Predicting the effective elastic property of human cancellous bone using the convolutional neural network method

Yongtao Lu[1,2,3*], Zhuoyue Yang[1], Hanxing Zhu[4], Chengwei Wu[1,2*]

[1]Department of Engineering Mechanics, Dalian University of Technology,

[2]State Key Laboratory of Structural Analysis for Industrial Equipment, Dalian University of Technology, No. 2 Linggong Road, 116024, Dalian, China

[3]DUT-BSU Joint Institute, Dalian University of Technology, Dalian, 116024, China

[4]School of Engineering, Cardiff University, Cardiff, UK

Corresponding author:

Prof. Chengwei Wu

Department of Engineering Mechanics,

Dalian University of Technology

No.2 Linggong Road, 116024, Dalian, China

Email: cwwu@dlut.edu.cn

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Abstract

The efficient prediction of biomechanical properties of bone plays an important role in the assessment of bone quality. However, the present techniques are either of low accuracy or of high complexity for the clinical application. The present study aims to investigate the predictive ability of the evolving convolutional neural network (CNN) technique in predicting the effective compressive modulus of porous bone structures. The T11/T12/L1 segments of thirty-five female cadavers were scanned using the HR-pQCT scanner and the images obtained from it were used to generate 10896 2 D bone samples, in which only the cancellous bony parts were processed and investigated. The corresponding 10896 heterogeneous finite-element (FE) models were generated, and then a CNN model was constructed and trained using the predictions of the FE analysis as the ground truths. Then the remaining 260 bone samples generated from the initial HR-pQCT images were used to test the predictive power of the CNN model. The results show that the coefficient of the determinant (R^2) from the linear correlation between the CNN and FE predicted elastic modulus is 0.95, which is much higher than that from the correlation between the BMD and the FE predictions (R^2 = 0.65). Furthermore, the 95th and 50th percentiles of relative prediction error are below 0.28 and 0.09, respectively. In the conclusion, the CNN model can efficiently predict the effective compressive modulus of human cancellous bone and can be used as a promising and clinically applicable method to evaluate the mechanical quality of porous bone.

Keywords: Convolutional neural network, cancellous bone, mechanical property, prediction error

1. Introduction

Prediction of the mechanical properties of the human bone tissues is of great importance for the assessment, prevention and early treatment of bone fracture. Currently, using the measurements of the bone mineral density (BMD), such as the areal bone mineral density (aBMD) obtained from the dual energy X-ray absorptiometry (DXA) and the volumetric BMD (vBMD) obtained from the quantitative computed tomography (QCT), are widely used in clinic. However, the aBMD obtained from the DXA contains neither the information on the bone microarchitecture nor any mechanical property of the bone tissues, and the vBMD cannot provide information on the distribution of the BMD and the bone microarchitecture. Because the increasing risk of bone fracture is caused not only by the loss of bone mass but also by the deterioration of the bone microarchitecture, neither aBMD nor vBMD can provide a good prediction of the mechanical property of the bone tissues and approximately only 50% of the variability in the vertebral fracture can be predicted by these BMD measurements (**Dong et al., 2018; Ebbesen et al., 2000; Lochmueller et al., 2002; Lu et al., 2015**).

In the last a couple of decades, the subject-specific finite element (FE) models of bone tissues have been widely used to predict the mechanical properties of bone tissues (**Chevalier et al., 2009; Lu et al., 2014, 2019; Pistoia et al., 2002; Wang et al., 2012**). It has been demonstrated that the three-dimensional (3D) FE models of bone have a higher ability for predicting the bone fracture loads than the densitometry measurements (aBMD and vBMD) (**Lu et al., 2014; Wang et al., 2012**). However, because of the high complexity in generating the 3D FE models of bone tissues (including the process of segmenting the bone tissues, mesh generation, etc.) and the high cost in performing the FE calculations, it is very challenging to transfer the subject-specific 3D FE modeling into the clinic for the routine use. In the recent years, the machine learning technique, e.g., the convolutional neural network (CNN), has emerged as a novel and crucial tool for predicting the properties of porous structures (**Alber et al., 2019; Alastruely-Lopez et al., 2020; Chandran et al., 2018; Rane et al., 2019**). For examples, Chandran et al. have managed the accurate prediction of the thickness of cortex using the supervised machine learning algorithm (**Chandran et al., 2018**); Rane et al. have managed the accurate prediction of the force of the skeletal muscles using the deep learning algorithm (**Rane et al., 2019**); Alastruely-Lopez et al. have developed the artificial neural network model to predict the impingement and the dislocation in the total hip arthroplasty (**Alstruey-Lopez et al., 2020**). In principal, the CNN technique takes the medical images, the patient's information (such as the gender, age), etc. as the input and then establishes the relationship between the input variables and the output (such as the bone fracture risk, etc.) using the learning process based on a large amount of datasets. Therefore, compared to the subject-specific FE modeling technique, the CNN technique has the clear advantages of being efficient, accurate and real-time and has the potential for the direct clinic routine use. Despite these, to the best of our knowledge, the application of the CNN technique in predicting the mechanical property of the vertebral bone tissues using the CT data has not been fully elaborated.

