Topical **N**itroglycerine **T**reatment for **R**adial **A**rtery **S**pasm **P**revention (**TNT-RASP**)

NCT02832115

September 19 2017

INFORMED CONSENT DOCUMENT FOR PARTICIPATION OF A SUBJECT IN A RESEARCH STUDY

Transdermal Nitroglycerine Treatment for Radial Artery Spasm Prevention

TNT-RASP

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INTRODUCTION

You are being asked to participate in a clinical trial, a type of research study. This consent document provides you with important information about the trial to decide if you want to participate. It will outline the purpose of the study, the procedures involved, any possible risks associated with participation, and your rights as a participant.

Please take time to completely and carefully read the consent document. You will be able to ask the study doctor and study staff any questions you may have. You may also discuss your participation in the trial with your primary physician and family.

If you agree to participate in this study, you will be asked to sign this consent form. You will then receive a copy of the signed document.

In order to participate in this study you will be required to sign both this consent document and the authorization document.

Your participation in this study is voluntary. You are free to say yes or no. If you choose not to participate, your regular medical care and legal rights will not be affected. If you decide to participate, you are permitted to withdraw your consent and stop at any time.

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

WHO IS CONDUCTING THIS STUDY?

Dr. **Prabhakaran Gopalakrishnan,** a Cardiology Fellow at Aultman Hospital, and Dr. **Nagapradeep Nagajothi**, an Interventional cardiologist and Program director of the Cardiology Fellowship at Aultman Hospital, are responsible for conducting this clinical study. Dr. **Brendan Duffy**, an interventional cardiologist is responsible for the study design and compliance with regulations.

DO I HAVE TO BE IN THIS STUDY?

You can decide whether to take part in this study or not. You are free to say yes or no. If you say no, your regular medical care will not change. Even if you join this study, you do not have to stay in it. You may stop at any time.

A research study is different from routine medical care in three ways: 1) there are extra risks that we will tell you about in this form; 2) you may have some extra medical tests and visits; 3) the study procedures, tests and visits follow a set plan that must be kept.

WHO CAN TAKE PART IN THIS STUDY?

You are being asked to take part in this study because you are having a cardiac catheterization by transradial approach (using the artery in your wrist).

WHAT IS THE USUAL APPROACH FOR CARDIAC CATHETERIZATION?

Cardiac catheterization can be done either by transfemoral approach (i.e., using the artery in your thigh) or transradial approach (i.e., using the artery in your wrist). While each approach has its merits and limitations, your provider has elected for you to undergo a transradial approach. While transradial approach has been shown to have lower risk of complications as well as improved patient discomfort, the smaller size of the radial artery (artery in wrist) may lead to difficulties during the procedure in a small fraction of patients undergoing the procedure. You will be asked to lie flat on the operating table and medications will be given to help you relax. Your provider will administer a subcutaneous local anesthetic injection (to block pain sensation)

as well as vasodilatory medications directly into the artery (to improve its size), during the procedure. A sheath (small tube) will be inserted into the radial artery. Medications are given through the tube to help relax the radial artery, which may cause a temporary burning sensation in the hand and arm. Blood thinners are also administered to help prevent the formation of blood clots within the artery. Then the catheters will be moved through the tube and guided to the heart. A coronary angiogram and, if required, stent placement may be performed. After the completion of the procedure, the catheters and tubes will be removed from the radial artery. An inflatable balloon type device will be placed on your wrist to help stop bleeding. If cardiac catheterization is unsuccessful by transradial approach, a transfemoral approach may be used to complete the cardiac catheterization based on your provider's clinical judgment.

EXPLANATION OF TERMS

- **Cardiac Catheterization** is a procedure that involves passing small catheters through your blood vessels in wrist or groin and injecting contrast dye to study the heart chambers (Ventriculogram) or blood vessels supplying the heart (Coronary Angiogram).

- **Coronary Angiogram** is a study of blood vessels supplying the heart (Coronary arteries). It is done by injecting contrast dye into the blood vessels and studying them with fluoroscopy (A type of imaging study using Xrays). It helps to identify any blockages in the blood vessels supplying the heart. A significant blockage in these arteries can be the cause of chest pain (angina) or heart attack (myocardial infarction).

- **Ventriculogram** is a study of ventricle (heart chamber). It involves injecting dye into the heart chamber and studying its size, shape and function using fluoroscopy.

- **Transfemoral:** Traditionally cardiac catheterization has been done by passing small catheters through the blood vessel in the groin called the Femoral artery. This is called the Transfemoral approach.

