

**Geniculate Artery Embolization for the Treatment of Knee Pain Secondary to
Osteoarthritis**

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University of North Carolina at Chapel Hill

Consent to Participate in a Research Study

Adult Participants

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IRB Study # 16-1969

Title of Study: Geniculate Artery Embolization for the Treatment of Knee Pain Secondary to Osteoarthritis

Principal Investigator: Ari Isaacson

Principal Investigator Department: Heart and Vascular - Vascular Interventional Radiology

Principal Investigator Phone number: (919) 966-4292

Principal Investigator Email Address: ari_isaacson@med.unc.edu

Co-Investigators: Sandeep Bagla, Daniel Del Gaizo, Daniel Nissman, Rachel Piechowiak

Funding Source and/or Sponsor: Boston Scientific Corporation

Study Contact Telephone Number: (919) 966-4997 or (919) 966-6957

Study Contact Email: terry_hartman@med.unc.edu or shanah_kirk@med.unc.edu

What are some general things you should know about research studies?

You are being asked to take part in a research study. To join the study is voluntary. You may refuse to join or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study. You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

The primary aims of this study are to determine if geniculate artery embolization (GAE) will reduce pain and disability (resulting from pain, stiffness and difficulty performing daily activities) caused by knee osteoarthritis (OA). Embolization is a procedure where physicians intentionally block the blood vessels to specific areas of the body to prevent blood flow to that region. By doing this, the decrease in blood flow will decrease the size of the area of interest. In this case, your physician will block the geniculate artery, which is located in the knee, with a goal to decrease the swelling around the knee, resulting in improvement of pain, stiffness, and difficulty performing daily activities from OA. Although embolization is used commonly throughout the body to treat bleeding and tumors, this technique has not yet been proven to improve OA in the knee, making this study experimental.

You are being asked to be in the study because you have moderate to severe pain that occurs in the knee even after at least 3 months of non-surgical therapies like medicines to reduce swelling, physical therapy, muscle strengthening, or injections of medicine, and have arthritis of the knee that has been seen and identified by medical imaging like an MRI or X-ray.

Are there any reasons you should not be in this study?

You should not be in this study if you have any of the following.

1. Current local infection
2. Life expectancy less than 6 months
3. Known advanced atherosclerosis (plaque that builds within the vessels that lead blood to the heart)
4. Rheumatoid or infectious arthritis
5. Prior knee surgery
6. Iodine allergy
7. Kidney disease
8. Inability to tolerate or undergo MRI

How many people will take part in this study?

A total of approximately 20 people will take part in this study, including approximately 10 individuals from UNC.

How long will your part in this study last?

You will be asked to participate for approximately 6 months of follow up. This will include the GAE procedure and all follow up visits. Follow up visits will be scheduled at 1 day, 1 month, 3 months, and 6 months. These visits will either in be in person, over the phone, or via teleconference. They will each last approximately 15 min to 2 hours. Prior to the procedure, you will also undergo some testing so that your physician can plan your procedure. This will include an MRI of the knee, which will last approximately 1 hour.

What will happen if you take part in the study?

During your initial visit, you will undergo the standard work-up for knee OA including a detailed history, physical exam, Western Ontario and McMaster University Osteoarthritis Index (WOMAC) questionnaire, visual analog scale (VAS), a knee radiograph (X-ray), and an MRI of the knee. This visit may be completed before enrolling in the study. If you have had an MRI of your knee within 90 days of the research procedure, you will not be asked to have another MRI of the knee. The WOMAC questionnaire will ask you about your symptoms, stiffness, pain and how it affects your ability to function. The VAS is a scale that will allow us to compare you pain level over time between visits.

Following this visit, you will be asked not to initiate any new pain therapy or escalate current therapy for 1 month prior to the GAE procedure. During this procedure, which is investigational, physicians intentionally block the blood vessels in the knee to prevent blood flow to that region. By doing this, the decrease in blood flow will decrease the size of the area of interest.

You will likely be released from the hospital the same day of your GAE procedure unless a complication arises that requires us to keep you over night. You may be given pain medications that you can take as needed for two weeks or less following your procedure.

