

Original Article

Biomechanical analysis of fracture risk associated with tibia deformity in children with osteogenesis imperfecta: a finite element analysis

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Abstract

Objectives: Osteogenesis imperfecta (OI) frequently leads to long-bone bowing requiring a surgical intervention in severe cases to avoid subsequent fractures. However, there are no objective criteria to decide when to perform such intervention. The objective is to develop a finite element model to predict the risk of tibial fracture associated with tibia deformity in patients with OI. **Methods:** A comprehensive FE model of the tibia was adapted to match bi-planar radiographs of a 7 year-old girl with OI. Ten additional models with different deformed geometries (from 2° to 24°) were created and the elasto-plastic mechanical properties were adapted to reflect OI conditions. Loads were obtained from mechanography of two-legged hopping. Two additional impact cases (lateral and torsion) were also simulated. Principal strain levels were used to define a risk criterion. **Results:** Fracture risks for the two-legged hopping load case remained low and constant until tibia bowing reached 15° and 16° in sagittal and coronal planes respectively. Fracture risks for lateral and torsion impact were equivalent whatever the level of tibial bowing. **Conclusions:** The finite element model of OI tibia provides an objective means of assessing the necessity of surgical intervention for a given level of tibia bowing in OI-affected children.

Keywords: Osteogenesis Imperfecta, Finite Element, Tibia Deformity, Tibia Nailing Surgery

Introduction

Osteogenesis imperfecta (OI) is the most frequent bone fragility disorder in children, with an incidence of 1 in 10 000¹ to 1 in 20 000 newborns². The disease is usually caused by mu-

tations in *COL1A1* or *COL1A2*, the genes that code for type I collagen³. OI is classified in several types, depending on the severity of clinical symptoms (Silence classification) and affected genes. Patients with OI type IV typically have bone fragility of intermediate severity, varying degrees of short stature, and progressive skeletal deformity. One reason for the bone fragility in children with OI type IV is low bone density. This lower bone mass is usually well corrected by intravenous bisphosphonate treatment, the current standard of care in such patients³.

With this treatment, most children with OI type IV achieve independent ambulation. However, despite the medical treatment, they often have progressive lower limb bowing, secondary to the bone fragility. Long bone bowing that causes repeated fractures can only be corrected by surgical intervention involving multiple osteotomies to re-align the bone and insertion of intramedullary rods. In order to judge the necessity for surgical intervention, the surgeon must predict whether a given bow is likely to lead to fracture during situations that occur in daily life. Unless the bone has already fractured due to the bow, the sur-

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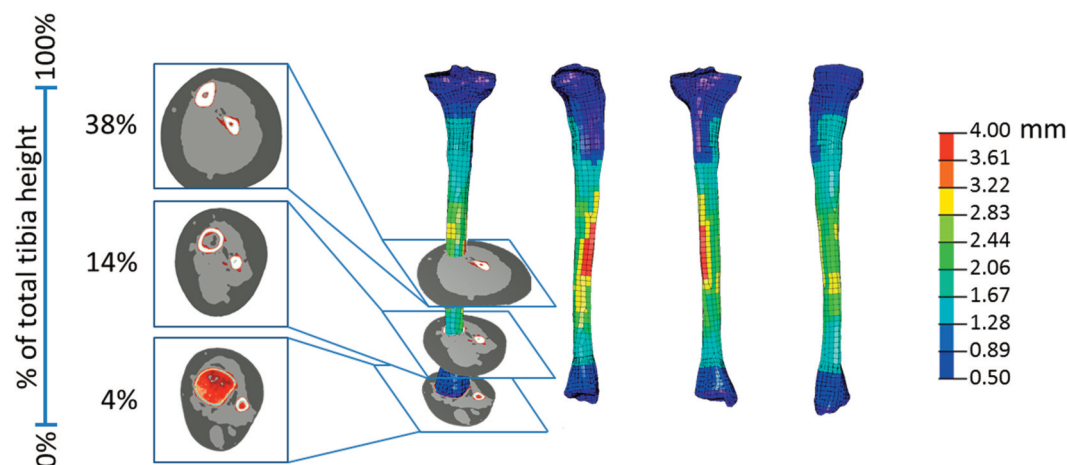


Figure 1. Mesh and thickness distribution in the model, with localization of pQCT slices (posterior, lateral, anterior and medial views).

geon's experience is essentially the only guide. Femoral bowing is frequently treated surgically once it progresses to more than 20-30 degrees or when the patient has fractures. However, clinical experience suggests that tibial bowing is better tolerated and the degree of bow requiring surgical intervention is less clear. Clinical decision-making could be put on a firmer basis if there was a more objective way to assess the effect of bowing on a bone's capacity to withstand loading. The purpose of the present study is to devise such a tool for tibial bowing.

