



MULTICENTER OSTEOARTHRITIS STUDY
LONGITUDINAL KNEE MRI MOAKS READING ASSESSMENTS
(144-MONTH TO 168-MONTH FOLLOW-UP)
DATASET DESCRIPTION AND READING PROTOCOL
MARCH 2023

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1. Introduction

1.1 Dataset and Documents

Dataset: MOSTV79MOAKS
Observations: 1854 knees (1854 participants)
Variable Guide: VariableGuide_V79MOAKS.pdf
Distributions: Distributions_V79MOAKS.pdf
Formats: FORMATS.SAS7BDAT

This dataset contains centrally performed longitudinal semi-quantitative (SQ) readings of OA related structural changes from MRI of the knee performed at Boston Core Imaging Lab (<http://www.bicl.org>) by 2 experienced radiologists under the supervision of Dr. Ali Guermazi. The MRI scans were read using the MOAKS (MRI Osteoarthritis Knee Score) scoring method¹. Any participant with at least one knee with pair of readable 144-month and 168-month visit MRIs had a unilateral MRI reading.

Variables assessed for using MOAKS in this project include:

- Scores for cartilage morphology (lesion size & depth) in 14 anatomical locations.
- Scores for the size and number of bone marrow lesions (BMLs) in 15 anatomical locations.
- Scores for meniscal damage for anterior horn, body and posterior horn of both medial and lateral menisci, plus meniscal signal abnormalities, root tears, meniscal hypertrophy and extrusion.
- A score for synovitis at infra-patellar fat pad and one for synovitis/effusion in the whole knee.
- Scores for ACL and PCL tears and extra articular features (e.g.: cysts, bursitis).

This publication¹ gives more details about the MOAKS scoring methods used:

- Hunter DJ et al. Evolution of semi-quantitative whole joint assessment of knee OA: MOAKS (MRI Osteoarthritis Knee Score). *Osteoarthritis and Cartilage* 2011; 19(8); 990-1002. PMID: 21645627; PMCID: PMC4058435; <http://dx.doi.org/10.1016/j.joca.2011.05.004>

Osteophytes and MRI signal in the ilio-tibial band were described as part of MOAKS but were not scored in this project. In addition to raw MOAKS scores for each feature/anatomical location, the dataset also contains summary calculated variables that can be used to address various questions. Sections 4 and 7 give information and examples about how raw variables can be combined to give various kinds of information such as:

- Does a knee have incident full thickness cartilage loss?
- Does a knee have any kind of meniscal tear at baseline?
- Does cartilage morphology in the medial tibio-femoral compartment worsen between the 2 visits?
- Has BML score in any patello-femoral location worsened between the 2 visits? (regardless of whether any patello-femoral locations have shown improvement of BML score)

1.2 Eligibility for MRI acquisition and selection for MOAKS Readings

MRI Acquisition at 144-month follow-up visit (V7)

New Cohort: To be enrolled in the study, participants in the new cohort were required to have an MRI in at least one knee. 98% of new cohort participants had bilateral MRIs.

Original Cohort: Participants in the original cohort who were eligible for a clinic visit were eligible for a **unilateral** MRI in either knee that had a KL<3 on most recent knee x-ray reading prior to 144-month and no TKR in that knee by the 144-month visit. In addition, the knee fit in the MRI scanner coil and the participant had no MRI contraindications. If both knees were eligible for an MRI, the knee with WORMS readings at 60-month/84-month visits was selected, and if the participant had neither knee with WORMS readings at 60-month/84-month, then the knee was chosen randomly. 97% of the original cohort had an MRI in one knee only.

MRI Acquisition at 168-month follow-up visit (V9)

All participants in both the new and original cohorts enrolled in the study were eligible for the 168-month visit, even if they missed 144m visit for any reason. Eligibility for MRI acquisition at 168-months was based on 144-month MRI status: participants were eligible for MRI at the 168-month visit if they had an MRI at the 144-month clinic visit, no new TKR or other contraindications reported. Therefore, new cohort participants were eligible for bilateral MRI (97% bilateral MRI obtained; 1% unilateral MRI obtained); original cohort participants were eligible for unilateral MRI (preferably on the same knee) (0.5% bilateral MRI obtained; 61% unilateral MRI obtained).

Selection of knees for reading

The MRI scans were read using the MOAKS (MRI Osteoarthritis Knee Score) scoring method⁽¹⁾. Readings were done on knees with a readable pair of 144-168m scans. One knee was read per participant. If only one knee had a readable pair, that knee was read. If both knees had a readable pair, the pair with better quality images was read, otherwise one knee was randomly selected for reading. See tables in Appendix B for further details of acquisitions and readings.

