Biomechanics of Osteogenesis Imperfecta: Current Concepts and Emerging Horizons

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INTRODUCTION

Osteogenesis imperfecta (OI) is associated with bone fragility. Long bone fractures are a common occurrence in individuals with OI. Although there have been significant advances in understanding the genetic defects associated with OI, the mechanisms behind bone fragility in this patient population are not yet well understood. This fragility is believed to stem in part from characteristic bone mass deficiencies. Research further suggests that the material properties of the bone are also compromised in individuals with this disorder. There is currently no quantitative method available to assess bone fracture risk in individuals with OI. This chapter examines several critical elements needed to assess bone fracture risk through a unified biomechanical modeling approach. Finite element modeling (FEM) lies at the core of this approach with reliance upon material property and load data. The former stems from micro- and macrostructural scale characterization of bone material properties while the latter derives from assessment of mobility and other activities. As improved tools are developed for fracture risk assessment, clinicians will be afforded more effective methods to examine interventional effects and rehabilitative strategies in the short- and long-term with an ultimate goal of fracture reduction.
MECHANICS AND MICROSTRUCTURE OF THE BONE MATERIAL

Bone Mass

Low bone mass is a characteristic of OI, as evidenced by very low areal bone mineral density as well as sparse material distribution in bone biopsies.\textsuperscript{1-4} These findings indicate that individuals with OI have less bone material available to support musculoskeletal loading, and that these loads are distributed over a smaller bone cross-sectional area, resulting in increased stresses (local intensity of forces per area) within the bone for a given load.

Bone Composition

Abnormalities related to bone tissue composition and microstructure in OI have been described, which, in addition to bone mass deficiencies, may contribute to bone fragility.

OI is the result of genetic defects related to type I collagen, an important structural component of bone, or to other proteins that interact with type I collagen for \textit{post-translational modification and/or folding}. For example, OI type I, a mild form, is attributed to an insufficient quantity of type I collagen;\textsuperscript{5-8} while OI types III and IV, which are more severe, are associated with defects within the collagen.\textsuperscript{8-10} Thus, it is perhaps not surprising that irregularities in collagen molecules size have been observed within this population.\textsuperscript{11-13}

Abnormalities in the mineral component of bone have also been observed in OI. The size, shape, and composition of the mineral crystals have been shown to be affected,\textsuperscript{11,14-17} and mineralization density was found to be higher than normal.\textsuperscript{4,17-19}

Bone Properties at the Microstructural Scale

The idea that bone material properties are compromised in OI is supported by findings from studies of mouse and human bone tissues.

Bone is a highly hierarchical material having distinct structural features at different length scales. Therefore, it displays different mechanical behavior depending on the scale at which it is tested. A few studies have used nanoindentation, a mechanical test in which a small diamond-tip is pressed into the polished surface of a specimen, to measure the mechanical...
properties of surgical and biopsy bone specimens from children with OI. In this test, the resulting indent is a few microns in width, allowing measurement of mechanical properties on a small area within the bone microstructure (e.g., intra-osteon).

From nanoindentation tests, two material properties can be determined: the elastic modulus, representing the material’s stiffness (i.e., resistance to non-permanent deformation); and hardness, representing the resistance to permanent deformation. Surveying the literature on nanoindentation testing of pediatric OI bone, the following observations are made regarding elastic modulus and hardness at the microstructural scale. Overall, these properties tend to be higher in children with mild vs. severe phenotypes;20 but they do not appear to differ between moderately severe and severe OI phenotypes.21 Importantly, however, there have been conflicting observations regarding how these properties compare with those of normal bone. In one study, higher elastic modulus and hardness were observed in children with severe and moderately severe OI (types III and IV),18 while in a more recent study these properties were lower in children with mild to severe OI vs. control specimens.17 These divergent observations have not been explained. However, these studies may have been focused on different regions within the bone microstructure. Nanoindentation properties have been shown to vary between interstitial versus secondary osteon lamellar regions.20

