CAROLINAS HEALTHCARE SYSTEM
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

The Effect of Botulinum Toxin Injections on Ankle Dorsiflexion Following Internal Fixation of Pilon Fractures

INTRODUCTION

Drs. Karunakar and his colleagues are asking you to participate in this research study of pilon fractures at OrthoCarolina and Carolinas HealthCare System (CHS). You are being asked to take part because you have a pilon fracture. The purpose of this study is to determine if botulinum toxin type A (Botox) injections at the time of surgery for your injury will improve ankle range-of-motion and functionality. You will be one of approximately 20 people involved in this research project at CHS, and your participation will last for 12 months.

Botox is not Food and Drug Administration (FDA) approved at this time for this particular indication, however it is currently being used "off-label" in a similar manner.

HOW THE STUDY WORKS

If you agree to participate, you will receive an injection of either Botox or saline placebo into your calf muscle while your injury is surgically repaired. You will be assigned by chance (like flipping a coin) to one of the two types of treatment being studied (this is called randomization):

- Group A: Injection Botox into calf muscle in operating room
- Group B: Injection of saline (the placebo or inactive medicine) into your calf muscle in operating room

Neither you, nor your physician will know the contents of the injection. We are using this method because it is not clear at the present time whether Botox improves ankle range-of-motion and functionality. Although you and your doctor will not know which treatment you are receiving, this information can be determined in the event of an emergency.

After you sign this informed consent and agree to be part of the study, the following things will happen:

- You will be assigned one of the two treatments
- You will be asked your demographic information

You will be placed in a splint for 2 weeks to allow your incisions to heal. After 2 weeks, the splint will be removed and you will begin a standardized rehabilitation protocol with stretching and range-of-motion exercises clearly outlined. Physical therapy is not mandated, but is available for patients who request it. You will return for regularly scheduled follow-up appointments with your surgeon to assess your progress consistent with current practices.
At 6 and 12 months following your surgery,

- You will be asked to complete two short questionnaires to assess your quality-of-life and ankle functionality.
- You will also have your ankle range-of-motion measured with a device specifically designed to do so accurately.

You will then undergo the same rehabilitation protocol plan currently used as standard of care for this injury.
At the conclusion of the study, the results of the information we gather will be compared between the two study groups.

RISKS

The study has several risks. First, you may be in the placebo (inactive medicine) group and have no active medicine. Currently, your injury is treated without this medicine and you will be treated exactly how we treat all patients with your injury. Being randomized into the placebo group is the same as not participating in the study at all. Second, it is possible that you will get the new treatment but do less well than you have been doing. Third, because the treatment is new, we may not yet know all of the side effects: something unexpected could happen. The known side effects are:

Likely

- Pain at the injection site
  - You will be asleep for all injections. Any residual pain will be minor if noticeable at all.
- Surrounding muscle weakness
  - Botox can spread in to closely associated muscles. This is a desired effect for this study. You will not begin using your lower leg until well after the effects of Botox have worn off.

Less Likely

- Generalized Weakness (rare)
- Flu-Like Symptoms (rare)
- Allergic Reactions (rare)
- Constipation (rare)
- Urinary Incontinence (rare)

Rare but serious

- Difficulty swallowing (extremely rare)
- Aspiration Pneumonia (extremely rare)
- Anaphylaxis (extremely rare)

As with all medications, side effects may include allergic reaction. Allergic reactions may range from minor itching or rash to major reactions which can result in death. A

serious reaction would occur during your first hospital stay where you can be adequately supported.

Reproductive Risks
Botox has not been studied in pregnant women. For this reason, we are excluding women who are pregnant or without a pregnancy test on file from this study. There is no foreseeable risk for women who become pregnant more than 1 week after the study injections as Botox remains primarily at the site where it is injected. Although systemic spread has been documented, it is very uncommon and cleared from the system in several days.

If you have problems that might be related to the drug, your doctor may "break the code" to find out which group you are in. You would then no longer be in the study, but you would still get $70-$100 per visit for the appointments you have kept**.**

EXCLUSION CRITERIA

- Younger than 18 years of age.
- Significant traumatic brain injury or cognitive disability that would interfere with post-operative rehabilitation and study questionnaires.
- Nerve, vascular, or tendon injury of the lower leg: injury to the tibial or peroneal motor nerves, injury to the posterior tibial artery requiring repair, or laceration of tendons that are involved in plantar flexion or dorsiflexion of the ankle which require repair.
- History of prior lower extremity fracture to the tibia or ankle of the affected limb.
- Incarcerated patients.
- Patients unable or unwilling to return for follow-up examination.
- Pregnant or patients who are breastfeeding.
- History of disease affecting the neuromuscular junction (ex: myasthenia gravis).
- Use of aminoglycoside antibiotics at the time of definitive fixation.
- Ipsilateral foot injury that will impair dorsiflexion exercises: Lisfranc injuries, fractures or dislocations of the talus, calcaneus, navicular, cuboid, cuneiforms, or metatarsals (phalanx fractures or dislocations will not be excluded).
- Patients receiving Botulinum Toxin A for other reasons.
- Patients with a known hypersensitivity to Botulinum Toxin A.
- Gustilo Anderson type III B and C.
- Patients with a weight greater than 115 kg – to ensure proper injection locations.

BENEFITS

This study may or may not improve your condition. The information gained from your case may benefit others with your condition. There is the potential for those in the treatment group to experience improved ankle range-of-motion, but this has never been shown. You should not enter the study with this expectation.