The aim of the present study was to assess the capability of the CNN method in predicting the mechanical property of the human cancellous bone tissues based on a large amount of the CT images of bone tissues.

2. Materials and Method

2.1. CT image datasets of the human cancellous bone

The high resolution CT images (HR-pQCT) of human cancellous bone instead of the clinical CT images were used in the present study, because the bone samples were from the elderly female patients and the microarchitecture of these bone tissues can be hardly characterized in the regular clinical CT images. The detailed procedure for the acquisition of the HR-pQCT images of the vertebral specimens is described in the previous studies (**Lu et al., 2014; 2015**). In brief, thirty-five cadavers were harvested from female patients with a mean age of 81.3 $\pm$ 7.2 year-old (range: 65 to 90 year-old). The spinal segment of T11/T12/L1 was dissected and the specimens were scanned during frozen using the HR-pQCT scanner (XtremeCT, Scanco Medical AG, Bruettisellen, Switzerland) operating at 59.4 kV, 900 μAs with an image voxel size of $82.0 \times 82.0 \times 82.0\ \mu m^3$.

2.2. The effective elastic modulus of the bone from the finite element analysis

The effective elastic moduli of the cancellous bone tissues calculated from the FE models were taken as the ground truth and used to train the CNN model constructed in the present study. To obtain the effective elastic modulus, the heterogeneous FE model of the human cancellous bone was created using the method previously developed (**Lu et al., 2019**). In brief, first, a volume of interest was cropped out from the vertebral body, which contained only the cancellous bone part (**Figure 1**). Second, the grayscale image datasets were smoothed using a Gaussian filter (sigma = 1.2, support = 2.0) to reduce the influence of the image noise and then each image voxel was converted to a two-dimensional (2D) 4-node plane stress element (PLANE182). In the FE mesh model generated, the heterogenous material model was defined by converting the image grayscale values to the corresponding Young's moduli (**Figure 2**). The image grayscale values were first converted into the vBMD values based on the linear calibration equation provided by the HR-pQCT scanner. The vBMD values were then converted into the bone ash densities using the relationship reported in the literature, i.e., $\rho_{ash} = 0.877 \times \rho_{HA} + 0.079$ (ρ_{ash} is the bone ash density, unit in mg/cm^3; ρ_{HA} is the HA-equivalent vBMD, unit in mg/cm^3) (**Knowles et al., 2016**). Young's modulus of each bone element was then calculated from the bone ash density using the following exponential density-modulus relationship (**Knowles et al., 2016**):

$$\mathrm{E} = \begin{cases} 0.1127 \times 1200^{1.746}, & \rho_{ash} > 1200 \\ 0.1127 \times {\rho_{ash}}^{1.746}, & 400 \le \rho_{ash} \le 1200 \\ 0.0104, & \rho_{ash} < 400 \end{cases} \quad (1)$$

In the above definition, an upper threshold of 1200.00 mg/cm^3 was set to eliminate the effect of the artificially high grayscale values. On the other hand, the material with the bone ash density lower than 400 mg/cm^3 was regarded as the bone marrow, and the corresponding Poisson' ratio was set to 0.49 (**Crawford et al., 2003**). The Poisson's ratio for the bone elements was set to 0.30. An example of the heterogeneous FE model is shown in **Figure 2(b)**, where the color map shows the distribution of the tissue Young's modulus and the black areas represent the pores.