2. MOAKS Anatomical Locations for Scoring

2.1 Locations for Cartilage Morphology and Bone Marrow Lesion Scoring

MOAKS scores cartilage morphology and bone marrow lesions in a large number of anatomical locations. Figure 1 shows the 3 MOAKS 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. In MOAKS, the anterior (or trochlear portion) 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 medial femoral condyle, which articulates with the medial facet of the patella is part of the patello-femoral compartment. Therefore the patello femoral compartment comprises 4 anatomical subregions, 2 from the femur and 2 from the patella. 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. For bone marrow lesions (BMLs) 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 tibio-femoral joint, but is not assigned to either medial or lateral compartment of that joint. Figure 2 also shows the line used to differentiate medial and lateral sides of the femur.

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

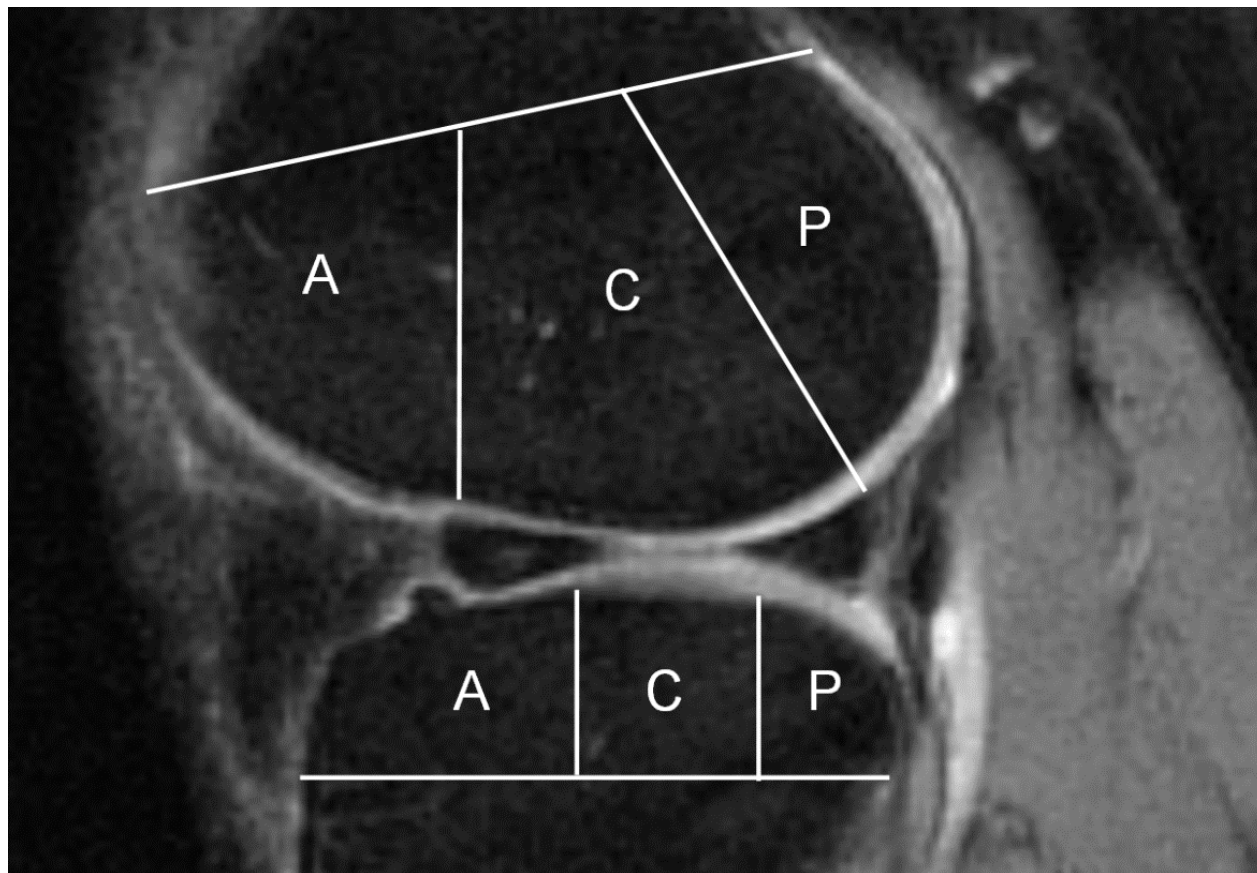
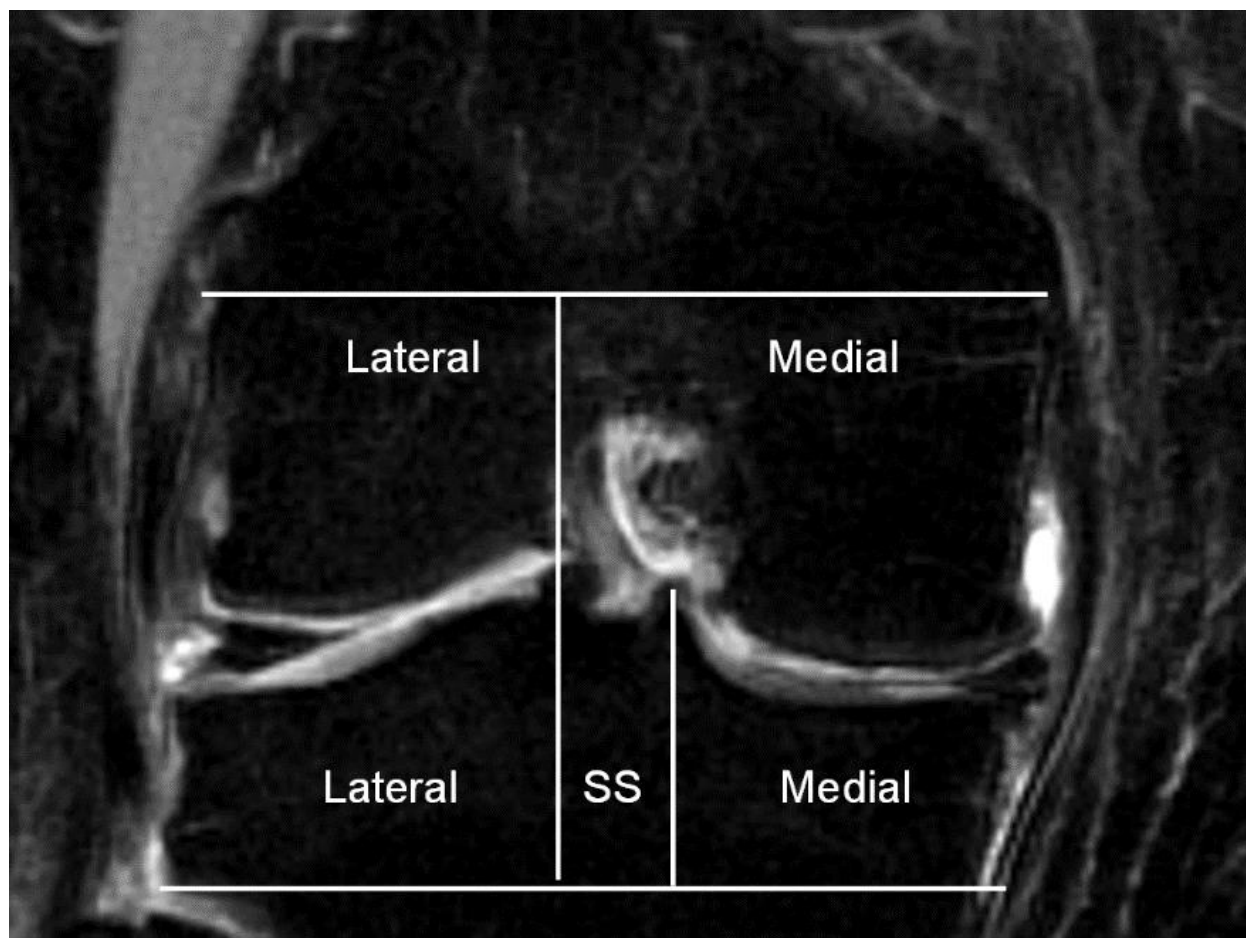


