THE UNIVERSITY OF TENNESSEE KNOXVILLE

July 09, 2019

IRB Protocol#: UTK IRB-15-02631-FB
Title: In vivo determination of THA kinematics and sound for subjects for normal, diseased and implanted hips

Richard David Komistek
UTK - College of Engineering - Mech Aero &Biomed Engineering

Dear Richard David Komistek:

The UTK Institutional Review Board (IRB) received a Form 7 indicating the project referenced above has been completed. The original date of approval date for the study is 12/17/2015. The effective date of closure is 07/09/2019. The IRB determined that no further information is required from you for this protocol.

As of the closure date, no further work is authorized by the IRB, including recruitment, consenting, data collection, or analysis of any related data. If this study received funding, no further monies are to be committed as of the closure date. For funded studies, a copy of this letter will be forwarded to the Office of Sponsored Programs.

The IRB determined that no further information is required from you for this protocol.

Sincerely,
Colleen P. Gilrane
Colleen Gilrane, Ph.D.
Chair

In vivo determination of THA kinematics and sound for normal, diseased and implanted hips

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In vivo kinematics and acoustics will be assessed for 20 subjects for this study: 10 normal hips and 10 ten hips will be diseased, requiring a THA and then those same ten diseased hips will be reanalyzed at least six months post-operative after implantation of a THA manufactured by DePuy Synthes by Dr. Charles DeCook of Northside Hospital Forsyth [1200 Northside Forsyth Drive, Cumming, GA 30041]: this is the location from which all study participants will be recruited. Ten subjects will be implanted with a similar surgical technique and will be implanted with either a Summit/Pinnacle THA or Corail/Pinnacle THA. All THAs should be judged clinically successful (Harris Hip Scores HHS> 90 points), without pain, functional deficits, or generalized inflammatory. All subjects must have demonstrated no evidence of post-operative hip subluxation or dislocation. The remaining ten subjects will have normal hips. None of the subjects can walk with a detectable limp and all subjects must be able to actively abduct their operated or healthy hip against gravity without difficulty.

Deciding which patients receive which of the two kinds of implants is up to the discretion of Dr. DeCook, according to his professional opinion. The determination as to which type of implant patients receive is outside the scope of this particular study. Participation in the study is entirely voluntary, and the patient's decision as to whether or not to participate will not impact the type or quality of care provided by the surgeon or his staff.

We will use the following inclusion criteria to recruit participants for the diseased/implanted cohort of this study:

1. Subjects will require a THA and will be implanted with either Summit/Pinnacle THA or Corail/Pinnacle THA by Dr. Charles DeCook.
2. For Phase 2, subjects must be at least six months post-operative with no other surgical procedures conducted within the past six months that will prohibit them from performing the study activities.
3. Subjects must be between 40-85 years of age.
4. Potential subjects will have a body weight of less than 250 lbs.
5. Participants must have Body Mass Index (BMI) of less than 38.
6. Potential subjects' THAs should be judged clinically successful with a HHS >90.
7. Subjects must have demonstrated no evidence of post-operative hip subluxation or dislocation.
8. Subjects must not walk with a detectable limp and must be able to actively abduct their operated hip against gravity without difficulty.

9. Participants must be able to walk on level ground, ascend and descend a ramp and rise from a chair without assistance.
10. Subjects from the physician's list who do not meet the study requirements will not be considered.
11. Subjects must be willing to sign the Informed Consent (IC)/HIPAA form to participate in the study.

Exclusion criteria:

1. Pregnant, potentially pregnant or lactating females. To satisfy radiation protocol, each female subject will be asked if she is pregnant, or possibly could be pregnant. A pregnant person will not be allowed to participate in the study.
2. Subjects without one of the two types of required hip implants.
3. Subjects who have had surgery within the past 6 months that would prohibit them from performing level walking, ascend and descend a ramp and rise from a chair without aid or support of any kind.
4. Subjects who are unable to perform level walking, ascend and descend a ramp and rise from a chair without aid or support.
5. Subjects with pain, functional deficits, or generalized inflammatory.
6. Subjects who walk with a detectable limp.
7. Subjects who cannot actively abduct their operated hip against gravity without difficulty.
8. Subjects who are unwilling to sign IC/HIPAA document.
9. Subjects who have a HHS <90.

