R1: Nano- and Microstructural Tissue Characterization for Improved Care of Children with Osteogenesis Imperfecta and Severe Clubfoot Deformity (Focus Topic)

O Co-Pl's

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Nano-

indentation (R1)

Gait analysis (R4)

SIMM (R

- Patient populations
 - Osteogenesis Imperfecta (OI): 45
 - Clubfoot (CF): 12

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What Is Osteogenesis Imperfecta (OI)?

- OI is a genetic disorder with increased bone fragility and low bone mass.
- Typical extraskeletal manifestations can be associated to a variable degree
 - Blue sclera
 - Dentinogenesis Imperfecta
 - Hyperlaxity of ligaments and skin
 - Hearing impairment
 - Wormian bones

Osteogenesis Imperfecta



The hierarchical structure of bone



Nanoindentation

- Microstructural level mechanical properties measurement without structural influence
- Static measurements: Young's modulus (E) and hardness (H)
- Dynamic Measurements







Results

For cortical and trabecular bone, modulus and hardness do not show any significant difference between OI type III and type IV.

The ratio of E/H shows <u>marginally significant decrease for</u> <u>type III cortical bone</u> and a <u>significant decrease for</u> <u>trabecular bone</u>.

Measurement	Values (GPa)					
	Type III	Type IV	P value			
Young's Modulus (Cortical)	19.67 (2.76)	19.19 (2.4)	0.61			
Hardness (Cortical)	0.70 (0.17)	0.66 (0.13)	0.43			
Young's Modulus (Trabecular)	19.23 (2.01)	18.27 (2.76)	0.29			
Hardness (Trabecular)	0.65 (0.12)	0.62 (0.14)	0.35			
Ratio of E/H (Cortical)	28.60 (4.38)	30.64 (4.44)	0.069			
Ratio of E/H (Trabecular)	28.62 (2.23)	31.27 (3.99)	0.002*			

Nanoindentation Studies of OI Bone Summary – Current Knowledge

Young's modulus, E: 11-24 Gpa

- cortical ≈ trabecular¹
- Iongitudinal ≈ transverse¹
- $||| \approx |V^2|$
- Iong bones ≈ iliac²
- OI > control (13%)³
- pamidronate: no significant effect on modulus³

1. Fan et al. 2006; 2. Fan et al. 2007; 3. Weber et al. 2006





1. Kinematics. The mean value of the type I OI group is plotted as a light blue band plus and minus one standard deviation.

75%

75%

75%

- 2. The control group is plotted in dark gray.
- 3. The x-axis represents the percent gait cycle.
- 4. Toe off occurs at 63.4% GC for the OI subjects and 60.6% GC for the control group.
- 5. The "*" indicates a peak significant difference between the groups.



- Kinetics. The mean value of the type I OI group is plotted as a light blue band plus and minus one standard deviation.
- 2. The control group is plotted in dark gray.
- 3. The x-axis represents the percent gait cycle.
- 4. Toe off occurs at 63.4% GC for the OI Subjects and 60.6% GC for the control group.
- 5. The "*" indicates a peak of significant difference between the groups.

Model Development

Tetrahedral elements

- Triangular shell elements for moments
- Material properties from nanoindentation literature
 - Young's modulus: 19 GPa
 - Poisson's ratio: 0.30
- Nodal manipulation to match femur geometry from x-ray
 - Shortened from 48.4 cm to 40 cm
 - Mild outward coronal bowing



Meshed models of normal femur (left) & OI type I femur (right) in Abaqus.

X-ray of OI type I femur

Results: Qualitative

- Contour plots on model show location of femur at highest risk
- Location of risk <u>migrates with gait phase</u> & <u>muscle loading</u>





Stress distribution for initial swing

RERC Directions in Fx Risk Assessment

- Mechanical Testing ... Strength
- µCT, Nano, µFE ... Effective Trabecular Modulus
- Synchrotron Radiation Micro CT, SR- µCT
- Better Musculoskeletal Models (UE & LE)
- Better Patient Specific FE Models (UE & LE)
- Better Statistical Models ... Clinical Outcomes
- Effects of Transition and Aging







RERC Directions in Clubfoot Tissue Assessment

- Mechanical Testing ... Tissue Bath / Longer Term Behavior
- Sample Collection (3 samples / 2 patients)
- Acoustic Evaluation (SAM)
- Histological Evaluuation
- Modeling Approaches (uni- and bi-axial tests)
- Clinical Application/Evaluation



R1 Time Line

Activity:	Year 1	Year 2	Year 3	Year 4	Year 5
Harvesting of OI bone specimens					
μCT of OI bone specimens					
Nanoindentation of OI bone specimens					
Micro-mechanical testing of OI bone specimens					
OI FEM development: generic, patient-specific					
Harvesting of clubfoot MFMT specimens					
μ CT imaging and analysis of MFMT specimens					
Mechanical characterization of clubfoot MFMT:					
testing, QLV+P modeling					
Clubfoot QLV+P FEM: development, simulations, verification					



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THANK YOU.







Rehabilitation Institute of Chicago

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