PARTICIPANT INFORMED CONSENT FORM AND AUTHORIZATION TO USE AND DISCLOSE MEDICAL INFORMATION

STUDY TITLE: Bone Marrow Concentrate Intradiscal Injection for Chronic Discogenic Low Back Pain: A Double Blind Randomized Controlled Trial.

PROTOCOL NO: BMC-1788

STUDY DOCTOR: David Levi, M.D.

STUDY SITE: APM Spine and Sports Physicians
1788 Republic Road
Virginia Beach, VA 23544

TELEPHONE: (757) 422-2966

SPONSOR: David Levi M.D.

You are being asked to participate in a medical research study. Your participation in this study is voluntary, meaning that you may or may not choose to take part. To decide whether or not you want to be part of this research, the risks and possible benefits of the study are described in this form so that you can make an informed decision. The process is known as informed consent. This consent form describes the purpose, procedures, possible benefits, and risks of the study. This form explains how medical information will be used and who may see it. You may have a copy of this form to review at your leisure or to ask advice from others.

The study doctor or study staff will answer any questions you may have about this form or about the study. Please read this document carefully and do not hesitate to ask anything about the information. This form may contain words that you do not understand. Please ask the study physician or staff to explain the words or information that you do not understand. After reading the consent form if you would like to participate in the study, you will be asked to sign this form. You will be given a signed copy of your consent form to take home and keep for your records.

BACKGROUND

You are being asked to participate in the study because you have been experiencing low back pain for more than six months and have not experience adequate relief from your current treatment.

Low back pain is a common cause of pain and disability. Low back pain can be caused by different parts of the back, but the disc between the vertebrae, specifically small tears in the outer portion of the discs may be that the main cause of 40-50% of all low back pain. The most common treatment options for low back pain include restricting activity, medications, physical therapy, chiropractic treatment, and steroid injections. Some patients do not experience pain relief from these treatments and may end up having surgery. Surgical options for pain coming from the disc include lumbar fusion and intervertebral disc replacement.

ABOUT THE STUDY PRODUCT

The ideal treatment for low back pain would be to heal the tears in the discs. Researchers want to know if bone marrow concentrate would help to heal these tears. Bone marrow concentrate includes stem cells which may promote growth of new healthy disc tissue.

PURPOSE

In the study, participants will be given a single injection of bone marrow concentrate injection or a placebo injection into one or more intervertebral discs. The purpose of this study is to evaluate the effectiveness and potential side effects of the single injection of bone marrow concentrate into one or more of the intervertebral discs causing chronic low back pain.

Bone marrow concentrate is made by aspirating (removing) approximately 50 mL of bone marrow from the pelvis bone. There is a drill aspiration system that is used in a sterile setting to aspirate the bone marrow from this area. The device used to complete this process is approved by the United States Food and Drug Administration (FDA). Using bone marrow concentrate injection to treat low back pain is investigational, which means doctors do not know if this will work for your pain and it is not approved by the FDA.

Approximately 60 men and women 18 to 55 years of age will participate in the study at one location in the United States.

In order to best determine if a treatment works, it may be compared to a pretend treatment, referred to as a placebo. The placebo treatment is a procedure in which a small amount of normal saline (equivalent to water) will be injected into a muscle in the back. The placebo is not expected to be of benefit or harm to you.

You do not have the choice of whether or not you are in the study treatment group or the placebo group. This will be randomly decided by a computer program. You have a 67% chance of being selected for the bone marrow disc injection and a 33% chance of being assigned to the placebo group. Only the doctor performing the procedure will know to which group you have been assigned. You will not know which procedure that you are receiving.

DURATION

Participation in this study will include a baseline visit, injection visit and follow up visits at 2 weeks post-injection, 4 weeks post-injection, 2 months, 6 months and 12 months post-injection. You may be in this study for 12 months.

PROCEDURES

If you agree to participate in this study you will be asked to read and sign this Participant Informed Consent Form and Authorization to Use and Disclose Medical Information before any study-related procedures are performed.

Baseline Visit

A baseline visit will be done to make sure you are eligible to participate in this study. This visit will take 40-60 minutes. At this visit the following procedures will take place.

- The study doctor or study staff will review your medical history.
- The study doctor or study staff will review your medication history. This includes prescription and over-the-counter medications, vitamins and herbal supplements.
- You will be asked to complete a questionnaire that includes questions about your back pain.
- You will be asked to complete a questionnaire that includes questions about how your back pain affects your normal daily activities.
- If you are a woman who is neither post-menopausal for one year nor surgically sterile, a pregnancy test will be performed.

