BROOKE ARMY MEDICAL CENTER
CONSENT TO PARTICIPATE IN RESEARCH

Title: Rotator Cuff Repairs With or Without BioEnthesis ™ Augmentation

Principal Investigator: Andrew Sheean, MD

You may be eligible to take part in this research study. This form gives you important information about the study.

Please take time to carefully review this information. You should talk to the researchers about the research study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or your personal physician) about your potential participation in this research study. You do not have to take part in this study. Participation is voluntary. You may also leave the research study at any time without penalization.

1. KEY INFORMATION:

The purpose of this research is to evaluate the safety and effectiveness of a shoulder repair product, BioEnthesis™, for surgical use in rotator cuff (RC) injuries. BioEnthesis™ is a biological graft (piece of tissue) derived from human cancellous (spongy) bone that provides enhanced strength during RC repair by interconnecting soft and hard tissues. This product has been classified by the United States (U.S.) Food and Drug Administration (FDA) as a human cell, tissue, and cellular and tissue-based product (HCT/P). You do not have to take part in this research. It is your decision. You can also choose to stop participating at any time during the study.

If you volunteer for this research study, you will be randomized to one of two groups, either:

1) Standard of care (SOC) surgical intervention group:
   Participants assigned to the SOC surgical intervention group will receive surgical treatment to repair their RC tear following traditional medicine techniques, which use anchors and sutures.

   - OR -

2) BioEnthesis™ surgical intervention group:
   Participants assigned to the BioEnthesis™ surgical treatment group will receive surgical treatment to repair their RC tear using BioEnthesis™.

This study is blinded, which means you will not know what group you are assigned to until you complete the study at the 12-month follow-up visit. Due to the nature of this study intervention, your surgeon will not be blinded to your study treatment.

If you participate in this study, you will be asked to complete self-report questionnaires and undergo measures of your shoulder function (i.e., strength and range of motion (ROM) testing), and complete magnetic resonance imaging (MRI), as applicable. There are a total of four study visits including: baseline/pre-operative, 3-, 6-, and 12-months post-surgery.

It is possible that you may benefit from participating in this research study since we are testing a new product which may enhance healing. This could include: less pain, faster return to work/active-duty, better shoulder-related outcomes, etc. Additionally, if you undergo the BioEnthesis™ procedure you may have a reduced risk of repeated rotator cuff tear. However, we cannot guarantee that you will directly benefit from your participation in this study.

The main risks from being in this study are the possible risks associated with BioEnthesis™ surgical treatment, including material performance (i.e., the allograft splits, frays, tears during the surgery or fails post-surgery), improper surgical placement, unintended consequences, and adverse reactions (e.g., inflammation from the allograft). Steps to minimize the risks are described later in this consent form.

If you are a biological female of child-bearing age and capacity, you will only be eligible to participate in this study and receive study treatment if you are not currently pregnant. If you become pregnant after enrolling in this study, please notify a study team member.

Your decision will not affect your future care at Brooke Army Medical Center (BAMC). If you decide to take part in this research study, you will be asked to sign this document. Before you sign this document, be sure you understand what the research study is about in all sections of the consent form, including the risks and possible benefits to you.

Please tell the researchers if you are taking part in another research study.

2. WHAT IS THE PURPOSE AND DURATION OF THIS RESEARCH AND WHO WILL TAKE PART?

You are being asked to take part in this research study because you are a DEERS-eligible adult, between the ages of 18-65 (inclusive), and have a rotator cuff tear that is indicated for surgical repair. The purpose of this research study is to learn about the safety and effectiveness of BioEnthesis™ used in surgical interventions to repair RC tears. The duration of participation per visit is about 30-45 minutes. An additional hour may be expected if an MRI is required.

There will be about 100 people taking part in this study overall, with about 50 participants to be enrolled at both BAMC at Walter Reed National Military Medical Center (WRNMMC) over a period of 3 years.

During the study, you will have an initial baseline/pre-operative study visit and up to three (3) in-person follow-up study visits at 3-, 6-, and 12-months post-surgery. Data will be collected during your operative visit, however, this will be done through medical records review and requires no additional time on your behalf.