Figure 2. Showing the lines delineating medial and lateral sides of the femur and tibia, along with the definition of the sub-spinous region (SS) used only for scoring bone marrow lesions in MOAKS



2.2 Locations for Scoring Meniscal Damage

For MOAKS, each meniscus (medial and lateral) was split into three subregions: anterior horn, meniscal body, and posterior horn. The presence and type of any meniscal tear was scored separately for each of those 6 subregions. Signal abnormalities that were not severe enough to be called tears were also recorded, as was the presence of any posterior root tears of either meniscus. Extrusion of the body of each meniscus (in the medio-lateral direction) was scored and anterior extrusion of the anterior horn was also scored.

2.3 Locations for scoring of Synovitis and Effusion

Synovitis was scored in the infra-patellar fat pad based on signal abnormalities in Hoffa's fat pad, and presence and size of synovial effusion was also scored. It is important to note that this effusion score can include both synovitis and effusion since it is impossible to differentiate the two using the non-enhanced MRI sequences used for this study.

3. MOAKS Variables and Grades for Scoring of OA Related Changes in Structure

3.1 Variable names and Naming Conventions

Variable names prefixed with V7 are for 144-month visit and V9 are for the 168-month visit in MOST. Detailed descriptions, examples and definitions of the different score values each feature scored are given in the original publications for MOAKS¹. Variables names tend to be made of 3 parts, (i) the visit prefix Vx, (ii) a short abbreviation of the type of score (e.g.: “MCM” for MOAKS cartilage morphology, “MBMS” for MOAKS bone marrow lesion size, “MMT” for MOAKS meniscal tear, and (iii) a short abbreviation of the anatomical location (e.g.: “FMP” for femur medial posterior, “TLP” for tibia lateral posterior, both of which apply for cartilage and bone marrow lesions, or “MB” for medial body, which applies to meniscus)-

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

1) Visit Prefix

In general, variables are prefixed by ‘Vx’ indicating the study visit with which the variable is associated, or Vxy to indicate changes between visits:

Visit Prefix	Description
V7	144-months
V9	168-months
V79	change from V7 to V9

There are some derived variables prefixed V7a_, V9a_, V79a_, V7b_, V9b_, V79b_ which are described in section 3.3 and are variables derived from the MOAKS cartilage morphology scores described in section 3.2.

