Reliability of Sacral Slope, Pelvic Femoral Motion and Cup Ante-inclination on AP Pelvic Radiographs in Healthy Pts

IRB: 0719-20-FB

NCT04687306

07/31/2023

Biomedical
SECTION I

Therapeutic/Non-Therapeutic
Does your research involve a drug, medical device, technique or other intervention or strategy (including means like diet, cognitive therapy, behavioral therapy, exercise) to diagnose, treat or prevent a particular condition or disease: "THERAPEUTIC RESEARCH"?
No

1. Title of Protocol:
Inter-observer reliability of sacral slope, pelvic femoral motion and cup ante-inclination on anteroposterior pelvic radiographs in healthy individuals.

2. Responsible Personnel:
A. Principal Investigator (PI):
Garvin, Kevin Lloyd - Orthopaedic Surgery - 402-559-5605 - kgarvin@unmc.edu - alt #: 402-559-8000 - degree: MD - address: LOC 4.14.023 UNMC Midtown (Zip 5640) - phone: 9-5605

B. Secondary Investigator (SI):
Apker, Kim (Kim) Ann - Dept Of Rad Diag Home - 402-559-3285 - kapker@unmc.edu - alt #: 402-559-3285 - degree: MD - address: UT4 1412C (Zip 1045) - phone: 9-3285

Kildow, Beau J. - Orthopaedic Surgery - 402-559-5511 - beau.kildow@unmc.edu - alt #: 402-559-8000 - degree: MD - address: LOC 4.14.016 UNMC Midtown (Zip 5640) - phone: 2-9653

Vincent, Scott Allen - Orthopaedic Surgery - 402-559-9171 - scott.vincent@unmc.edu - alt #: 402-559-8000 - degree: MD - address: LOC 4.14.037 UNMC Midtown (Zip 5640) - phone: 9-9171

C. Participating Personnel:
Buckner, Brandt C - Orthopaedic Surgery - 402-559-5614 - brandt.buckner@unmc.edu - alt #: 402-559-8000 - degree: MD

Khela, Monty - Orthopaedic Surgery - 9164259074 - montykhela@creighton.edu - degree:

Student

Ohnoutka, Cole Joseph - Orthopaedic Surgery - 402-559-8591 - cohnoutka@unmc.edu - alt #: 402-559-8000 - degree: MD - address: LOC 4.14.052 UNMC Midtown (Zip 5640) - phone: 9-8591

D. Lead Coordinator:
Danielson, Pete Wade - Orthopaedic Surgery - 402-559-1703 - peter.danielson@unmc.edu - alt #: 402-559-1703 - degree: BS - address: LOC 4.14.014 UNMC Midtown (Zip 5640) - phone: 9-1703

E. Coordinator(s):
Schwarz, Dana M - Orthopaedic Surgery - 402-559-4167 - dschwarz@unmc.edu - alt #: 402-559-4167 - degree: RN, MS - address: LOC 4.14.032 UNMC Midtown (Zip 5640) - phone: 9-4167

F. Data/Administrative Personnel:
Lyden, Elizabeth Ruby - COPH Biostatistics - 402-559-6061 - elyden@unmc.edu - alt #: 402-559-6061 - degree: MS - address: MCPH 3046 UNMC Midtown (Zip 4375) - phone: 9-6061

G. Are you a student or house officer?
No

3. Funding Source:
Check all that apply and provide the source of the funding.
Cooperative Group:
Center for Clinical and Translational Research (CCTR)
Federal (e.g., NIH) Grant - Provide source:
Other Grant:
♦ Departmental funding
Commercial - Provide company name:
Department of Defense
♦ Other - Provide source (e.g. personal funding): An application to CCTR is being made requesting coverage for radiographs

4. Deadline for IRB Approval:
Yes - Explain and provide date:
♦ No

5. Contract:
Is there a contract associated with this study?
No

6. Agreements
Is there a Material Transfer Agreement (MTA) associated with this study?
No

Is there a Data Use Agreement (DUA) associated with this study?
No

Is there a Data Transfer Agreement (DTA) associated with this study?
No

7. Study Sites:
A. Provide the names and locations of all study sites where this research will be conducted under the oversight of the UNMC IRB or Joint Pediatric IRB.
UNMC and The Nebraska Medical Center, Dept. of Orthopaedic Surgery and Radiology.

B. Will the research be conducted at external sites under the oversight of an external IRB?
No

C. Does UNMC, TNMC, CHMC or UNO serve as the lead site with responsibility for data and/or safety monitoring?
No

D. Does this study involve any international sites where the PI will either; 1) conduct 2) supervise or 3) receive / ship HBM or data to / from UNMC?
No

E. Does this study involve face to face contact with subjects?
Yes

8. Principal Investigator Assurance

The PI understands and accepts the following obligations to protect the rights and welfare of research subjects in this study:

I certify that:

- **I have carefully reviewed this application and all supporting documents. I have determined that the application is accurate, complete and ready for submission to the IRB.**
- **I, and all listed research personnel, have the necessary qualifications, expertise, and hospital credentials to conduct this study in a manner which fully protects the rights and welfare of research subjects.**
- **There are, or will be, adequate resources and facilities to safely initiate, carry out and complete this research at the study sites specified in Section I.7. This includes sufficient staff, funding, space, record keeping capability, and resources necessary to address adverse events and any unanticipated problems involving risk to the subject or others. If the necessary resources become unavailable I will promptly notify the IRB.**
- **All listed research personnel, including external investigators, will be given a copy of the final IRB approved application and any other relevant study-related documents in accordance with their defined responsibilities.**
- **All listed research personnel, including external investigators, will be notified promptly of any changes in protocol, in accordance with their defined responsibilities.**
- **Research personnel, including data and administrative personnel who have access to protected health information (PHI) or subject identifiers will have adequate training in confidentiality and protection of PHI.**
- **The minimum amount of protected health information (PHI) or other identifiers necessary will be used and disclosed to conduct this research study (if applicable). I will implement reasonable safeguards to protect the PHI/identifiers at all times.**
- **I and all other personnel listed in Section I.3A-E of the IRB Application have disclosed all potential financial conflicts of interest as required and are in full compliance with the UNMC Conflict of Interest Policy #8010 and HRPP Policy. I further certify that all potential financial conflicts of interest are appropriately managed in order to ensure protection of the rights and welfare of subjects.**

