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Biomechanical Investigation of the Effect of Bone Disorders on Pediatric Femur Fracture Potential
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PIs: A. Thompson and G. Bertocci– University of Louisville

FINAL SUMMARY OVERVIEW

Purpose

Child abuse is the leading cause of trauma-related fatalities in children less than four years of age. Children one year of age and younger are particularly at risk; approximately 1 out of every 43 children in this age group is a victim of abuse or neglect.[1] Cases of physical child abuse are sometimes mistaken for accidental trauma. If the abuse goes unrecognized, the child may be placed back into a high-risk environment where abuse may continue and escalate in severity of injuries. Early detection of abuse is critical to prevent repeat occurrences of physical trauma. Clinicians, child protective services, and law enforcement personnel are often faced with determining whether a child's injuries are the result of accidental causes or whether abuse should be suspected. These assessments are particularly challenging in cases where children have bone fragility disorders. Children who have bone disorders sometimes present with fractures that are misdiagnosed as abuse. Conversely, speculative bone disorders may be provided as false explanations for fractures by defense experts in criminal prosecution of child abuse.[2] However, presence of a bone fragility disorder does not rule out the possibility child abuse. Thus, there is a need for scientific evidence comparing fracture potential in children with bone disorders to that of healthy children so as to improve the accuracy of forensic analysis and child abuse assessments in cases involving fracture.

There are several bone fragility disorders that place patients at an increased risk of fracture. Osteogenesis imperfecta (OI) and rickets are two disorders which are associated with differences in both bone morphology (shape) due to differing skeletal development and material properties (e.g. stiffness and density) compared to that of healthy children. Our research goal was to determine how material property and morphologic bone differences in children with bone disorders affect fracture potential. For example, if the same force is applied to the femur of a healthy child and the femur of a child with a bone disorder, will there be a difference in likelihood of fracture? Would there be a difference in the resulting fracture morphology (i.e. type, extent and location of fracture along the bone)? Knowledge of differing fracture potential in children with bone disorders may improve assessment of injury and history compatibility (i.e. assessing the likelihood that a particular child could have sustained a specific fracture type in the given scenario). This study had two specific aims: (**1) Characterize femur morphology and identify differences in morphology between healthy children (ages 0-3 years) and those with bone disorders (OI and rickets), and (2) Determine the influence of bone health on femur fracture potential for children aged 0-3 years.**

Project Subjects

For this study, radiographic images and medical data were collected for children aged 0-3 years that were healthy and those with diagnosed bone disorders including OI and rickets. Data were obtained from 4 sites: Norton Children's Hospital (formerly Kosair Children's Hospital) in Louisville, KY, Ann & Robert H. Lurie Children's Hospital in Chicago, IL, Children's Hospital of Philadelphia (CHOP) in Philadelphia, PA, and the New Mexico Office of the Medical Investigator (OMI) in Albuquerque, NM. Additionally, radiographs and subject data for 40 subjects from a prior study at the University of Pittsburgh were reviewed.

Subjects 0-3 years old with a radiograph (x-ray or CT) of the femur were included in the study. Each subject was classified as healthy (with regards to bone health), diagnosed OI or rickets, or having another disorder or condition that could potentially affect bone health (e.g. congenital syndromes, taking certain medications, premature birth). Subjects with 2D radiographs (x-rays) were included in the analysis for Aim 1. Only subjects with CT scans were included in model development as part of Aim 2.

Specific Aim 1: There were 228 subjects with available femur x-rays across all enrollment locations; 42% were female and 58% were male. Subjects were 67% White/Caucasian, 12% Black/African American, 1% Asian/Pacific Islander, 13% Native American Indian, and 7% unspecified.

Specific Aim 2: There were 97 healthy subjects with a CT (all from OMI) that were used for development of the finite element model; 65% were male, 35% were female. Subjects were 63% White/Caucasian, 3% Black/African American, and 34% Native American Indian.

