MULTICENTER OSTEOARTHRITIS STUDY
KNEE MAGNETIC RESONANCE IMAGING ASSESSMENTS
(BASELINE TO 15-MONTH AND 30-MONTH FOLLOW-UP WORMS)
DATASET DESCRIPTION AND READING PROTOCOL

JUNE 2011

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I. Overview

Three MOST Knee Magnetic Resonance Image Assessment datasets are publicly available:

1) Baseline/15-Month Incident Knee Symptoms Cases and Controls (V01WORMS)
   Dataset: MOSTV01WORMS.sas7bdat
   Observations: 415 (1 record per knee: variable KNEE, 'L'=Left and 'R'=Right)
   Annotated Forms: AnnotatedForms_V012WORMS.pdf
   Variable Guide: VariableGuide_ V01WORMS.pdf
   Distributions: Distributions_ V01WORMS.pdf
   Formats: FORMATS.SAS7BDAT (contains all the formats used for the dataset)

   Description: The dataset includes knees with no OA symptoms at baseline and selected for reading at a pre-specified ratio of 1 case (all available among those knees that developed symptoms at the 15-month follow-up) to 2 controls (those who did not develop symptoms at the 15-month follow-up). The selection was frequency matched by clinic. The variable V1_SXMRI identifies selection for reading as cases or controls with the values '1:Case read' and '2:Control read'.

   In MOST, OA symptoms are defined as the presence of frequent knee pain (FKP): pain on most days within the past 30 days reported at 2 contact points within the visit. FKP status is derived from the calculated variables VxR_FKP and VxL_FKP in the clinical datasets VxEnroll (see Variables and Naming Conventions, page 8).

2) Baseline/30-Month Subset of Knees with Baseline OA (V02WORMS_BLROA)
   Dataset: MOSTV02WORMS_BLROA.sas7bdat
   Observations: 597 (1 record per knee: variable KNEE, 'L'=Left and 'R'=Right)
   Annotated Forms: AnnotatedForms_V012WORMS.pdf
   Variable Guide: VariableGuide_ V02WORMS_BLROA).pdf
   Distributions: Distributions_ V02WORMS_BLROA).pdf
   Formats: FORMATS.SAS7BDAT (contains all the formats used for the dataset)

   Description: The dataset includes knees with baseline radiographic whole-knee OA that was not end stage OA (tibiofemoral and patellofemoral end stage OA) randomly selected for reading among those eligible for progression at the 30-month follow-up. The variable TFPFPG identifies progression status with the values '0: no change' and '1: progression'.

3) Baseline/30-Month Incident Radiographic OA (V02WORMS_INCIDENTROA)
   Dataset: MOSTV02WORMS_INCIDENTROA.sas7bdat
   Observations: 443 (1 record per knee: variable KNEE, 'L'=Left and 'R'=Right)
   Annotated Forms: AnnotatedForms_V012WORMS.pdf
   Variable Guide: VariableGuide_ V02WORMS_INCIDENTROA.pdf
   Distributions: Distributions_ V02WORMS_INCIDENTROA.pdf
   Formats: FORMATS.SAS7BDAT (contains all the formats used for the dataset)

   Description: The dataset includes knees with no baseline radiographic OA and selected for reading at a pre-specified matched ratio of 1 case (all available among those knees that developed radiographic OA at the 30-month follow-up) to 2 controls (knees which did not develop radiographic OA at the 30-month follow-up). The selection was frequency matched by clinic. The variable V2_ROAMRI identifies selection for reading as cases or controls with the values '1:Case read' and '2:Control read'.

II. MRI Scoring Methods

The Whole Organ MRI Scoring (WORMS) method, described by Peterfy et al[1], was used with minor modifications to score the MR images for structural changes related to knee OA. This method, combined with the types of MR images acquired in MOST, has been shown to be suitable for semi-quantitative evaluation of osteoarthritis of the knee[2,3]. Appendix A shows the details of the 1.0T extremity scanner MRI acquisition protocol used in MOST.

A. Time Points Scored

Dataset (Vxx) and variable prefixes (Vx) contain numeric indicators of the time points scored. Images were assessed from the following time points:

- Baseline visit identifier = V0
- 15-month follow-up visit identifier = V1 (a subset of the cohort was examined)
- 30-month follow-up visit identifier = V2

- Longitudinal: Baseline to 15-month change visit identifier = V01
- Longitudinal: Baseline to 30-month change visit identifier = V02

All incident symptoms readings were paired baseline and 15-month follow-up images read together in known chronological order. Radiographic OA readings were done by reading either the single baseline or paired baseline and 30-month follow-up images.

B. Knee Selection for Reading

Several nested-case control and cohort subsamples were selected for reading in order to address the specific aims of the NIA-funded MOST grant proposals. Image quality criteria also played a role in which knees were read.

