

MULTICENTER OSTEOARTHRITIS STUDY

MOST Dataset Description Ancillary Study 04-07 (AS04-07) "Structural Correlates of Knee Pain" (David Felson)

V2MRI15T_gadolinium

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1. Dataset description and Analyst Notes

Dataset: V2MRI15T_gadolinium.sas7bdat

Observations: 587 records (587 knees, 1 knee per participant) Documentation:

- VariableGuide_V2MRI15T_gadolinium.pdf
- Distributions_V2MRI15T_gadolinium.pdf
- AS0407AnnotatedForms_30m.pdf

V2MRI15T_gadolinium dataset contains 587 records; one record per knee/participant with a Gadolinium enhanced 1.5T MRI collected during 30m clinic visit for selected group of participants (one knee per person) who met study inclusion criteria.

For a MOST Ancillary study which was part of R01HD043500 (PI Leena Sharma "Laxity and Malalignment in a Large Cohort Study of OA") - called the "Laxity Study" in this document, MOST participants who agreed to get a 1.5T MRI scan for quantitative assessment of cartilage at the baseline visit were also eligible to get a 1.5T MRI scan at the 30-month follow-up visit (V2). These people were also then eligible for the 1.5T Gadolinium study. Other MOST participants were also eligible for the 1.5T Gadolinium Study if they had been randomly selected for biospecimen sample collection at the 30-month visit (see description below).

Exclusion by participant:

- Deceased or withdrew consent
- Both knees not eligible: K/L grade of 3.5 or 4; TKR; inflammatory arthritis

Exclusion by knee:

- No baseline MRI
- Knee MRI ineligible (contraindication prior to clinic visit)
- Excluded due to missing patella, osteonecrosis, or amputation below knee
- Knee not eligible: K/L grade of 3.5 or 4 (end stage OA) or KR.

Inclusion criteria:

- One knee per participant with K/L grade between 0 and 3
- Had BL+30M 1.0T knee MR (Baseline MRI obtained, no contraindication for 30m MRI recorded)
- Select knee with lower K/L grade

• If K/L grade is the same in both knees, use dominant knee (right is default if leg dominance is missing) <u>Note</u>: There were three reading projects completed with additional Self-Administered Questionnaire (SAQ) completed by subset of participants (details below).

Dataset structure:

- Variables #1 to #3 included from tracking forms.
- Variables #4 to #12 reading parameters and summary of synovitis from reading project 1 (synovitis related readings).
- Variables #13 to #57 reading parameters from paired MRI1.0T (w/o gadolinium) and MRI1.5T (with gadolinium) from reading project 2.
- Variables #58 to #63 calculated variables from reading project 2 (Synovitis/Cysts/Cartilage Morphology readings).
- Variables #64 to #116 reading parameters from paired MRI1.0T (w/o gadolinium) and MRI1.5T (with gadolinium) from reading project 3.
- Variables #117 to #119 calculated variables from reading project 3 (Bone Attrition/Bone Marrow Lesion and Synovitis readings).
- Variables #120 to #152 selected SAQ questions completed for subset of participants who returned to clinic to obtain 1.5T MRI with gadolinium contrast at the later time. See AS0407AnnotatedForms_30m.pdf. For user convenience, each variable has prefix (G2) corresponding to the main visit collected values (dataset V2ENROLL, prefix V2).
- Variables #136, #140, #148 and #152 calculated scores from SAQ questions

2. MRI 1.5T with Gadolinium selection and reading status

Figure 1. Flow-chart

Completed CV at 30m	2713
Knee selected for Gadolinium study ⁽¹⁾	1179
MRI 1.5T with gadolinium contrast obtained	587
MRI 1.5T (with gadolinium) read for Synovitis (Reading project 1)	574
MRI 1.5T (with gadolinium) paired with MRI 1.0T and read for additional projects 2 and 3	SY/CY/CM ⁽²⁾ 405 BA/BM/SY ⁽³⁾ 458

