Association of MR Relaxation Times with Muscle Morphology and Functional Loading at the Knee

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OABiomarker Global Initiative OARSI

BACKGROUND

Knee OA: Scope of the Problem

- Need for early identification in knee osteoarthritis (OA)
  - since it is too late once structural changes occur
  - because current management ineffective at long-term symptom modification or any disease modification[3,4]
  - to develop sub-group specific preventative interventions
  - depends on ability to detect early biochemical changes
  - using promising quantitative MR imaging techniques[3,4]

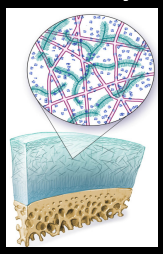
1. Zhang et al. 2008
2. Zhang et al. 2009
3. Mosher et al. 2004
4. Li et al. 2007

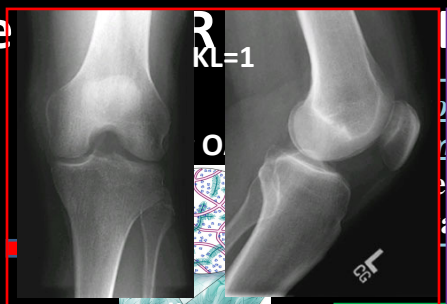
BACKGROUND

MQIR

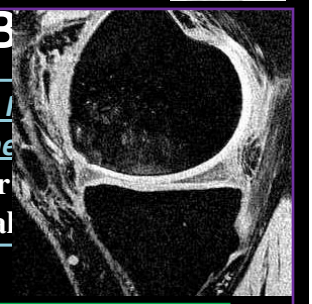
Knee

Healthy





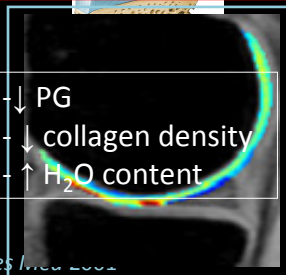
Radiographs



SPGR images

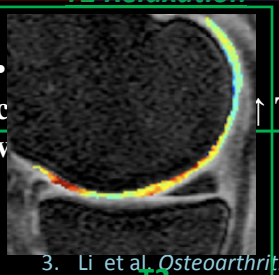
T1ρ Relaxation

- ↓ PG
- ↓ collagen density
- ↑ H_2O content

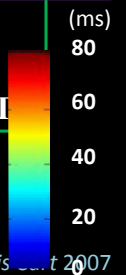


T1ρ

T2 Relaxation



T2



1. Akella et al. *Magn Res Med* 2001
2. Mosher et al. *Semin Musculoskelet Radiol* 2004
3. Li et al. *Osteoarthritis Cart* 2007
4. Li et al. *Magn Res Imag* 2010

PURPOSE

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Knee OA: Risk Factors

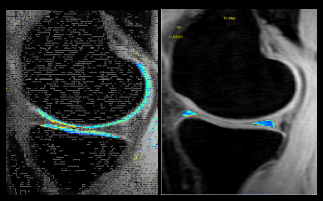
Alignment

↑incidence & progression[1]

↑ adduction moment (KAM)

– Young healthy / old with knee OA[4,5]

Articular & Meniscal Cartilage T1ρ/T2 Relaxation Times



1. Sharma et al. 2010
2. Sharma et al. 1999
3. Barrios et al. 2010
4. Miyazaki et al. 2002
5. Kumar et al. 2011
6. Koo et al. 2010

Association of MR relaxation times with risk factors in young healthy adults

METHODS

Subjects

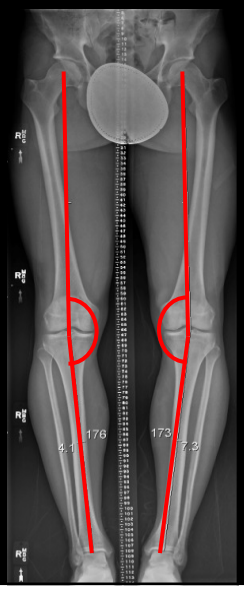
	n	Mean (SD)
Age	25 (42 knees)	27.9 (4.1)
BMI	25 (42knees)	22.7 (2.2)

- Physically active
- No knee pain
- No h/o knee trauma, surgery

METHODS

Mechanical Axis (Alignment)

- Standard weight-bearing long limb radiographs
- Internal angle
  - Center of femur head to center of the knee
  - Center of the knee to the center of talar dome
  - Smaller angle = greater varus
  - Available from 27 knees

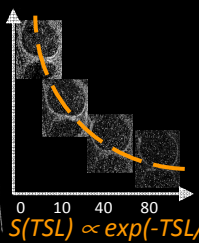


METHODS

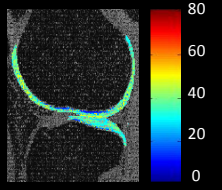
Quantitative MRI of Cartilage

- 3 Tesla MRI with 8 channel T/R knee coil

Sequence	Parameters	Variables
Sagittal 3D fat-saturated high-resolution SPGR	TR/TE = 15/6.7 ms, FA = 18, FOV = 14 cm, matrix = 512 x 512, ST= 1 mm, BW = 31.25 kHz, NEX = 1	Articular Cartilage Thickness
$T_{1\rho}/T_2$ quantification	TSL = 0/10/40/80 ms, prep TE = 0/13.7/27.3/54.7 ms, FOV = 14 cm, matrix = 256 x 128, time of recovery = 1.2 sec, ST = 4 mm	$T_{1\rho}/T_2$ Relaxation times



