Long-Term Effectiveness of Walking Training in Patients with Knee Osteoarthritis

NCT02767570

09/29/2019

Title of Study: Long-Term Effectiveness of Walking Training in Patients with Knee Osteoarthritis	
Title of Consent (if different from Study Title):	
Principal Investigator: **Julie A. Kolesar, PhD**	VAMC: VA Palo Alto HCS

Are you participating in any other research studies? _____ yes _____no

PURPOSE OF RESEARCH

You are invited to participate in a research study to investigate novel methods for treating individuals with early to moderate knee osteoarthritis that is isolated to the inside (medial) half of knees. The methods involve training individuals to maintain a consistent angle that their feet point relative to their direction of walking. We hope to learn if these methods provide a long-term benefit in terms reducing pain and improving function. You were selected as a possible participant in this study because you have early or moderate knee pain from osteoarthritis primarily in the medial side of your knees.

This study is being done together by researchers at VA Palo Alto and Stanford University.

This research study will screen/consent up to 400 people, and will enroll up to 100 people with isolated, medial compartment knee osteoarthritis. Enrollment will occur only in the United States, and will require multiple visits to research laboratories at VA Palo Alto Health Care System and Stanford University.

VOLUNTARY PARTICIPATION

Your participation in this study is entirely voluntary. Your decision not to participate will not have any negative effect on you or your medical care. You can decide to participate now, but withdraw your consent later and stop being in the study without any loss of benefits or medical care you are entitled to.

DURATION OF STUDY INVOLVEMENT

Participants will be actively involved in the study for one year with optional follow-up activities in years 2, 3 and 4. During your year of participation you will have eleven visits (see table below) to the Stanford University or to VA Palo Alto for analysis of your walking biomechanics or other related research activities. The time required for each visit will vary, with most visits taking 1.25 hours, but with the longest two visits lasting 3 to 4 hours. Additionally, an MRI scan of the knee will be obtained at the beginning of the study as well as at week 52. Knee X-rays may also be taken at the beginning of the study, and knee X-rays will be required at week 52. Between visits to our research labs, you will be expected to practice a new walking pattern during daily walking activity throughout the course of the year-long intervention.

Optional knee X-rays and MRI scans may be taken during years 2, 3 and 4. Those follow-up X-rays and MRI scans in years 2, 3 and 4, however, are optional and are not required for participation in the study.

Research Visits

Visit	Activity	Approximate Duration
Week 0	Screening and Consenting; Questionnaire; X-ray (if needed);	1.5 hours
Optional	Visit Human Performance Lab to practice treadmill walking	30 minutes
1) Week 1	Gait Analysis; Assign pedometer & smart shoes for one week of use	2.5 hours
2) Week 2	Return pedometer & smart-shoe; MRI; Treadmill walking with gait training	3 hours
3) Week 3	Treadmill walking with gait training	1 hour
4) Week 4	Treadmill walking with gait training	1 hour
5) Week 5	Treadmill walking with gait training	1 hour
6) Week 6	Treadmill walking with gait training	1 hour
7) Week 7	Treadmill walking with gait training; Questionnaire; Assign pedometer & smart shoes for one week use prior to remaining visits	1.25 hours
8) Week 11	Questionnaire; Gait Analysis; Possible refresher gait training	1.25 hours
9) Week 25	Questionnaire; Gait Analysis; Possible refresher gait training	1.25 hours
10) Week 39	Questionnaire; Gait Analysis; Possible refresher gait training	1.25 hours
11) Week 52	Return pedometer and smart shoes; Questionnaire; Gait Analysis; MRI; X-ray	4 hours
12) Month 24 (optional)	MRI; X-ray	2 hours
13) Month 36 (optional)	MRI; X-ray	2 hours
14) Month 48 (optional)	MRI; X-ray	2 hours

PROCEDURES

Initial Study Visit

If you decide to participate in this study, Dr. Kolesar or a member of the study team will schedule an appointment for you to come to our research laboratory, describe the study to you, and answer any of your questions. During your first visit to our laboratory we will assess your eligibility for the study. We will have you complete a questionnaire about the health of your knees and we will have you assign a score to your average knee pain for the previous week. During that visit we will also take an initial set of knee X-rays if needed, and arrange for you to have magnetic resonance images of your knee.

Randomization

There are two groups in this study who will participate in all of the same procedures, with the only difference being the walking modification that each group adopts. 50% of subjects are randomized into each group following the initial study visit.

