

MULTICENTER OSTEOARTHRITIS STUDY

LONGITUDINAL KNEE RADIOGRAPH ASSESSMENTS (BASELINE TO 15-MONTH, 30-MONTH, 60-MONTH AND 84-MONTH FOLLOW-UP) AND MEASUREMENTS FROM BASELINE FULL LIMB RADIOGRAPHS

DATASET DESCRIPTION AND READING PROTOCOL JULY 2016

Table of Contents

Overview2
Introduction2
Variables
Missing Data5
Methods
Image Type6
Time Points6
Reading Methods6
Calculated Variables6
Definitions of Incident Radiographic OA and Progression9
References10
APPENDIX A: Measurements from Full Limb Radiographs
APPENDIX B: Knee X-ray Reading Discrepancy Adjudication13
APPENDIX C: Image Inventory16

Overview

Dataset:MOSTV01235XRAYObservations:3026 (1 record per study participant)Annotated Forms:AnnotatedForms_V01235xray.pdfVariable Guide:VariableGuide_V01235xray.pdfDistributions:Distributions_V01235xray.pdfFormats:FORMATS.SAS7BDAT (contains all the formats used for the dataset)

At present, data from baseline thru 84-month follow-up visit are released.

This dataset contains x-ray readings of Kellgren and Lawrence grades and OARSI joint space narrowing grades along with scores for other individual radiographic features (IRFs) such as osteophytes and sclerosis, along with variables for longitudinal changes between all possible paired combinations of visits.

There is a separate dataset (OUTCOMES) which has special variables for cumulative incidence of radiographic OA (ROA), and for progression of radiographic OA from the baseline visit. The documentation for that dataset, and page 9 of this document, give more information on the different definitions of incident ROA and progression of ROA that can be used. So for analyses involving incidence or progression of ROA, we recommend that the OUTCOMES dataset should be used.

Limb alignment measurements from baseline visit full-limb radiographs are also in this dataset.

Introduction

MOST serial knee radiographs were read at the Boston University Clinical Epidemiology Research and Training Unit. The radiographs were read with visits grouped and temporal order known, from baseline to 15, 30, 60 and 84-month follow-up visits, by 2 readers for Kellgren-Lawrence grade (KLG) and Individual Radiographic Features (IRFs, see page 5). Knees without follow-up images were scored for baseline KLG only or baseline KLG and other features. The number of knees with various combinations of assessments is shown in the table below:

Assessments	Right Knee	Left Knee
Five x-ray Baseline to 15M, 30M,60M, and 84M Assessments	160	157
Quadruplet Baseline to 15M, 30M, and 60M Assessments	33	34
Quadruplet Baseline to 15M, 30M, and 84M Assessments	12	12
Quadruplet Baseline to 15M, 60M, and 84M Assessments	3	3
Quadruplet Baseline to 30M, 60M, and 84M Assessments	1508	1504
Triplet Baseline to 15M and 30M Assessments	58	53
Triplet Baseline to 15M and 60M Assessments	2	2
Triplet Baseline to 15M and 84M Assessments	1	1
Triplet Baseline to 30M and 60M Assessments	245	260
Triplet Baseline to 30M and 84M Assessments	79	82
Triplet Baseline to 60M and 84M Assessments	39	35
Paired Baseline to 15M Assessments	20	23
Paired Baseline to 30M Assessments	472	461
Paired Baseline to 60M Assessments	23	26

 MOST Longitudinal Knee Radiograph Assessments & Baseline Visit Full Limb Radiograph Measurements
 2 of 17

 Dataset Description And Reading Protocol
 7/25/16

Assessments	Right Knee	Left Knee
Paired Baseline to 84M Assessments	15	17
Baseline KLG Only (Participants with baseline readings and no follow-up		
images)	209	210
Baseline KLG and Other Features (Subset of participants with baseline		
readings and no follow-up images)	98	89
No Assessments (baseline KR or other x-ray exclusion)	49	57
Total	3026	3026

At the baseline visit, MOST full limb radiographs were acquired in almost all participants. This dataset contains central measurements of frontal plane lower limb mechanical alignment using hip-knee-ankle (HKA) angle. The analysis of these images was performed by OAISYS Inc (Dr. Derek Cooke <u>http://www.oaisysmedical.com</u>) with support of staff at Queen's University, Kingston, Ontario.