*In orthopaedics, the Harris Hip Score (HHS) evaluates clinical outcomes to determine the patient's post-operative results. A patient who receives a HHS score > 90 is considered excellent.

We will use the following inclusion criteria to recruit participants for the normal hip cohort of this study:

1. Subjects must not have any kind of hip implant.
2. Subjects must not have had any type of hip surgery or any pathological hip conditions, including osteoarthritis, or hip pain.
3. Subjects must be between the ages of 18 and 65.
4. Potential subjects will have a body weight of less than 250 lbs.
5. Participants must have BMI of less than 38.
6. Pregnant or potentially pregnant females will be excluded from the study. To satisfy radiation protocol, each female subject will be asked if she is pregnant, or possibly could be pregnant. A pregnant person will not be allowed to participate in the study.
7. Participants must be able to walk on level ground, ascend and descend a ramp and rise from a chair without aid of any kind or have had any kind of surgical procedure within the past 6 months that would affect his/her ability to perform the study activities.
8. Subjects must be willing to sign the IC and HIPAA forms to participate in the study.
9. Subjects must be between 160cm (5'3) and 193cm (6'4) tall.

Exclusion criteria:

1. Pregnant, potentially pregnant or lactating females. To satisfy radiation protocol, each female subject will be asked if she is pregnant, or possibly could be pregnant. A pregnant person will not be allowed to participate in the study
2. Subjects with any kind of hip implant.
3. Subjects who have had any past hip surgery, have pathological hip conditions and/or hip pain.
4. Subjects who have had surgery within the past 6 months that would prohibit them from performing level walking, ascend and descend a ramp and rise from a chair without aid or support of any kind.
5. Subjects who are unable to perform level walking, ascend and descend a ramp and rise from a chair without aid or support.
6. Subjects who are unwilling to sign IC/HIPAA document.

Study locations

Subject Recruitment (both diseased/implanted and normal groups):
Practice of Dr. Charles DeCook:
Northside Hospital- Forsyth
1200 Northside Forsyth Dr.
Cumming, GA 30041

Computer Tomography (CT) scans:
Northside Hospital- Forsyth
1200 Northside Forsyth Dr.
Cumming, GA 30041

Pre-operative, diseased and normal hip fluoroscopic exams performed on all 20 subjects:
Dougherty Engineering Building
The University of Tennessee
1512 Middle Dr.
Knoxville, TN 37996

Post-operative fluoroscopy data collection for implanted subjects performed:
Abercrombie Radiology
Weisgarber Medical Center
1112 Weisgarber Rd.
Knoxville, TN 37909

Analysis will take place at the University of Tennessee's Center for Musculoskeletal Research laboratories:
Science and Engineering Research Facility
1414 Circle Dr.
Knoxville, TN 37996

CMR administrative offices:
Perkins Hall
1506 Middle Dr.

Knoxville, TN 37996

Recruitment and Consenting of Diseased Hip/Implanted Subjects
Dr. DeCook will recommend eligible patients for recruitment that require THA who will be implanted with either the DePuy Summit/Pinnacle THA or Corail/Pinnacle THA. Dr. DeCook's staff will review those patients' medical records to determine if they meet the remaining eligibility requirements for the study according to the study-specific criteria. Dr. DeCook may discuss participation with potentially eligible participants during regularly scheduled office visits or may recommend certain patients who are eligible to his staff who will then contact the patients to explain the study via telephone utilizing a script and inquire as to whether or not they are interested in participating; if a patient is agreeable to participate, s/he will schedule a visit to Dr. DeCook's practice where s/he will be consented by Dr. DeCook's staff. Dr. DeCook will not be present during the consenting process or during any of the procedures to be conducted to avoid possible patient coercion to participate.