Subsequent Study Visits

During subsequent visits to our gait laboratory, we will have you walk either over-ground or on a treadmill while we measure and record the biomechanics of your movements. The biomechanical measurements include one or more of the following:

3D Motion Capture – We will place approximately 30 small reflective markers onto your skin to track the movements of your body. A 10-camera motion capture system will capture the three-dimensional location of the markers as you walk in order to record your movement patterns.

Force Plate analysis – You will walk across floor-embedded force plates and on an instrumented treadmill capable of measuring the force between your foot and the treadmill belt. The forces we measure will be used in combination with the joint and limb motions to determine internal forces at your ankle, knee, and hip joints.

Electromyography – We may record the electrical activity of your muscles as you walk using electromyography (EMG). Small surface electrodes will be placed onto the skin over 16 muscles of your lower limb. This information is used to determine which muscles are active and the magnitude and duration of their activity.

Vibration Feedback devices – While walking on a treadmill, you may be asked to wear up to four small vibrating devices, called tactors, affixed to your legs, similar to the vibrating motor in a cell phone. These tactors will provide you with feedback about how you walk and give suggestions for how to adopt the target investigational movement pattern.

Other Research Activities & Procedures

Free-Living Walking – During your year of participation, you will be asked to walk at least 20 minutes each day and to try to walk with a consistent angle of your feet relative to your direction of walking. Walking more frequently has been shown to reduce pain and improve walking function in patients with early to moderate knee osteoarthritis, and we believe that walking with a consistent foot angle will enhance that benefit. The walking training plus additional walking that we ask you to do is the investigational component of this study. At several time points in the study for a week at a time we will ask you to use a pedometer to record your walking steps and we may ask you to use a pair of “smart shoes”. The smart shoes look like typical athletic shoes, but they contain a small sensor embedded within the shoes that measures and records your walking characteristics. You will be asked to record your minutes of daily walking activity using an activity log and we will make a copy of your log at each visit.

MRI (Magnetic Resonance Imaging) – MRI machines use a strong magnet and radiofrequency magnetic fields to make images of the body interior. The scanning procedure is very much like an X-ray or CT scan. You will be asked to lie on a long narrow couch for approximately 40 minutes while the machine gathers data. During this time you will not be exposed to X-rays, but rather a strong magnetic field and radiofrequency magnetic fields, which you will not feel. You will, however, hear repetitive tapping noises that arise from the Magnetic Resonance (MR) scanner. We will provide earplugs or headphones that you will be required to wear. The space within the large magnet in which you lie is somewhat confined, although we have taken many steps to relieve the "claustrophobic" feeling. A locker will be provided for you to secure all your items and valuables.

Women of Childbearing Potential

If you are a woman who is able to become pregnant, it is expected that you will use an effective method of birth control to prevent exposing a fetus to a potentially dangerous agent with unknown risk. If you are pregnant or currently breast feeding, you may not participate in this study. You understand that if you are

pregnant, if you become pregnant, or if you are breast-feeding during this study, you or your child may be exposed to an unknown risk.

To confirm to the extent medically possible that you are not pregnant, you agree to begin the study after the onset of your next menstrual period. You must agree to avoid sexual intercourse or use a birth control method judged to be effective by the investigator and which will not interfere with the proposed investigation. You must accept the risk that pregnancy could still result despite the responsible use of reliable method of birth control. You agree to notify the investigator as soon as possible of any failure of proper use of your birth control method, or if you become pregnant, either of which may result in your being withdrawn from the study.

Data Storage for Future Research

As part of this research we may save your data for future research use. Your data will be stored on secure servers at the Palo Alto VA or Stanford University and may be used for future research on musculoskeletal health. Your data will be stored until no longer needed. Your data and information about you will be stored with a code that does not contain your name, initials, SSN, date of birth, or other ways that identify who you are. Any future research using your data will be done for research purposes only and we will not tell you or your doctor about the results of the research.

The research we conduct using your data may result in inventions or discoveries that could be used to make new products or diagnostic or therapeutic agents. You will not receive any money or other benefits from any commercial or other products that are made using your data.

PARTICIPANT RESPONSIBILITIES

As a participant, your responsibilities include:

- Follow the instructions of the investigators and study staff.
- Keep your study appointments. If it is necessary to miss an appointment, please contact the investigators or research study staff to reschedule as soon as you know you will miss the appointment.
- Tell the investigators or research study staff about any side effects, doctor visits, or hospitalizations that you may have.
- Tell the investigators or research staff if you believe you might be pregnant or gotten your partner pregnant.
- Complete your questionnaires as instructed.
- Ask questions as you think of them.

