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Short communication

Determine the equilibrium mechanical properties of articular cartilage from the short-term indentation response

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ABSTRACT

Indentation testing is widely used to evaluate the mechanical properties of articular cartilage. However, most curve-fitting solutions for indentation analysis require the deformation data of cartilage at the equilibrium state, which often takes the tissue hours to reach. The lengthy testing time reduces the efficiency of indentation, increases the chance of tissue deterioration, and prevents *in vivo* applications. To overcome these limitations, a novel technique based on principal component analysis (PCA) was developed in this study, which can predict the full indentation creep curve based on the first few minutes' deformation history and the principal components. The accuracy of this technique was confirmed using the indentation data from 40 temporomandibular joint condylar cartilage samples and 17 bovine knee joint samples. The mechanical properties determined by biphasic curve-fitting using predicted and experimental data are in good agreement, with the difference between the two less than 5%. For TMJ and knee cartilages, it is found that any number of full tests beyond eight will not lead to any increase larger than 1% in the accuracy, indicating a low sample number required for prediction. In addition, the principal components of indentation creep curves are consistent for the same type of cartilage tested with identical protocols, but significantly different between two distinct cartilages. Therefore PCA may also represent a new method to compare the mechanical behaviors of different cartilages, as it avoids the assumptions associated with mechanical constitutive models and relies purely on the experimental data.

1. Introduction

Indentation testing is widely used to determine the mechanical properties of articular cartilage (Mow et al., 2005). Since the tissue is left untouched on the bone and tested in its natural state without disturbing the structure and pre-stress in the solid matrix, indentation serves as a major technique for the *in situ* or potentially *in vivo* evaluation of cartilage mechanical properties. As the testing device only records the history of tissue deformation or force response, mechanical properties of the tissue have to be obtained by analyzing the experimental data with a proper constitutive model for cartilage. Hayes et al. (Hayes et al., 1972) developed an indentation solution based on linear elastic theory, which correlates the Young's modulus and Poisson's ratio with indentation force and deformation by a closed-form equation. However, one of the two properties, usually Poisson's ratio, has to be assumed *a priori* to determine the other property using this equation (Hoch et al., 1983; Mow et al., 1989). Later a technique utilizing multiple creep tests on a sample with different-sized indenter tips was developed which can extract both elastic properties of cartilage (Jin and Lewis, 2004). Another widely used indentation solution was developed by Mow et al. based on biphasic theory and the Hayes elastic solution (Mow et al., 1980; Mak et al., 1987; Mow et al., 1989), which can simultaneously determine the aggregate modulus, shear modulus and permeability of the tissue using a single indentation creep test (Athanasiou et al., 1991). With the advent of finite-element software and advanced porous media theories, complex constitutive models such as triphasic mixture theory are also used to analyze indentation data (Le and Fleming, 2008; Lu et al., 2010). Most of these analytical solutions for indentation require the equilibrium deformation data for curve-fitting, since the deformation-load correlation at equilibrium stage (with no fluid flow) can be defined by the closed-form Hayes solution (Hayes et al., 1972; Mow et al., 1989; Jin and Lewis, 2004; Lu et al., 2004). Due to the significant viscoelastic behavior of cartilage, however, it may take up to several hours for the tissue to reach a final steady state, where the characteristic time of creep is defined as $t=a^2/H_a*k$ (a=indenter tip size, H_a=tissue modulus, and k=hydraulic permeability) (Spilker et al., 1992; Bae et al., 2006; Han et al., 2011). Such a long testing time reduces the efficiency of indentation and

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hinders *in vivo* applications. For example, creep testing of five regions on a small animal joint could take a dozen hours (Lu et al., 2009), which considerably increases the possibility of tissue degeneration during testing.

The primary objective of this study is to develop a data processing technique using principal component analysis (PCA) which can predict the full indentation creep curve based on the transient data obtained in the first few minutes of indentation testing. The accuracy of the prediction is verified using experimental data from two types of articular cartilage - bovine knee cartilage and condylar cartilage from the porcine temporomandibular joint (TMJ). The mechanical properties determined by biphasic theory based on predicted curves are compared with those from full experimental data in order to validate the accuracy of this method.

