IRB Approved at the
Protocol Level
Jul 11, 2019

In vivo Three-Dimensional Determination of OA Brace Effectiveness

Richard D Komistek, PhD
University of Tennessee
1506 Middle Drive
310 Perkins Hall
Knoxville, TN 37996
Phone: (865) 974-4159
Fax: (865) 946-1787
Email: rkomiste@utk.edu

In vivo knee kinematics will be assessed for 20 subjects that have been clinically diagnosed with substantial unicompartmental osteoarthritis (OA) by one of the surgeons of Colorado Joint Replacement; this is the location from which participants will be recruited.
Enrollment will be increased to 24 subjects to account for any dropouts. Medial joint space narrowing will be clinically assessed in all patients on standing anteroposterior radiographs. The objective of this study will be to analyze subjects with symptomatic unicompartmental osteoarthritis under in vivo dynamic, weight-bearing conditions using video fluoroscopy to determine if present-day OA knee braces provide separation of the femoral condyle from the tibial plateau, thus avoiding excessive loads on the degenerative compartment.

The study will be submitted to Western IRB (WIRB); the University of Tennessee's IRB and Centura Health/Catholic Health Initiatives (for Colorado Joint Replacement/Porter Adventist Hospital) have waived oversight to WIRB. The required Reliance Agreements will be included with this submission to WIRB.

We will use the following inclusion criteria to recruit participants for this study:

1. Must be a patient of Colorado Joint Replacement.
2. Must be diagnosed with marked unicompartimental degenerative joint space narrowing.
3. Bilateral subjects may not be included in the subject population.

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 who are unable to perform normal walking.
3. Subjects who are unwilling to sign Informed Consent/ HIPAA documents.
4. Does not speak English.

Investigators

Richard D. Komistek, Ph. D. (PI)
Douglas A. Dennis, MD (Co-PI)
Jason Jennings, MD (Sub-I)
Michael T. LaCour, Ph. D. (Sub-I)
Jacob Elkins, MD (Sub-I)
Lindsay Kleeman-Forsthuber, MD (Sub-I)

Study locations
Subject Recruitment will take place at Colorado Joint Replacement:
Colorado Joint Replacement
2535 S Downing St., Suite 100
Denver, CO 80210
(720) 524-1367

Fluoroscopic exams, ultrasound exams and CT exams will be performed on all 20 (or possibly 24) subjects at: Porter Adventist Hospital
2525 S Downing St.
Denver, CO 80210
(303) 778-1955

Satellite sites:
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:
310 Perkins Hall
1506 Middle Dr.
Knoxville, TN 37996

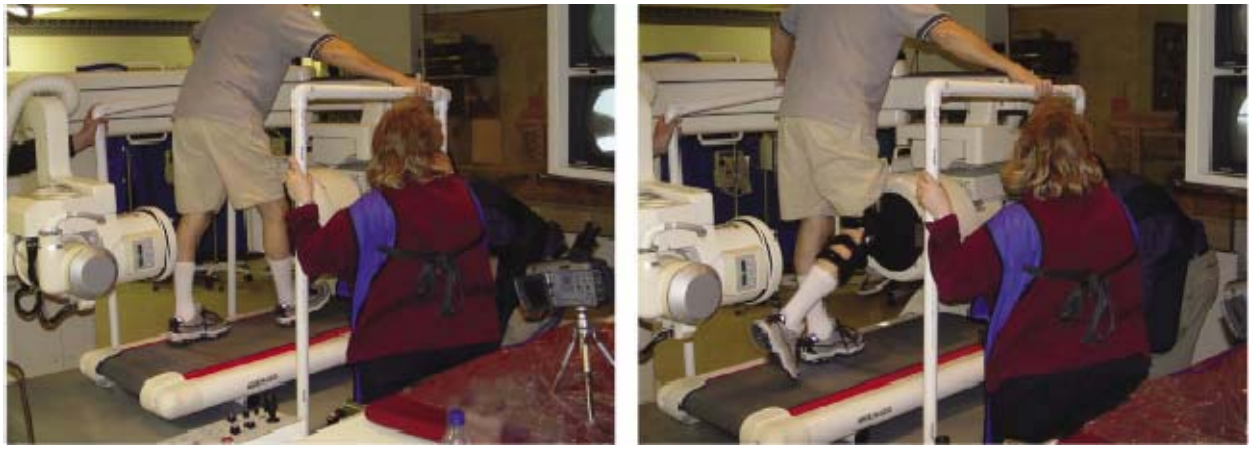
Recruitment
Patients of Colorado Joint Replacement in Denver, Colorado will recommend eligible subjects for recruitment who have been clinically diagnosed to have marked unicompartimental degenerative joint space narrowing. Since there are no inclusion criteria other than being a patient of Colorado Joint Replacement and having unicompartmental OA, review of patient medical files prior to contacting about participation is not necessary. No inclusion/exclusion checklists will be used to ensure eligibility since no other criteria must be met other than being a patient of Colorado Joint Replacement, having the unicompartimental degenerative joint space narrowing, being able to speak English and perform normal walking. The surgeons of Colorado Joint Replacement will be aware of which of their patients have this joint condition. Even though a HIPAA waiver for recruitment will not be necessary, patient medical files will need to be accessed in order to acquire contact information for each potential subject.

