OARSI Year in Review:
Mechanics

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Mechanics ↔ Biology ↔ OA

Gait and Joint Mechanics

Molecular Mechanics

PCM / ECM Matrix Mechanics

Cell Mechanics

Tissue Mechanics
Baseline knee adduction and flexion moments during walking are both associated with 5 year cartilage changes in patients with medial knee osteoarthritis.

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Knee adduction moment

Knee flexion moment
**Baseline knee adduction and flexion moments during walking**

- Medial compartment contact force best approx. by a combo of KFM and KAM, rather than KAM alone
- **5-year** prospective study; subjects with medial knee OA
- Baseline (60 yr) & 5-year MRI to assess KAM and KFM

**Conclusions:**

- **KAM** had greater influence on:
  - femoral cartilage changes (medial-to-lateral cartilage thickness ratio);
  - subjects with more severe OA
- **KFM** had greater influence on:
  - tibial cartilage thickness;
  - subjects with less severe OA

**Implications** for reducing OA progression: focusing only on KAM may not be sufficient….pain modifies joint loading…..
Gait, Knee OA, Kinematics; Cartilage, **Muscle**...

From: Knee Joint Muscle Forces & Tissue Stresses-Strains During Gait: Severe OA vs Normal; [M. Adouni, A. Shirazi-Adl;](#) (JOR 2014)

- OA changes in rotations/moments influence activation levels of lower extremity musculature.....
- Muscle forces dropped at nearly all stance periods.....
Chondrolabral contact mechanics

- Labrum in dysplastic hips is more significant in hip mechanics than in normal hips
- Labrum in dysplastic hips experiences loads 3-4 times larger than in normal hips
- The labrum in dysplastic hips should be preserved during surgery
• There is now improved ability….. to perform complex 3-D contact analysis.
• Numerical methods based on FE analysis…..will soon enable patient-specific analysis of joint contact mechanics based on medical imaging data
Mechanics ↔ Biology ↔ OA

Gait and Joint Mechanics

Meniscus-to-Cartilage Joint → Tissue Mechanics

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Differences in profile of contact stresses → medial and lateral menisci carry load at different points in the gait cycle.

Posterior aspect of medial meniscus distributes load during early phase of stance; posterior aspect of lateral meniscus distributes load during early & late phases of stance.
Meniscus Injuries Alter the Kinematics of Knees With Anterior Cruciate Ligament Deficiency

Ali Hosseini,* PhD, Jing-Sheng Li,*+, MS, Thomas J. Gill IV,* MD, and Guoan Li,*+, PhD

Investigation performed at the Bioengineering Laboratory, Massachusetts General Hospital

Knee kinematics during stair climbing (21 patients):

- **Combined meniscus + ACL injury** alters kinematics of ACL-injured knees in a different way compared to knees with isolated ACL tears, depending on the pattern of the meniscus tear.

MRI + Biplanar Fluoroscopy
In vivo cartilage strain increases following medial meniscal tear and correlates with synovial fluid matrix metalloproteinase activity

Teralyn E. Carter a, Kevin A. Taylor a, Charles E. Spritzer b, Gangadhar M. Utturkar a, Dean C. Taylor a, Claude T. Moorman III a, William E. Garrett a, Farshid Guilak a, Amy L. McNulty a, Louis E. DeFrate a,*

a Department of Orthopaedic Surgery, Duke University Medical Center, Durham, NC, United States

• Measured in vivo tibiofemoral contact patterns (during quasi-static lunge) and biomarkers in the synovial fluid of patients with meniscus tears

• Cartilage strain (medial & lateral) increased significantly at max flexion angle....

• Correlated with total MMP activity (via fluorogenic substrates)
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Mechanobiology
Recently identified mechanically activated ion channels Piezo 1/2 were found to be expressed by chondrocytes.

Cell compression evoked Ca++ signals!!

Studied primary chondrocytes and pig cartilage explants: role of Piezos in mechanically induced cell death.
• In primary chondrocytes, mechanically evoked Ca2+ transients produced by AFM were inhibited by the Piezo blocking peptide GsMTx4 (from tarantula venom), and by Piezo1- or Piezo2-specific siRNA.....

• GsMTx4 also inhibited cell death around a biopsy wound induced by cutting into porcine explant...a potential therapeutic target....

• High strain mechanical cues are thereby linked to mechanically sensitive ion channels, functionally linked to the cytoskeleton
• Calcium signaling in intact cartilage differs from isolated cells

• Intact rabbit patellar bone-cartilage samples w. Ca-sensitive dyes imaged continuously under 10-40% compression...

• Ca signaling mainly caused by dynamic loading; greatly increased above 10% strain....
Biomechanics of Animal Joint Cartilage
All the animals at Mr. Jones' Farm assemble to hear a pig describe a dream about a world where all animals live free from the tyranny of humans........
George Orwell, 1945:

“Four legs good, two legs bad.”

“All animals are equal, but some animals are more equal than others.”
Basic Biology

Biomechanics of Mouse Cartilage
Nanomechanical phenotype of chondroadherin-null murine articular cartilage

Mike Batista, Dick Heinegård, Patrik Önnerfjord, Lin Han

- CHAD-deletion resulted in ~70–80% reduction in the indentation modulus of the superficial zone knee cartilage of 11 weeks, 4 months and 1 year old CHAD−/− mice compared to wild type.
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High-bandwidth AFM-based rheology is a sensitive indicator of early cartilage aggregan degradation relevant to mouse models of osteoarthritis

Hadi T. Nia\textsuperscript{a}, Stephanie J. Gauci\textsuperscript{b}, Mojtaba Azadi\textsuperscript{a}, Han-Hwa Hung\textsuperscript{c}, Eliot Frank\textsuperscript{c}, Amanda J. Fosang\textsuperscript{b}, Christine Ortiz\textsuperscript{d}, Alan J. Grodzinsky\textsuperscript{a,c,e,f,*}
Dramatic **decrease in high frequency stiffness** and increased hydraulic permeability of GAG-depleted superficial zone cartilage (even with intact collagen network): cartilage **of mice and men** can no longer resist impact loads relevant to traumatic injury.
Wide Range of Loading Rates

- Traumatic impact
- Jumping - landing
- Jumping - take off
- Running
- Kicking - soccer
- Walking

Heiner...Brown, Cartilage, 2012

Loading Time scale (s)

Loading Frequency Content (Hz)

1,000 Hz

milli sec
Mechanics ↔ Biology ↔ OA

Gait

Tissue Mechanics

Molecular Mechanics
Molecular-Level Nanomechanics

Aggrecan Nanoscale Solid–Fluid Interactions Are a Primary Determinant of Cartilage Dynamic Mechanical Properties

Hadi Tavakoli Nia, Lin Han, Iman Soltani Bozchalooi, Peter Roughley, Kamal Youcef-Toumi, Alan J. Grodzinsky,* and Christine Ortiz*
Molecular-Level Nanomechanics: Aggrecan provides basis for cartilage poroelasticity

AFM- Nanomechanics: Random Binary Sequence loading profile used to maximize signal-to-noise ratio

Nia+, ACS Nano 2015
Normal Cartilage  GAG-depleted Cartilage  Aggrecan Monolayer

Hadi Nia+, ACS Nano 2015
GAG - electrostatic repulsion
inter-GAG fluid flow and pressurization

GAG-associated Molecular Mechanism

Daily Activity

slow loading (low frequency)
fast loading (high frequency)
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