Interestingly, elastic modulus and hardness measured by nanoindentation were not found to be altered by pamidronate treatments;18 and these properties are not correlated with age in children with OI.20-22 A positive correlation, however, has been observed between elastic modulus and local tissue mineral density.17

**Bone Properties at the Macrostructural Scale**

Due to limited access to bone tissue specimens from humans with OI, little data is yet available to describe their material strength. Recently, a testing methodology was developed and validated to enable measurement of bone material strength using small bone specimens obtained from osteotomy procedures used to correct long bones deformities.23,24 These small, irregular-shaped osteotomy specimens can be machined into even smaller rectangular-shaped beams, from which the material strength can be determined. Preliminary results indicate that this bone material property is reduced in children with OI relative to typical children.23,24 Further research is needed to confirm whether this is consistently true in all forms of OI, and
how this property is affected by factors such as age, gender, anatomic site, and genotype. Nonetheless, the consequence of low bone material strength is that the bone tissue itself is less resistant to internal loading, and will fracture more easily.

**Bone Microstructure**

In a recent study of three-dimensional bone microstructure, several abnormalities have been noted in cortical bone specimens from children with OI versus control tissues. In particular, abnormally elevated vascular porosity was observed in cortical bone tissue in OI. This observation is consistent with those of a recent two-dimensional scanning electron microscopy study. These findings indicate that, in contrast with normal bone, cortical bone tissue in OI has a highly porous structure, which can affect internal stress distribution within the material.

**Future Directions**

Further study is warranted toward exploring relationships between bone material properties at the microscale and the local variations in mineral and collagen composition with respect to the various OI genotypes. Future studies should also aim to establish relationships between bone properties at the mesoscale and the three-dimensional microstructure. Finally, future directions in material characterization of bone tissues in OI should explore how the bone material properties and microstructure are affected by factors such as: donor age, genotype, antiresorptive therapies, mobility level, and anatomic site.

**STRUCTURAL MECHANICS OF WHOLE LONG BONES**

Several studies have characterized the structural and material-level mechanical properties of bones in murine models of OI.

In Mov13 mice, a model for OI type I, cortical bone material is weaker than that of control mice. However, the Mov13 whole femur as a structure exhibits load to failure similar to that of controls, which appears associated with greater cross-sectional area and bending moment of inertia.

In the oim/oim mouse, a model of OI type III, reduced whole bone structural strength is associated with reduced material strength and toughness. In that mouse model, the collagen is weaker than normal. However,
demineralized bone properties do not differ from those of controls, indicating that the weakness of bone tissue in the oim/oim mouse is likely attributed to incompetent mineral-matrix interaction rather than to the collagen matrix itself.\textsuperscript{30}

The Brtl mouse, a model representative of OI type IV, exhibits reduced whole bone structural strength, which, interestingly, increases as the animal aged.\textsuperscript{33,34} This improvement of whole bone strength with age is associated with an increased material strength rather than an improvement in the cross-section geometry.\textsuperscript{33,34}

It is not clear whether all the above observations are also true in the human forms of OI, nonetheless, these models offer valuable insight into the mechanisms of the bone fragility in OI. Moreover, the availability of murine models has enabled the evaluation of several therapies for OI and their impact on bone structure and strength. For example, therapies such as alendronate, pamidronate, RANKL inhibition, \textit{in utero} transplantation of adult bone marrow, scleritin antibody, and whole body vibration have been studied in various murine models of OI.\textsuperscript{29,31,34-39}

**Finite Element Studies of Human OI Bones**

Structurally, OI bone exhibits characteristics that point to decreased strength even in response to everyday loading. Histomorphometric data indicates that OI bone exhibits decreased cortical and trabecular thickness as well as reduced bone volume fraction.\textsuperscript{24} Normal human long bone develops with the bulk of its material aligned with the mechanical axis of loading, such as predominantly along the length of the femur. This partially explains why bone is strongest in compression along its longitudinal axis. However, OI long bones often exhibit deformations consisting of bowing in the lateral or anterior directions or a combination of both along with torsional deformations. Such geometric alterations shift the locus (area and mass moment) of the material with respect to the ideal mechanical loading axis. As more bone material is moved away from this axis, this bone undergoes higher stresses and becomes an increased risk for fracture.

