A simulation study of marrow fat effect on bone biomechanics

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***Abstract*—Bone marrow was assumed to be negligible on the aspect of bone mechanical behavior, where bone mass and bone mineral density were most studied. As a result, if the bone marrow, especially the marrow fat, plays a role in the bone mechanical properties is unknown yet. Marrow fat content was found increased in osteoporotic bone. However, the relationship between such change of bone marrow and bone strength is not clear yet. This study was proposed to investigate the effect of marrow fat on the bone biomechanical performance by computer simulations. A finite element model was established based on trabecular structure extracted from quantitative CT at L3 vertebrae. Simulations were conducted on the models with and without marrow fat under the same condition, respectively. The results showed that the cancellous bone with marrow fat had a 7.56%~18.81% higher maximum stress in trabeculae. Further, trabeculae with higher Young's modulus tend to sustain a higher maximum compressive stress when considering the marrow fat. As a conclusion, the marrow fat has effect on bone biomechanics, which cannot be ignored. Such effect in osteoporosis should be further investigated in deep.**

I. Introduction

Bone fracture is the key problem of osteoporosis [1], which is characterized by lower bone mass and degraded microstructure. Approximately 90 million (7.01% of the populace) osteoporotic suffers have been reported in China. In order to understand the mechanism of osteoporotic fracture, huge of studies have focused on the key factors of fracture. Especially in recent 10 years, bone strength is more and more emphasized rather than bone mineral density (BMD) because the latter factor cannot explain the osteoporotic fractures solely [2]. Currently, finite element analysis (FEA) is the most popular method for bone strength study by analyzing the biomechanical properties in terms of trabecular architecture and microstructure. Gibson [3] considered the trabecular bone as a cellular material and simplified the structure into four models according to the differences of bone density. Rietbergen [4] reconstructed the bone architecture by the combination of high-resolution CT image and FE model. Based on the system, Pistoia [5] explored that the application of FEA can lead to a better prediction of the bone failure than DXA (dual-energy X-ray absorptiometry) measurements and structural parameters.

Mechanical behavior of trabecular bone has been intensively investigated for more than 40 years [6]. The hard tissue, i.e. the trabecula, has become the focus in such studies. As a consequence, many technologies were developed to examine its property. Tensile testing [7], ultrasonic [8] and nanoindentation [9] were used to enhance the bone mineral density measurement. However, as a whole structure, the cancellous bone contains not only the hard tissue, but also the bone marrow, filling in the inter-trabecular spaces of the hard tissue. Ochoa [10] reported the biomechanics effect of bone marrow as inter-trabecular fluid and intraosseous pressure, which should be considered in bone strength investigation. Some other studies also revealed the bone marrow's mechanical effect on bone strength from different aspects. In vitro, experiments have demonstrated that marrow is responsive to hydrostatic pressure, fluid shear and local compositional factors such as medium viscosity. Gurkan [11] indicated that changes in mechanical and compositional environment of marrow may affect the fate of resident stem cells, which in turn may alter the homeostasis of bone in vivo. Coughlin [12] suggested that fluid induced shear stress affects bone anabolism by low magnitude high frequency vibrations on three-dimensional finite element models. It appears that bone marrow is not negligible in bone biomechanical investigations.

On the other hand, it was reported that marrow fat was increased in osteoporotic bone [13], indicating that more fat content filled in the inter-trabecular spaces during bone loss procedure. Whether such marrow fat increase contributes to bone strength deterioration is unknown yet. Under such circumstance, this study was proposed to investigate the marrow fat's effect on bone biomechanical properties. Two finite element models were established for cancellous bone with and without bone marrow respectively. The biomechanical properties of the two models were evaluated individually and compared with each other. Further, the model with marrow fat had simplified bone marrow as pure fat content.

II. Methodology

Research supported by the Basic Research Foundation (Outstanding Young Investigator Track) of Shenzhen (JC201005260124A), Research Grants Council of the Hong Kong Special Administrative Region, China (Project No. 465111), High-end Talent Oversea Returnees Foundation of Shenzhen (KQC201109020052A), and National Natural Science Foundation of China (81000647).

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A. Data acquisition and model construction

One female aged 63 years was chosen to take one hundred and ten QCT images (quantitative CT, by Lightspeed VCT 64) at L3 lumbar spine. The subject involved had normal BMD. Figure 1 displayed one image slice of the obtained data.