2) Feature/Subregion

The central part of the name indicates the feature scored and subregion if applicable. Section 2 of this document describes anatomical subregions used in MOAKS, and sections 3.2-3.5 the details for each individual feature. Abbreviations are identified below:

Feature	Abbreviation	# of subregions	Section
Cartilage Morphology Score	MCM	14	3.2
Cartilage Morphology Score (Area)	a_MCM	14	3.3
Cartilage Morphology Score (Full Thickness)	b_MCM	14	3.3
Bone Marrow Lesion Size Score	MBMS	15	3.4
Number of Bone Marrow Lesions	MBMN	15	3.4
Bone Marrow Lesion % Cystic	MBMC	15	3.4
Meniscal Tears + Root tears	MMT	6 + 2	3.6
Meniscal Extrusion	MMX	6	3.6
Meniscal Hypertrophy	MMH	6	3.6
Meniscal Cysts	MMC	6	3.6
Infra-patellar Synovitis	MSY	1	see Ref #1
Effusion	MEF	1	see Ref #1
ACL (tear, repair, associated BML)	MACL	1 x 3 features	see Ref #1
PCL (tear, repair, associated BML)	NPCL	1 x 3 features	see Ref #1

This publication¹ gives more details about the MOAKS scoring methods used and sections 3.2-3.5 give information specific to this project:

- Hunter DJ et al. Evolution of semi-quantitative whole joint assessment of knee OA: MOAKS (MRI Osteoarthritis Knee Score). *Osteoarthritis and Cartilage* 2011; 19(8); 990-1002. PMID: 21645627 PMCID: PMC4058435 <http://dx.doi.org/10.1016/j.joca.2011.05.004>

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 V79= 144-month to 168-month change. (See Subregion Change Scores, section 7.1, and Compartment, Joint and Whole Knee change scores, section 7.2).
- Eligibility for a specific measure is indicated by the suffix ‘_E’. (See “Prevalence and Eligibility for Incidence or Progression at the Compartment and Knee Level”, section 7.3).

So, for example, the 144-month and 168-month visit cartilage morphology scores for the posterior subregion of the medial femoral condyle are recorded in variables V7MCMFMP and V9MCMFMP. Change from 144-month to 168-month visit in the same feature and location is recorded in variable V79MCMFMP_C. Eligibility for worsening and the presence or absence of worsening of the cartilage morphology medial TF compartment aggregate from 144-month to 168-month visit is recorded in the variables V79MCMMTF_E, V79MCMMTF_C. All eligibility indicator variables are paired with a change variable.

3.2 Cartilage Scores

MOAKS scores the size of any cartilage lesions on a 4 point scale based on the percentage of the subregions that the lesion(s) affect. There is also a separate score for the percentage of the subregion that is affected by full thickness cartilage loss. Table 1 shows the thresholds used for each of these scores.

Table 1. Showing the values for MOAKS scores of cartilage morphology for size of lesion and the amount of full thickness lesion relative to the area of the region

Size of any cartilage loss (partial or full thickness) as a % of the surface area of the subregion	% full thickness cartilage loss in the subregion
0: none	0: none
1: < 10% of the surface area of the region	1: < 10% of the surface area of the region
2: 10-75% of the surface area of the region	2: 10-75% of the surface area of the region
3: >75% of the surface area of the region	3: >75% of the surface area of the region

These two scores are combined to form 10 categories (see Table 2) and in the dataset, these categories are identified numerically by combining two separate features scores into a single number where the portion before the decimal point represents the score for the size of the lesion and the portion after the decimal point represents the score for the amount of full thickness cartilage loss.

Table 2. Showing the coding for MOAKS values of the MOAK cartilage morphology variables in the dataset.

Score	Description
0.0	Normal
1.0	1-10% Area, No FT
1.1	1-10% Area, 1-10% FT
2.0	10-75% Area, No FT
2.1	10-75% Area, 1-10% FT
2.2	10-75% Area, 10-75% FT
3.0	>75% Area, No FT
3.1	>75% Area, 1-10% FT
3.2	>75% Area, 10-75% FT
3.3	>75% Area, >75% FT

For example, a value of 1.0 represents a small isolated cartilage lesion that covers less than 10% of the surface area of the subregion and there is no full thickness cartilage loss, and a grade 3.1 lesion represents a large lesion that covers more than 75% of the surface area of the subregion, but has only a small amount of full thickness cartilage loss covering less than 10% of the surface area of the subregion. Readers could also record definite within-grade worsening of cartilage (and in rare cases they recorded within-grade improvement). Calculated variables for the change between visits (see section 7) can be used to identify this.