IMPORTANT: Investigators need to exercise caution when combining subsamples of MRI readings to address a research question. Combining such samples for analysis can cause problems stemming from the impact of the sampling mechanism on bias in estimating association between predictors and outcomes. This can occur in several common situations.

A) Using observations from nested case-control samples in MOST in order to study a predictor of an outcome other than the one defining the original case and control samples. When there is an association between the new outcome variable and case–control status the analysis can give biased results if it does not take the original case–control sampling design into account.

B) Combining observations from additional subsamples (knees or subjects) with the observations from a case-control sample in order to study a predictor of the original case-control outcome. When the selection criteria for the additional subsample are associated with case-control status and are effects of the predictor, an analysis that does not take the complex sampling design into account can give biased results.

These situations have in common that observations come from subsamples selected using criteria that are related to the outcome under investigation. It is essential to seek guidance from a statistician when considering or attempting such analyses. For information about MOST sub-sample selection, contact MOSTOnline@pgs.ucsf.edu. Also see Lee, McMurchy, and Scott[6] and Scott[7].

C. Articular Surface and Related Features scored using WORMS

The following five articular surface and related features were scored in a large number of different anatomical locations as described in Appendix B.

1) Cartilage Morphology

Cartilage morphology was scored from 0 to 6 in each of the five subregions in the medial and lateral compartments, and in four subregions of the patello-femoral joint for a total of fourteen subregions. Appendix B describes these anatomical locations in detail.

Score/Value	Description	Any Cartilage Lesion	Full Thickness Loss
0	Normal thickness	No	No
1*	-	-	-
2	Partial thickness focal defect <1 cm in greatest width	Yes	No
2.5	Full thickness focal defect <1 cm in greatest width	Yes	Yes
3	Multiple areas of < 1 cm partial-thickness (grade 2) defects intermixed with areas of normal thickness, or a partial thickness defect wider than 1 cm but <75% of the region	Yes	No
4	Diffuse (>75% of the region) partial-thickness loss	Yes	No
5	Multiple areas of full-thickness loss (grade 2.5) or a grade 2.5 lesion wider than 1 cm but <75% of the region	Yes	Yes
6	Diffuse (>75% of the region) full-thickness loss	Yes	Yes

* *Signal abnormalities (scored as grade 1 in WORMS from T2 weighted images) were not used when scoring MOST MR images.*

Due to the large amount of change required to cause full grade changes in certain situations, readers could record longitudinal changes in cartilage scores for a given subregion that were not large enough to score a full grade increase. In such cases, the baseline and follow-up scores have the same grade recorded, but the reader indicates a partial "within" grade change. The value of the longitudinal change variable (see Calculated Variables for Change and Prevalence, page 11) in such cases will indicate "worsening."

For example, a grade 3 lesion at baseline which had enlarged by follow-up but had not become large enough to be grade 4, and had not developed the full thickness loss required for grade 5, would be scored by the readers with a within grade change indicator. Thus the score for the subregion at the follow-up visit remains a grade 3, but there was worsening in comparison to the prior visit.

2) Bone Attrition

Bone attrition severity, which records presence of deformation of the normal shape of the subchondral bone surface, was scored on a four-point scale in the same fourteen subregions (Appendix B) as cartilage morphology.

Score/Value	Description
0	Normal
1	Mild
2	Moderate
3	Severe

3) Osteophytes

Osteophyte size, scored 0 to 7, was scored in sixteen subregions. The anatomical subregion divisions used for those locations are described in Appendix B.

Score/Value	Description
0	None
1	Equivocal
2	Small horizontal spur
3	Moderate horizontal or small curved spur
4	Large horizontal or moderate curved spur
5	Moderate-large curved spur
6	Large exuberant spur
7	Very large irregular spur

In MOST, a score >=2 at an anatomical location defines the presence of a definite osteophyte.

4) Bone Marrow Lesions (BMLs)

BMLs – diffuse hyperintense lesions on the MOST MR images - were scored from 0 to 3. BMLs were scored in fifteen articular surface subregions as described in Appendix B.

Score/Value	Description
0	None
1	< 25% of subregion
2	25%-50% of subregion
3	>50% of subregion

As with cartilage lesions, readers were allowed to record whether within grade changes in BMLs had occurred longitudinally, compared to baseline, but since BMLs are reversible in nature, readers could record both within grade worsening and improvement.

5) Subchondral Cysts

Subchondral cysts – hyperintense lesions with well defined boundaries on the MOST MR images - were scored from 0 to 3 in the same subregions as used for BML scoring.

Score/Value	Description
0	None
1	< 25% of region
2	25%-50% of region
3	> 50% of region

D. Other Main Structural Features Scored in WORMS

1) Meniscal Tears and Signal Abnormalities

Meniscal tears were graded as described by Peterfy et al[1] in the anterior horn, the body segment, and the posterior horn of the medial and lateral meniscus. Definite meniscal damage or pathology was defined as a tear, maceration, and (or) destruction (=any grades >1).