ALTERNATIVE PROCEDURE/TREATMENT

There are no alternative procedures to prevent the loss of ankle range-of-motion for your injury at this time. By participating in this study, you are not forgoing any other treatment options that may be beneficial. The alternative to being in the study is to not participate. This would in no way harm your relationship with your doctor or CHS.

ADDITIONAL COST

There are additional costs associated with receiving Botox injections for this study. You will not be responsible for the cost of Botox injections as these will be paid for by funds from our research grant. You will however be responsible for charges for the cost of care for your injury, as you would if you did not participate in this study.

COMPENSATION

In the event that you are harmed as a direct result of your participation in this study, we will provide or arrange for treatment as necessary. This treatment, as well as other medical expenses, will be billed to you or your insurance company in the usual manner.

You will also be provided financial compensation for your time in completing questionnaires and having your ankle range-of-motion measured. You will receive $70 for your 6-month visit and $100 for your 12-month visit.

WITHDRAWAL

Your participation in this study is completely voluntary. You should feel under no pressure to be in the study. If you decide not to be in the study, it will not in any way harm your relations with your doctors or with Carolinas HealthCare System. You are free to withdraw from the study if you change your mind after entering it. This would not harm your relations with your doctors or Carolinas HealthCare System.

We will tell you about new medical findings that may affect your willingness to continue in the study.

CONFIDENTIALITY:

The records of this study will be kept private. In any sort of report we might publish, we will not include any information that will make it possible to identify a patient. However, your record for this study may be reviewed and/or photocopied by Carolinas HealthCare System, or by representatives of the Food and Drug Administration or other government agencies. To that extent, confidentiality is not absolute. 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.

AUTHORIZATION:

If you wish to take part in this clinical study, you will be asked to sign this consent form. It allows the study sponsor and the study investigator to collect, process and pass on to the sponsor

organizations any relevant personal health information collected from you during the study. These are activities routinely carried out during all clinical studies.

You have been told that personal information about you (including sensitive personal health information, such as your medical history and your racial/ethnic origin if relevant to the study) will be reviewed, collected on a computer database, stored in electronic or manual files, audited, and/or otherwise processed by:

- the clinical study investigators (Karunakar, Cohen, Ellington, Ruffolo, Bosse, Kellam, Sims,Hsu Haines), and research staff
- regulatory or other governmental authorities of the United States and other countries,
- Carolinas HealthCare System employees,
- other persons or agencies as required by law or allowed by federal regulations.

You have been told that your personal data are being collected and processed to:

- check your suitability to take part in the study,
- monitor your treatment with the study medication,
- compare and pool treatment results with those of other subjects in clinical studies.

You have been told that your personal information may be processed within the U.S. or elsewhere in the world or transferred to or from the U.S. for review, processing and/or storage by an associated company or a carefully selected third-party organization. By signing this document, you explicitly consent to the transfer of your personal information, including sensitive personal information, collected during this clinical study, for review, processing and/or storage. Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the Privacy Rule. However, the groups are committed to keeping your personal health confidential.

You may refuse this authorization to transfer your personal information. If you choose not to agree to this authorization, you might be ineligible to participate in the study. If you decide not to sign this authorization, that will not harm your relations with your doctors or with Carolinas HealthCare System.

You have the right to inspect your medical record at any time. Your research record may be unavailable until the conclusion of the study. At that point, it will be available. Please speak with the study doctor if you desire to access your record.

You have been told whenever your personal information is processed; it will be kept confidential and secure, to the best of our ability. It will be used only for the purpose for which it was collected.

This Authorization does not have an expiration date. You have been told that according to the guidelines for good clinical practice, the study investigator and sponsor will keep your personal information for at least 6 years. If you do not withdraw this Authorization in writing, it will remain

in effect indefinitely. If you wish to revoke authorization to use your personal information, you will notify the study doctor, Dr. Karunakar (contact information listed below) in writing. Some of the data obtained from your record prior to your revocation may still be used if considered necessary for the study.

FINANCIAL INTEREST OF INVESTIGATOR

None of the doctors asking you to participate in this study have received or will receive money or other benefits for personal use from the study sponsor. However, the sponsor will give money or other benefits to a research fund, foundation, educational institution, or other organization with which the doctor or study staff is associated.

QUESTIONS

The researchers doing the study at Carolinas HealthCare System are Drs. Karunakar, Cohen, Ellington, Seymour, Hsu, and Ruffolo. You may ask them any questions you have now. If you have questions later, you may contact Dr. Karunakar at:

Department of Orthopaedic Surgery
Carolinas Medical Center
1025 Morehead Medical Dr.
Charlotte, NC 28203
Telephone 704-355-4638

The Institutional Review Board is a group of people who review the research to protect your rights. If you have questions about the conduct of this study or about your rights as a research subject, you may call the chairperson of the Institutional Review Board of Carolinas HealthCare System for information regarding patients' rights in a research study. You can obtain the name and number of this person by calling (704) 355-3158.

CONSENT

I have read the above information. I have asked any questions I had, and those questions have been answered. I agree to be in this study and authorize the use of my personal health information. Dr. Karunakar will give me a copy of this form.

Patient [guardian] Print Name	**Date**	**Time**
Patient [guardian] Signature	**Date**	**Time**
Signature of Person Obtaining Consent	**Date**	**Time**
Investigator Signature	**Date**	**Time**

Identity of representative:
___Next of Kin
___Parent/Guardian
___Healthcare Power of Attorney