Age distribution of all subjects is shown in Figure 1.

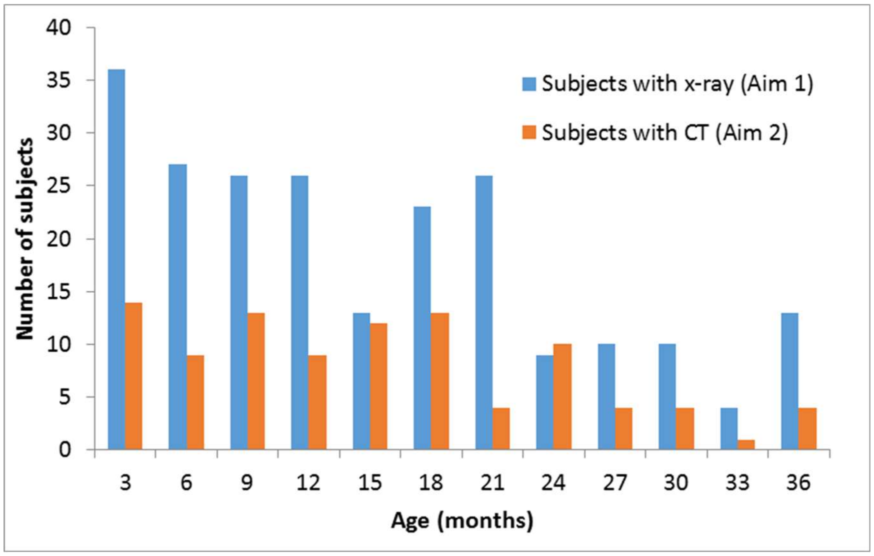

Figure 1. Age distribution of subjects.

Project Design and Methods

To determine the effect of material property and morphologic bone differences in children with bone disorders on fracture potential, this study aimed to (1) characterize differences in femur morphology between healthy children and those with bone disorders, and (2) to evaluate the effect of differences measured in Aim 1 on fracture potential using a finite element model of a femur**.** Aim 1 was accomplished through a retrospective review of medical records and identification and measurement of femur morphology parameters on 2D femur radiographs. Aim 2 was accomplished by developing a parametric finite element model (FEM) of a pediatric femur using 3D femur models generated from subject CTs. Parametric FEMs are useful for describing shape variability for a population based upon a small sample. Using this approach, one can determine the average shape for a population or generate new, realistic models for "virtual" subjects. These virtual femur models would not be from actual human data, but computer-generated models representative of potential variations in femur shape based on the original sample population. Under simulated loading conditions, relative fracture potential could be evaluated through comparisons of FEM-predicted stresses and strains.

Study procedures were approved by Institutional Review Boards at each location: University of Louisville IRB#15.0263, Ann & Robert H. Lurie Children's Hospital IRB#2016-472, and Children's Hospital of Philadelphia IRB#16-013225.

Medical Records Review

Medical records were reviewed for eligible subjects and relevant data including age, height, weight, gender, race, ethnicity, any medical conditions or diagnoses relating to bone health, mobility status, and cause of death (for OMI subjects only) were recorded in a custom-developed research database. De-identified anterior-posterior femur radiographs from the left and/or right femur were obtained and saved for further analysis.

Morphology Characterization

A custom, user-guided image analysis tool was developed using mathematical analysis software (MATLAB R2016b, MathWorks, Natick, MA) to perform key measurements from radiographs. The assessment tool guides the user to select points on the radiograph corresponding to bony landmark locations, which are then used to determine desired morphological measures. Up to 104 morphological measures were documented for each subject including assessments of femur length, diameter, cortical thickness, and radius of curvature. Normalized ratios of morphological measures were also determined. Radiographs and morphology measurements were stored within the research database for further analysis.

Data Analysis

Morphology measures were characterized using descriptive statistics and trends with age and weight were assessed for healthy bone subjects. A mixed design ANOVA with age as a covariate was performed to examine the effect of bone health status (healthy versus unhealthy) on key morphological measures.

