COMPUTATIONAL MODELLING OF TRABECULAR BONE STRUCTURE USING FLUID-STRUCTURE INTERACTION APPROACH

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This work is dedicated to ALLAH SWT for all His guidance

This work is dedicated also to all my family members, as a token of love and appreciation. To my husband, Fahmi Bahri, who always loves, patient and supports me through good and bad times. To my parents for their love and always encourage me to go on every adventure, especially this one.

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In the name of Allah, the Most Gracious and the Most Merciful

ABSTRACT

While doing daily physiological activities, trabecular bone will experience certain amount of deformation, which causes movement of the bone marrow. The bone marrow movement could affect the bone remodelling process. The properties of the bone will also be affected as the bone marrow acts as a hydraulic stiffening to the trabecular structure. Previous studies on trabecular bone remodelling did not consider the effects of bone marrow movement. Thus, there is a need to perform combined analyses of the bone marrow movement with trabecular structure to assess its effects on the remodelling process under a realistic condition. The aim of this study is to determine the effect of bone marrow movement onto the trabecular bone structure under mechanical loading using fluid-structure interaction (FSI) approach. Two different models of the trabecular bone, namely idealised and actual were constructed. The idealised models were used to correlate the bone marrow behaviour to the trabecular bone morphology. The actual trabecular bone models were constructed to mimic the presence of the bone marrow within the trabecular bone structure during physiological loading. The effects of different orientation of the trabecular structures were also examined. Three numerical approaches which are finite element method, computational fluid dynamics and FSI were employed to evaluate the importance of bone marrow movement effect towards the trabecular bone mechanical properties. The findings show that the bone cells are able to stimulate the bone remodelling process under the normal walking gait loading. The bone marrow behaviour such as shear stress, pressure and permeability, together with bone porosity and surface area, have a significant relationship with a p-value < 0.05. The longitudinal permeability and stiffness were respectively 83% and 56% higher, compared to the transverse orientation. The shear stress during a normal walking phase was in a range of 0.01-0.27 Pa. These are sufficient to regulate cell response. It was also found that the stiffness of the trabecular bone structure is 22% higher compared to the models without the bone marrow. This finding suggests that the presence of the bone marrow could help to reduce the deformation and stresses on the trabecular bone structure.

ABSTRAK

Semasa melakukan aktiviti fisiologi harian, tulang trabekular akan mengalami perubahan bentuk yang menyebabkan pergerakan sumsum tulang. Pergerakan ini boleh menjejaskan proses pembentukan semula sel tulang. Sifat-sifat tulang itu sendiri juga terjejas dengan peranan sumsum tulang sebagai pengekalan hidraulik pada trabekular. Kajian terdahulu menganalisis tulang trabekular tanpa mengambil kira pergerakan sumsum tulang. Oleh itu, untuk menyerupai keadaan sebenar adalah penting untuk mempertimbangkan analisis gabungan sumsum tulang dengan struktur trabekular. Tujuan kajian ini adalah untuk mengenal pasti kesan pergerakan sumsum tulang pada struktur trabekular terhadap beban mekanikal dengan menggunakan pendekatan Interaksi Struktur-Bendalir (FSI). Dua jenis model yang berbeza iaitu model unggul dan tulang trabekular sebenar dibina. Model unggul digunakan untuk mengukur hubungan ciri-ciri sumsum tulang kepada morfologi tulang trabekular. Manakala, model tulang trabekular sebenar dibina untuk mengkaji keadaan sebenar sumsum tulang dalam struktur semasa beban fisiologi. Orientasi struktur trabecular yang berbeza juga diperiksa. Tiga pendekatan berangka yang mana merupakan kaedah unsur terhingga, dinamik cecair pengkomputeran dan FSI digunakan untuk menilai kesan kepentingan pergerakan sumsum tulang ke arah sifat mekanik tulang trabekular. Penemuan menunjukkan sel tulang mampu untuk bertindak balas terhadap proses pembentukan semula tulang dengan beban gait berjalan secara normal. Perilaku pergerakan sumsum tulang seperti tekanan ricih, tekanan dan kebolehtelapan dengan keliangan dan kawasan permukaan trabekular mempunyai hubungan yang signifikan dengan nilai-p < 0.05. Kebolehtelapan dan kekakuan orientasi membujur adalah 83% dan 56% lebih tinggi berbanding orientasi melintang. Dalam kajian beban gait, nilai tegasan ricih sepanjang fasa berjalan secara normal didapati dalam julat 0.01-0.27 Pa. Ini didapati cukup untuk mencerna tindak balas sel seperti yang dinyatakan dalam kajian sebelumnya. Kekakuan tulang trabekular adalah 22% lebih tinggi berbanding model tanpa sumsum tulang. Penemuan ini mencadangkan kehadiran sumsum tulang boleh menyebabkan perubahan bentuk dan tekanan pada struktur trabecular berkurang.