Footnotes

⁽¹⁾ Selection criteria:

Inclusion criteria:

- One knee per participant
- Had BL+30M 1.0T knee MR (Baseline MRI obtained, no contraindication for 30m MRI recorded)
- Select knee with lower K/L grade
- If K/L grade is the same in both knees, use dominant knee (right is default if leg dominance is missing)

⁽²⁾ SY/CY/CM stands for Synovitis/Cysts/Cartilage Morphology readings

⁽³⁾ BA/BM/SY stands for Bone Attrition/Bone Marrow Lesion/Synovitis readings

3. Related MOST Analysis Plans and Publications

The data in this dataset are related to three MOST Analysis plans, and analyses based on the data have been published:

- AP06-07 Baker "Relation of synovitis to knee pain using contrast-enhanced MRIs" [1]
- **AP07-09 Crema** "Contrast-enhanced MRI of subchondral cysts in patients with or at risk for knee osteoarthritis:"[2]
- **AP07-10 Marra** "Peripatellar synovitis: comparison between non-contrast-enhanced and contrast-enhanced MRI and association with pain"[3]

The data were collected as part of three separate reading projects:

- Reading Project 1: Synovitis scored from 1.5T enhanced MRI scans.
- Reading Project 2: Synovitis, cyst and cartilage morphology scored from paired MRI 1.0T and MRI1.5T (with gadolinium) images
- **Reading Project 3:** Bone attrition, bone marrow edema, effusion, synovitis and periarticular lesions from paired MRI 1.0T and MRI1.5T (with gadolinium) images

Details of the reading projects are given below, and more information has also been published [1,2,3].

4. Reading project 1: Synovitis

Synovitis parameters on 6 parapatella sites scored from MRI1.5T (with gadolinium) read by Kristin Baker (KRB), and results[1] and scoring method[4] have been published.

Reading parameters: contains readings for 574 knees.

- V2_SPP V2_IFP are scored:
 - 0 normal synovium
 - 1 diffuse, even thickening
 - 2 nodular thickening
 - 3 gross nodular thickening
 - .U unreadable

V2_MPC and V2_LPC are scored 0=absent/1=present. Further details and examples of this grading system have been published[4]

Table 1. Variables scored or defined for Reading Proje	ct 1.
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Variable	Label
V2_SPP	30M synovitis, suprapatella pouch
V2_MPR	30M synovitis, medial parapatella recess
V2_LPR	30M synovitis, lateral parapatella recess
V2_IFP	30M synovitis, infrapatella fat pad (Hoffa's)
V2_MPC	30M synovitis, medial posterior condylar
V2_LPC	30M synovitis, lateral posterior condylar
V2_synovDetails	30M synovitis overall category (3 levels)
V2_synovSum	30M synovitis summary category (4 levels)

The 4 level summary variable (V2_synovSum) has values (see [1] for definitions):

- 0 = normal
- 1= mild synovitis
- 2= moderate synovitis
- 3= extensive synovitis

5. Reading project 2: paired MRI 1.0T and MRI1.5T (with gadolinium) images

Synovitis, cyst and cartilage morphology parameters from MRI1.0T (without contrast) and MRI1.5T (with gadolinium contrast) paired images read by two readers (AG and FR) and analyses have been published [2,3].

<u>Reading parameters:</u> the dataset contains readings for 405 knees. See the variable labels (Table 2) for description of which MRI images the features are read from. The meaning of the values for each variable are given below:

SYnnn values when read from MRI1.0T (no Gadolinium) assess intercondylar and infrapatellar synovitis:

- 0 normal
- 1 mild
- 2 moderate
- 3 severe

SYnnn values when read from MRI1.5T (with Gadolinium) assess synovitis in 11 locations:

- 0 no synovial enhancement
- 1 0-2mm synovial enhancement
- 2 2-4mm synovial enhancement
- 3 >=4mm synovial enhancement