At the end of this research study, the clinical results, including research results about you, will only be shared with you if they are relevant to your clinical care, and only at the discretion of your attending medical provider (i.e., orthopaedic surgeon).

3. SCREENING PROCESS TO QUALIFY FOR PARTICIPATION IN THIS STUDY

Before you can take part in this study, you will need to have some tests and provide some information so that the Investigator can confirm that you qualify for the study. This is called the "Screening Process." These tests may have been done or this information collected as a part of your regular medical care.

4. WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH?

If you agree to participate in this research, you will be asked to complete the following study procedures after you sign the informed consent and Health Insurance Portability and Accountability (HIPAA) authorization forms:

Baseline Data Collection:

As part of formal screening procedures, your final eligibility status will be confirmed from diagnostic magnetic resonance imaging (MRI) indicating you have an RC tear that is indicated for surgical repair and meets all eligibility criteria. The MRI that you completed as SOC at the time of your injury diagnosis will be accessed and reviewed by a study team member. If you do not meet the required eligibility criteria, you will be formally withdrawn from the study and unable to receive study treatment.

You will be asked complete 3 questionnaires to collect your contact information, demographics, and self-report measures of your current use of medications and your shoulder function and pain. Additionally, you will be asked to complete a brief assessment of your shoulder strength and ROM.

Randomization:

You will be randomly assigned to one of two groups. Randomization is a process like flipping a coin and means you will have a 50% chance of being assigned to either of the groups. Participants assigned to the SOC surgical intervention group will receive surgical treatment to repair their RC tear following traditional medicine techniques, which use anchors and sutures. Participants that are assigned to the BioEnthesis™ surgical treatment group will receive surgical treatment to repair their RC tear using BioEnthesis™.

This research study is a double-blind study, which means that you will not know which study treatment you received until after study completion at your final follow-up visit. Due to the nature of this study intervention, your surgeon will not be blinded to your study treatment. However, the biostatistician and study team members assessing your objective outcome measures (i.e., strength and ROM) will be blinded to the study treatment you received.

Study Intervention:

If you are randomized to the SOC surgical intervention group, you will undergo surgical repair of your RC tear using standard techniques (i.e., sutures and anchors). The surgical intervention received as SOC is not a study-specific research procedure and will not be dictated as such; however, information will be collected from your operative report regarding surgical approach/technique.

If you are assigned to the BioEnthesis™ surgical treatment group, you will receive surgical treatment to repair your RC tear using BioEnthesis™. Your surgeon will place the single-use BioEnthesis™ allograft to interconnect the soft and hard tissues of your RC, and anchors will be

inserted through the graft. Over time, the graft can be expected to integrate with your body tissues and strengthen the connection of your tendon to the bone in your shoulder joint.

If your RC repair fails and you require a revision procedure, you will be promptly unblinded to your treatment group and withdrawn from the study. Your surgeon will perform a revision surgery to repair your RC per SOC procedures.

Follow-Up Data Collection:

3-Month Follow-Up:
You will be asked to complete a brief follow-up questionnaire for your shoulder pain, return to activities, medication use, and shoulder immobilization status. This visit may be completed either in-person or remotely.

6-Month Follow-Up
You will be asked to return to the clinic to complete a follow-up questionnaire for your shoulder pain and function, return to activities, medication use, and shoulder immobilization status. You will also complete follow-up assessments of your shoulder strength and ROM.

12-Month Follow-Up
You will be asked to return to the clinic to complete a follow-up questionnaire for your shoulder pain and function, return to activities, medication use, and shoulder immobilization status. You will complete follow-up assessments of your shoulder strength and ROM. Follow-up diagnostic MRI will be ordered by an authorized medical provider, and you will be asked to complete the appropriate imaging procedures. Once you complete your final study visit, you will be unblinded to the study group you were assigned to. Your study participation will end after the completion of your 12-month follow-up visit.

Medical Record Review:
During the course of your involvement in this study, the study team will complete a chart review of your electronic medical record to collect information regarding your surgery, medical events, adverse events, and overall healthcare resource utilization. A study visit is not required on your behalf.

