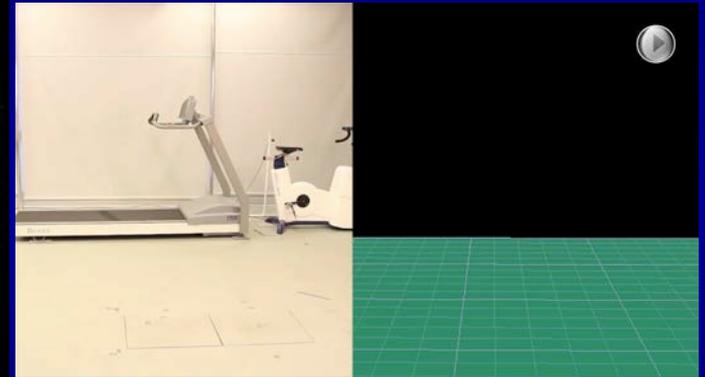
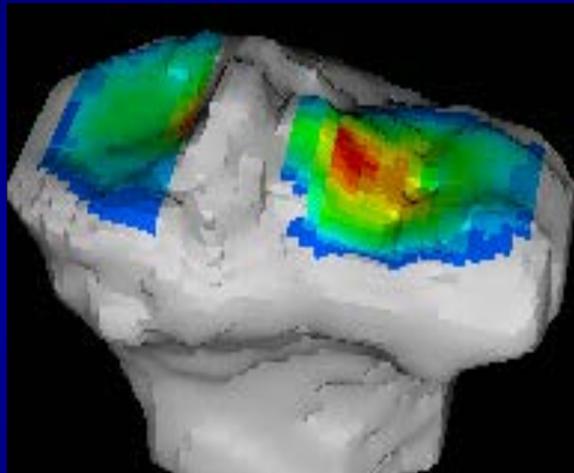
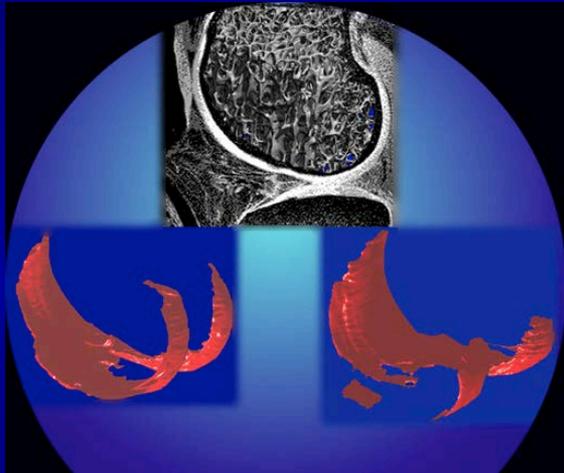




# QUANTITATIVE MRI

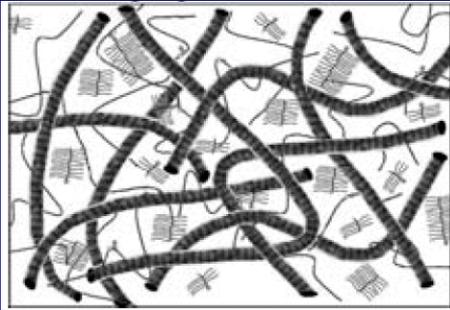


**Sharmila Majumdar, PhD**  
**Musculoskeletal Quantitative Imaging Research Group**  
**Dept. of Radiology and Biomedical Imaging**  
**University of California, San Francisco**



# OSTEOARTHRITIS

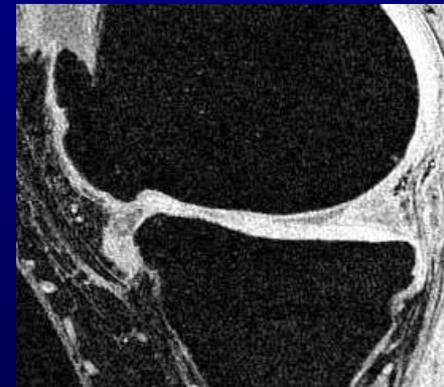
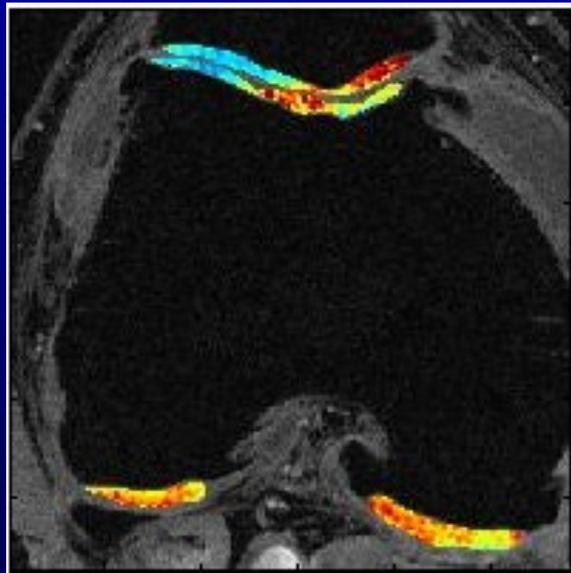
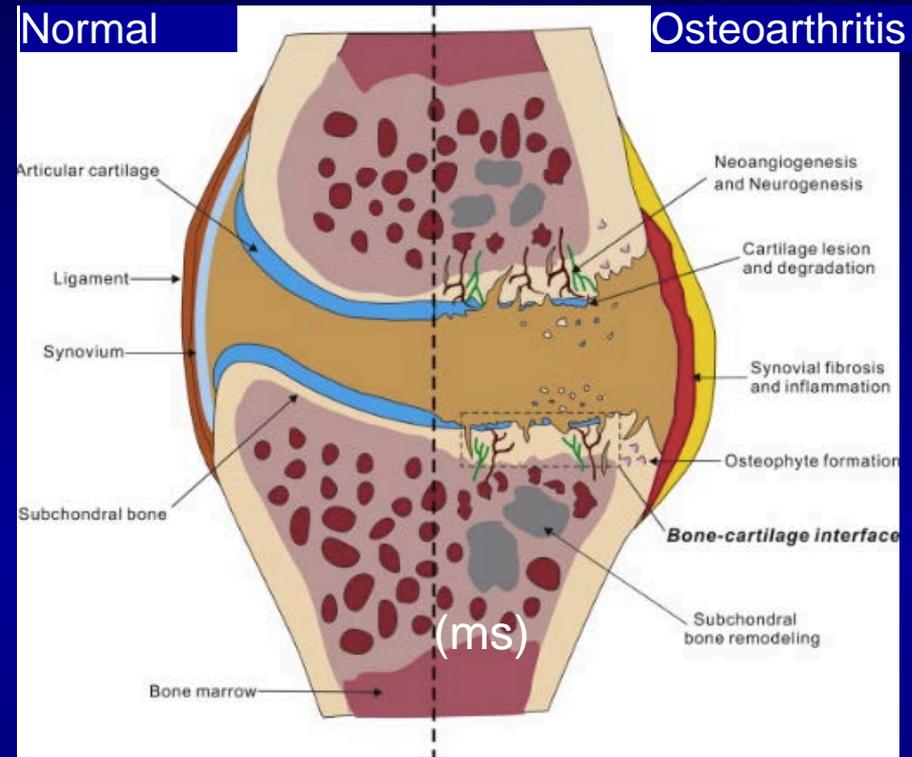
## Early Stage: Cartilage Biochemical Changes