I recognize that:

- **As the PI it is my responsibility to ensure that this research and the actions of all research personnel involved in conducting the study will comply fully with the IRB-approved protocol (including all amendments), all applicable federal regulations, state laws, and HRPP policies.**
- **It is my responsibility to ensure that valid informed consent/assent will be obtained, as appropriate, from all research subjects or their legally authorized**

representative(LARs).

I will:

- Ensure that all research personnel involved in the process of consent/assent are properly trained and are fully aware of their responsibilities relative to the obtainment of informed consent/assent according to federal regulations, state laws, and HRPP policies.
- Promptly inform the IRB of internal adverse events, as well as any unanticipated problems involving risk to the subjects or to others, as required within the time frame defined by HRPP policies. I will analyze each internal adverse event/reported problem to determine if it impacts the risk-benefit relationship of the study, the safety of the subjects, or informed consent.
- Analyze each MedWatch/safety report to determine if it impacts the risk/benefit relationship of the study, the safety of the subjects, or informed consent.
- Promptly submit external adverse event reports in accordance with HRPP policies.
- Promptly inform the IRB if I become aware of 1) any complaints from research subjects, LARs, or others about research participation, 2) violations of federal regulations or state law, 3) violations of the HIPAA Rule, or 4) violations of HRPP policies.
- Promptly inform the IRB of the results of external audits performed by sponsors, Contract Review Organizations (CROs), cooperative groups, FDA, or other external groups.
- Not initiate any change in protocol without IRB approval except when it is necessary to reduce or eliminate a risk to the subject, in which case the IRB will be notified as soon as possible.
- Promptly inform the IRB of any significant negative change in the risk/benefit relationship of the research as originally presented in the protocol and approved by the IRB.
- Maintain all required research records on file and I recognize that representatives from the IRB, OHRP, HHS, FDA, and other Federal Departments or Agencies may inspect these records in accordance with granted authority.

I understand that:

- Continuing review by the IRB is required at least annually, or as per Federal Regulations and HRPP Policy, in order to maintain approval status. I will maintain IRB approval as long as this study is active.
- I am responsible for appropriate research billing in accordance with UNMC Clinical Trial Professional and Technical Fee Billing Policy #8008 or applicable Children's Hospital & Medical Center policy.

Failure to comply with the Common Rule, applicable Subparts B, C, and D of HHS regulations at 45 CFR 46, applicable FDA regulations, the HIPAA Rule, applicable state

law, HRPP policies, and the provisions of the IRB-approved protocol may result in suspension or termination of IRB Approval of my research project and/or other administrative or legal actions.
Garvin, Kevin Lloyd - 2023-07-31 14:09:51.487

9. Principal Investigator Financial Interest Disclosure
A. As the PI, I declare:
♦ I have no financial interest in this research.
I have a financial interest in this research.

B. As the PI, I understand
♦ I must disclose any change in my financial interest during the course of this research within five (5) business days from the time the change becomes known.

C. As the PI, I certify that:
♦ No Responsible Personnel have a financial interest in this research.
The Responsible Personnel listed below have informed me that they have a financial interest in this research.

D. I have informed all Responsible Personnel that if there is any change in their financial interests during the course of this study it must be disclosed within five (5) business days from the time the change becomes known.
Garvin, Kevin Lloyd - 2023-07-31 14:09:51.487

11. Scientific/Scholarly Merit and Resource Review Certification
Scientific Reviewer:
Mormino, Matthew Allen - Orthopaedic Surgery - 402-559-5624 - mamormin@unmc.edu - alt #: 402-559-8000 - degree: MD - address: LOC 4.14.040 UNMC Midtown (Zip 5640) - phone: 9-5624

As the Scientific Reviewer,
♦ I do not have a financial conflict of interest associated with this study.
I do have a financial conflict of interest associated with this study.

My signature certifies that:

- **this application has been reviewed for scientific/scholarly merit and available resources. It has been determined that the application merits consideration by the IRB based upon the following:**

- **The proposal has an acceptable level of scientific/scholarly merit which justifies the involvement of human subjects.**
- **The proposal has a sound research design in consideration of the stated objectives,**
- **The PI has the necessary qualifications, experience and credentials to conduct this research.**
- **The PI has or will have the necessary funding to support this research**
- **There is or will be adequate physical space required for the research interventions at all study sites specified in Section I.7. In addition, there is or will be adequate laboratory and administrative support, data storage capability, and any other resources necessary to complete this research.**
- **At all study sites specified in Section I.7, there is or will be emergency equipment, personnel, or services necessary to respond promptly to adverse events or unanticipated problems involving risk to the subject or others.**
- **I will promptly notify the IRB if the necessary resources to support this research become unavailable.**

Mormino, Matthew Allen - 2020-12-03 07:09:32.900

Do you have any additional comments that you wish the IRB to consider during the review of this application?
No

SECTION II

PROTOCOL ABSTRACT

1. Provide a brief (less than 2500 characters) abstract of the research protocol. (2500 characters)
This summary should include: 1)) a brief description of the purpose of the study, 2) eligibility criteria, 3) interventions and evaluations and 4) follow-up.
Currently, there are no validated anatomical landmarks that can be used to predict risk of and diagnose abnormal patterns of pelvic motion.This proposed study will measure sacral slope, pelvic femoral angle and cup ante-inclination in both sitting and standing positions, using healthy individuals without a history of spinal and/or lower extremity pathology. Two total radiographs will be taken on each participant. All radiographs will be evaluated for the three measurements by four individuals with the intent of evaluating inter-observer reliability. Determining the reproducibility of these angles between observers will give insight into the potential clinical utility of these measurements in evaluating and treating patients with hip-spine syndrome.