<u>Variables</u>

The Variable Guide (VariableGuide_V01235xray.pdf) is a complete list of all variables in the dataset, their SAS variable names, descriptive variable labels, and attributes. If you are unfamiliar with the data, it may be useful to begin by reviewing the annotated data collection forms (AnnotatedForms_V01235xray.pdf) to look for variables of interest.

The dataset contains five types of variables, listed below. The first type is related to measurements of HKA from full limb radiographs and the remaining 4 types are related to readings of bilateral PA view radiographs:

- 1. Measurements of HKA angle (in degrees) where neutral alignment is represented by 0 degrees with varus deviations negative and valgus deviations positive. (eg: V0XLHKA is left limb hip-knee-ankle angle).
- 2. Raw radiograph reading from a specific visit (for example, V0XRKL: Right knee KLG at the baseline visit).
- 3. Change score between two visits for a specific measure (for example, V02XRKL_C: Right knee KLG change from baseline to 30 months).
- 4. Derived status of a knee or person meeting the criteria for a specific measure (for example, V0XRTFROA: Right knee tibiofemoral radiographic OA).
- Derived indicator of a knee meeting the criteria for a specific outcome measure (for example JSN progression: V02XRTFJSL_P: Right knee joint space narrowing progression from baseline to 30 months).

Variables are prefixed VxXs indicating the visit(s) and side (right or left). For example, in the prefix V0XR, V0 = Baseline visit, XR = Right side. The following suffixes are used to identify derived indicator variables:

- _C: Change score between two visits (between any pair of visits).
- _P: Joint space narrowing progression status (from baseline to follow-up visits).
- k (lower case): Indicator of which knee meets the criteria for a specific measure.

The dataset contains the following prefix and suffix combinations:

Prefixes	Visit/Side	Suffix
V0XR, V0XL	Baseline right/left knee	
V1XR, V1XL	15M right/left knee	

Prefixes	Visit/Side	Suffix
V2XR, V2XL	30M right/left knee	
V3XR, V3XL	60M right/left knee	
V5XR, V5XL	84M right/left knee	
V01XR, V01XL	Right/left knee change from BL to 15M	_C
V02XR, V02XL	Right/left knee change from BL to 30M	_C
V03XR, V03XL	Right/left knee change from BL to 60M	_C
V05XR, V05XL	Right/left knee change from BL to 84M	_C
V12XR, V12XL	Right/left knee change from 15M to 30M	_C
V13XR, V13XL	Right/left knee change from 15M to 60M	_C
V15XR, V15XL	Right/left knee change from 15M to 84M	_C
V23XR, V23XL	Right/left knee change from 30M to 60M	_C
V25XR, V25XL	Right/left knee change from 30M to 84M	_C
V35XR, V35XL	Right/left knee change from 60M to 84M	_C
	Right/left knee progression determined by	
V02XR, X02XL	change from BL to 30M	_P
	Right/left knee progression determined by	
V03XR, X03XL	change from BL to 60M	_P
	Right/left knee progression determined by	
V05XR, X05XL	change from BL to 84M	_P
V0X	Which knee at baseline	k (lower case)
V1X	Which knee at 15M	k (lower case)
V2X	Which knee at 30M	k (lower case)
V3X	Which knee at 60M	k (lower case)
V5X	Which knee at 84M	k (lower case)

Variables assessed from Bilateral Full Limb Radiographs:

• Measurement of hip-knee-ankle (HKA) angle in right and left limbs (see Appendix A for more information).

Variables assessed from Bilateral PA View Knee Radiographs:

 KLG (see Kellgren and Lawrence¹) scored in whole grades, 0 to 4. Scores correspond to tibiofemoral osteoarthritis (TFOA) status, as follows:

KLG Score	OA Status
KLG = 0 KLG = 1	No TFOA
KLG=1.9*	Possible incident TFOA
KLG = 2 KLG = 3	Definite TFOA
KLG = 4	End stage TFOA
KLG = 8	<u>KR/Poor Quality</u> : Special missing score denoting that reading was discontinued due to knee replacement or poor quality image.
KLG = 9	Excluded: Special missing score denoting that reading was discontinued due to rheumatoid arthritis, osteonecrosis, machine failure, or other criteria.

* Non-standard; see below.