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LIST OF ABBREVIATIONS

FSI	-	Fluid-Structure Interaction
MSCs	-	Mesenchymal Stromal Cells
HSCs	-	Hematopoietic Stem Cells
MIL	-	Mean Intercept Length
SMI	-	Structure Model Index
3D	-	Three-Dimensional
FEA	-	Finite Element Analysis
µCT scan	-	Micro-Computed Tomography Scan
BV/TV	-	Bone Volume Fraction
BS/TV	-	Bone Specific Surface-To-Volume
Tb.Th	-	Trabecular Thickness
Tb.Sp	-	Trabecular Separation
Tb.N	-	Trabecular Number
Conn.D	-	Connectivity Density
DA	-	Degree of Anisotropy
QCT	-	Quantitative Computed Tomography
BMD	-	Bone Mineral Density
SI	-	Singh Index
ALE	-	Arbitrary Lagrangian-Eulerian
ANFH	-	Avascular Necrosis of The Femoral Head
S.G	-	Steroid Injection Group
C.G	-	Controlled Group
ARF	-	Activation-Resorption-Formation
BMU	-	Basic Multicellular Unit
MRI	-	Magnetic Resonance Imaging

pQCT	-	Peripheral Quantitative Computed Tomography
CSM	-	Computational Solid Mechanic
CFD	-	Computational Fluid Dynamic
BMI	-	Body Mass Index

LIST OF SYMBOLS

k	-	intrinsic permeability of the trabecular bone
Q	-	volumetric flow rate
μ	-	viscosity
t	-	specimen thickness
A	-	cross-section area
ΔP	-	pressure difference
ρ	-	density
u	-	velocity
p	-	pressure
ε	-	porosity
V_0	-	total volume of the structure
V	-	volume that the structure occupies

CHAPTER 1

INTRODUCTION

1.1   Background of Study

Bone is an ultimate biomaterial which is light, robust, able to adapt to its functional demand and can also repair itself. Bone roles as structural support, shield vital organs from distress, maintains mineral homoeostasis (calcium and phosphorus), and serve as attachment sites for muscles. The four shapes of bone include short, long, flat and irregular shape and different shape has different purpose and position in the human body.

There are two types of bone tissue; cortical bone and trabecular bone. As shown in Figure 1.1, the cortical bone is the outside shell of the bone that forms the tube of the long bone, while the trabecular bone is the porous cellular solid that absorb load. Up to 80% of the bone mass is composed of the cortical bone since it is compact dense and solid, and the balance, which only 20% carried by trabecular bone [1]. Due to the trabecular bone is porous structure, the bone is strong but light in weight. The cortical bone is a bone tissue that has a porosity less than about 30% [2]. Thus, porosity can be used to differentiate between the cortical bone and trabecular bone [3]. Furthermore, the trabecular bone is also known as spongy bone or cancellous bone.

The trabecular bone structures arranged in order to withstand the stresses from usual standing and walking. In addition, the irregular lattice small rods and plates on the trabecular bone tissue called trabeculae and the pores of the trabecular bone filled with bone marrow.

Figure 1.1: Structural types of bone; compact and spongy bone

The bone tissue is composed of organic phases, inorganic phases, and water. The organic phase consists of fibrous type I collagen and amorphous ground substance, while the inorganic phase contains calcium phosphate crystal. Organic and inorganic phase contribute to the tensile strength and compressive strength respectively to the bone tissue [4]. There are several cells in the bone such as osteoclasts, osteoblasts, osteocytes, lining cells, etc. All these bone cells have their functions in bone growth and recovery, also known as bone remodelling process.

Studies on mechanobiological movement through the trabecular bone needed to sustain the bone quality. Previous researchers reported that various physiological activities had affected the bone remodelling process and nutrient supply. Moreover, bone is well known as a self-repairing structural material that altered mechanical

loading. In addition, the bone marrow contained by the trabecular bone will have displacement while bone is subject to mechanical loading.

It is widely known that the trabecular bone is a highly porous structure with a significant volume of bone marrow. A compressive or tensile force on the trabecular bone will result in bone marrow movement with respect to the trabecular bone structure. Hence, the interaction between the fluid and trabecular bone will occur, and this incident might have several effects on the trabecular structure. Therefore, the Fluid-Structure Interaction (FSI) approach were used to find out the effect of fluid to the trabecular and vice versa. With the purpose of understanding the bone marrow interaction inside the trabecular bone, the knowledge of bone marrow properties is essential. Even though there are some previous researches on bone marrow, the literature available on the fluid flow characteristic of bone marrow in the trabecular bone is still lacking. As the trabecular bone experience loading conditions, the bone marrow will have a resistance to the trabecular bone structure. Since the trabecular bone is known as an anisotropic material, by measuring the permeability of bone at a different orientation more understanding of the trabecular bone orientation can be understood. Moreover, knowledge of shear stresses that occur within the bone during daily activities is necessary to comprehend how the bone marrow can affect the trabecular structure properties.

