JOURNAL OF THE MECHANICAL BEHAVIOR OF BIOMEDICAL MATERIALS 65 (2017) 90–101

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Research Paper

Contribution of fluid in bone extravascular matrix to strain-rate dependent stiffening of bone tissue – A poroelastic study

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ARTICLE INFO

Article history:
Received 18 April 2016
Received in revised form
22 July 2016
Accepted 6 August 2016
Available online 13 August 2016

Keywords:
Bone mechanics
Poroelasticity
Hydraulic stiffening
Strain rate
Tissue microstructure

ABSTRACT

Osteoporotic fractures represent an increasing cost to society, and its diagnosis methods based on bone density still lack accuracy in identifying risk of fracture. This is why a better understanding of mechanical behavior of bone tissue is of importance, especially when it comes to relating experimental observations to realistic physiological fall loading conditions. This study aims at exploring the stiffening effect of pore fluid in bone extravascular matrix subject to high strain rate loading that is more realistic to simulate a physiological fall. A computational approach is used, where bone tissue microstructure extracted from micro-CT images is modeled using finite elements. The solid phase of bone tissue is modeled as a poroelastic material, a porous matrix filled with fluid. When the extravascular matrix experiences certain volumetric deformation, the fluid in pores presents load carrying capacity, which consequently varies the apparent stiffness of bone tissue. It is shown that effects of fluid stiffening in bone can be significant, depending on the chosen material properties, the amount of volumetric strain in tissue and the loading rate with respect to hydraulic conductivity and drainage conditions. It is also shown that such stiffening effect is influenced by bone microstructure, and is more significant in cortical bone than in trabecular bone.

1. Introduction

Bone is a porous medium filled with fluid, which can be found in pores at several length scales ranging from millimeters to approximately 1 μm. Trabecular bone, often found in the head of long bones and in vertebrae, is formed of a spongy structure. The solid matrix of the trabecular bone is formed by trabeculae that are spatially connected and its void is filled with bone marrow. The average distance between trabeculae is found to be of dimension of 0.5–1 mm (Ulrich et al., 1999). The vascular porosity of cortical bone, i.e. the denser bone forming the outer shell of long bones, is formed of microscopic canals of dimension in the order of 100 μm (Wang et al., 2003). The solid phase of these two types of bone tissue, often referred to as bone extravascular matrix, can also be seen as a porous medium, although at a lower length scale.

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http://dx.doi.org/10.1016/j.jmbbm.2016.08.016
1751-6161/

Its porosity, often referred to as the lacunar-canalicular network, is formed by the lacunae containing osteocytes (of a dimension between 5–20 μm (Dong et al., 2014)) and spatially inter-connected by small channels, the canaliculi, of a diameter between 0.2–0.5 μm (Varga et al., 2015).

Osteoporosis, the loss of bone mass density with age, is a major health issue whose socio-economic cost increases with aging population. Current approaches against osteoporosis-related fractures include prevention of falls, exercise, nutrition and the administration of anabolic or antiresorptive drugs (Kanis et al., 2013). Clinical diagnosis relies on measurement of bone mineral density (BMD) using Dual-energy X-ray absorptiometry (DEXA) which can be further enhanced by patients risk factors, FRAX (Kanis et al., 2008), or the analysis of bone turnover biological markers (Kanis et al., 2013). Unfortunately these methods present certain limitations. BMD, for example, which is an index that takes into account bone size, porosity and mineral density, is somewhat incapable of accounting for the differences in bone loss pattern at the microstructural scale (Seeman and Delmas, 2006). Quantitative computed tomography micro finite element (micro-FE) models have been proved to provide more accurate prediction of femoral strength than BMD by accounting for bone microstructure (Dall'Ara et al., 2013).

