Determination of Fracture Risk on Patient-specific Model of Femur with Osteogenesis Imperfecta

Siti Fatima Zahra' Ahmad¹, Mohd Hanafi Mat Som¹⁎, Khairul Salleh Basaruddin¹, Ruslizam Daud¹ and Mohd Shukrimi Awang²

¹School of Mechatronic Engineering, Universiti Malaysia Perlis, Pauh Putra Campus, 02600 Arau, Perlis, Malaysia.
²Kuliyyah of Medicine, International Islamic University Malaysia, Jalan Sultan Ahmad Shah, Bandar Indera Mahkota, 25200 Kuantan, Pahang.

⁎mhanafi@unimap.edu.my

Abstract. Osteogenesis Imperfecta (OI) is a group of genetic disorder that affects the bones. It causes bone to break easily. For severe case, it can lead the patient to death. However, doctors still have no quantitative method to predict fractures. Therefore, this study aims to investigate the fracture risk for OI femoral bone under load of activities in daily living and various loading direction. A finite element model reconstructed from radiography CT images was developed. The variations of daily activities were subjected to the femoral model. In standing and walking configuration, the model of OI has the ability to perform without having any fracture. However, during jumping, both configurations cause the OI femoral fractured. We can conclude that when the OI patients more active in their daily life, the higher chances for fracture to occur. The risk of fracture increases with increasing the intensity of the activity. Thus, early prediction of fracture risk could help prevent or treating fracture for OI patients.

1. Introduction

Osteogenesis Imperfecta (OI) or brittle bone disease is a genetic disorder. It is characterized by easily broken bones or ‘imperfectly formed bones’. OI's patient has genetic defect that impairs the formation of strong bones [1]. This disease is caused by a mutation in COL1A1 and COL1A2, genes that encode type I collagen. Type I collagen is the main structural protein of the extracellular matrix of bone, skin, and tendons [1] [2]. A person with skeletal abnormalities tends to have very low bone mass and bone strength, which will lead to an easy and frequent fracture. Generally, OI is divided into 4 main types, Type I, Type II, Type III and Type IV. These types are divided based on radiography structures and clinical [3].

The main issue of Osteogenesis Imperfecta is the prediction of bone fracture. It is important to investigate the ability of the bone to resist the force before bone fracture occurs [4,5]. Currently, there is no established method in determining fracture risk for OI patients [6]. In order to estimate the fracture risk and plan the preventive interventions, it is necessary to determine the strength of bone accurately [7,8]. Finite Element Analysis (FEA) is broadly used in analysing bone structures and mechanical behaviours. The bone structures are divided into finite elements and each of the elements was assigned to proper material properties [6].

Wanna et al. used finite element model of OI to study the effect of bowing angles during standing [9]. A fracture risk assessment model of the femur in children with osteogenesis imperfecta (OI) during gait [6]. The findings showed that the risk of fracture is influenced by various load impact
and gait cycle. In finite element, the key parameters of the femoral model comprised the mechanical properties of material, the boundary conditions, and the geometry of the model. These parameters make an important contribution to the analysis of fracture.

In this study, the OI finite element model of a femur was reconstructed based on radiography CT images of a real OI patient. This patient-specific model was used to analyse the distribution of mechanical stress, fracture risk, and fracture load under various loads of daily activities (ADL)—standing, walking, and jumping. The result of this simulation might provide important information in the determination of fracture risk in OI patients.

2. Methodology

2.1. Reconstruction of Femoral Model

A set of 310 CT images was obtained from a 13 years old female patient of IIUM Medical Centre. The patient was diagnosed with type III OI. The bone and soft tissues were segmented using global thresholding method as described by Mansor et al. [10]. A 3D femoral model was created using the segmented bone images on VOXELCON (Quint Corporation, Japan). Each voxel was assigned with 1 mm of width, 1 mm of height, and 1 mm of slice pitch of a pixel, thus resulting in 1 mm$^3$ of voxel. Figure 1(a) shows the lower limb of the patient where it was apparent that the bones were bowed at a certain angle. Figure 1(b) shows the resulted 3D femoral model created using the VOXELCON software.

![Figure 1](image1.png)

Figure 1. (a) CT image showing the lower limb of a type III OI patient. (b) 3D femoral model generated from the segmented images using VOXELCON.

2.2. Material Properties

The material properties of the reconstructed OI bone was assigned as isotropic linear elastic. The femur was assumed to has similar properties of cancellous bone, where Young’s Modulus was set to 19 GPa and Poisson ratio of 0.3 [11]. The voxel element size of the femur model was generated based on the pixel size of the original image, thus eliminating the needs for convergence test.

2.3. Boundary and Load Conditions

The boundary condition was set to be in static condition. Boundary constraint was set at the distal of femur as to support the OI femoral model and prevents it from moving. A set of compressive forces were applied on the femoral head simulating the loads of ADL. In standing position, the compressive force was assumed as one-third of body weight. While walking, the femur needs to absorb three to seven times of body weight. Whereas during jumping, the femur takes approximately 15 to 20 times of body weight [12]. Since the body weight was not recorded, it is assumed that patient’s weight is 37.5 kg (367.9 N) based on the study by Graff et al. [13]. Figure 2 illustrate the setup of the femur throughout the study.
2.4 Fracture Risk Analysis

Five loading conditions were applied to the distal part of femoral model to simulate standing, walking, and jumping. The fracture risk is calculated based on formulation created by Keyak et al. [14]. It is a test to measure the fragility of the bone. Based on nanoindentation test done by Fan et al. [11], the fracture strength was assumed to be 115 MPa. The von Mises stress value obtained through the simulation.