CYnnn values (read from paired 1.0T (no Gadolinium) and 1.5T (with Gadolinium) score the size of subchondral cysts (integer part of score) and whether they enhance the Gadolinium (decimal portion):

- 0.0 none
- 1.0 < 25% | no enhancement
- 1.1 < 25% | partial enhnancement
- 1.2 < 25% | full enhancement
- 2.0 25%-50% | no enhancement
- 2.1 25%-50% | partial enhancement
- 2.2 25%-50% | full enhancement
- 3.0 > 50% | no enhancement
- 3.1 > 50% | partial enhancement
- 3.2 > 50% | full enhancement

CMnnn values (read from MRI1.0T (no Gadolinium) assess cartilage lesion depth:

- 0 normal
- 1 partial thickness lesion
- 2 full thickness lesion

POPCYST values read from MRI1.0T (no Gadolinium) assess the size of any popliteal/Baker's cyst::

- 0 normal
- 1 mild
- 2 moderate
- 3 severe

Table 2 shows the variables scored (Table 2a) or calculated (Table 2b) from Reading Project 2.

This SAS code shows how the calculated variables listed in Table 2b are defined for each compartment:

```
misCMmedTF =nmiss(of CM001 CM002 CM007 CM008 CM009);
maxCMmedTF =max(of CM001 CM002 CM007 CM008 CM009);
misCMlatTF =nmiss(of CM004 CM005 CM011 CM012 CM013);
maxCMlatTF =max(of CM004 CM005 CM011 CM012 CM013);
misCMPF =nmiss(of CM003 CM006 CM014 CM015);
maxCMPF =max(of CM003 CM006 CM014 CM015);
```

Variable	Label
SY001	Synovitis: Intercondylar - MRI1.0T
SY002	Synovitis: Infrapatellar - MRI1.0T
SY003	Synovitis: Suprapatellar - MRI1.5T with gadolinium
SY004IP	Synovitis: Infrapatellar - MRI1.5T with gadolinium
SY004IC	Synovitis: Intercondylar - MRI1.5T with gadolinium
SY005	Synovitis: Parapatellar (Medial) - MRI1.5T with gadolinium
SY006	Synovitis: Parapatellar (Lateral) - MRI1.5T with gadolinium
SY007	Synovitis: Around ACL - MRI1.5T with gadolinium
SY008	Synovitis: Around PCL - MRI1.5T with gadolinium
SY009	Synovitis: Perimeniscal (Medial) - MRI1.5T with gadolinium
SY010	Synovitis: Perimeniscal (Lateral) - MRI1.5T with gadolinium
SY011	Synovitis: Around Loose Bodies - MRI1.5T with gadolinium
SY012	Synovitis: Bakers Cyst - MRI1.5T with gadolinium
CY001	Cysts: Posterior Medial Femur
CY002	Cysts: Central Medial Femur
CY003	Cysts: Anterior Medial Femur
CY004	Cysts: Posterior Lateral Femur
CY005	Cysts: Central Lateral Femur
CY006	Cysts: Anterior Lateral Femur
CY007	Cysts: Posterior Medial Tibia
CY008	Cysts: Central Medial Tibia
CY009	Cysts: Anterior Medial Tibia
CY010	Cysts: Sub Sp. Tibia
CY011	Cysts: Posterior Lateral Tibia
CY012	Cysts: Central Lateral Tibia
CY013	Cysts: Anterior Lateral Tibia
CY014	Cysts: Medial Patella
CY015	Cysts: Lateral Patella
CM001	Cartilage: Posterior Medial Femur
CM002	Cartilage: Central Medial Femur
CM003	Cartilage: Anterior Medial Femur
CM004	Cartilage: Posterior Lateral Femur
CM005	Cartilage: Central Lateral Femur
CM006	Cartilage: Anterior Lateral Femur
CM007	Cartilage: Posterior Medial Tibia
CM008	Cartilage: Central Medial Tibia
CM009	Cartilage: Anterior Medial Tibia
CM011	Cartilage: Posterior Lateral Tibia
CM012	Cartilage: Central Lateral Tibia
CM013	Cartilage: Anterior Lateral Tibia
CM014	Cartilage: Medial Patella
CM015	Cartilage: Lateral Patella
POPCYST	Popliteal Cyst: Intercondylar - MRI1.0T

Table 2(b) Calculated variables from Reading Project 2.