- Loss of proteoglycan
- Disorganization of collagen structure



## Late Stage: Morphological Changes

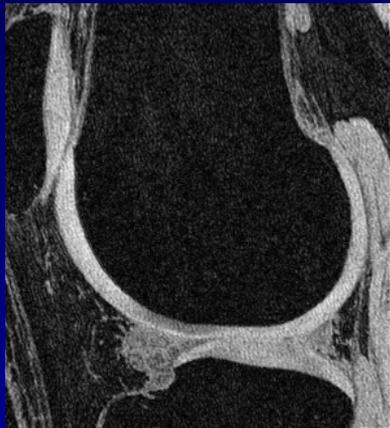


$T_{1\rho}$ ,  $T_2$

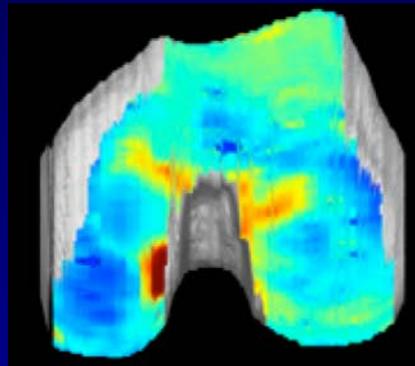
# PRECISION IMAGING & OSTEOARTHRITIS

Later Stage:

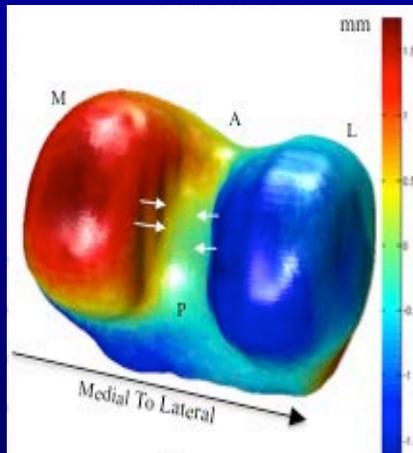
Early Stage: Cartilage



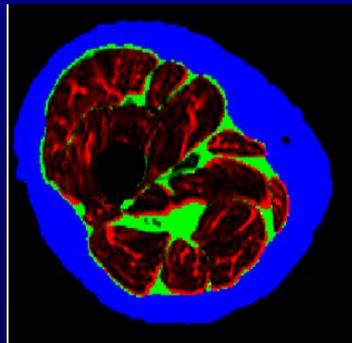
*Radiological  
Diagnosis*



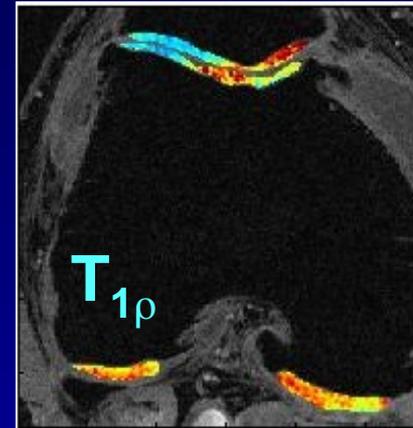
*Cartilage Morphology*



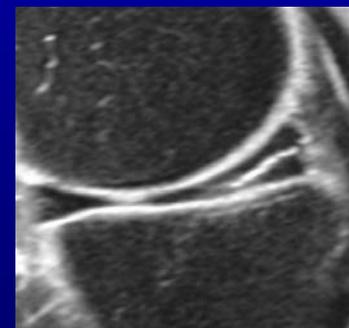
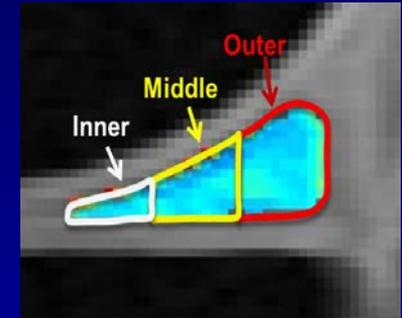
*Bone Shape*



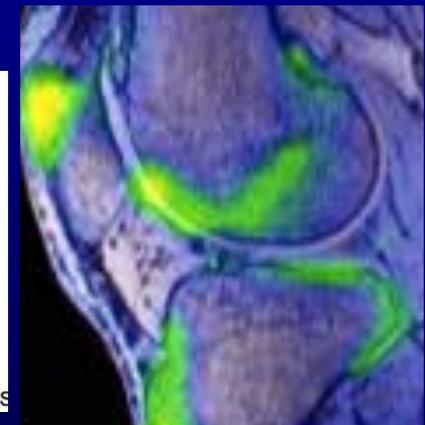
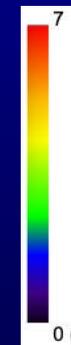
*Muscle Composition &  
Size*