$S(TSL) \propto exp(-TSL/T1\rho)$



$T_{1\rho}$ Map

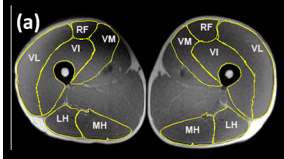
Cartilage	Menisci
- FT, PF - Global - Medial - Lateral -M:L Ratio	- Medial - Lateral - Global -M:L Ratio

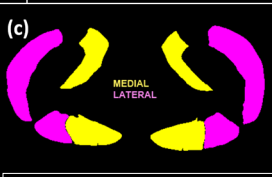
METHODS

Quantitative MRI of Thigh Muscle

- 3 Tesla MRI with 8 channel T/R knee coil

Sequence	Parameters	Variables
Midthigh Axial T1-W	TE/TR = 6.41/800, slice thickness = 10 mm, matrix = 384 x 1932, ETL = 2, bandwidth = 150 kHz, NEX = 4	Quadriceps and Hamstrings Cross-sectional Area



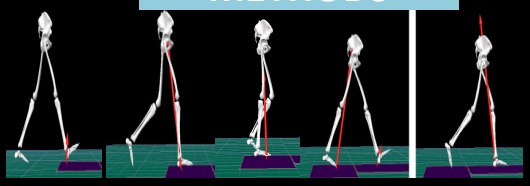


-Mid-thigh
-Mean of 4 slices

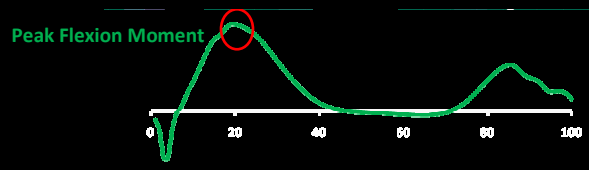
- Quadriceps
- Hamstrings
- Q:H Ratio

- Medial
- Lateral
- Quads M:L ratio
- Overall M:L Ratio

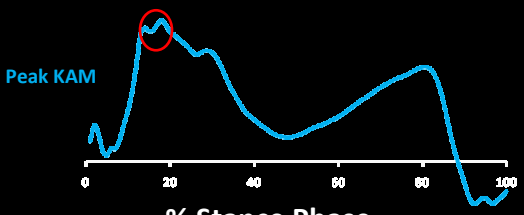
METHODS



Walking Patterns



Sagittal knee Moment (Also : Sagittal Rate of Loading)



Frontal knee Moment (Also: KAM Impulse, Frontal ROL,)

METHODS

Statistics

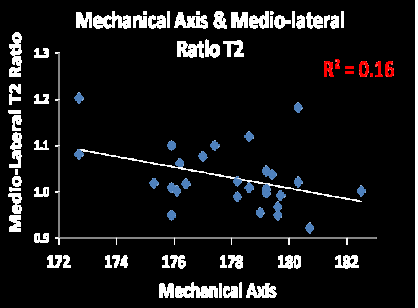
- Mechanical Axis and Cartilage Parameters
  - Pearson's correlations
- Muscle morphology, Loading and Cartilage Parameters
  - Generalized Estimating Equations (GEE)
  - Accounting for age, BMI, gender, walking speed and data from both knees

RESULTS & DISCUSSION

Alignment and qMRI

Correlation	Lateral Cartilage		Medio-lateral Ratio	
	$T_{1\rho}$	T_2	$T_{1\rho}$	T_2
r	0.357	0.489	-0.241	-0.395
p	0.067	0.010	0.225	0.042

- ↑ Varus related to ↑ medio-lateral ratio of cartilage T_2
  - collagen in medial compartment more disorganized compared to lateral
  - Changes evident as early as 3rd decade

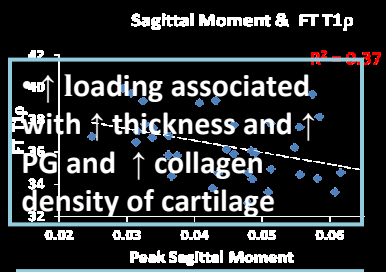


RESULTS & DISCUSSION

Loading & T1ρ/T2 Relaxation Times

Cartilage

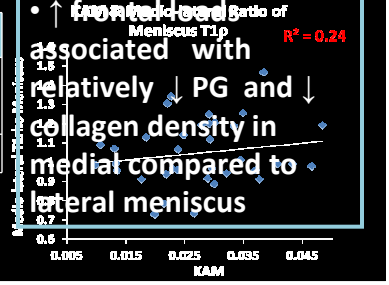
MR variable	Predictors	p
FT, Global T1ρ	Peak Sag Moment	< 0.001
FT , PF, Global T2	Peak Sag Moment	< 0.001