- Tell the investigators or research staff if you change your mind about staying in the study.

WITHDRAWAL FROM STUDY

If you first agree to participate and then you change your mind, you are **free to withdraw** your consent and stop your participation at any time. If you decide to withdraw from the study, you will not lose any benefits to which you would otherwise be entitled [(if applicable) and your decision will not affect your ability to receive medical care for your condition].

If you want to stop being in the study you should tell the investigators or study staff. You can do this by phone by calling Dr. Julie Kolesar at (650) 493-5000 ext. 67677.

If you withdraw from the study, or the study is stopped for any reason, you must return any study-related supplies, such as the pedometer and the smart shoes.

The investigators may also withdraw you from the study without your consent for one or more of the following reasons:

- You do not meet the inclusion/exclusion criteria of the study.
- Failure to follow the instructions of the investigators and/or study staff.
- The investigators decide that continuing your participation could be harmful to you.
- Pregnancy (if applicable).
- You need treatment not allowed in the study.
- The study is cancelled.
- Other administrative reasons.
- Unanticipated circumstances.

POSSIBLE RISKS, DISCOMFORTS, AND INCONVENIENCES

There are risks, discomforts, and inconveniences associated with any research study. These deserve careful thought. The procedures may involve risks that are currently unforeseeable. You should talk with the Protocol Director if you have any questions.

1. *MRI*

   Magnetic fields do not cause harmful effects at the levels used in the MRI machine. However, the MR scanner uses a very strong magnet

that will attract some metals and affect some electronic devices. If you have a cardiac pacemaker or any other biomedical device in or on your body, it is very important that you tell the operator/investigator immediately. As metallic objects may experience a strong attraction to the magnet, it is also very important that you notify the operator of any metal objects (especially surgical clips), devices, or implants that are in or on your body before entering the magnet room. This includes biomedical devices such as pacemakers and aneurysm clips, prostheses, and any other metallic objects embedded in the body such as bullets, buckshot, shrapnel, and any metal fragments from working around metal. All other metallic objects must also be removed from your person prior to entering the magnet room or approaching the magnet to prevent them from becoming a projectile or being pulled by the magnet. This includes keys, jewelry, body piercing, pocket knives, money clips, paper clips, safety pins, hair pins, and barrettes. In addition, objects such as watches, credit cards, and hearing aids could be damaged in the presence of the magnetic field. You will be provided a way to secure these items. If you have any history of head or eye injury involving metal fragments, if you have ever worked in a metal shop, or if you could be pregnant, you should notify the operator/investigator. You should also notify the operator/investigator if you have any tattoos on your body. Tattoos could become warm and irritated during the scan and remain so for several days due to the exposure to the RF electromagnetic field. If you would prefer not to participate in the MR scan due to the presence of tattoos on your body, please inform a research team member. If you are or are trying to get pregnant, the effects of the scan on the fetus are unknown and, therefore, we will not perform the examination at this time.

The scans performed in this study are for specific research purposes and are not optimized to find medical abnormalities. The investigators for this project may not be trained to perform medical diagnosis. The investigators and Stanford are not responsible for failure to find existing abnormalities with these MRI scans. However, on occasion the investigator may notice a finding on an MRI scan that seems abnormal. When this occurs, a physician will be consulted as to whether the findings merits further investigation, in which case the investigator will contact you and your primary care physician and inform you of the finding. The decision as to whether to proceed with further examination or treatment lies solely with you and your physician. The investigators, the consulting physician, and Stanford are not responsible for any

examination or treatment that you undertake based on these findings. Because the images collected in this study may not comprise a proper clinical MRI scan, these images will not be made available for diagnostic purposes.

There is a possibility that you will experience a localized twitching sensation due to the magnetic field changes during the scan. This is expected and should not be painful. Dizziness or nausea may occur if you move your head rapidly within the magnet.

Some of the radio frequency imaging coils, imaging software and devices being used in your scan are not approved by the FDA but are similar to counterparts that have been approved by the FDA. There is a small risk of heating from radiofrequency imaging coils and their cables. Please report any heating sensation immediately. You may have the scan stopped at any time if this occurs.

If you feel discomfort at any time, notify the operator and you can discontinue the exam at any time.