Development of 3D femur models using CT scans

CT scans were reconstructed using Mimics software (Materialise, Plymouth, MI) and segmented to identify portions of the image corresponding to bone (Figure 2). Following segmentation (selection of the femur bone tissue), a 3D model of the left femur was created for each subject.

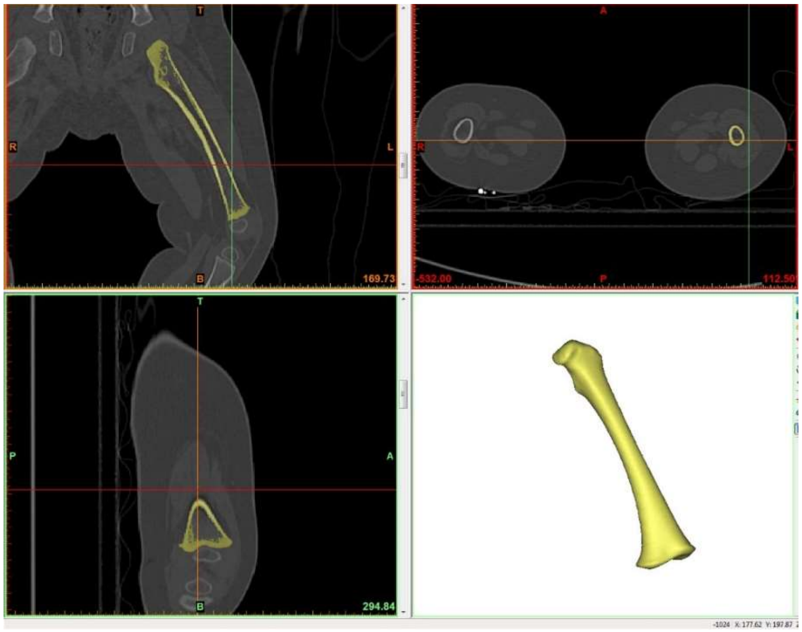

Figure 2. Reconstruction of CT in Mimics. Anterior-posterior (top left), superior-inferior (top right), and medial-lateral (bottom left) views with 3D model (bottom right) are shown with left femur bone tissue highlighted in yellow.

Statistical Shape Analysis

To develop the parametric finite element model, a baseline finite element mesh (dividing the 3D bone into small tetrahedral shaped elements where each corner forms a node) was created for a 10-month-old subject. This baseline mesh was then morphed to 3D femur models for remaining subjects so that each 3D femur would have the same number of elements and nodes. Principal component analysis was conducted using the data set containing the nodal locations from each mesh to create the statistical shape model, a model describing the 3D shape variation in the femur set. Through regression, the principal components were linked to key subject parameters (age, height, and weight); this enabled generation of femur meshes at various ages with specified height/weight beyond those in our data set.

Finite Element Analysis

Healthy femurs of various ages (1, 6, 11 months) were generated using the results of the statistical shape analysis (Figure 3). Femur meshes were imported into Solidworks (Dassault Systémes, Waltham, MA) for finite element simulations. In this preliminary study investigating the effect of bone disorders on fracture potential, the femur was represented as a solid structure (no medullary canal) and cortical bone properties were assigned as elastic, homogenous and isotropic. A sensitivity analysis was conducted to determine the effect of age and material properties (elastic modulus or stiffness of the bone tissue) on femoral stress and strain under bending loading. Due to high porosity of the bone tissue in OI, the elastic modulus associated with OI has been reported to be lower than that of healthy children (approximately 5 GPa compared to 13 GPa in healthy controls).[3, 4] The elastic modulus in children with rickets has not been measured, but is also expected to be lower than that of healthy children due to lower bone mineralization.