Recruitment and Consenting of Normal Hip Subjects
For the ten normal hips, these participants will be recruited from the surgeon's office by means of a displayed recruitment flyer. Potential subjects will be advised per the flyer to contact Dr. DeCook's assistant to inform her of their willingness to participate and schedule a visit to Dr. DeCook's practice to discuss any questions they may have about the study and collect the information from inclusion criteria listed above from the subjects to ensure eligibility requirements are met. After Dr. DeCook's staff has determined eligibility requirements are met, s/he will consent the subject, using the IC/HIPAA as a guide, including the risks and benefits associated with participation and will answer any questions potential subjects may have about participation. Signing this form gives Dr. DeCook's staff the ability to relate the information collected from the normal hip subjects during the consenting visit to UT researchers to aid in the interpretation of the results and correlate clinical outcomes versus kinematic results. After the subject is officially enrolled in the study (i.e., has signed IC/HIPAA form), Dr. DeCook will examine the subject's hip to determine the normalcy of it and s/he will be scheduled for the CT scan.

Procedures
Computer Tomography
Since the normal and diseased, pre-operative hip subjects will undergo a computer tomography (CT) scan of the hip so researchers can create the bone models necessary to analyze the hip data acquired after the fluoroscopy collection. These normal and pre-operative bone models will be compared to the computer-aided designed (CAD) bone models created from data acquired from DePuy's implant-specific information (size, reference and lot numbers), all of which will be used in the analysis of the fluoroscopy and sound data obtained during data collection.

The CT scans for the normal subjects and diseased/pre-operative THA patients will take place at Northside Hospital Forsyth [1200 Northside Forsyth Drive, Cumming, GA 30041] six inches distally on the femur and six inches proximally on the pelvis. The study will be submitted to Northside Hospital's Institutional Review Board for review and approval. After CT scans have been conducted, they will be provided to UT researchers by mail/courier or secure electronic transfer to CMR researchers.

Fluoroscopy Data Collection at the University of Tennessee
Subjects with a normal hip will travel to Knoxville for the fluoroscopy/sound data collection one time, while subjects with a diseased and then implanted hip will travel to Knoxville for data collection twice, once pre-operatively and a second time at least 6 months post-operatively.

In addition to fluoroscopy video, subjects will be videotaped from the torso down (to maintain patient anonymity) while performing the activities (live feed perspective). The speed level of each trial will be based on the comfort level of the subject. Activities will be performed without the aid of handrails; however, one of the researchers will be ready and in close proximity to assist each patient in case the participant requires help. This precaution will be practiced for all participants, regardless of physical wellbeing, age or prior results; no assumptions will be made as to any participant's capabilities.

Subjects will be video-recorded from the waist down while performing the activities while under fluoroscopy surveillance. The speed level of each trial will be based on the comfort level of the patient. The fluoroscopic images will be stored digitally for subsequent analysis on secure servers and workstations at UT. In vivo hip kinematics will be assessed for all 10 normal subjects, the 10 diseased hip/pre-operative subjects who will be assessed again after they have been implanted with THA at least six months post-operatively.

On the day of data collection, there will be at least three UT researchers present to conduct the fluoroscopic evaluations, as well as a State of Tennessee or ARRT certified Radiation Technician (RT) to run the x-ray component of the machine. These three UT researchers, graduate research assistants (GRAs), will be appointed by either Drs. Richard Komistek or William Hamel and will have significant experience with this particular tracking fluoroscope system (TFS).

