Official Title: Blood Flow Restriction Therapy Following Acute Shoulder Injury Patients: Assessment of Efficacy in Return to Activity

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ADVOCATE HEALTH

Wake Forest University School of Medicine

Department of Orthopedic Surgery and Rehabilitation

Blood Flow Restriction Therapy Following Acute Shoulder Injury Patients: Assessment of Efficacy in Return to Activity

Informed Consent Form to Participate in Research

Kristen Nicholson, PhD, Principal Investigator

1. SUMMARY

You are invited to participate in a research study. The purpose of this research study is to assess the efficacy of blood flow restriction (BFR) therapy in patients undergoing non-operative treatment of rotator cuff and biceps tendonitis. You are invited to be in this study because you have been diagnosed with a non-operative rotator cuff and/or biceps tendonitis and have met the inclusion criteria for our study. Your participation in this research will involve 2 additional visits outside those of required physical rehabilitation and last about 1.5 hours each.

Participation in this study will involve undergoing routine physical rehabilitation for treatment of your condition which may involve blood flow restriction therapy, measurement of muscle cross-sectional areas using ultra-sound, strength testing, and taking of blood samples at 3 different time points within the study. All research studies involve some risks. A risk to this study that you should be aware of include those associated with taking of blood samples as well as administration of the blood flow restriction tourniquet. Risks of blood draws include bruising as well as infection at the site of the blood draw. Risks of blood flow restriction tourniquet include development of a blood clot, which could result in breathing complications if the clot travels to the lung. These risks have been minimized by excluding patients with risk factors for blood clots, as well as ensuring that the cuff is inflated to standard measurements that limit this risk. Other risks for tourniquet use include pain and discomfort at the site. However, the standard protocol limits the compression of the tourniquet to 30 second intervals, and there are no reports of persistent pain after sessions. You may or may not benefit from participation in this study.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. There may be other choices available to you. Some other choices may include routine non-operative physical rehabilitation without using a tourniquet, or rest from activity and watchful waiting. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions if you need help deciding whether to join the study. If you have questions, suggestions, or concerns regarding this study or you want to

withdraw from the study please contact the Principal Investigator at Phone: [redacted] Email: [redacted]

If you have any questions, suggestions, or concerns about your rights as a volunteer in this research, you should contact the Chairman of the IRB at [redacted] or the Research Subject Advocate at [redacted].".

2. Introduction

You are invited to be in a research study. Studies help researchers learn new information that may help other people in the future. You are being asked to take part in this study because you have been formally diagnosed with rotator cuff or biceps tendinopathy amenable to treatment with physical rehabilitation. Your participation is voluntary. You do not have to be a part of this study if you do not want to. Please take your time in making your decision if you would like to join. Ask the researchers to explain any words or information in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

This study will take place at Atrium Health Wake Forest Baptist.

3. Why Is This Study Being Done?

The purpose of this research study is to evaluate the effect of BFR therapy has on your shoulder recovery time, shoulder strength, and muscle mass. Additionally, we are attempting to better understand the mechanism of action BFR therapy has on the healing process of your injury.

In this study blood flow restriction therapy in addition to routine physical rehabilitation will be compared to a placebo (i.e. routine physical rehabilitation alone). A placebo is a substance, like a sugar pill, that is not thought to have any effect on your disease or condition. In this study you will either receive physical therapy, with or without the use of a BFR tourniquet. Placebos are used in research studies to see if the drug being studied really does have an effect.

4. Who is Sponsoring this Study?

This study is being sponsored by the Department of Orthopedic Surgery at Atrium Health Wake Forest Baptist. The sponsor is providing money or other support to the researchers to help conduct this study.

5. How Many People Will Take Part in the Study?

Up to 24 people at this research site will take part in this study. Some people may be screened but will not be eligible to participate as they may not qualify to be included in the study.

6. How Long Will I Be in the Study?

You will be in the study from the beginning of physical rehabilitation through 12 months after being cleared for return to sport.

You can stop participating at any time. If you decide to stop participating in the study, we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. There are no serious health consequences for withdrawal from the study. If

you withdraw from the study, you will be encouraged to continue physical rehabilitation for your injury either at the same clinic or elsewhere based on your preference until you are cleared for physical activity by your clinician.

7. What Is Involved 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. You will have a one in two chance of being placed in any group.

The principal investigator will not know which study therapy protocol you are receiving. This is done so that a fair evaluation of results can be made. This information is available to the researchers if needed in an emergency.