Ms. Roseann Johnson will contact the patients to explain the study using an approved script and inquire as to whether or not they are interested in participating. A partial waiver of HIPAA has been included for this. The surgeons of Colorado Joint Replacement may also bring the study to patients' attention during regular office visits and will use language similar to that in the script. If a patient is agreeable to participate, s/he will be scheduled to visit Porter Adventist Hospital on the day of data collection. On this scheduled day, UT researchers will travel to Porter to collect the kinematic data of participants' knees under fluoroscopic surveillance using a C-arm fluoroscopic unit while subjects perform normal treadmill walking in the frontal plane. The fluoroscopic images will be stored on password protected computer workstations for subsequent analysis.

Data Collection

Fluoroscopy

On the scheduled day of data collection, here will be at least two UT researchers present (which could also include the PI), as well as a study PI, (Drs. Komistek, Dennis; Jennings, Elkins, Kleeman-Forsthuber, LaCour [Sub-Investigators]) to conduct the fluoroscopic evaluation. Each subject will be asked to perform gait without the assistance of an offloading brace (Figure 1a). Then, each subject will be fitted with a Breg, off-the-shelf OA brace and will perform normal gait while under fluoroscopic surveillance (Figure 1b). To ensure each brace was fitted properly, Breg will be asked to send either a sales representative or an engineer to the evaluation site. Therefore, the sales representative or engineer will be asked to fit their brace on each of the subjects. This individual will sign a pledge of confidentiality.



a b

Figure 1. Subject on a treadmill perform gait without a brace (a) and with a brace (b).

A Radiation Technician (RT) employed by Porter Adventist Hospital will perform the actual fluoroscopy procedure, following the subjects' OA knee with the unit as the activity is performed with and without the OA brace; only the knee joint (from the fluoroscopy machine) will be recorded on the fluoroscopy footage. The UT researchers, graduate research assistants (GRAs), which may include any of the following - Garett Dessinger, Jarrod Nachtrab, Milad Khasian, Lauren Smith, Seth Coomer – will be present, although they will not perform the actual fluoroscopy procedure. They will be present during the fluoroscopy procedure to walk subjects through the activities, answer any questions that may arise, ensure data collection equipment is set up as needed and serve as consultants to the RT.

Any of these UT individuals, or study staff from Colorado Joint Replacement, will consent the participants. They will meet with each potential participant individually to make sure s/he has been properly informed of the procedures and to help with any of the IC form. CMR researchers will inform all subjects that they do not have to participate and are free to leave if they wish and will answer any questions subjects may have about the study. Participation is entirely voluntary.

Participants will be asked to practice the activity to ensure they can comfortably complete it and experience no pain with the fluoroscopy machine off (no radiation). The practice portion of the data collection without radiation will not be video-recorded.

Multiple trials of each activity may be conducted to ensure usable images have been acquired to complete the study. Radiation time will be kept as low as reasonably achievable (ALARA) and will not exceed two minutes. The RT will start the fluoroscope just prior to the subject beginning the activity trial and will stop the fluoroscope immediately after the subject completes each activity trial to ensure that the subject is not exposed during idol periods. On-time will be recorded on the subject's IC, as well as any output the fluoroscopy unit is able to provide.

In addition to fluoroscopy video, subjects will be videotaped from the shoulders down (to maintain subject anonymity) while performing the activities (live feed perspective). The speed level of each trial will be based on the comfort level of the subject. 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. The participant will be allowed to rest as necessary and be instructed to stop the activity at the first sign of pain.

The fluoroscopic and video footage for the study activities will be stored on digital video files on a secure computer workstation and stored securely by UT researchers. It will then be uploaded onto the secure CMR database by these researchers. Once the data has been uploaded, identifiers are removed from the data automatically by the database, and a study and subject-specific identifier will be assigned to each subject.

JointVue three-dimensional ultrasound

Since the skeletal geometry is different for every person, computer aided design (CAD) models of the femur and tibia will be created for each specific subject. In order to create these CAD models, each subject will be asked to undergo a three-dimensional (3D) ultrasound using the JointVue proprietary software to reconstruct 3D femoral and tibial bones (Figure 2). A representative from JointVue will be present during data collection to conduct the ultrasound procedure in order to create the CAD models. This individual will sign a statement of confidentiality.

Study data will then be uploaded onto a secure server that University of Tennessee researchers will use to conduct the kinematic analysis using a model-fitting approach, the relative pose of knee implant components will be determined in 3D from a single-perspective fluoroscopic image by manipulating a CAD model in 3D space.

Using a model-fitting technique, the 3D bones will be overlaid onto the fluoroscopic images to determine amount of medial OA offloading. Successive fluoroscopic images of each subject's stance phase, with and without the OA brace, will be downloaded to a computer. Images will be captured at five instances during stance-phase of gait: heel strike, 33% of stance phase, mid-stance, 66% of stance-phase and at toe-off. A comparative analysis will be conducted for each subject while wearing the OA brace and with their non-braced test. Then, the amount of medial condylar separation will be assessed for each subject.