The non-standard value of 1.9 (described as KLG=2N), represents a knee that has developed a definite osteophyte, but has no joint space narrowing. This value only exists for follow-up visits. The change from KLG=1 to KLG=1.9 (2N) is represented in change variables as a "within-grade" change, and represents a weaker definition of incident radiographic OA than transition from KLG<=1 to KLG>=2. See page 9 for more information on these two definitions of incident radiographic OA used in MOST.

Grade changes and reliability of the scoring method are described by Felson et al².

 Individual Radiographic Features (IRFs) such as osteophytes and joint space narrowing (JSN) in specific anatomic locations, based on published atlases³.

Non-integer grades for joint space narrowing (JSN) variables <u>at a follow-up visit</u> represent the same OARSI grade as at the previous visit, but differ by a fraction of an integer to denote definite progression within an OARSI grade. This means that non-integer grades (eg: x.2, x.4, x.5, x.7 and x.9) are used, and indicate whether JSN has narrowed, but by less than a whole OARSI grade. An example of this would be a knee scored JSN=2 at baseline, JSN=2.2 at 15-month follow-up, JSN=2.4 at 30-month follow-up, JSN=2.4 at 60-month, and JSN=3 at 84-month follow-up. This would indicate that the knee has an OARSI JSN grade=2 at all visits, except the 84-month visit, but that the readers had agreed that narrowing had occurred between baseline and 15-months, and again between 15-months and 30-months, but that there was no narrowing between 30-month and 60-months. There was then also narrowing between 60-months and 84-months, and that the 84-month visit OARSI grade was 3. For more detail about the method see Felson *et al*².

Non-integer grades for joint space narrowing (JSN) variables <u>at the baseline visit</u> are used to indicate a special situation where the readers consider that the baseline score is very close to the next highest JSN grade (eg: V0XLJSM=2.5 means that the baseline visit left knee medial joint space is very close to zero and could be considered "bone-on-bone" and it usually represents a situation where a later timepoint has VxXLJSM=3 indicating no medial joint space width and a JSN grade of 3.) Users might want to treat knees with a baseline grade of JSN=2.5 as a special case of knees that are very close to end-stage.

IMPORTANT NOTE: These non-integer grades SHOULD NOT be used as equivalent to specific fractional amount of joint space narrowing (i.e. 2.2 to 2.4 does not represent two tenths of a grade change) but rather indicate only a perception of a qualitative increase in JSN within the same OARSI grade compare to another time point.

Missing Data

The dataset includes records for 3026 participants. Where expected data do not exist for a knee, special missing values are assigned to denote why the data were not acquired. The special missing values include:

.P	Not expected: Data missing because the exam was not done (appears only in
	follow-up data since all 3026 participants have a baseline exam).
.S	End stage OA: Data is missing because the maximum value was reached at the
	initial time point (used for change variables and progression status).
.Χ	X-ray not read: Baseline feature other than KLG was not read because only a

	single time point was available to be read.
.Z	Not determined: The value cannot be determined because the calculation is
	dependent on missing data (for example, if there is no tibiofemoral OA and
	patellofemoral radiographic OA was not read, whole knee OA cannot be
	determined).

<u>Methods</u>

Image Type:

Bilateral, weight-bearing fixed-flexion posteroranterior (PA) and lateral knee radiographs were acquired in MOST, along with Full Limb Radiographs. See the <u>Knee and Full-Limb Radiography</u> (X-ray) Operations Manual for the acquisition protocol.

Time Points:

<u>Full Limb Radiographs:</u> Baseline and 60-month follow up visits.

<u>Bilateral PA View Knee Radiographs and Lateral Knee Radiographs:</u> Baseline, 15-month follow-up (subset of cohort), 30-month, 60-month and 84-month follow-up visits.

Reading Methods:

Full Limb Radiographs:

For information about measurements taken from full limb radiographs, see Appendix A.

Bilateral PA View Knee Radiographs:

The rest of this section describes the reading methods for longitudinal semi-quantitative (SQ) assessments of the bilateral PA View Knee radiographs. Two expert readers, blinded to subject's clinical data, assessed each participant's films. Baseline and follow-up films were scored while viewed simultaneously. Readers were not blinded to chronological order of the images. When readers disagreed on key features, or changes in key features, an adjudication procedure was followed (see Appendix B for more information).

Calculated Variables:

Radiographic tibiofemoral (TF), patellofemoral (PF), and whole knee (WK) OA status were defined for each knee at each visit if the corresponding features were read.