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

- Before to beginning rehabilitation, you will undergo muscle mass measurements using ultrasound. Ultrasound will be used to quantify the changes in rotator cuff muscle and distal biceps cross-sectional area before and after therapy.

- On your first day of rehabilitation, upper extremity strength will be measured, and will be compared to your strength half-way through the rehabilitation protocol and once you have been cleared to return to sport.

- Your rehabilitation protocol will be outlined by your physical therapist at Wake Forest Baptist Health. This protocol has been standardized previously by our team for all individuals with your type of shoulder injury. If you are in the study group without BFR therapy, you will be going through therapy using this protocol. If you are in the study group with BFR therapy, you will be going through this protocol in addition to the BFR therapy protocol outlined by your physical therapist at Wake Forest Baptist Health. The standard BFR protocol that is implemented by the Wake Forest physical therapists and recommended by expert opinion involve performing 4 separate exercises during each session. Each exercise will be done 4 consecutive times, starting with 30 repetitions, followed by 15 repetitions performed 3 times. Each set will be separated by 30 seconds break. After the finishing the 4 sets for one specific exercise, the patient will rest for 2 minutes prior to beginning the next 4 sets. In summary, the patient will perform 4 sets of 4 different exercises, perming the following repetitions: 30-15-15-15. While the cuff inflates, it will squeeze your arm in a similar fashion to a blood pressure cuff. Patients will be required to attend 2 physical rehabilitation sessions a week. The BFR therapy protocol will not prolong your treatment, as it is carried out in parallel with your routine rehabilitation schedule.

- Once you have been cleared to return to physical activity by your therapist, we will once again be testing your upper extremity strength, as well as measuring the muscle mass of your shoulder using ultrasound.

- After therapy, we will be following up via electronic questionnaires to evaluate your shoulder function and whether you have remained injury-free. These questionnaires will be sent electronically at 6 and 12 months after you have been cleared for physical activity.

You will have approximately 1 tablespoon of blood withdrawn from a vein twice at the beginning, middle, and end of your rehabilitation. The total amount of blood withdrawn during the study will be approximately 6 tablespoons.

If you agree to participate in this study, some of the samples will be kept and may be used in future research to learn more about other diseases. The sample will be stored and it will be given only to researchers approved by the PI, Dr. Kristen Nicholson. An Institutional Review Board (IRB) must also approve any future research study using your blood sample.

The research that may be performed with your blood sample is not designed to help you specifically. There is no personal benefit to you from taking part in this aspect of the research study. The results of the research performed with your blood will not be given to you or your doctor. The results will not be put in your medical record. The research using your blood sample will not affect your care.

Your blood sample will be used only for research and will not be sold.

Your blood sample will be stored with a unique identifier and will not include any identifiable information about you such as your name, address, telephone number, or social security number. The unique identifier will be a randomly assigned number and only the principal investigator will have access to the code that links the unique identifier to you.

8. WILL I RECEIVE THE RESULTS OF THE STUDY?

Research results that are not clinically relevant will not be disclosed to you.

9. WHAT ARE THE RISKS OF THE STUDY?

Being in this study involves some risk/inconvenience to you. You should discuss the risk of being in this study with the study staff. These can be physical, emotional, financial, or social. Many side effects go away, but sometimes they can be serious, long-lasting, or may never go away. There may be other side effects that we do not know about yet, so be sure to tell the study doctor about any unusual symptoms. Risks and side effects related to BFR therapy are studying include:

- You may experience discomfort, bruising and/or bleeding where the needle is inserted. Occasionally some people become dizzy lightheaded or feel faint. Infection may occur on rare occasions. Frequent donation of blood can result in low iron in your blood (iron deficient anemia). If you donate blood to the American Red Cross, you should talk with the study doctor about whether or not it is safe to do so while participating in this study.

You should not donate blood more than 2 times per week and no more than approximately one pint (about 500 ml) of blood in an eight week period.

- Risks of blood flow restriction tourniquet includes development of a blood clot, which could result in breathing complications if the clot travels to the lung. These risks have been minimized by excluding patients with risk factors for blood clots, as well as ensuring that the cuff is inflated to standard measurements that limit this risk.

- Other risks for tourniquet use include pain and discomfort at the site. However, the standard protocol limits the compression of the tourniquet to 30 second intervals, and there are no reports of persistent pain after sessions.