After the procedure, you will have 4 follow-up that will be scheduled for 1 day, 1 month, 3 months, and 6 months after the procedure. At these visits, you will complete the WOMAC questionnaire and VAS pain score similar to your initial visit. During your 1 month follow up visit, you will also receive an MRI of the knee. Most of these visits may be conducted in the clinic or by phone or teleconference. However, the MRI will be obtained at the hospital. Additional MRIs may be acquired during follow up visits if they are needed by your physician to guide your care.

What are the possible benefits from being in this study?

Research is designed to benefit society by gaining new knowledge. The benefits to you from being in this

study may be that your pain, stiffness and difficulty performing daily activities associated with OA may decrease. It is also possible that you no longer may require other means to treat your OA such as medications or injections.

What are the possible risks or discomforts involved from being in this study?

There may be uncommon or previously unknown risks. You should report any problems to the research team.

There is a minimal risk of a breach of your confidentiality. In order to minimize this risk, you will not be identified by name in any of our study data. You will be identified by a study ID number. This study ID number will be stored separately to protect your identity.

Procedural discomfort or complications of geniculate artery embolization (GAE): You may experience pain or discomfort in the thigh or knee area where the catheter was placed from the development of bruising or the collection of a small amount of blood under the skin. If the pain or discomfort is severe or does not go away, you should contact your physician. In addition, there is a small risk of developing a skin infection at the thigh or knee.

Non-target embolization resulting in ischemia of the leg, foot, or toes is a rare complication that may occur. Ischemia is a restriction of blood supply to the tissue that results in a lack of oxygen or glucose to those tissues. Non-targeted embolization is where an area outside of the area of interest is embolized (blocked) and the tissue may be irreversibly damaged.

Additional risks that are anticipated but occur infrequently after any procedure that involves the arteries include infection, pain, swelling of clotted blood within the tissues that forms because of a leaking vessel, or a tear in the blood vessels.

The use of the contrast agent during the study treatment procedure has a small chance of causing kidney damage.

Most of these complications resolve themselves without treatment or can be treated with medications that may be taken for a short period of time, such as antibiotics. If a long-term complication occurs, such as tissue loss, you will be referred to the appropriate physicians. Any costs associated with complications will be paid by you and/or your insurance company.

A detailed table is below is included below:

	Risk or Side Effect	Source of Risk or Side Effect	Possible	Less Possible	Rare Event
Potential Risks Associated Study Enrollment &	Discomfort	Blood draw for lab test, or MRI	X		
	Clot in artery or vein, bruising, bleeding, blood clot, or fainting	Blood draw for lab tests		X	
	Anxiety or claustrophobia	MRI scan		X	
	Mental discomfort	Clinical Trial Enrollment			X
	Infection	Blood draw for lab tests			X

Study Procedures	Allergic reaction	MRI contrast injection			X
	Gadolinium contrast adverse reaction (ie. kidney damage or severe skin reaction from contrast agent only reported in patients with kidney dysfunction)	MRI Contrast injection			X
	Confidentiality breach from medical records	Medical Record Keeping			X
	Groin or anesthetic injection causing nerve injury, discomfort, or Pain	Pressure during arterial access and after catheter removed at the leg/femoral artery site	X		
Risks of the GAE Procedure and Postoperative care	Radiation exposure	GAE procedure			X
	Kidney dysfunction	Contrast injected during procedure		X	
	Joint infection	GAE Procedure		X	
	Adverse or allergic reaction	Intravenous contrast agent or medications administered as part of procedure or follow-up care (ie. MRI contrast)		X	
	Tissue damage to muscle, skin or other structure in legs from non-target embolization	GAE procedure			X
	Minor bruising or bleeding	GAE procedure			X
	Bleeding requiring transfusion or surgery	GAE procedure			X
	Joint inflammation related symptoms including pain, stiffness, or limited joint mobility	GAE procedure	X		
	Post-embolization Syndrome, including fever, tiredness, headache, and body aches	GAE procedure		X	
	Internal bleeding, such as gastrointestinal bleeding	Medications taken after the procedure (ie. Ibuprofen)			X
	Infection	Catheter site in the leg/groin			X
	Blood vessel injury or cuts, bruising	Procedure/ Closure device (clip) on the artery			X
	Clot in artery, vein, or lung	GAE procedure and immobility			X
Heart attack	GAE procedure including moderate sedation/sedative medication			X	

