Written Consent to Participate in a Research Study

Project Title: Biological Response to Platelet-rich Plasma and Corticosteroid Injections
Principal Investigator Name: Dr. James Keeney
IRB Assigned Project Number: 2092036

Key Information About the Study

We request your participation in this study with the goal of figuring out how two different injections that are used to treat patients with knee osteoarthritis, steroid and platelet-rich plasma, may affect a patient's pain and function. Secondarily, we are also interested in knowing how the two types of injections that will be given may affect what happens in your joint cartilage. If you agree to take part in this study, you will receive one of two injection types at your visit. There will be surveys to complete (around 10 questions) about your knee and your overall function. We will ask these same questions on seven separate occasions. In addition, we will ask you to provide blood and urine samples at our clinic before your first knee injection and before any other injection that is needed over the course of the study. During the injections, fluid will be collected from your knee as part of the injection procedure. If you decide to go to surgery to help relieve your pain from osteoarthritis at any point during the study, we ask that we are allowed to collect material from your knee that would be normally discarded as medical waste. Possible benefits of this study include relief of your knee pain and return of function. Steroid injections have been used in injections for over 60 years and have shown to provide symptom relief for patients suffering from osteoarthritis. Platelet-rich plasma injection has over the past decade appeared as another means of reducing pain associated with osteoarthritis. Some possible risks with both injections and drawing blood may include pain, bruising, bleeding, infection, and damage to surrounding structures, such as nerves and blood vessels. Other risks associated with steroid injection include skin discoloration, elevated blood sugar, and allergic reaction. If there is a concern with the risks associated with the study, you should ask your provider for more information about the risk of injection to your specific health conditions.

Please read this form carefully. We encourage you to discuss this study, along with its potential benefits and side effects, with your family, friends, or doctor. Let us know if you have any questions before taking part. The research team can explain words or information that you do not understand. **Research is voluntary and you are not compelled to take part. If you do not wish to take part or choose to start then stop later, there will be no penalty or loss of benefits to which you are otherwise entitled.**

Purpose of the Research

You are being asked to take part in this study because you are experiencing knee pain associated with your osteoarthritis. The purpose of the study is to see how two different injections that are used to treat patients with knee osteoarthritis may affect your pain and function. We are also interested in knowing how the two types of injections affect what happens in your joint cartilage.

The two types of injections that we are using for this study are already being used today to treat patients with osteoarthritis. One of the medications, triamcinolone, is a steroid approved by the

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Food and Drug Administration (FDA) for its use in treating osteoarthritis of the knee. Its effects have been studied thoroughly because of its accessibility. The other medication, platelet-rich plasma (PRP), an injectable made from your own concentrated blood, is being used in an "off-label" manner. "Off-label" means that the FDA has not approved the use of PRP in knee injections for treating knee pain caused by osteoarthritis. In collecting the results of this study, we will better understand its effects on your pain, function, and joint cartilage.

What will happen during the study?

Prior to the first injection, you will be asked to answer approximately 10 questions about your knee and your overall function. To help us understand the effects of the injections, PRP will be compared to steroid injection in two different, randomized study groups.

"Randomize" means that you will be put into a group by chance. It is like flipping a coin or pulling a number from a hat. You will have a one in two chance of being placed into a particular group. A computer program chooses which group you will be assigned to. You and your doctor cannot choose which group you are assigned to.

There will be *70 patients* randomized to one of two treatment groups:

Treatment Groups	First Injection
Steroid Group	Triamcinolone 40 mg/1 mL (Kenalog) injection with 5 mL of 1% lidocaine
PRP Group	Platelet-rich plasma

This study is also "blinded," which means that you will not know which injection you are receiving. If at any time you feel the need to receive an injection for your knee pain, please call to schedule for an evaluation. At this visit, you will be informed of which injection you had received. If it has been greater than 3 months since your last visit, you can choose which type of injection to receive. If before 3 months, options for injection will be based on your initial treatment arm. If you received PRP you will be eligible for a steroid injection if your physician deems it necessary. A discussion is needed with your physician on what may be best to alleviate your pain.

Parts of the study are classified as "research-only" and the cost of these procedures or events will be covered by our research team. There will be parts of the study that are classified as "standard of care," which means they are tests and procedures you would receive without being in this study. These procedures or events will be billed to you or your health insurance company.

If you choose to take part in this study, you will take part in the following surveys, tests, and procedures:

On seven separate occasions during the study, we will ask participants to answer the same questions in the form of a brief (<5 minute) survey. When surveys align with an office visit, the

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questions can be completed at the time of your appointment. At times when an office visit is not needed, surveys can be completed at your convenience and by the method of your choice (e.g., email, telephone).
This will occur:

- Before your first injection
- 2 weeks after injection
- 1 month after injection
- 2 months after injection
- 3 months after injection
- 6 months after injection
- 12 months after injection

1) We will ask you to come in for an office visit at 1 month. The 1 month is classified as research-only and will not billed to you or your health insurance.