Scores used for assessing meniscal tears in MOST are as follows:

Score/Value	Description
0	Intact
1	Minor radial tear or parrot-beak tear
2	Non-displaced tear or prior surgical repair
3	Displaced tear or partial resection
4	Complete maceration/destruction/resection

2) Joint Effusion

Abnormally large amounts of synovial fluid effusion were graded from 0 to 3 in terms of the estimated maximal distention of the synovial cavity as originally described by Peterfy et al [1].

Score/Value	Description
0	None
1	< 33% of maximum potential distention
2	33%-66% of maximum potential distention
3	> 66% of maximum potential distention

3) Other OA Features

For scoring of other features from WORMS, see Variables and Naming Conventions, page 8, in addition to the original WORMS publication by Peterfy et al[1] for more details.

E. Modifications

Modifications to the original WORMS method are as follows:

1) Reversible vs. Irreversible Change

When scoring bone marrow lesions, we considered change to be reversible, and therefore never considered to be at an end stage. Other features, such as periarticular cysts and bursitis, and loose bodies are considered reversible, either naturally or because surgery or other procedures can cause them to resolve. Meniscal extrusion (MX) is also considered reversible.

We considered change (worsening) to be irreversible in the following six WORMS features and, therefore, when the maximum value (end stage) was reached in these features, they were not eligible for change.

1) Cartilage morphology
2) Osteophytes
3) Bone attrition
4) Subchondral cysts
5) Meniscal tears
6) Ligaments tears

2) Within Grade Changes

For longitudinal readings of cartilage morphology, readers were allowed to indicate a partial "within" grade change in cases where change was seen, but the change was not enough to score a full grade change. In such cases, the baseline and follow-up scores have the same grade recorded, but the value of the change variable will be recorded as "worsening" (within grade increase). See Cartilage Morphology, page 4.

For longitudinal readings of bone marrow lesions, readers were also allowed to indicate a within grade change for both worsening (within grade increase) and improvement (within grade decrease). Again, the baseline and follow-up scores have the same grade recorded, but the value of the change variable will be recorded as worsening or improvement. See Bone Marrow Lesions, page 5.

3) Meniscal Extrusion

Meniscal extrusion of the medial and lateral meniscal body was scored on the coronal plane as described by Englund et al[4] and graded as follows: 0 = no meniscal extrusion, 1 = extrusion < 50%, 2 = extrusion > 50%.

Score/Value	Description
0	None
1	< 50% extruded
2	> 50% extruded

3) Synovitis

Signal changes related to synovitis in Hoffa's fat pad were scored on a 3-point scale on the sagittal non-enhanced PD fat suppressed sequences at the superior edge of the fat pad adjacent to the patella (=''superior'') and the internal fat pad (=''internal''), as previously described by Roemer et al[4].

Score/Value	Description
0	None
1	Mild
2	Moderate
3	Severe

4) Unscoreable Features

For any feature, when it was not possible to score at a particular location for any given exam time point, the readers indicated "not scored" by entering the value of -9.

III. Variables and Naming Conventions

See the variable guide for each dataset for a complete list of all the 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_V012WORMS.pdf) to look for variables of interest.

All the WORMS variables for a knee at a given time point (or pair of time points) are contained in a single, unique record in the dataset (1 row per knee).

Variable names take the form: [*visit prefix*] - [*feature/subregion*] - [*type suffix*].

1) Visit Prefix

Variables are prefixed by 'Vx' indicating the study visit(s):

Visit Prefix	Description
V0	Baseline
V1	15 months
V01	Baseline to 15-month change
V2	30 months
V02	Baseline to 30-month change

2) Feature/Subregion

The central part of the name indicates the feature scored and subregion if applicable. Abbreviations are identified in the next section

3) Type Suffix

Two special types of variables will have the feature/subregion identifier(s) of the variable name followed by a suffix comprised of an underscore and type indicator:

- Where change from one time point to another has been calculated, the suffix '_C' is added, and the prefix indicates both time points, for example V02=Baseline to 30-month change. (See Subregion Change Scores, page 11, and Compartment and Whole Knee Change Scores, page 12.)

- Eligibility for a specific measure is indicated by the suffix '_E'. (See Calculating Prevalence and Eligibility for Incidence or Progression of MRI Features at the Compartment And Knee Level, page 13).

So, for example, the baseline and 30-month cartilage morphology scores for the posterior subregion of the medial femoral condyle is recorded in variables V0CMFMP and V2CMFMP.

Change from baseline to 30-month follow-up in the same feature and location is recorded in variable V02CMFMP_C.

Eligibility for worsening and the presence or absence of worsening of the cartilage morphology medial TF compartment aggregate from baseline to 30 months is recorded in the variables V02CMMTF_E V02CMMTF_C. All eligibility indicator variables are paired with a change variable.

IV. Features And Subregions Assessed (See AnnotatedForms_V012WORMS.pdf)

The following five WORMS features are scored in a large number of individual subregions (see Appendix B). Abbreviations used for the feature identifier variable names are given in parentheses.