PURPOSE OF THE STUDY AND BACKGROUND

2. Purpose of the Study
What are the specific scientific objectives of the research?
The purpose of this study is to evaluate the mechanics and influence of spinopelvic motion and balance from normal healthy subjects for the purpose of establishing radiographic measurements which are reliable and reproducible and which could give insight into the potential clinical utility of these measurements as future predictors of who may/may not have spinal pelvic issues and in evaluation and treatment of patients with hip-spine syndrome.

This specific objective of this study will be to measure sacral slope, pelvic femoral angle and cup ante-inclination via radiographs in both sitting and standing positions. The radiographs will be evaluated for the three measurements by four individuals with the intent of evaluating inter-observer reliability.

3. Background and Rationale
Describe the background of the study. Include a critical evaluation of existing knowledge, and specifically identify the information gaps that the project is intended to fill.
Low back pain, diagnosed as degenerative joint disease of the hip and/or lumbar spine, is one of the most common chief complaints evaluated by primary care physicians. While isolated degeneration of the hip or lumbar spine is possible, symptomatology of the two

often overlap and can be difficult to distinguish one from the other [7]. More recently, the interplay between hip and spine pathologies has gained more recognition [6]. Increased spinal stiffness is part of the normal aging process. Not well understood though, is why some joints with a lesser degree of pathology become symptomatic while others that appear worse clinically do not become symptomatic. Studies investigating the biomechanics underlying hip-spine syndrome have consistently shown that the body is able to maintain functionality despite increased spinal stiffness by gaining 0.9° of femoral motion for every 1° of spinal motion lost [1-5]. These changes in the hip-spine relationship have more recently been identified as a risk factor for late dislocation of THA [1-5].

Heckman et. al. unexpectedly found that many patients with late THA dislocation have normal component position on standard anteroposterior pelvic radiographs [5]. In the aforementioned study, three measurements were obtained from lateral spine-pelvis-hip radiographs: 1) sacral slope -- the angle formed by the first sacral vertebrae end-plate (S1) and a horizontal line, 2) pelvic femoral motion -- based on a line drawn from the center of the superior S1 end plate to the center of the femoral head and a second line drawn parallel to the femoral diaphysis, and 3) cup ante-inclination -- the sagittal cup position formed by a line bisecting the long axis of the cup and a transverse line [5]. Changes in these angles were calculated for sitting versus standing positions. The study concluded spinopelvic imbalance resulting from increased spinal stiffness as the cause of late THA dislocation in the event of within normal limits component positioning [5]. But, the question remains as to whether there is a precise measure that can predict whether a joint will become symptomatic.

Currently, there are no validated anatomical landmarks that can be used to predict risk of and diagnose abnormal patterns of pelvic motion. Similar to the study performed by Heckman et. al., the proposed study will measure sacral slope, pelvic femoral angle and cup ante-inclination in both sitting and standing positions, using 30 healthy individuals without a history of spinal and/or lower extremity pathology. All radiographs will be evaluated for the three measurements by four individuals with the intent of evaluating inter-observer reliability. Determining the reproducibility of these angles between observers will give insight into the potential clinical utility of these measurements in evaluating and treating patients with hip-spine syndrome.

CHARACTERISTICS OF THE SUBJECT POPULATION

4. Accrual

A. Is this study conducted solely at sites under the oversight of the UNMC IRB (e.g. UNMC, Nebraska Medicine, CHMC, UNO)?

Yes

1. How many subjects will need to be consented (per group, as applicable) in order to achieve the scientific objectives of the research?
30 subjects (15 female and 15 male) are needed to complete the study.

Allowing up to 20% withdrawal or 6 subjects (3 Female and 3 Male) who may sign a consent and then decide does not want to complete x-rays or x-rays may not be of sufficient quality for accurate readings or subject may have identified on the xray signs of exclusionary criteria (such as arthritis) that subject was not aware of.

We will consent up to 36 (18 Females and 18 males) to ensure we have enough subjects to complete the study.

2. What is the statistical or other justification for the total number of subjects described above?
The intraclass correlation coefficient (ICC) will be used to evaluate the consistency of the 4 providers in measuring the sacral slope, pelvic femoral angle and cup ante-inclination via radiographs in both sitting and standing positions. A sample size of 30 subjects with 4 observations per subject (i.e. the 4 providers assessment of the radiograph of any one of the three measurements of interest [sacral slope, pelvic femoral angle or cup ante-inclination]) achieves 80% power to detect an intraclass correlation of 0.81 under the alternative hypothesis when the intraclass correlation under the null hypothesis is 0.65 using an F-test with a significance level of 0.05.

5. Gender of the Subjects
A. Are there any enrollment restrictions based on gender?
Yes

Provide justification.
We will have 2 separate groups (female and male). We need an equal amount in each group and so one gender group may have reached accrual while we are still recruiting for another gender group thus limiting recruitment to just one gender at that time.

