# *My Aching Knees – Osteoarthritis: Prevention, Detection, and Treatment*
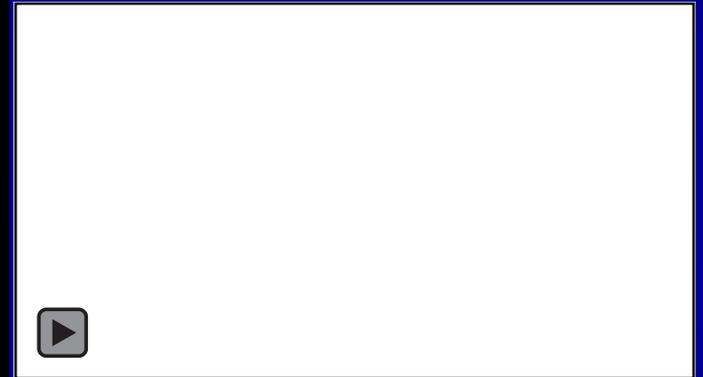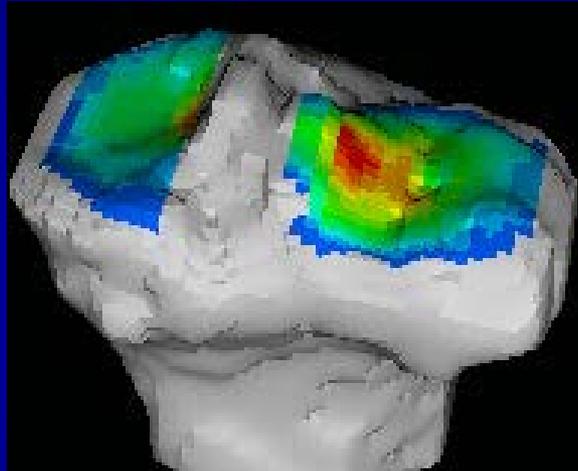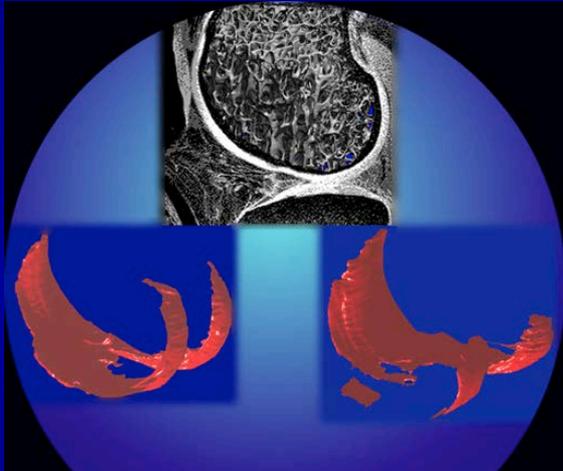
**Sharmila Majumdar, PhD**
**Musculo-skeletal Quantitative Imaging Research Group**
**Dept. of Radiology and Biomedical Imaging**
**University of California, San Francisco**
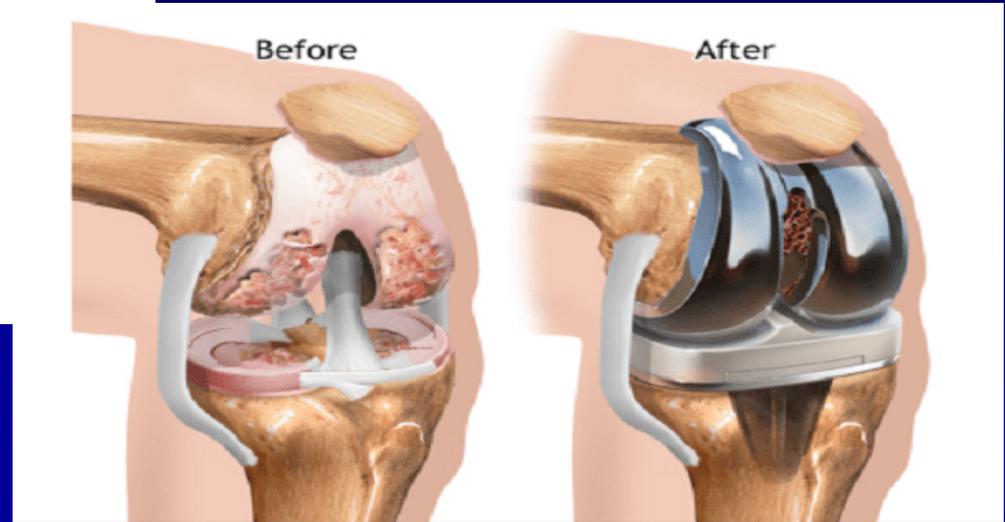
Contributors to pain
are poorly understood

- **52.5 million** (22.7%) adults - self-reported doctor-diagnosed OA
- **22.7 million** (9.8% adults) have arthritis-attributable activity limitation.
- Based on 2010-2012 data – by **2040**
  - **78 million** (26%) adults 18 years or older will have doctor-diagnosed OA
  - **35 million** adults - arthritis-attributable activity limitations

# TOTAL KNEE REPLACEMENT (TKR)
# TOTAL HIP ARTHROPLASTY (THA)



Legend: ■ Number TKR ■ Number THA ■ Total

Y-axis: 0; 500,000; 1,000,000; 1,500,000; 2,000,000; 2,500,000; 3,000,000; 3,500,000; 4,000,000; 4,500,000