5. WHAT ARE THE RISKS OR DISCOMFORTS FROM BEING IN THIS RESEARCH?

If you choose to take part in this study, there are risks associated with:

- Diagnostic Imaging:
  Possible risks include: anxiousness from being in a confined space, exposure to loud noises and heat that can cause harm if adequate protection isn't used. There are also additional risks associated with persons with certain metal or electronic devices in the body. Standard procedures for screening for these issues will occur to avoid harm or injury.

- SOC Surgical Treatment:
  The SOC surgical treatment risks are the standard risks associated with rotator cuff surgery. These risks will be discussed with you by your surgeon as part of standard surgical

counseling. If your SOC surgical intervention fails post-surgery, it will be documented; your surgeon will perform a revision surgery to repair your RC per SOC procedures.

- BioEnthesis ™ Surgical Treatment:
  Possible risks from BioEnthesis ™ surgical treatment include: material performance (i.e., the allograft splits, frays, tears during the surgery, or fails post-surgery), improper surgical placement and/or insecure placement of the allograft, unintended consequences, and adverse reactions (e.g., inflammation from the allograft). These risks are largely mitigated by preliminary data analysis and surgical approach. If your BioEnthesis™ allograft fails post-surgery, it will be documented; your surgeon will not implant a second BioEnthesis ™ allograft is this occurs, and instead, you will undergo a second surgery to repair your RC per SOC procedures.

- Physical Exams:
  Follow-up exams may elicit discomfort, however the physical exams included in this study are the same routine physical exams that would be conducted by clinicians during their evaluation of rotator cuff injuries.

- Data Collection:
  Although efforts are made to protect your research study records, there is always a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.

All available measures to minimize risks will be taken in accordance with standard clinic protocols.

BioEnthesis ™ has not been shown to cause birth defects.

There may also be other risks of taking part in this study that we do not yet know about.

6. WHAT ARE THE POSSIBLE BENEFITS FROM THIS RESEARCH?

The possible benefits to you as a research participant in this study include decreased pain, faster return to duty/work, improved function, reduced healthcare utilization, and lower cost of care. Additionally, if you undergo the BioEnthesis™ procedure you may have a reduced risk of repeated rotator cuff tear. However, there is no guarantee that you will benefit from being in this research.

7. WHAT ARE THE ALTERNATIVES TO TAKING PART IN THIS RESEARCH?

There may be other options for treating your rotator cuff tear. Alternative treatments and/or procedures that may be available to you include continuing your current course of treatment and standard of care surgical repair of your rotator cuff tear. You should talk with your personal physician (if applicable) about these options.

Choosing not to take part in this research study is also an option.

There may be other research studies involving experimental treatments that could be helpful to your condition.

8. <u>IS THERE COMPENSATION FOR YOUR PARTICIPATION IN THIS RESEARCH?</u>
Yes, for your participation, you may receive a $50 gift card after each fully completed study visit, up to a maximum of $200. "Fully completed" means completing all aspects of that time point, which may include surveys, objective measures (strength and ROM), and MRI scan, as applicable. The study visits that you may be compensated for include:

1. Baseline/ pre-operative visit ($50),
2. 3-month follow-up visit ($50),
3. 6-month follow-up visit ($50), and
4. 12-month follow-up visit ($50)

Greenphire will act as an agent of The Geneva Foundation to manage the payments for your participation. You will be issued a Greenphire ClinCard card which is a visa debit card that your funds are loaded onto. When a study visit is completed, funds will be approved and loaded onto your card. The funds will be available within approximately 2-5 business days and can be used at your discretion. You will be issued one card for the duration of your participation. If your card is lost, the site can replace it for you-once at no cost. The card will expire within 3 years of distribution.

Payment received as compensation for participation in research is considered taxable income. If your payments exceed $600 in any one calendar year, The Geneva Foundation will file a 1099 (Miscellaneous Income) form. The Geneva Foundation will need to collect certain information about you, on a W-9 including: name, address, date of birth and Social Security Number. All information is stored in a secure fashion.

If you are active duty or a federal employee, you must be on leave or off-duty at the time of your visit to receive compensation.

9. <u>ARE THERE COSTS FOR PARTICIPATING IN THIS RESEARCH?</u>
No, there are no costs to you for taking part in this research study.