6. Age Range of Subjects
A. Will adults be enrolled ?
Yes

1. What is the age range of the adult subjects?
25-50

2. What is the rationale for selecting this age range?

This study is limited to adults which is defined as skeletal mature. Skeletal maturity is attained when the epiphyseal plates close, closure usually begins in childhood and is complete by the age of 25 which is the minimum age for our study.

This study is recruiting "healthy" volunteers with no history of spine/hip/pelvis issues. Therefore, we have made our maximum age limit at 50 as co-morbidities such as hypertension, diabetes type 2, hyperlipidemia and heart disease increase with aging. Osteoarthritis (OA) is a classic age-related disorder. It is often described as a chronic degenerative disease and thought by many to be an inevitable consequence of growing old. In OA, degradation and loss of the articular cartilage is a central feature that is sometimes attributed to "wear and tear".

B. Will children (18 years of age or younger) be included in this research?
No

1. What is the justification for excluding children from participating in this research?
Research is irrelevant to children (e.g. disease or condition rarely encountered in children).
Knowledge being sought in the research is already available for children or will be obtained from another ongoing study.
A separate study in children is warranted and preferable.
Insufficient data are available in adults to judge the potential risk in children.
♦ Other. Explain. Do not have skeletal maturity and data would not be relevant to our study.

7. Race and Ethnicity
Are there any subject enrollment restrictions based upon race or ethnic origin?
No

8. Vulnerable Subjects
A. Will prisoners be included in the research?
No

B. Select from the list all of the vulnerable populations that will specifically be recruited to participate in this research.
Decisionally-impaired persons

Critically ill patients
Students of the investigator
Employees of the investigator
Educationally disadvantaged individuals
Socially or economically disadvantaged individuals
Individuals with a stigmatizing illness or condition
Individuals from a marginalized social or ethnic group
Other.
♦ No vulnerable subjects will be specifically recruited

9. Inclusion Criteria
What are the specific inclusion criteria?
1. Males or females
2. aged 25-50
3. Healthy individuals without major co-morbidities and without spine/hip/pelvis issues including previous injuries or surgeries.

10. Exclusion Criteria
What are the specific exclusion criteria?
Females of child bearing potential who are pregnant or trying to become pregnant.

11. Pregnancy and Contraception Requirements
A. Are women of child bearing potential (WOCBP) included in this research?
Yes

a. Are there any specific contraception requirements for subjects?
No

1. Provide justification for absence of contraception requirements
There are no interventions that are likely to be of risk to a fetus
Investigational drug(s) is (are) not systemically absorbed
Investigational drug(s) is (are) systemically absorbed, but there is no evidence from human studies, or from clinical experience, that there is risk to a fetus
♦ Other A negative pregnancy test is required prior to obtainment of the one time x-rays.

B. Are pregnant women included in this research?
No

1. Provide justification for excluding pregnant women

Investigational drug(s) is (are) absorbed systemically, and there is evidence from animal or human studies, or from clinical experience, that there is risk to a fetus **OR** investigational drug(s) is (are) absorbed systemically, and there is a well-understood mechanism of action that may result in risk to a fetus

♦ Intervention includes a procedure expected to be of risk to a fetus (eg, exposure to ionizing radiation, maximal exercise test)

Research is not relevant to pregnant women (e.g. disease or condition rarely encountered in pregnant women)

Knowledge being sought in the research is already available for pregnant women or will be obtained from another ongoing study

A separate study in pregnant women is warranted and preferable

Physiology of pregnancy precludes generalization to other populations

Other - explain

2. Describe how pregnancy status will be assessed (eg, self-report, urine pregnancy test, blood pregnancy test) and the frequency of monitoring during participation in the research.

Females of child bearing potential will have a urine pregnancy test which must result negative prior to obtaining x-rays. If the test is positive, the subject will be withdrawn from the study. (Those who have had a tubal ligation or hysterectomy or are 2 years post menopause will not be required to have a pregnancy test). Radiographs occur just one time so there will be no further testing or monitoring for pregnancy status.

The pregnancy test will be performed at the Nebraska Medicine lab within the LOC. As with all medical tests, the results will be kept in the electronic chart. The study staff will look at the results in their chart prior to any radiographs being performed.

3. Describe the plan should a female subject, or the partner of a male subject, become pregnant while research interventions are on-going (or during the period that contraception is required following the completion of the intervention).

If a female subject tests positive for pregnancy following their study visit and that they may have been pregnant during their study visit when they obtained radiographs, despite having had a negative pregnancy test at that time or have had reported a prior tubal ligation, hysterectomy or claimed 2 years post menopause - the PI will make provisions for the subject as appropriate by referring her to her primary care physician or OB/GYN and if she does not have an established MD, a referral to one would be arranged.

C. Are breast feeding women included in this research?

Yes

Provide justification

According to www.babycenter.com it is perfectly safe for a breastfeeding mom to get any kind of x-rays.The radiation in an may kill off a few of the living cells in any breast milk present at the time of the scan, but it won't expose baby to radiation.

METHODS AND PROCEDURES (NON-THERAPEUTIC)

12. Methods and Procedures Applied to Human Subjects
A. Describe the research plan, including all procedures, interventions, evaluations and tests. If subjects will be randomized to a specific intervention, the randomization plan should be explained.
After obtaining consent, the male subject will have a total of two (2) radiographs of the pelvis and spine in both the standing and sitting positions. The one time study visit will last approximately 1 hour.

Consenting is expected to take under 20 minutes; to offer a urine sample at the lab for pregnancy testing is expected to take about 10 minutes; checking into radiology, changing into gown and completing the radiographs is expected to 30 minutes, (If a female wishes to complete everything in one visit, the wait time for the pregnancy test which needs to be transported by courier from Lauritzen Outpatient Care Center to main lab may take up to 2 hours).