1) Cartilage morphology (CM)
2) Osteophytes (OS)
3) Bone attrition (BA)
4) Bone marrow lesions (BM)
5) Subarticular cysts (SC)

The different anatomical subregions in which these features are scored are identified by abbreviations that follow the feature identifier in the variable names. These subregions can be grouped into different compartments of the knee, as outlined below:

- Tibiofemoral Medial Compartment (MTF)
  - Tibial subregions: anterior (TMA), central (TMC) and posterior (TMP)
  - Femoral subregions: central (FMC) and posterior (FMP)
- Tibiofemoral Lateral Compartment (LTF)
  - Tibial subregions: anterior (TLA), central (TLC) and posterior (TLP)
  - Femoral subregions: central (FLC) and posterior (FLP)
- Tibiofemoral Joint (TF)
  - Tibiofemoral Medial Compartment (MTF)
  - Tibiofemoral Lateral Compartment (LTF)
- Patello-Femoral Joint (PF)
  - Patellar subregions: medial (PM) and lateral (PL)
  - Femur (Anterior) subregions: medial (FMA) and lateral (FLA)
- Whole Knee (WK)

So, for example, the variable V0CMTMA is the cartilage morphology score (CM) at baseline visit (V0), in the anterior subregion of the medial tibial plateau (TMA).

The ten tibiofemoral subregions together comprise a combined tibiofemoral joint, which can be combined with the four patello-femoral subregions to form a whole knee.

For bone marrow lesions (BM) and cysts (SC) there is an additional tibial sub-spinous region (abbreviation=BMTSS, or SCTSS) which lies directly below the tibial spines and is in neither of the tibiofemoral or the patello-femoral joints.

For osteophytes (OS), there are two additional patello-femoral subregions for the patella (inferior=OSPI, and superior-OSPS).

Medial and lateral meniscal tear scores are identified using the following abbreviations following the visit prefix:

- Meniscal tears (MT) - medial (MTM) and lateral (MTL) menisci. Each section of meniscus is then identified by further abbreviations: anterior horn (A), body (B) and posterior horn (P)

The remaining WORMS features, which are not scored in multiple subregions, are identified in the variable names by the following abbreviations in parentheses. These abbreviations follow the visit prefix:

- Meniscal extrusion – medial (MXM) and lateral (MXL)
- Synovitis – infra-patellar (SYIP) and inter-condylar (SYIC)
- Effusion – whole knee (EFWK)
- Collateral Ligaments – medial (MCL) and lateral (LCL)
- Cruciate Ligaments – anterior (ACL) and posterior (PCL)
- Meniscal Cysts – medial (MENCYM) and lateral (MENCYL)
- Popliteal/Baker's cysts (POPBAK)
- Tibio-fibular cysts (TFCY)
- Anserine Bursitis (ANSBUR)
- Patellar Bursitis (PATBUR)
- Loose Bodies (LBOD)

V. Special Scores and Missing Values

Where 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:

Value	Description
-9	Data is missing because the feature was not scored.
.	Data is missing because the MRI exam was not done.
.S	End stage OA: Data is missing because the maximum value (end stage OA) was reached at the initial time point. This value is used only for change variables of irreversible features.
.Z	Not determined: The value cannot be determined because the calculation is dependent on missing data.

VI. Calculated Variables for Change and Prevalence

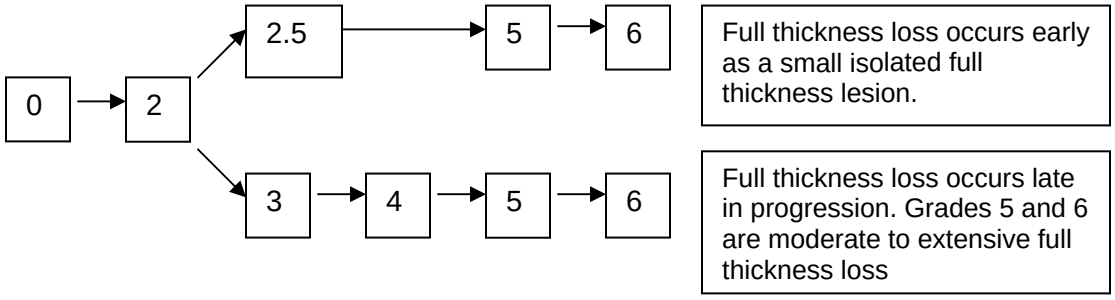
Note that the way in which we have calculated the following variables and aggregated them into compartment, joint, and knee level variables is not the only way to calculate change scores. Consult your analyst and other investigators about the most appropriate way to address these issues for your own analyses.

A. Subregion Change Scores

For each WORMS feature scored, at each anatomical location, a change variable is calculated ('_C' suffix). For example, V02BMFMP_C is the change score variable calculated for the posterior of the medial femoral condyle from baseline to 30-month follow-up.