Fractures in osteoporotic bone usually occur after a fall at high loading rate. Although experimental measurement of strain in bone during fall conditions remains challenging (Grassi and Isaksson, 2015), recent development of drop tower tests, where a mass is dropped onto a femur from a certain height in order to reproduce a fall configuration (Gilchrist et al., 2013), has led to an estimate of strain rates above 20 s^{-1} (Ariza et al., 2015). Experiments on tissue samples of trabecular (Carter and Hayes, 1977) and cortical bones (Cloete et al., 2015; Hansen et al., 2008; McElhaney, 1966) have shown a notable strain rate dependency of bone elastic modulus. Although early studies determined a logarithmic relationship between the apparent Young's modulus and strain rate (Carter and Hayes, 1977; McElhaney, 1966), some studies reported a drastic transition in strain rate sensitivity over a critical range of strain rate, over which the apparent stiffness of tissue increases significantly (Cloete et al., 2015; McElhaney, 1966). Nanoindentation of bone matrix has also shown such an increase of the derived Young's modulus with respect to strain rate (Fan and Rho, 2003; Isaksson et al., 2010).

Incorporating such strain rate dependency into Finite Element models to assess bone quality can be done through the use of empirically derived viscoelastic models (Cloete et al., 2015; Johnson et al., 2010; Sasaki et al., 1993). The empirical nature of these models, where two or more time constants are determined to fit the experimental results, do not allow discriminating different physical relaxation mechanisms, which may include fluid motion in canals and viscoelasticity of collagen fibers (Lakes and Katz, 1979). It is worth noting that such physical mechanisms might be affected, to different extents, by tissue microstructure, loading and boundary conditions of the chosen sample. Although it has been reported that collagen viscoelasticity could result in time dependent behavior in bone, the role of fluid phase in bone at high strain rate still remains unclear.

On one hand, there has been a long standing debate concerning whether or not bone, at organ level, could undergo hydraulic stiffening as a result of marrow pressurization (Bryant, 1995). Experiments where small holes were drilled in canine femoral heads in order to disrupt the fluid boundary conditions showed a significant reduction in bone stiffness due to altered fluid drainage (Ochoa et al. 1991). It has however been advanced that their loading scenario lacked relevance to physiological loading conditions (Bryant, 1995). Other experiments have shown a clear increase in stiffness and strength of trabecular bone samples at high strain rate, due to the presence of bone marrow, under undrained and confined compression tests (Carter and Hayes, 1977). But once again, the relevance to physiological loading conditions could be discussed. On the other hand, at the nanometer scale, bone mechanical properties clearly vary depending on its water content. Indeed, several nanoindentation studies (Guidoni et al., 2010; Wolfram et al., 2010) have reported higher elastic moduli for dehydrated compared to hydrated samples, which demonstrates an influence of water content in the mechanical properties of bone tissue. Based on the aforementioned experimental evidence from the literature, it is therefore important to investigate the role of fluid phase in the bone mechanical behavior, particularly at high strain rate, which is crucial for assessment of fracture risk in realistic fall conditions.

In this study, poroelasticity is employed, with the aim of understanding the physical mechanism of the stiffening effect in bone tissue subject to high strain rate, to explore how fluid in the bone extravascular matrix affects its time dependent behavior. Modeling of poroelasticity in human tissues has been extensively investigated for cartilage (Mow et al., 1984). Bone is a much stiffer material however, with a Young's modulus much higher than cartilage, and it is expected that pore fluid might have a different effect on its macroscopic mechanical behavior. We use a micro-FE approach based on bone microstructures to study the interplay between the poroelastic behavior of bone extravascular matrix and bone microstructure at tissue scale. We then further investigate how fluid phase affects bone apparent stiffness at different strain rates. It is worth mentioning that although a poromechanics approach has already been used in literature to model bone tissue (Cowin, 1999; Hellmich and Ulm, 2005; Sandino et al., 2015) either from a theoretical or computational perspective, it is still unclear how various factors, such as the wide range of existing material properties, boundary conditions, loading rates, and tissue microstructures, affect the assessment of bone mechanical behavior, especially under high strain rates. Therefore, a key issue in this study is to determine the loading and boundary conditions relevant to physiological conditions that may better reflect the tissue behavior *in vivo*, for numerical investigations as well as experimental setups. Quantifying the stiffening effect of bone fluid in its apparent properties, depending on the aforementioned factors, could therefore lead to an improved assessment of bone fracture risk under realistic loading scenarios.

2. Materials and methods

2.1. Poroelasticity formulation of the bone extravascular matrix

When applying mechanical loading on a porous microstructure filled with fluid, fluid sustains part of the load due to