2. Materials and methods

2.1. Indentation testing

Indentation creep tests were performed on condylar cartilage from porcine TMJ and bovine knee cartilage, as described in previous studies (Lu et al., 2004; Lu et al., 2009). Briefly, seventeen 2 cm × 2 cm rectangular cartilage-bone blocks were harvested from the trochlear groove of mature bovine knee joints. Samples were mounted onto a step-loading indentation device equipped with a rigid flat-ended porous–permeable indenter tip (ϕ=2.1 mm). At the start of the creep test, a 50 mN tare load was applied for 0.5 h, followed by a 200 mN step load for another 1 h to generate the creep data. Additionally, eight TMJs were harvested from mature porcine heads, and five regions (anterior, posterior, central, medial, and lateral) on the condylar head were indented by a custom-built micro-indenter with a porous-permeable indenter tip (ϕ=1.6 mm), by the same loading protocol detailed for bovine cartilage (Lu et al., 2009).

2.2. Principal component analysis

The creep displacement of each sample was first resampled at 1 Hz by linear interpolation and denoted as an $n \times 1$ vector t. Vectors from m samples were further combined into an $m \times n$ matrix. Principal component analysis (PCA) (Jackson, 1991) was then conducted on this matrix without centering, which generated m principal components. Each obtained principal component is an $n \times 1$ unit vector, denoted as PC_i. Based on the PCA definition, the creep curve (vector t) can be decomposed by the principal component matrix PC as

$$\begin{bmatrix} t_1 \\ t_2 \\ \vdots \\ t_n \end{bmatrix} = \begin{bmatrix} PC_{1_1} & PC_{2_1} & \cdots & PC_{m_1} \\ PC_{1_2} & PC_{2_2} & & PC_{m_2} \\ \vdots & & \ddots & \vdots \\ PC_{1_n} & PC_{2_n} & \cdots & PC_{m_n} \end{bmatrix} \begin{bmatrix} c_1 \\ c_2 \\ \vdots \\ c_m \end{bmatrix} \quad or\ t = \sum_{i=1}^{m} c_i \times PC_i \ where\ c_i = t \cdot PC_i \qquad (1)$$

Here c_i is the two norm of vector t's projection on PC_i. We now hypothesize that the principal components are consistent for the same type of cartilage tested with an identical protocol. Therefore the creep curves of the other samples, which are not initially included in the m samples for PCA, can also be decomposed by the above principal components PC. To verify this assumption, we performed PCA on 50 different combinations of five indentation creep curves that were randomly selected from either bovine knee joint samples or TMJ samples, *i.e.*, 50 PCA for each type of cartilage. The variances of 50 obtained PCs at each time point (n total points) were calculated to determine the consistency of PCs.

Based on the PCA consistency assumption, the short-term creep displacement ($\hat{t}$) of a new sample can be decomposed by the principal component matrix PC as

$$\begin{bmatrix} \hat{t}_1 \\ \hat{t}_2 \\ \vdots \\ \hat{t}_k \end{bmatrix} \approx \begin{bmatrix} PC_{1_1} & PC_{2_1} & \cdots & PC_{m_1} \\ PC_{1_2} & PC_{2_2} & & PC_{m_2} \\ \vdots & & \ddots & \vdots \\ PC_{1_k} & PC_{2_k} & \cdots & PC_{m_k} \end{bmatrix} \begin{bmatrix} \hat{c}_1 \\ \hat{c}_2 \\ \vdots \\ \hat{c}_m \end{bmatrix} \quad or\ \hat{t}(1:k) = \sum_{i=1}^{m} \hat{c}_i \times PC_i(1:k),\ \mathrm{k} < n. \qquad (2)$$

Here vector $\hat{t}(1:k)$ contains only k components ($k \ll n$) since it represents only the first k seconds of a creep curve. $PC_i(1:k)$ denotes the first k components of PC_i. If the shortened principal component matrix is denoted as B, the coefficient vector $\hat{c}$ can be calculated as

$$\hat{c} = \left(B^T B\right)^{-1} B^T \hat{t}(1:k) \qquad (3)$$

Note that $\hat{c}$ is the coefficient vector with m components. The long-term creep deformation of the sample after k seconds, $\hat{t}(k+1:n)$, can be estimated using $\hat{c}$ and matrix PC.