*Cartilage and Meniscus  
Biochemistry*



*Meniscus*



*PET-MR: +Bone remodeling*

# - COLLAGEN CONTENT & ORIENTATION

Superficial Zone

Transition Zone

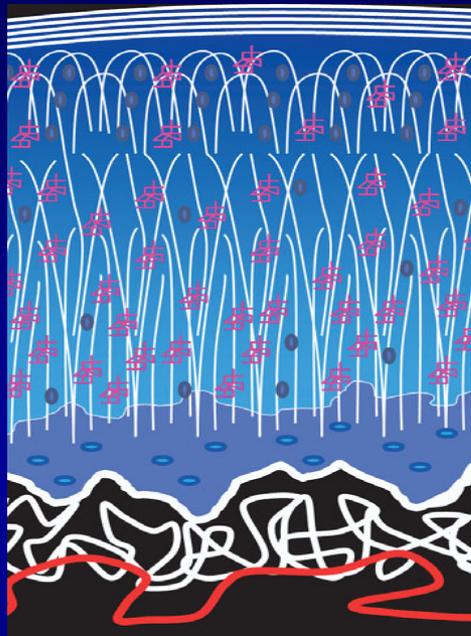
Radial Zone

Tidemark  $\rightarrow$

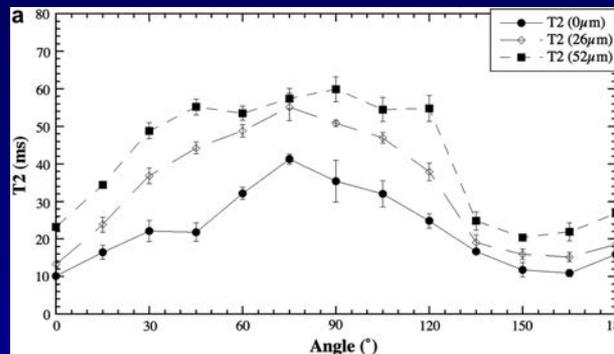
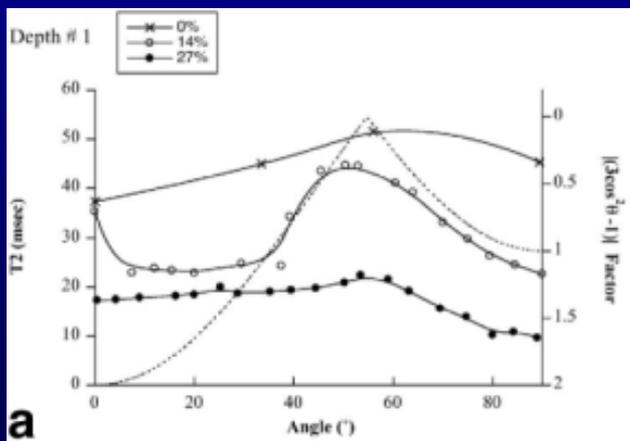
Calcified cartilage

Subchondral bone plate

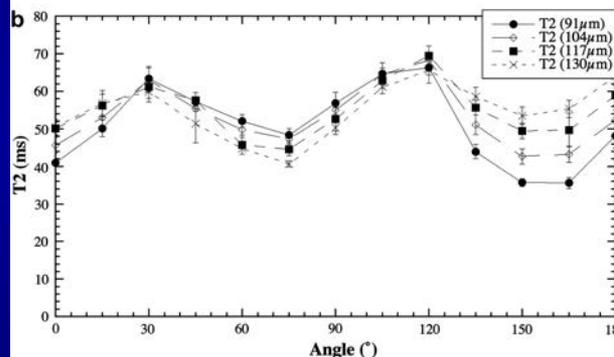
Vascular plexus



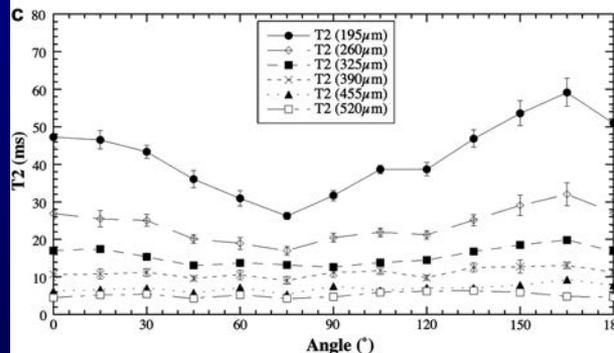
Under Load



Superficial



Transition



Radial

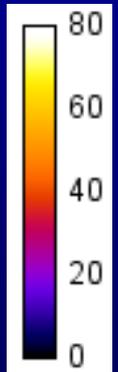
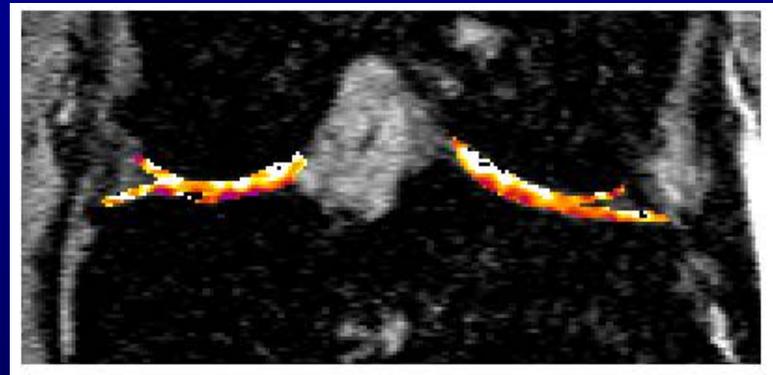
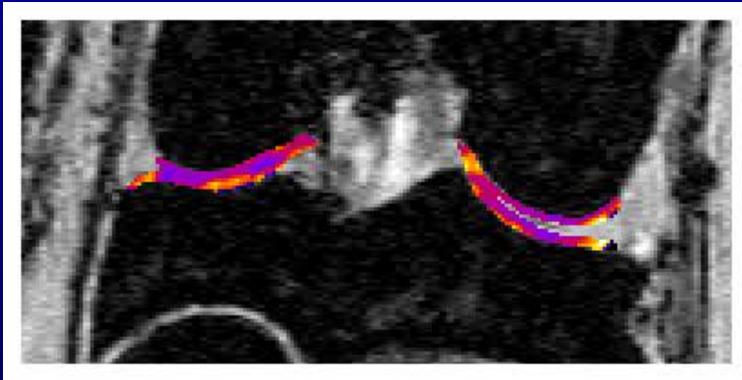
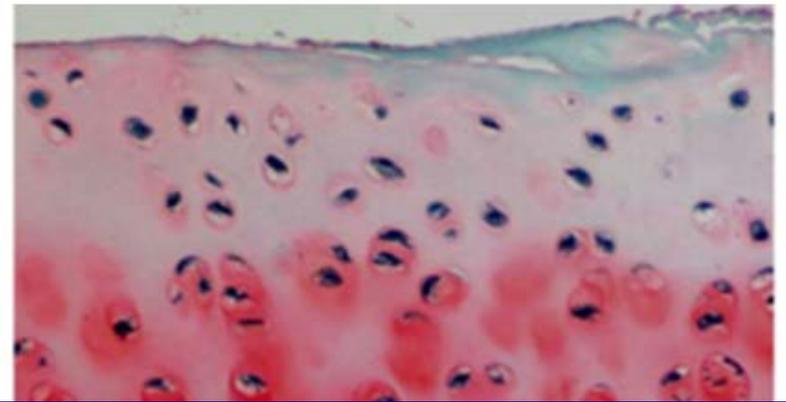
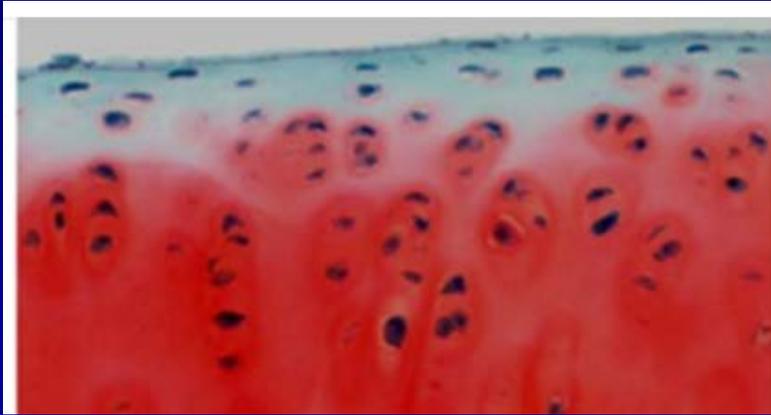
Zheng and Xia Lab, Osteoarthritis and Cartilage, 2009