The representative volume element (RVE) method was used to calculate the effective elastic properties of the cancellous bone, which has been widely used to calculate the mechanical properties of complex composites (**Omairey et al., 2019**). In the present study, the FE model of the 2D bone sample was taken as the RVE and periodic boundary conditions (PBCs) were applied to the RVE, which can be expressed as:

$$u_i^{b+} - u_i^{b-} = \bar{\varepsilon}_{ik} \Delta x_k^b \tag{2}$$

where, u_i^{b+} and u_i^{b-} are the displacements on a pair of nodes x_k^{b+} and x_k^{b-} of two opposite boundary surfaces, and $\Delta x_k^b = x_k^{b+} - x_k^{b-}$ with the superscript b indicating a quantity pertaining to boundary.

The elastic stiffness components C_{ijkl} can be determined from the calculation results of RVE by:

$$\bar{\sigma}_{ij} = C_{ijkl} \bar{\varepsilon}_{kl} \tag{3}$$

In the present study, a plane stress problem is assumed and thus the effective Young's modulus E of the cancellous bone can be derived as:

$$E = \frac{C_{1111} + C_{2222}}{2}(1 - v^2) \tag{4}$$

where, v is the Poisson's ratio and

$$v = \frac{2C_{1122}}{C_{1111} + C_{2222}} \tag{5}$$

To enable the process of a large amount of the bone samples, all the pre-processing and post-processing were automated using the in-house developed Matlab (R2019, MathWorks, Natick, Massachusetts, U.S.A.) code and the finite element analysis was performed using the Ansys APDL (v18.0, ANSYS, Inc., Canonsburg, PA, U.S.A.).

2.3. Training and cross-validation of the CNN model

In the present study, a convolutional neural network (CNN) model was developed to predict the effective elastic modulus of the vertebral cancellous bone. The procedure for the training and testing of the CNN model is presented in **Figure 3**. The training process of the CNN model can be briefly described as below: 10636 2D human vertebral cancellous bone samples covering a large range of the bone porosities and bone microarchitectures were processed. Their effective Young's moduli were calculated from the FE analysis and served as the ground truth for the effective modulus of the cancellous bone tissue. The distribution of the effective elastic moduli of the bone samples is shown in **Figure 4**, where the 50th percentile of the elastic moduli is 988.7 MPa. The 10636 bone samples were randomly divided into two parts: one part has 8000 samples used for training the CNN model and the other has 2636 samples used for the cross-validation of the CNN model.

The CNN model constructed is shown in **Figure 5**, which can be briefly described as below: First, several nonlinear layers were applied to gradually extract the features in the bone images; afterwards, the grayscale CT image was transformed to a numerical value as the output of the CNN. In the present study, the grayscale image with the size of 14.9×14.9 mm^2 (182×182) was taken as the input for the CNN model. Eight convolution layers, four pooling layers and four fully connected layers were applied to the image. The convolution kernels were trained in a hierarchical manner, which consisted of the low-level features to generate more complex patterns. The size of all the convolution kernels was set to 3×3. The maximal pooling was applied after the convolutional layers to simplify the information of the output neurons (**Li et al., 2019**). To improve the accuracy of the CNN model, the 20% dropout was used in the four pooling layers, and the batch normalization was used to mitigate the effects of the initialization and to accelerate the training of the CNN model (**Li et al., 2019**). In the present study, the grayscale images of the human vertebral cancellous bone tissues were taken as the input for the CNN model constructed and the corresponding effective elastic modulus for each bone sample was the output from the CNN model.

In the training process, the CNN model learned the valid representation describing the geometric features of the vertebral cancellous bone tissues and discarded those features less important. A loss function was defined to quantify the difference between the effective elastic moduli predicted from the CNN model and those calculated from the FE analysis. Then, the kernels and biases in the convolutional layers and the weights in the fully connected layers were adjusted using the backpropagation algorithm (**Rubio et al., 2011**). Iterative adjustments were made to minimize the loss function using a large amount of bone image datasets. In the present study, the mean absolute error (MAE) was set as the objective function:

$$\mathrm{MAE}[Y, f(X)] = \frac{1}{n}\sum_{i=1}^{n}|Y - f(X)| \quad (6)$$

where, Y is the effective elastic modulus of the bone tissues calculated from the FE analysis; $f(X)$ is the corresponding effective elastic modulus calculated from the CNN model and n is the number of samples used for the cross-validation ($n = 2636$ in the present study).

The training process was conducted on a desktop computer with the setting of i7-8700 CPU, 32G RAM, and the Nvidia GTX1060. The batch size was set to 128 and the training was iterated for 200 epochs. The training process took approximately 2.0 hours.