Formatted Change Score	Description
-1:Improvement	The follow-up visit score is less than the baseline visit score – or – (BMLs only) the scores were the same but the reader indicated a within grade improvement.
0: No change	The baseline and follow-up visit scores are the same – or – (for irreversible features only) the follow-up visit score is less than the baseline visit score or there is missing data at baseline and the follow-up visit score is zero.
1: Worsening	The follow-up visit score is greater than the baseline visit score (increase) – or – (CM or BMLs only) the scores were the same but the reader indicated a within grade worsening.

For cartilage morphology scores, due to the nature in which WORMS uses a single score to asses both the size of the cartilage lesion and the amount of the subregion in which full thickness cartilage has occurred, calculating change scores is more complex. The following progression of cartilage scores constitutes a full grade increase between each of the following sequential the steps:



Any change in cartilage morphology scores between baseline and follow-up visits which represents one or more steps rightwards in either of the above diagram paths is assigned the value "worsening" for the change score.

B. Compartment, Joint, and Whole Knee Change Scores

IMPORTANT: The WORMS cartilage scores do not form a demonstrated ordinal scale, so we *do not add cartilage subregion scores together to form composite cartilage scores* for neither compartments nor the whole knee. Similarly, there has been no evaluation of the scaling properties of composite scores for the other WORMS features, calculated by adding together the subregion scores of one feature or adding together the scores from multiple features. Therefore *no variables have been created for composite scores derived by adding raw subregion scores together to form higher level composite scores*.

For the features cartilage morphology (CM), osteophytes (OS), bone attrition (BA), bone marrow lesions (BM), and subarticular cysts (SC), change scores at the medial tibiofemoral (TF), lateral tibiofemoral compartment, and patello-femoral (PF) compartments were calculated, and the suffix at the end of the variable name indicates the level at which the change score was calculated:

Suffix	Description	Calculation is derived from …
MTF_C	Medial TF compartment change	the 5 medial TF subregions
LTF_C	Lateral TF compartment change	the 5 lateral TF subregions
TF_C	TF joint change	all 10 TF subregions
PF_C	PF joint change	– the 6 PF subregions for osteophytes – the 4 PF subregions for all other features
WK_C	Whole knee change	– all 14 subregions for cartilage morphology and bone attrition – all 16 subregions for osteophytes – all 15 subregions for bone marrow lesions and subarticular cysts

For example, for cartilage morphology from baseline to 30 months, V02CMLTF_C is the tibiofemoral lateral compartment change score, V02CMPF_C is the patellofemoral joint change score, and V02CMWK_C is the whole knee change score.

Compartment/joint/knee change scores are calculated in the following manner:

- If the feature is irreversible and all subregion change scores in the compartment are '.S: end stage OA', then the compartment change score is also '.S: end stage OA'.
- Otherwise, if any of the subregion change scores in the compartment are '1: worsening', then the compartment change score is also '1: worsening'.
- Otherwise, if all of the subregion change scores in the compartment are '0: no change', then the compartment change score is also '0: no change'.
- Otherwise, for reversible features only, if any of the subregion change scores in the compartment are '-1: improvement', and none of the subregion change scores are '.Z: not determined', then the compartment change score is also '-1: improvement'.
- Otherwise, if any of the subregion change scores are '.Z: not determined', then the subregion change score is also '.Z: not determined'.

This algorithm handles missing subregion scores by: a) never assuming that no change or improvement has occurred in compartments with missing data; b) always defining a compartment as worsening if any subregion worsens, even if there are also subregions with missing data or that show improvement; and c) only defining a compartment as improvement if at least one subregion improved and no subregions worsened, and no subregions have missing data.

C. Calculating Prevalence and Eligibility for Incidence or Progression of MRI Features at the Compartment and Knee Level

Calculating prevalence and eligibility for incidence or progression of MRI features at the compartment and knee level is complicated by missing values at the subregion level.

Variables for prevalence and eligibility for change in a given feature for an individual subregion have not been calculated. These can be created, as needed by the user, following the principles below.

For each compartment, joint, and knee level change score variable, there are associated calculated variables with a '_E' suffix that are useful for determining:

- Prevalence of a feature in the compartment/joint/knee
- Whether a compartment/knee is eligible for determining progression or improvement of a prevalent feature
- Whether the compartment/knee is eligible for determining incidence of the feature

These variables define whether a given feature is present or not in a joint, compartment, or knee. These variables should be used in conjunction with the change score for the compartment to determine incidence of the feature, or whether progression or improvement of a prevalent feature has occurred. Also, there are situations where missing values for scores means that incidence cannot be determined, even though the feature is known to have worsened. When scores are missing, analysts can assume that prevalence or worsening can be determined from the non-missing scores. However, eligibility for incidence and improvement can not be determined when scores are missing.