Finite element analysis (FEA) is widely used in engineering for the analysis of complex mechanical and/or geometrical problems such as the present one^{4,5}. FEA uses mesh generation techniques to divide a structure into small subdivisions ("finite elements"), thus allowing for the accurate representation of complex geometries and the inclusion of heterogeneous material properties. Several subject-specific models exist to evaluate fracture risks in the femoral neck for various loadings such as walking and stumbling⁶⁻⁸. These models rely on CT-scan exams for geometric reconstruction and use heterogeneous material properties (density, elasticity and strength) distributions estimated from attenuation coefficient measurement values of the CT-scan. Using these techniques, stresses and strains can be estimated with good accuracy⁷. The maximal principal strain has been shown to be a good criterion to determine risk of fracture as compared to stress-based criteria⁸. Finite element models of the tibia have been used to evaluate the types of loading (compression with bending, torsion) likely to cause fractures in athletes⁹, to evaluate the effect of varus/valgus misalignment on bone strains in the proximal tibia after total knee arthroplasty¹⁰, or to predict the pattern of fracture for a given load¹¹. In certain cases, finite element models are better at predicting fracture than DXA or QCT exams¹².

One published finite element model of the femur of an OI patient¹³ featured a numerically deformed version of the standard femur model available for download through the International Society of Biomechanics mesh repository. Geometric

reconstruction of a patient's femur was based on frontal plane bowing evaluated from a single radiograph (sagittal bowing was not evaluated). Bone elastic modulus was adapted to data obtained from nanoindentation tests performed on pediatric OI bone specimens^{14,15}, and boundary conditions were based on gait cinematic data of a subject with OI. The study concluded that the particular femur that was investigated was not at risk of fracture during walking. An equivalent model to assess the effect of tibia curvatures on fracture risk has not been described.

Subject-specific finite element analyses of the lower limbs are sensitive to the geometry of the bones^{16,17}. The healthy adult tibial bone has been shown in cadaveric studies to be optimized to carry compressive loading in its distal part (from 5 to 40% of its total height)¹⁸, and to resist the bending moment created in the sagittal plane by an impact force delivered to its distal extremity¹⁹. The effect of bowing on the tibia ability to carry compressive loads has not been quantified. Numerous finite element models have shown that cortical thickness is an important parameter related to fracture risk in long bones^{4,20}. Cortical diaphysis of lower limb long bones from OI type IV patients usually have reduced diameter and thinner cortex than normal pediatric bones³. Treatment with bisphosphonates will enhance cortical thickness, but will not correct bowing. The biomechanical effect of this bowing and reduced cortical thickness on fracture risk is not precisely known.

The objective of the current study is to develop a patient-specific finite element model of the lower leg that is adapted to OI bone. This model will be used to create a predictive fracture model for patients with OI, and to assess the effect of tibial bowing on fracture risk.

Materials and methods

Patient data

The patient whose radiographs served as a baseline for the current study is a 7 year old girl with OI type IV due to a

Model	Sagittal plane bowing	Coronal plane bowing	Combined bowing angle (angle with respect to the coronal plane)
0 (Asymptomatic geometry)	2.0°	8.0°	8.2° (46.8°)
1 (Actual Patient geometry)	11.8°	10.8°	15.8° (44.7°)
2	12.3°	12.2°	17.1° (45.0°)
3	13.2°	13.7°	18.7° (45.1°)
4	14.2°	15.3°	20.4° (45.3°)
5	15.3°	16.5°	22.0° (45.3°)
6	16.3°	18.2°	23.7° (45.5°)
7	16.8°	20.1°	25.4° (45.9°)
8	17.1°	21.4°	26.5° (46.1°)
9	17.7°	22.0°	27.2° (46.1°)
10 (Most deformed geometry simulated)	18.3°	24.2°	29.2° (46.5°)

Table 1. Deformation angles measured on the asymptomatic geometry, patient geometry and over-deformed geometries.

COL1A1 mutation, who had undergone bilateral intramedullary rodding to correct bowing in the femurs two years previously. She has also received bisphosphonate treatment at regular intervals to increase her bone density. Calibrated lateral and frontal radiographs of the right tibia were taken using the low-dose EOS system (EOS imaging, Paris) during a routine follow-up visit. Peripheral quantitative computed tomography (pQCT) slices were taken at 4%, 14% and 38% of tibial height (see Figure 1), as per standard protocol for this technique²¹. The patient was also asked to hop on two feet on a force platform²² to provide a personalized load case that will be further detailed in the boundary conditions section.