X-axis: 2000, 2005, 2010, 2030
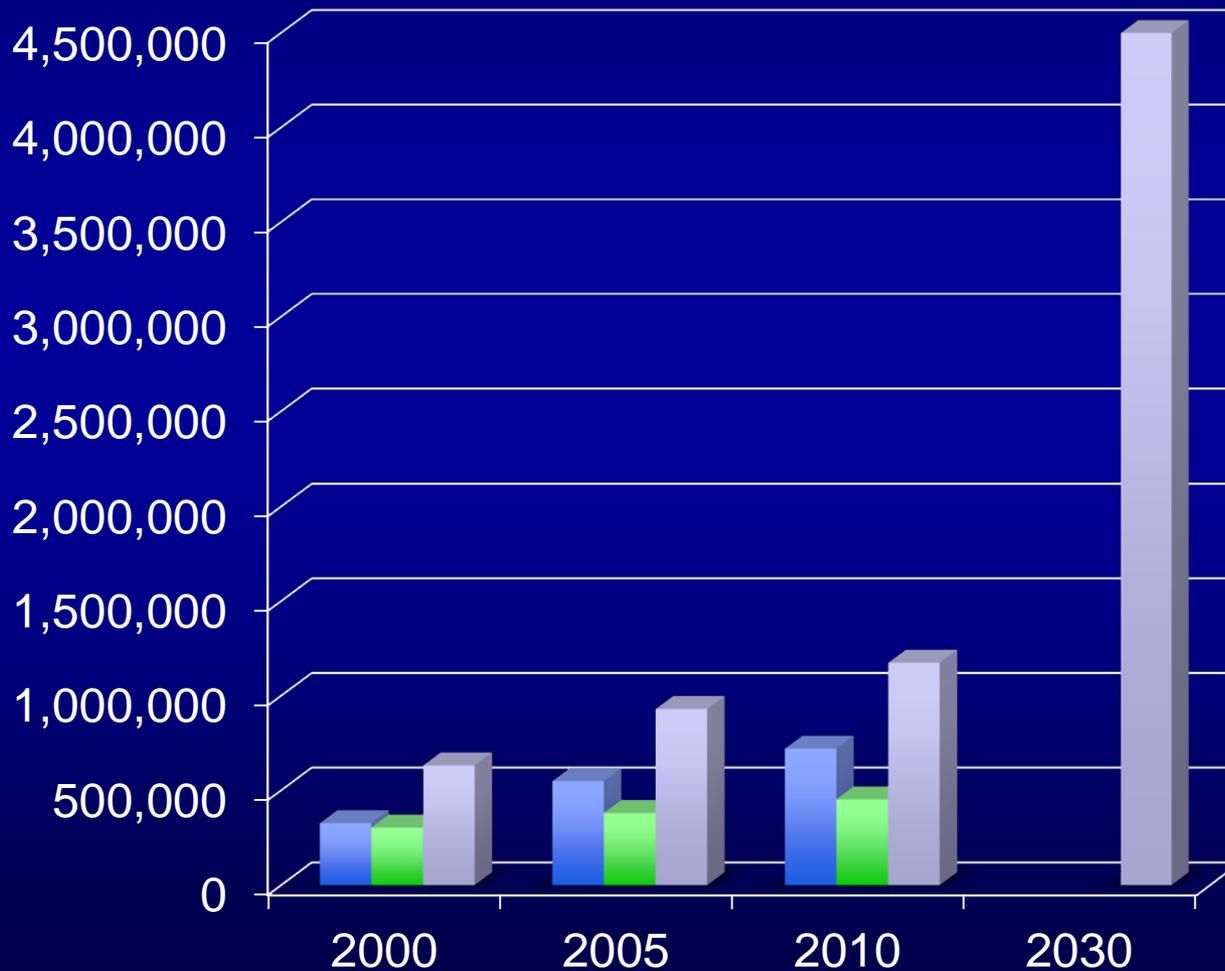
# ECONOMIC IMPACT

| Year | Inflation Adjusted $ in Billions |
|------|----------------------------------|
| 2000 | 8.9 |
| 2005 | 14.7 |
| 2010 | 19.7 |
| 2030 | 50 |

A 10% reduction in surgeries will have major impact on healthcare costs – estimated reduction is likely to be 5 billion in 2030 based on the predictions above.

# MY FOCUS IS TO ADDRESS EMERGING PRECISION IMAGING METHODS THAT…

- *Will ultimately reduce the number of knee replacements*

# THE KNEE JOINT



Lateral Collateral Ligament

Anterior Cruciate Ligament

Meniscus

Patella (kneecap)