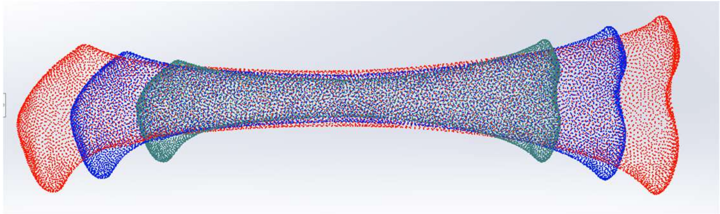

Figure 3. Femur models generated for 50th percentile (based on height and weight) children ages 1, 6, and 11 months.

In addition to changing material properties, the 6-month-old femur was morphed to represent key deformities seen in children with bone disorders. An important deformity in OI and rickets is bowing of the femur. The femur was morphed to represent 15 degrees of bowing (angle measured from the longitudinal axis) similar to that seen in subjects with bone disorders (Figure 4) to generate a 3D model of an unhealthy femur.

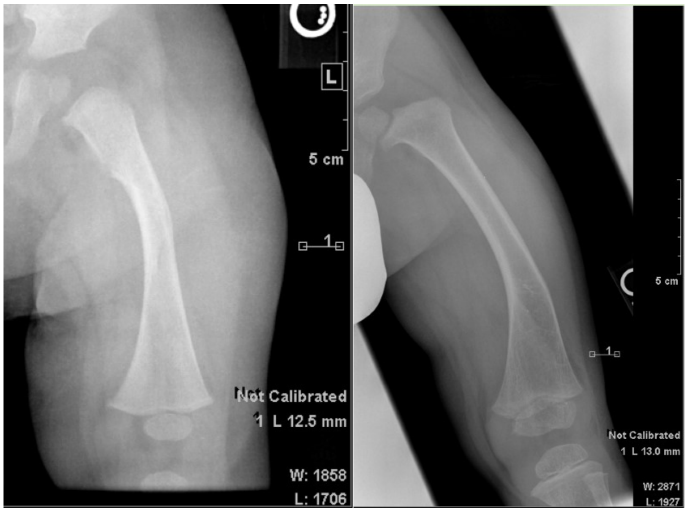

Figure 4. Bowing of femur in 6-month-old child with type I osteogenesis imperfecta (left) and 36-month-old with rickets.

In prior studies, bending and compression loads produced the highest femur strains in short-distance fall simulations[5, 6]. Average loads for feet-first falls (3-point bending of 10 Nm and axial compression of 375 N) were applied to femur models. Stress and strain distributions were evaluated along with magnitude and location of peak values. Higher stress and/or strain values are indicative of a higher fracture risk.

Findings

Femur Morphology Assessment

Figures 5-6 illustrate how 2 representative morphology measures (minimum diaphysis outer diameter and lateral cortical thickness) vary with age for both healthy and unhealthy subjects. Differences in 4 key morphological measures were found between healthy and unhealthy bone (Table 1). Healthy children tend to have larger femur diameters (measured mid-shaft), a thicker lateral cortex (measured mid-shaft at the lateral aspect of the femur), and a larger radius of curvature (i.e. straighter femurs) compared to children with bone disorders. These morphological differences likely contribute to a higher fracture risk in children with bone disorders.