Geometry reconstruction

The tibia mesh was obtained from a previously developed comprehensive finite element model of the lower limb²³. The model was developed using the explicit finite element code RADIOSS (Altair HyperWorks, Troy, Michigan, USA) and was adapted to perform dynamic analysis. This mesh was made of shell elements for cortical bone (1744 elements of 3.25 mm length) and solid elements for trabecular bone (2232 elements of 3 mm length) and was initially constructed from MRI images (scanning step of 1 mm in joint parts and range of 5 to 10 mm in other regions) of a healthy adult male (50th percentile). Convergence of the mesh and its ability to properly simulate tibial fracture due to impact loading was verified in a previous study²⁴. Shell thicknesses were adjusted based on the cortical bone measured on this initial MRI. The model (mesh and shell thicknesses) was first scaled at 55% to fit the height of the OI pediatric patient (asymptomatic geometry). To reproduce the tibial bowing found on the medio-lateral and antero-posterior radiographs of the patient, a lateral force was applied to the tibial shaft and the model was solved. This was repeated up until the mesh matched the tibial shape on the radiographs (see Figure 2). The stresses were reinitialized to zero and this deformed geometry was then used as the initial geometry in the OI model

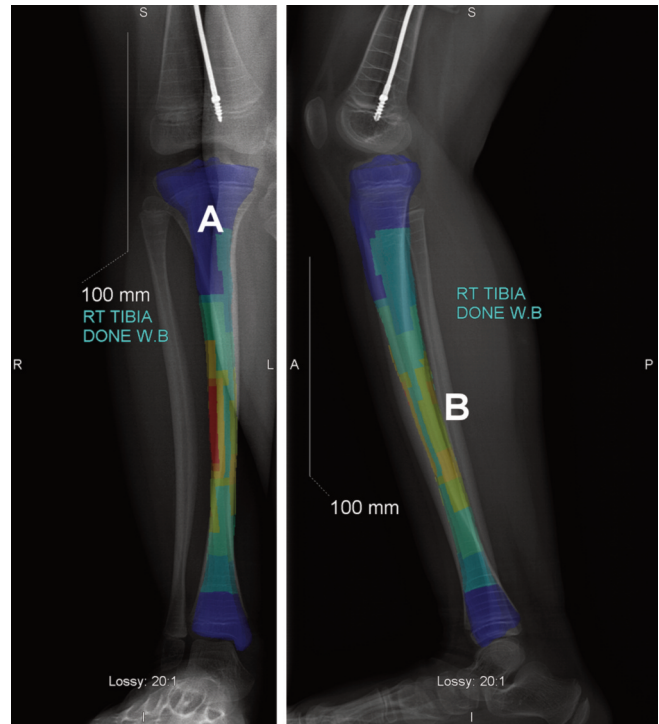


Figure 2. Patient coronal and lateral radiographs, with deformed mesh superimposed.

(OI patient geometry). The same technique was applied to obtain ten different levels of simulated bows (see Table 1) in the tibia (OI geometries). Bowing in the anterior direction (coronal plane) and medial direction (sagittal plane) was measured between lines drawn in the middle of proximal and distal epiphysis on the patient radiographs, as per the current standard in clinical practice. The combined angle and angle of the curvature

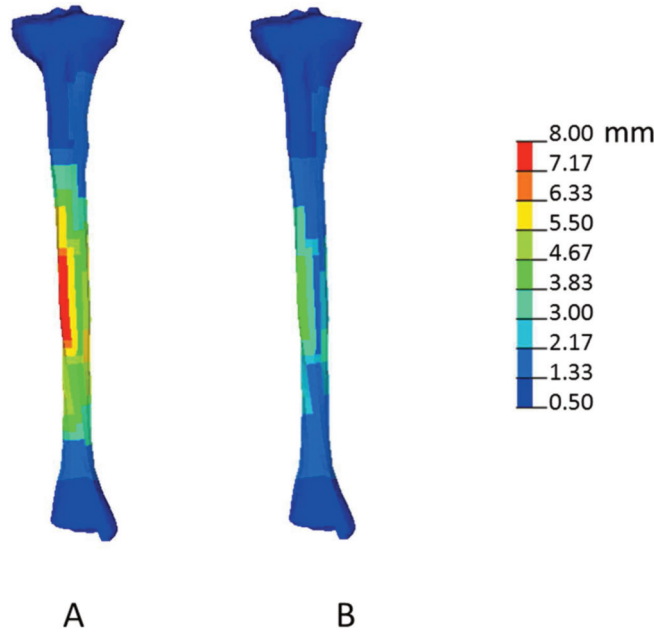


Figure 3. Shell thickness distribution for the two models used in the current study a) initial model (asymptomatic cortical bone thickness, non-OI model) b) initial thickness scaled down and adjusted to cortical thicknesses measured on pQCT slices (patient-specific OI model).

plane with respect to the coronal plane are also provided as reference. Model 0 refers to the asymptomatic geometry, model 1 refers to the geometry fitted to patient radiographs, and models 2-10 refer to over-deformed geometries.

Cortical thickness, which is usually reduced in OI, was adjusted in the current model. Cortical thicknesses from the initial (non-OI) model were first scaled down by 55%. The pQCT images were used to measure cortical thicknesses at 15° intervals around the diaphysis diameter of each level and local adjustments were made to the OI model to improve the fit to these values. The resulting thickness for the two models (non-OI and OI) is shown on Figure 3.

