

Computational Modeling of Trabecular Bone Marrow

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Introduction

Trabecular bone is located at the end of long bones, in irregular bones such as the sternum and the skull, and in the vertebral bodies of the spine. Found within the porous structure of trabecular bone is bone marrow. This is a highly specialised environment home to numerous cell types. It is the origin of many of the cells in the body and as such is one of the most vital tissues. Since it was found that during normal loading rates marrow does not contribute to the overall stiffness of the bone, the mechanics of bone marrow have largely been ignored [1]. In recent years there has been an increased focus on mechanical environment of bone marrow with the reason for this being that marrow is home to Mesenchymal Stem Cells (MSCs). MSCs are capable of forming a number of cell types and tissues such as bone cartilage and fat. The unique micro-environment in which MSCs reside is termed the stem cell niche. It consists of a host of different cells including hematopoietic progenitors and their progeny, as well as MSCs and their progeny including fibroblasts, endothelial cells, adipocytes, osteoblasts, osteocytes found embedded in bone and osteoclasts (Kuhn and Tuan, 2010). Schofield identified the niche as having three main functions (1) maintaining quiescence, (2) promoting cell number and (3) directing differentiation [2]. As MSCs are known to be mechano-sensitive *in vitro* [3]; [4] an understanding of the mechanical environment of which they experience *in vivo* will help to delineate the role of mechanical loading in the niche. The aim of this study is to validate an idealized trabecular bone structure by analysing the permeability using Darcy's Law. Results are compared to experimentally determined values of permeability for trabecular bone. Methods are then applied to novel Fluid Solid Interaction (FSI) models of the bone and marrow and finally applied to realistic geometries determined from micro CT scans.

Materials and Methods

Models of trabecular bone and marrow were established using Abaqus Explicit and Abaqus CFD (v6.11). For initial studies an idealized structure for trabecular bone was used with the marrow being the inverse shape (Fig. 1(a)) [5] [6]. To validate the use of such a structure analyses were performed to calculate the permeability using Darcy's Law.

$$U_D = \frac{Q}{A_s} = \left(\frac{k}{\mu} \right) \frac{P_u - P_d}{L_s}$$

where U_D is the Darcy's velocity, Q is the volume flow rate, A_s is the CSA of the model, k is the permeability, μ is the viscosity (water 1mPa.s), P_u is the upstream pressure, P_d is the downstream pressure and L_s is the length of the bone (Fig. 1(b)).

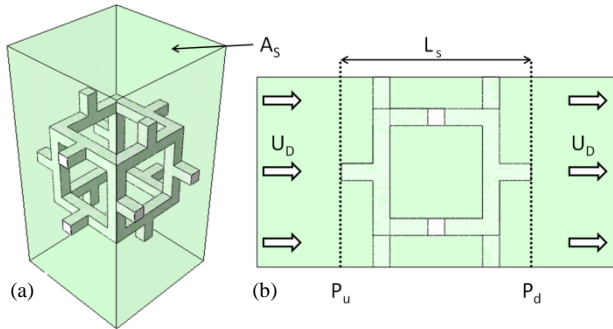


Figure 1: (a) Idealized trabecular bone based on [5] [6] and (b) analysis for permeability study using Darcy's Law.

Different bone volume fractions were examined, to determine the effect of lower bone fractions associated with disease states such as osteoporosis. FSI models were also examined for different mesh densities to determine the effect of fluid/structure meshes and how they interact. The pressure in the marrow and shear stress at the bone/marrow interface was examined for different volume fractions to determine the influence of bone volume on the possible mechanical stimulation experienced by MSCs in the marrow. The viscosity of the bone marrow was determined experimentally to be 1Pa.s and was used in the FSI

analyses. FSI models of realistic trabecular bone geometries were created using previously developed software (FEEBE [7]).

Results

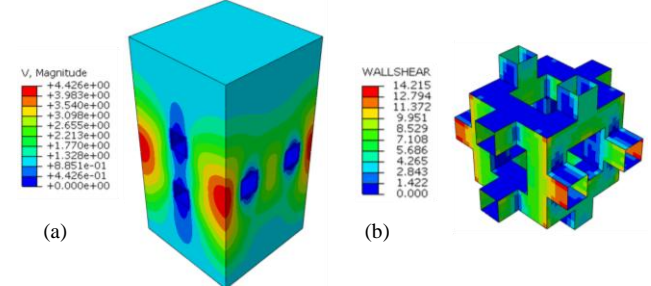


Figure 2: (a) Velocity magnitude (mm/s) for 20.4% bone volume for Darcy's law investigation and (b) wall shear stress (Pa) at the bone/marrow interface for FSI analysis.

Fig. 2(a) shows the velocity in the marrow of a 20.4% bone volume model. A linear relationship between the average pressure gradient and the Darcy velocity was confirmed and the permeability of the idealized trabecular bone structures was found to fall within known ranges of trabecular bone [8] with $3.01 \times 10^{-7} \text{ m}^2$ (6.8% bone volume), $2.33 \times 10^{-9} \text{ m}^2$ (13.98%) and $7.49 \times 10^{-11} \text{ m}^2$ (20.4%). When the pressure within the marrow was examined it was found that the higher bone volume (20.4%) produced higher pressure (2 kPa) in the marrow (50 times greater than the 6.8% bone volume) and wall shear stress (Fig. 2(b)) at the bone marrow interface compared to the lower bone volumes (~100 times greater than the 6.8 and 13.98% bone volumes). Fig.3 shows the FSI methods applied to realistic geometries.

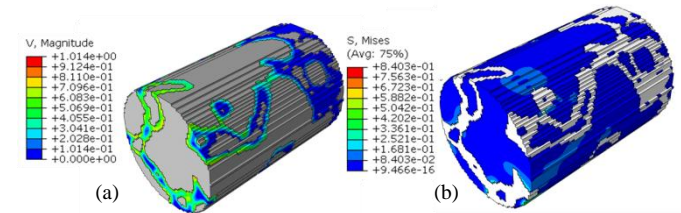


Figure 3: (a) velocity (mm/s) within FSI model of realistic trabecular bone and marrow, bone in grey for clarity, (b) stress (MPa) within the bone from the same FSI model of trabecular bone and marrow, marrow in white for clarity.

Discussion and Conclusion

The idealized structures and repeating cell approach was found to be appropriate for determining micro-mechanical effects within the bone marrow, based on values of permeability obtained. The novel FSI models here move away from previous modeling approaches which either modeled the bone as rigid or the marrow as a soft solid. Results from this study give a unique insight into the micromechanical environment of the stem cell niche for different bone volume fractions. Values for pressure and wall shear stress suggest that the 20.4% volume fraction is producing the greatest stimulatory effect for new bone formation, showing the detrimental effect of lower bone volumes associated with diseases like osteoporosis. Further work will involve the comparisons of different realistic geometries, identifying the mechanical loading which stem cells are susceptible under different regimes.

References

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