Fluoroscopy Activity
Normal Gait (walking)

1. With the fluoroscopic unit in the off position (no radiation), the subject will be asked to practice the activity.
2. The subject will begin standing in a resting position and when ready will take a step leading with her/his implanted (or normal in case of normal subjects) hip in focus and proceed to walk at a comfortable pace for approximately 10 paces, or until instructed to stop.
3. Once the subject and researchers are ready to begin after the practice, the subject will return to starting position.
4. The radiation technician (RT) will start the fluoroscopic machine (x-ray on).
5. The subject will perform the gait activity as the mobile fluoroscopy unit tracks the implanted hip.
6. The RT will stop the fluoroscopic procedure after the patient successfully performs the maneuver twice or after two minutes of fluoroscopic "on-time" elapses.

Participants will be asked to practice the activity to ensure they can comfortably complete them and experience no pain with the fluoroscopy machine off (no radiation). The practice portion

without radiation will not be video-recorded. During the fluoroscopy procedure, the implanted hip will be tracked by the mobile fluoroscopy machine and the hip joint is the only area in which radiation will be directed. The subject will perform the activities until successful movements of each activity have been acquired, or a fluoroscopic "on-time" of two minutes is achieved. The participant will be allowed to rest as necessary and be instructed to stop the activities at the first sign of pain.

The fluoroscopic footage for these activities will be stored on digital video files on a computer workstation, and participant information will be removed and replaced with identifiers by researchers selected by Dr. Komistek to lead the study, which will include graduate research assistants and other researchers. All researchers with access to identifiable subject data will sign statements of confidentiality. This de-identified data will then be uploaded onto a secure server. Each participant will be under fluoroscopic surveillance for less than or equal to 2 minutes and only the hip joint (from the fluoroscopy machine) will be recorded on the videotape. Individual still frames will be collected from the fluoroscopic video and these frames will be evaluated for hip sliding or separation. These frames from subject fluoroscopy will be loaded into a database for analysis.

Mobile Tracking Fluoroscopy System (TFS)
The TFS is similar to a standard fluoroscope in that it emits x-rays in a stream that produces a motion picture x-ray of the object in question, in this case, the implanted joint. The difference between the standard fluoroscope and the TFS is that the TFS is motorized with an automatic tracking system that monitors the surrounding environment and itself. This allows the subject to move freely while the implanted joint is accurately tracked by the machine.

The TFS is not currently FDA approved, and each study wherein the machine will be used must be approved by the State of Tennessee for use within the State of Tennessee. Approvals from both the State of Tennessee and the IRBs of UTK and Northside Hospital were acquired for the pre-operative stage of the study.

Sound Data Acquisition
Previously, the Center for Musculoskeletal Research has used in vivo sound sensors to detect sound within the hip and knee joints. These sensors have detected some remarkable sounds for different bearing surfaces that represent variable interactive conditions. Patients with normal knees, degenerative osteoarthritic knees and well-functioning THAs have been analyzed under in vivo conditions using video fluoroscopy and vibration sensors while performing various normal day activities.

For this study, the data capture set-up will consist of video cameras, accelerometers, signal conditioners, a data acquisition system, and a synchronization trigger. Sound/vibration data collection will be performed simultaneously with the fluoroscopic exam to ensure the vibration data completely correlates with the 3D kinematics.

Private Health Information/Medical Record Data
The surgeon and his staff will provide subjects' clinical information from their medical records – PHI – to Dr. Komistek and his researchers to aid in the interpretation of the results and correlate

clinical outcomes versus kinematic results, although only researchers present during data collection or those appointed by Dr. Komistek to lead the study will have access to PHI; they will sign confidentiality statements.

The clinical/demographic information acquired from the medical records with participant authorization obtained as required by HIPAA will include:

- the range-of-motion (pre-operative and 6 months post-operative),
- activity level,
- athletic activities able to perform,
- DOB (or age at time of surgery), body weight, height, Body Mass Index (BMI)
- date of surgery
- pre-operative and post-operative HHS
- previous medical assessments that are not a part of this particular research study, that may alter the kinematic results, such as previous hip x-rays,
- post-operative time and any other conditions that may alter the kinematic results, such as back problems, ankle fusion, or contra-lateral hip problems.