Bone tissue material properties

Material properties were assumed to be isotropic, following a symmetric and strain-rate dependent elasto-plastic material law. This material law allows accounting for the initiation of bone fracture: when the equivalent stress is lower than the yield stress (115 MPa in the current study¹³), the material behaves as linear elastic. Once the critical value of strain is reached locally in the bone, failure is modeled by removing the ruptured elements from the model. This modeling approach was used in similar projects to simulate vertebral fractures^{25,26}. The elastic modulus of OI cortical bone was set to 19 GPa; the value was obtained from nanoindentation tests conducted on pediatric OI type IV bone specimens^{15,27}. Trabecular bone elastic modulus was adjusted with bone mineral density values

from the pQCT exams and the equation of Varghese et al.²⁸ (see Equation 1, where $E_{\text{trabecular}}$ is trabecular bone elasticity modulus and ρ is bone apparent density) was used to convert bone density to elasticity modulus:

$$E_{\text{trabecular}} = 3 \cdot \rho^{1.8} \quad (1)$$

A normalized bone fracture criterion based on principal strain in tension ($\epsilon_{\text{tension}}$) and compression ($\epsilon_{\text{compression}}$) was calculated for each simulation (see Equation 2). Values of 7,300 $\mu\epsilon$ in tension and 10,900 $\mu\epsilon$ in compression were used for the analysis of fracture initiation, based on data from the literature²⁸. The “fracture criterion” was calculated as the maximal ratio between the principal tension and compression strains and their respective fracture values (Equation 2). Thus, the risk of fracture increases as the value of the calculated fracture criterion approaches the fracture threshold of 1.0, when whole bone fracture is predicted to occur. This fracture criterion was shown to be able to accurately predict the onset of femoral neck fracture on cadaveric femora⁸. The strains observed in the OI patient (model 1) for the hopping test will obviously be below the fracture threshold. However, using the 9 other models of different tibia curvatures, we expect that the stress will increase with the bone curvature. For the torsion and horizontal impact cases, the simulated loads were increased up until the fracture criterion reached the fracture threshold to obtain a maximal loading reference.

$$\text{Bone fracture criterion} = \max \left(\frac{\epsilon_{\text{tension}}}{\epsilon_{\text{fracture initiation tension}}}, \frac{\epsilon_{\text{compression}}}{\epsilon_{\text{fracture initiation compression}}} \right) \quad (2)$$

Loading cases and Boundary conditions

Seven different loading cases were simulated, corresponding to (1) the forces that occur under physiological conditions during two-legged hopping, (2-3) internal and external twisting of the tibia along the diaphyseal axis (twisting load case), (4 to 7) a direct hit on the tibia from a horizontal direction in the lateral, medial, anterior and posterior directions (impact load cases).

For the first loading case, data from the mechanographic clinical test was used. The maximum value of three recordings was used for analysis. During hopping the lever arm (foot) about the ankle joint has a ratio of about 3:1 relative to the Achilles tendon. Therefore, resulting total force acting on the tibia was estimated at four times the ground reaction force data. Peak force of this load case (665 N) was here considered the maximum physiological loading the bone is subjected to in daily life and causes the highest strains in the bone tissue²².

For all load cases, the FE model was fully constrained (no displacement or rotations allowed) at the tibial plateau, and a distributed joint contact force was applied to the distal tibia. The load was applied vertically for the hopping load case, internal and external rotation were simulated until fracture for the twisting load cases, and loading was applied laterally and medially (frontal plane impact) and posteriorly and anteriorly (sagittal plane impact) for the impact load cases. Loading was applied at the same speed as the mechanography load case (9400 N/s) and increased until rupture of the tibia. Bending and torsional stiffness were also evaluated.