	Stroke	GAE procedure including moderate sedation/sedative medication			X
	Disability	GAE procedure including moderate sedation/sedative medication			X
	Death	GAE procedure including moderate sedation/sedative medication			X

Unrelieved or worsening pain in knee: There is a chance that your knee pain may not improve or even worsen after GAE. If this were to occur, you would be permitted to take more pain medication or undergo other pain treatments as needed. In this circumstance, the experimental treatment (GAE) will have failed to achieve the goal of this study.

Duracef or Clindamycin: Along with its needed effects, the antibiotics we use may cause some unwanted effects. Side effects are not likely, but possible. Listed below are those that have been reported. Check with your doctor immediately if any of the following severe side effects occur while taking either antibiotic.

Common side effects of Duricef:

- Diarrhea
- Yeast Infection of Vagina and Vulva

Infrequent side effects of Duricef:

- Burning Stomach
- Feel Like Throwing Up
- Indigestion
- Infection due to the Candida Fungus
- Stomach Cramps
- Throwing Up

Rare side effects of Duricef:

- Abnormal Liver Function Tests (severe)
- Allergic Reaction causing Serum Sickness (severe)
- Clostridium Difficile Bacteria Related Colitis (severe)
- Decrease in the Blood-Clotting Protein Prothrombin (severe)
- Decreased Blood Platelets (severe)
- Deficiency of Granulocytes a Type of White Blood Cell (severe)
- Erythema Multiforme (severe)
- Fever caused by Administration of a Drug (severe)
- Giant Hives (severe)
- Hallucination (severe)
- Hemolytic Anemia (severe)
- Hemorrhage (severe)
- Hepatitis (severe)
- Hives (severe)
- Increased Eosinophils in the Blood (severe)
- Inflammation of the Large Intestine (severe)

- Interstitial Nephritis (severe)
- Itching (severe)
- Kidney Disease (severe)
- Kidney Failure (severe)
- Life Threatening Allergic Reaction (severe)
- Rash (severe)
- Reaction due to an Allergy (severe)
- Seizures (severe)
- Stevens-Johnson Syndrome (severe)
- Yellowing of Skin or Eyes from Bile Flow Problems (severe)
- Confused
- Dizzy
- Feeling Restless
- Genital Itching
- Head Pain
- Joint Pain
- Low Energy
- Numbness and Tingling

Common side effects of clindamycin HCl:

- Clostridium Difficile Bacteria Related Colitis (severe)
- Diarrhea
- Feel Like Throwing Up
- Stomach Cramps
- Throwing Up

Infrequent side effects of clindamycin HCl:

- Decreased Blood Platelets (severe)
- Decreased Neutrophils a Type of White Blood Cell (severe)
- Hives (severe)
- Inflammation of Skin caused by an Allergy (severe)
- Itching (severe)
- Rash (severe)
- Reaction due to an Allergy (severe)
- Redness of Skin (severe)
- Genital Itching
- Thrush
- Yeast Infection of Vagina and Vulva

Rare side effects of clindamycin HCl:

- Abnormal Liver Function Tests (severe)
- Acute Pustular Eruptions on Skin
- Blockage of Normal Bile Flow (severe)
- Deficiency of Granulocytes a Type of White Blood Cell (severe)
- Erythema Multiforme (severe)
- Hepatitis caused by Drugs (severe)
- Increased Eosinophils in the Blood (severe)
- Kidney Disease (severe)
- Life Threatening Allergic Reaction (severe)
- Toxic Epidermal Necrolysis (severe)
- Ulcers of Esophagus (severe)

- Yellowing of Skin or Eyes from Liver Problems (severe)
- Arthritis
- Azotemia
- Discolored Spots and Small Elevations of the Skin

MR Imaging: A standard screening form will be used to ensure that you have no contraindication to MR imaging. If you experience claustrophobia during the imagining, you may immediately stop the scan and exit the magnet. Please let us know if you feel uncomfortable at any time.