There are no further interventions, assessments, or questionnaires for the subject.

The female subject of child bearing potential will have a urine pregnancy test after signing the consent form and must have a negative result before obtaining radiographs. The pregnancy test will be a urine pregnancy test. Pregnancy test results could take up to 2 hours so the subject may choose to return at a different time for the x-rays rather than wait (a pregnancy test is valid for 7 days per policy).
Per Nebraska Medicine Pregnancy Testing Policy (MS72), a negative pregnancy test within 7 days prior to the intervention of interest should be considered current.

Arrangement have been made to utilize the same rad tech for all x-rays for consistency.

Radiographs will be read by radiology and then de-identified and evaluated for three measurements by four individuals with the intent of evaluating inter-observer reliability. Measurements of the radiographs will be sacral slope, pelvic femoral angle and cup ante-inclination in both sitting and standing positions.

Radiographs read by radiology which have important incidental findings (a tumor for an

example) will be reported to the PI, who will consult if needed a specialist in that area, and will inform the subject of the findings, provide the radiographs to the subject, offer to provide same information to subject's primary care physician and/or offer to make a referral to an appropriate specialist for further follow-up.

All radiographs and initial standard reading of by radiologist will become part of the subject's permanent medical record and the subject may re quest that these be sent to his/her primary care physician.

B. Are all of the procedures, interventions, evaluations and tests being performed solely for research purposes?
Yes

C. Describe briefly the statistical methods used to analyze the data (or reference the appropriate section of the detailed protocol or grant).
We will calculate ICC values with 95% confidence intervals using linear mixed effects models for each of the three measurements separately: sacral slope, pelvic femoral angle and cup ante-inclination. Descriptive statistics will include model adjusted means and standard errors of each of the measurements. Analysis will be done in SAS and SPSS. A p-value < 0.05 will be considered statistically significant.

References
Walter, S.D., Eliasziw, M., and Donner, A. 1998. 'Sample Size and Optimal Designs For Reliability Studies.' Statistics in Medicine, 17, 101-110.
Winer, B.J. 1991. Statistical Principles in Experimental Design (Third Edition). McGraw-Hill. New York, NY.

D. Does this study involve the collection of blood, urine, saliva or other human biological material (HBM)?
Yes

1. Does this research involve genetic testing including Genome Wide Association Studies (GWAS), Whole Genome Sequencing (WGS) or Whole Exome Sequencing (WES)?
No

E. Does this study involve the creation of a tissue bank for future unspecified research? This includes un-used (excess) blood, urine, or tissue, obtained for clinical indication or for research, or additional human biological material collected specifically for future research.

No

DRUGS, BIOLOGIC DRUGS AND DEVICES

13. Drugs and Biologic Drugs
1. Does this research involve the use of drugs or biologics?
No

14. Devices
1. Does this research involve a medical device(s)?
No

CONFIDENTIALITY AND PRIVACY

15. Confidentiality and Privacy
A. Describe where research data will be stored. Check all that apply.
♦ On a secure server at UNMC, CHMC, Nebraska Medicine, and/or UNO (including REDCap)
On a secure cloud server - Specify the secured cloud serve:
On a firewall protected database accessible through the internet - Specify who has administrative responsibility for maintenance of the server:
On an encrypted, password protected local hard drive
On an encrypted, password protected portable computer
On an encrypted, password protected flash drive
♦ In hard copy
Other

a. Please provide justification for use of hard copies
Radiographs are downloaded and read electronically. Other than a consent form and enrollment log there will be no hard copies. These hard copies will be kept in a Regulatory binder located in the coordinator's locked office which is in a restricted access area. All data collected from radiographs will be entered into excel sheets which are stored on an institutional secured server.

b. Will hard copies will be transported from one site to another, on or off campus?
No

B. Will any of the following subject identifiers be recorded (at any time) in association with the research data?

Yes

1) Indicate the subject identifiers that will be recorded. Check all that apply.
♦ Name
♦ DATES (e.g. date of study visit, date of sample collection, birth, admission, discharge)
Postal address information: street address, city, county, precinct, ZIP code
Telephone numbers
Fax numbers
Electronic mail addresses
Social Security numbers
♦ Medical Record numbers
Health plan beneficiary numbers
Account numbers
Certificate/license numbers
Vehicle identifiers and serial numbers, including license plate numbers
Device identifiers and serial numbers
Web Universal Resource Locators (URLs) Internet Protocol (IP) address numbers
Biometric identifiers, including finger and voice print
Full face photographic images [and any comparable images]
No Identifier

2) Will a unique subject identifying number (e.g., S1, S2, S3), characteristic or code be used to link data to any of the identifiers listed above?
Yes

a. Where will the key (that links the unique subject identification code to the subject's name or other identifier) be stored?
In the locked office of the study coordinator located in a restricted access area.

b. Does the code number include the subject's initials or other subject identifier as part of the code?
No

3) What is the justification for recording the specific subject identifiers listed above? Check all that apply.
Schedule appointments
Collect continuous clinical information from the medical records
♦ Follow-up with subjects
Link stored tissue with subject identification for it to be withdrawn in the future if requested

Compensation
Other. Explain.

4) How long will the subject identifiers be maintained in association with the research data?
Per institutional policy for 7 years as part of the research.

5) How will all of the identifiable research data be destroyed (e.g., all identifiers stripped from the data and destroyed, hard copies shredded etc) when the identifiable data is no longer required?
After 7 years, all identifiers are removed or destroyed.