Eligibility variables ('_E' suffix) take the following values:

'_E' Score values	Description
0: Not eligible	Any situation in which none of the other 3 values occurs.
1: Eligible for incidence	All subregions in the compartment have a baseline feature score of normal* and the compartment '_C' score is not '.Z: not determined'.
2: Prevalence not determined	There is at least one subregion in the compartment for which the baseline visit score is missing and all other subregions have normal* feature scores.
3: Prevalence	There is at least one subregion in the compartment for which the baseline feature score is abnormal*, regardless of how many subregions have missing baseline visit scores.

** Osteophytes scores >1 are abnormal, and scores <=1 are normal. All other features, scores > 0 are abnormal, and scores =0 are normal.*

When then combined with the related '_C' change scores for the compartment and feature, these eligibility variables allow determination of incidence or progression.

VII. Knee MRI Reading Procedures and Calibration

Images were read blinded to the alpha-numeric study participant identifier, clinical status, selection status, and the results of any x-ray readings. Images from baseline and follow-up visits were read paired with known chronological order. In reading batches, the selection status was always mixed, so one reader could never read images for a single selection.

IMPORTANT: Analysts using the data are advised to control for reader (the variable ReaderID, identified in the dataset by number) and site (the variable SITE in the clinical dataset VxEnroll, also identified by number).

Reader Calibration and Verification:

All readers received training in the use of WORMS by the senior reader. Post-training readers undertook a set of readings of images previously read by the senior reader. Inter-reader reliability for various WORMS features was then calculated from these duplicate knee readings to verify that readers had a high-level of agreement for WORMS features. Also, during the reading process, a random selection of knees read by other readers were checked by the senior reader for any serious errors in scoring. For inter-reader reliability reports, contact MOSTOnline@pgs.ucsf.edu.

VIII. Comparison with Large-Bore 1.5T MR Imaging

In a small subset of MOST participants for whom 1.5T large-bore MRI scans of the knee were also acquired, semi-quantitative scoring of the 1.0T MRI scans has been shown to have high agreement with the results of scoring the 1.5T scans[2].

IX. References

[1] Peterfy CG, Guermazi A, Zaim S, Tirman PFJ, Miaux Y, White D, et al. Whole-organ magnetic resonance imaging score (WORMS) of the knee in osteoarthritis. Osteoarthritis and Cartilage 2004; 12: 177-190.

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[4] Englund M, Guermazi A, Roemer FW, Aliabadi P, Yang M, Lewis CE, Torner J, Nevitt MC, Sack B, Felson DT. Meniscal tear in knees without surgery and the development of radiographic osteoarthritis among middle-aged and elderly persons: The Multicenter Osteoarthritis Study. Arthritis Rheum. 2009 Mar;60(3):831-9. PMID: 19248082.

[5] Roemer FW, Guermazi A, Zhang Y, Yang M, Hunter DJ, Crema MD, et al. Hoffa's fat pad: evaluation on unenhanced MR images as a measure of patellofemoral synovitis in osteoarthritis. AJR Am J Roentgenol 2009; 192: 1696-700.

[6] Lee AJ, McMurchy L, Scott AJ. Re-using data from case-control studies. Stat Med. 1997 Jun 30;16(12):1377-89. PMID: 9232759.

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

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APPENDIX A: MRI Acquisition Protocol

MRIs were obtained with a 1.0 Tesla dedicated MR system (OrthOne™ ONI Inc., Wilmington, MA) with a circumferential extremity coil using fat-suppressed fast-spin echo (FSE) proton density-weighted sequences in two planes, sagittal and axial, and a STIR sequence in the coronal plane. A few participants also had a coronal FSE sequence and/or a sagittal 3-point Dixon fat suppressed sequence with intermediate weighting.

For MRI acquisition protocol details, see the MOST 1.0T Knee MRI Operations Manual. To summarize, the main sequences used for WORMS readings were acquired with the following parameters, with slight variations (particularly in TR) depending on the number of slices acquired:

Scan Parameters	Axial	Sagittal	Coronal STIR
Fat suppression	Fat Sat	Fat Sat	STIR
TR	2500 msec	5800 msec	7820 msec
TE	35 msec	35 msec	15 msec
TI	-	-	100 msec
Slice thickness	3 mm	3 mm	3 mm
Interslice gap	0 mm	0 mm	0 mm
Slices (varies)	20	32	28
Frequency x Phase	288 x 192	288 x 192	256 x 256
Band width	45	-	-
NEX	2	2	2
Prescan	water	-	-
Flip angle	-	90	90
FOV	140	140	140
Frequency direction	A/P	H/F	H/F
Echo train length	8	8	8
Set center frequency	water	water	-
Scan time	2 min 59 sec	4 min 44 sec	< 6 min