If you are eligible to participate you will be scheduled for the study injection visit, either Bone Marrow Concentrate (BMC) or placebo procedure. The doctor or physician assistant performing the consent process and follow up visits will not know if you will receive the study treatment or the placebo.

Injection Visit

The injection procedure will last 60-90 minutes. Before the procedure you will be offered a sedative by mouth or IV (intravenous). Pain medicine may be given by IV or alternatively, you may be offered a pain medicine that may be injected into a muscle in the buttocks. The sedative will help you to relax and feel sleepy. The pain medicine will help with the discomfort of the procedure.

You will be asked to lie on your stomach for the bone marrow aspiration. The area for bone marrow aspiration will be cleaned. The area for the aspiration will be numbed using Lidocaine. X-ray will be used for guidance to the posterior iliac spine and the area around the bone will also be numbed. A drill will be placed on the needle to access the bone marrow. You will hear this drill. A little more than 3 tablespoons (50mL) of bone marrow will be aspirated. The needle will be removed and the area cleaned and a bandage placed. The bone marrow will be processed into bone marrow concentrate form, which will take about 15 minutes.

You will be asked again to lie on your stomach for the bone marrow concentrate injection. The area where the needle goes into the skin will be cleaned. Lidocaine will be injected into your skin to numb the area where the needle goes. Throughout the procedure x-ray guidance will be used by the study doctor in order to get correct needle placement into the disc or discs affected. Contrast dye will be used to help the disc tissue to be seen on x-ray. There will be antibiotics mixed into the contrast to help prevent infection. Once the needle has been placed into the disc the BMC will be injected.

Throughout the procedure, your heart rate, blood pressure, breathing will be monitored. If you experience any problems, the study doctor will stop the procedure immediately.

If you have been assigned to the placebo group, the study doctor will not actually perform the bone marrow aspiration. Rather, he will simulate the procedure so it will be difficult for you to tell if it is actually being performed. He will also simulate the discs being injected with the bone marrow concentrate, but no injection into the disc will occur.

After the injection you will be monitored for 30 minutes. During that time, your heart rate, blood pressure and breathing will be monitored every 15 minutes. When the study doctor or study staff determines it is safe for you to leave, you will be discharged from the study clinic and given the following instructions:

- You should not drive or operate machinery for 12 hours following the procedure.
- You should call the study doctor or study staff if you have any bowel or bladder problems, worsening of low back symptoms that last longer than 2 days after the procedure, severe low back pain at any time, new or worsening leg symptoms.
- You will be given written instructions on how to contact the study doctor with 24-hour availability.
- You will be offered a prescription pain medication if you do not already have one.
- You should not engage in any strenuous activities for 2 weeks after the procedure.

Follow up Telephone Calls

The study staff will call you during the week after the injection procedure to see how you are feeling and if you have any side effects. These phone calls will last 3-5 minutes.

Follow up Study Clinic Visits

You will be asked to come to the study clinic for follow up visits 2 weeks, 4 weeks, 2 months, 6 months and 12 months post-injection. These visits will last 5-20 minutes. At these visits you will be asked:

- To tell the study doctor or study staff any symptoms or side effects since your procedure or last visit
- To complete a questionnaire that includes questions about your back pain
- To complete a questionnaire that includes questions about how your back pain affects your normal daily activities
- To complete a questionnaire about prescription and over-the-counter pain medication use

After a 12-month visit, your participation in the study will be complete

POTENTIAL RISKS, SIDE EFFECTS, DISCOMFORTS, INCONVIENCES

While you are participating in this study you may experience side effects. The most common occurring side effects as well as rare, but serious side effects are described below. There may be side effects that are unknown at present time.

You are at risk of experiencing all, some or none of these side effects. Side effects that do occur may vary in severity. Some side effects may be serious, long lasting or permanent.

Risks of the injection procedure are considered the same risks as a discogram and are as follows:

- Pain
- Redness at the injection site
- Because the needle passes close to nerve roots, there is a small risk of nerve damage
- Infection in the disc
- Bowel injury
- Bleeding
- Severe allergic reactions to the contrast dye, local anesthetic, or antimicrobial skin prep. Symptoms of allergic reaction can include a rash, hives, itching and/or difficulty breathing, closing of the throat, swelling of the lips, tongue or face and rarely, death. You will be closely monitored for any of these symptoms. There are trained medical personnel and emergency medicines and equipment at the study center to treat you in the event of a severe allergic reaction. **If you think you are having a severe allergic reaction after you leave the study clinic, call 911 and seek medical attention immediately.**
- Feeling faint or fainting
- Muscle pain
- New or increased pain, numbness or weakness in the legs
- Needle puncture of the disc which may cause the disc to degenerate faster and increase the risk of disc herniation over a 10 year period.
- Decreased breathing rate
- Irregular heart rhythm
- Stroke
- In very rare cases, paralysis or death