C. Will research data that contain subject identifiers be disclosed to:
Other investigators at UNMC, NM, UNO or CHMC who are not listed in Section I of this application?
No

2. Investigators outside of UNMC, NM, UNO or CHMC?
No

3. Will research data that contain subject identifiers be disclosed to any commercial sponsor or contract research organization (CRO), or to any other external organization or entity (e.g., NCI cooperative groups)?
No

D. What provisions will be in place to protect the subject's privacy? Check all that apply.
♦ Ensuring that only personnel listed on the IRB application Section I.3(A-E) are present during the consent process.
♦ Ensuring that the fewest number of individuals possible are aware of the subject's participation in the research.
♦ Ensuring that the research activities are performed in as private of a place as possible.
Other. Explain.

E. Does this research involve data banking at UNMC, NM, UNO or CHMC, or by an outside organization (e.g. NCI Cooperative Group, pharmaceutical company) for future research that is not related to this study?
No

RISK/BENEFIT ASSESSMENT

16. Potential Risks
What are the potential risks associated with each research procedure, intervention, evaluation and/or test? If data are available, estimate the probability that a given harm may occur and its potential reversibility.
1. Potential for the loss of confidentiality, however, safeguards are in place to help prevent that from happening.

2. Radiation exposure from the x-rays. The scientific unit of measurement for radiation dose, commonly referred to as effective dose is the millisievert (mSv). We are exposed to radiation from natural sources all the time. The average person in the U.S. receives an effective dose of about 3mSv per year from naturally occurring radioactive materials and cosmic radiation from outer space. A spine x-ray approximate effective radiation dose is 1.5mSv which is comparable to natural background radiation for 6 months. (RadiologyInfo.org)

3. Females of childbearing potential may discover they are pregnant.

17. Risk Classification
What is the overall risk classification of the research?
Minimal risk
♦ Greater than minimal risk

18. Minimization of Risk
A. Describe how the subjects of the research will be monitored by the investigators and other research personnel to ensure their safety.
This is a one time only study visit, two visits if females who have a pregnancy test choose to return for x-rays rather than wait for pregnancy results. Subjects will be provided the names and contact information of research personnel should an emergency arise or they have any questions following their study visit.

B. Describe how the data collected will be monitored to ensure the safety of subjects. Identify who will perform the ongoing data and safety analysis, and describe the frequency of data analysis. If there is an independent Data and Safety Monitoring Board (DSMB) provide the charter, or describe (1) the composition of the DSMB membership, (2) the frequency of DSMB meetings and reports.
There will not be an independent Data and Safety Monitoring Board. This is a clinical trial that is not investigating a drug, device or procedure. The research includes a one time only study visit where radiographs are obtained. Female subjects of child bearing potential may

have a urine pregnancy test if they are unsure of their pregnancy status. All institutional and department guidelines and policies will be followed to ensure the safety of subjects which includes also the subject's right to privacy, COVID screening and precautions and appropriate data de-identification and storage.

Any incidental findings will be managed by the PI and discussed with the patient promptly. The PI will assist the patient in referring them to the correct type of physician to deal with their findings. All IF's will be handled in conjunction with HRPP policy.

These findings will be also reported on the continuing review applications for the study.

C. Describe the auditing plan for research conducted. Identify who will conduct the audits and specify the audit frequency.
Annual continuing reviews will be completed by the Research Coordinator and submitted to the Institutional Review Board with the Principle Investigator overseeing and reviewing.

D. Describe the specific subject withdrawal criteria.
An investigator may withdraw a subject if the radiographs obtained would show conditions such as arthritis that the subjects may not have been aware of and this study wants xrays only from healthy individuals with no known history of spine/hip issues.

E. Describe the stopping rules for the research (e.g., the specific criteria for halting or early termination of the study).
There are no stopping rules for this research. This is not a clinical trial investigating a drug, device or procedure but rather the recruitment of healthy subjects for xray imaging so that inter-observer variance can be completed by MDs who are reading xrays.

F. Describe plans and resources available to promptly address any subject injury.
All institutional and departmental policies and plans will be followed from COVID screening at point of entry into the building to the escort of patient to the private clinical exam room and what to do in case of an accidental slip/fall. All staff are BLS certified and know where emergency equipment is located such as a defibrillator and what numbers to call in event of an emergency.

19. Potential Benefits to the Subject
Is there the prospect for direct benefit (eg, research on diagnosis or treatment of disease)?
No

20. Potential Benefits to Society

Describe the potential benefits to society that may reasonably be expected to result from this research.

An increase in knowledge. Currently, there are no validated anatomical landmarks that can be used to predict risk of and diagnose abnormal patterns of pelvic motion. Study radiographs from healthy individuals with no history of spine/pelvis hip issues will be evaluated by various observers with the intent of evaluating inter-observer reliability. Determining the reproducibility of these angles between observers will give insight into the potential clinical utility of these measurements in evaluating and treating patients with hip-spine syndrome.

FINANCIAL OBLIGATIONS AND COMPENSATION

22. Financial Obligations of the Subject

A. Who will pay for research procedures, interventions, evaluations and tests? Check all that apply.

Sponsor
Grant
CRC, CCTR
Costs or fees waived by Nebraska Medicine, UNMC- P, CHMC or CSP
♦ Department/Section funds
♦ Other. Explain The department is applying for a CRC,CCTR grant for costs of radiographs and PG testing.

B. Will any of these procedures, interventions, evaluations and tests will be charged to the Subject, the Subject's health insurance, or Medicare/Medicaid?

No

C. Are there any other financial obligations that the subject will incur as a result of participating in the study?

No

23. Compensation to the Subject for Participation

A. Will the subject receive any compensation for participation?

Yes

1. Describe the form of compensation, dollar amount (if applicable) and the prorated compensation plan (if applicable).

A $25.00 Visa gift card for the subject's (male or female of non-child bearing potential) time and travel after completion of the one time study visit.