Tibia
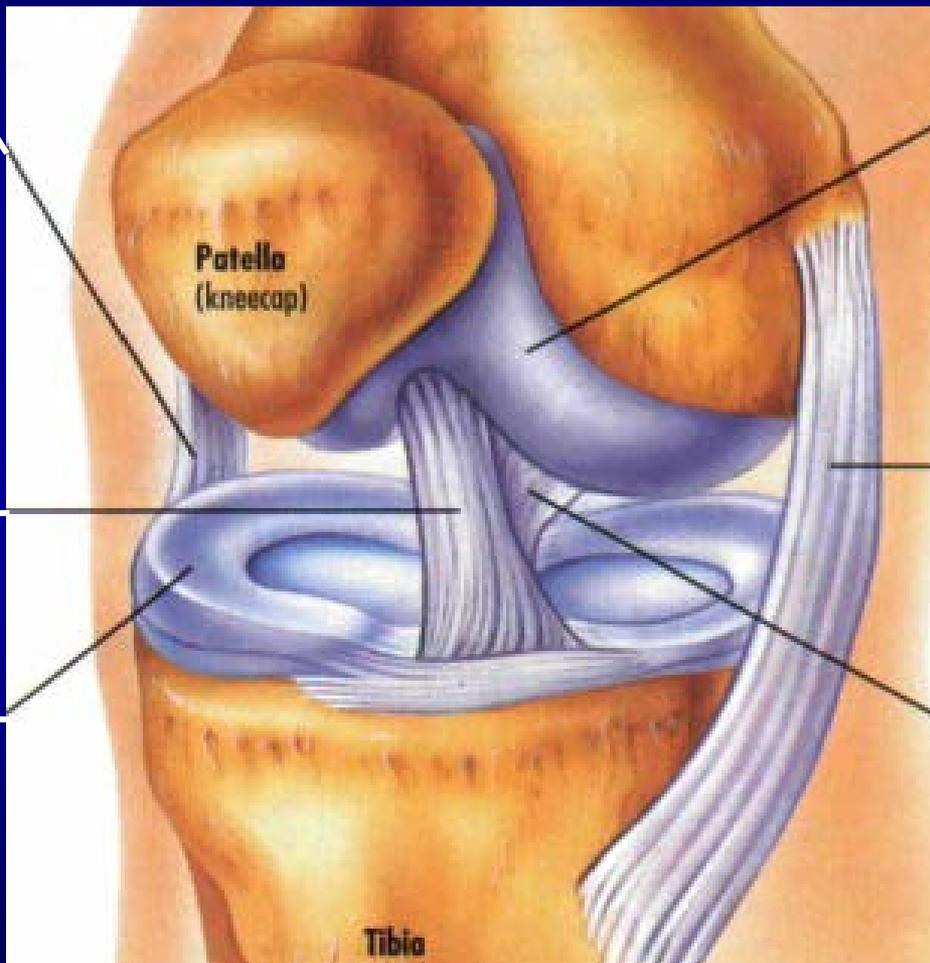
Cartilage

Medial Collateral Ligament

Posterior Cruciate Ligament

# OSTEOARTHRITIS

## Early Stage: Cartilage
Biochemical Changes
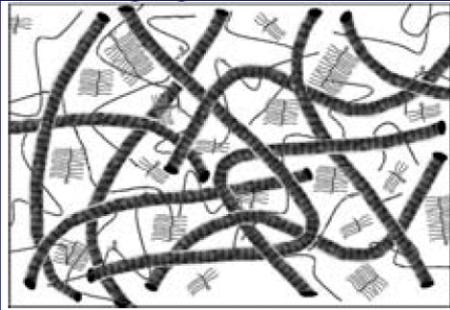


- Loss of proteoglycan
- Disorganization of collagen structure
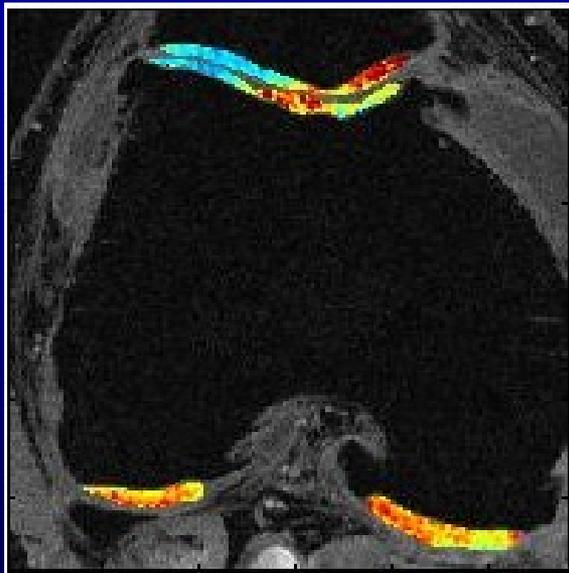


$T_{1\rho}, T_2$

## Late Stage: Morphological Changes

Normal | Osteoarthritis



Articular cartilage

Ligament

Synovium

Subchondral bone

Bone marrow

Neoangiogenesis and Neurogenesis

Cartilage lesion and degradation

Synovial fibrosis and inflammation

Osteophyte formation

*Bone-cartilage interface*

Subchondral bone remodeling

(ms)

80
60
40
20
0
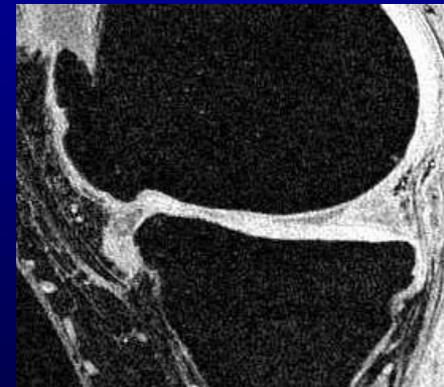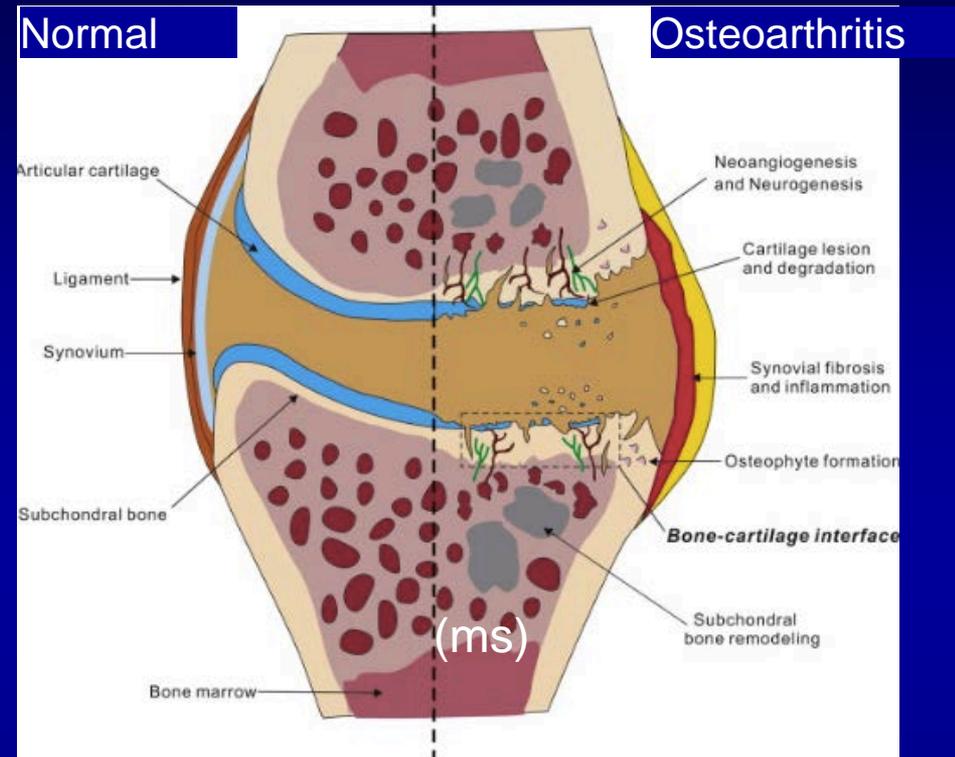
# PRECISION IMAGING & OSTEOARTHRITIS

## Late Stage:

## Early Stage: Cartilage
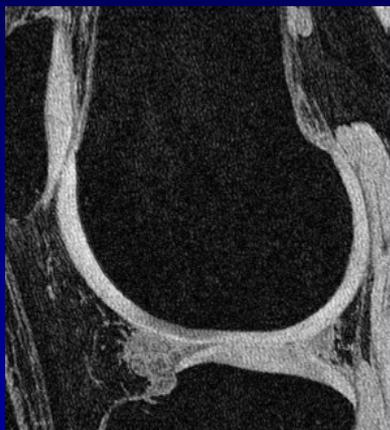


*Radiological Diagnosis*
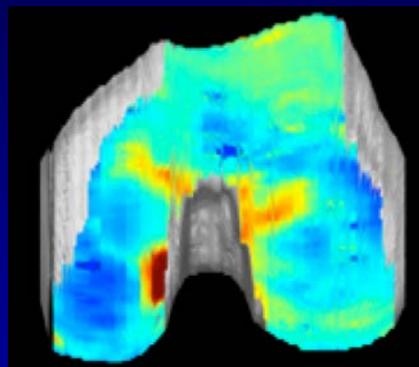
*Cartilage Morphology*
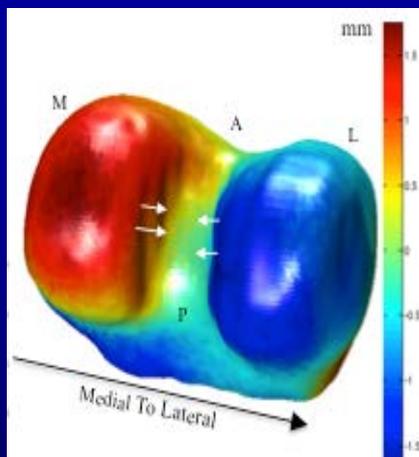
*Bone Shape*
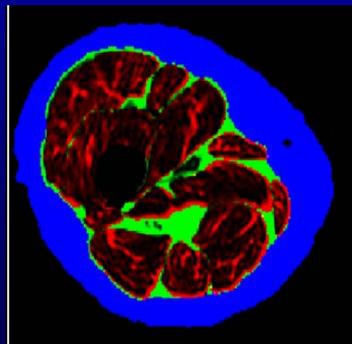
*Muscle Composition & Size*