- **Transradial:** Cardiac catheterization can also be done by passing small catheters through the blood vessel in the wrist called the Radial artery. This is called the Transradial approach. Compared to transfemoral approach, transradial approach has less complications and patient comfort is more. When performed by providers experienced in transradial approach it is generally considered safer than transfemoral approach. In about 5-10% of the patients, transradial approach can be unsuccessful and a transfemoral approach may be needed.

WHAT ARE MY OTHER CHOICES IF I DO NOT TAKE PART IN THIS STUDY?

If you decide not to take part in this study you may choose to have the usual approach described above.

WHY IS THIS RESEARCH STUDY BEING DONE?

The purpose of this study is to improve the success of cardiac catheterization by transradial approach and increase patient comfort by reducing radial artery spasm. Transradial approach chosen by your provider improves patient comfort and reduces bleeding complications significantly compared to the transfemoral approach (using the artery in the groin). Since the radial artery is smaller than the femoral artery, it is more prone to spasm. Cardiac catheterization by transradial approach may be difficult in some patients and they may need a switch to transfemoral approach to complete the procedure.

This study is designed to look at the possibility of using topical nitroglycerine, a vasodilator, to increase the radial artery size and reduce radial artery spasm. This may:

- increase patient comfort;
- improve success of the transradial approach; and
- avoid the need for switching to transfermoral approach.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

There will be up to 300 people taking part in this study.

WHAT ARE THE STUDY GROUPS?

If you decide to take part in the study, in addition to the above mentioned usual treatment, you will receive topical lidocaine ointment, a local anesthetic (numbing cream), applied on your wrist one hour before the procedure. This may reduce pain felt during the lidocaine injection given as part of usual approach. Additionally, based on your random study assignment you will receive either topical nitroglycerine ointment (a vasodilator) or placebo applied to your wrist. The nitroglycerine may increase size of the radial artery and potentially improve the success of the procedure as well as your comfort during and after the procedure.

EXPLANATION OF TERMS

- **Local anesthetic** is a medication that acts locally on the nerves and blocks pain sensation. This is generally used during procedures involving manipulation of skin and superficial tissues to ensure patients do not experience pain or discomfort during the

procedure. It can be in the form of an ointment applied to the skin or a solution injected into the skin and tissues immediately below the skin.

- **Vasodilator** is a medication that dilates blood vessels.

You will be randomly assigned to one of two groups:

1. Treatment group: Will receive a combination of topical lidocaine and topical nitroglycerine applied to the wrist while waiting in the holding area.

2. Placebo group: Will receive a combination of topical lidocaine and placebo applied to the wrist while waiting in the holding area.

This is a double-blind study; neither you nor your doctor will know what group you are in. After informed consent is obtained, you will be randomized to the treatment group or placebo group. Patients and physicians will be blinded to the administered drug (topical nitroglycerine vs. placebo).

- **Randomization** is a standard procedure used in clinical trials where subjects are assigned by chance to one study group or another. It is used to make sure that the results of the study are not influenced by the selection of subjects/patients in one group as compared to the other. This is important to make certain that study results are accurately interpreted and therefore beneficial to future patients. In this study, you have a 50:50 chance of being assigned to one group or another.
- **Double Blinding** is a process used in clinical trials where neither the person giving the treatment [doing the research] nor the patient [research subject] knows which treatment the patient [research subject] is receiving, or which group the research subject is participating in. It is used in order to make sure that the subject and the person giving the treatment are not influenced by knowledge of the type of treatment that is being used.
- **Placebo** is an inactive substance (with no drug in it, often called a "sugar pill" or "dummy pill") that is compared to a drug in a clinical trial to see if the drug has a real effect. A placebo is often used in clinical trials in order to "blind" the study so that the doctor and the subject cannot be influenced by his/her expectations of the effects of the drug. The study can be "un-blinded" in case of an emergency.

WHAT WILL HAPPEN IF I TAKE PART IN THE STUDY?

Once you agree to participate in the study, you will receive all the standard treatment for cardiac catheterization by transradial approach, as described above.

On the day of the procedure you will report to Ambulatory Cardiac Unit (Same Day Unit) opposite to Cardiac Catheterization Lab in the Bedford building.

As part of standard care, nurses will do the routine pre-procedure evaluation including vital signs, verifying lab data, etc.

As part of the research study a brief ultrasound exam of your radial artery (wrist artery) will be done to measure its size. You will answer a brief 6 question survey to assess your anxiety level before the procedure. Based on the randomized assignment of your treatment, a combination of topical lidocaine (local anesthetic) and nitroglycerine or placebo will be applied to your wrist at least 60 minutes before the procedure.