Additionally, the very rare complication of thickening or scarring of the skin and internal organs after gadolinium contrast injection, which is known as Nephrogenic systemic fibrosis. This complication has only occurred in patients with severe kidney problems. We exclude individuals from our study that have kidney problems in order to keep the risk to you extremely low.

Radiation: The GAE procedure in this study uses fluoroscopy, which is similar to an X-ray “movie.” Fluoroscopy projects the X-ray images on to a screen so that your physician can see the area of interest using these images during the procedure.

The fluoroscopic procedure used in this study involves exposure to radiation. The estimated additional amount of radiation exposure that you will receive in this study is 0.225 rem (rem is a unit used to measure doses of radiation). For comparison, the average person in the United States receives a radiation exposure of 0.3 rem per year from natural background sources. The radiation dose that you will receive in this study is equivalent to the radiation exposure that everyone receives in 9 months from natural background radiation.

This radiation exposure involves a small risk and is necessary to obtain the information desired. The radiation exposure described here is what you will get from this research study only. It does not include any exposure you may have received or will receive from other tests outside of this study that are a part of your medical care.

If you choose not to be in the study, what other treatment options do you have?

If you decide not to participate in this study, your physician may suggest exercise and education, oral medication, creams, or surgery to replace damaged portions of the joint with a metal, plastic, or ceramic device. Minor symptoms can be managed with medications like Tylenol, Ibuprofen, or Advil.

What if we learn about new findings or information during the study?

You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

How will information about you be protected?

In order to protect your privacy, your information will be stored with a study number that is unique to you. Your information will not be stored with your name or any other identifying information. The file that links your identifiable information with your unique study ID will be stored separately from all research data. Only a limited set of individuals among the research team will have access to your identifiable information.

Participants will not be identified in any report or publication about this study. Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives

of the University, research sponsors, or government agencies (for example, the FDA) for purposes such as quality control or safety.

What will happen if you are injured by this research?

All research involves a chance that something bad might happen to you. This may include the risk of personal injury. In spite of all safety measures, you might develop a reaction or injury from being in this study. If such problems occur, the researchers will help you get medical care, but any costs for the medical care will be billed to you and/or your insurance company. The University of North Carolina at Chapel Hill has not set aside funds to pay you for any such reactions or injuries, or for the related medical care. You do not give up any of your legal rights by signing this form.

What if you want to stop before your part in the study is complete?

You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

Will you receive anything for being in this study?

You will not be compensated for participating in this study.

Will it cost you anything to be in this study?

The experimental procedure and all follow up care will be paid for by the Sponsor. You and your insurance company will be responsible for all initial work-up costs associated with OA. These costs include a physical exam and history, WOMAC questionnaire, VAS questionnaire, and a knee radiograph. Your physician may not order an MRI of your knee as a part of this standard workup. Therefore, the costs associated with an MRI of the knee will be covered by the Sponsor. We will work with you to schedule this MRI. If you had an MRI within the past 90 days for clinical reasons, we will not repeat this scan and you would not be reimbursed for the MRI conducted before enrolling in the study. Please note that your treating physician may include other testing during this initial workup that are clinically indicated based on your medical history that would also be your responsibility. Associated travel costs, including parking and lodging, will also be your responsibility.

Who is sponsoring this study?

This research is funded by Boston Scientific Corporation (the Sponsor). This means that the research team is being paid by the sponsor for doing the study. In addition, Sandeep Bagla, the external site PI, has received money from Boston Scientific Corporation for work that is not part of this study. These activities may include consulting, service on advisory boards, giving speeches, or writing reports.

A review of these financial arrangements was conducted at the University of North Carolina at Chapel Hill. They concluded that the possible benefit to the person(s) listed above is not likely to affect your safety or the scientific quality of the study. If you would like more information, please ask the researchers listed on the first page of this form.

What if you have questions about this study?

You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

What if you have questions about your rights as a research participant?

All research on human volunteers is reviewed by a committee that works to protect your rights and

welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

Signature of Research Participant

Date

Printed Name of Research Participant

Signature of Research Team Member Obtaining Consent

Date

Printed Name of Research Team Member Obtaining Consent