$T_{1\rho}$
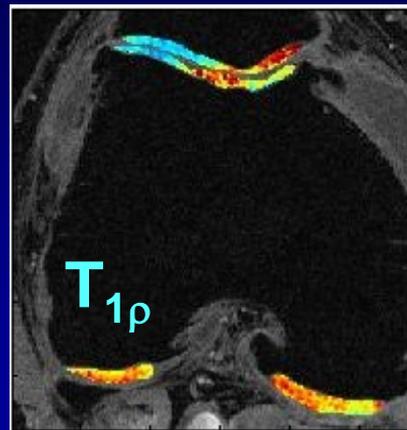
*Cartilage and Meniscus Biochemistry*
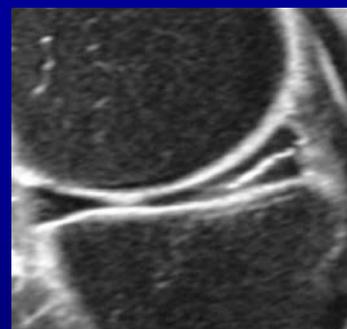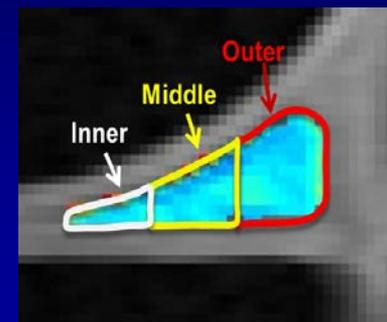
*Meniscus*
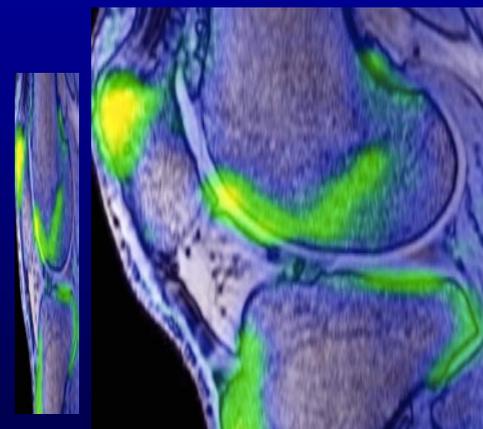
*PET-MR: +Bone remodeling*
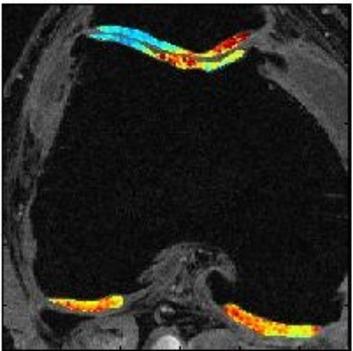
# *Early changes in Cartilage Biochemistry*

- *Association with OA (disease)*
- *Association with pain*
- *Association with joint load*

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



Difference between OA and non OA
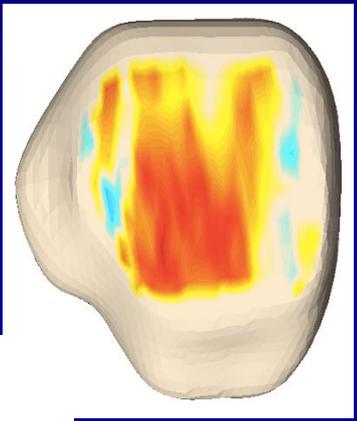
Greater the degeneration -- Higher the pain and symptoms

(-0.43, <0.001)

Symptoms
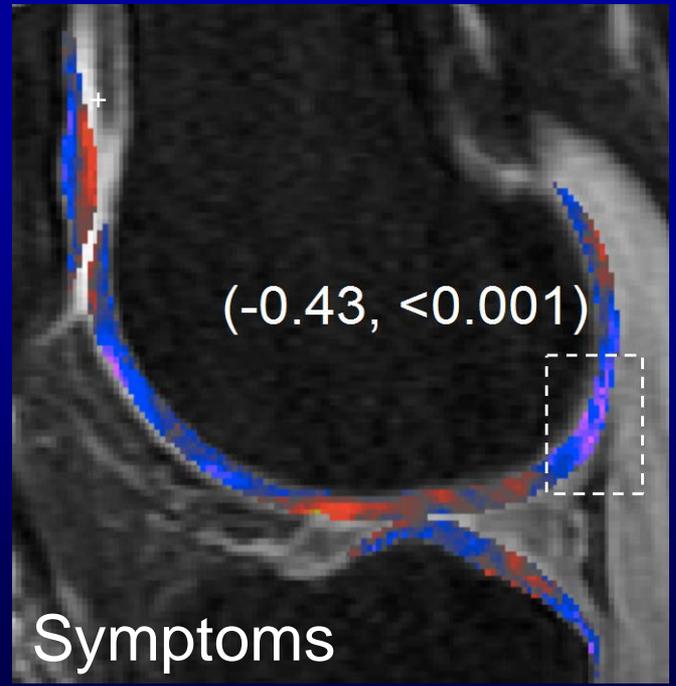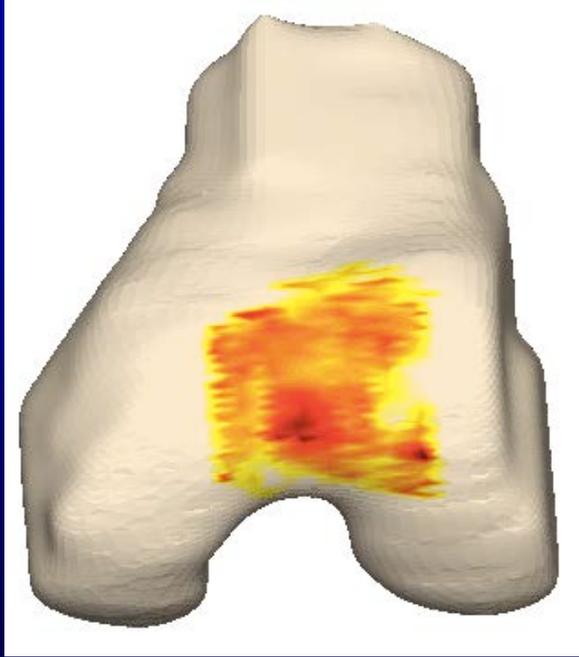
# $T_{1\rho}$ – Biochemical degeneration is higher with higher joint loads
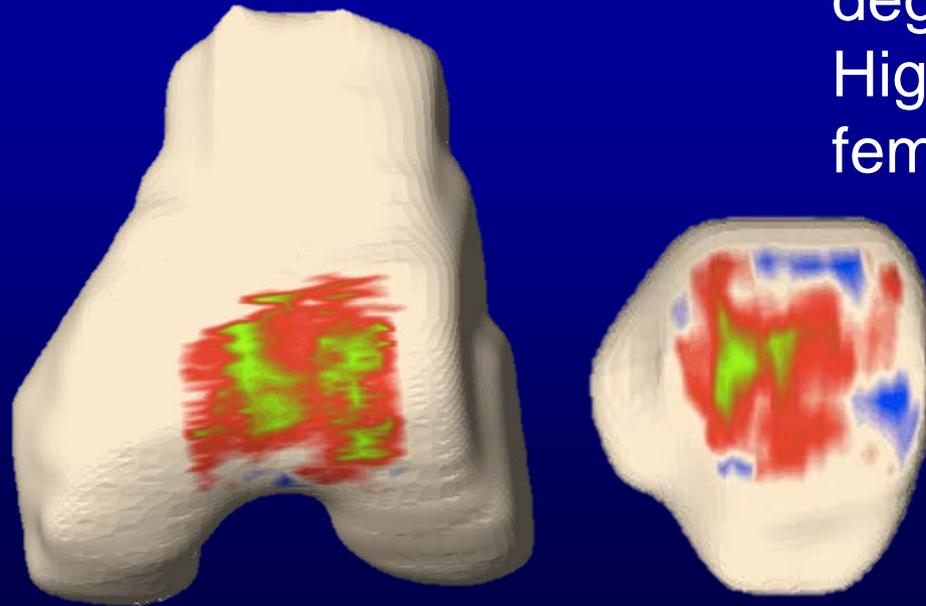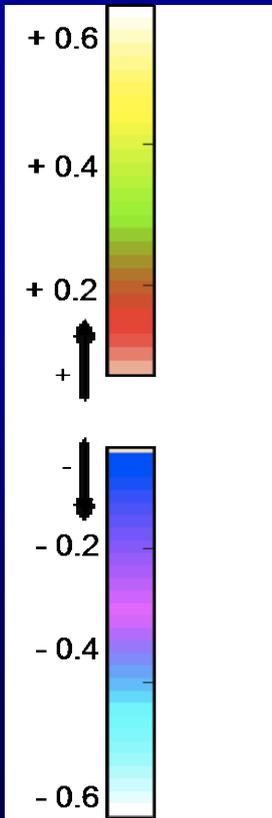