- Radiographic TF OA Status (Variable names: VxXsTFROA)
 - 0: No, KLG 0-1
 - 1: Yes, KLG 2-4
- Radiographic PF OA Status (Variable names: VxXsPFROA)
 - 0: No
 - 1: Yes= Any osteophyte >=2 or JSN >= 1 plus any osteophyte, sclerosis, or cyst >= 1 in the PF joint
- Radiographic WK OA Status (Variable names: VxXsWKROA) (See Felson et al.⁴)
 0: No, neither TF nor PF radiographic OA (see above definitions)
 - 1: Yes, either TF or PF radiographic OA (see above definitions)

The presence of radiographic TF OA, PF OA, and WK OA was determined for right and left knees of each participant at each visit.

- Knees with radiographic TF OA (Variable names: VxXTFROAk)
 - 0: None
 - 1: Right
 - 2: Left
 - 3: Both
- Knees with radiographic PF OA (Variable names: VxXPFROAk)
 - 0: None
 - 1: Right
 - 2: Left
 - 3: Both
- Knees with radiographic whole knee OA (Variable names: VxXWKROAk)
 - 0: None
 - 1: Right
 - 2: Left
 - 3: Both

Symptomatic (Sx) OA status was defined for each knee at each visit if the whole knee OA status was known at the visit or any prior visit, and the knee pain symptoms questionnaires (telephone and clinic interview) had no missing values. Symptomatic OA is derived from the variables VxXsWKROA (see above) and frequent knee pain (FKP) variables VxR_FKP / VxL_FKP (right and left) in the clinical datasets (VxENROLL).

- Symptomatic OA status (Variable names: VxXsSxOA)
 - 0: No, whole knee radiographic OA was not present (see above definition) or knee pain questionnaires had no missing values and the answers were any combination other than Yes/Yes*
 - 1: Yes, whole knee radiographic OA was present and knee pain questionnaire answers were Yes/Yes* at both time points

* Yes/Yes means that at both time points (telephone and clinic interview), the participant reported knee pain, aching, and stiffness on most days for at least one month in the past 12 months.

- Knees with symptomatic OA status (Variable names: VxXSxOAk)
 - 0: None
 - 1: Right
 - 2: Left
 - 3: Both

<u>Note</u>: Symptomatic OA status at each visit is based on radiograph whole knee OA and frequent symptoms status at the indicated visit. Frequent symptom status can change over time, so a knee with symptomatic OA at baseline may not be classified as having symptomatic OA at follow-up if the participant no longer reports frequent symptoms in that knee. Investigators⁵ have noted this pain fluctuation pattern in longitudinal studies of

knee OA. MOST recruited and enrolled study participants with knee symptoms, so the prevalence of symptomatic OA was higher than in the general population.

Five-level JSN change variables between two visits were calculated for the medial TF compartment, lateral TF compartment, TF joint, and PF joint for each knee if the corresponding compartments or joint had JSN score < 3 in the corresponding compartment or joint at the earlier visit. It is not required that radiographic OA be present at baseline.

- Change of medial TF JSN (Variable names: VxxXsTFJSM_C) <u>Note</u>: If JSN change was different on PA view and lateral view in the medial compartment, change in medial TF JSN was classified based on the view with the greatest change.
 - 1: decrease
 - 2: no change
 - 3: within grade increase
 - 4: full grade increase
 - 5: more than full grade increase
- Change of lateral TF JSN (Variable names: VxxXsTFJSL_C) <u>Note</u>: If JSN change was different on PA view and lateral view in the lateral compartment, change in lateral TF JSN was classified based on the view with the greatest change.
 - 1: decrease
 - 2: no change
 - 3: within grade increase
 - 4: full grade increase
 - 5: more than full grade increase
- Change of TF JSN in either medial or lateral compartments (Variable names: VxxXsTFJS_C) <u>Note</u>: If JSN change was different in compartments. TF JSN was classified based on the compartment with the greatest change.
 - 1: decrease
 - 2: no change
 - 3: within grade increase
 - 4: full grade increase
 - 5: more than full grade increase
- Change of PF JSN (Variable names: VxxXsPFJS_C)
 - 1: decrease
 - 2: no change
 - 3: within grade increase
 - 4: full grade increase
 - 5: more than full grade increase

Four-level KLG change variables between two visits were defined in TF joint for each knee if the knee had KLG < 4 in the corresponding joint at the earlier visit, remembering that KLG=3.5 is bone-on-bone (end stage) on the PA view x-ray.