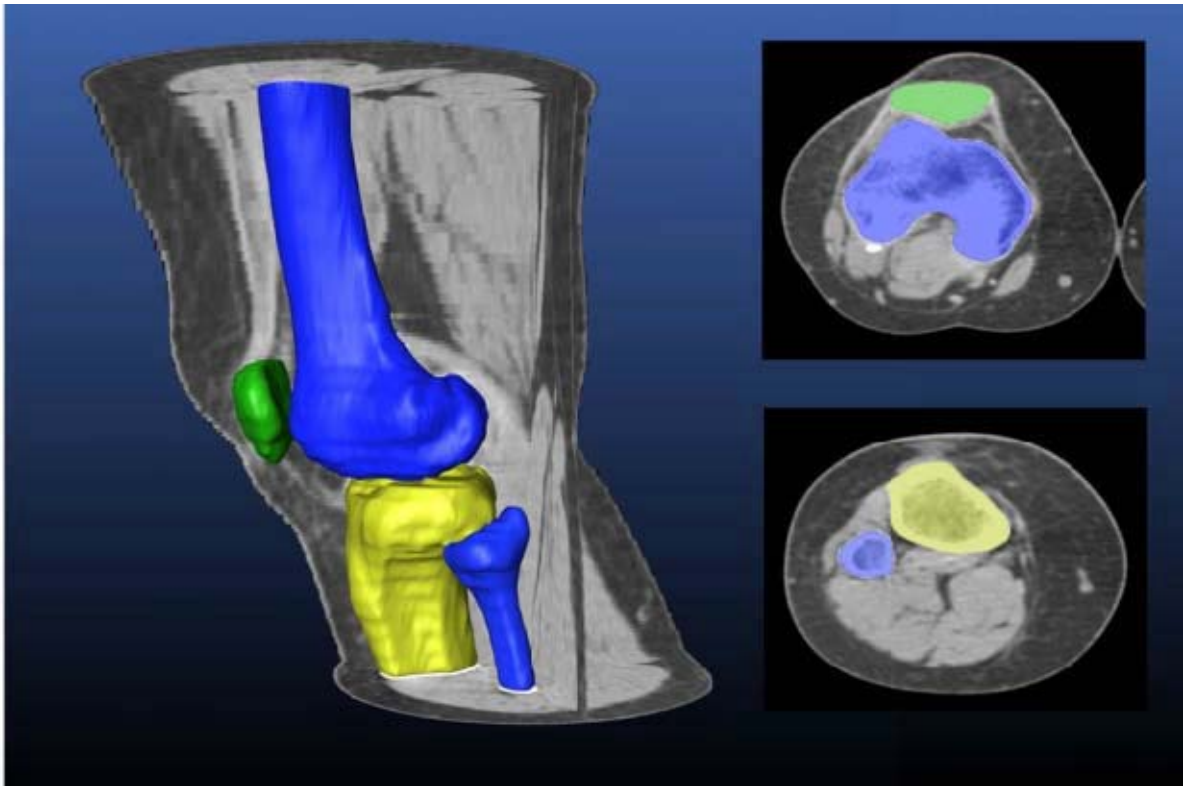


Figure 2. Example of 3D bone creation.

CT Scan
Participants will be asked to schedule a CT scan at Porter Adventist Hospital at their convenience within 1 month of the initial data collection day. To ensure subject safety, CT will be limited to the affected knee and the rest of patient's body will be protected from radiation with lead protection. The CT scan will be limited to the study knee and will image 6 inches distal on the tibia and 6 inches proximal on the femur.

Private Health Information/Medical Record Data
It is not anticipated that the subjects' medical files should need to be accessed for any PHI for the study for recruitment or for the conduct of the study itself. However, contact information from patient files will be acquired for inquiring as to whether or not patients would be willing to participate. The only subject-specific data that will be necessary will be measurements of medial condyle separation from the medial tibial plateau for each subject with and without a brace. Researchers will acquire the measurements with the brace while they are conducting the data collection. Researchers may also acquire the subjects' medial condyle separation without the brace while they are present for data collection. However, if this is not possible or time does not permit, Colorado Joint Replacement staff may send that information to UT researchers via secure transfer (e.g., UT Vault).

The subject data – fluoroscopy frames, video footage and ultrasound– will be uploaded and stored on CMR's secure server for use in this and future studies (if participant permission is obtained via IC) by the researcher(s) who attend data collection or appointed by Dr. Komistek. Once data has been uploaded, the database automatically removes subject identifiers and assigns an ID for each subject. Only these files of de-identified data are now available for researchers to review and analyze. Only Dr. Komistek, Dr. LaCour and Garett Dessinger have access to the

identifiable data that was originally uploaded by the GRA, as it remains in a password-protected portion of the secure server. Only Dr. LaCour and Mr. Dessinger can grant access to this identifiable password- protected portion of the database by changing a user's level of authentication with different privilege levels.

Researchers would like to retain this study 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 orthopaedic products. Participants will be asked if their study data may remain a part of the CMR data collection for use in future studies in the IC. Likewise, should a subject 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 destroyed from CMR records; subjects choosing to withdraw will be asked to complete a Revocation of Consent wherein they may indicate their preference regarding the data collected from them.

On the day of data collection, the list of patient names will be given to UT researchers and the researchers will generate subject-specific identifiers for each participant. A table will be generated for this study, indicating the participant's name and generated ID number; this table with subject names and corresponding ID numbers will be provided to Colorado Joint Replacement staff, so the staff will be aware of which identifier is linked with each subject. If necessary (i.e., time not permitting during data collection; researchers unable to collect measurement), Colorado Joint Replacement staff may relate the measurements of medial condyle separation from the medial tibial plateau for each subject without a brace securely to UT researchers via the UT Vault https://vault.utk.edu/.