2. *Biomechanics*

   The collection of video, motion capture data, ground reaction forces, and EMG signals are all non-invasive and pose minimal risk to individuals during testing. You might feel some discomfort when the electrodes and markers are removed due to the double sided tape used to attach the markers and electrodes to the skin. There are inherent risks of walking on a treadmill, however they are no greater than the risks of walking on a treadmill at a fitness club.

   If you feel discomfort at any time, notify the operator and you can discontinue the exam at any time.

3. *Knee X-rays*

   The effective radiation dose from the baseline x-ray (4 knee views with a full-leg view) is 53 microSv which is equivalent to less than 7 days of background radiation. The x-rays taken at years 1, 2, 3, and 4 include 4 knee views which is about 4 microSv (12 hours of background radiation) at each time point. If you participate in all 5 time points, you will be exposed to 69 microSv which is equivalent to 8.63 days of background radiation. If you only participate in the baseline and 1 year x-rays, you will be exposed to 57 microSv which is equivalent to 7.13 days of background radiation.

4. *Use of Smart Shoes*

   Wearing the smart shoes poses no greater risk than wearing any new pair of athletic shoes. There is the minor risk of developing a blister if the shoes don't fit properly, however, we will have an assortment of sizes to offer you to provide an acceptable fit. Another minor risk is that the insole will have an arch that is not to your liking, but we will have an assortment of insoles in different sizes and styles if the default arch is uncomfortable.

POTENTIAL BENEFITS

During this study you may experience reduced knee pain from increasing the amount that you walk and/or by changing your walking pattern. Additionally, you may receive a copy of any X-ray image taken for research purposes during this study.

WE CANNOT AND DO NOT GUARANTEE OR PROMISE THAT YOU WILL RECEIVE ANY BENEFITS FROM THIS STUDY.

ALTERNATIVES

The alternative to participating in this study is simply not to participate.

PARTICIPANT'S RIGHTS

You should not feel obligated to agree to participate. Your questions should be answered clearly and to your satisfaction.

You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study.

ClinicalTrials.gov

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 the results. You can search this Web site at any time.

CONFIDENTIALITY

We will keep your name and all the information about you used in this study as confidential as possible. We may publish the results of this study for others to read about, but you will not be identified in any articles about the study by name, social security number, address, telephone number, or any other direct personal identifier. Also, other federal agencies as required, such as the VA Office of Research Oversight and the VA Office of the Inspector General may have access to your information.

Because this study involves an investigational device, the Food and Drug Administration may also have access to information about you collected in this study.

Photographs and/or videos may be taken during data collection sessions if you consent. In any photographs or videos your identity will be concealed by placing a black box over your face. If you do not wish to have photographs or videos taken, this decision will have no impact on the rest of the study.

I consent to being photographed or videoed: Yes_____ No_____

Health Information Portability and Accountability Act (HIPAA)

There are rules to protect your private health information. Federal and state laws and the federal medical law, known as the HIPAA Privacy Rule, also protect your privacy. By signing this form, you provide your permission called your 'authorization,' for the use and disclosure of information protected by the HIPAA Privacy Rule.

How will my health information be used in the study?

In this study we will investigate novel methods for treating individuals with early to moderate knee osteoarthritis that is isolated to the inside half of knees (sometimes called "medial compartment knee OA"). The methods involve training individuals to maintain a consistent angle that their feet point relative to their direction of walking. We expect that individuals participating in the study will have a reduction in knee pain over the course of the 52-week intervention.

What Personal Health Information Will Be Used or Shared?

The following health information about you will be used for this research:

- Medical history and physical examination information
- Progress notes
- Operative reports
- X-ray and MR scans
- Survey/Questionnaire responses
- Photographs, videotapes, other images
- Demographic information such as name, age, race
- Gait analysis data
- Walking pattern & activity records

Who May Use or Share Your Health Information?

By signing this document, you allow the following individuals and entities to obtain, use and share your health information for this research study:

- The Principal Investigator (Dr. Julie Kolesar) and members of the VA research team.
- Departments within the VA Health Care System responsible for the oversight, administration, or conduct of research.
- The Stanford University Administrative Panel on Human Subjects in Medical Research and other Stanford University Officials responsible for the oversight, administration, or conduct of research.

Who May Receive and Use Your Health Information

The investigators may share your health information with the following individuals as part of this research study.