Developing a better understanding of OI bone biomechanics as well as when and why fractures may occur in OI bone would be largely beneficial to the population. However, it is often not feasible to study bone biomechanics \textit{in vivo}. Thus, modeling has the potential to play a key role in understanding how OI bones respond to loading experienced during various activities,
especially ambulation. Biomechanical modeling can provide insight into bone fracture risks, such as fracture type and location, from single applied loads or repetitive loading. One method for obtaining this information is via finite element analysis (FEA).

Finite element analysis (FEA) has long been used to assess the response of materials to various loading conditions through computational modeling. Finite element (FE) models can be developed and processed for loading conditions that would be too costly, time consuming, or impractical to perform with traditional mechanical testing. The application of FEA to biomechanics was introduced in 1972 by Brekelmans et al. to investigate the stresses experienced in human bone under physiologic loading conditions.\(^\text{40}\)

Since that time, FEA has been widely used in orthopaedic biomechanics and bone assessments as it allows estimations of \textit{in vivo} responses of biological tissues to various loading conditions.\(^\text{41,42}\) Patient-specific FE models have been an effective tool for both bone strain and fracture strength assessment.\(^\text{43,44}\) One important developing application is the use of FEA to predict fractures in OI.\(^\text{45,46}\)

The first FE model for OI was published by Fritz et al. in 2009 and examined the fracture risk of the right femur during normal ambulation of a 12-year-old female with OI type I.\(^\text{45}\) It is a patient-specific model that incorporated loading from inverse dynamics and muscle activations based on clinical gait analysis. The model was analyzed across all seven phases of gait. Material property assignment in this model was taken from literature on nanoindentation testing of bone specimens from children with mild OI. Model geometry (size and lateral bowing) was matched to the patient based on her femoral x-rays by scaling and manipulating an existing three-dimensional (3D) model for FEA of the standardized femur. Initial analysis showed that the femoral stresses were highest during mid-stance and located at the lateral aspect of the bowing deformity and migrated through the gait cycle.\(^\text{45}\) Fritz et al. also examined the sensitivity of the model to changes in applied loading from muscle forces during mid-stance. They concluded that the model was sensitive to force changes from the gluteus maximus and gluteus medius muscles.\(^\text{46}\) Since their initial work, Fritz and colleagues have implemented an improved mesh and updated the material property assignments to reflect the most recent OI bone mechanical property data.\(^\text{24,45,46}\)
Other FE models for assessing OI bones have recently been developed. Orwoll et al. used FEA to estimate vertebral strength in a study of the effects of teriparatide treatment in adults with OI.\textsuperscript{47} Caouette et al. have developed FE models of tibias to biomechanically assess fracture risk in children with OI.\textsuperscript{48} These tibia models examined fracture risk via principal strain criteria through the modeling of two-legged hopping loading, lateral loading, and torsional loading. Geometry of the tibia models was created by combining 3D reconstructions from peripheral quantitative computed tomography (pQCT) and bi-planar tibial x-rays matched to a standardized 3D tibial model into a 3D model for FE analysis. Material property (elastic modulus and Poisson’s ratio) data was assigned based on nanoindentation data from a group of children with OI type IV (cortical regions),\textsuperscript{21,49} or estimated based upon patient-specific bone apparent density measures obtained at three different sites by pQCT (trabecular regions).\textsuperscript{48} Although this method did not enable site-specific assignment of material properties throughout the whole tibia, it provided patient-specific estimates of bone properties with limited radiation exposure to the patient compared to a whole bone computed tomography (CT) scan. This approach also provided more specific estimates of effective trabecular properties than would have the use of data obtained from non patient-specific \textit{in vitro} mechanical studies.