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\text{Fracture Risk} = \frac{\text{Fracture Strength}}{\text{von Mises Stress}}
\]  

3. Result and discussion

(a) Standing : 1/3 × BW  
(3.56 MPa)

(b) Walking (min) : 3 × BW  
(32.1 MPa)

(c) Walking (max) : 7 × BW  
(74.7 MPa)

(d) Jumping (min) : 15 × BW  
(159.7 MPa)

(e) Jumping (max) : 20 × BW  
(213.9 MPa)

Figure 3. Maximum Von Mises stress on the femoral model upon compressive force under different ADL.
The results are represented as a contour map of stress distribution on the surface of femur as shown in Figure 3. The minimum von Mises stress was normalized to 0 MPa and maximum 30 MPa and the contour range were applied to all results. The contour plot highlights the location of high fracture risk. The area that appears as red colour indicates high von Mises stress level. Both scenario of jumping resulted in von Mises stresses that exceed the fracture stress of 115 MPa.

Figure 4 shows the plot of fracture risk against the coefficient of body weight based on ADL. The dotted line indicates the point when the fracture occurs. For standing condition, the result shows that OI model able to stand without causing any fracture. Significant decrease of fracture risk values in relative to standing condition were observed for both minimum and maximum walking condition. However, the forces acting on the femur did not cause any fracture as indicated by the fracture risk values of 3.58 and 1.54. This finding is supported by previous study by Wanna et al. where the OI patient can stand and walk on their own without causing any femur fracture [5]. This finding also supported by Fritz et al. where their study proved that all OI patient were able to perform full gait cycle without causing any bone fracture [6]. On the contrary, both minimum and maximum jumping resulted in fracture of femur as implied by the contour plot and fracture risk values calculated. The fracture risk value below 1 indicate that the bone is fractured as suggested by Keyak et al. [14]. Thus, that the more the compressive force is subjected to the OI femur, the higher the chances of femur to fracture. Based on the power regression, it was found that the fracture will be initiated on the femur when the body weight coefficient is 11.

**Figure 4.** Fracture risk curve against the coefficient of body weight based on ADL

### 4. Conclusion

The fracture risk analysis of patient-specific OI femur has been performed using various loadings based on ADL. The simulation results showed that the standing and walking activities did not cause pose fracture risk to the femur. However, when the body weight coefficient is higher than 11, the femur started to fracture. Jumping activity have the body weight coefficient between 15-20, hence resulted in femur fracture. As a conclusion, OI patient have to be careful when performing activities in the daily life as excessive forces may result in fracture of the bone.

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References

[1] Alharbi S A 2016 A Systematic Overview of Osteogenesis Imperfecta 5 1–9

[2] Forlino A and Marini J C 2016 Osteogenesis imperfecta Lancet 387 1657–71

[3] Silience D O, Senn A and Danks D M 1979 Genetic heterogeneity in osteogenesis imperfecta. J. Med. Genet. 16 101–16

[4] Wanna S B C, Basaruddin K S, Mat Som M H, Mohamad Hashim M S, Daud R, Abdul Majid M S and Sulaiman A R 2017 Prediction on fracture risk of femur with Osteogenesis Imperfecta using finite element models: Preliminary study Journal of Physics: Conference Series vol 908 p 012022

[5] Wanna S B C, Basaruddin K S, Mat Som M H, Sulaiman A R, Shukrimi A, Khan S F, Abdul Majid M S and Ridzuan M J M 2018 Fracture risk prediction on children with Osteogenesis Imperfecta subjected to loads under activity of daily living IOP Conference Series: Materials Science and Engineering vol 429 p 012004

[6] Fritz J M, Guan Y, Wang M, Smith P A and Harris G F 2009 A fracture risk assessment model of the femur in children with osteogenesis imperfecta (OI) during gait Med. Eng. Phys. 31 1043–8

[7] Bessho M, Ohnishi I, Matsuyama J, Matsumoto T, Imai K and Nakamura K 2007 Prediction of strength and strain of the proximal femur by a CT-based finite element method J. Biomech.

[8] Sulong I, Basaruddin K S, Mat Som M H and Daud R 2018 Nanoindentation measurement on mechanical properties of Osteogenesis Imperfecta (OI): A review ARPN J. Eng. Appl. Sci. 13 3435–40

[9] Wanna S B C, Basaruddin K S, Som M H M, Salleh A F and Sulaiman A R 2018 Effect of loading direction on fracture of bone with osteogenesis imperfecta (OI) during standing AIP Conference Proceedings vol 2030 p 020094

[10] Mansor N, Beh Y M, Mat Som M H, Basaruddin K S, Mustafa N, Yazid H and Salleh A F 2018 Reconstruction of cortical and cancellous bone in tibia with osteogenesis imperfecta J. Telecommun. Electron. Comput. Eng. 10 115–9

[11] Fan Z F, Smith P, Rauch F and Harris G F 2007 Nanoindentation as a means for distinguishing clinical type of osteogenesis imperfecta Compos. Part B Eng. 38 411–5

[12] Pria Bankoff A D 2012 Biomechanical Characteristics of the Bone Human Musculoskeletal Biomechanics

[13] Graff K and Syczewska M 2017 Developmental charts for children with osteogenesis imperfecta, type I (body height, body weight and BMI). Eur. J. Pediatr. 176 311–6

[14] Keyak J H, Rossi S A, Jones K A and Skinner H B 1997 Prediction of femoral fracture load using automated finite element modeling J. Biomech. 31 125–33