You will be transferred to the Cardiac Catheterization Lab and the procedure will be done as per standard approach described above. As part of the research study a repeat ultrasound exam of your radial artery (wrist artery) may be done immediately before the beginning of the procedure.

HOW LONG WILL I BE IN THIS STUDY?

You will be part of the study from the time of consent and enrollment, which will take place during your office visit or in the ambulatory cardiac unit (same day unit), until discharge from the Cardiac Catheterization Lab or admission to the inpatient unit after completion of the procedure. If you are hospitalized after your procedure, your participation will end 120 minutes, or 2 hours, after the removal of the TR band or comparable product, which is a compression band placed on your wrist during the procedure.

WHAT EXTRA TESTS WILL I HAVE IF I TAKE PART IN THIS STUDY?

An extra test necessary for this study is the measurement of the size of your radial artery (wrist artery) with a portable ultrasound device. This is a brief noninvasive test done bedside and involves no risk of injury or pain.

WHAT POSSIBLE RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?

There are minimal risks associated with this study such as a drop in your blood pressure and headache. The drop in blood pressure should be mild and easily reversed with removal of the medication and or administration of intravenous (IV) fluids. The risk of drop in blood pressure is lower with topical nitroglycerine compared to the risk with intraarterial nitroglycerine (directly into the artery) given to all patients (both patients enrolled and not enrolled in the study) as part of standard approach. If headache occurs, the patient will be given acetaminophen (Tylenol) for relief.

Pregnancy, Breastfeeding Women, Women of Childbearing Potential, and Contraception

Women who are pregnant or nursing a child cannot participate in this trial. You must confirm, to the best of your knowledge, that you are not now pregnant, that you do not intend to become

pregnant, and that you will use highly effective methods of contraception during study treatment. Highly effective methods of contraception include:

- Total abstinence
- Barrier methods of contraception
- Use of oral, injected, or implanted hormonal methods of contraception or other forms of hormonal contraception that have comparable efficacy
- Placement of an intrauterine device (IUD) or intrauterine system (IUS)
- Female sterilization (have had surgical bilateral oophorectomy with or without hysterectomy) or tubal ligation before taking study treatment.
- Male sterilization (prior to screening).

If you suspect being pregnant during study treatment, you must inform the Study Doctor immediately. You will not be allowed to receive study treatment if you are pregnant.

WHAT POSSIBLE BENEFITS CAN I EXPECT FROM TAKING PART IN THIS STUDY?

Taking part in this study may or may not provide additional benefits.

The treatment group to which you are assigned may prove to be more effective and/or have fewer side effects than the other treatment group(s).

Both treatment and control groups will receive topical lidocaine and you may

- feel less or no pain at the time of lidocaine injection.

Patients in the study group will receive topical nitroglycerine and it may

- improve your comfort during the procedure,
- improve the success of the procedure, and/or
- reduce the need for changing to transfemoral (groin) approach.

CAN I STOP TAKING PART IN THIS STUDY?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. Even if you decide not to continue in the study, no therapy will be withheld, and you will still receive standard treatment, follow–up, and clinical monitoring. In addition, no changes will be made with regard to confidentiality and release of medical information.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

WHAT ARE MY RIGHTS IN THIS STUDY?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

If you have any questions about YOUR RIGHTS AS A RESEARCH SUBJECT, contact the Aultman Health Foundation Human Research Review Board in the Office of Research, 2600 Sixth Street SW, Canton, Ohio 44710 [330-363-6793] [e-mail: HumanResearch.ReviewBoard@aultman.com]. You may also contact them if you feel under any pressure to enroll or continue to participate in this study.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

It is expected that you will not have any additional costs to participate in this study. You will receive topical lidocaine and topical nitroglycerine (or placebo) at no charge. Any tests that are outside the standard of care will be covered by research. All costs not related to the study, including those related to the standard treatment of your disease will be your responsibility.

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

WHAT HAPPENS IF I AM INJURED OR HURT BECAUSE I TOOK PART IN THIS STUDY?

If you feel you have been injured or hurt as a result of taking part in the study, it is important that you contact **24 hour emergency number** at **330-454-8076 immediately.** You will get medical treatment if you are injured or hurt as a result of taking part in this study.

Immediate and necessary care for research-related adverse events will be provided at Aultman Hospital if you are injured because of participation in this research project. Any costs associated with providing this care not paid for by your insurance will be your responsibility. Aultman Hospital has not arranged to provide compensation for any injury you may suffer as a direct consequence of the non-negligent performance of the procedures described above. However, by signing this form, you do not give up your right to seek payment for harm you receive while participating in this study.