Alkahladled And Xia Lab, JMRI, 2005

# $T_{1\rho}$ - PROTEOGLYCAN

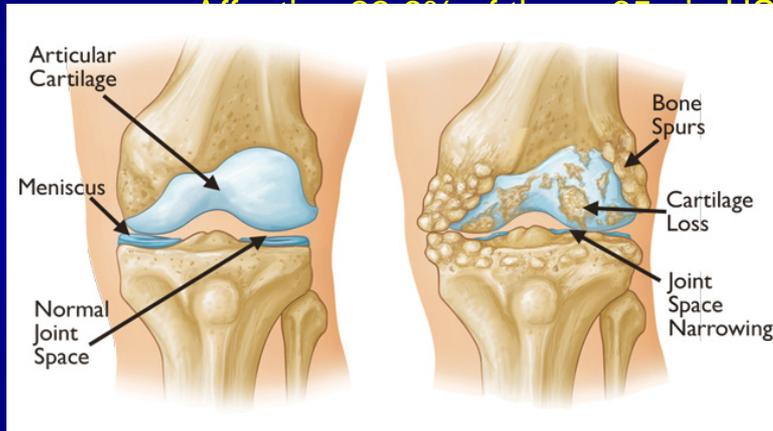
3 month old

9 month old



# ACL INJURY AS A MODEL FOR OSTEOARTHRITIS

Osteoarthritis (OA): degenerative cartilage disease



<http://orthoinfo.aaos.org/figures>



<http://faculty.washington.edu>



<https://usatthebiglead.files.wordpress.com/>

ACL Injury is associated with OA

- Young and active population
- Despite surgical reconstruction
- Abnormal joint biomechanics
- Unclear connection between injury and cartilage degeneration

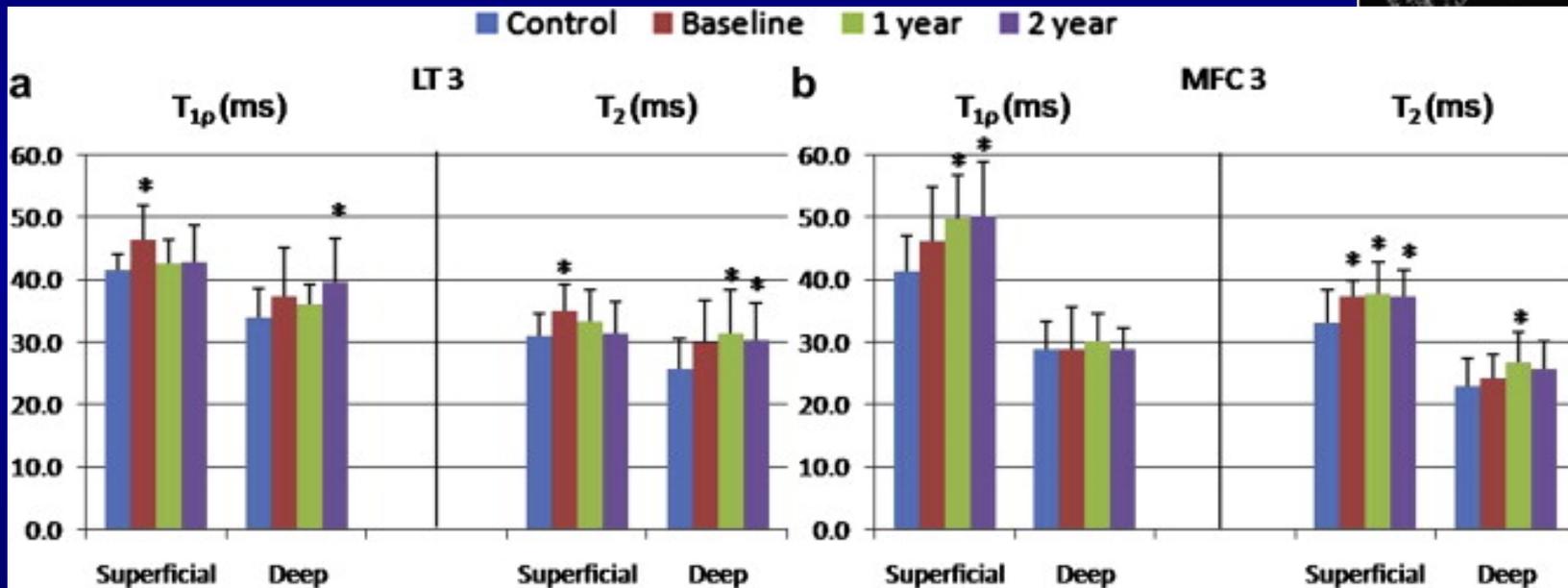
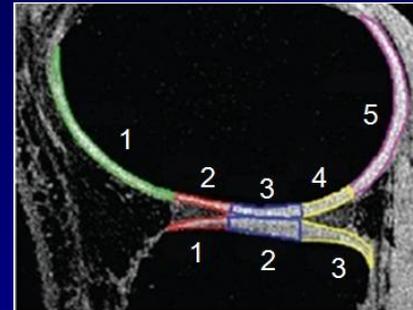


Meniscus – Plays a major role in whole Joint Function

<sup>1</sup> Center for Disease Control (CDC): <http://www.cdc.gov/arthritis/basics/osteoarthritis.htm>