SPECIFIC RISKS AND PROTECTION MEASURES

1. Fluoroscopic Procedures

As with every clinical study, there may be some risks. However, doses of radiation exposure received will be much lower than those known to produce detectable health effects. Previously reported literature shows that fluoroscopy-based procedure (angiography) on the lower limb result in a typical effective dose of 0.83 mSv per min (0.083 rem per min) (Verdun [1]). Mettler, et al. have reported that the typical effective dose for a conventional knee procedure is 0.005 mSv (0.0005 rem)[2]. According to either estimate, the additional risk of a fluoroscopic procedure involving the knee ranges between "Negligible" to "Low" for a 2 minute exam (Verdun). A previous fluoroscopy TKA study conducted at another hospital with a 2 minute on-time limit shows that the average effective dose was 0.14 mSv (0.0014 rem) with a maximum dose of 0.27 mSv (0.027 rem). The additional risk for all subjects in this previous study would be considered "Negligible." To account for subject variability and differences in imagining techniques, all subjects enrolled in this study will receive less than 2.0 rem. 2.0 rem is considered "Low" risk. It is unlikely that anyone in this study will approach the 2.0 rem limit. Since the fluoroscopy data will be collected in one session, there will only be one day in which the participants will be exposed to this amount of radiation.

2. CT Scan

In addition to the radiation exposure from the fluoroscopy procedure, all subjects will be exposed to radiation from the CT scan of the knee (which is considered an "extremity"), estimated at 0.01 rem, according to the American Nuclear Society's Radiation Dose Chart,

http://www.ans.org/pi/resources/dosechart/ (Attachment 4). The radiology department at Porter Adventist hospital uses a software program call Caredose that automatically keeps the dose as low as possible on all CT exams. Insofar as the amount of time for the CT scans taking place, we estimate approximately 30 minutes for the exam itself.

In conclusion, a participant who will be fluoroscoped for less than two minutes will be exposed to a maximum amount of only 2.0 rems of radiation. This means that the maximum total exposure rate will be less than 2.0 rems per subject for the entire experiment. The participant's knee joint will be fluoroscoped using negligible to low risk levels of radiation according to published literature.

The participant has the right to stop the procedure at any time; researchers or the RT can end the procedures at any time if they feel the participant is at risk, but the participant can choose to remain in the study if s/he feels that there is no risk to her/his surgical procedure or recuperation.

3. Participant Confidentiality

The investigators will ensure subject confidentiality to the extent that is permissible by law is maintained throughout the study and after. Researchers not notated as Investigators of this study that have access to subjects during data collection will sign pledges of confidentiality. Complete confidentiality cannot be guaranteed.

Computer Database

As noted, on the day of data collection, the list of patient names will be given to UT researchers and researchers will generate subject-specific identifiers; Colorado Joint Replacement staff will be provided with this list of subject names and corresponding generated identifiers. These assigned identifiers will be uploaded into an excel spreadsheet created by UT researchers. Colorado Joint Replacement staff will be aware of each subject's respective identifier from the table provided to them on the day of data collection after UT researchers generate the subject-specific identifiers

Researchers present during data collection or appointed by Dr. Komistek will upload the subject data, including fluoroscopy, video and ultrasound, into the CMR digital data collection. Consequently, student researchers in CMR who assist in data analysis cannot access subject-specific information. All participant queries (lookups) generate the participant identification number and no subject identifiers. No identifiable images exist in the database. This study data will be kept indefinitely on the secure CMR database for possible future research (with the permission of each participant – requested in the IC). In the case of participant withdrawal from the study, the Revocation of Consent that the participant will be asked to complete requests that the participant indicate whether or not data collected prior to withdrawal may be used for data analysis purposes, or if it should be removed from the CMR data collection completely and destroyed.

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 participant study data:

List of Persons Involved in Research:

- Dr. Richard Komistek, PI, UT Professor, Biomedical Engineering
- Dr. Michael LaCour, Sub-Investigator, UT Research Assistant Professor, Biomedical Engineering
- Dr. Douglas Dennis, Co-PI, Colorado Joint Replacement, Orthopaedic Surgeon
- Dr. Jason Jennings, Sub-Investigator, Colorado Joint Replacement, Orthopaedic Surgeon
- Jacob Elkins, Sub-Investigator, Colorado Joint Replacement, Orthopaedic Surgeon
- Lindsay Kleeman-Forsthuber, Sub-Investigator, Colorado Joint Replacement, Orthopaedic Surgeon
- Clinical Research Staff, including Ms. Roseann Johnson, Ms. Anna Brady and Ms. Aviva Pollet, Colorado Joint Replacement
- Radiation technician(s) will operate the fluoroscopy machine, Porter Adventist Hospital
- Required MD present during the fluoroscopy procedure
- Rebecca Robertson, Research Coordinator, UT staff
- Researchers present during data collection at the University of Tennessee and/or the lead researchers appointed by Dr. Komistek.
    - Graduate students:
        - Garett Dessinger
        - Jarrod Nachtrab
        - Milad Khasian
        - Lauren Smith
        - Seth Coomer
    - * Undergraduate student researchers employed by CMR will be involved in analyzing the data after it has been collected and transferred to CMR's digital data collection. Since subject 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 subjects. They will only have access to the study data that has been uploaded onto the secure CMR digital collection. These undergraduate student researchers will not have contact with subjects.
- Institutional Review Boards
    - The University of Tennessee will/has waived oversight to WIRB. Reliance Agreement included.
    - Centura Health/Catholic Health Initiatives will/ has waived oversight to WIRB. Reliance Agreement included.
    - Western Institutional Review Board.
- A representative from Breg, Inc. will be present at data collection to fit subjects with the brace properly. This individual will sign a pledge of confidentiality.
- A representative from JointVue will be present at data collection to acquire 3 dimensional bone images using JointVue's ultrasound procedure and software. This individual will sign a pledge of confidentiality.