OR

A $40.00 Visa gift card for women of child bearing potential who are required to have a pregnancy test and either wait for the results or return for a 2nd visit to have the radiographs.

PRIOR REVIEW

24. Prior IRB Review
A. Has this study (or one substantially similar) been previously submitted to the UNMC IRB (or the Joint Pediatric IRB) and then withdrawn by the investigator for any reason?
No

B. To the best of your knowledge, has this study (or one substantially similar) been considered by another IRB and disapproved?
No

SUBJECT IDENTIFICATION & RECRUITMENT

25. Method of Subject Identification and Recruitment
A. Will prospective subjects be identified through initial contact by the investigator?
No

B. Will prospective subjects make the initial contact with the research personnel to inquire about the study?
Yes

1. Potential Subjects learn about the research through: Check all that apply.
Referral by clinician or other parties specifically for the research
Printed advertisements (including bulletins, newsletters, posters, fliers, and magazine or newspaper ads)
Radio and Television advertisements
Electronic advertisements (including social media or other on-line venue)
♦ Word of mouth
Public UNMC study database
♦ Other. Explain. Advertisement in the UNMC Today

C. Will this study be listed in the clinical trial registry at www.clinicaltrials.gov?
Yes

1. Provide the NCT#.
NCT 04687306

2. Identify who holds the NCT#
♦ PI
Sponsor

OBTAINMENT OF INFORMED CONSENT

26. Waiver or Alteration of Informed Consent
A. Is a complete waiver or alteration of consent requested?
No

27. Waiver of Signed Consent
Is a waiver to obtain signed consent requested?
No

29. Process of Informed Consent
A. When will the prospective subject/parent(s)/guardian(s)/LAR be approached relative to their/the subject's actual participation in the study?
Interested subjects who become aware of the study, will initiate contact with the research coordinator and then come in for a screening visit to be consented with the research coordinator and/or PI.

B. Where will informed consent be obtained, and how will the environment be conducive to discussion and thoughtful consideration?
Consent will be obtained in a private clinical exam room which is conducive to discussion and thoughtful consideration by the subject.

Prior to the subject coming to research study visit, the subject would have contacted research persons to inquire about the study in response to advertisement. Research personnel would have provided an overview of the study with the subject over the phone and answered any questions the subject may have had and a copy of the consent form would have been mailed to subject to read and review. If the subject was then further interested, the subject would contact research again and scheduled a time to come in for purpose of consenting and then have the radiographs. Registering the subject as a patient

in order to enter radiograph orders would occur at time of second contact with research.

C. Who will be involved in the process of consent and what are their responsibilities?
The research coordinator or PI will obtain consent from the subject after having thoroughly reviewed the consent form and answering any questions the subject may have.

D. How much time will be allotted to the process of consent?
As much time as is needed, however, consent is expected to take 20 minutes at the study visit. (Prior to the scheduled study visit, the subject will have contacted research in response to an advertisement and will have been the consent form to read and review).

E. How will the process of consent be structured for subjects who are likely to be more vulnerable to coercion or undue influence?
The subject will have been sent the consent form in advance to read and review and discuss with friends/family if he/she so chose.. There is a $25. or $40. gift card to Walmart for participation which is not a high amount in which to coerce into participation but rather to reimburse for time and travel. The adult subject will need to be their own guardian and be able to verbalize an understanding of the research and their role in it. If the subject is unable to read or has vision challenges, the consent will be read to them, word by word, stopping at each paragraph to assess the subject's understanding and ask the subject if they have any questions. Vulnerable populations are not being recruited for this study. Each subject is informed that they do not have to participate if they do not want to and can withdraw at any time for any reason.

F. Will non-English speaking subjects be enrolled in this research?
No

Provide justification for exclusion of non-English speaking subjects
This study requires only a small number of subjects, is investigator initiated and non funded, (although a grant from CRC is being applied for to cover the costs of the radiographs), the institution has not previously provided interpreters for research related visits and the study does not have funding to pay interpreters or have the consent form translated.

G. How will it be determined that the subject/parent(s)/guardian(s)/LAR understood the information presented?
Subjects will be asked to verbalize an understanding of the research and their role in it.

30. Documentation of Informed Consent and Assent
Select who will obtain consent from the subject/parent(s)/LAR.
Danielson, Pete Wade

Garvin, Kevin Lloyd

Kildow, Beau J

Schwarz, Dana M

Vincent, Scott Allen

31. Consent Forms and Study Information Sheets
Indicate the type of consent forms and study information sheets to be used in this research. Check all that apply.
♦ Adult consent form
Legally authorized representative (LAR) consent form
Parental/Guardian consent form
Youth study information sheet
Child study information sheet
Adult study information sheet (decisionally-impaired)
Screening consent form
Addendum consent form
Other. Explain.

32. Information Purposely Withheld
Will any information be purposely withheld from the subject during the research or after completion of the research?
No

RESOURCES

33. Describe the resources available to safely conduct this study at <u>each</u> study sites specified in Section I.7.
The clinic is providing space for research to obtain consent in a private exam room with the subject which includes PPE availability. The department has a dedicated research personnel staff and office equipment and supplies needed for research activities.

LITERATURE REVIEW

34. References
Provide a full listing of the key references cited in the background (Section II.3). The references should clearly support the stated purpose of the study.