10. <u>PRINCIPAL INVESTIGATOR</u> (the person(s) responsible for the scientific and technical direction of the study):
Andrew Sheean, MD
Brooke Army Medical Center
Orthopedic Surgery
3551 Roger Brooke Dr
Fort Sam Houston, TX 78234
210-916-7846
andrew.j.sheean.mil@health.mil

11. <u>STUDY SPONSOR (the organizations or persons who oversee the study and are responsible for analyzing the study data):</u>
As the sponsor of this research, the Department of Defense may have access to your research data in accordance with DoDI 3216.02.

12. SOURCE OF FUNDING:
Research funding is provided from the Department of Defense (DoD) through the Congressionally Directed Medical Research Program (CDMRP).

13. LOCATION OF THE RESEARCH:
Brooke Army Medical Center

14. DISCLOSURE OF FINANCIAL INTERESTS AND OTHER PERSONAL ARRANGEMENTS:
There are no financial interests or other personal arrangements to disclose.

15. WHO WILL SEE MY INFORMATION (PRIVACY) AND HOW WILL IT BE PROTECTED (CONFIDENTIALITY)?
Records of your participation in this research study may only be disclosed in accordance with state and federal law, including the Federal Privacy Act, 5 U.S.C.552a, and its implementing regulations. DD Form 2005, Privacy Act Statement - Military Health Records, contains the Privacy Act Statement for the records. A copy of DD Form 2005 can be given to you upon request, or you can read on-line at: https://www.esd.whs.mil/Portals/54/Documents/DD/forms/dd/dd2005.pdf

The research team will keep your research records. These records may be looked at by staff from the BAMC Research Office, the San Antonio Institutional Review Board (IRB), and the DoD Higher Level Review as part of their duties. These duties include making sure that the research participants are protected. Confidentiality of your records will be protected to the extent possible under existing regulations and laws but cannot be guaranteed.

Procedures to protect the confidentiality of the data in this study include but are not limited to:

- With the exception of the signed consent form, signed HIPAA authorization, master list and intake form, your research data will be identified only by a unique coded study number (and not by your name, social security number, DoD ID, or other protected identifier). The unique coded study number cannot be linked to your name except at the clinic where you complete visits.

- The BAMC research team will maintain a confidential electronic enrollment log (i.e., master list) which matches the unique coded study numbers with participants' names, date of consent, date of birth, and DoD ID number. This enrollment log will be stored separately from all other electronic research data in a secure, password-protected database on a DoD computer and network that requires CAC access.

- All paper research records will be stored in a locked cabinet inside of a locked room accessible only by authorized staff. The BAMC research team will maintain a paper intake form that collects your preferred contact information; this form will be stored separately from your coded research records.

- Your coded study data will be entered into Research Electronic Data Capture (REDCap), a secure, access controlled, and password protected electronic data capture and management

system housed on a DoD server and maintained by the Uniformed Services University (USU) in Bethesda, MD. No identifiable information will be entered into REDCap. Once your coded data is entered in REDCap, it will only be accessible by authorized study team members and oversight officials, the local BAMC research office, the San Antonio IRB, authorized staff from USU, and authorized staff from Musculoskeletal Injury Rehabilitation Research for Operational Readiness (MIRROR), which is based out of the Department of Physical Medicine & Rehabilitation at USU, and is serving as the data coordinating center for this study. Representatives of MIRROR/USU will not have access to your identifiable information.

- The BAMC research team will keep this consent form and your signed HIPAA authorization for six (6) years following study closure. They will keep your coded paper research forms for five (5) years following study closure. The master code list which connects your identity with your unique study code will be destroyed at study closure.

Researchers will make every effort to protect your privacy and confidentiality; however, there are risks of breach of information security and information loss.

If applicable, 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 results. You can search this Web site at any time.

Complete confidentiality cannot be promised for military personnel because information regarding your health may be required to be reported to appropriate medical or command authorities to ensure the proper execution of the military mission, including evaluation of fitness for duty.

Those listed below will have access to your records and agree to safeguard your protected health information by using and disclosing it only as permitted by you in this consent or as directed by state and federal law:

- The members of the research team
- The BAMC Human Research Protection Program (HRPP) Research Office
- The San-Antonio Institutional Review Board (IRB)
- The DoD Higher Level Review
- The United States Food and Drug Administration (FDA)

Information gained from your participation in this research study may be published in literature, discussed for educational purposes, and used generally to further science. You will not be personally identified when your information is shared in these ways; all information will be de-identified.