Clinical Observations:

There are no clinical observations made during this data collection or from the images obtained through data collection. UT researchers do not require any kind of report from the radiology

department. Unless the data collection site requires such a report, 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 physician's office for evaluation or review. However, if researchers see anything in the imaging that is extremely out of the ordinary (*e.g.,* floating body, severe dislocation, potential tumors [spots of incredibly dense tissue on bones and skin]), they will bring this to the attention of Drs. Dennis or Jennings or their staff.

It is not anticipated that the imaging collected during this study would potentially provide benefit to specific subjects by influencing the physician's treatment plan.

BENEFITS

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

- Better understanding of the joints analyzed with the same technique in the past.
- Future brace design improvements based on the kinematic findings.
- There is no intention of any direct benefit to participants of the study. Information related to the data gathered may be provided to Drs. Dennis or Jennings by the researchers if something out of the ordinary is seen during the imaging. However, researchers are not radiologists and cannot interpret anything they may see. If there is something within the imaging that is obviously wrong as mentioned above, then this could result in potential modification of a subject's treatment plan if images collected as a result of this study reveal any kind of "significant problem."

COMPENSATION

The participants in this study will receive a $50 onetime payment in the form of a check for participation that will be mailed to the participate after completion of their CT Scan.

METHODS TO OBTAIN "INFORMED CONSENT" FROM PARTICIPANTS

Informed consent will be obtained prior to any procedures being conducted. Subjects who are agreeable to participate will be scheduled to visit Porter Adventist Hospital on the day that UT researchers will travel there for data collection. Appointed staff from Colorado Joint Replacement and/or UT researchers will be responsible for consenting the participants, giving them ample time to review and complete the forms and assist the participants with review of the documentation, if the participants are unable to read the form on their own. Only upon signed consent will the subject be allowed to participate in the study. If the subject chooses to be removed from the study after participating, his/her video, fluoroscopy footage and ultrasound data that was collected will be managed according to the subject's response on the Revocation of Consent form. A copy of his/her Revocation of Consent will be attached to his/her IC and placed in a separate, secure file for IRB review. These consent forms will be stored at UT, Knoxville and will be accessible by only the aforementioned personnel.

Drs. Dennis and Jennings will not be present during the consenting process to avoid possible subject coercion to participate. Subjects may contact Colorado Joint Replacement with any questions they may have.

From previous studies, we have determined that it takes approximately 15 minutes to consent a subject and answer any questions that s/he may have. We have also estimated approximately 20 minutes for researchers to guide the subject through the steps of the procedure, allow the subject

to practice the activity and then to actually perform the activity under fluoroscopic surveillance; actual radiation exposure will be up to, but not more than two minutes. The ultrasound portion of the data collection should take approximately 10 minutes. We have estimated a total time of approximately 45 minutes for each subject to be consented and complete the fluoroscopy and ultrasound procedures.

ATTACHMENT 1

Verdun FR, Bochud F, Gundinchet F, Aroua A, Schnyder P, Meuli R. Quality Initiatives Radiation Risk: What You Should Know to Tell Your Patient 1. *Radiographics* 2008 Nov 28(7):1807-16.

Table 2
Generic Dose-Area Products, Conversion Factors, and Effective Doses at Angiography in a Standard Adult Patient

Examination*	Fluoroscopy time (min)	Dose-Area Product (Gy • cm^2)	Conversion Factor (mSv/Gy • cm^2)	Effective Dose (mSv)
Cerebrum	12	75	0.04	3.0
Coronary arteries	4	75	0.20	15.0
Abdomen	8	80	0.25	20.0
Lower limbs	6	50	0.10	5.0

Source.—Adapted from reference 27.
*Including image acquisition.

Table 3
Generic Dose-Length Products, Conversion Factors, and Effective Doses at CT in a Standard Adult Patient

Examination	Dose-Length Product (mGy • cm)	Conversion Factor (mSv/mGy • cm)	Effective Dose (mSv)
Head	1000	0.0023	2.3
Neck	400	0.0054	2.2
Chest	300	0.017	5.1
Abdomen-pelvis	500	0.015	8.0
Lower limbs (excluding pelvis)	500	0.0012	0.6

Sources.—References 21 and 32.

Table 4
What to Tell Your Patients concerning Additional Risk of Death from Cancer

Effective Dose (mSv)	Risk	Quantification	Examination
<0.1	$<10^{-6}$	Negligible	Radiography of the chest (postero-anterior), extremities, or teeth
0.1–1.0	10^{-5}	Minimal or extremely low	Abdomen, lumbar spine
1.0–10	10^{-4}	Very low	CT of the brain, chest, or abdomen
10–100	10^{-3}	Low	Multiphase CT
>100	$>10^{-2}$	Moderate	Interventional procedures,* repeat CT

Sources.—References 10 and 22.
*Including the determinist effects of ionizing radiation (skin burns).

ATTACHMENT 2

Mettler, et al. "Effective Doses in Radiology and Diagnostic Nuclear Medicine." *Radiology* 248.1 (2008): 254-263. http://radiology.rsna.org/content/248/1/254.full.pdf+html

Results

Representative values and ranges of effective doses reported in the literature for various examinations and procedures are presented in Tables 1–5.

In addition to effective dose, absorbed organ doses are important for some procedures that either involve high doses or include sensitive tissues in the primary radiation beam. For CT scanning, organs in the beam can receive doses that are 10–100 mGy but are usually in the range of 15–30 mGy per single CT sequence (162–169).

Doses to the lens of the eye during CT scanning of the head have been reported to be 30–50 mGy (170–174). Values depend on whether the lens is in the direct beam or out of the beam when the gantry is angled. Angulation of the gantry for head CT studies can reduce the eye dose by 90%, to about 3–4 mGy. For many new scanners, such as portable intensive care unit scanners, positron emission tomography/CT scanners, and dual-tube multidetector CT scanners, the gantry cannot be angled, which will result in higher eye doses when head CT examinations are performed.