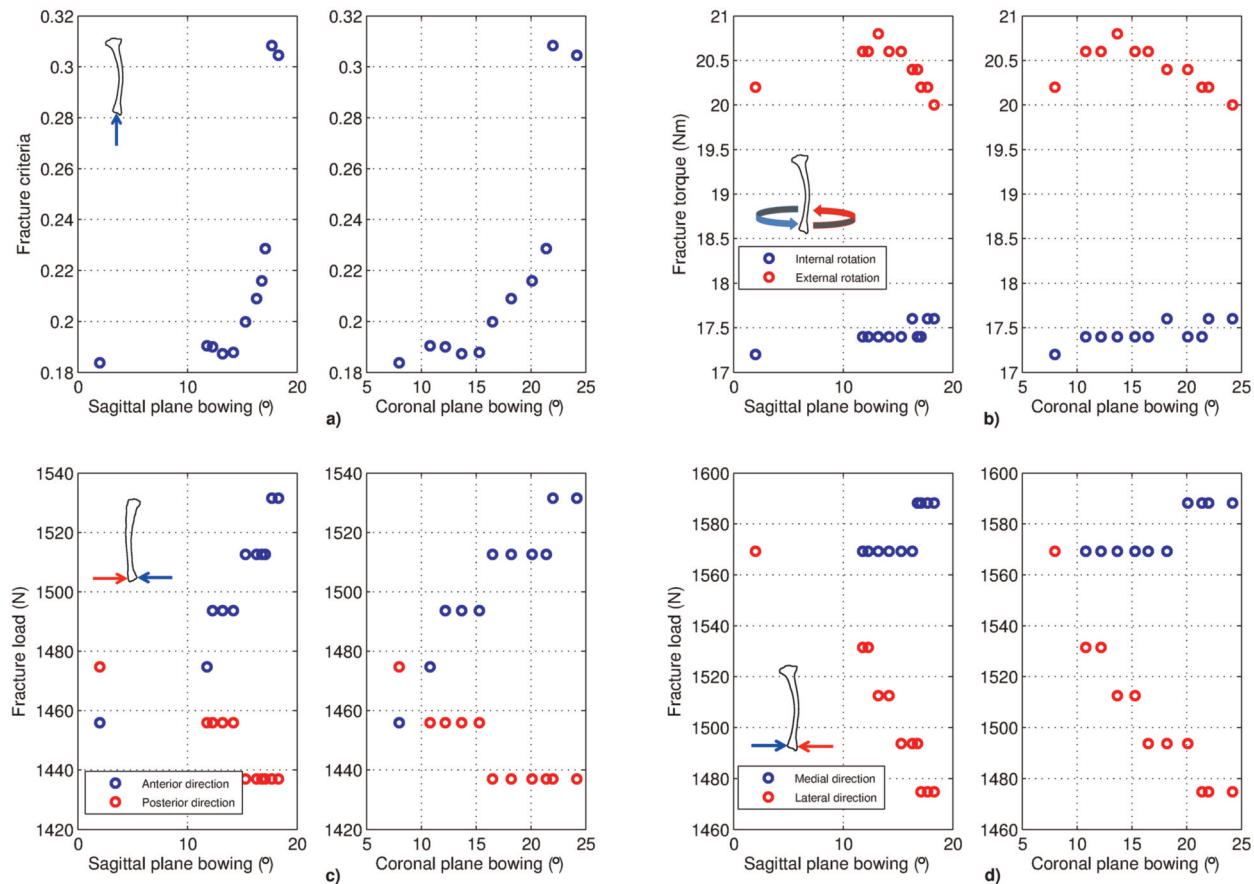


Figure 4. a) Fracture criterion as a function of sagittal and coronal plane bowing for the hopping load case b) Fracture torque as a function of bowing for torsional load case c) Fracture load as a function of bowing for frontal plane impact d) Fracture load as a function of bowing angles for sagittal plane impact.

Thickness approximation scheme used	Maximal value of fracture criterion (hopping load case)	
	Asymptomatic geometry	Most deformed geometry
OI model (adjusted to cortical thickness from pQCT slices)	0.184	0.305
Non-OI model	0.160	0.239

Table 2. Maximal value of fracture criterion for the hopping load case and the two thickness approximation schemes used.

Results

The patient-specific reconstructed tibia (model 1) is shown on Figure 2. The general shape and bowing of the patient bone is reproduced by the finite element mesh, with discrepancies below 2 mm for most of the tibia surface. The patient's tibial metaphysis (zone A on Figure 2) has a more widened shape (33 mm) than the original scaled-down mesh (26 mm). The

patient's diaphysis as seen on the frontal radiograph has reduced diameter (10 mm) compared with the scaled-down mesh (12 mm, zone B on Figure 2). The tibia bending stiffness was evaluated at 1300 Nm and 1350 Nm in sagittal and frontal planes respectively. Torsional stiffness in internal and external rotation was 5.8 Nm/°.

Table 2 shows the effect of cortical thickness on the maximal value of the fracture criterion, for the hopping load case

and two geometries (asymptomatic geometry and the most deformed geometry). The OI model thickness adjusted to cortical thicknesses measured from the pQCT images on each level has the highest fracture criteria for both geometries. All values are below the fracture threshold of the fracture criteria, as expected from a load case obtained from clinical measurements that did not cause bone fracture in the patients.

Figure 4a shows fracture criteria as a function of sagittal and coronal plane bowing for the hopping load case. For sagittal and coronal plane, tibial bows inferior to 15° and 16° respectively (22° combined angle), the fracture criterion remains below 0.2. For higher degrees of bowing, there is an increase of the fracture criteria, up to 0.31 for sagittal plane bowing of 18° and coronal plane bowing of 22° (27° combined angle). This maximal value of 0.31 is below the fracture threshold of the fracture criteria. Maximal values of the fracture criteria occur in the proximal part of the tibia for all geometries. The diaphysis remains less stressed than the distal and proximal parts of the tibia for all levels of curvature.