WHO WILL SEE MY MEDICAL INFORMATION?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the

researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations and individuals that may inspect your records. These organizations and individuals are required to make sure your information is kept private. Some of these organizations and individuals are:

- The Human Research Review Board, HRRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The research staff, including the Principal Investigator and Sub-Investigators listed on page one of this document, along with other members of the research team responsible for collecting and analyzing data.
- The Food and Drug Administration

WHERE CAN I GET MORE INFORMATION?

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.

WHO CAN ANSWER MY QUESTIONS ABOUT THIS STUDY?

You can talk to **Dr. Prabhakaran Gopalakrishnan**, the Principal Investigator, about any questions or concerns you have about this study or to report side effects or injuries. Contact **Dr. Prabhakaran Gopalakrishnan** at the telephone number and address listed on the first page.

If you have any questions about COMPENSATION OR MEDICAL TREATMENT FOR RESEARCH-RELATED INJURIES contact the Aultman Health Foundation Human Research Review Board in the Office of Research, 2600 Sixth Street SW, Canton, Ohio 44710 [330-363-6793] [e-mail: HumanResearch.ReviewBoard@aultman.com]

If you have any questions about YOUR RIGHTS AS A RESEARCH SUBJECT, contact the Aultman Health Foundation Human Research Review Board in the Office of Research, 2600 Sixth Street SW, Canton, Ohio 44710 [330-363-6793] [e-mail: HumanResearch.ReviewBoard@aultman.com]. You may also contact them if you feel under any pressure to enroll or continue to participate in this study.

Authorization to Use and/or Disclose (Release) Individually Identifiable Health Information for Research Purposes

You have rights regarding the privacy of your medical information collected prior to and in the course of this research study. These rights are protected by a federal law that requires the Aultman Health Foundation and its affiliated hospitals and clinics, researchers, health care providers and physicians (collectively, "Aultman") to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health and conditions ("protected health information").

Before researchers use or share any health information about you as part of this study, Aultman is required to obtain your authorization. This Authorization helps explain to you how this information will be used or shared with others involved in the study.

- The Aultman Health Foundation and its hospitals, clinics, health-care providers and researchers are required to protect the privacy of your health information.
- You should have received a Notice of Privacy Practices when you received health care services here. If not, let us know and a copy will be given to you. Please carefully review this information. Ask if you have any questions or do not understand any parts of this notice.
- If you agree to take part in this study your health information will be used and shared with others involved in this study. Also, any new health information about you that comes from tests or other parts of this study will be shared with those involved in this study.
- Health information about you that will be used or shared with others involved in this study may include your research record and any health care records at Aultman. For example, this may include your medical records, x-ray or laboratory results. Psychotherapy notes in your health records (if any) will not, however, be shared or used. Use of these notes requires a separate, signed authorization.
- If you decide to participate in this research study, your protected health information will be used and shared with others as explained below.

Purpose of Use and/or Disclosure of Health Information

By signing this form, you are giving permission to Aultman Health Foundation, Aultman Hospital, Cardiovascular Clinical Trials, and all other Aultman Health Foundation affiliated

health care provider organizations to use and/or disclose your health information that individually identifies you for the purposes of the research study ("Study") listed above.

What Health Information May be Used and/or Disclosed?

To do this research study, we need your permission to collect and use some of your health information, or you cannot be in the study. This information may come from questions we ask, forms we ask you to fill out, or your medical record, as described below. We will only collect and use information needed for the study.

Aultman may use and/or disclose your past, present and future records and information as described in the study protocol approved by the Human Research Review Board which may include:

- Lab test results (which may include genetic tests, HIV/AIDS tests and/or tests for other communicable diseases if part of my records)
- Procedure reports
- Hospitalization records
- Operative reports
- Outpatient/Office visits, exams, consultations, phone call records and notes
- Radiology/x-ray images and/or reports
- Registration and billing information
- Emergency room reports
- Medication information including drugs, vitamins, and herbal remedies
- Questionnaires and diaries
- Pathology reports
- Other (describe):

Why will protected health information [PHI] about me be used or shared with others?

The main reasons include:

- To conduct and oversee the research described in the consent document and for all purposes necessary to conduct and ensure the integrity of the study.
- To ensure the research meets legal, institutional, and accreditation requirements; and
- To conduct public health activities (including reporting of adverse events or situations where you or others may be at risk of harm).

Other reasons may include for treatment, payment or health care operations. For example, some medical information produced by this study may become part of your hospital medical record because the information may be necessary for your medical care.