Radiation dose to the breast tissue is of critical importance, especially in girls and young women. Chest CT scanning results in relatively high doses to breast tissue. Doses have been estimated to be 20–60 mGy for a CT examination performed for pulmonary embolism, 50–80 mGy for a CT coronary angiography examination, and even 10–20 mGy to the inferior part of the breast for an abdominal CT examination (175–177). Even though lower x-ray energies are used, as a comparison, for mammography, the American College of Radiology and the Mammography Quality Standards Act of 1992 regulations require that the mean glandular dose for a single mammogram to a normal-sized breast with 50% glandularity be less than 3 mGy.

Discussion

As mentioned earlier, effective dose is a calculated age- and sex-averaged value that is used as a robust measure to compare detriment from cancer and hereditary effects due to various procedures involving ionizing radiation. Martin (178) has pointed out a number of limitations in its use, including about ±40% uncertainty for a reference patient. Often, effective dose is calculated and expressed to a much greater precision than is warranted, and we have expressed values to only one significant digit. There clearly are additional problems in trying to apply the sex-averaged effective dose to procedures that predominantly involve one sex (such as mammography).

The sources of information reviewed were variable in quantity, qual-

Table 1

Adult Effective Doses for Various Diagnostic Radiology Procedures

Examination	Average Effective Dose (mSv)	Values Reported in Literature (mSv)
Skull	0.1	0.03–0.22
Cervical spine	0.2	0.07–0.3
Thoracic spine	1.0	0.6–1.4
Lumbar spine	1.5	0.5–1.8
Posteroanterior and lateral study of chest	0.1	0.05–0.24
Posteroanterior study of chest	0.02	0.007–0.050
Mammography	0.4	0.10–0.60
Abdomen	0.7	0.04–1.1
Pelvis	0.6	0.2–1.2
Hip	0.7	0.18–2.71
Shoulder	0.01	...
Knee	0.005	...
Other extremities	0.001	0.0002–0.1
Dual x-ray absorptiometry (without CT)	0.001	0.001–0.035
Dual x-ray absorptiometry (with CT)	0.04	0.003–0.06
Intravenous urography	3	0.7–3.7
Upper gastrointestinal series	6*	1.5–12
Small-bowel series	5	3.0–7.8
Barium enema	8*	2.0–18.0
Endoscopic retrograde cholangiopancreatography	4.0	...

* Includes fluoroscopy.

Table 2

Adult Effective Doses for Various CT Procedures

Examination	Average Effective Dose (mSv)	Values Reported in Literature (mSv)
Head	2	0.9–4.0
Neck	3	...
Chest	7	4.0–18.0
Chest for pulmonary embolism	15	13–40
Abdomen	8	3.5–25
Pelvis	6	3.3–10
Three-phase liver study	15	...
Spine	6	1.5–10
Coronary angiography	16	5.0–32
Calcium scoring	3	1.0–12
Virtual colonoscopy	10	4.0–13.2

ATTACHMENT 3

HEALTH PHYSICS SOCIETY

RADIATION RISK IN PERSPECTIVE

POSITION STATEMENT OF THE HEALTH PHYSICS SOCIETY*

Adopted: January 1996
Revised: July 2010
Further revised: May 2016

Contact: Brett Burk
Executive Director
Health Physics Society
Telephone: 703-790-1745
Fax: 703-790-2672
Email: HPS@BurkInc.com
http://www.hps.org

The Health Physics Society advises against estimating health risks to people from exposures to ionizing radiation that are near or less than natural background levels because statistical uncertainties at these low levels are great.

The average annual equivalent dose[1] from natural background radiation in the United States is about 3 mSv. A person might accumulate an equivalent dose from natural background radiation of about 50 mSv in the first 17 years of life and about 250 mSv during an average 80-year lifetime.

Substantial and convincing scientific data show evidence of health effects following high-dose exposures (many multiples of natural background). However, below levels of about 100 mSv above background from all sources combined, the observed radiation effects in people are not statistically different from zero.

Scientists evaluate and estimate radiation risk using several assumptions that, taken together, may lead to a range of hypothetical health risk estimates for any given exposure scenario.

For radiation protection purposes and for setting radiation exposure limits, current standards and practices are based on the questionable premise that any radiation dose, no matter how small, could result in detrimental

[1] Dose is a term used to express or quantify the amount of radiation a person or object has received. Equivalent dose to an organ or tissue is a quantity derived from the absorbed dose. Equivalent dose is used in radiation protection to relate absorbed dose to the probability of a stochastic radiation effect (cancer induction and hereditary changes) in that organ or tissue. The equivalent dose represents the sum of all of the contributions from radiations of different types multiplied by their respective radiation qualities.

health effects such as cancer or heritable genetic damage. Implicit in this linear no-threshold (LNT) hypothesis is the core assumption that detrimental effects occur proportionately with radiation dose received (NAS/NRC 2006). However, because of statistical uncertainties in biological response at or near background levels, the LNT hypothesis cannot provide reliable projections of future cancer incidence from low-level radiation exposures (NCRP 2001).

Molecular-level radiation effects are nonlinear

Studies show that dose-response relationships are typically nonlinear (Tubiana and Aurengo 2006; Tubiana et al. 2006). Substantial scientific data indicate that the LNT model of radiation effects oversimplifies the relationship between dose and response. Linearity at low dose may be rejected for a number of specific cancers, such as bone cancer, lymphoma, and chronic lymphocytic leukemia. Heritable genetic damage has not been observed in human studies.