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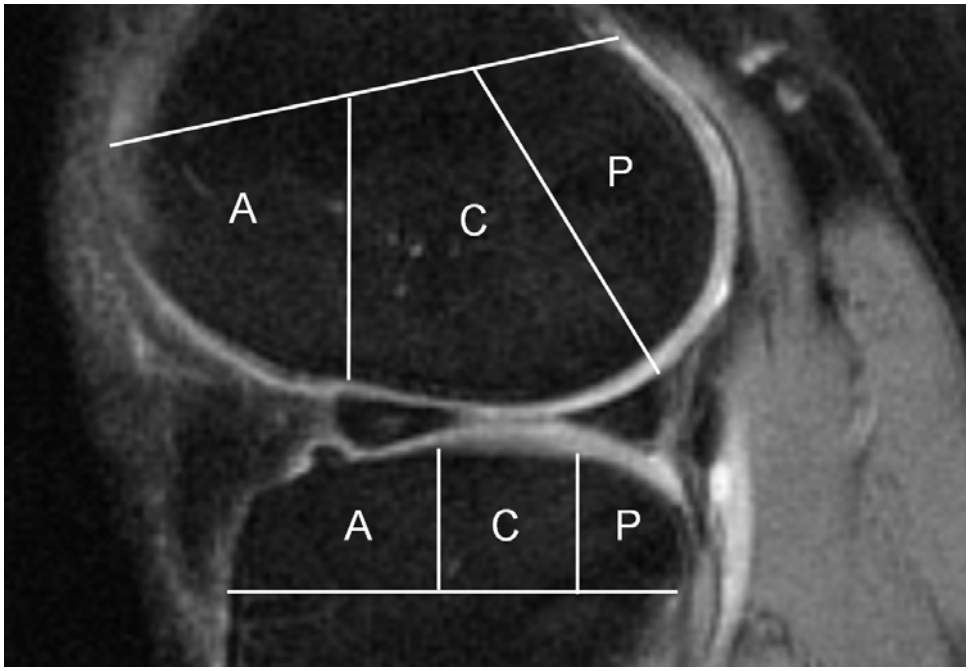
APPENDIX B: Anatomical Subregions used in WORMS

For the articular surface and related features scored in WORMS (cartilage morphology, osteophytes, bone attrition, bone marrow lesions, subchondral cysts), we suggest reading the WORMS publication[1] for detailed information about anatomical subregion definitions, but the following summarizes how the knee is divided into different locations for scoring.

Figure 1 shows the 3 subregions of the lateral tibial plateau (A = anterior, C=central and P=posterior), along with the 2 subregions of the femoral condyle (C=central and P=posterior) which together make up the 5 subregions of the lateral tibio-femoral compartment. There are 5 similar anatomical locations on the medial side of the joint which make up the medial tibio-femoral compartment.

The anterior of the lateral femoral condyle (A) is considered part of the patello-femoral compartment since it articulates with the lateral facet of the patella. Similarly, the anterior of the medal femoral condyle, which articulates with the medial facet of the patella is part of the patello-femoral compartment. Therefore the patello femoral compartment comprised 4 anatomical subregions, 2 from the femur and 2 from the patella.

Figure 1. Showing the anterior (A), central (C) and posterior (P) subregions of the lateral femoral condyle and lateral tibial plateau. There are similar regions defined for the medial side of the knee.



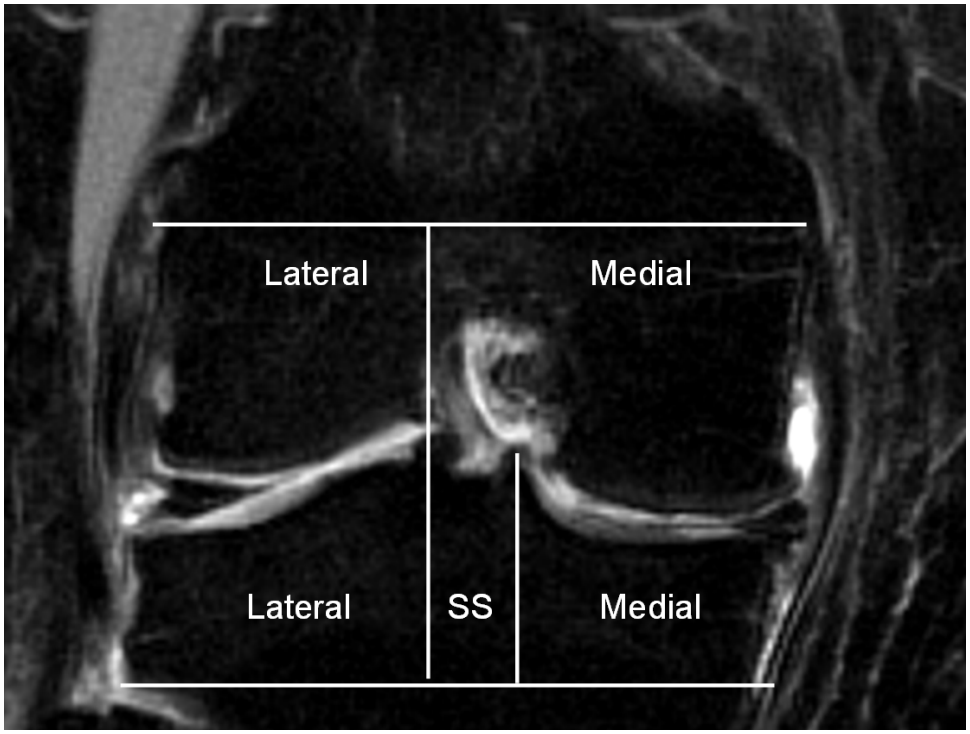
The 4 patello-femoral compartment subregions, along with the 5 medial tibio-femoral compartment subregions and 5 lateral tibio-femoral compartment subregions comprise the 14 subregions used for scoring cartilage morphology and bone attrition.

