OARSI Year in Review: Mechanics

#### Alan J. Grodzinsky

Center for Biomedical Engineering Departments of Biological Engineering, Mechanical Engineering, Electrical Engineering and Computer Science MIT

#### Mechanics $\leftrightarrow$ Biology $\leftrightarrow$ OA



#### Gait, Knee OA, Kinematics; Cartilage, Muscle...

Baseline knee adduction and flexion moments during walking are both associated with 5 year cartilage changes in patients with medial knee osteoarthritis OAC 2014

E.F. Chehab † ‡ \*, J. Favre †, J.C. Erhart-Hledik † §, T.P. Andriacchi † § ||

Department of Mechanical Engineering, Stanford, CA, United States



#### Osteoarthritis and Cartilage



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; <u>M. Adouni, A. Shirazi-Adl</u>; (JOR 2014)

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

#### Continued emphasis: Patient-Specific Analysis/Treatment

Patient-specific analysis of cartilage and labrum mechanics in human hips with acetabular dysplasia OAC 2014

C.R. Henak <sup>†a</sup>, C.L. Abraham <sup>†‡</sup>, A.E. Anderson <sup>†‡§</sup>, S.A. Maas <sup>†</sup>, B.J. Ellis <sup>†</sup>, C.L. Peters <sup>‡</sup>, J.A. Weiss <sup>†‡\*</sup>

+ Department of Bioengineering and Scientific Computing and Imaging Institute, University of Utah, Salt Lake City, UT 84112, USA



#### 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

#### Toward patient-specific articular contact mechanics (hip)

Gerard A. Ateshian<sup>a</sup>, Corinne R. Henak<sup>b</sup>, Jeffrey A. Weiss<sup>c</sup>

<sup>a</sup> Department of Mechanical Engineering, Columbia University, New York, NY 10027, USA J Biomech 2015

<sup>b</sup> Department of Biomedical Engineering, Cornell University, Ithaca, NY 14850, USA

<sup>c</sup> Department of Bioengineering, Department of Orthopaedics, and Scientific Computing and Imaging Institute, University of Utah,



- 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 $\leftrightarrow$ Biology $\leftrightarrow$ OA



Dynamic contact stress patterns on the tibial plateaus during simulated gait: A novel application of normalized cross correlation Hongsheng Wang<sup>a,1</sup>, Tony Chen<sup>a,1</sup>, Peter Torzilli<sup>b</sup>, Russell Warren<sup>c</sup>, Suzanne Maher<sup>a,\*</sup> <sup>a</sup> Department of Biomechanics, Hospital for Special Surgery, New York, NY 10021, United States J Biomech 2014



Contact stress under 1kN static loading

- Differences in profile of contact stresses → medial and lateral menisci carry load at different points in the gait cycle
- Posterior aspect of <u>medial</u> <u>meniscus</u> distributes load during early phase of stance; posterior aspect of <u>lateral meniscus</u> distributes load during early <u>&</u> late phases of stance.

#### Meniscus Injuries Alter the Kinematics of Knees With Anterior Cruciate Ligament Deficiency Othop J Sports Med 2014

Ali Hosseini,\* PhD, Jing-Sheng Li,\*<sup>†</sup> MS, Thomas J. Gill IV,\* MD, and Guoan Li,\*<sup>‡</sup> PhD *Investigation performed at the Bioengineering Laboratory, Massachusetts General Hospital/* 



MRI + Biplanar Fluoroscopy

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 *In vivo* cartilage strain increases following medial meniscal tear and correlates with synovial fluid matrix metalloproteinase activity Teralyn E. Carter<sup>a</sup>, Kevin A. Taylor<sup>a</sup>, Charles E. Spritzer<sup>b</sup>, Gangadhar M. Utturkar<sup>a</sup>, Dean C. Taylor<sup>a</sup>, Claude T. Moorman III<sup>a</sup>, William E. Garrett<sup>a</sup>, Farshid Guilak<sup>a</sup>, Amy L. McNulty<sup>a</sup>, Louis E. DeFrate<sup>a,\*</sup>