- Change of KLG (Variable names: VxxXsKL_C)
 - 1: decrease
 - 2: no change
 - 3: within grade increase
 - 4: full grade increase

5: more than full grade increase

<u>Note</u>: Value of 3 (within grade increase) was assigned to change between KLG=1 and special situation of KLG=2N (see below for more information on KLG=2N).

Two-level JSN progression variables between baseline and each follow-up visit were calculated for the medial TF compartment, the lateral TF compartment, the TF joint, the PF joint, and the whole knee for each knee <u>if the knee had radiographic OA but did not reach the end stage in the corresponding joint at the baseline visit</u>.

- Progression of medial TF JSN (Variable names: V0yXsTFJSM_P)
 0: decrease or no change
 - 1: any increase, including within grade increase
- Progression of lateral TF JSN (Variable names: V0yXsTFJSL_ P)
 0: decrease or no change
 - 1: any increase, including within grade increase
- Progression of TF JSN (Variable names: V0yXsTFJS_ P)
 0: decrease or no change
 - 1: any increase, including within grade increase
- Progression of PF JSN (Variable names: V0yXsPFJS_P)
 - 0: decrease or no change
 - 1: any increase, including within grade increase
- Progression of whole knee JSN (Variable names: V0yXsWKJS_P)
 - 0: decrease or no change
 - 1: any increase, including within grade increase

Definitions of Incident Radiographic OA and Progression:

Typically incident radiographic OA at a specific visit is the development of structural changes scored as KLG >= 2 at a follow-up visit, where the earlier visits were scored KLG 0 or 1.

Following this standard, incident radiographic knee OA occurred when a knee with a KLG of 0-1 became a grade 2 or higher at a subsequent visit.

In addition, the readers classified the incident KLG 2 radiographic OA as resulting from either:

- a) new or enlarging definite osteophyte with normal joint space (described as KLG of 2N, represented by a value 1.9 in the variables VxXsKL),
- or
- b) the new combination of a definite osteophyte and joint space narrowing in a knee that did not have this combination at previous visits (denoted by a new KLG of 2).

The reason for doing this is related to the different definitions of each KLG that have been used over the years, where KLG=2 in particular was sometimes defined as an unimpaired joint space, and other times defined having joint space narrowing⁶.

Definition (a) is a weaker definition of incident ROA and definition (b) is a stronger definition. In this dataset, knees which are KLG 0-1 at early visits, but which become KLG=2 at a later visit

represent knees which meet either of these two definitions. For analyses which might want to separate out knees which meet each of these two separate definitions, we recommend use of the OUTCOMES dataset which contains separate variables (V99ELXKL2N for left knee, V99ERXKL2N for right knee) that can used to identify knees with incident ROA which meets either definition (a) or (b) and separate variable (V99ELXKL2 for left knee, V99ERXKL2 for right knee) which identifies knees which only meet the stronger definition (b) of incident ROA. See the documentation for the OUTCOMES dataset for further information about these variables.

We define progression of ROA as a worsening of JSN score (including within-grade worsening) in a knee which has radiographic OA at the initial time point of the analysis. As well as variables V99ELXKL2N, V99ERXKL2N, V99ELXKL2 and V99ERXKL2 which indicate prevalence, incidence of radiographic OA from the baseline visit, the OUTCOMES dataset also contains variables for indicating cumulative worsening of joint space from baseline (eg: V99ELXJSNM/ V99ERXJSNM for medial tibio-femoral joint space, V99ELXJSNL/ V99ERXJSNL for lateral tibio-femoral joint space). Again the documentation for the OUTCOMES dataset provides further information about these variables.