# ✓ Changes in Compartments and Layers of Cartilage Reflect Degeneration

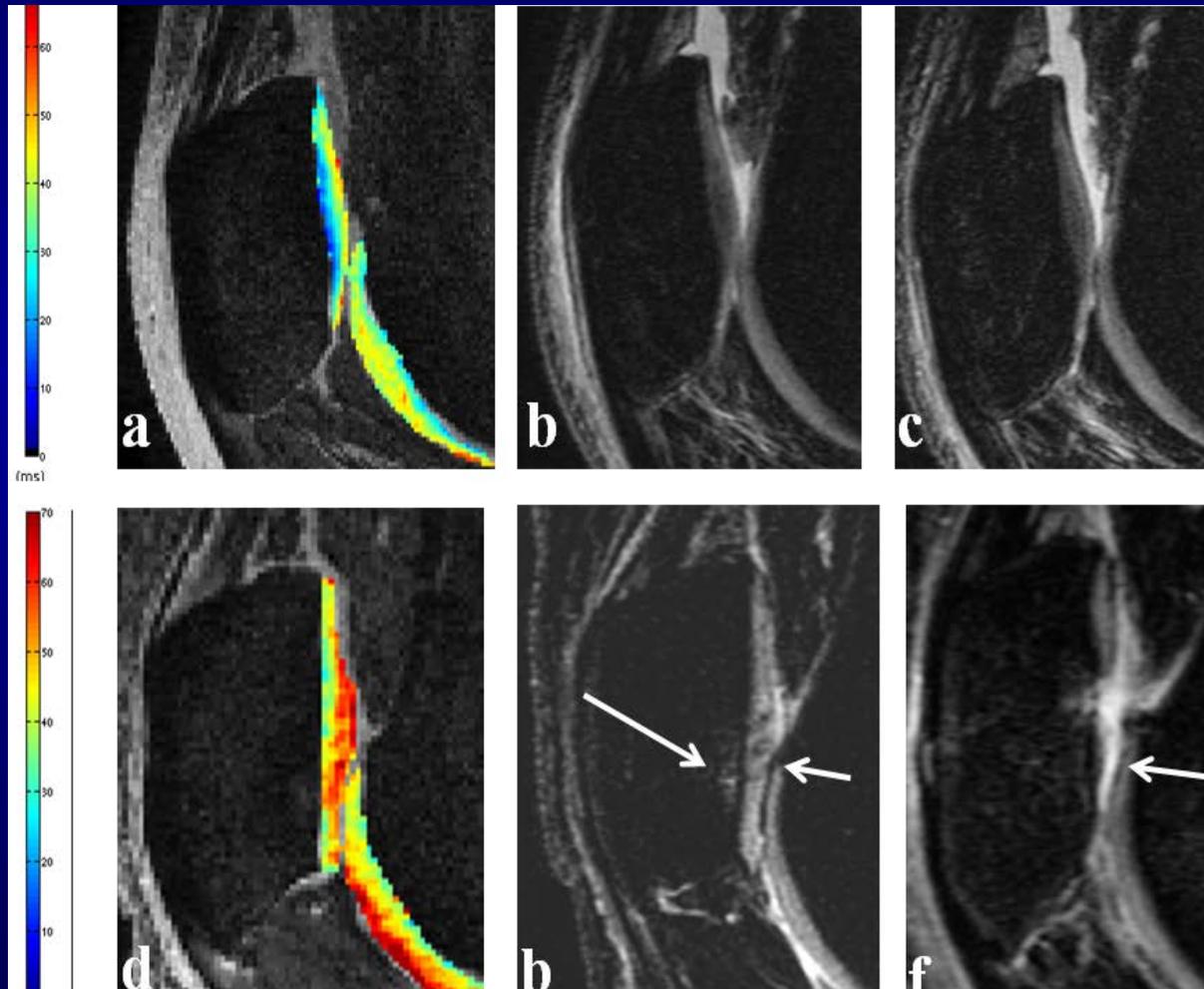
## 2-YEAR FOLLOW UP



\* p < 0.05 compared to controls

# ✓ $T_{1\rho}$ and $T_2$ predict cartilage loss over 2 yrs

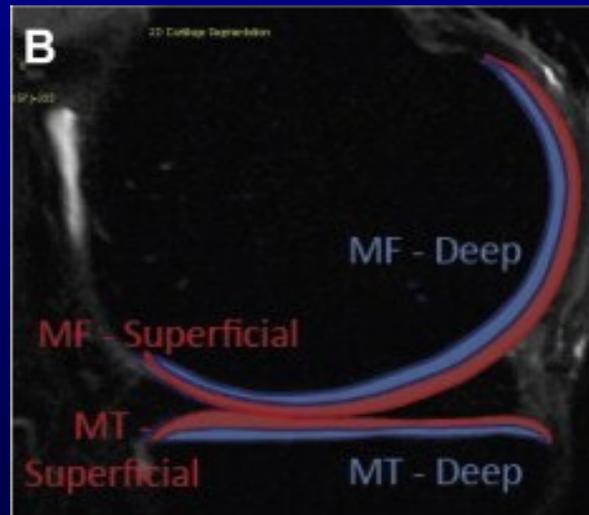
*55 subject with no or mild OA Follow-up over 2 years  
2 groups with and without progression*



# ✓ $T_{1\rho}$ and $T_2$ - Compartments and Layers of Cartilage Reflect Degeneration

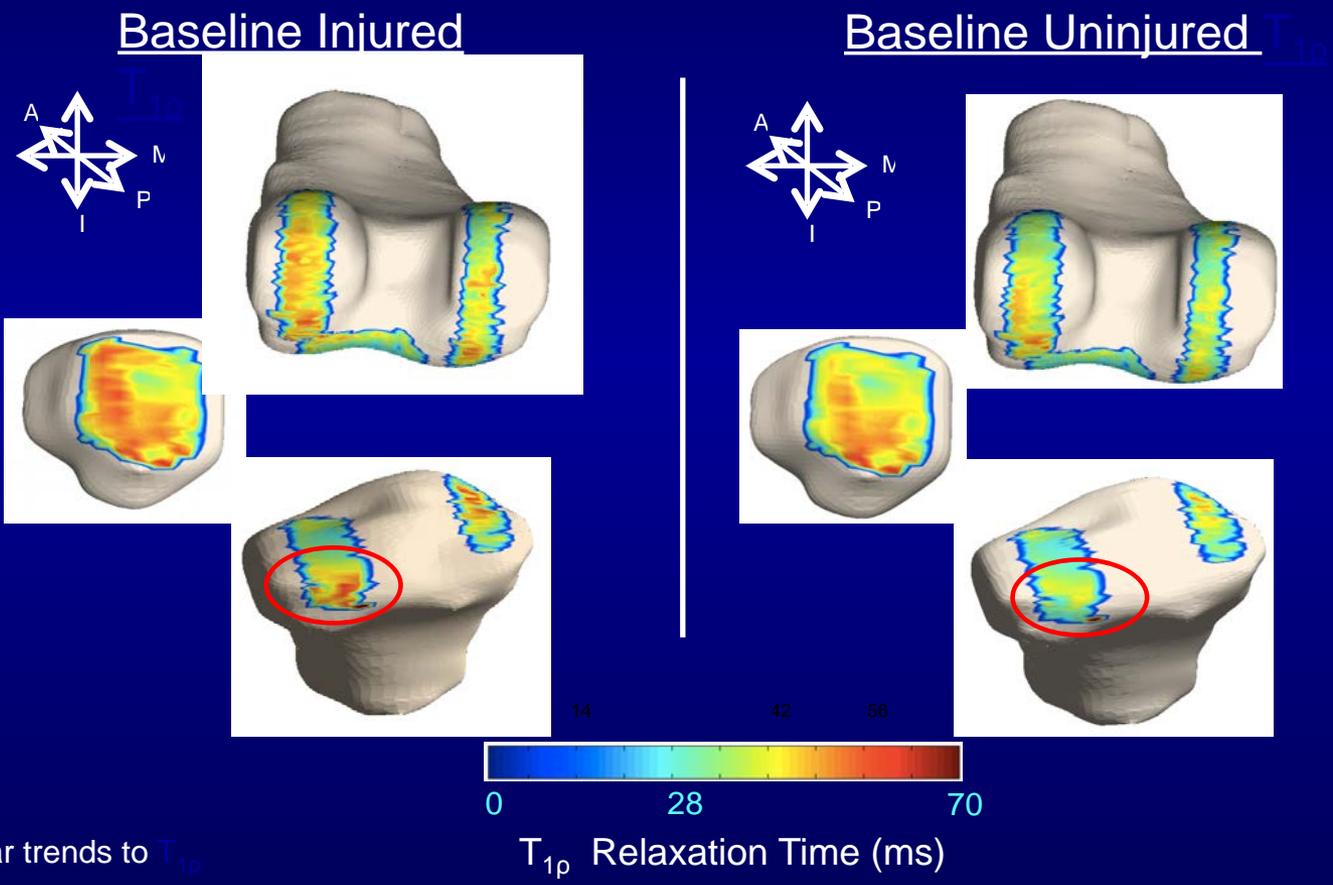
## In 120 subjects with and without knee OA