**Future Directions**

Advancing knowledge of bone mechanical properties and musculoskeletal biomechanics associated with OI increases the capabilities of FE modeling for fracture risk assessment of OI bones. Patient-specific parameters for FE models include material properties, geometry, boundary, and loading conditions. Along with the implementation of new mechanical properties of OI bone, researchers are looking to understand how musculoskeletal biomechanics and muscle activation patterns and levels may vary in persons with OI compared to normal data. Muscle activation timing and levels play a key role in the direct loading exerted on long bones at each muscle attachment site. Fritz et al. showed that the stresses within the femur are sensitive to changes in muscle forces from the gluteus maximus and gluteus medius during the mid-stance phase of gait in an FE model of an OI femur.\textsuperscript{46} This observation has led to implementation of additional surface electromyography (EMG) data being collected during gait analysis studies of minors with OI and age-matched controls. Future investigations into the exact forces being exerted on OI bones by muscle activation may further benefit from musculoskeletal modeling and simulation. Advanced knowledge of muscle forces along with motion analysis during various
activities will provide patient-specific data for the boundary and loading conditions necessary for FE models of OI bones. A better understanding of the dynamic application of loads during various activities (walking, running, jumping, etc.) will enable estimation of the stresses and strains that these loads induce within bones. Ultimately, these models will help to evaluate the load levels that may induce fracture and locate the site within the bone where a fracture is most likely to occur.

The heterogeneity of the OI population requires that these FE models take into account the patient’s clinical severity (phenotype and possibly genotype) and physical activity level, and how these factors affect the bone from a mechanical perspective. A more precise method for applying patient-specific material properties for FE models of bones involves the acquisition of CT scans of the bone to be modeled. Geometric and mechanical property data can both be extracted from CT scans.\textsuperscript{50} However, this comes with the caveat of radiation exposure, which is not desirable or feasible in minors with OI who already undergo frequent x-ray scans due to fractures and routine clinical examinations.

Future work should examine the necessity of acquiring 3D images of OI bones for geometric modeling. As discussed earlier, not all current models are created from direct 3D reconstructions of the patient’s bone. Fritz et al. use a method that employs planar x-ray data to scale an existing 3D femur model while Caouette et al. use a combination of pQCT and scaling to create their tibia models.\textsuperscript{45,48} Magnetic resonance imaging (MRI) data collection may be a safer – though expensive – alternative to acquiring exact 3D geometry of patients without radiation exposure. As discussed earlier, the altered geometry of OI bones often leads to more material being moved away from the mechanical axis and, thus, leaving long bones more susceptible to fracture during routine loading conditions such as ambulation.

Long bone loading during ambulation is generally associated with the lower extremities, specifically the femur and tibia. However, many persons with OI use assistive devices, such as walkers, Lofstrand crutches, or wheelchairs, for ambulation. While the use of these devices offloads the lower extremity bones, higher magnitudes of cyclic loads are imposed on the upper extremity bones when compared to unassisted ambulation. Upper extremity motion analysis models along with instrumented crutches have provided insight into the joint loading and potential overuse injuries.\textsuperscript{51} Such upper extremity load data could be incorporated into FE bone models to assess the impact of these
assistive devices on fracture risk. During assistive device ambulation, the humerus becomes analogous to the femur and geometric alterations such as bowing move material away from the mechanical axis. Like the femur, this is likely to cause increased stress levels and concentrations at the apex of bowing.

Technology and knowledge advances continue to assist in the development of patient-specific FE models for fracture risk assessment. This tool may ultimately prove invaluable for quantification of fracture risk. By simulating various activities, these models could help identify those activities that pose greater risk and thus reduce the risk of fractures through activity modification. These models could also enable persons with OI to participate actively and safely in a broader range of activities that are assessed to pose lower risk. Finite element fracture risk models may also provide novel quantitative insight in deciding if and when a patient’s bowing deformity should be surgically corrected.