<sup>a</sup> Department of Orthopaedic Surgery, Duke University Medical Center, Durham, NC, United States





- Measured <u>in vivo tibiofemoral contact</u> <u>patterns</u> (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)



#### Mechanics $\leftrightarrow$ Biology $\leftrightarrow$ OA



**Gait and Joint Mechanics** 



### Mechanobiology

#### PNAS 2014

#### Synergy between Piezo1 and Piezo2 channels confers high-strain mechanosensitivity to articular cartilage

Whasil Lee<sup>a</sup>, Holly A. Leddy<sup>b</sup>, Yong Chen<sup>a</sup>, Suk Hee Lee<sup>a</sup>, Nicole A. Zelenski<sup>b</sup>, Amy L. McNulty<sup>b</sup>, Jason Wu<sup>c</sup>, Kellie N. Beicker<sup>d</sup>, Jeffrey Coles<sup>e</sup>, Stefan Zauscher<sup>e</sup>, Jörg Grandl<sup>c</sup>, Frederick Sachs<sup>f</sup>, Farshid Guilak<sup>b,e,1</sup>, and Wolfgang B. Liedtke<sup>a,c,g,1</sup>

- 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 Piezo2specific 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

#### The effect of compressive loading magnitude on in situ chondrocyte calcium signaling Biomech Model Mechanobio 2014

Ryan M. J. Madden · Sang-Kuy Han · Walter Herzog

- 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....





**Fig. 3** a Exemplar field of view (x–y plane) showing fluorescently labeled cells (*scale bar* =  $50 \,\mu$ m).





Pre-Clinical & Safety

## 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.....

Pre-Clinical



George Orwell, 1945:

Pre-Clinical

"Four legs good, two legs bad."

"All animals are equal, but <u>some</u> <u>animals are</u> <u>more equal than</u> others."



# OARSI

## **Biomechanics of Mouse Cartilage**

Nanomechanical phenotype of chondroadherin-null murine articular cartilage Matrix Biology 2014

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 aggrecan degradation relevant to mouse models of osteoarthritis J Biomechanics 2015 Hadi T. Nia<sup>a</sup>, Stephanie J. Gauci<sup>b</sup>, Mojtaba Azadi<sup>a</sup>, Han-Hwa Hung<sup>c</sup>, Eliot Frank<sup>c</sup>, Amanda J. Fosang<sup>b</sup>, Christine Ortiz<sup>d</sup>, Alan J. Grodzinsky<sup>a,c,e,f,\*</sup>



Dramatic <u>decrease in high frequency stiffness</u> and increased hydraulic permeability of <u>GAG-depleted</u> <u>superficial zone cartilage</u> (even with intact collagen network): cartilage <u>of mice and men</u> can no longer resist impact loads relevant to traumatic injury



#### Wide Range of Loading Rates Heiner...Brown, Cartilage, 2012 milli sec Loading Time scale (s) 10<sup>-3</sup> 10<sup>-1</sup> 10<sup>0</sup> -4 -2 10 traumatic impact jumping - landing jumping - take off running kicking - soccer walking 2 10<sup>0</sup> 3 10<sup>1</sup> 4 10 10 10 Loading Frequency Content (Hz) 1,000 Hz

#### $\textbf{Mechanics} \leftrightarrow \textbf{Biology} \leftrightarrow \textbf{OA}$



#### **Molecular-Level Nanomechanics**

# Aggrecan Nanoscale Solid—FluidACS Nano 2015Interactions Are a PrimaryDeterminant of Cartilage DynamicMechanical PropertiesMathematical Properties

Hadi Tavakoli Nia, Lin Han, Iman Soltani Bozchalooi, Peter Roughley, Kamal Youcef-Toumi, Alan J. Grodzinsky,<sup>\*</sup> and Christine Ortiz<sup>\*</sup>



# Molecular-Level Nanomechanics: Aggrecan provides basis for cartilage poroelasticity





Hadi Nia+, ACS Nano 2015



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