Fracture load as a function of tibial bowing for the torsional load cases is shown on Figure 4b. There is a small increase in fracture load for internal rotation with increasing deformity (+0.5 Nm). For external rotation, fracture load increases until the bowing reaches 13° and 14° in the sagittal and frontal plane respectively (19° combined angle) then decreases below the fracture load of the asymptomatic geometry (from 20.8 Nm at its peak to 20.0 Nm).

Fracture load for lateral impacts in the sagittal and frontal planes are shown in Figure 4c and Figure 4d respectively. Failure occurred in about 0.16 seconds for all lateral impact load cases. Fracture load is slightly higher for impact in the sagittal plane (medial and lateral direction) than in the frontal plane (anterior and posterior directions), but the difference is small (± 100 N). For impact loading applied in the direction that increases the tibial bow, the maximal load decreases slightly, and increases for loading applied in the direction that decreases the tibial bow.

Discussion

The patient-specific finite element model presented in the current study is a first step in the development of a clinically useful numerical tool allowing the identification of patients with OI requiring surgical intervention for tibial bowing. For the compressive vertical load case, the fracture criterion remains relatively constant for simulated tibial bowing below 15° in the frontal and sagittal planes (22° combined bowing). The fracture criteria then increases in a much more rapid fashion as compared with the asymptomatic geometry (68% increase of the fracture criterion for the most deformed OI model relative to the asymptomatic model). At 0.305 for the most-deformed geometry OI model and the hopping load case, the fracture criterion is still well below the fracture threshold (1.0) that would indicate probable whole bone fracture for this patient. The model also allowed the estimation of fracture loads for a variety of load cases and deformities without placing the patient at risk.

The patient-specific reconstructed tibia used in the current study showed discrepancies of up to 2 mm over most of the tibia surface, but the reduced diaphysis diameter and widened shape of the tibial metaphysis typical of OI type IV pediatric patients, who have had bisphosphonate treatment, were not reproduced. Geometric reconstruction of OI patients long bones is challenging because of the lack of 3D information: CT-scans cannot be obtained without compelling reasons from these young patients who will undergo numerous radiological exams through their lives. The reconstruction method employed in the current study used calibrated bi-planar radiographs and three pQCT slices to obtain an approximate geometry that reproduces the general bowing. Geometry affects the predictions of FE models of long bones¹⁶, but the effect of these reconstruction errors on the calculated fracture criteria is not known. The current model also showed significant changes of the fracture criterion (from 0.160 to 0.184 for the healthy geometry and from 0.239 to 0.305 for the most deformed geometry) for altered cortical thickness distribution. Whole bone strength is affected by reduction of cortical thickness²⁰; cortical thickness is in fact the best predictor of whole bone load fracture⁴. The reconstruction method used in the current study has one feature particularly well suited to the study of OI: it allows over-deformation of the tibia to create geometries representing progression of the OI deformity. These theoretical models can be used to determine how much more bowing can be tolerated for this particular patient before the fracture risk increases too much. An improved reconstruction method for OI deformed bones is required to include this feature. The reconstruction method also has to be improved to better reproduce the bone as seen on the radiographs, as well as cortical thickness as measured from pQCT images. A sensitivity study on the effects of geometric reconstruction errors and cortical thickness variations should be further conducted on this improved reconstruction method to assess their effect on the calculated fracture risks.

Genuine model validation is not possible due to unavailability of whole bone pediatric specimens for *in vitro* mechanical testing. However, model bending and torsional stiffness was compared to data from the literature obtained for cadaveric adult specimens²⁹. Results were found to agree reasonably well for bending stiffness (1600 Nm vs 1300 Nm in the current study for bending in the sagittal plane and 1200 Nm vs 1350 Nm in the current study for bending in the frontal plane) and torsional stiffness (5.0 Nm/° vs 5.8 Nm/° in the current study). Fracture loads obtained for lateral impacts (range of 1440 to 1550 N) are inferior to those found in the literature for three-point bending tests³⁰, which vary from 2500 to 12 000 N. However, these tests were conducted at the maximal travel speed of the testing machine (15 mm in 50 ms), which is much faster than the loading rate used in the current study (15 mm in 500 ms for the lateral impact cases) and is more representative of high speed impacts such as pedestrian car crashes. Lateral impacts conducted at higher speed (15 mm in 250 ms) on the current model yielded fracture loads of up to 2500 N, indicating that stress stiffening effects due to inertial forces were at work

in the study by Rabl et al.³⁰. Such effects are negligible for loadings applied at speeds seen in stumbling load cases³¹ and were therefore not considered in the current study. Fracture loads obtained for the torsional load case (17 to 21 Nm) are in the lower range of values found in the literature for torsional fracture of cadaver tibias (from 25 to 100 Nm in a study by Grutter et al.³², and from 12 to 82 in a study by Hong et al.³³). This is consistent with the reduced thickness tibia featured in the current study.