The pressure differences across the trabecular bone along with viscosity and permeability values were used in these studies to quantify the shear stresses occurring on the trabecular surfaces. Currently, no literature is available regarding the nature and behaviour of bone marrow that occur in trabecular bone during physiological loading condition. So far, however, there has been little discussion on the fluid in bone area, and most of the researchers focused on the bone fluid flow within the lacunar-canalicular porosity. Therefore, in this study, the main concern is on the FSI of the bone marrow within the trabecular bone with the purpose of finding a correlation between fluid characteristics and mechanical properties of the trabecular bone and how the trabecular bone reacts on the interaction of bone marrow.

1.2   Problem Statement

As mentioned earlier, this study is based on the effect of bone marrow movement to the trabecular bone during the physiological activities. It is commonly known, bone marrow always coexisting with the trabecular structure. However, previously most of studies have modelled the fluids and solid components separately. Thus, unable to capture the real conditions which occur within the trabecular bone and bone marrow. Due to the load applied to the bone while daily activities were performed, such as standing, walking and running, the trabecular structure will have a stress and deformation. Consequently, the bone marrow within the trabecular would have movement, while also providing a hydraulic stiffening effect to the trabecular structure. The hydraulic stiffening effect will be slowing down the trabecular bone deformation [5]. Additionally, the movement of bone marrow can cause shear stress to the trabecular bone structure. These mechanical effects to the trabecular bone are crucial to be understood with the purpose of developing artificial trabecular bone or scaffold.

Furthermore, the mechanical environments of bone marrow are not yet clearly understood. Other than a function of hydraulic stiffening of bone, bone marrow also acts importantly in the bone remodelling process. In fact, bone marrow also functions as a home for progenitor cells; osteoclast and osteoblast, also, as a host to others cells such as immune cells, blood cells, adipocytes, mesenchymal stromal cells (MSCs), hematopoietic stem cells (HSCs), etc. [6]. The remodelling process was controlled by osteocytes mechanobiological signalling which was diffuse to the bone marrow. Likewise, it is known that when there is mechanical loading due to the physiological activities, the bone marrow within the trabecular structure was compressed. This phenomenon causes a pressure drop in the trabecular bone structure. Thus, the bone marrow will have a fluid flow through the porous structure. Furthermore, the interaction between the bone marrow flow and the trabecular wall will generate shear stress. These mechanical stimuli will affect the bone formation which also in control of trabecular design structure. Over the time, the bone cells within the bone marrow

will respond to the remodelling process and adapt to the induced mechanical loading to resist the loading and become stronger. Thus, the trabecular bone and marrow intimate interaction recommend that they both needed to be considered in parallel.

Most of the bone-related diseases were prone in involve elderly such as hip, wrist and spine fracture, required additional focus in understanding the biomechanics of bone. Due to the primary function of bone in withstand load during daily life activities, it is needed to understand the mechanical factors of bone. Improving understanding of bone metabolism and bone fracture aetiology is vital with the purpose of preventing fracture and identify the risk at an early stage. Therefore, the fluid-structure interaction between the bone marrow and trabecular bone need to be examined. With the purpose of understanding the bone marrow interaction between the trabecular bone and how it will have affected to mechanical properties, the finite element method was used. The simulation was designed to imitate real condition within trabecular bone during mechanical loading. These mechanical stimuli study may direct to the development of new approaches for enhancing bone healing while also help in preventing bone fracture. Therefore, current study might cover the following research questions;

1. How is the morphology of trabecular structure affecting the bone marrow characteristic.
2. How the orientation affects the local stress of trabecular structure and bone marrow flow properties at the tissue level.
3. What are the effects of morphology parameter indices correlation to the trabecular structure properties and bone marrow characteristics in physiological activity.
4. How the bone marrow within the structure contributes to trabecular bone strength.

1.3   Objective

This study is set out with the aim of assessing the importance on the interaction between the bone marrow and trabecular structure during physiological loading by using the FSI approach.

The specific objectives of this research are:
1.   To determine the relationship of structure morphology and mechanical stimuli of bone marrow.
2.   To investigate the effects of trabecular bone loading orientation to bone marrow characteristic.
3.   To identify the flow characteristics of bone marrow with respect to the normal walking loading conditions as a daily physiological activity.
4.   To determine the effect of bone marrow to the trabecular structure stiffness.