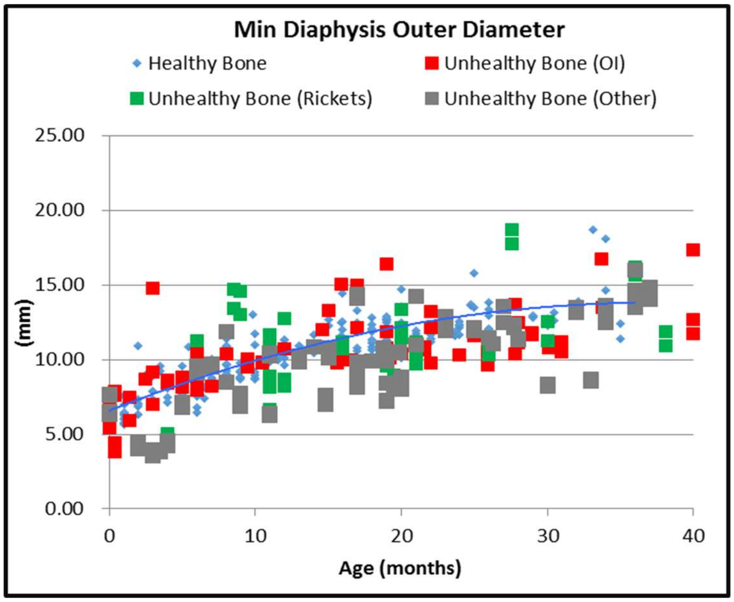

Figure 5. Minimum diaphysis outer diameter from radiographs of healthy (n=205) and unhealthy (n=209) femurs. A quadratic curve of best fit overlies Healthy Bone data. Unhealthy Bone includes femur measurements from subjects with OI, rickets, and other medical diagnoses.

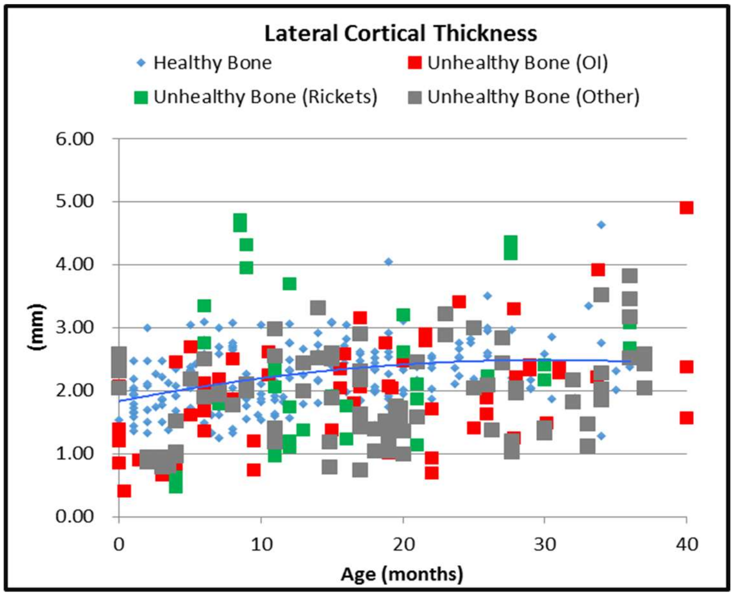

Figure 6. Lateral cortical thickness from radiographs of healthy (n=204) and unhealthy (n=192) femurs. A quadratic curve of best fit overlies Healthy Bone data. Unhealthy Bone includes femur measurements from subjects with OI, rickets, and other medical diagnoses.

Table 1. Results of ANOVA comparing healthy/unhealthy femur measures

Morphological Measure	F statistic	Sig.
Mid diaphysis outer diameter	F(1, 141) = 10.10	p <0.01
Lateral cortical thickness	F(1, 134) = 6.18	p =0.014
Femur radius of curvature	F(1, 136) = 19.79	p <0.01
Cortical Index	F(1, 134) = 0.51	p =0.475
Mid diaphysis outer diameter to femur length ratio	F(1, 136) = 7.41	p<0.01

Finite Element Analysis

Finite element analyses showed that changes in material stiffness (elastic modulus) and morphology due to age affect peak strains (and thus likelihood of fracture) under bending loads (Figure 7). Peak strain increased with higher elastic modulus values and decreased age. Peak strains occurred at the midshaft of the femur (where transverse fractures most often occur). Under a combined loading scenario representative of a short distance feet-first fall, a bowed femur representing an OI bone with a lower elastic modulus experienced much higher peak strains than a healthy age-matched control (1.1% for OI compared to 0.4% for healthy, Figure 8). This suggests a higher fracture risk for the OI femur under the same loading conditions. These results are preliminary; additional factors such as reduced cortical wall thickness and a lower ultimate strength associated with OI bone were not accounted for in our model and would likely further increase fracture risk in this bone. Additionally, simulations of other loading scenarios (e.g. bending in different directions, torsional loads, shear loads) are needed to better understand relative fracture risk.