↑ loading associated with ↑ thickness and ↑ PG and ↑ collagen density of cartilage

Meniscus

MR variable	Predictors	p
Medial, M: L T1ρ	Peak KAM	0.001 – 0.031
M:L T2	Frontal ROL	0.002



- ↑ [illegible] ratio of associated with relatively ↓ PG and ↓ collagen density in medial compared to lateral meniscus

RESULTS & DISCUSSION

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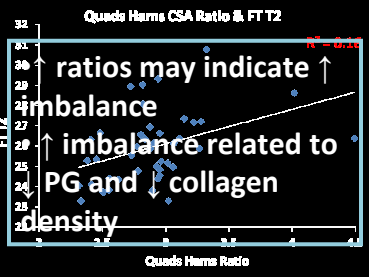
Muscle CSA & T1ρ/T2 Parameters

Cartilage

MR variable	Predictors	p
TF , PF, Global T2	Quads Hams Ratio	0.007-0.045
Medial T1ρ, T2	Quads M:L Ratio	0.052-0.057

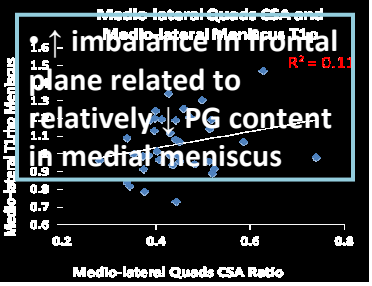


↑ ratios may indicate ↑ imbalance

↑ imbalance related to ↑ PG and ↓ collagen density

Meniscus

MR variable	Predictors	p
Medial T1ρ	Quads M:L Ratio	0.002
M: L Ratio T1ρ	Quads M:L Ratio	0.006



↑ imbalance in frontal plane related to relatively ↓ PG content in medial meniscus

RESULTS & DISCUSSION

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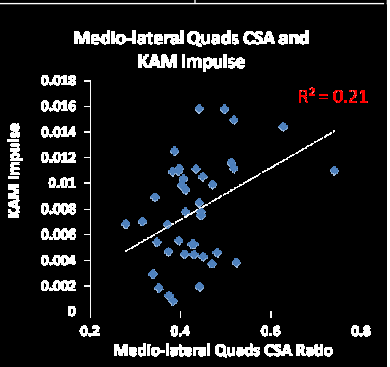
Muscle CSA & Walking Patterns

Gait variable	Predictors	p
Peak KAM	Q: H ratio, Quads M:L Ratio	< 0.001
KAM impulse	Quads M:L Ratio	< 0.001
Frontal ROL	Q: H Ratio	0.002

- ↑ imbalance related to ↑KAM, KAM impulse and frontal ROL
  - ↑ imbalance related to walking patterns that predispose to knee OA
  - ? mechanism by which muscle imbalance impacts cartilage health



CONCLUSIONS

- T1ρ and T2 relaxation times are sensitive to mechanical loading
  - could be used in interventional and clinical studies.
- Malalignment and KAM are associated with medio-lateral imbalances of cartilage composition
  - as early as 3rd decade, which could progress to OA.
- Impact of loading more pronounced on the meniscus than articular cartilage
  - ? Meniscus degenerates first
- Muscle imbalance is related to walking patterns known to predispose to OA as well as higher MR relaxation times
  - importance of targeted muscle balance training in addition to strengthening

FUTURE STUDIES

- From this dataset
  - Association of spatial distribution of T1ρ and T2 relaxation times and texture parameters to OA risk factors
  - Focus on weight-bearing cartilage regions
- In people with knee OA and matched controls
  - Cross-sectional analysis of risk factors with cartilage morphology, T1ρ and T2 relaxation times
  - Longitudinal analysis of relationship of walking patterns, muscle activation patterns, strength changes with cartilage degradation
- General questions
  - Meniscus relaxation times and biochemical correlation

Thank You

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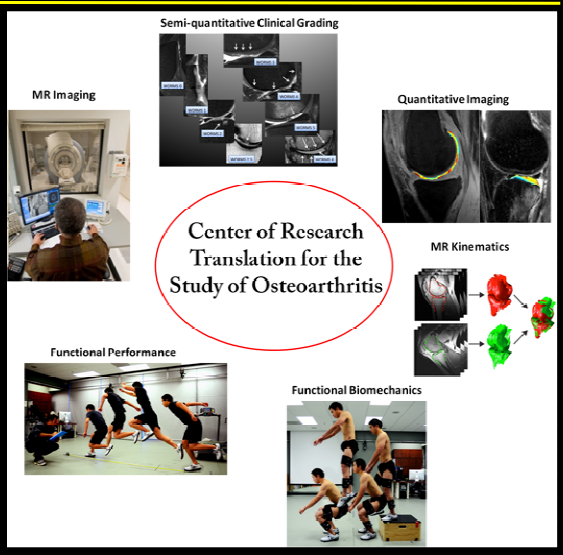
- NIH- NIAMS R01AR046905-11A1



http://www.radiology.ucsf.edu/research/centers/translation-study-osteoarthritis