2) We will take fluid from your knee joint (as a part of the injection procedure) for assessment before injections are given at the first visit and will aspirate fluid at the 1-month visit. Fluid will be drawn from the knee as part of the procedure if another injection is given during the 12-month study period.

3) We will ask you to provide blood and urine samples at the first- and 1-month visits. These collections are research-only events and not billed to you or your health insurance.

4) If you or your doctor decide that surgery is needed to help relieve your pain from osteoarthritis at any point during the study, we ask you to allow us to collect material from your knee that would be normally discarded as medical waste to help figure out the effects of your earlier injections.

Will you share with me any results or health problems/issues that you learn about me while in the study?

We do not expect to find any clinically relevant results involving your health while collecting and analyzing your blood, urine, and knee tissue.

How long will I be in the study?

If you agree to take part in this study, your participation is expected to last for a period of 12 months after the injection. This time requirement is implemented to give the research team the proper amount of time to gather the information needed to answer our research question. After 12 months, you will be released from the study.

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Are there benefits to taking part in the study?

Potential benefits of taking part in this study include relief of your knee pain and return of your function. Steroid and PRP injections have been shown to provide symptom relief for patients suffering from osteoarthritis. We hope to show a difference in the ability to treat osteoarthritis with steroid and PRP injections, which would help guide future clinical decision-making. Longer term, insurance companies may choose to accept and reimburse for PRP injections.

What are the possible risks of participating in this study?

We do not expect any significant medical risks associated with your treatment. Most of the risk associated with this study is related to piercing the skin by injection with synovial fluid collection and the venous blood draw. These can include the following: pain, bruising, bleeding, infection, and damage to surrounding structures, such as nerves and blood vessels. You may already be familiar with the process of having an injection placed into your knee. The risks of PRP injections include local infection and pain at injection site. The risks of steroid injections include pain at injection site, skin discoloration, elevated blood sugar, infection, cartilage deterioration, and allergic reaction. Synovial fluid collection in this study is part of the injection process and a stand-alone procedure at the 4-week visit. It has the same risk as the risk for injections listed previously. If there is a concern with the risks associated with the study, you are recommended to ask your provider for more information regarding the risks of the injection to your specific health condition. At any point, you have the right to withdraw from the study without recourse.

To help lower these possible risks, only professionally trained individuals will take part in the collection of the specimens. You will also be monitored for 5-10 minutes after injection. We will tell you about any new important information we learn that may affect your decision to continue to take part in this study.

We want you to report any problems that may arise. All noted issues and observation by the investigator/research staff will lead to a physical exam for your safety. If the events meet the criteria for IRB reporting, they will be reported to the IRB within five days.

If any serious problems are noted to be in direct association with the injections or blood draw or there is a change in the study design that leads to your injury, we will notify you immediately to ensure your safety.

What other choices do I have if I do not want to be in this study?

You do not have to be in this study. You can simply choose not to take part. You can look for other research projects you may be interested in instead of this study. The research team can share other options that may be available to you.

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Will I receive compensation for taking part in this study?

You will not be compensated for taking part in this study. It is to be disclosed that exposure from this study may lead to financial benefit for the organization conducting the study. The remote possibility exists for your information gathered from your surveys and specimens may be used for commercial profit, but you will not share in this commercial profit.

Are there any costs for participating in this study?

You should not expect any added costs from taking part in this study. The study will pay for all research tests and procedures. You and/or your health plan/insurance will not be billed for tests and procedures that are done for research-only.

We are applying for a research grant to help cover the costs of PRP injections and to cover all the expenses associated with the blood, urine, joint fluid, and cartilage testing.

The source of funding for the research is a non-profit research fund (Department of Orthopaedic Surgery)

You and/or your health plan/insurance will be billed for everything that is considered standard of care. This includes tests and procedures you would receive without being in this study. Some health plans/insurance companies will not pay for these costs for people who are in research studies. Check with your plan/company to find out what they will pay for.

Standard of care events within study design that will be billed to your insurance:
- Initial office visit
- Any injection after the initial office visit

Other costs to you from being in this study may include testing or treatment for existing or new health conditions, insurance co-payments for doctor visits, transportation, parking, childcare, and/or time off work.

A social worker and financial counselor are available to discuss concerns with you. Please let the research staff know if you would like to visit with them and an appointment will be made.

Please discuss any questions about costs with the researchers before agreeing to take part.

Will information about me be kept private?

The research team is committed to respecting your privacy and keeping your personal information confidential, including health information. We will make every effort to protect your information to the extent allowed by law. All subjects will have a de-identified Subject Study ID number. All subject information in electronic format will be kept in password-protected storage. All subject

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information in paper format will be kept in locked cabinets in a secured suite at the Missouri Orthopedic Institute with access granted only to the designated research personnel.