IMPORTANT: although the separate components of the scores can be considered ordinal, the coded decimal scores are categorical. Although some are obviously more severe than others, the following situations have to be considered:

- whether 1.1 is worse or better than 2.0
- whether 1.1 is worse or better than 3.0
- whether 2.1 is worse or better than 2.0
- whether 2.1 is worse or better than 3.0
- whether 2.2 is worse or better than 3.1

The decision depends on whether the overall size of the lesion is considered more important than the amount of full thickness lesions. In calculated variables for change (described in section 7), we have considered that longitudinally these changes are a worsening since the overall area of the subregion affected by cartilage loss has increased.

3.3 Derived MOAKS Variables for Cartilage Lesion Size and Full Thickness Cartilage Loss

As pointed out in the previous section, the MOAKS cartilage morphology score assesses both the overall lesion size and the amount of full thickness loss. This portion of the score before the decimal point in the V7MCM... and V9MCM... variables has been converted into a 4 point ordinal scale in variables V7a_MCM... and V9a_MCM.... Although this score is ordinal, its use longitudinally can reach end stage for lesions that are only partial thickness, and it may therefore not be useful for assessing knees/subregions with moderately severe features of OA.

In an analogous manner to the derived score for cartilage lesion size, a score for the amount of full thickness loss has been derived from the portion of the MOAKS score after the decimal point. This ordinal score may be insensitive for assessing structural changes in knees with mild features of OA since it can remain 0 in all subregions until full thickness cartilage loss has occurred.

Table 3. Showing the coding for the two variables derived from the MOAKS subregion cartilage scores for the two separate features of lesion size (V7a_MCM) and amount of full thickness loss (V7b_MCM).

Derived Score	Description for V7a_MCM...variables	Description for V7b_MCM...variables
0	Normal	No full thickness loss
1	1-10% Area	1-10% Area has full thickness loss
2	10-75% Area	10-75% Area has full thickness loss
3	>75% Area	>75% Area has full thickness loss

3.4 BML Scores

For each subregion analyzed, MOAKS has 3 separate scores related to Bone Marrow Lesions (BMLs):

- a score for the % of the volume of the subregion that is affected by BML
- a score for the number of BMLs within the subregion
- a score for the % of the lesion that is BML, as opposed to cyst.

Table 4 shows size thresholds used for this. As with cartilage scoring, readers could also record definite within-grade worsening or within-grade improvement of BML size scores. Calculated variables for the change between visits (see section 7.1) can be used to identify this.

Table 4. Showing the scoring system for BMLs

Size of BML (including any associated cysts)	Number of BMLs counted within the subregion	% of lesion that is BML (vs cyst)
0: none	0: no BMLs in subregion	0: none
1: < 33% of subregional volume	1: a single BML in the subregion	1: < 33%
2: 33-66% of subregional volume	2: a pair of BMLs in the subregion	2: 33-66%
3: >66% of subregional volume	etc	3: > 66%

3.5 Osteophyte Scoring

Osteophyte scoring was described in the original MOAKS publication¹, but was not performed for this project.

3.6 Meniscus Scoring

For each meniscus (medial and lateral), MOAKS scores are recorded for the anterior horn, body of the meniscus and the posterior horn using the following numeric values to indicate different categories:

- 0: normal meniscus
- 1: signal abnormality that is not severe enough to be considered a meniscal tear
- 2: radial tear
- 3: horizontal tear
- 4: vertical tear
- 5: complex tear
- 6: partial maceration
- 7: progressive partial maceration (only used for follow-up visit scores)
- 8: complete maceration

Although these are numeric values, they are not a completely ordinal scale. Values 0 and 1 represent a meniscal subregion without a definite tear, and a value of 1 can be considered worse than a value of 0. Values of 2, 3 and 4 are not of increasing severity, and are simply different categories; they are definite tears that can be considered worse than 1 but not as severe as 5, which is a complex tear that generally involves a complex combination of 3, 4 or 5 in the same subregion. Complete maceration can be considered “end-stage” and worse than any other value. Partial maceration is simply a loss of normal meniscal tissue and not necessarily worse than the various categories of tear. Detailed definitions of these are given in the original MOAKS publication¹.

In addition, the presence of meniscal hypertrophy (a definite increase in the meniscal volume compared to normal), meniscal extrusion, meniscal root tears or meniscal cysts are also recorded.

4. Compartment-specific Variables, Predictors and Outcomes

4.1 Compartment-specific grouping of variables

The various anatomic locations used for cartilage morphology and bone marrow lesions can generally be grouped into one of the 3 compartments of the knee joint: For cartilage morphology and bone marrow lesion scores, the following grouping can be used.