Greater the degeneration -- Higher the patellar femoral stress
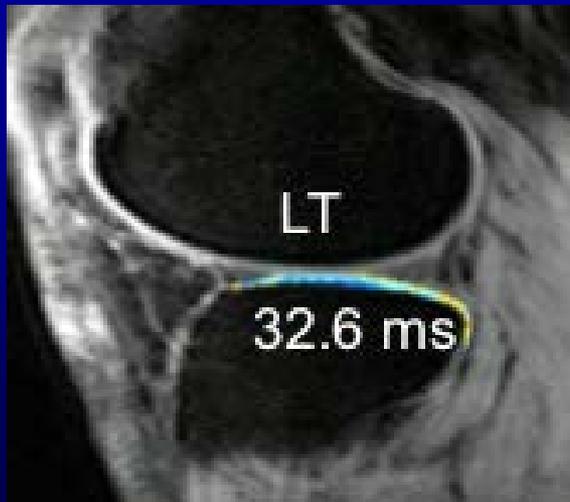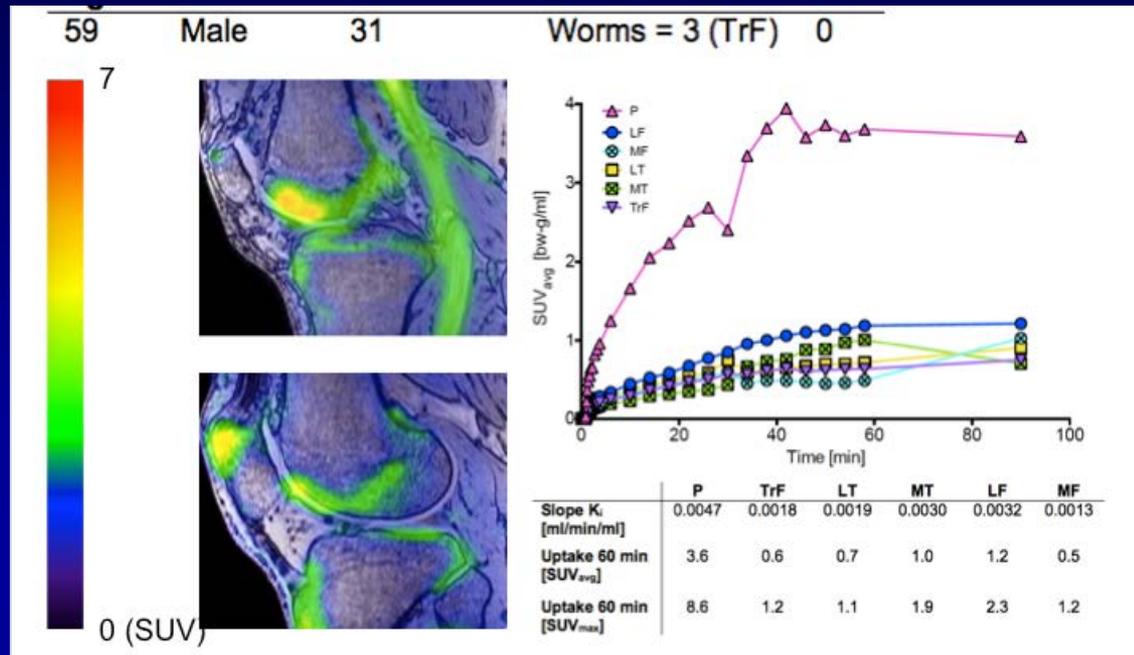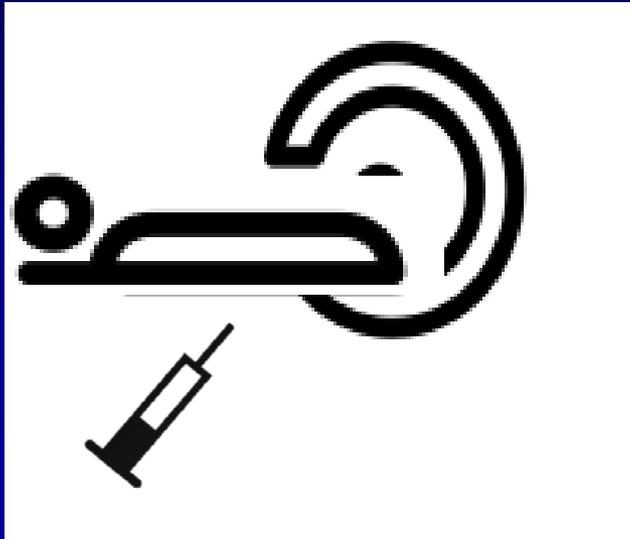
Simultaneous assessment of cartilage biochemical changes and bone remodeling and blood flow is possible with PET-MR