Pearson's $r$ (P value)	Self-report Symptoms	Self-report Pain	Self-report ADL	Physical Function
Femoral Superficial $T_{1\rho}$	0.29 (0.014)	0.29 (0.001)	0.25 (0.006)	0.23 (0.039)
Tibial Deep $T_{1\rho}$	0.25 (0.007)	0.25 (0.007)	0.25 (0.007)	ns



# ✓ Going Beyond Averaging Compartments and Layers Reflect Local Degeneration

## $T_{1\rho}$ & $T_2$ (Increased in ACL Injury at baseline)



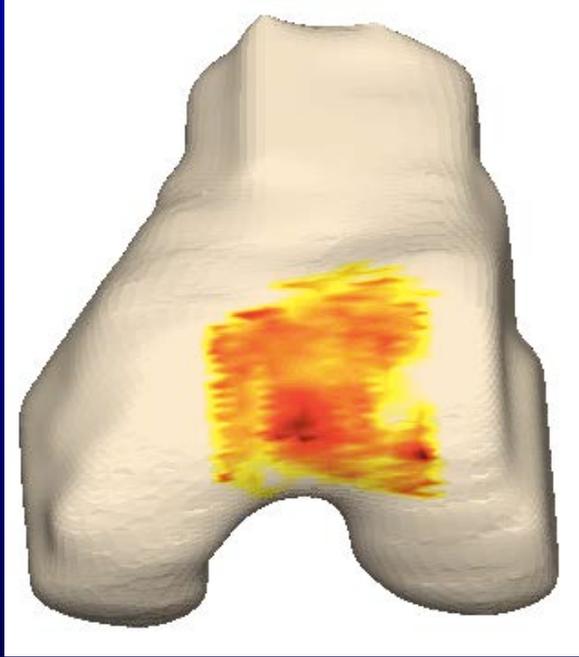
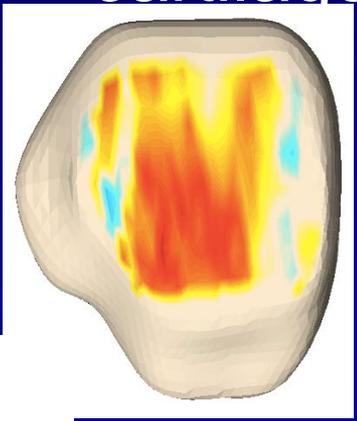
\*  $T_2$  showed similar trends to  $T_{1\rho}$

# ✓ Going Beyond Averaging Compartments and Layers Reflect Local and Higher Correlations with Symptoms/Pain

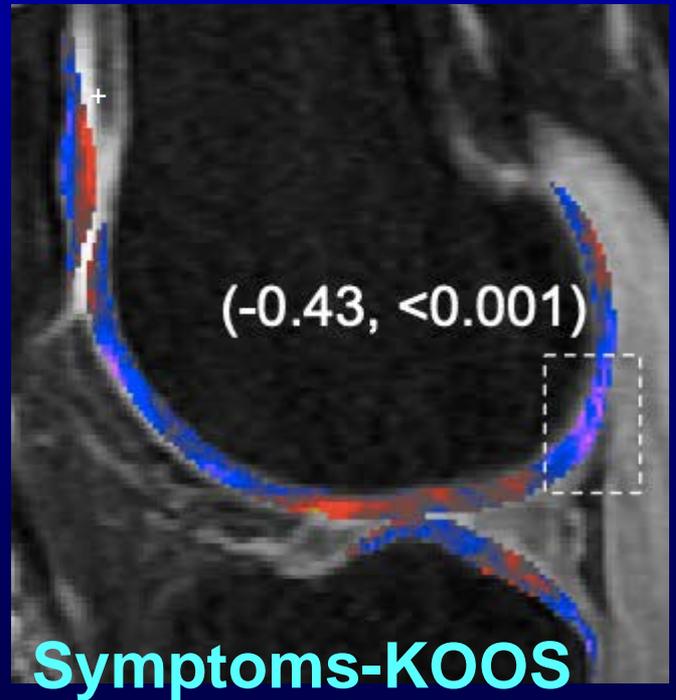
$T_{1\rho}$  – Biochemical degeneration is higher in osteoarthritic