The medial tibio-femoral compartment comprises the 5 anatomical locations which are listed below along with the abbreviations used in the relevant variable names:

- FMC – femoral condyle (medial) central region
- FMP – femoral condyle (medial) posterior region
- TMA – tibia (medial) anterior region
- TMC – tibia (medial) central region
- TMP – tibia (medial) posterior region

The lateral tibio-femoral compartment comprises the 5 anatomical locations which are listed below along with the abbreviations used in the relevant variable names:

- FLC – femoral condyle (lateral) central region
- FLP – femoral condyle (lateral) posterior region
- TLA – tibia (lateral) anterior region
- TLC – tibia (lateral) central region
- TLP – tibia (lateral) posterior region

The patella-femoral compartment comprises the 4 anatomical locations which are listed below along with the abbreviations used in the relevant variable names:

- FMA – femur (medial) anterior region
- FLA – femur (lateral) anterior region
- PM – patella medial facet
- PL – patella lateral facet

For bone marrow lesions, there is a region under the tibial spine (see Figure 2) which is considered neither medial nor lateral:

- TSS – tibial sup-spinous region

4.2 Calculating Predictors, Longitudinal Changes and Outcomes

It is important to remember that the raw values for MOAKS variables for cartilage morphology and meniscal damage have to be thought of as categorical variables, and are scored in multiple locations. See section 8 for information about a variety of variables that have been calculated for this. If users want to determine a compartment-specific predictor or outcome that is not already described in section 8, multiple values/variables have to be considered.

So, for example, if the aim is to determine if the medial tibio-femoral compartment has any full thickness cartilage loss, the variables V7MCMTMC, V7MCMTMP, V7MCMTMA, V7MCMFMC, V7MCMFMP have to be considered. If **ANY** of them is non-integer (take the value n.x where x is 1, 2 or 3), then that knee has full thickness cartilage loss in the medial tibio-femoral sub-compartment. If **ALL** of the 5 subregions have an integer valued score (0, 1, 2 or 3), then the compartment has no full thickness loss. It is important to note that if any of the 5 subregions have a missing score, it is still possible to determine that full thickness loss exists, but it is impossible to determine if it does not exist.

For cartilage morphology scores (V7MCM... and V9MCM...), a subregion can be considered as having worsened over time if any of the following occur between two visits:

- (a) The size of the lesion has changed (i.e.: the integer portion of the score has gone from 0->1, or from 1->2 or from 2->3)
- (b) The amount of full thickness loss has increased (i.e.: the decimal portion of the raw score has increased (i.e.: 1.0->1.1, or 2.0->2.1, or 2.0->2.2, or 3.0->3.1, or 3.0->3.2, or 3.0->3.3, or 3.1->3.2, or 3.1->3.3, or 3.2->3.3)
- (c) Readers could record within-grade changes for worsening or improvement although in some analyses. Such within-grade changes may be considered as no-change when a stricter definition of change is required and, in those cases, the score at the previous visit needs examining. These are recorded in special variables described in section 7.1.

For the ordinal, derived cartilage scores for cartilage lesion size (V7a_MCM...) and amount of full thickness loss (V7b_MCM...) worsening was defined as an increase in value between two visits, and within-grade worsening was also recorded (section 7.1).

For meniscal damage, scores of 0 or 1 are considered to not be tears. The remaining values are categorical and it is important to note that values of 2 “radial tear”, 3 “horizontal tear” and 4 “vertical tear” are not necessarily of increasing severity. A value of 5 “complex tear” or 8 “complete maceration” could be considered to be worse than values less than 5, but there is no reason to consider 6 “partial maceration” as worse than 5 “complex tear”, although 6 “partial maceration” is definitely less severe than 8 “complete maceration”.

These issues need careful consideration when using the raw values of variable to determine the status and severity of damage in compartments or knees, and even more careful consideration when determining longitudinal changes and calculation of outcomes of structural worsening in the knee.

NOTE: See section 7 for information about various calculated variables for predictors, outcomes and changes at the whole knee, compartment and subregion levels provided in this dataset

4.3 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, meniscal hypertrophy, synovitis and effusion are also 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 3 MOAKS features and, therefore, when the maximum value (end stage) was reached in these features, they were not eligible for change (see section 7 for information about calculated variables related to eligibility for change):

- 1) Cartilage morphology
- 2) Meniscal tears
- 3) Ligament tears and repair

5. Selection for reading and missing data

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 (usually due to image quality issues)
.	Data is missing because the MR images were not provided to the reader (because they were unreadable), or were not acquired.
.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.

For irreversible features, when the 144-month visit score is missing, but the 168-month visit score is “normal”, then in spite of that missing value, the subregion calculated change score (see section 8) is imputed to be “no change”.

6. Reading Protocol

6.1 Image type

In MOST, sagittal, coronal and axial fat-suppressed FSEfw images from a 1.5T GE MSK Extreme 1.5T scanner were acquired. For the MRI acquisition protocol, see the PDF provided with this document, or the “MRI Manual” available at https://agingresearchbiobank.nia.nih.gov/studies/most/documents/?f=Manual_of_Procedures

6.2 Time points

Paired MRIs from the 144-month and 168m visit were read with the readers knowing the chronological order, but blinded to other participant information.

7. Calculated Variables for Change and Prevalence

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. See section 3.2 for information about the MOAKS cartilage score values being categorical rather than ordinal.