1.4   Scope of Study

This study concentrates on the fluid flow interaction within the trabecular bone of bovine femur. The bone marrow movements inside the trabecular bone were investigated in order to find out how it is affected by the bovine trabecular bone structure. Thus, the bone remodelling process behaviour from the bone marrow can be explored with the purpose of understanding the fluid characteristic phenomena. More specifically, the scope of this thesis study can be simplified as follow;

i.   Idealise models were constructed based on parameters from literature review studies.

ii. The real samples of trabecular bone are harvested from the bovine femur.

iii. Different orientations are considered for the morphology study and the FSI analysis.

iv. All harvested bovine specimens are scanned using high-resolution micro-CT scanner (Skyscan1172).

v. The scanning data were then being studied by using the ImageJ software for morphology study.

vi. The morphology parameters, such as trabecular thickness, trabecular separation, trabecular number, volume fraction, connectivity, Mean Intercept Length (MIL) and Structure Model Index (SMI) are obtained from the ImageJ software.

vii. The morphology data are compared with the previous study from the literature.

viii. The scanning images were constructed to three-dimensional (3D) images by using Mimics software.

ix. From the 3D images, the models of the trabecular bone structure are imported into the Comsol software for analysis.

x. Load and boundary conditions are applied to the trabecular structure with bone marrow surrounding the trabecular model.

xi. The movement of the bone marrow are studied while the different load applied such as uniaxial load and gait loading based on normal physiological activity.

xii. The relationship between morphology parameters of bovine trabecular bone and physical activities with bone marrow characteristics were determined.

1.5   Significant of Finding

Trabecular bone consists of a hierarchical complex structure which constantly changing under certain factors of mechanical and chemical. These structures of trabecular bone play the main role in the distribution of stress in the skeletal system. By the time, the bone will lose its mass, and the structure will experience deterioration [7]. As a result, the bone becomes fragile, and its structure might break. This condition called as osteoporosis disease. More than 8.9 million fractures were caused by osteoporosis annually [8] and in fact, 1 in 5 men and 1 in 3 women aged over 50, will experience osteoporotic fractures [9]. In the year 2000, 9 million of new osteoporotic fracture were estimated [10], and by the year 2050, the occurrence of hip fracture will increase by 240% to 310% [11]. Studies from previous research have consistently found that treatments can reduce the risk of osteoporotic fracture depending on the patients' population and drug used [12, 13]. However, with the bone remodelling process and adequate nutrient transport within the bone, the osteoporotic fracture can be prevented.

The key to bone health that can prevent bone fractures is the mechanism which involves bone loss and formations of new bone called bone remodelling. Undoubtedly, bone remodelling process also requires adequate nutrient transport through the bone cells. Amazingly the bone can heal itself when there is external loads act upon the cells which can trigger the signals to the bones and start building themselves up. These loads come from human daily life activities which also include house chores, daily walking, and sports activity. Then again, the loads from human daily life will lead to the movement of the bone marrow within the trabecular structure which will cause the shear stress. This shear stress is one of the factors which trigger the bone cells to start the bone remodelling process. The capability of remodelling its structure and mass in adapting to biomechanical loading in daily life activities brand the bone as the highly efficient material.

Since the osteoporotic fractures are one of the health burdens which causes impairment, morbidity, mortality and decreases the quality of life in elderly, it is vital to increase understanding on how the bone cells mechanical stimuli actually works. Moreover, the previous study only focusing on the bone material properties itself while overlooking the functions of bone marrow within the trabecular structures [14-18]. Therefore, the present study was focusing on quantification of the trabecular bone behaviour with a presence of bone marrow to improve the accuracy and validity of trabecular failure and prediction of the bone remodelling process, which was failed to be submitted by previous assessments. Moreover, accurate bone remodelling process through the bone cell was predicted by using the FSI approach. Subsequently, this study will contribute to the future development of strategies towards enhancing the bone healing process and osteoporotic fracture preventions.

1.6 Thesis Structure and Organisation

Chapter 1 presents an introduction to this research which provides an overview and the importance of FSI in the trabecular bone study. It consists of a background of study, problem statement, objective, scope and significance of this research. Then, continue with Chapter 2 is the literature review which contains review on bone, trabecular bone, bone remodelling process and FSI in the trabecular bone application based on study of previous researchers. Chapter 3 explain on what steps used to complete this research. Starts from model developments for the simulation purpose, morphological study of trabecular sample, Finite Element Analysis (FEA), results validation to the statistical analysis. The results and discussions were delivered in Chapter 4 which is divided into five main sections; the morphology indices on the trabecular bone model, behaviour of bone marrow towards physical structure, FSI modelling of bone marrow through trabecular bone under uniaxial compression, trabecular bone mechanic of gait loading with a presence of bone marrow, and the effect of bone marrow within the trabecular structure by comparing between multiphysics and single approach. Lastly, Chapter 5 concludes the findings accomplished in this study. The limitations and recommendations also are highlight for future works.

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