Lateral and torsion load cases caused fracture to occur first in the distal part of the tibia. This could be explained by the fact that the tibial bone is optimized to carry compressive loads in its distal portion (from 5 to 40% of its height) and is therefore more vulnerable to lateral impact and torsion load cases in that section¹⁸. The study by Cristofolini et al.¹⁹ also showed that the tibia is optimized to resist antero-posterior impact loading in particular. Our results do not show such a trend: fracture load for lateral impact in the antero-posterior direction was comparable to that of all other directions of impact. Fracture torque showed clinically insignificant variations with increasing tibial bow. Torsional stiffness and strength are well correlated to the cross-sectional area and polar moment of inertia, as shown in a cadaveric study by Grutter et al.³². Because they were kept constant when the bow was increased, the current study found very limited effect of bowing on fracture torque. Increased bowing was associated with increased fracture risks in the case of compressive loading only. The addition of a bow decreased resistance to compressive loading by adding a flexion moment to the load carried by the tibia, as in a curved beam under compressive loading³⁴. It has also been noted in the literature that the oblique fracture pattern usually seen in traumatic fractures of long bones is associated with combined loading including torque, but loads were applied one type at a time in the current study and their effects on fracture risk evaluated separately.

Bone tissue was assumed to behave isotropically in the current study, and the elastic modulus of cortical bone was adjusted to fit nanoindentation tests conducted on samples from OI type IV patients, as were cortical thicknesses throughout the tibia. The increased trabecular bone density induced by bisphosphonate treatment was accounted for by adjusting mechanical properties based on density from the pQCT slices. OI bone has been shown to be less anisotropic than normal bone¹⁴. However, the allowable stress in the bone was taken from literature data and corresponds to adolescent healthy bone. OI bone is more brittle than healthy bone: properties related to crack initiation and propagation such as fracture toughness, energy to failure and stress intensity factor have been shown to be reduced in OI bone^{15,27}. This was not taken into account in the current study, which only considered the effect of bowing on fracture risk: hence, the calculated fracture risks are underestimated. The fracture loads obtained are therefore overestimated and should be taken as an indication of the trend caused by bony bowing and not as absolute values. A failure criterion specially developed for OI bone would also be needed for more accurate evaluation of fracture risks.

The model in its current version allows the evaluation of the effect of increased tibial bowing on fracture risk. It can be extended to build a semi-parametric model that could be fitted to patients and used to evaluate other clinical problems related to OI. For instance, this semi-parametric model can be used to evaluate severely deformed bones, and maximal loads can be estimated. It can also be used to run series of simulations in which structural (bone tissue properties) and geometrical (angles of bowing, plane of bowing, cortical thickness) parameters are varied within their possible ranges, allowing the development of an abacus of bowing associated risks. Such a model could eventually be used to study other clinical situations related to OI, such as the effect of nail diameter in the rodding procedure often used to correct bowing.

A finite element model of the tibia in OI for the evaluation of the effect of bowing on whole bone fracture load was developed which allows the evaluation of tibia fracture risks in OI children. The model showed increased fracture risk associated with tibial bowing for vertical compressive loading, but not for lateral impact or twisting. The patient-specific model outlined requires improvements to further analyze the effects of geometric features typical of OI such as the widened metaphysis.

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References

1. Glorieux FH. Osteogenesis imperfecta. *Best Pract Res Clin Rheumatol* 2008;22:85-100.
2. Michell C, Patel V, Amirfeyz R, et al. Osteogenesis imperfecta. *Curr Orthop* 2007;21:236-241.
3. Rauch F, Glorieux FH. Osteogenesis imperfecta. *Lancet* 2004;363:1377-85.
4. Ural A, Bruno P, Zhou B, et al. A new fracture assessment approach coupling HR-pQCT imaging and fracture mechanics-based finite element modeling. *J Biomech* 2013.
5. Ascenzi M-G, Kavas NP, Lutz A, et al. Individual-specific multi-scale finite element simulation of cortical bone of human proximal femur. *J Comput Phys* 2013;244:298-311.
6. Keyak JH, Rossi SA, Jones KA, et al. Prediction of femoral fracture load using automated finite element modeling. *J Biomech* 1997;31:125-33.
7. Taddei F, Cristofolini L, Martelli S, et al. Subject-specific finite element models of long bones: An *in vitro* evaluation of the overall accuracy. *J Biomech* 2006;39:2457-67.
8. Schileo E, Taddei F, Cristofolini L, et al. Subject-specific finite element models implementing a maximum principal strain criterion are able to estimate failure risk and fracture location on human femurs tested *in vitro*. *J Biomech* 2008;41:356-67.
9. Sonoda N, Chosa E, Totoribe K, et al. Biomechanical