The surgeon's office will also relate the implant component information:

- Size of (including offsets): acetabular cup, acetabular liner, femoral stem, femoral head
- Product/Reference # of: acetabular cup, acetabular liner, femoral stem, femoral head
- Lot # of: acetabular cup, acetabular liner, femoral stem, femoral head

The subject data – fluoroscopy frames, video footage, and sound – will be de-identified by the researcher(s) who attend data collection or appointed by Dr. Komistek and then stored on CMR's secure server for use in future studies (if participant permission is obtained via IC); the individuals not indicated as Investigators with access to PHI will sign a pledges of confidentiality. Researchers would like to retain this de-identified data in our secure database so as to continue to add relevant, current data to our digital collection to help us work with manufacturers in the future to create better implants that last longer and will not require revision surgery. Participants will be asked if their de-identified data may remain a part of the CMR data collection for use in future studies in the IC. Likewise, should a patient choose to withdraw from the study, s/he will have the option as to whether or not data collected from them at the point of withdrawal may be used for data analysis or if their information should be provided to them and destroyed from CMR records; patients choosing to withdraw will be asked to complete a Revocation of Consent wherein they may indicate their preference regarding the data collected from them.

Participant Confidentiality

The investigators will ensure subject confidentiality is maintained throughout the study and after. Researchers not notated as Investigators of this study that have access to PHI will sign pledges of confidentiality.

Hard Copy:

In compliance with HIPAA regulations, all participants will have their identities withheld from all public files. Individuals not indicated as investigators below will have access to participant information and they will sign pledges of confidentiality. The personnel in the following list will have access to private participant information:

List of Persons Involved in Research:

- Dr. Richard Komistek, PI, UT Professor, Biomedical Engineering
- Dr. William Hamel, Co-PI, UT Professor, Mechanical Engineering
- Dr. Charles DeCook, Co-PI, Northside Hospital, Orthopaedic Surgeon
- Selected staff from Dr. DeCook's office**.**
- Radiation technician(s) will operate the fluoroscopy machine.
- Rebecca Robertson, Research Coordinator III.
- Researchers present during data collection at the University of Tennessee and/or the lead researchers appointed by Dr. Komistek.
    - * Undergraduate student researchers employed by CMR will be involved in analyzing the data after it has been collected, de-identified and transferred to CMR's digital data collection. Since patient information will be removed and replaced with the assigned identifiers before the data is transferred to the database, it will not be possible for these undergraduate students to be able to identify patients. They will only have access to the de-identified data that has been uploaded onto the secure CMR digital collection. These student researchers will not have contact with patients.
- Institutional Review Boards
    - The University of Tennessee
    - Northside Hospital

BENEFITS

The potential benefits from this study include, but are not limited to:

- Subject stipend
- Better understanding of the joints analyzed with the same technique in the past.
- Future implant design improvements based on the kinematic findings.
- New and advanced surgical techniques for THA based on the results.
- There are no direct health benefits to participants of the study.

Remuneration/Compensation for Travel Expenses

Subjects were paid a stipend agreed upon by the sponsor and were also compensated for their travel to Knoxville.

Clinical Observations:

There are no clinical observations made during this data collection or from the images obtained through data collection. There will be no radiology report generated for this procedure conducted as a result of this study. Therefore, no RT will review such a report for the procedures, which would be the only way such a "significant problem" would be determined. No data will be returned to the surgeon's office for evaluation or surgeon review, and therefore, the imaging

collected during this study will not potentially provide benefit to specific patients by influencing the physician's treatment plan.