2.4. Predictive power of the CNN model

To assess the predictive power of the CNN model constructed, 260 new bone samples were processed. The effective elastic moduli of these bone samples were calculated using the trained CNN model and the FE analysis, respectively. The FE predictions were served as the ground truth and the predictive power of the CNN model was obtained by comparing the values obtained from the CNN and the FE models (**Figure 3b**). To quantify the accuracy of the CNN model, the relative prediction error (RPE) was used, which is defined as below:

$$\mathrm{RPE} = \frac{|\mathrm{P^{CNN}} - \mathrm{P^{RVE}}|}{\mathrm{P^{RVE}}} \times 100\% \quad (7)$$

where, $\mathrm{P^{CNN}}$ is the effective elastic modulus calculated from the CNN model, $\mathrm{P^{RVE}}$ is the corresponding value calculated from the FE analysis.

3. Results

3.1 Training and cross-validation of the CNN model

The relation between the mean absolute error (MAE) and the training iteration is shown in **Figure 6**. Because the initial values of the weights and biases are randomly assigned, the MAE at the first a few iterations is high. However, after several iterations, the MAE rapidly descends and the MSE is below 100.0 MPa after 100 training epochs. Therefore, no over-fitting is observed in the cross-validation.

3.2 Predictive power of the CNN model

The comparison using the 260 testing bone samples shows that the predictions from the CNN model are highly correlated with those from the FE analysis (R^2 = 0.91). The slope of the correlation line is 0.79, which is a bit deviated away from the diagonal line ($y = x$) (**Figure 7**), implying that some prediction errors are present in the CNN model. The distribution of the relative prediction error (RPE) shows that 95th and 50th percentiles of the relative prediction error are below 0.28 and 0.09, respectively (**Figures 8 and 9**).

4. Discussion

In the present study, a convolutional neural network (CNN) model for the quick and accurate prediction of the elastic mechanical property of the porous bone tissues was presented. The predictive power of the CNN model was assessed, and a good accuracy was achieved, i.e., the 95th and 50th percentiles of the relative prediction error are below 0.28 and 0.09, respectively.

The present study was motivated by the lengthy and complex nature of the nonlinear FE analysis on human bone tissues. To obtain the effective mechanical property of human bone, in the previous studies (**Lu et al. 2014; 2019**), it took more than 8 hours to obtain the result using the 3D FE modeling technique (including the image processing, the FE model generation, the nonlinear calculation, etc.), and more than 4 hours to obtain the result using the 2D FE modeling technique. In contrast, it takes only less than one minute to obtain the result using the CNN technique without compromising the predictive power. The quick and accurate prediction of the effective mechanical property of bone tissues is crucial in the clinical settings, because in the scenario of bone trauma, a surgical plan has to be quickly decided, which can only be made possible by a quick and accurate assessment of the bone quality. Additionally, the ‘easy to use’ feature of the CNN technique is another important factor in the clinical setting because the tool has to be easily operable by the clinical staff. The CNN technique takes only the 2D CT images of the bone tissues as the input and can quickly output the effective mechanical properties of the bone tissues within a few minutes and thus meets the requirements. In the present study, to obtain the effective elastic modulus of the bone tissue, it takes approximately 40 minutes using the FE analysis (including the process of the image segmentation, the model generation, the FE calculation, the post-processing, etc.), but it only takes approximately 30 seconds using the CNN model constructed.

In the present study, the machine learning (ML) method of the CNN was used. Compared to other ML techniques, e.g., the support vector machine (**Hao, 2009**), the CNN is the most appropriate one for the specific challenges presented in the present study. First, the CNN model takes the medical image, which is readily available in the clinic, as the input. Second, the CNN technique uses the convolution kernel to extract the features from the medical image and consequently the model parameters and complexity are largely reduced (**Li et al., 2019; Ye et al., 2019**).