cartilage

Difference between OA and non OA

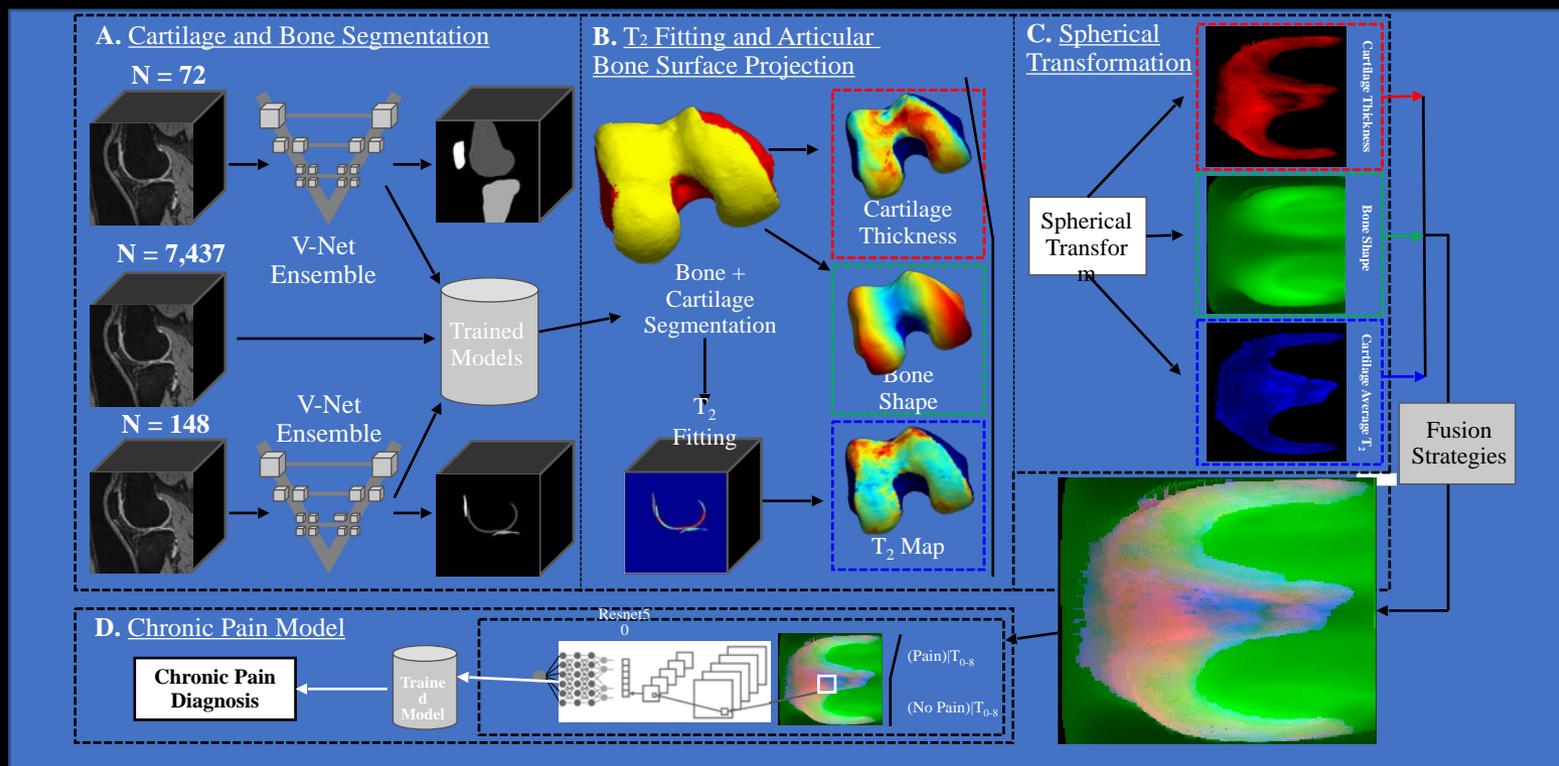


Greater the degeneration -- **Higher the pain and symptoms**



# The Role of Deep Learning and the OAI Dataset

## *DeepPain: Uncovering Associations Between Data-Driven Learned qMRI Biomarkers and Chronic Pain*



Chronic knee pain was defined as patient timepoints which reported knee pain, aching, or stiffness over half of the days of the month for more than six months of the past 12 months.

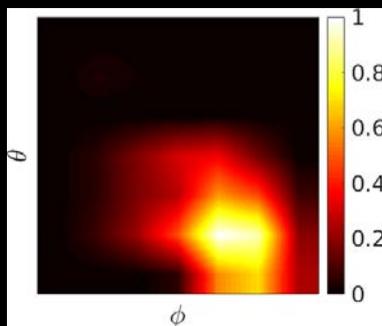
# Pain Correlations cannot be determined using a single biomarker, region of interest

Better feature extraction to combine with other biomarkers

**Bone shape shows ethnic differences, and related to OA**

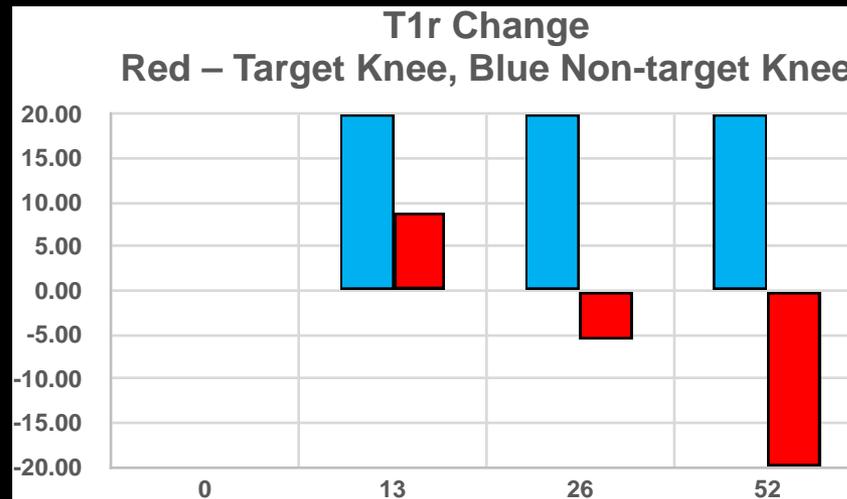
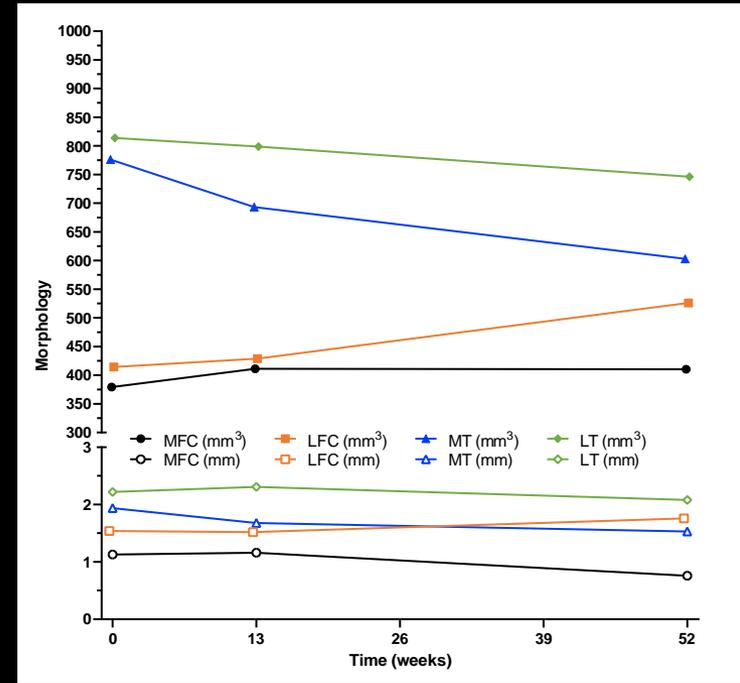
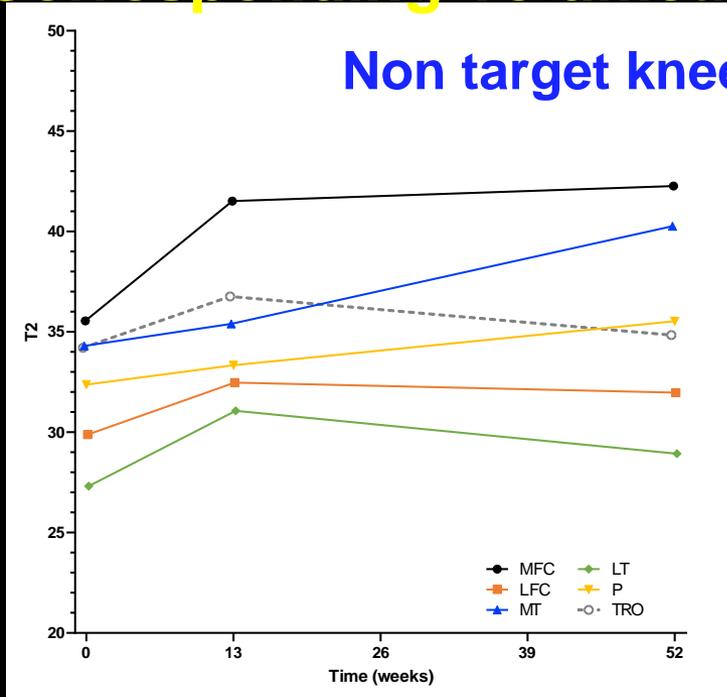
**Test Set ROC (Sensitivity/Specificity/AUC) (Mean  $\pm$  CI95)**