1. An VVG, Phan K, Sivakumar BS, Mobbs RJ, Bruce WJ. Prior lumbar spinal fusion is associated with an increased risk of dislocation and revision in total hip arthroplasty: A meta-analysis. J Arthroplasty. 2018 Jan;33(1):297-300.
2. Blizzard DJ, Sheets CZ, Seyler TM, Penrose CT, Klement MR, Gallizzi MA, Brown CR. The impact of lumbar spine disease and deformity on total hip arthroplasty outcomes. Orthopedics. 2017 May 1;40(3):e520-5.
3. Buckland AJ, Puvanesarajah V, Vigdorchik J, Schwarzkopf R, Jain A, Klineberg EO, Hart RA, Callaghan JJ, Hassanzadeh H. Dislocation of a primary total hip arthroplasty is more common in patients with a lumbar spinal fusion. Bone Joint J. 2017 May;99-B(5):585-91.
4. Garvin KL. Spinopelvic stiffness and the lax hip arthroplasty: A conundrum for the aging population: Commentary on an article by nathanael heckmann, MD, et al.: "late dislocation following total hip arthroplasty. spinopelvic imbalance as a causative factor". J Bone Joint Surg Am. 2018 Nov 7;100(21):e140.
5. Heckmann N, McKnight B, Stefl M, Trasolini NA, Ike H, Dorr LD. Late dislocation following total hip arthroplasty: Spinopelvic imbalance as a causative factor. J Bone Joint Surg Am. 2018 11/07;100(21):1845-53. Available from: https://library1.unmc.edu/login?url=http://search.ebscohost.com/login.aspx?direct=true&db=cmedm&AN=30399079&login.asp&site=ehost-live&scope=site
6. Diebo BG, Day LM, Lafage R, et al. Radiographic Categorization of the Hip-spine Syndrome in the Setting of Hip Osteoarthritis and Sagittal Spinal Malalignment.*J Am Acad Orthop Surg*. 2019;27(17):659-666. doi:10.5435/JAAOS-D-18-00295
7. Devin CJ, McCullough KA, Morris BJ, Yates AJ, Kang JD. Hip-spine syndrome.*J Am Acad Orthop Surg*. 2012;20(7):434-442. doi:10.5435/JAAOS-20-07-434

SECTION III

SUBMISSION DEADLINE

A. Full Board Review:
The IRB meets twice monthly, on the first and third Thursday of the month, with the exception of January and July when the IRB meets only on the third Thursday of the month. No more than 15 applications (e.g., initial review of a new study, re-review of a tabled study) will be reviewed at each meeting. All reviews are performed on a first-come first-served basis. The IRB meeting schedule and deadline dates can be found on the IRB website at www.unmc.edu/irb.

B. Expedited Review
Applications that qualify for expedited review have no submission deadline and can be reviewed independent of the IRB meeting schedule. Call the Office of Regulatory Affairs for assistance in determining if your study meets the requirements for expedited review.

ADDITIONAL REVIEW REQUIREMENTS

Final IRB approval and release of studies is contingent upon approval by the following UNMC committees or departments. Check the appropriate boxes:
UNMC and NM - Pharmacy & Therapeutics (P&T) Committee (Required for studies involving drugs)
Fred & Pamela Buffett Cancer Center Scientific Review Committee (SRC) (Required for studies involving cancer)
Institutional Biosafety Committee (IBC) (Required for studies involving the use of gene transfer and vaccines)
Investigational Device Review Committee (IDRC) Review by the IDRC is required for all protocols involving the use of investigational or marketed devices
Billing Grid (Required for all studies involving billing for hospital/clinic services)
Coverage Analysis (Departments requiring this analysis have been specified by the Organization)
Conflict of Interest (COI) Management Plan (Required for all studies with declared COI by study personnel)
Sponsored Programs Administration (SPA)/UNeHealth grants and contracts
Pathology approval for collection of tissue samples required for this study
Radiation Committee Approval
Other Review
♦ **None of the above organizational requirements apply to this study**

SECTION IV

COVID-19

1. Written documentation
List all of the location(s) that will be used for informed consent, visits, or other procedures. Provide the name and title of the person(s) granting permission AND written documentation that the researchers have permission to conduct the study in all location(s) proposed.
This study is a one-time visit and consent will occur in the privacy of a clinical exam room in Orthopaedic Surgery department at the LOC. X-ray orders will be placed in EPIC and completed in radiology at the LOC which is walk-in and first come. We are choosing to group the consenting and radiograph obtainment to Friday afternoons 2pm-4pm which is the slowest part of the week for the clinic and radiology.

2. Describe mask, visitor, and other guidance or policies required by each site.
As is the standard of care currently in place - All persons are screened at all points of entry into the LOC and are required to wear a mask while inside the LOC. Hand and washing or sanitizing is also required of all entering persons. All staff at all times are required to wear a mask and hand sanitize when entering and leaving a room. All exam rooms and any surface area that a patient may have had contact with or touched is wiped down with approved cleaning wipes after a patient leaves the room. Institutional policy currently does not allow visitors or care givers to accompany outpatients to visits unless the patient has mental or physical challenges which require personal assistance.

3. Describe the source of PPE.
Masks are provided at points of building entry if the patient does not have one. All staff have masks and goggles provided by the department. Each clinic exam room is stocked with gloves, and cleaning wipes. There is hand sanitizer in each clinic exam room and various areas in hallways available to patients and staff. This is institutional and department required and provided.

4. Describe other plans to be instituted by investigators enhance safety of subjects, such as social distancing, remote visits, flexible scheduling, etc.
This is a one time study visit, all safety precautions as previously described will be used per institutional and department policies.

5. Describe plans for site and/or equipment cleaning, and the source of appropriate cleaning supplies.
Anything a patient may have had contact with or touch is cleaned with approved cleaning sanitizing wipes as per policy when the patient is finished and leaves and prior to another

patient being escorted in.

6. Describe when COVID-19 screening questions will be asked of each research subject, and by whom.
By the screeners found at all points of building entry.