Variable	Label					
misCMmedTF	# of missing cartilage scores MTF compartment					
maxCMmedTF	Worst Cartilage Score MTF compartment					
misCMlatTF	# of missing cartilage scores LTF compartment					
maxCMlatTF	Worst Cartilage Score LTF compartment					
misCMPF	# of missing cartilage scores PF compartment					
maxCMPF	Worst Cartilage Score PF compartment					

6. Reading project 3: paired MRI 1.0T and MRI 1.5T (with gadolinium) images.

Bone attrition (BAnnn) parameters from MRI1.5T (with gadolinium contrast); bone marrow edema (BMnnn) and effusion (EFFnnn) parameters from MRI1.0T (without contrast) and MRI1.5T (with gadolinium contrast) paired images; synovitis (SY001_BM, SY002_BM) and periarticular lesions from MRI1.0T (without contrast) read by one reader (MC), and analyses have been published [2,3].

<u>Reading parameters:</u> contains readings for 458 knees. The variable labels contain information about the anatomical subregion scored and which MRI images (1.0T, or 1.5T with Gadolinium) were used for scoring a particular variable. The meaning of the values for each variable are given below:

BAnnn values (read from MRI1.5T) to assess bone attrition severity:

- 0 normal
- 1 mild
- 2 moderate
- 3 severe

BMnnn values (read from MRI1.0T and MRI1.5T) assess bone marrow edema lesion size:

- 0 none
- 1 <25% of region
- 2 25-50% of region
- 3 >50% of region

For variables scored from the 1.5T MRI with Gadolinium:

- +0.5 larger post Gd, but same grade as on 1.0T MRI
- -0.5 smaller post Gd, but same grade as on 1.0T MRI

EFnnn values (read from MRI1.0T and MRI1.5T) assess effusion:

- 0 none
- 1 < 33% of maximum potential distention
- 2 33%-66% of maximum potential distention
- 3 > 66% of maximum potential distention

SYnnn_BM values (read from MRI1.0T) assess intercondylar and infrapatellar synovitis:

- 0 normal
- 1 mild
- 2 moderate
- 3 severe

PERILESION values (read from MRI1.0T) record presence of peri-articular lesions:

- 0 absent
- 1 present

and when present, the type of lesion is provided in the PERILISIONTYPE text variable.

Table 3. Variables scored as part of Reading Project 3.