- analysis for stress fractures of the anterior middle third of the tibia in athletes: nonlinear analysis using a three-dimensional finite element method. *J Orthop Sci* 2003; 8:505-13.
10. Perillo-Marcone A, Taylor M. Effect of varus/valgus malalignment on bone strains in the proximal tibia after TKR: an explicit finite element study. *J Biomech Eng* 2007;129:1-11.
11. Wong C, Mikkelsen P, Hansen LB, et al. Finite element analysis of tibial fractures. *Dan Med Bull* 2010;57:A4148.
12. Edwards WB, Schnitzer TJ, Troy KL. Torsional stiffness and strength of the proximal tibia are better predicted by finite element models than DXA or QCT. *J Biomech* 2013;46:1655-62.
13. Fritz JM, Guan Y, Wang M, et al. A fracture risk assessment model of the femur in children with osteogenesis imperfecta (OI) during gait. *Med Eng Phys* 2009;31:1043-8.
14. Fan Z, Smith PA, Eckstein EC, et al. Mechanical properties of OI type III bone tissue measured by nanoindentation. *J Biomed Mater Res A* 2006;79A:71-7.
15. Fan ZF, Smith P, Rauch F, et al. Nanoindentation as a means for distinguishing clinical type of osteogenesis imperfecta. *Compos Part B-Eng* 2007;38:411-5.
16. Taddei F, Martelli S, Reggiani B, et al. Finite-element modeling of bones from CT data: sensitivity to geometry and material uncertainties. *IEEE Trans Biomed Eng* 2006; 53:2194-200.
17. Eberle S, Göttlinger M, Augat P. An investigation to determine if a single validated density-elasticity relationship can be used for subject specific finite element analyses of human long bones. *Med Eng Phys* 2013;35:875-83.
18. Capozza RF, Feldman S, Mortarino P, et al. Structural analysis of the human tibia by tomographic (pQCT) serial scans. *J Anat* 2010;216:470-81.
19. Cristofolini L, Angeli E, Juszczuk JM, et al. Shape and function of the diaphysis of the human tibia. *J Biomech* 2013;46:1882-92.
20. Pistoia W, van Rietbergen B, Rügsegger P. Mechanical consequences of different scenarios for simulated bone atrophy and recovery in the distal radius. *Bone* 2003; 33:937-45.
21. Anliker E, Rawer R, Boutellier U, et al. Maximum ground reaction force in relation to tibial bone mass in children and adults. *Med Sci Sports Exerc* 2011;43:2102-9.
22. Veilleux LN, Rauch F. Reproducibility of jumping mechanography in healthy children and adults. *J Musculoskelet Neuronal Interact* 2010;10:256-66.
23. Arnoux PJ, Cesari D, Behr M, et al. Pedestrian Lower Limb Injury Criteria Evaluation: A Finite Element Approach. *Traffic Inj Prev* 2005;6:288-97.
24. Mo F, Arnoux PJ, Jure JJ, et al. Injury tolerance of tibia for the car-pedestrian impact. *Accident Anal Prev* 2012; 46:18-25.
25. El-Rich M, Arnoux P-J, Wagnac E, et al. Finite element investigation of the loading rate effect on the spinal load-sharing changes under impact conditions. *J Biomech* 2009;42:1252-62.
26. Garo A, Arnoux PJ, Wagnac E, et al. Calibration of the mechanical properties in a finite element model of a lumbar vertebra under dynamic compression up to failure. *Med Biol Eng Comput* 2011;49:1371-9.
27. Fan Z, Smith PA, Harris GF, et al. Comparison of nanoindentation measurements between osteogenesis imperfecta Type III and Type IV and between different anatomic locations (femur/tibia versus iliac crest). *Connect Tissue Res* 2007;48:70-5.
28. Bayraktar HH, Morgan EF, Niebur GL, et al. Comparison of the elastic and yield properties of human femoral trabecular and cortical bone tissue. *J Biomech* 2004;37:27-35.
29. Cristofolini L, Conti G, Juszczuk M, et al. Structural behaviour and strain distribution of the long bones of the human lower limbs. *J Biomech* 2010;43:826-35.
30. Rabl W, Haid C, Krismer M. Biomechanical properties of the human tibia: fracture behavior and morphology. *Forensic Sci Int* 1996;83:39-49.
31. Bergmann G, Graichen F, Rohlmann A. Hip joint contact forces during stumbling. *Langenbecks Arch Surg* 2004; 389:53-9.
32. Grutter R, Cordey J, Wahl D, et al. A biomechanical enigma: why are tibial fractures not more frequent in the elderly? *Injury* 2000;31(Suppl 3):C72-7.
33. Hong Y, Parks BG, Miller SD. Biomechanical analysis of tibial strength after harvest of unicortical tibial grafts from two different sites. *Foot Ankle Int* 2006;27:190-5.
34. Boresi AP, Schmidt RJ. *Advanced mechanics of materials*. New York:Wiley; 2003.