Who will use or share protected health information about me at the Aultman Health Foundation

Those who oversee the study will have access to your information, including:

- Researchers and staff at Aultman will use, share and receive your personal health information for this research study. They will make every reasonable effort to protect the information and keep it confidential.
- The only Aultman Hospital employees allowed to handle your health information are those on the study team, and those on the Aultman Human Research Review Board, the committee that oversees research at Aultman, and Aultman officials who review the research plan and check the research activities to make sure the hospital's rules are followed.
- Authorized Aultman staff not involved in the study may be aware that you are participating in a research study and have access to your information. If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic or physician's office records. As a result, this research information may be seen by authorized members of the Aultman workforce who need to access your medical record in the performance of their duties (for example, to provide treatment, to ensure integrity of the research, accounting or billing matters, etc.)

Will my protected health information be shared with people outside the Aultman Health Foundation?

We may share your information with people who do not work at Aultman Hospital because they planned this study, pay for this study, or work with us on this study. The federal Privacy Rule may no longer protect your health information once it leaves Aultman Hospital. Once your health information has been disclosed, the information may no longer be protected under the laws and regulations that apply to Aultman. The recipients may share the information with others without your permission, if permitted by laws governing them.

There are organizations that may inspect your records for quality assurance and data analysis. These organizations are required to make sure your information is kept private, unless required by law to provide information. For this study, we plan to share information with those doctors, researchers or government representatives working with us on this study at the institutions or companies listed here:

Your health information may also be shared with federal and state agencies that have oversight of the study or to whom access is required under the law. These may include:

- The Food and Drug Administration (FDA).

How long will protected health information about me be used or shared with others?

If you sign this form, we plan to keep your information for 10 years after the research study ends in case we need to check it again for this study.

We will not use your health information for a different study without your permission, or the permission of the Aultman Human Research Review Board. Once all personal identification is removed, the information might be used or released for other purposes without asking you.

May I have access to my medical information that results from my participation in this research study?

In accordance with the Aultman Health Foundation Notices of Privacy Practices document that you have been provided, you are permitted access to information (including information resulting from your participation in this research study) contained within your medical records filed with your health care provider.

During your participation in this study, you will have access to your medical record and any study information that is part of that record.

Statement of Privacy Rights

If you change your and later and do not want us to collect or share your health information, you need to send a letter to the Principal Investigator at the mailing address on the first page. The letter must say that you have changed your mind and do not want the researcher to collect and share your health information. If you change your mind and revoke the authorization, you will not be allowed to continue to participate in the Study.

If you revoke this authorization, Aultman may not continue to use and/or disclose your health information for this Study, except that:

- Your health information that has already been disclosed before you revoked this Authorization cannot be taken back; and
- Aultman and the recipients may continue to use and disclose your health information **already** collected for this research Study for the purposes of maintaining the integrity of the Study, and for regulatory compliance.

You have the right to limit the use and sharing of your PHI, and you have the right to see your medical records and know who else is seeing them.

You have the right to refuse to sign this authorization. You do not have to give this permission for use of your PHI. If you decide not to provide permission, you will not be able to participate in this research study. Your health care outside of the study, payment for your health care, and your health care benefits will not be affected if you choose not to sign this form.

Publication of results or use for teaching purposes

The information from this study may be published in scientific journals or presented at scientific meetings but your identity will be kept strictly confidential. Your name or other identifiers will not be used in any publication or teaching materials without your specific permission.

CONSENT TO PARTICIPATION IN TNT-RASP

By signing my name below, I confirm the following

- I have read (or had read to me) this entire consent document. All of my questions have been answered to my satisfaction.
- The study's purpose, procedures, risks and possible benefits have been explained to me.
- I agree to let the study team use and share the health information and other information gathered for this study.
- I voluntarily agree to participate in this research study. I agree to follow the study procedures as directed. I have been told that I can stop at any time.

IMPORTANT: You will be given a copy of this signed document for your records. A second copy will be kept together with the Investigator's research records on this study. A third copy will be placed in your Aultman Hospital medical record.

Please keep it where you can find it easily. It will help you remember what we discussed today

Research Participant's Name [PRINT]:

Research Participant's Signature: Date/Time

INVESTIGATORS CONFIRMING STATEMENT

I have given this research subject information on the study, which in my opinion is accurate and sufficient for the subject to understand fully the nature, risks and benefits of the study, and the rights of a research subject. There has been no coercion or undue influence.

INVESTIGATOR/INDIVIDUAL OBTAINING CONSENT Date/Time

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