7.1 Subregion change scores

For each MOAKS feature scored, at each anatomical location, a change variable is calculated (‘_C’ suffix). For example, V79MBMSFMP_C is the change score variable calculated for bone marrow lesion size in the posterior of the medial femoral condyle from 144-month to 168-month.

The table below gives the values assigned to the change scores:

Formatted Change Score	Description
0: decrease	The baseline visit score is worse than the follow-up visit score
1: within grade decrease	The baseline and follow-up visit scores are the same but the reader scored a within-grade improvement between baseline and follow-up (for cartilage and bone marrow lesion size score only)
2: No change	The baseline and follow-up visit scores are the same – or – (for irreversible features only) there is missing data at baseline and the follow-up visit score is zero
3: within grade worsening	The baseline and follow-up visit scores are the same but the reader scored a within-grade worsening between baseline and follow-up (for cartilage and bone marrow lesion size scores only)
4: full grade worsening	The follow-up visit score was one grade worse than the follow-up visit score (for cartilage this meant that and integer part and/or the decimal part of the score increase by 1)
5: more than full grade worsening	Any worsening that isn’t either of the previous 2 categories (change score 3 or 4)

Collapsing this in various ways can create various binary outcomes (e.g.: 0,1,2 vs 3,4,5 would be not worsening vs worsening). It would also be possible to perform sensitivity analyses by first initially allowing within-grade changes to be considered as an outcome and then rerunning an analysis where they are considered “no change”.

7.2 Compartment, Joint and Whole Knee Change Scores

IMPORTANT: The MOAKS cartilage score categories do not form a demonstrated ordinal scale (see section 3.2). Similarly, there has been no evaluation of the scaling properties of composite scores (calculated by adding together the subregion scores of one feature or adding together the scores from multiple features) for the other MOAKS features. Therefore, we do not add cartilage subregion scores together to form composite cartilage scores for either compartments or the whole knee. No variables have been created for composite scores derived by adding raw subregion scores together to form higher level composite scores.

Change scores were calculated for the whole knee (WK), medial tibiofemoral (TF), lateral tibiofemoral, and patello-femoral (PF) compartments for the cartilage morphology (MCM) and bone marrow lesion (MBMS, MBMN, MBMC) features. The suffix at the end of the variable name indicates the level at which the change score was calculated:

The table below indicates the abbreviations used in variable names to indicate compartment and whole knee-level changes:

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 4 PF subregions
WK_C	Whole knee change	– all 14 subregions for cartilage morphology and bone attrition – all 15 subregions for bone marrow lesions

For example, for cartilage morphology from 144-months to 168-months, V79MCMLTF_C is the tibiofemoral lateral compartment change score, V79MCMPF_C is the patellofemoral joint change score, and V79MCMWK_C is the whole knee change score.

7.3 Prevalence and Eligibility for Incidence or Progression 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.

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 an abnormal* 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 the subregions of 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 cannot 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.

** scores = 0 are considered normal, and scores > 0 are considered abnormal*

When combined with the associated ‘_C’ change scores for the compartment and feature, these eligibility variables allow determination of incidence or progression.

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

7.4 MRI Cartilage Outcomes for MOST Primary Aims

In MOST, the primary structural outcome is development of a full thickness cartilage lesion at V9 (168 month visit) in a knee which had no full thickness loss at V7 (144-month visit).

Variables V79b_MCMWK_E and V79b_MCMWK_C can be used to define this outcome, as can be seen from the table below. Also note that a “within-grade increase” for knees that are eligible for incidence of a full thickness lesion indicates that a lesion has become deeper, but not to the level of being full thickness (so those knees are considered to have not reached the outcome).

Table 5. Showing the frequency of incident full thickness lesions in the main 144-month/168-month paired readings.

Table of V79b_MCMWK_E by V79b_MCMWK_C							
V79b_MCMWK_E(cartilage morphology FT, Whole knee worsening eligibility indicator)	V79b_MCMWK_C(cartilage morphology FT, Whole knee (144m-168m change))						
Frequency	.Z:Not Determined	1:within grade decrease	2:no change	3:within grade increase	4:full grade increase	5:more than full grade increase	Total
0:not eligible	2	0	0	0	0	0	2
1:elig for incidence	0	0	670	1	108	9	788
3:prevalence	53	2	575	94	281	59	1064
Total	56	2	1244	95	389	68	1854

Knees in the “1: elig for incidence” row are those that have no full thickness loss at V7 and have no missing subregion cartilage scores, and those highlighted in grey are ones that have a full thickness lesion at V9. Those in the “3: prevalence” row already have full thickness loss at V7 and aren’t eligible for the outcome.