**MOBILITY**

The need for quantitative mobility and activity assessment is fundamental to the FEM process that lies at the core of fracture risk assessment. Dynamic load application during ambulation, assisted ambulation, and other activities induces stresses and strains within the bones. Analysis of these dynamic loads has become a critical phase of the fracture risk assessment.

Human motion analysis offers a sophisticated laboratory method for characterizing loads during ambulation. This process of analysis is used frequently today for clinical and research applications and has evolved well beyond basic descriptions of ambulatory patterns to include triaxial joint kinematics and kinetics (dynamics) as well as surface and fine-wire EMG. Knowledge about body segment anthropometry and segmental kinematics can be combined with EMG and muscle evaluation data to drive further models of muscle contributions to bone and joint loading. SIMM (Musculographics Inc., Santa Rosa, CA), OpenSim (Simbios,NIH), Biomechanics of Bodies (The MathWorks Inc., Natick, MA), AnyBody (AnyBody Technology Inc., Salem, MA) and MADYMO (Tass International, Livonia, MI) are a few examples of simulation models that offer various options for including muscle contributions to joint dynamics.

Historically, lower extremity motion analysis has played a vital role in the advancement of surgical treatment of children and young adults from the
days of isolated procedures to the current comprehensive, multilevel approaches.\textsuperscript{52-55} Lower extremity motion analysis has long proven useful in studies of neuromuscular disorders\textsuperscript{56-60}, joint replacement\textsuperscript{61-71}, athletic performance and injury\textsuperscript{72-75}, prosthetics\textsuperscript{76-80}, orthotics\textsuperscript{81-84}, and assistive devices.\textsuperscript{85-87} While simple observational analysis of ambulation by a trained observer is clinically useful, current technology supports precise analysis of joint angles, angular velocities and angular accelerations; ground reaction forces; joint reaction moments and forces; joint power generation and absorption; and EMG. This technology also supports analyses of upper extremity contributions to assisted ambulation and other activities with similar precision. In children and young adults with OI, mobility assessment has included analysis of ambulation during use of wheelchairs and assistive devices.

**Ambulation**

The largest predictor of walking ability in a study of 70 children with OI (types I, III and IV) is reported by Engelbert et al. to be the severity of collagen defect.\textsuperscript{88} While all children of the type I group were able to ambulate, 85\% were able to ambulate household distances without assistive devices. In an examination of functional limitations, Takken et al. reported that children with OI type I fatigued easily, possibly due to muscle weakness and diminished peak maximal oxygen consumption.\textsuperscript{89} Studies have also been performed to improve the process of evaluation of children with OI by assessing gait and selected functional measures. These have extended to a broader investigation of bony fracture through biomechanical modeling and material characterization as described earlier in this chapter. In a study of ten subjects with OI type I and 22 age-matched controls, Graf et al. performed gait analysis, including kinematics and kinetics.\textsuperscript{90} Gait data was collected at 120 frames per second using a passive-reflective marker set and a 14 Vicon MX camera motion analysis system (Vicon Motion Systems, Ltd., Oxford, UK). Spherical reflective markers were placed at anatomical landmarks on the pelvis and lower extremities in accordance with the validated Vicon Plug-in-Gait Model (Vicon Workstation v 5.2.4).\textsuperscript{91-93} Twin force plates (AMTI, Newton, MA) were used to measure ground reaction forces. System calibration assured an accuracy of less than 1 mm.\textsuperscript{94,95} Participants walked at a freely selected pace for 10 to 15 trials with a minimum of three trials selected for analysis. Kinematics and kinetics were computed for all trials.