Data will be stored on the Department of Orthopaedic Surgery shared drive and/or Patient IQ, a HIPAA-compliant cloud-based platform that is contracted with the Department of Orthopaedic Surgery.

The results of this study may be published in a medical book or journal or used for teaching purposes. We will remove all identifying information so it will not be known who provided the information. Your information will be kept as secure as possible to prevent your identity from being shown.

We may share what we collected from you as part of this research, after removing your identifiers, for future research without additional informed consent from you.

We will scan a copy of this consent form into your medical record. We may also record your research information, including the results of tests and procedures, in your medical record if the information could be useful for future treatment.

Permission to Use your Protected Health Information:

State and federal privacy laws, HIPAA (Health Insurance Portability and Accountability), protect the use and release of your health information. If you decide to take part in this study, you also give us your permission to use your private health information, including the health information in your medical records and information that can identify you.

You have the right to refuse to give us your permission for us to use your health information. However, doing so would mean that you could not take part in this study.

Some identifiers about you will be obtained from your health records and are necessary for this research. The identifiers will include your Medical Record Number, Community Medical Record Number (UEI), Name, Date of Birth, Age, Gender, Race, Height, Weight, Body Mass Index, Risk Class (ASA), Telephone number, and Email.

We may share any of this information with the following:

- Authorized members and staff of the University of Missouri Institutional Review Board (IRB).
- Dr. James A. Keeney, (Principal Investigator), other Co-Investigators, and the study staff at the University of Missouri.
- Government agencies and public health authorities, such as the Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS), and the Office for Human Research Protections (OHRP)

Any research information shared with outside entities will not contain your name, address, telephone or social security number, or any other personal identifier unless it is necessary for review or required by law.

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The people who get your health information may not be required by Federal privacy laws (such as the HIPAA Privacy Rule) to protect it. Some of those people may be able to share your information with others without your separate permission. Your permission for us to use and/or release your information will expire at the end of the study unless you cancel your permission in writing.

You can cancel your permission at any time by writing to:
James Keeney, MD
Department of Orthopaedics
Missouri Orthopaedic Institute
1100 Virginia Ave
Columbia, MO 65212

The information we have already collected may still be used for this research study, but we will not collect any more information after we receive your letter.

You will not be allowed to access your protected health information that is obtained or created during this research project until the end of the study.

If you have not already received a copy of the University of Missouri Health Care Privacy Notice, you may request one. If you have any questions or concerns about your privacy rights, you may contact the Privacy Officer at 573-882-9054.

What if I am injured during the study?

It is not the policy of the University of Missouri to compensate human subjects in the event the research results in injury.

The University of Missouri, in fulfilling its public responsibility, has provided medical, professional, and general liability insurance coverage for any injury in the event such injury is caused by the negligence of the University of Missouri, its faculty and staff. The University of Missouri also will provide, within the limitations of the laws of the State of Missouri, facilities and medical attention to subjects who suffer injuries while taking part in the research projects of the University of Missouri.

In the event you have suffered injury as the result of participation in this research program, you are to contact the Risk Management Officer, telephone number 573-882-1181, at the Health Sciences Center, who can review the matter and provide further information. This statement is not to be construed as an admission of liability.

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Where can I get more information about this clinical trial?

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.

Who do I contact if I have questions or concerns?

If you have questions about this study or experience a research-related injury, you can contact the University of Missouri researcher, Dr. James Keeney, at 573-882-6449 or a member of the research team at 573-884-9017

If you have questions about your rights as a research participant, or have problems or complaints, please contact the University of Missouri Institutional Review Board (IRB) at 573-882-3181 or muresearchirb@missouri.edu. The IRB is a group of people who review research studies to make sure the rights and welfare of participants are protected.

If you want to talk privately about any concerns or issues related to your participation, you may contact the Research Participant Advocacy at 888-280-5002 (a free call) or email muresearchrpa@missouri.edu.

Do I get a copy of this consent?

You will receive a copy of this consent for your records.

We appreciate your consideration to take part in this study

Contacts

Privacy Officer: 573-882-9054

Risk Management Officer: 573-882-1181

Dr. James Keeney: 573-882-6449 or 573-884-9017

University of Missouri Institutional Review Board (IRB): 573-882-3181

Research Participant Advocacy: 888-280-5002

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Consent to Participate - Signatures

My initials state my choice about allowing my information/biospecimens to be stored and used for future research:

Yes_____ No_____

By signing my name below, I confirm the following:

• I have read/had read to me this entire consent form.

• All my questions were answered to my satisfaction.

• The study's purpose, procedures, risks, and possible benefits were explained to me.

• I voluntarily agree to take part in this research study. I have been told that I can stop at any time.

Subject's Signature	**Date**

Investigator Authorized to Obtain Consent	**Date**

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