As well as this “whole knee” outcome, compartment specific outcomes can be calculated:

- Medial Tibio-Femoral: cross-tabs of V7b_MCMMTF_E x V7b_MCMMTF_E
- Lateral Tibio-Femoral: cross-tabs of V7b_MCMLTF_E x V7b_MCMLTF_E
- Patello-Femoral: cross-tabs of V7b_MCMPF_E x V7b_MCMPF_E

8. References

1. Hunter DJ et al. Evolution of semi-quantitative whole joint assessment of knee OA: MOAKS (MRI Osteoarthritis Knee Score). *Osteoarthritis and Cartilage* 2011; 19(8); 990-1002. PMID: 21645627 PMCID: PMC4058435 <http://dx.doi.org/10.1016/j.joca.2011.05.004>

Appendix A. MRI Operations Manual Chapter – Table of Contents

KNEE MRI 1.5T

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The entire MRI operations manual can be downloaded from
https://agingresearchbiobank.nia.nih.gov/studies/most/documents/?f=Manual_of_Procedures

Appendix B. 144- and 168-Month MRI Summary Report

MOST 144m Knee MRI summary; data received between 16MAR2016 and 28SEP2018

Table 1. Knee MRI summary report

	Existing cohort		New cohort		Total	
	N	col%	N	col%	N	col%
Total CV	1309	100.00%	1525	100.00%	2,834	100.00%
MRI status						
1:unilateral MRI done	809	61.80%	5	0.33%	814	28.70%
2:bilateral MRI done	27	2.06%	1506	98.75%	1,533	54.00%
5:not done, cancelled	14	1.07%	4	0.26%	18	0.60%
6:equipment failure	2	0.15%	4	0.26%	6	0.20%
7:refusal	8	0.61%	0	0.00%	8	0.20%
8:not done, reason unknown	71	5.42%	5	0.33%	76	2.60%
8:not done, not eligible	378	28.88%	1	0.07%	379	13.30%

Table 2. Summary of Clinic Visit by images collected

	Existing cohort		New cohort		Total	
	N	col%	N	col%	N	col%
Total CV	1309	100.00%	1525	100.00%	2,834	100.00%
CV type						
0:Visit With CT/MRI/X-Ray	587	44.84%	1459	95.67%	2,046	72.10%
1:Visit With MRI/X-Ray	236	18.03%	51	3.34%	287	10.10%
2:Visit With CT/X-Ray	42	3.21%	13	0.85%	55	1.90%
3:Visit With CT/MRI	4	0.31%	1	0.07%	5	0.10%
4:Visit With CT only	2	0.15%	0	0.00%	2	0.00%
5:Visit With MRI only	9	0.69%	0	0.00%	9	0.30%
6:Visit With X-Ray only	155	11.84%	0	0.00%	155	5.40%
7:Visit Without images	274	20.93%	1	0.07%	275	9.70%

Table 3. Summary of paired MRI reading - reported only if 144m acquired

	Existing cohort		New cohort		Total	
	N	col%	N	col%	N	col%
Total CV with MRI	836	100.00%	1511	100.00%	2,347	100.00%
Paired MRI reading						
0:pair MRI not available	165	19.74%	244	16.15%	409	17.43%
0:pair MRI not readable	66	7.89%	18	1.19%	84	3.50%
1:MRI reading complete	605	72.37%	1249	82.66%	1,854	78.90%

MOST 168m Knee MRI summary; data received between 25APR2018 and 16DEC2020

Table 1. Knee MRI summary report

	Existing cohort		New cohort		Total	
	N	col%	N	col%	N	col%
Total CV	1323	100.00%	1298	100.00%	2,621	100.00%
MRI status						
1:unilateral MRI done	810	61.22%	12	0.92%	822	31.30%
2:bilateral MRI done	7	0.53%	1265	97.46%	1,272	48.50%
5:not done, cancelled	3	0.23%	3	0.23%	6	0.20%
6:equipment failure	1	0.08%	0	0.00%	1	0.00%
7:refusal	9	0.68%	2	0.15%	11	0.40%
8:not done, reason unknown	62	4.69%	16	1.23%	78	2.90%
8:not done, not eligible	431	32.58%	0	0.00%	431	16.40%

Table 2. Summary of Clinic Visit by images collected

	Existing cohort		New cohort		Total	
	N	col%	N	col%	N	col%
Total CV	1323	100.00%	1298	100.00%	2,621	100.00%
CV type						
1:Visit With MRI/X-Ray	806	60.92%	1269	97.77%	2,075	79.10%
5:Visit With MRI only	11	0.83%	8	0.62%	19	0.70%
6:Visit With X-Ray only	137	10.36%	21	1.62%	158	6.00%
7:Visit Without images	369	27.89%	0	0.00%	369	14.00%

Table 3. Summary of paired MRI reading - reported only if 168m acquired

	Existing cohort		New cohort		Total	
	N	col%	N	col%	N	col%
Total CV with MRI	817	100.00%	1277	100.00%	2,094	100.00%
Paired MRI reading						
single 168m - not readable	9	1.10%	0	0.00%	9	0.40%
single 168m - readable	137	16.77%	10	0.78%	147	7.00%
0:pair MRI not readable	66	8.08%	18	1.41%	84	4.00%
1:MRI reading complete	605	74.05%	1249	97.81%	1,854	88.50%