	Patella	Tibia	Femur	PTF
All Biomarkers Fusion	65.5 $\pm$ 0.381	52.5 $\pm$ 0.369	56.6 $\pm$ 0.368	57.3 $\pm$ 0.367
Biomarkers	63.9 $\pm$ 0.255	71.8 $\pm$ 0.235	76.2 $\pm$ 0.207	75.2 $\pm$ 0.207
Fusion	70.3 $\pm$ 0.251	66.4 $\pm$ 0.250	72.5 $\pm$ 0.223	73.0 $\pm$ 0.233



- The activations are quite varied across each bone
- Pointing to a multifactorial combination of biomarkers behind chronic knee pain
- Differs in different individuals

# ✓ An example in a DMOAD trial $T_{1\rho}$ and $T_2$ Mapping with Corresponding Volumetric and Thickness Measurements



# ✓ Issues with $T_2$ and $T_{1\rho}$ Mapping and Solutions

- Lack of standardized data acquisition and processing
- Needs documentation of inter-vendor variations
- Needs standardized and automated processing
- Needs fast imaging

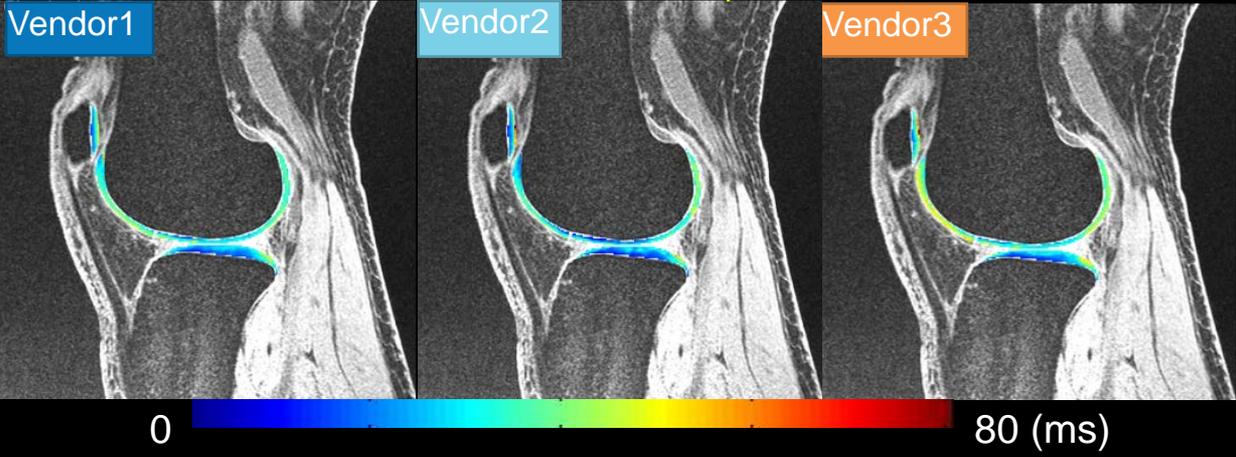
QIBA MSK Committee: 70+ members (30+ active members) from 40+ academic institutes and industrial partners



QIBA Profile: MR-based cartilage compositional biomarkers ( $T_{1\rho}$ ,  $T_2$ ) for risk prediction, early diagnosis and monitoring of treatment of degenerative joint disease

# ✓ Multi-vendor Multi-site $T_{1\rho}$ and $T_2$ Imaging

MAPSS  $T_{1\rho}$  Maps



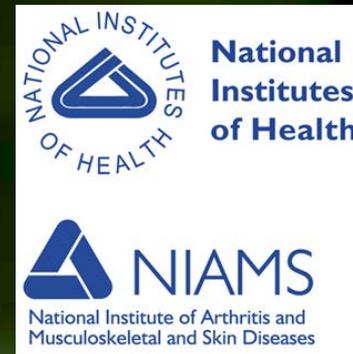
- Implemented MAPSS  $T_{1\rho}$  and  $T_2$  imaging on major MR platforms
- Harmonized protocols and central processing: inter-vendor inter-site variations  $\sim 10\%$ <sup>1</sup>
- Further mitigate variations and develop fast imaging
- Develop a MSK phantom with NIST with reference  $T_1$ ,  $T_2$ ,  $T_{1\rho}$  values



<sup>1</sup>Kim et al Osteoarthritis Cartilage 2020

Sponsored by Arthritis Foundation and NIH/NIAMS R01AR077452

# Thank You



OREF/Goldberg Arthritis  
Research Award

Arthritis Foundation

AOSSM