$$\begin{bmatrix} \hat{t}_{k+1} \\ \hat{t}_{k+2} \\ \vdots \\ \hat{t}_n \end{bmatrix} \approx \begin{bmatrix} PC_{1_{k+1}} & PC_{2_{k+1}} & \cdots & PC_{m_{k+1}} \\ PC_{1_{k+2}} & PC_{2_{k+2}} & \cdots & PC_{m_{k+2}} \\ \vdots & & \ddots & \vdots \\ PC_{1_n} & PC_{2_n} & \cdots & PC_{m_n} \end{bmatrix} \begin{bmatrix} \hat{c}_1 \\ \hat{c}_2 \\ \vdots \\ \hat{c}_m \end{bmatrix} \quad or\ \hat{t}(\mathrm{k}+1:\mathrm{n}) = \sum_{i=1}^{m} \hat{c}_i \times PC_i(k+1:n) \qquad (4)$$

Thus PCA of the full creep curves from a small group of samples can generate the principal component matrix, and then the long-term creep data of the other samples can be predicted by their short-term response using this matrix.

2.3. Accuracy of predicted data

To test the accuracy of the predicted curve, eight sets of full indentation data were randomly selected for each type of cartilage to generate the corresponding principal components, and the first 10 min' data from the unselected samples were used to predict their long-term response with PCA. The predicted curves were directly compared with the actual long-term experimental data. Moreover, the mechanical properties (aggregate modulus, Poisson's ratio, permeability) were obtained for both the predicted curve and the actual experimental data using a biphasic curve-fitting program (Mow et al., 1989). The agreement between the two sets of mechanical properties was then examined (Martin Bland and Altman, 1986).

3. Results

To understand the effectiveness of PCA for predicting cartilage indentation data, PCA of all the creep curves were performed to obtain the contribution to the total variance of each principal component (PC) (Fig. 1). The first PC alone contributes 98.5% and 99.8% to the total variance for TMJ and knee cartilage, respectively. The first and second PCs contribute over 99.5% of the variance for both tissues. Thus, in the following PC consistency analysis, only the first two PCs were presented, as the third and higher PCs contribute little to the total variance. For each type of tissue, average and standard deviation of the first two PCs from 50 analyzed groups are shown in Fig. 2. The standard deviations are close to 0 for PC1 at all points, *i.e.*, PC1 remains constant for any five randomly selected indentation curves. The standard deviations of PC2 are larger than PC1, but PC2 explains only 1.4% and 0.1% of variance for TMJ and knee cartilages, respectively. Therefore, it can be concluded that the principal components are consistent for the same type of cartilage. In contrast, indentation curves of TMJ and knee cartilage have drastically different PCs in terms of magnitude and distribution over time (Fig. 2).

Two typical experimental creep curves for each cartilage are plotted in Fig. 3 together with the PCA prediction. The first 10 min' data and the PCs based on eight creep curves are able to provide an accurate prediction of the long-term indentation responses for both types of cartilage. The average difference of equilibrium deformation

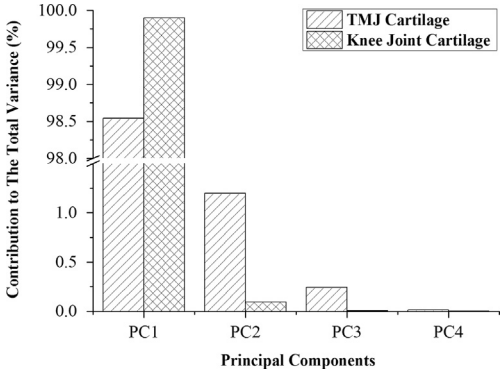

Fig. 1. Contribution of principal components to the total variance of indentation creep curves. The first principal component (PC1) explains 98.5% and 99.8% of the total variance for TMJ cartilage and knee joint cartilage, respectively. The third principal component contributes less than 0.5%.