Variable	Label							
BA001	Attrition: Medial Patella - MRI1.5T with gadolinium							
BA002	Attrition: Lateral Patella - MRI1.5T with gadolinium							
BA003	Attrition: Posterior Medial Femur - MRI1.5T with gadolinium							
BA004	Attrition: Central Medial Femur - MRI1.5T with gadolinium							
BA005	Attrition: Anterior Medial Femur - MRI1.5T with gadolinium							
BA006	Attrition: Posterior Lateral Femur - MRI1.5T with gadolinium							
BA007	Attrition: Central Lateral Femur - MRI1.5T with gadolinium							
BA008	Attrition: Anterior Lateral Femur - MRI1.5T with gadolinium							
BA009	Attrition: Posterior Medial Tibia - MRI1.5T with gadolinium							
BA010	Attrition: Central Medial Tibia - MRI1.5T with gadolinium							
BA011	Attrition: Anterior Medial Tibia - MRI1.5T with gadolinium							
BA012	Attrition: Posterior Lateral Tibia - MRI1.5T with gadolinium							
BA013	Attrition: Central Lateral Tibia - MRI1.5T with gadolinium							
BA014	Attrition: Anterior Lateral Tibia - MRI1.5T with gadolinium							
BM001	BME: Posterior Medial Femur - MRI1.0T							
BM002	BME: Central Medial Femur - MRI1.0T							
BM003	BME: Anterior Medial Femur - MRI1.0T							
BM004	BME: Posterior Medial Femur - MRI1.5T with gadolinium							
BM005	BME: Central Medial Femur - MRI1.5T with gadolinium							
BM006	BME: Anterior Medial Femur - MRI1.5T with gadolinium							
BM007	BME: Posterior Lateral Femur - MRI1.0T							
BM008	BME: Central Lateral Femur - MRI1.0T							
BM009	BME: Anterior Lateral Femur - MRI1.0T							
BM010	BME: Posterior Lateral Femur - MRI1.5T with gadolinium							
BM011	BME: Central Lateral Femur - MRI1.5T with gadolinium							
BM012	BME: Anterior Lateral Femur - MRI1.5T with gadolinium							
BM013	BME: Posterior Medial Tibia - MRI1.0T							
BM014	BME: Central Medial Tibia - MRI1.0T							
BM015	BME: Anterior Medial Tibia - MRI1.0T							
BM016	BME: Posterior Medial Tibia - MRI1.5T with gadolinium							
BM017	BME: Central Medial Tibia - MRI1.5T with gadolinium							
BM018	BME: Anterior Medial Tibia - MRI1.5T with gadolinium							
BM019	BME: Sub Sp. Tibia - MRI1.0T							
BM020	BME: Sub Sp. Tibia - MRI1.5T with gadolinium							
BM021	BME: Posterior Lateral Tibia - MRI1.0T							
BM022	BME: Central Lateral Tibia - MRI1.0T							
BM023	BME: Anterior Lateral Tibia - MRI1.0T							
BM024	BME: Posterior Lateral Tibia - MRI1.5T with gadolinium							
BM025	BME: Central Lateral Tibia - MRI1.5T with gadolinium							
BM026	BME: Anterior Lateral Tibia - MRI1.5T with gadolinium							
BM027	BME: Medial Patella - MRI1.0T							
BM028	BME: Lateral Patella - MRI1.0T							
BM029	BME: Medial Patella - MRI1.5T with gadolinium							
BM030	BME: Lateral Patella - MRI1.5T with gadolinium							
EF001	Effusion: MRI1.0T							

EF002	Effusion: MRI1.5T with gadolinium					
EF003	Synovitis in Effusion: MRI1.5T with gadolinium					
SY001_BM	Synovitis: Intercondylar - MRI1.0T					
SY002_BM	Synovitis: Infrapatellar - MRI1.0T					
PERILESION	Periarticular Lesion					
PERILESIONTYPE	Periarticular Lesion Type					
MisBM	N of sites with enhanced BML score missing					
MaxBM	maximum of enhanced BML scores in 15 sites					
sumBM	sum of enhanced BML scores in 15 sites					

SAS code for calculated variables:

array nogado{15} BM001 BM002 BM003 BM007 BM008 BM009 BM013 BM014 BM015 BM019 BM021 BM022 BM023 BM027 BM028; array postgado{15} BM004 BM005 BM006 BM010 BM011 BM012 BM016 BM017 BM018 BM020 BM024 BM025 BM026 BM029 BM030; array bm{15} BM01 BM02 BM03 BM04 BM05 BM06 BM07 BM08 BM09 BM10 BM11 BM12 BM13 BM14 BM15; do i=1 to 15; if postgado{i} in (-0.5,0.5) then bm{i}=nogado{i}; else bm{i}=postgado{i}; end; MisBM=nmiss(of BM01 BM02 BM03 BM04 BM05 BM06 BM07 BM08 BM09 BM10 BM11 BM12 BM13 BM14 BM15); MaxBM=max(of BM01 BM02 BM03 BM04 BM05 BM06 BM07 BM08 BM09 BM10 BM11 BM12 BM13 BM14 BM15); if MisBM=0 then sumBM=sum(of BM01 BM02 BM03 BM04 BM05 BM06 BM07 BM08 BM09 BM10 BM11 BM12 BM13 BM14 BM15);