METHODS TO OBTAIN INFORMED CONSENT FROM PARTICIPANTS

Informed consent will be obtained prior to any procedures being conducted. Subjects from both cohorts who are agreeable to participate will schedule a visit to Dr. DeCook's practice where s/he will be consented by Dr. DeCook's staff. Dr. DeCook was not present during the consenting process to avoid possible patient coercion to participate. Consenting staff will use the IC/HIPAA as a guide, including the risks and benefits associated with participation and will answer any questions potential subjects may have about participation.

Phase 2: Post-Operative Fluoroscopy data collection

For Phase 2 of the study, only seven of the ten hips that were diseased and required a THA that participated in Phase 1 of the study in Knoxville were reachable to participate in post-operative fluoroscopy at Abercrombie. Radiology in Knoxville, TN Weisgarber Medical Center, 1112 Weisgarber Rd., Knoxville, TN 37909.

The following inclusion criteria were used to ensure hip subjects that participated in Phase 1 meet eligibility for continuing participation in Phase 2:

1. Subjects required a THA and were implanted with either Summit/Pinnacle THA or Corail/Pinnacle THA by Dr. Charles DeCook.
2. All subjects are well past the required six months post-operative time.
3. Subjects must be between 40-85 years of age.
4. Potential subjects will have a body weight equal to or less than 300 lbs.
5. Participants must have Body Mass Index (BMI) of less than 40.
6. Potential subjects' THAs should be judged clinically successful with a HHS >90.
7. Participants must be able to walk on level ground without assistance.
8. Subjects from the physician's list who do not meet the study requirements will not be considered.
9. Subjects must be willing to sign the Informed Consent (IC)/HIPAA form to participate in the study.

To ensure that all subjects who participated in Phase 1 of the study still met all study eligibility requirements prior to undergoing the post-operative fluoroscopy procedure, a subject specific form was completed for each of the subjects prior to contact for scheduling of post-operative fluoroscopy visit. Dr. DeCook's office staff will be responsible for reviewing the medical files of the subjects that participated in Phase 1 and using the checklist to ensure all subjects meet study criteria. If subjects meet the criteria, they will then be contacted by Dr. DeCook's office to inform the subjects that the second phase of the study is underway and to schedule their appointments to Abercrombie Radiology in Knoxville.

The same reimbursement of travel expenses applied to Phase 2 as was in place for Phase 1. To facilitate implanted subject post-operative participation and compensate for the delay between data collections, the stipend for the implanted group was increased.

Due to protocol revisions (only performing gait activity), change in post-operative fluoroscopy

data collection location (Abercrombie Radiology instead of UT campus), and increase in stipend, each subject will be consented again by UT researchers so subjects are aware and understand the changes to the study. After signing the revised IC form, s/he will be fitted with non-invasive, surface-based sound/vibration sensors placed at the closest distance to the hip joint interface, allowing for the capturing of sound emissions during the gait activity. The sensor will be securely attached using a spica dressing, a tight-fitting, sleeve-like article of clothing, designed for the purpose of the study, and adjusted to subject size using integrated Velcro strips. The sensors will be connected to a data acquisition system that will also be connected to the subject by thin, ultra-lightweight cables while s/he performs the level walking (gait) activity.

In addition to fluoroscopy video, subjects will be videotaped from the torso down (to maintain subject anonymity) while performing the activity (live feed perspective) under fluoroscopy surveillance. The speed level of each trial will be based on the comfort level of the subject. The activity will be performed without the aid of handrails; however, one of the researchers will be ready and in close proximity to assist each subject in case the participant requires help. This precaution will be practiced for all participants, regardless of physical wellbeing, age or prior results; no assumptions will be made as to any participant's capabilities.

In vivo hip kinematics will be assessed for all 10 normal subjects, 10 diseased hip/pre-operative subjects and the same 10 subjects will be assessed again after they complete the post-operative

Statistical Analysis

Basic descriptive statistics (mean and standard deviation) were analyzed for femoral head center displacement from the acetabulum center for both implanted (post-operative) and non-implanted (normal, pre-operative) cases. This was evaluated for one complete gait cycle for each subject.