References

- 1. Kellgren JH, Lawrence JS. <u>Radiological assessment of osteo-arthritis</u>. Ann Rheum Dis. 1957;16:494–502. PMID: 13498604.
- Felson DT, Nevitt MC, Yang M, Clancy M, Niu J, Torner JC, Lewis CE, Aliabadi P, Sack B, McCulloch C, Zhang Y. <u>A new approach yields high rates of radiographic progression in</u> <u>knee osteoarthritis</u>. J Rheumatol. 2008 Oct;35(10):2047-54. PMID: 18793000. PMCID: PMC2758234.
- 3. Altman RD, Gold GE. <u>Atlas of individual radiographic features in osteoarthritis, revised</u>. Osteoarthritis Cartilage. 2007;15 Suppl A:A1-56. PMID: 17320422.
- Felson DT, McAlindon TE, Anderson JJ, Naimark A, Weissman BW, Aliabadi P, Evans S, Levy D, LaValley MP. <u>Defining radiographic osteoarthritis for the whole knee</u>. Osteoarthritis Cartilage. 1997 Jul;5(4):241-50. PMID: 9404469.
- Zhang Y, Nevitt M, Niu J, Lewis C, Torner J, Guermazi A, Roemer F, McCulloch C, Felson D. <u>Fluctuation of knee pain and changes in bone marrow lesions, effusions and synovitis on</u> <u>MRI: The MOST study</u>. Arthritis Rheum. 2011 Mar; 64(3): 691-9. PMID: 21360498.
- 6. Croft P. <u>An introduction to the atlas of standard radiographs of arthritis</u>. Rheumatology 2005; 44(Suppl 4) iv42. PMID: 16306482.

Additional imaging background literature is available on MOST Online under Data and Documentation (<u>http://most.ucsf.edu/datadocs.asp</u>).

<u>APPENDIX A</u>: Measurements from Full Limb Radiographs

In general, frontal plane lower limb alignment is measured from standing bilateral radiographs of the lower limbs in their entirety, with knees fully extended (called 'full-limb' radiographs in MOST). Positional reliability is provided for by aligning the 'knee flexion plane' ahead. Frontal alignment may be defined as the angle between the mechanical axes of the femur and tibia. This angle has been termed the hip-knee-ankle (HKA) angle or the mechanical axis angle. The measurements in this dataset have been made from digital full-limb images using software programs (OAISYS Inc) to obtain the measurement of alignment. These publications give more details about the methods and measurement performance:

- Cooke TD, et al. Frontal plane knee alignment: a call for standardized measurement. J Rheumatol. 2007; 34(9):1796-801. PMID: 17787049.
- Cooke TD, et al. Analysis of limb alignment in the pathogenesis of osteoarthritis: a comparison of Saudi Arabian and Canadian cases. Rheumatol Int. 2002; 22(4):160-4. PMID: 12172956
- Sled E, et al. Reliability of lower limb alignment measures using an established landmark-based method with a customized computer software program. Rheumatol Int. 2011: 31:71-7

From the anatomical and functional perspective, the orientation of the femur and tibia at the knee is best described in terms of the bones' mechanical axes. The orientation of these axes reflects alignment in stance, which may be neutral, varus (bowlegged), or valgus (knock-kneed) (Figure 1).

The mechanical axis of the femur (FM) is located as a line from the center of the femoral head running distally to the mid-condylar point between the cruciate ligaments. In the case of the tibia, the mechanical axis (TM) is a line from the center of the tibial plateau (interspinous intercruciate midpoint) extending distally to the center of the tibial platond. The angle between these two axes is the hip-knee-ankle (HKA) angle. In the neutrally-aligned limb the HKA angle approaches 180°. At this point FM and TM are co-linear, pass through the knee center, and are coincident with the load-bearing axis (LBA) which is the line of ground reaction force passing from the ankle to the hip (Figure 1B).

In *varus* the knee center is lateral to the LBA (Figure 1A), whereas in *valgus* the knee center is displaced medially (Figure 1C). As a convention the HKA is expressed as its angular deviation from 180° (i.e. HKA = 0° in neutral alignment). Varus deviations are negative and valgus ones are positive. The choice of varus as a negative value and valgus as positive is based on the general observations of a more serious problem of loading and damage in the varus knee.