Savic, et. al. Molecular Imaging, 2017, Pedoia ISMRM, 2017

# *Early changes in Bone Remodeling*

- *Association with pain*
- *Association between bone and cartilage changes*

## $^{18}$F-NaF PET-MR: BONE
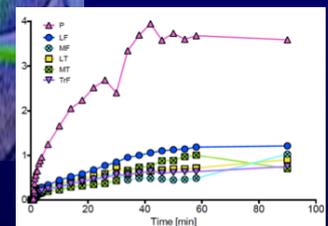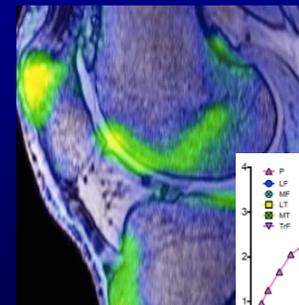
K$_i$ [min$^{-1}$]   K$_i$ [min$^{-1}$]   Association with pain

Femur

Tibia

Patella

0.012
0.008
0.004
0

0.6
0.4
0.2
0
-0.2
-0.4
-0.6
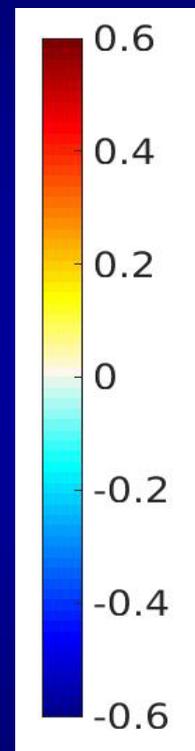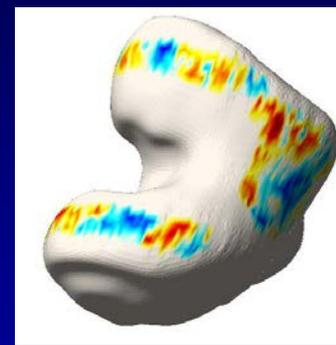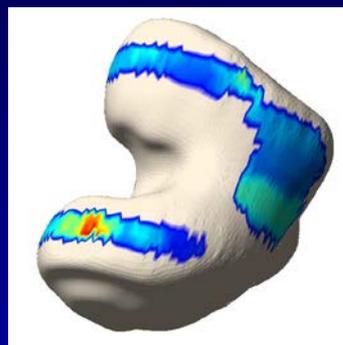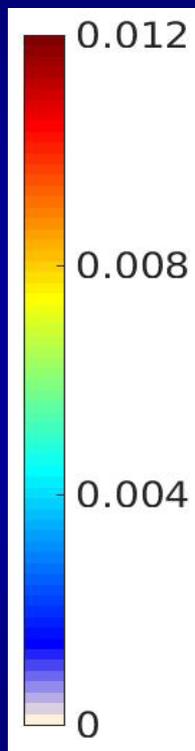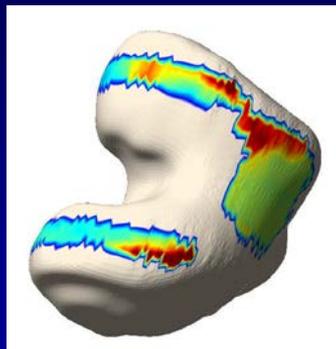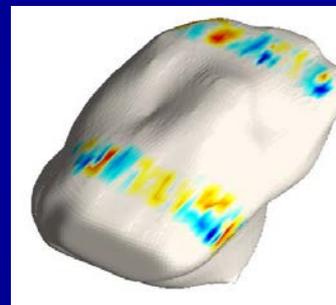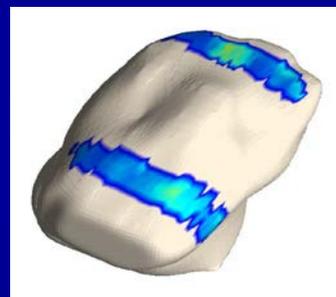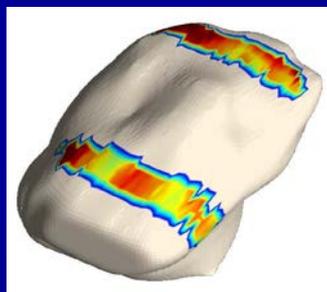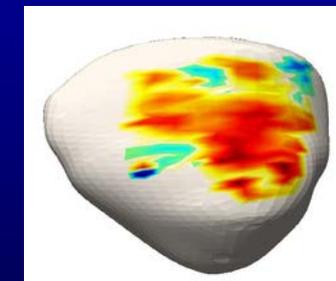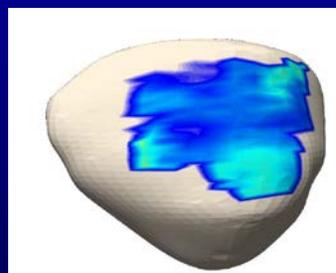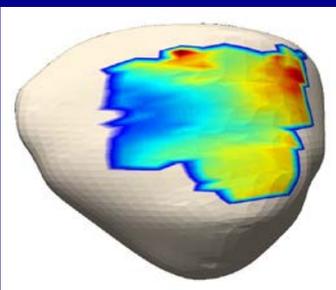
with Pain          No Pain          *Strong correlations – PET (bone) and Pain*

K$_i$ [min$^{-1}$]     K$_i$ [min$^{-1}$]     Association with cartilage biochemistry