Recent low-dose research indicates that biological response mechanisms such as DNA repair, bystander effects, and adaptive response modulate radiation-induced changes at the molecular level. Cellular transformation leading to carcinogenesis by mutation of genetic material appears to be a complicated, multistep process that is not reflected in the LNT model.

Radiogenic health effects have not been consistently demonstrated below 100 mSv

Due to large statistical uncertainties, epidemiological studies have not provided *consistent* estimates of radiation risk for whole-body equivalent doses less than 100 mSv. Underlying dose-response relationships at molecular levels appear mainly nonlinear. The low incidence of biological effects from exposure to radiation compared to the natural background incidence of the same effects limits the applicability of radiation risk coefficients at organ equivalent doses less than 100 mSv (NCRP 2012).

The references to 100 mSv in this position statement should not be construed as implying that health effects are well established for doses exceeding 100 mSv. Considerable uncertainties remain for stochastic effects of radiation exposure between 100 mSv and 1,000 mSv, depending upon the population exposed, the rate of exposure, the organs and tissues affected, and other variables. In addition, it is worth noting that epidemiological studies generally do not take into account the dose that occupationally or medically exposed persons incur as natural background; thus, the references to 100 mSv in this position statement should generally be interpreted as 100 mSv above natural background dose.

Dose-rate issues

Risk estimates commonly used to predict health effects in exposed individuals or populations are based primarily on epidemiological studies of Japanese atomic bomb survivors and other populations exposed to relatively high doses delivered at high dose rates. Animal, cellular, and molecular studies all demonstrate that at any level of biological organization, the responses following low-dose-rate exposure are less than observed after the same dose delivered at a high dose rate (Dauer et al. 2010). Epidemiological studies have not consistently demonstrated adverse health effects in persons exposed to small (less than 100 mSv) doses protracted over a period of many years.

Collective dose and radiation protection planning

A common approach in many circles, not recommended here, involves extrapolating the calculated risk derived at high doses to low-dose levels. Extrapolation may be convenient for setting radiation protection guidelines. However, when used prospectively to predict future risk to an exposed population, the multiplication of small risk coefficients by large population numbers leads inevitably to unsupportable claims of cancer risk from ionizing radiation (NCRP 1997, 2012).

Significant dosimetry uncertainties for individual subjects characterize most epidemiological studies. Actual doses and individual responses to radiation may be highly variable. It follows, therefore, that the collective population dose (the sum of individual whole-body equivalent doses expressed in units of person-sievert) is a highly uncertain number. Since the risk coefficient at low dose is uncertain, and the individual contributors to collective population dose are also uncertain, the resultant uncertainty is greater than each of the individual contributions—and should not be used with confidence to predict cancer incidence in an exposed population.

Equivalent dose is not defined for short-term deterministic effects

The concept of equivalent dose applies only to population group averages (reference models) for radiation protection purposes and not to biological risk for individual subjects. Since the radiation-weighting factors used to derive equivalent dose were developed only for stochastic effects, the equivalent dose is not applicable to deterministic biological effects. Therefore, equivalent dose should not be used for evaluating organ or tissue toxicity from radiation.

References

Dauer LT, Brooks AL, Hoel DG, Morgan WF, Stram D, Tran P. Review and evaluation of updated research on the health effects associated with low-dose ionising radiation. Radiat Protection Dosimetry 140:103–136; 2010.

National Academies of Science/National Research Council. BEIR VII Phase 2: Health risks from exposure to low levels of ionizing radiation. Washington, DC: National Academies Press; 2006.

National Council on Radiation Protection and Measurements. Uncertainties in fatal cancer risk estimates used in radiation protection. Bethesda, MD: National Council on Radiation Protection and Measurements; NCRP Report No. 126; 1997.

National Council on Radiation Protection and Measurements. Evaluation of the linear-nonthreshold dose-response model for ionizing radiation. Bethesda, MD: National Council on Radiation Protection and Measurements; NCRP Report No. 136; 2001.