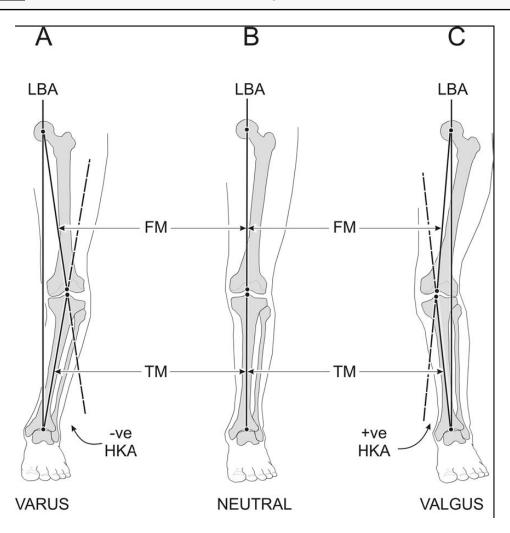


Figure 1. Common frontal plane lower limb alignment patterns. A. Varus alignment: knee center is lateral to the LBA (HKA is negative). B. Neutral alignment: knee center is located on the LBA (HKA = 0°); femoral and tibial mechanical axes are colinear. C. Valgus alignment: knee center is medial to the LBA (HKA is positive). LBA: load-bearing axis, HKA: hip-knee-ankle angle, FM: femoral mechanical axis, TM: tibial mechanical axis.

APPENDIX B: Knee X-ray Reading Discrepancy Adjudication

Overview

Films were read independently by two primary readers and discrepancies adjudicated in order to allow comparison of key findings that the senior reader may have missed and to ensure high quality data by reducing measurement error.

Pre-specified discrepancies between readers were adjudicated in a consensus session with films viewed simultaneously and a third reader participating. The values in this dataset are the final, adjudicated readings. When a variable was not adjudicated for discrepancies, the value in the dataset is from the senior reader.

Reader disagreements that were adjudicated were TF OA and PF OA status (Y/N) and its change in all knees, and progressive JSN (Y/N) in those knees with OA in the TF and/or PF joints at one or more time points.

Adjudication rules for the key variables are listed below. For all of these variables, readings for only these variables were adjudicated if the two readers did not agree on the variable.

PA Radiographs

Knee OA status and its progression was classified into one of the following four groups for each two consecutive visits, and the readings adjudicated if the two readers did not agree on the classification:

- No OA at either time point.
- Incident OA (no OA at baseline, OA at follow-up).
- Prevalent OA at the earlier visit, no progression in KLG in the follow-up visit.
- Prevalent OA at the earlier visit, progression in KLG in the follow-up visit.

A knee was not adjudicated if:

- Both readers agreed there was 'No OA' longitudinally but one reader scored KLG progression while the other did not (e.g. KLG 0 → 1 by one reader vs. other reader scored knee as 1 → 1).
- Both readers agreed there was incident OA but the KLG at either visit differed by reader (e.g. reader one scored 1 → 2; reader two scored 1 → 3).
- Both readers agreed there was prevalent OA at the earlier visit but the KLG at either visit differed by reader as long as both agreed there was/was not KLG progression (e.g. reader one scored 3 → 3; reader two scored 2 → 2).

<u>Note</u>: When a variable was not adjudicated, the value in the dataset is from the senior reader.

APPENDIX B: Knee X-ray Reading Discrepancy Adjudication (continued)

Joint Space Narrowing (JSN)

Joint space narrowing was scored 0-3 based on the OARSI Radiographic Atlas. However, when follow-up film clearly showed worsening JSN Knee X-ray Reading compared to the film from the previous visit, but narrowing for both films was still within one OARSI grade, readers were permitted to use non-integer grades (e.g. $2 \rightarrow 2.2$). Progression was defined as present when there was an increase in score by a grade of >=0.2. Progression status was classified into one of the following two groups for each two consecutive visits, and readings were adjudicated if the two readers did not agree on the classification:

- JSN progression in either the medial and/or lateral compartments in the follow-up visit.
- JSN progression in the follow-up visit but in different compartments (e.g. one reader scored progression in the medial compartment whereas other reader scored it in the lateral).

A knee was not adjudicated if:

- The two readers agreed there was no progression, even if one reader scored JSN as being present but the other reader did not.
- The two readers agreed there was progression, even if one reader scored JSN as being present but the other reader did not.
- Both readers scored progression but disagreed on the amount of progression (e.g. one reader scored an increase in one grade whereas the other reader scored an increase of two grades).

Lateral Radiographs

TF and/or PF JSN Progression

Change of TF JSN and/or PF JSN was classified into one of the following two groups for each two consecutive visits and the knee was adjudicated if the two readers did not agree on the classification:

- TF JSN progression in the follow-up visit.
- PF JSN progression in the follow-up visit.

A knee was not adjudicated if:

- One reader scored TF JSN and/or PF JSN but the other reader did not, as long as neither read progression in JSN.
- The two readers agreed on progression but differed on the amount of progression.