16. <u>USE OF INFORMATION:</u>

The information that we obtain from you for this study might be used for future studies. We may remove anything that might identify you from the information. If we do so, that information may then be used for future research studies or given to another investigator without getting additional

permission from you. If we do, a review board will decide whether or not we need to get additional permission from you.

If you consent to participate in this research study, your de-identified data, meaning that all of your personal identifiers have been removed, collected as part of this research may be kept for future research studies or given to others for future approved research studies without additional permission from you. ****If you would NOT like your de-identified data collected as part of this research to be kept for possible future research, you should not consent to participate in this research study.****

Your de-identified research data will be securely sent to Musculoskeletal Injury Rehabilitation Research for Operational Readiness (MIRROR) and stored at the Uniformed Services University (USU) alongside other de-identified research data. This de-identified research data will be kept indefinitely, or as long as it is practical to maintain, and may be used in future research studies.

Any future research using your retained data will require a research protocol for the proposed study reviewed and approved by an Institutional Review Board (IRB) (a committee responsible for protecting research participants), an Exempt Determination Official (EDO), or other authorized official responsible for protecting human subjects of research. The data protections for privacy and confidentiality described in this consent form will apply to any future use of your stored data.

Future Use of Identifiable Information:
While this study is ongoing and the master list exists, your data will be coded; this is considered identifying information and can be traced back to you. When the master list is destroyed at study closure, your data will be de-identified; this is considered not identifying information and cannot be traced back to you.

The investigators in this study are asking for your permission to store your *identifiable* data for future use in other research studies. The specifics of these future research studies are unknown at this time, but these studies will frequently be in the area of orthopaedics. You will be provided choices at the end of this consent form to either allow or deny the use of your identifiable data in future research studies.

If you choose to allow researchers to store your identifiable information, your study data will remain coded indefinitely, or as long as it is practical to maintain. When the study master list is destroyed at study closure, your identifiable information from the study master list will be retained and transcribed to a new master list for long-term storage; this includes your name, DOD ID, date of birth, and phone and email contact information. The new master list will be kept in a secure, password-protected document at BAMC, the lead study site, on a computer and network that requires CAC access, and will only be accessible by authorized research staff. This new master list will be maintained by the overall study PI.

17. INCIDENTAL FINDINGS

There is a possibility that while reviewing your test results we may see an abnormality that we did not expect to see in this study. This is what is called an "incidental finding."

We will let you know if we see such an incidental finding. Depending on the type of incidental finding, we may contact you by phone. In the case of a potential serious emergency, the researcher will inform you right away. We will also give information about this incidental finding to your primary doctor or we will refer you to an appropriate doctor for further evaluation.

- An incidental finding may cause you to feel anxious.
- Since an incidental finding will be part of your medical record, you could face greater difficulty in getting health or life insurance.

The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study. These costs would be your responsibility. If you are a DoD beneficiary, you will have access to care through standard Military Health System and TRICARE procedures.

You will not have the option to decline receiving information about an incidental finding.

18. VOLUNTARY PARTICIPATION

The decision to take part in this research study is completely voluntary on your part which means you do not have to take part if you do not want to. You may also leave the research study at any time. If you choose not to take part in this research study or if you leave the study before it is finished, there will be no penalty or loss of benefits to which you are otherwise entitled.

You will be informed if significant new findings develop during the course of this research study that may relate to your decision to continue participation.

19. WHAT HAPPENS IF I WITHDRAW FROM THIS RESEARCH?

Should you choose to withdraw, you must contact the Principal Investigator or a member of the study team in writing via mail or email using the contact information provided in this document.

If you decide to no longer participate in this research study, the researchers may keep and analyze data that was collected during your participation in this study. However, no additional data will be collected after the time of your withdrawal.

If you are receiving treatment as part of this research study, you will no longer be eligible for such research-related treatment. Contact your personal physician to discuss medical treatment for your condition.