Femur

Tibia

Patella

0.012

0.008

0.004

0

0.6

0.4

0.2

0

-0.2

-0.4

-0.6
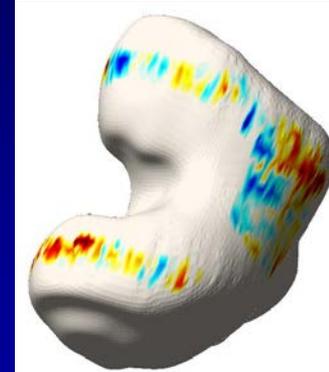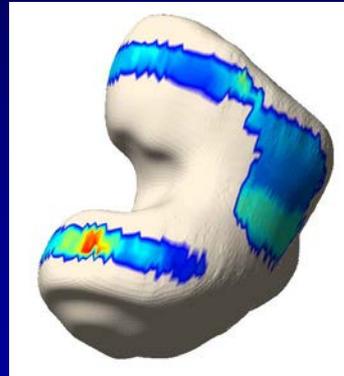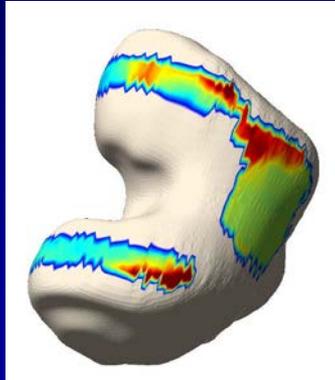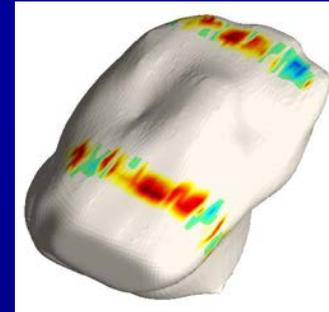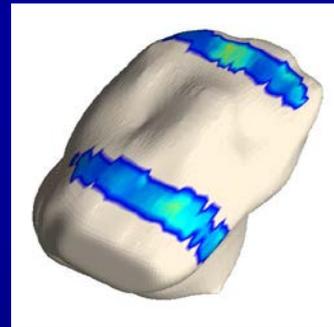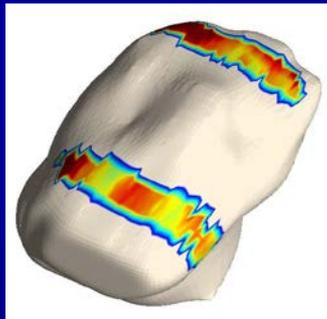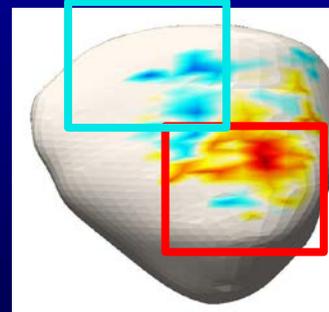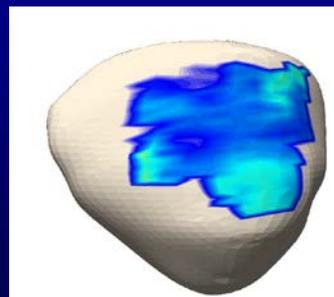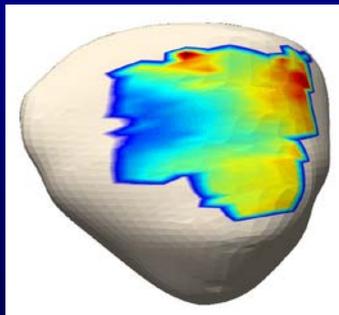
with Pain          No Pain

*Strong correlations – PET (bone) and Cartilage*

# PRECISION IMAGING IN ACHING KNEES

- Precise localization of early OA cartilage and bone changes are possible
- Correlations exist with pain
- Correlations exist  with joint loading/stress

# WHAT IF DISEASE HAS PROGRESSED BEYOND THE EARLY STAGES: CAN PRECISION IMAGING PLAY A ROLE

- Is there a way to precisely stage lesion progression?

- Are there some lesions that are indicators for total knee replacement?

# Artificial Intelligence for **multi-tissue segmentation and lesion detection**
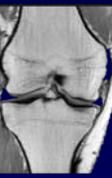


● Cartilage    ● Meniscus    ● Bone    ● Ligaments
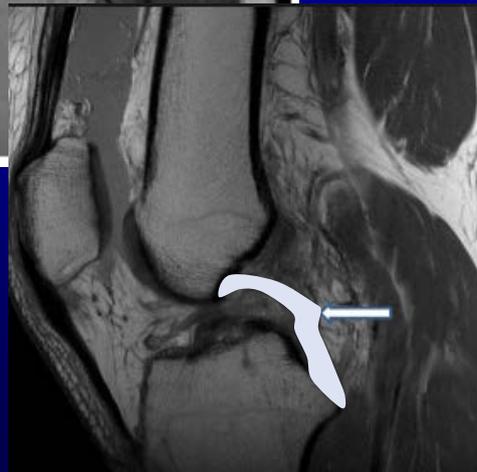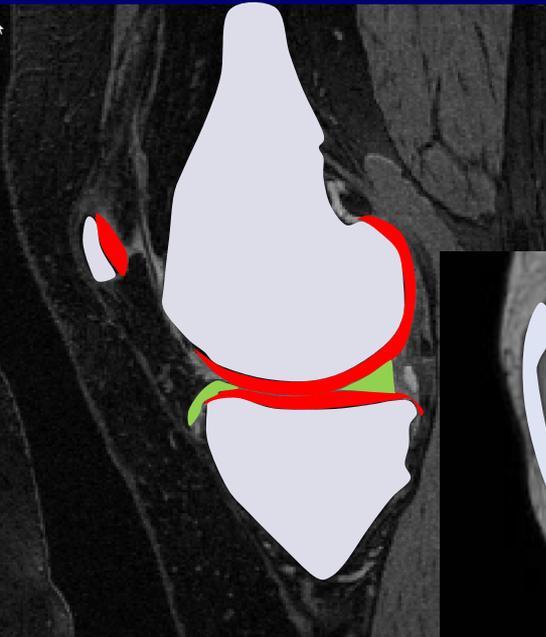
**Automatic** 3D Morphology Analysis
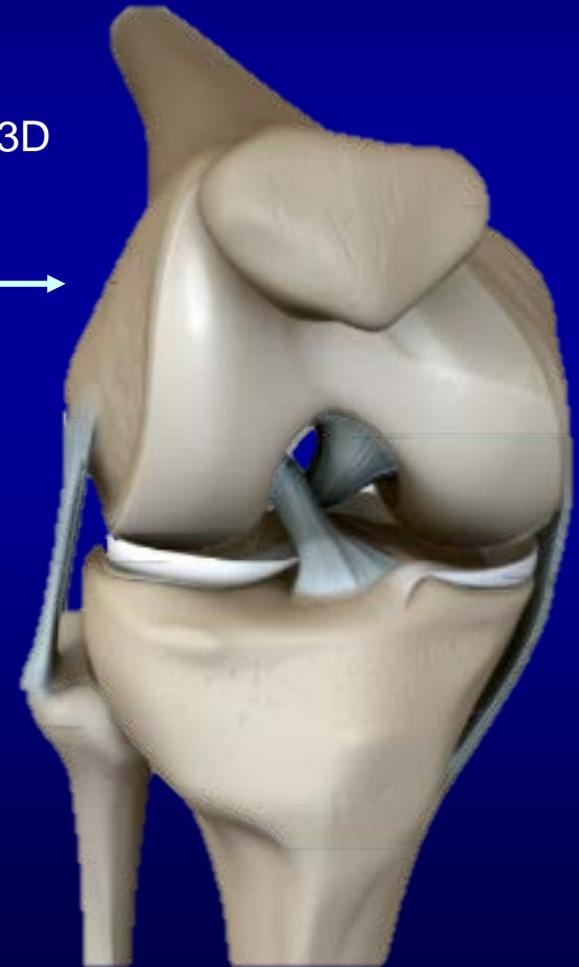
# *What if……*