APPENDIX B: Reader Discrepancy Adjudication (continued)

PF Osteoarthritis (PF OA: 0=No PFOA; 1=Definite PFOA) and Progression

Knee PF OA status and its progression was classified into one of the following three groups for each two consecutive visits and the knee was adjudicated if the two readers did not agree on the classification:

- No PF OA longitudinally.
- Incident PF OA (no PF OA at initial radiograph; PF OA present at the follow-up radiograph).
- Prevalent PF OA at the initial radiograph.

Adjudication sessions were held approximately every month. These sessions were attended by both primary readers and a third reader. All adjudicated readings were arrived at by consensus of readers and the adjudicated score was recorded on the senior reader's scoring sheet. After consensus was reached, the dataset was updated. When readers' data are in agreement, both are archived and the dataset of the senior reader will be used in analysis.

Other features were not adjudicated (e.g. cysts, osteophytes, sclerosis). For these features, the senior reader's readings were used. However, to make the data consistent after adjudication, some of the scores for these variables were changed during adjudication, e.g. if KLG and/or progression was changed during adjudication to be consistent with the adjudicated score. For example, if the adjudicated score was KLG 2 and the senior reader had '0' for all osteophytes, then this was reevaluated by the readers to create logical consistency of all feature scores.

APPENDIX C: Image Inventory

When MOST radiograph image sets are requested, an image inventory dataset will be provided to the recipient.

Dataset

Dataset:	V01235XRAYinv.sas (inventory of all available images)
Observations:	3026 (1 record per study participant)
Variable Guide:	VariableGuide_ V01235XRAYinv.pdf
Distributions:	Distributions_ V01235RAYinv.pdf

Variables

The dataset includes the following variables:

Full Limb Radiographs: Number of images available in the dataset for each participant

Variable	Description
V0_FL	Baseline Full Limb Radiograph - Bilateral
V3_FL	60M Full Limb Radiograph - Bilateral

PA Views: Number of images available in the dataset for each participant

Variable	Description
V0_PA	Baseline PA view – Bilateral knees
V1_PA	15M PA view – Bilateral knees
V2_PA	30M PA view – Bilateral knees
V3_PA	60M PA view – Bilateral knees
V5_PA	84M PA view – Bilateral knees

Lateral Views: Number of images available in the dataset for each participant

Variable	Description
V0R_Lat	Baseline Lateral view - Right knee
V1R_Lat	15M Lateral view - Right knee
V2R_Lat	30M Lateral view – Right knee
V3R_Lat	60M Lateral view - Right knee
V5R_Lat	84M Lateral view - Right knee
V0L_Lat	Baseline Lateral view - Left knee
V1L_Lat	15M Lateral view - Left knee
V2L_Lat	30M Lateral view – Left knee
V3L_Lat	60M Lateral view - Left knee
V5L_Lat	84M Lateral view - Left knee

<u>Values</u>

0= None (The participant has no images available)

1= 1 view (The participant has one image available)

2= 2 views (The participant has two images available)

APPENDIX C: Image Inventory (continued)

Beam Angles

Beam angles used for PA view knee radiographs (5, 10, and 15 degrees) are stored in the DICOM Series Description. When a participant had more than two PA views taken, the two best were selected for release by the MOST MR Imaging Quality Assurance readers. Some participants have two PA views available for a given beam angle because a single film could not include the entire anatomy of both knees. No more than one lateral view per knee is available.

De-identification

For de-identification purposes, the images have been altered as follows:

- 1. Gender and clinic site are not revealed in the images.
- 2. Exam date is not revealed in the images. The images for all participants are dated by study visit:
 - Baseline = 1/1/2005
 - 15 Months = 1/1/2006
 - 30 Months = 1/1/2007
 - 60 Months = 1/1/2008
 - 84 Months = 1/1/2009

When repeat exams were done and those images are in the image set, the January month in the date is replaced with February, March, etc., to distinguish the sequence of repeat exams.

Hard Drive Return

Image sets are transferred on a loaned UCSF hard drive. Recipients are responsible for the return of the hard drive within ten working days to the following:

Maria Klemm UCSF Dept. Epidemiology and Biostatistics 550 16th Street, 2nd Floor, Box 0560 San Francisco, CA 94143 (for **FedEx** use 94158) United States of America Ph: (415) 514-8177 Email: mrivera@psg.ucsf.edu

Study Contacts

Questions and problems: Email <u>MOSTOnline@psg.ucsf.edu</u>.