The DICOM (Digital Imaging and Communications in Medicine) data obtained from QCT was imported into Simpleware (Exeter) for FE models creating. Briefly, bone density (1.2g/cm^3) was calculated from Hounsfield absorption coefficient. To select the threshold for segmentation a measuring line (the yellow line in Fig. 2a) was drawn. Then image processing method was used to reconstruct the three dimensional gray image accordingly. As an inevitable result of image segmentation, noise points appeared as red arrows marked in Fig. 2b. Isolated island filter was applied several times to remove the noise points. Then a region of interest (ROI) with the dimension of 10×10×11 mm^3 was separated from the image and converted into 85 092 tetrahedral finite elements. By such procedure, the FE model of trabecular bone, namely Model-N was established. The model with marrow were created by Boolean operations since spongy bone is a complex network of intersecting curved plates and tubes filled with bone marrow. Model-N and Model-M hereinafter referred to the model with merely trabecula and the model filled with fat marrow (Fig. 2c and Fig. 2d).

B. Biomechanical compression simulations

In order to study the effect of fat marrow on bone mechanism, Model-N was set as the control group with the same boundary conditions. It is important to note that both the bone and fat marrow were assumed to be linear elastic material. The finite element analyses used poroelastic field with the elastic modulus calculated as Kenneth's formula:

$$E = \begin{cases} 2014\rho^{2.5} & \rho \le 1.2 \quad \mathrm{g/cm^3} \\ 1736\rho^{3.25} & \rho > 1.2 \quad g/cm^3 \end{cases} \qquad (1)$$

where ρ stands for the apparent bone density. The modulus turned to be 3 GPa, according with the accepted range from 0.4 GPa to 20 GPa. Other relevant parameters for bone (ν =0.3) and marrow (E=2 MPa, ν =0.17) were set as Lacroix [14].

The uni-axial compression simulations were performed in three manners. In the first manner, unified displacements equivalent to preset apparent strain were applied on the top surface (red color plane in Fig. 2c & d). The given apparent strain increased from 0.04% to 4%, where the corresponding displacement increased from 0.0044 mm to 0.44 mm. In the second manner, a compressive motion driven by loading velocities in the axial direction was introduced. The velocities were set as 0.08 mm/s, 0.1 mm/s and 0.2 mm/s (equivalent to strain rates as 0.007 s^{-1}, 0.009 s^{-1} and 0.018 s^{-1}). On the other hand, previous studies indicates that bone elastic modulus situation, elastic modulus in the simulation were performed from 0.1 GPa to 17 GPa [7-9].

No constraint was applied to the elements in X and Y directions. Interfaces of trabecular bone and marrow were assumed to be internal continuum boundaries, ensuring the two volume moved together as the biological confinement of bone marrow by trabeculae. This setting guaranteed the lateral elements could deform in horizontal and perpendicular to loading. The maximum and average apparent stress, and the bone tissue stress were selected as bone mechanical features.

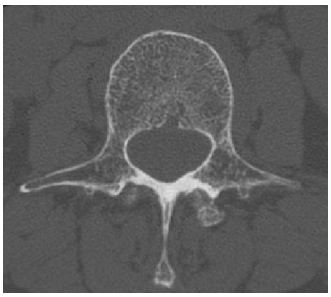
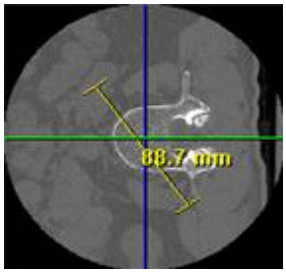
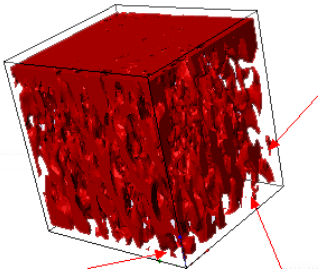


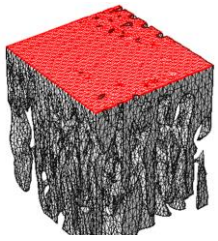
Figure 1. One slice of QCT image at L3 vertebrae, the subject is female, 63 years old, with normal BMD