Risks of Bone Marrow Concentrate injected into the disc:

- Local soreness at injection and/or aspiration site
- Injury to the disc
- Leaking of the BMC into the epidural space and/or movement into the subarachnoid space which could cause nerve injury or paralysis
- Allergic reaction to the anticoagulant. Symptoms of allergic reaction can include a rash, hives, itching and/or difficulty breathing, closing of the throat, swelling of the lips, tongue or face and rarely, death. You will be closely monitored for any of these symptoms. There are trained medical personnel and emergency medicines and equipment at the study center to treat you in the event of a severe allergic reaction. **If you think you are having a severe allergic reaction after you leave the study clinic, call 911 and seek medical attention immediately.**

Risks of Aspiration of bone marrow:

- Bleeding

- Infection
- Damage to nearby tissues, nerves, blood vessels or organs
- Unlikely risks include injury to the bone itself, including fracture and continued pain in the area.
- Extremely unlikely risks include: paralysis, cardiac arrest, brain damage and/or death

Risks of Placebo bone marrow aspiration:

- Bleeding
- Infection
- Damage to nearby tissues, vessels, nerves or organs

Risks of Placebo bone marrow concentrate injection

- Bleeding
- Infection
- Muscle pain
- Severe allergic reactions to the contrast dye, local anesthetic or antimicrobial skin prep

Risks of venipuncture for IV sedation and IV sedation:

- Bleeding
- Infection
- Nerve injury
- Risks of IV sedation include: low blood pressure, low oxygen level, decrease in respiration, cardiovascular compromise, stroke, severe allergic reaction and death.

You may feel uncomfortable undergoing the BMC procedure.

Women Who Can Get Pregnant or are Breast-feeding

You may not take part in this study if you are breast-feeding, are pregnant, think you may be pregnant, or are trying to get pregnant. If you are pregnant or breast-feeding, there may be risks to you and the baby that are not known at this time.

High doses of radiation can cause changes in a baby's rapidly growing cells. It is possible that these changes could increase a baby's risk of birth defects or certain cancers, such as leukemia. However, the typical dose of radiation associated with a diagnostic x-ray doesn't post this risk. You must avoid getting pregnant in order to take place in this study. Therefore, you must agree to use a medically acceptable method of birth control approved by your study doctor. Medically acceptable methods include oral medication (the pill), an intrauterine device (IUD), a hormonal implant (such as Nexplanon), a hormonal injection (such as Depo-Provera), a hormonal patch (Ortho-Evra), a hormonal vaginal ring (NuvaRing) or a barrier method (such as a condom or diaphragm with spermacide).

It is important for you to tell the study doctor at once if you get pregnant or think that you might be pregnant while you are in the research study. If this happens, the study doctor will discuss with you what you should do. If you get pregnant, you will be asked to stop taking part in the study. You may also be asked questions about your pregnancy and baby.

POTENTIAL BENEFITS

Your back pain may improve, but this cannot be assured. Your condition may stay the same or get worse. Your participation in this study will provide information that may help patients with low back pain in the future.

ALTERNATIVE TREATMENTS

You do not have to participate in this study to receive treatment for your low back pain. Other treatments available include: surgery, medication, physical therapy, steroid injection, other intradiscal treatments such as platelet-rich plasma and alternative or complementary medicine such as acupuncture, or homeopathic remedies. You may also decide not to treat your low back pain. The study doctor will discuss these options and the risks and benefits of each.

NEW INFORMATION

You will be informed in a timely manner of new information that may influence your willingness to continue participation in the study.

COMPENSATION TO YOU

You will not be compensated for the consent or procedure portion of the research study.

There will be compensation for the 3-, 6-, and 12-month follow-up visits/study paperwork visits in the amount of $30.00 per visit.

COST TO YOU

You will not be charged for the bone marrow concentrate aspiration or injection.

Fees for follow up visits will be billed to your insurance carrier. Co-pays for office visits are collected at time of visit. You should check with your insurance company to make sure that your participation in this study does not affect the conditions of your policy.

VOLUNTARY PARTICIPATION/WITHDRAW

Your decision to participate in this study is entirely voluntary. You may elect to receive alternative treatment. You may refuse to participate or withdraw from the study at any time, without penalty or loss of benefits to which you are otherwise entitled. Your ongoing medical care will not be affected by your decision to be in this study or to withdraw from the study. If you

decide to withdraw from the study, please talk to your study doctor to make sure this is done easily.