- *We could detect Osteoarthritis early*
- *Predict the combination of factors that may lead to knee replacements later*
- *Treat people and thus reduce pain and the number of knee replacements*

Early → OA

Many yrs later → TKR

OA → No TKR

No OA

?
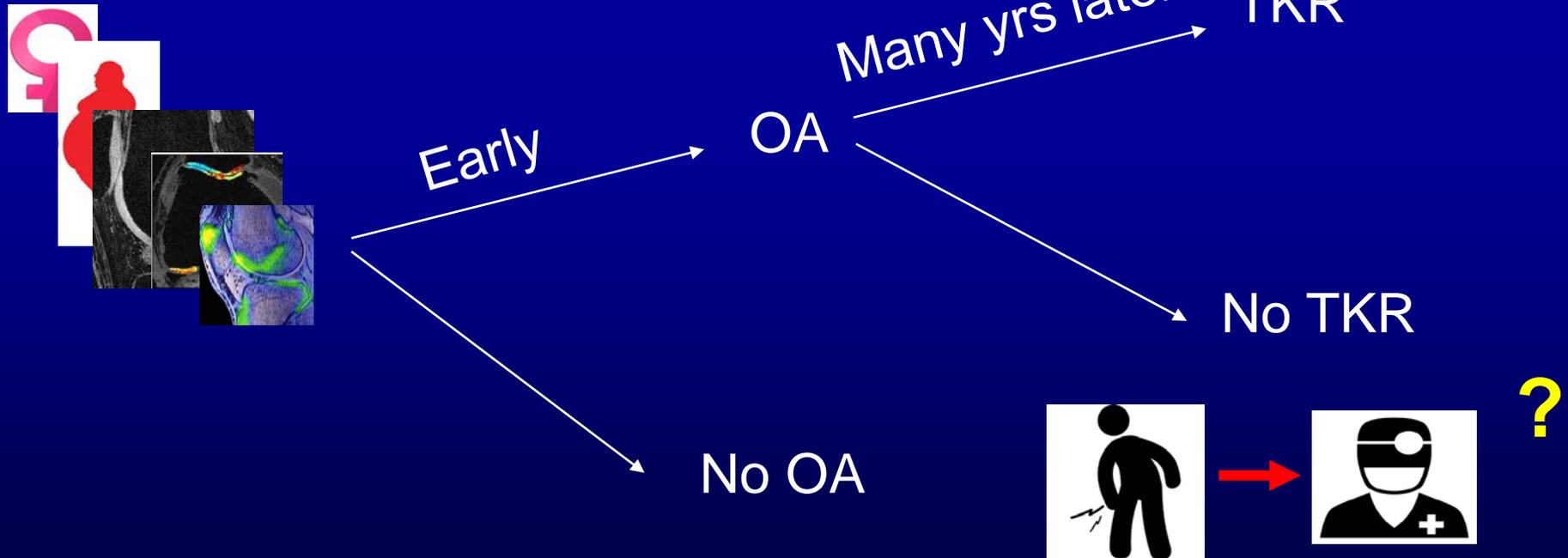
# Big Data Analytics in Osteoarthritis The What if?
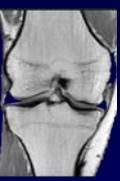
**Demographics:** *Age, Gender, Genetics, BMI*

**PROMs:** *Koos, Marx, Ipaq*

**X-Ray:** *Kellgren and Lawrence (KL)*

Femur

osteophyte

reduced joint space

sclerosis

Tibia

## TKR?

**Biomechanics:** *Kinematics Kinetics*

OA
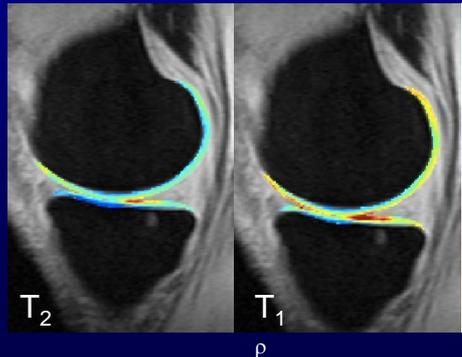
**Morphometry and Morphological MRI Grading:**

synovitis

subchondral cyst

bone marrow edema

A

B

C

partial-thickness lesion

full-thickness lesion

osteophyte formation

D

E

F

**Compositional MRI, Bone**

$T_2$

$T_1$

$\rho$

Methods
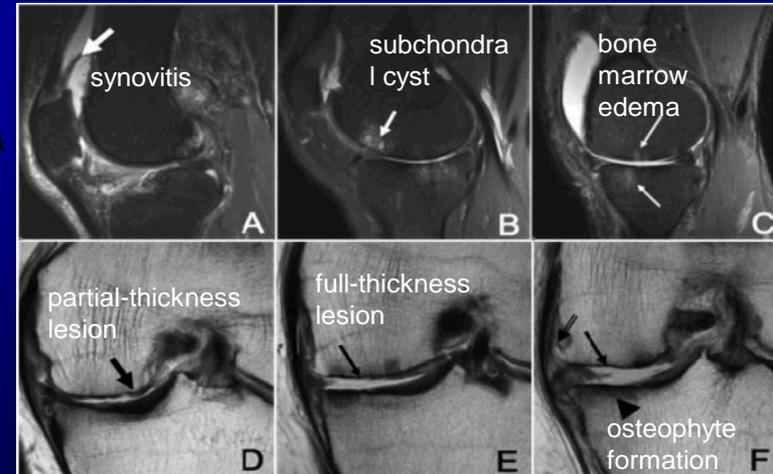
# *Getting Close to the What if…….*

*We are on our way to*
- *understanding  the cause of the achy knee*
- *detect Osteoarthritis early*
- *predict the combination of factors that may lead to knee replacements later*

IMAGING RESEARCH

COMPUTATION POWER

PEOPLE

WITH DIVERSE SKILLS

What Do We Need to Get There?

# Thank You