Please note that withdrawing your consent to participate in this research does not fully revoke your HIPAA Authorization Form to use/disclose your protected health information. If you do not wish for the study team to continue to collect any health information at all for study purposes, please provide written confirmation at the time of study withdrawal. To make that revocation, please send a letter to the principal investigator as discussed in the HIPAA Authorization Form.

The Principal Investigator of this research study may terminate your participation in this research study at any time if they determine this to be in your best interest, if you are unable to comply with the procedures required, or if you no longer meet eligibility criteria.

20. WHAT HAPPENS IF YOU ARE INJURED AS A RESULT OF THIS RESEARCH?

If you think that you have a research-related injury, notify your Principal Investigator immediately using the contact information in the section below.

If you are injured because of your participation in this research and you are a DoD healthcare beneficiary (e.g., active-duty military, dependent of active-duty military, retiree), you are authorized space-available medical care for your injury within the DoD healthcare system, as long as you remain a DoD healthcare beneficiary. This care includes, but is not limited to, free medical care at DoD hospitals or DoD clinics.

If you are injured because of your participation in this research and you are not a DoD healthcare beneficiary, you are authorized space-available medical care for your injury at a DoD hospital or an DoD clinic; medical care charges for care at a DoD hospital or a DoD clinic will be waived for your research-related injury. If you obtain care for research-related injuries outside of a DoD or DoD hospital or clinic, you will not be reimbursed for those medical expenses.

For DoD healthcare beneficiaries and non-DoD healthcare beneficiaries: Transportation to and from hospitals or clinics will not be provided or paid for by DoD. Unless you are covered by TRICARE, no DoD reimbursement is available if you incur medical expenses to treat research-related injuries. No compensation is available for research-related injuries. You are not waiving any legal rights.

21. CONTACT INFORMATION:

Principal Investigator (PI)

The Principal Investigator or a member of the research staff will be available to answer any questions throughout this study.

Principal Investigator: Andrew Sheean, MD
Phone: 210-916-7846
Mailing Address: 3551 Roger Brooke Drive, Fort Sam Houston, TX 78234

BAMC Human Research Protection Program (HRPP) Office

The Human Research Protection Program Office Point of Contact and/or Human Protections Administrator (HPA) will be available to answer questions or discuss concerns you may have about this research study.

Human Protections Administrator/HRPP POC: Jennifer Sadler
Phone: 210-916-9425

Institutional Review Board (IRB) Office

If you have any questions about your rights as a research participant or if you have concerns or complaints about the research study, please contact the IRB Office at:

San Antonio IRB Office, Brooke Army Medical Center
ATTN: MCHE-ZQ, Department of Quality and Safety
3551 Roger Brooke Drive, Fort Sam Houston, Texas 78234-4504
Phone: 210-916-2598

IF THERE IS ANY PORTION OF THIS DOCUMENT THAT YOU DO NOT UNDERSTAND, ASK THE INVESTIGATOR BEFORE SIGNING. YOU MAY CONSULT WITH YOUR PERSONAL PHYSICIAN OR LEGAL ADVISOR, IF YOU WISH.

A signed and dated copy of this document will be given to you.

Please initial the sentences that reflect your choices, and then sign below:

_____ I do not authorize the storage of my *identifiable* data collected as a part of this study for future use in research studies.

_____ I do authorize the storage of my *identifiable* data collected as a part of this study for future use in research studies.

With regard to future research studies done on stored data that has a link to your personal identity.

_____ I do not wish to be notified by investigators in the event of research findings of potential impact to my family members or myself.

_____ I do wish to be notified by investigators in the event of research findings of potential impact to my family members or myself. I agree that my current principal investigator may use any appropriate identifier to locate me in the future.

SIGNATURE OF PARTICIPANT

By signing below, I agree that I have been provided time to read the information describing the research study in the consent form. The content and meaning of this information has been explained to me. I have been provided with the opportunity to ask questions. I voluntarily consent to participate in this study.

By signing this form, I have not given up any of my legal rights as a research participant.

_____
Printed Name of Participant

_____ _____
Signature of Participant Date

SIGNATURE OF INDIVIDUAL ADMINISTERING CONSENT
(Can only be signed by an investigator or staff approved to administer consent)

_____
Printed Name of Administering Individual

_____ _____
Signature of Administering Individual Date