Your participation may be stopped without your consent by the study doctor or the Sterling Institutional Review Board for any reason. For example, your participation may be stopped if:

- It is deemed to be in the best interest of your health and welfare
- You have a severe allergic reaction or unacceptable side effects
- You have failed instructions

STUDY COMPLICATIONS AND COMPENSATION

Every effort to prevent a study-related injury will be taken by the study doctor and staff. Medical care will be made available to you to treat any physical injury incurred by you as a direct result of the study procedures. In the event you are injured as a direct result of the study in accordance with the study doctor's instructions and the study protocol, you should immediately contact Dr Levi or his staff and emergency treatment will be provided. **You and/or your insurance company or third-party payer will be billed for this treatment.**

However, you do not waive any of your legal rights or release anyone from liability for negligence by signing this document.

CONFIDENTIALITY AND AUTHORIZATION TO COLLECT, USE AND DISCLOSE YOUR MEDICAL INFORMATION

As a part of this research study, records that contain information or data about you and your health may be collected and used. These records may identify you and will be kept as confidential as possible. To the extent permitted by applicable laws and regulations, the records identifying you will not be made publicly available.

Under the privacy laws, you have the right to decide who can use your protected health information (called PHI). When you sign this form, you are saying that you will allow the use of your protected health information for this study.

The information that may be collected about you as part of this research study includes:

- Name
- Address
- Telephone number
- Birth date
- Race
- Sex
- Family medical history
- Allergies
- Medications you take (past and present)
- Results of the study tests and procedures

- Other information from other medical providers, doctors office, clinic and/or hospital

Information collected about you for the study will be kept in a research file that is separate from your medical chart. You will not be able to see your research file until after the study is complete.

The study team will know your identity; however, your records will be labeled using your initials and a code that will be randomly assigned to you. The research staff are the only people who will have access to this code and key.

The following groups may review and use your study information. They may review your study information to make sure it is correct. They may review your information to be sure that the study is being conducted properly.

- The study sponsor (or sponsor representatives such as monitors and/or auditors)
- Sterling Institutional Review Board (IRB)
- The Department of Health and Human Services (DHHS)
- Other doctors and health care professional who are involved in the study.

Your study information may be released to the groups listed above. If your study information is reviewed by these groups, they may need to see your entire medical record. It is possible that your Social Security Number may be included in the records reviewed. Because of this, it cannot be assured that your confidentiality will always be protected. However, this access to your records will be granted without violating your confidentiality to the extent permitted by applicable laws and regulations. By signing this form, you are authorizing this access to your records.

The results of this study, including your information, may also be presented at meetings or in articles written about the study (publications). If the results of the study (including your research or health information) are published, your identity will remain confidential.

This permission (also called an authorization) will have no end date.

You have a right to see your study records; however, you will not be able to see your study records until after the study has ended. You may also take away (or withdraw) your permission for the use of your protected health information at any time. If you choose to withdraw your permission, you must write your study doctor a letter.

The study doctor’s mailing address is:

APM Spine and Sports Physicians
1788 Republic Road
Virginia Beach, VA 23545.

The study doctor will still be able to use the health information collected about you before you withdrew your permission. Information that has already been sent to the sponsor of the study cannot be taken back.

If you withdraw your permission after you have entered the study, you cannot continue participating in the study. If you refuse to give permission or withdraw your permission, your medical care and your relationship with the health care providers at the study center will not be affected.

QUESTIONS

If you have any questions, concerns, or complaints about the research study or you experience a research-related injury; please contact Dr Levi or the research study staff at 757-422-2966.

If you have questions regarding your rights as a research participant, or if you have questions, concerns or complaints about the research, would like information, or would like to offer input, you may contact the Sterling Institutional Review Board Regulatory Department, 6300 Powers Ferry Road Suite 600.Atlanta, Georgia 30339 (mailing address) or at telephone number 1-888-636-1062 (toll free).

PARTICIPATION STATEMENT AND AUTHORIZATION

I will have read the Participant Informed Consent Form and Authorization to Use and Disclose Medical Information and I agree to participate voluntarily in this study. I give my permission to the study doctor to use and disclosed my protected health information as described in the consent form.

I will receive a signed copy of this form, which has 11 pages.

All of my questions have been answered.

I have not waived any of my legal rights by signing this document.

_____
Printed name of Participant

_____ _____
Signature of Participant Date

_____
Printed name of Person Explaining Consent

_____ _____
Signature of Person Explaining Consent Date

_____ _____
Signature of Principal Investigator Date

_____
Printed Name of Witness to Participant Signature*

_____ _____
Signature of Witness to Participant Signature* Date

*A witness is not required unless the subject is unable to read (e.g. blind or illiterate) or unless required by state or local laws or indicated in the protocol. If a witness is present, however, the witness must observe the entire informed consent process.