For scoring of osteophytes, there are 2 additional anatomical locations used: superior tip of the patella and inferior tip of the patella. These locations are considered part of the patello-femoral joint.

APPENDIX B: Anatomical Subregions used in WORMS (continued)

For bone marrow lesions (BMLs) and cysts, there is an additional sub-spinous region (Figure 2) which is associated with the insertion of the cruciate ligaments rather than being associated with an articular surface. This feature is associated with the tibia, but is not assigned to either medial or lateral compartment of the tibiofemoral joint. Figure 2 also shows the line used to differentiate medial and lateral sides of the femur.

Figure 2. Showing the lines delineating medial and lateral sides of the femur and tibia, along with the definition of the sub-spinous region (SS) used only for scoring bone marrow lesions and cysts



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APPENDIX C: Image Readability Report

MRIs were determined readable overall if the axial, sagittal, and coronal STIR sequences were acquired and the overall image quality was acceptable for scoring cartilage morphology, bone marrow lesions, meniscal damage, and osteophytes in the majority of Whole-Organ Magnetic Resonance Imaging (WORMS) subregions.

MOST 1.0T Knee MRI Readability Among Study Participants with Bilateral or Unilateral Scans Acquired

	Baseline		15 Months		30 Months	
Bilateral acquired						
- Bilateral readable	2112	86.7%	172	70.2%	1691	83.7%
- Unilateral readable	246	10.1%	48	19.6%	255	12.6%
- None readable	77	3.2%	25	10.2%	74	3.7%
Total	**2435**		**245**		**2020**	
Unilateral acquired						
- Unilateral readable	142	86.1%	284	86.1%	172	83.9%
- None readable	23	13.9%	46	13.9%	33	16.1%
Total	**165**		**330**		**205**	

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APPENDIX D: Image Inventory

An inventory dataset will be provided to recipients of the MR images.

Dataset

Dataset: MOSTV012MRIinv.sas
Observations: 3026 (1 record per study participant)
Variable Guide: MOSTVarGuideDistributions_ V012MRIinv.pdf
Distributions: MOSTVarGuideDistributions_ V012MRIinv.pdf

Variables

The dataset includes ten variables for each study visit indicating the availability of images for the indicated sequences: Axial, Saqittal, Coronal FSE (baseline only), Coronal STIR, and 3-point Dixon. The variable prefix 'Vx' (V0, V1, V2) indicates the study visit: Baseline, 15-month follow-up, or 30-month follow-up.

Variable	Description	Variable	Description
VxR_Ax	Right knee Axial FSE	VxL_Ax	Left knee Axial FSE
VxR_Sag	Right knee Sagittal FSE	VxL_Sag	Left knee Sagittal FSE
VxR_Cor	Right knee Coronal FSE	VxL_Cor	Left knee Coronal FSE
VxR_STIR	Right knee Coronal STIR	VxL_STIR	Left knee Coronal STIR
VxR_Dix	Right knee 3-Point Dixon	VxL_Dix	Left knee 3-Point Dixon

Values:

- 0 = None (the participant has no images available for the indicated sequence)
- 1 = The participant has 1 set of images available for the indicated sequence
- 2 = The participant has 2 sets of images available for the indicated sequence
- 3 = The participant has 3 sets of images available for the indicated sequence
- 4 = The participant has 4 sets of images available for the indicated sequence

Two additional variables for each study visit indicate whether the MR images for a knee were determined overall to be readable for WORMS scoring. However, images determined not readable may have images that can be scored for individual features.

Variable	Description	Variable	Description
VxR_RDBL	Right knee images readable	VxL_RDBL	Left knee images readable

Values:

- . (Missing) = Not applicable because no images are available
- 0 = Not readable overall for WORMS scoring
- 1 = Readable overall for WORMS scoring

APPENDIX D: Image Inventory (continued)

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

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 Rivera
UCSF Dept. Epidemiology and Biostatistics
185 Berry Street, Lobby 5
Suite 5700
San Francisco, CA 94107

(415) 514-8177
mrivera@psg.ucsf.edu

Study Contacts

Questions and problems: Email MOSTOnline@psg.ucsf.edu.