- Stanford University collaborating investigators and research staff.
- The Office for Human Research Protections in the U.S. Department of Health and Human Services
- Other outside individuals or entities hired by the VA Palo Alto Health Care System to do certain work in support of the VA Health Care System
- The Food and Drug Administration

We will protect your health information as required by all laws, however health information shared with others may no longer be protected by Federal laws or regulations and might be shared by the parties above.

Do I have to sign this form?

No. Signing this form is voluntary. The VA may not condition treatment, payment, enrollment or eligibility for benefits based on signing this form. If you decide not to sign the form, you will not be able to take part in this study.

If I sign now, can I decide later not to continue in the study?

Yes. You are free to take back your permission and stop being in the study. The investigators will not collect any more information about you after you take back your permission, but they can continue to use your information that was collected before you took back your permission.

Your request to take back your permission must be done in writing. Either give your written request to the investigator or send it by mail to:
Dr. Julie A. Kolesar
Musculoskeletal Research Laboratory (Mail Code 153); Bldg T6
VA Palo Alto Health Care System

3801 Miranda Avenue
Palo Alto, CA 94394

Does My Permission for the use of my Personal Health Information Expire?

Yes. Your information cannot be used forever. Your permission related to the use and sharing of your health information expires on October 1, 2050.

HIPAA regulations require you to give separate written permission (signature) for the use of your protected health information.

_____ _____
Signature of Participant Date

_____
Print Name of Participant

FINANCIAL CONSIDERATIONS

Payment
You will receive nominal payments of $100 after your week 7, week 25 and week 52 visits. In addition you will receive a $50 completion bonus after your week 52 (1 year) visit.

Payments may only be made to U.S. citizens, legal resident aliens, and those who have a work eligible visa. You may need to provide your social security number to receive payment.

After your final visit (52-weeks of participation) you will also be offered an Omron pedometer to keep. The pedometer has a retail value of approximately $25.You may need to provide your social security number to receive payment.

Costs

You will not have to pay anything to be in this study, although you will have to provide for your own transportation to and from the study visits.

Sponsor
The Department of Veterans Affairs is providing financial support and/or material for this study.

COMPENSATION for Research Related Injury

If you are injured as a direct result of being in this study, medical treatment will be available. If you are eligible for veteran's benefits, the cost of such treatment will be covered by the VA. If not, the cost of such treatments may still be covered by the VA depending on a number of factors. In most circumstances, the treatment must be provided in a VA medical facility. No other form of compensation for injuries is available. However, by signing this form you have not released the VA from liability for negligence. For further information, you may call the Human Protections Administrator at (650) 493-5000, ext. 67593 or the V.A. Regional Counsel at (415) 750-2288.

CONTACT INFORMATION

Questions, Concerns, or Complaints: If you have any questions, concerns or complaints about this research study, its procedures, risks and benefits, or alternative courses of treatment, you should ask the principal investigator, Dr. Julie Kolesar at (650) 493-5000 ext. 67677. You should also contact him/her at any time if you feel you have been hurt by being a part of this study.

Independent Contact: If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a participant, please contact the Stanford Institutional Review Board (IRB) to speak to someone independent of the research team at (650) 723-5244 or toll free at 1-866-680-2906. You can also write to the Stanford IRB, Stanford University, 3000 El Camino Real, Five Palo Alto Square, 4th Floor, Palo Alto, CA 94306.

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

As a research participant you have the following rights. These rights include but are not limited to the participant's right to:

- be informed of the nature and purpose of the experiment;

- be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- be given a description of any attendant discomforts and risks reasonably to be expected;
- be given an explanation of any benefits to the subject reasonably to be expected, if applicable;
- be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
- be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
- be given an opportunity to ask questions concerning the experiment or the procedures involved;
- be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
- be given a copy of the signed and dated consent form; and
- be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

May we contact you about future research studies that may be of interest to you? ____Yes _____ No

May we contact you about the optional MRI and x-ray imaging visits at years 2, 3, and 4? ____Yes _____ No

Would you be interested in learning more about a study that will assess markers of inflammation in your blood at two time points over the course of this study with Protocol Director Dr. Bill Robinson? If so we will pass your name and contact information on to Dr. Robinson's research group. Your response to this question does not affect your participation in the present study. _____Yes _____ No

Signing your name means you agree to be in this study and that you will receive a copy of this signed and dated consent form.

_____ _____
Signature of Participant Date

_____
Print Name of Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Print Name of Person Obtaining Consent

HIPAA regulations require the participant to give separate written permission (signature) for the use of their protected health information.

☐ Confirm the participant signed the VA HIPAA Authorization section of this consent form.