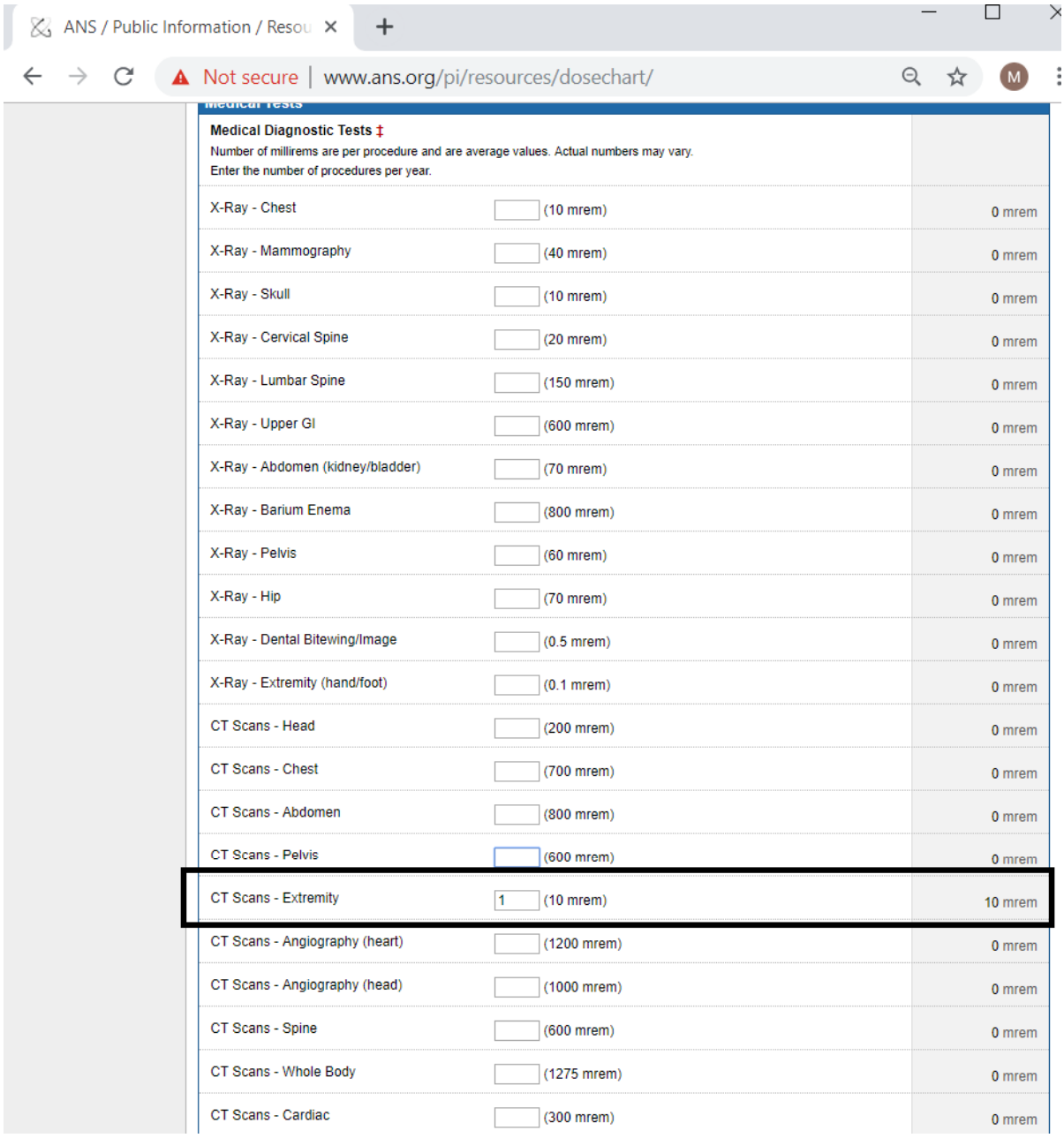
National Council on Radiation Protection and Measurements. Uncertainties in the estimation of radiation risks and probability of disease causation. Bethesda, MD: National Council on Radiation Protection and Measurements; NCRP Report No. 171; 2012.

Tubiana M, Aurengo A. Dose-effect relationship and estimation of the carcinogenic effects of low doses of ionizing radiation: The joint report of the Académie des Sciences (Paris) and of the Académie Nationale de Médecine. Int J Low Radiat 2 (3/4); 2006.

Tubiana M, Aurengo A, Averbeck D, Masse R. Recent reports on the effect of low doses of ionizing radiation and its dose-effect relationship. Rad Environ Biophys 44(4):245–251; 2006.

*The Health Physics Society is a nonprofit scientific professional organization whose mission is excellence in the science and practice of radiation safety. Since its formation in 1956, the Society has represented the largest radiation safety society in the world, with a membership that includes scientists, safety professionals, physicists, engineers, attorneys, and other professionals from academia, industry, medical institutions, state and federal government, the national laboratories, the military, and other organizations. Society activities include encouraging research in radiation science, developing standards, and disseminating radiation safety information. Society members are involved in understanding, evaluating, and controlling the potential risks from radiation relative to the benefits. Official position statements are prepared and adopted in accordance with standard policies and procedures of the Society. The Society may be contacted at 1313 Dolley Madison Blvd., Suite 402, McLean, VA 22101; phone: 703-790-1745; fax: 703-790-2672; email: HPS@BurkInc.com.

ATTACHMENT 4



Medical Diagnostic Tests ‡

Number of millirems are per procedure and are average values. Actual numbers may vary.
Enter the number of procedures per year.

X-Ray - Chest		(10 mrem)	0 mrem
X-Ray - Mammography		(40 mrem)	0 mrem
X-Ray - Skull		(10 mrem)	0 mrem
X-Ray - Cervical Spine		(20 mrem)	0 mrem
X-Ray - Lumbar Spine		(150 mrem)	0 mrem
X-Ray - Upper GI		(600 mrem)	0 mrem
X-Ray - Abdomen (kidney/bladder)		(70 mrem)	0 mrem
X-Ray - Barium Enema		(800 mrem)	0 mrem
X-Ray - Pelvis		(60 mrem)	0 mrem
X-Ray - Hip		(70 mrem)	0 mrem
X-Ray - Dental Bitewing/Image		(0.5 mrem)	0 mrem
X-Ray - Extremity (hand/foot)		(0.1 mrem)	0 mrem
CT Scans - Head		(200 mrem)	0 mrem
CT Scans - Chest		(700 mrem)	0 mrem
CT Scans - Abdomen		(800 mrem)	0 mrem
CT Scans - Pelvis		(600 mrem)	0 mrem
CT Scans - Extremity	1	(10 mrem)	10 mrem
CT Scans - Angiography (heart)		(1200 mrem)	0 mrem
CT Scans - Angiography (head)		(1000 mrem)	0 mrem
CT Scans - Spine		(600 mrem)	0 mrem
CT Scans - Whole Body		(1275 mrem)	0 mrem
CT Scans - Cardiac		(300 mrem)	0 mrem