Temporal analysis showed that the period of double limb support was increased and that foot off occurred later in the gait cycle in the OI group
when compared to controls. Cadence (steps/min), single limb support duration, and walking speed were not significantly different between groups. Kinematic analysis showed a significantly reduced mean peak ankle plantar flexion during third rocker for the OI group (mean: -3.6°) as compared to the controls (mean: -12.1°). There was a significantly reduced ankle range of motion during stance in the OI group (OI: 21.5°; controls: 28.0°). Significant differences were also found at the pelvis, with greater downward obliquity during stance in the OI group (OI: -4.4°; controls: -2.4°). With regard to event timing, peak ankle dorsiflexion during stance phase occurred at 52% gait cycle (GC) for the OI group and 43% GC for controls. Several other events occurred significantly later in the GC for the OI group including: peak hip extension, peak knee extension, and peak external foot progression angle (all during stance) and peak knee flexion during swing. In the kinetic analysis, the OI group peak ankle push off power (generation) was significantly reduced and occurred significantly later during the gait cycle (2.7 W/kg at 58% GC) when compared to the controls (3.7 W/kg at 52% GC).

Peak ankle power generation during push off in the OI group was significantly less than that of the controls. This decrease was thought to be related to the flexibility of the OI foot as well as an avoidance of excess force in the presence of bone fragility. Further developments, findings, and expanded opportunities for contribution to a better understanding of ambulation in children and young adults with OI can be found in the chapter by Adam Graf and colleagues later in this book.

**Wheeled Mobility**

Slavens et al. have reported on unique quantitative, three-dimensional (3D) evaluations of upper extremity (UE) joint dynamics at the shoulder complex, elbow, and wrist during pediatric wheelchair use. Work on pediatric-wheeled mobility assessment has also been reported by Schnorebne et al. with an advanced biomechanical model for evaluation of UE joint dynamics. An inverse dynamics model was used to characterize 3D UE joint kinematics and kinetics during pediatric wheelchair mobility using a SmartWheel (Mesa, AZ) instrumented hand rim system. The bilateral model included thorax, clavicle, scapula, upper arm, forearm, and hand segments, as well as the sternoclavicular, acromio-clavicular, glenohumeral, elbow, and wrist joints. Previous, validated UE models for the evaluation of pediatric assisted mobility provided a foundation for development of this model which incorporated International Society of Biomechanics (ISB) recommendations as well as custom features specific to the pediatric
population. The marker set used to describe the thorax was refined to reduce the influence of shoulder girdle movement on thoracic kinematics. A regression method was applied for determining glenohumeral (GH) joint center that used the positions of five markers on the scapula. A tracking method was described for the scapula markers to reduce the effects of skin motion artifact as well as possible marker-wheelchair interaction. Body segment parameters were calculated with equations specifically developed for pediatric application. The model was applied to an adolescent to demonstrate utility in identifying motion and loading patterns. This model may provide valuable new insight and is biomechanically appropriate for application in children and young adults with OI.

**Assistive Devices – Crutches and Walkers**

Upper extremity dynamics during crutch-assisted gait have been of interest for several decades following an early history of work done to characterize the lower extremities. Premature development of degenerative arthritis and disruption of the rotator cuff associated with assistive device usage has been of concern to a number of authors who have initiated UE studies. Model limitations, however, have tended to slow progress. An early study by Requejo et al. contributed information on kinematics and kinetics for a single subject with spinal cord injury. Complete UE dynamics were later reported in a study by Slavens et al. in 2007 for five children with myelomeningocele during Lofstrand crutch-assisted gait. This work incorporated standards suggested by the ISB Standardization and Terminology Committee and analyzed two types of gait patterns, reciprocal and swing-through. The study found that walking speed, cadence, and stride length were highest during swing-through gait. For both patterns, the thorax and elbows remained in flexion while the shoulders exhibited both flexion and extension throughout the gait cycles. Larger ranges of motion were seen in swing-through gait for all UE joints. Peak forces were noted in the crutches during swing-through gait. This work supported continued testing and development for pediatric assessment. A follow-up study comparing reciprocal and swing-through gait patterns was reported in 2009 by Slavens et al. for nine children with myelodysplasia. Temporal and distance parameters showed significant differences between the two gait patterns in terms of stride length and stance duration. Joint ranges of motion were all greater during swing-through gait. Kinetics were significantly different between the two gait patterns at all joints for superior/inferior force, range of force, and maximum inferior force. The authors also reported that functional outcomes were correlated with joint dynamics. In 2011, Slavens...
et al. presented a UE inverse dynamics model for pediatric Lofstrand crutch-assisted gait. The model described dynamics at the shoulders, elbows, wrists, and crutches and was compliant with the ISB recommended standards. A custom designed Lofstrand crutch system with four, six degree-of-freedom dynamometers was used with the model to assess triaxial UE joint reaction forces and moments. The pediatric system was demonstrated in children with diplegic cerebral palsy, incomplete spinal cord injury, and OI type I. A continuation of this combined modeling and instrumentation approach is described in the chapter by Slavens et al. later in this text with a specific focus on children with OI.