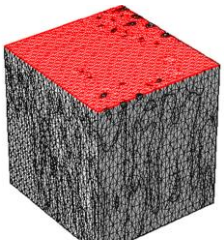
a. Threshold extraction from the QCT image



b. ROI with a dimension of 10×10×11 mm^3 (red arrows pointing at isolated noise points)



c. Model-N: FE model with merely trabecular bone



d. Model-M: FE model of trabecula filled with fat marrow

Figure 2. The procedure of three-dimensional reconstruct for spongy bone and fat marrow

III. Results

Both models were subjected to similar compressive simulation tests using COMSOL MUTIPHYSICS, and the top surface and the bottom surface of models were selected as the compression plate, where the bottom surface was fixed and the top surface had a uniform displacement or a velocity. Apparent stress and compressive stress in tissue of both models were investigated. For Model-N, the apparent stress under 1% strain is 21.61 MPa, whereas 23.24 MPa for Model-M. These values are comparable to the previous study [15]. Based on the model, we further investigated the biomechanical properties of bone to evaluate the effect of marrow fat.

A. *Unconfined compressive test under displacement control*

The von Mises stress distribution from Model-N and Model-M under 1% apparent strain are displayed in Fig. 3. The maximum compressive stress in tissue for Model-N and Model-M are 311.95 MPa and 370.62 MPa respectively. The average compressive stress in tissue in Model-N and Model-M are 15.33 MPa 16.90 MPa. It shows the marrow fat effect on the biomechanics, i.e. in maximum compressive stress by 18.81% increase and in the average stress by 10.25% increase than the model with merely trabecular bone.

The model performance was further investigated under different apparent strain conditions with results summarized in Fig. 4. The displacement, which equivalent to 4% apparent strain on the top surface, results in a maximum apparent stress with 86.42 MPa and 92.95 MPa in the Model-N and Model-M respectively. The average stress in Model-N is 25.98 MPa, which is about 16.67% lower than 30.31 MPa in the Model-M.

B. *Unconfined compressive tests under strain-rate control*

Three different velocities (0.08mm/s, 0.1mm/s, 0.2mm/s) are employed in current study, where the corresponding strain rates are 0.007 s^{-1}, 0.009 s^{-1}, 0.018 s^{-1} respectively, which meet the strain rate in daily acticities[16]. The strain rate is 0.008 s^{-1} and 0.02 s^{-1} in daily activities and at severe impact fractures respectively [16]. The termination time of the simulation are 1.42s, 1.11s, 0.55s, which equavalent to 1% strain of the model.The result in Fig. 5 indicated that the maximum apparent stress in both models decreased with the larger strain rate. Relevant parameter values were marked on the histogram for comparation.

C. *Simulation with varied Young's modulus*

The elastic modulus of trabecular bone vary widely with aging and disease. To figure out the possible explaination of this phenomenon, the study also focused on the variation trend of growth rate of models with elastic modulus increased from 0.1 GPa to 17 GPa (Fig. 6). The growth rate is the quotient of D-value and the corresponding stress in Model-N. All the simulations were finished with prescribed 1% apparent strain. For the maximum apparent stress, the growth rate is 22% at 0.1 GPa and it gradually reduces to a stable value (7%) with the Young's modulus increasd to 5.4 GPa. Similarly, the average apparent stress decreased from 42% (0.1 GPa) to 15% (13.4 GPa), and the average compressive stress in tissue decreased from 22% (0.1 GPa) to 10% at 3 GPa. However the maximum compressive stress in tissue had absolutely different behavior. The model without marrow suffered larger

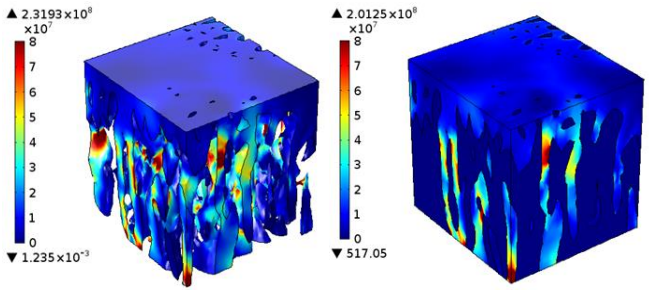


Figure 3. The von Mises stress distribution under 1% apparent strain

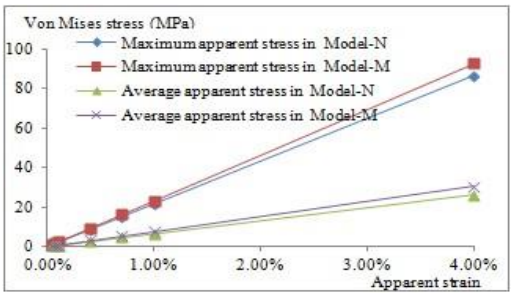


Figure 4. Maximum and average apparent stresses (MPa) in Model-N and Model-M with apparent strain increased from 0.04% to 4%