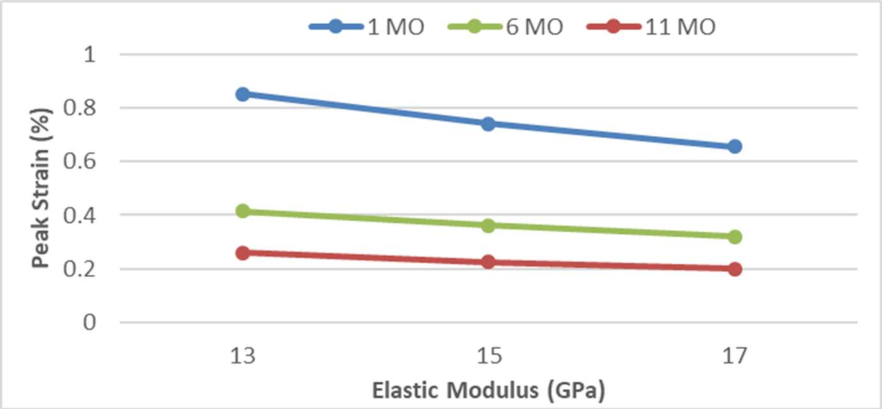

Figure 7. Peak strain measured in finite element analyses simulating bending loading applied to femur models that vary in age and material properties. Increased strain values are associated with higher likelihood of fracture.

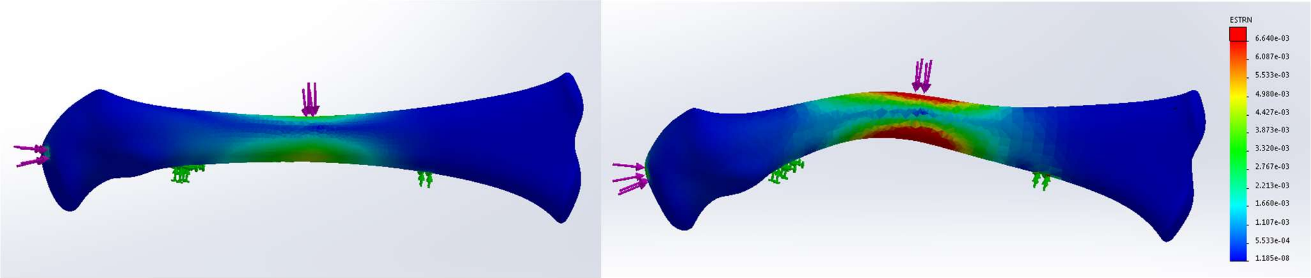

Figure 8. Strain distribution resulting from combined compression and bending load associated with feet-first falls applied to healthy 6-month-old femur (left) and bowed 6-month-old femur representing OI (right). Color mapping indicates a relatively high level (red) of strain at the mid-diaphysis of the OI bone suggesting a higher likelihood of fracture.

Implications for Criminal Justice Policy and Practice in the United States

Femur fractures are a common injury in both child abuse and accidents; there is a paucity of objective data to aid in distinguishing between the two, particularly when a child is suspected to have a bone fragility disorder. By addressing the question of how bone disease alters fracture potential, we will provide objective information to aid in determining biomechanical compatibility between fracture and stated cause – critical in the forensic investigation of child abuse and to the role a bioengineering expert fulfills in a judicial setting. Although this study focused on a single loading scenario in the femur, findings provide the foundation for future work investigating fracture potential in other loading scenarios and in other long bones. Furthermore, by building computational tools using radiographic images, this study may serve as a model for development of future subject-specific injury assessment tools. Results of this study have the potential to improve accuracy in child abuse diagnoses, forensic investigations, and legal proceedings.

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