Upper extremity assessment during walker-assisted gait has also been a topic of interest and development for several decades. As with work in crutch-assisted gait, walker assessment largely began with analysis of the lower extremities. In the case of walkers, however, much attention was and continues to be devoted to a comparison of differences in anterior versus posterior walker use. In 2008, Strifling et al. reported on a comparison of UE kinematics in children with cerebral palsy using anterior and posterior walkers. Ten children were analyzed in the comparative study in which each participant was tested using both types of walker following a period of acclimation. Overall results were similar. Shoulders were extended, elbows flexed and wrists extended with both walkers. Energy expenditure, walking speed, and stride lengths were also similar for both walker types. While not statistically significant in the relatively small population, anterior torso tilt was reduced with the posterior walker and shoulder extension and elbow flexion were increased. A year later in 2009, Strifling et al. presented findings from an UE study of GH joint forces in children using anterior and posterior walkers. Weight bearing on the GH joints was analyzed in five children with cerebral palsy using both anterior and posterior walkers fitted with six-axis handle transducers. In general, posterior walker use created larger GH joint forces. While not statistically significant, the authors noted that, over time and with repetitive loading, the findings could bear clinical significance. In a similar population study, Konop et al. reported on a biomechanical analysis of UE kinetics in children with cerebral palsy using anterior and posterior walkers. Upper extremity joint kinetics were calculated for ten children with cerebral palsy using both anterior and posterior walkers. Triaxial joint reaction forces and moments were fully characterized for the wrist, elbow, and shoulder joints for both walker types. Statistical comparisons showed no significant differences in kinetic joint parameters between walker types. Joint reaction forces at the shoulder ranged from
5.7% body weight (BW) in the superior direction to 4.3% inferiorly, 7.4% posteriorly, and 2.3% medially. Joint reaction moments were similar to values reported by others in previous studies. Posterior joint reaction forces at the GH joints were similar or larger in magnitude compared to superior forces. The greatest joint reaction moments seen at the shoulders were lateral bending and external rotation. In concluding, the authors noted that identification of risk factors could support changes in gait training routines, walker prescription, or walker design. Unique technical and model design details specific to UE joint demands during walker use in a child with OI are provided in the chapter by Konop et al. later in this text.

**Future Directions**

Quantitative mobility and activity assessment is fundamental to the FEM process that lies at the core of fracture risk assessment. Dynamic loading induces stresses and strains within the bones and must be well described in order to advance the process of fracture risk assessment. Current work in assessing children with OI has shown promise with unique findings, and these research efforts will likely continue to offer new clinical insight with future applications. Anticipated areas for expansion include improved musculoskeletal modeling and simulation approaches, and development of more refined multi-segmental models for kinetic assessment of joint loads.

From a technical perspective, it is encouraging to know that more advanced methods are becoming available for quantitative analysis of joint demands arising from a variety of mobility and daily living activities. Through a better understanding of the underlying biomechanics and associated joint loads, it is anticipated that improved methods will evolve for fracture risk assessment, activity prescription, and clinical approaches to care. Future work will likely address these issues through development of more precise biomechanical models, larger and more focused clinical studies of children with OI, and exploration of new methods to improve mobility while reducing joint demands. Advances in technology and reductions in cost will also drive opportunities to migrate much of this advanced technology to the community and home environments.

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