7. References

- Baker K, Grainger A, Niu J, Clancy M, Guermazi A, Crema M, Hughes L, Buckwalter J, Wooley A, Nevitt M, Felson DT. Relation of synovitis to knee pain using contrast-enhanced MRIs. Ann Rheum Dis. 2010 Oct;69(10):1779-83. doi: 10.1136/ard.2009.121426. Epub 2010 May 14. PMID: 20472593; PMCID: PMC3885343. <u>https://pubmed.ncbi.nlm.nih.gov/20472593/</u>
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8. Appendix - Summary report

	1.5T MRI (w Gado) vs 1.0T MRI (non-Gado) image acquisition									
site	N images Start date		Stop date	Same day as 1.0T MRI (non-Gado)	Within 90 days from 1.0T MRI (non-Gado)	More than 90 days between 1.5T MRI (with Gado) and 1.0T MRI (non-Gado)				
				N(%)	N(%)	N(%)	Range (days)			
Both clinics	587	Aug 2006	May 2008	507 (86.4%)	25 (4.3 %)	51 (8.7%)	[178 – 613]			
UAB	213	Oct 2006	May 2008	175 (82.2%)	6 (2.8%)	31 (14.6%)	[178 – 613]			
Ulowa	374	Aug 2006	Nov 2007	332 (88.8%)	19 (5.1%)	20 (5.4%)	[181 – 483]			

Table A1. Timing for 1.5T MRI (w gadolinium) and 1.0T MRI (non-gadolinium) acquired –by clinic.

*Total 4 knees: 1.5T MRI (w gadolinium) was obtained, but 1.0T MRI (non-gadolinium) was not obtained by clinic.

Table A2. Final sample – MRI 1.5T gadolinium images obtained by sex, race and age (at baseline) category.

	Age 50-59		Age 60-69		Age 70-79		Subtotal		Total
	Female	Male	Female	Male	Female	Male	Female	Male	
White or Caucasian	147	133	97	97	30	38	274	268	542
African American or Other non- white race	17	11	10	4	2	1	29	16	45
Total	164	144	107	101	32	39	303	284	587

Table A3. Comparison between participants not enrolled in the study and participants enrolled in the study (1.5T MRI with gadolinium acquired)

30m clinic visit completed	Not enrolled in AS		Enrolled in AS and 1.5 acqu	Total	
	Ν	Row %	Ν	Row %	
Total	2,126	78.3%	587	21.6%	2,713
UAB	1,113	83.9%	213	16.0%	1,326
Ulowa	1,013	73.0%	374	26.9%	1,387
Sex/Gender					
Female	1,319	81.3%	303	18.6%	1,622
Male	807	73.9%	284	26.0%	1,091
Age (mean (SD))	63.2(8.1)		59.9 (7.2)		62.4 (8.0)
Age at BL, 3 categories					
Age 50-59	730	70.3%	308	29.6%	1,038
Age 60-69	875	80.7%	208	19.2%	1,083
Age 70-79	521	88.0%	71	11.9%	592
Race					
White or Caucasian	1,751	76.3%	542	23.6%	2,293
Af-Am or other non-white	375	89.2%	45	10.7%	420
BMI at clinic visit (mean(SD))	30.9 (6.1)		29.7 (5.0)		30.7 (5.9)
Body mass index, 3 Categories					
.M:Missing	2	100.0%	0	0	2
Under 25	302	75.6%	97	24.3%	399
25 to under 30	773	76.6%	235	23.3%	1,008
30 or more	1,049	80.4%	255	19.5%	1,304