability insurance coverage for any injury in the event such injury is caused by the

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negligence of the University of Missouri, its faculty and staff. The University of Missouri also will provide, within the limitations of the laws of the State of Missouri, facilities and medical attention to subjects who suffer injuries while participating in the research projects of the University of Missouri. In the event you have suffered injury as the result of participation in this research program, you are to contact the Risk Management Officer, telephone number (573) 882-1181, at the Health Sciences Center, who can review the matter and provide further information. This statement is not to be construed as an admission of liability.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Participation in this study is voluntary. You do not have to participate in this study. Your present or future care will not be affected should you choose not to participate. If you decide to participate, you can change your mind and drop out of the study at any time without affecting your present or future care in the University Hospital at the University of Missouri. Leaving the study will not result in any penalty or loss of benefits to which you are entitled. In addition, the investigator of this study may decide to end your participation in this study at any time after she has explained the reasons for doing so and has helped arrange for your continued care by your own doctor, if needed.

You will be informed of any significant new findings discovered during the course of this study that might influence your health, welfare, or willingness to continue participation in this study.

Where Can I Get More Information About This Study?

A description of this clinical trial will be available on 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.

Who Can Answer My Questions About The Study?

If you have more questions about this study at any time, you can call Dr. Murray or Kate Muzzey, RN, BSN (Urology Nurse Navigator) at 573-884-2384. Dr. Murray can also be contacted at any time at 573-884-4057 or 573-884-8768.

You may also contact the University of Missouri Institutional Review Board (IRB) if you:

- Have any questions about your rights as a study participant;

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- Want to report any problems or complaints; or
- Feel under any pressure to take part or stay in this study.

The IRB is a group of people who review research studies to make sure the rights of participants are protected. Their phone number is 573-882-3181.

If you want to talk privately about your rights or any issues related to your participation in this study, you can contact University of Missouri Research Participant Advocacy by calling 888-280-5002 (a free call), or emailing MUResearchRPA@missouri.edu.

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WE WILL GIVE YOU A COPY OF THIS CONSENT FORM. PLEASE KEEP IT WHERE YOU CAN FIND IT EASILY. IT WILL HELP YOU TO REMEMBER WHAT WE DISCUSSED TODAY.

SIGNATURE

I confirm that the purpose of the research, the study procedures, the possible risks and discomforts as well as potential benefits that I may experience have been explained to me. Alternatives to my participation in the study also have been discussed. I have read this consent form and my questions have been answered. My signature below indicates my willingness to participate in this study.

Subject/Patient*	Date
Legal Guardian/Advocate/Witness (if required)**	Date
Additional Signature (if required) (identify relationship to subject)***	Date

*A minor's signature on this line indicates his/her assent to participate in this study. A minor's signature is not required if he/she is under 7 years old. Use the "Legal Guardian/Advocate/Witness" line for the parent's signature, and you may use the "Additional Signature" line for the second parent's signature, if required.

**The presence and signature of an impartial witness is required during the entire informed consent discussion if the patient or patient's legally authorized representative is unable to read.

***The "Additional Signature" line may be used for the second parent's signature, if required. This line may also be used for any other signature which is required as per federal, state, local, sponsor and/or any other entity requirements.

"If required" means that the signature line is signed only if it is required as per federal, state, local, sponsor and/or any other entity requirements.

SIGNATURE OF STUDY REPRESENTATIVE

I have explained the purpose of the research, the study procedures, identifying those that are investigational, the possible risks and discomforts as well as potential benefits and have answered questions regarding the study to the best of my ability.

Study Representative****	Date

****Study Representative is a person authorized to obtain consent. Per the policies of the University of Missouri Health Care, for any 'significant risk/treatment' study, the Study Representative must be a physician who is either the Principal or Co-Investigator. If the study is deemed either 'significant risk/non-treatment' or 'minimal risk,' the Study Representative may be a non-physician study investigator.

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