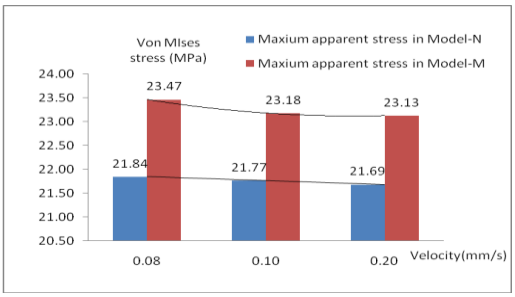


Figure 5. Von Mises stresses (MPa) in the volume with loading velocity increased from 0.08 mm/s to 0.2 mm/s

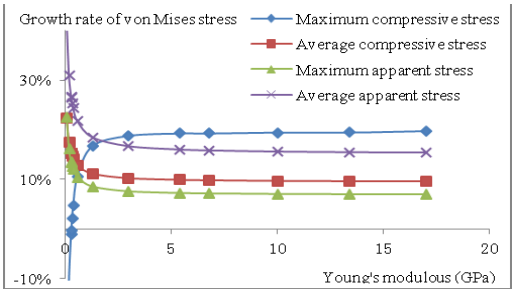


Figure 6. Growth rate of von Mises stress with Young's modulus increased from 0.1 GPa to 17 GPa

maximum tissue stress when the modulus is less than 0.31 GPa. After that the model with marrow suffered larger and the growth rate increased to 20% at 17 GPa.

IV. Discussion

Carter [17] firstly considered bone marrow in compression test on cancellous bone. He confined cylindrical trabecular bone samples with rigid annulus and reported that the presence of bone marrow increased the strength only at high strain rate of 10 s^{-1}. The conclusion was argued by Zysset P K [18] for its inappropriate classification of cortical bone and spongy bone. However, the marrow effect on bone mechanics is still debatable due to different experiment condition or varied simulation approaches. In addition, no study specifically investigated the yellow marrow's effect on the bone strength. An increased marrow fat content in subjects with lower bone mineral density was reported by Griffith [19,20] by a series of MRI based studies. The marrow fat becomes another concern on the decreased bone strength in osteoporosis.

In this study two approaches were adopted to evaluate the mechanical properties of trabecular bone under different

loading conditions. For unconfined compressive tests under the same boundary conditions, Model-M suffered larger apparent stress and compressive stress in tissue. This result is in agreement with a previous study by Rosen [21], who suggested the physiological existence of fat marrow could magnify trabecular stress. From the simulation, we can also observe that stress distribution was well balanced in Model-M. Under mechanical loadings, trabecular bone fracture is more likely to occur in Model-N for its unbalanced deformation. These observations may imply that bone marrow fat may decrease the risk of bone fracture. In conclusion, the marrow augmented the stress but balance its distribution. For samples with different velocities, the peak value decreased with increasing strain rate which accords with the anatomical sample tests by Chaari F.

In terms of the wide range for trabecular tissue modulus, Ladd [22] reported a reduction of elastic modulus with increasing age. Therefore it is of clinical relevance to discover how much of this variation affects the mechanical behavior of bone. This study explored elastic modulus effect (0.1 GPa to 17 GPa) in displacement control compression tests and discovered the same phenomenon that stress distribution was well balanced in Model-M. Another unexpected result is the growth rate of apparent stress in Model-M decreased with the increasing trabecular elastic modulus. This indicates that for the osteoporotic suffers, the increased trabecular Young's modulus and increased marrow fat could decrease the trabecular stress.

Using finite element method, the stress simulation can be applied on the same architecture repeatedly to study the maximum stress and find better physical method to simulate the vivo. With the enhancive displacement, linearly increased maximum stress was found and this fits the poroelastic medium set for bone. However, some limitations of this study must be considered. The primary one is the simplification of bone and marrow as solid homogeneous material with constant Young's modulus. In future, anisotropy material and red marrow should be taken into consideration.

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