- There also may be other risks that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

- The benefit of BFR therapy in shoulder injury is unknown. It is possible that by being in the BFR rehabilitation group, your rehabilitation process may be slower than undergoing rehabilitation with BFR included.

- Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

10. 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 benefit to you. We hope the information learned from this study will benefit other people in the future.

Based on experience with BFR therapy in healthy animal and human studies, researchers believe BFR may be as good as standard therapy you could receive without being in the study but with fewer side effects, or it may be of benefit to subjects with your condition. Because individuals respond differently to therapy, no one can know in advance if it will be helpful in your particular case.

11. What Other Choices Are There?

You do not have to be in this study to receive treatment. You should talk to your doctor about all the choices you have. Instead of being in this study, you have these options:

You could be treated with the standard rehabilitation protocol without BFR therapy even if you do not take part in the study.

12. What Are the Costs?

All study costs, including any study medications and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

- BFR tourniquet cuff provided by Atrium Health Wake Forest Baptist:

  Neither you nor your insurance company will be billed for the BFR tourniquet cuff. You and/or your insurance company **will not** be billed for the cost of any BFR procedure(s). Costs for regular physical rehabilitation will be billed to you or your insurance.

13. Will You Be Paid for Participating?

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

14. Will Your Research Records be Confidential?

Your participation in this research and any study records created about your participation will be kept as confidential as possible. The overall results of this study may be presented at scientific or medical meetings or published in scientific journals. Your identity will not be shared unless you give your permission or is required by law to protect you or others.

Your information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity.

A description of this clinical trial will be available on http://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 Web site at any time.

I give permission to Atrium Health, Wake Forest University Health Sciences, and their respective affiliated entities and representatives (including third-party agents if applicable) to contact me by text message at the number I provided to send information, reminders, and to communicate with me about the research study. I understand that I am responsible for the standard text message rate of my carrier. I also understand that text messaging is not a secure form of communication and I accept the risk that individuals not involved in the research study may be able to access the text messages. I also understand that texting is not to be used for emergency situations.

By providing my email address, I give permission for Atrium Health, Wake Forest University Health Sciences, and their respective affiliated entities and representatives (including third-party agents if applicable) to send me information, reminders, and messages about the research study

by email. I understand that these email messages may not be encrypted, and I understand and accept the risks that individuals not involved in the research study may be able to access unencrypted email messages. I also understand that email is not to be used for emergency situations.

15. WHAT IF I AM HARMED FROM BEING IN THE STUDY?

If you get hurt or sick from being in this study, you should seek medical care. Be sure to tell the researcher as soon as possible. You may receive care at Advocate Health. There is no plan to pay for lost income or any non-medical costs that might result from the illness or injury.

Advocate Health - Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for treatment of injuries or illnesses. To the extent research insurance coverage is available under this policy, the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. To the extent research coverage is not available, you or your insurance company may be charged for the costs of medical care. You may receive care at Wake Forest University Baptist Medical Center and/or Atrium Health.

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

16. WHO WILL SEE MY PROTECTED HEALTH INFORMATION?

Who may have access to my information:	***Purpose:***
Any sponsor, including future sponsors, of the study and anyone working on behalf of a sponsor or future sponsor	To oversee the study and make sure the information is correct.
Consultants and employees of Advocate Health – Wake Forest University School of Medicine, including IRB members.	To protect the rights and safety of subjects and make sure the study information is correct.
Organizations that regulate research (such as the FDA, Office for Human Research Protections (OHRP), or similar government agencies in the US and other countries).	To make sure applicable laws are being followed.
Organizations that grant accreditation to hospitals and research programs.	For Advocate Aurora Health to remain accredited.
Monitors, auditors, IRB or other regulatory agencies may be granted direct access to your medical record.	To verify clinical trial procedures or data.

By signing this form, you are giving the researchers permission to use and share your personally identifiable health information. This includes direct access to your medical records.

Please note that the study doctor or study staff may also share personal information about you if required by law (for example, if the study doctor or study staff suspects that you are going to harm someone or yourself, reporting of communicable disease (HIV, hepatitis, tuberculosis, etc.). If you have questions about this, please ask the study doctor.

How will my information be used for this study?
You must authorize the use and sharing of your information by signing this form or you cannot be in the study.

The study principal investigator and study staff will collect, use, and share identifiable health information about you for the following reasons:

- to conduct this research study.
- to review the study, and to check the safety and results of the study.
- to seek government approval of an investigational study drug, vaccine, device or product if such was involved in the trial.
- to assist a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury, or disability, and conducting public health surveillance, investigations, or interventions.

Information used and shared may include:

- information from your medical records related to the research or your routine medical care.
- information collected about you during the research and any follow-up related to study visits, tests, procedures, outcomes, etc.

The collected information may contain your name, address, telephone number, health plan number, date of birth, medical record numbers, dates relating to various medical procedures, and/or other identifying information.

How will my information be kept confidential?
We will keep your personal health information as confidential as possible. Your identity will be protected as required by law and according to any policies described in the study consent form. Researchers may share your information with representatives and agents of the sponsor(s) for the purposes of managing and overseeing the study. Usually, the health information sent to sponsors does not directly identify participants (for example, by name or address). Instead initials and a code number are used. Some personal information, such as date of birth, will usually be included but will not be used to identify you.

Once your information leaves the organization we cannot control how it is used, and the law may not require other groups to protect the privacy of your information.

To maintain the integrity of this research, you might not have access to any health information

developed as part of this study until it is completed. At that point, you generally will have access to your health information.

If this study is designed so that you are intentionally not told what treatment or study intervention you are receiving (called a blinded study), you will not have access to health information in your medical record that was collected as part of this study until those who run the study determine it is no longer necessary to keep you blinded. This usually occurs after everyone in the study has completed study treatment or intervention but can sometimes last until all study data is collected and analyzed.

How do I cancel my authorization?

You can cancel your authorization to use and share your information at any time by writing a letter to the study doctor. If you cancel your authorization, you will not be able to continue in the study. If some aspects of the study were optional, you may cancel your authorization for the optional part(s) of the study and still remain in the main study.

Kristen Nicholson, PhD

[redacted]

If you cancel your authorization, no new information will be collected without your permission. The study doctor and study staff will still be able to use and share your information that has already been collected to maintain the integrity of the study.

When will my authorization expire?

This authorization to use and share your information expires at the end of the research study when data analysis is complete, and study records have been destroyed.

If study information is used for scientific publications or educational purposes, all identifying information will be removed.

17. What Are My Rights as a Research Study Participant?

Taking part in this study is voluntary. You may choose not to take part, or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because your condition worsened, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped. Information that identifies you may be removed from the data or specimens that are collected as part of this study and could be used for future research or shared with others

without additional consent.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

You may be asked to complete a survey about your experiences participating in a research study.

18. WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, Dr. Kristen Nicholson, PhD at [redacted] during normal business hours. After hours and on weekends and holidays, call the after hours' pager. If calling the after hour's pager, dial [redacted] and then enter the pager id number 4313 and press #. You will then enter your telephone number starting with the area code where you wish to be called back at and press # again.

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted] or the Research Subject Advocate at [redacted].

19. Signatures

Subject name: _____

- I have read this form and the research study has been explained to me.
- I have had ample time to consider participation in the study and have been given the chance to ask questions, and my questions have been answered. I have been told who to call if I have more questions.
- I understand the research study and voluntarily agree to be in the research study described above.
- I will receive a copy of this consent form after I sign it. A copy will be put in my medical record and/or study record.
- I am not giving up any of my legal rights by signing this form.
- I agree to follow the investigator's instructions.
- I understand and agree that representatives from the sponsor, regulatory authorities and the institutional review board will be granted direct access to my medical records.
- I understand that I may decide to refuse participation or stop participating at any time without penalty and without affecting the quality of my health care or the relationship with the study doctor.
- I understand that there may be consequences to my withdrawal from the study as noted within this document.
- I understand and agree that personal information about me will be collected in this study and from my medical records, and used and processed (manually and by computer) for the

purposes of the study by the manufacturer of a medical device used in my treatment or any other designated party that is involved in the study (e.g. hospital, study doctor, regulatory authorities, ethics committees).

- If I so choose, I have provided the name of a person to be contacted by the principal investigator in case I cannot be reached for follow-up.

Participant signature Date Time AM/PM

For Site Use only:

My signature below certifies the following:

- The subject has been given enough time and an adequate place to read and review this form.
- All elements of the study, as contained in this document, were explained, and discussed with the subject **before** research-related procedures began.
- The subject has had a chance to ask questions and receive answers about this study.
- The subject expressed understanding of the study.
- The subject/LAR will receive a copy of the signed and dated consent form/authorization.

Name of person obtaining informed consent (print)

Signature of person obtaining informed consent Date Time AM/PM