In the present study, the 95th and 50th percentiles of the relative prediction error are below 0.28 and 0.09, respectively, which are comparable to the values reported in the literature for solving the similar problems. For examples, Ye et al. developed the deep neural network method for predicting the mechanical properties of porous composites and a relative error of smaller than 3.0% was achieved (**Ye et al., 2019**); Li et al. developed the deep learning method for predicting the effective mechanical property of heterogeneous materials and a relative error below 3.0% was reported (**Li et al., 2019**); Jiang et al. developed the support vector machine model for predicting the hip fracture risk and an accuracy of 74.0% Area Under Curve (AUC) was achieved. However, it should be noted that in the previous studies (**Jiang et al., 2015; Li et al., 2019; Ye et al., 2019**), the large datasets are artificially generated using the computer program, while the real clinical CT datasets are used in the present study. Therefore, the factors, such as the image noise and the partial volume effect, are taken into account in the CNN model constructed and consequently the results from the present study can be of the direct clinical translation.

The present study showed that if a large amount of the clinical image datasets can be obtained, the CNN model can be trained and used to predict the mechanical property of the bone tissues. This is crucial for clinical applications. For example, the model can be used to assess the bone fracture risk in case of a fall event (**Bhattacharya et al., 2018**), to predict the long-term quality of the bone tissues so as to help the design of the bone implant (**Metz et al., 2019**), etc. It should be noted that not only one apparent mechanical property of the bone tissue (demonstrated in the present study) can be predicted by the CNN technique, but also the distribution of the stress/strain within the human tissue can be predicted using the CNN technique (**Liang et al., 2018; Li et al., 2021**). Therefore, the CNN technique has the potential to act as a surrogate for the FE method in the medical engineering analysis. Taking use of the advanced ability of the CNN technique, i.e., the prediction of the strain distribution in the bone region, the mechanically weakest region in the bone tissue can be identified and consequently the specific bone region can be targeted for the effective prevention and treatment of the bone fracture. It should be noted that in the present study, the 2D numerical models are presented, which cannot consider the 3D architecture of the cancellous bone tissues. Therefore, to achieve a higher power for predicting the bone fracture risk, the future work should address the challenges related the 3D problems, e.g., the collection of a large amount of the medical image datasets, the automation of the processing of the 3D medical images, the automation of the 3D FE analysis, etc.

Despite the advantages and potentials of the CNN technique, some limitations in the present study should be discussed. First, the HR-pQCT images, which have a higher image resolution than the regular clinical CT images, are used in the present study. In the present study, the bone samples from the elderly donors are harvested and their cancellous bone tissues have some extent of osteoporosis. Therefore, the HR-pQCT images have to be used to accurately obtain the mechanical property of the porous bone tissues. Although this complies with the aim of the present study, i.e., the demonstration of the CNN technique in predicting the mechanical property of the porous bone tissues, the feasibility study using the clinical CT images should still be investigated in the future. Second, only the CT images of the bone tissue are taken as the input for training the CNN model. The mechanical properties of the bone tissue are determined not only by the tissue modulus and the microarchitecture of the bone sample, but also by the factors such as the chemical compositions and gene sequence which are not reflected in the medical CT images. Therefore, more input information, such as the patient's body weight, gender, family medical history, etc., should also be used for training the CNN model. The authors of the present study are in the process of collecting a large amount of clinical datasets and investigating whether the predictive power of the CNN model can be improved by adding more bone information into the model training. Third, in the present study, the results from the FE analysis are taken as the ground truth for the mechanical property of the bone tissue. It should be noted that generally the results from the in vitro mechanical testing should be taken as the ground truth (**Dong et al., 2018; Lu et al., 2014**), because some behaviors of the bone tissue, such as the propagation of the bone micro crack, can be hardly captured in the FE analysis. However, the mechanical property of the bone tissue cannot be obtained from the in vitro testing in the clinical setting. Furthermore, it has been shown in the previous studies (**Lu et al. 2014; 2019**) that the predictions from the FE analysis have a high correlation with the results obtained from the in vitro mechanical testing. Additionally, the aim of the present study is to find an accurate and efficient surrogate approach for the FE analysis. Therefore, it is reasonable to take the predictions from the FE analysis as the ground truth for assessing the predictive power of the CNN model.

In conclusion, the convolutional neural network (CNN) technique can be used to accurately and efficiently predict the mechanical properties of the porous cancellous bone tissues. Compared to the FE modeling technique, the CNN technique can be easily translated to the clinic for the routine use, e.g., the quick assessment of the bone quality. It should be noted that the CNN technique can also be used to calculate other physical properties of the porous/composite materials, e.g., the heat conductivity, the fatigue life, the roughness (fracture toughness?), etc.

Conflict of interest

The authors declare that they do not have any financial or personal relationships with other people or organizations that could have inappropriately influenced this study.

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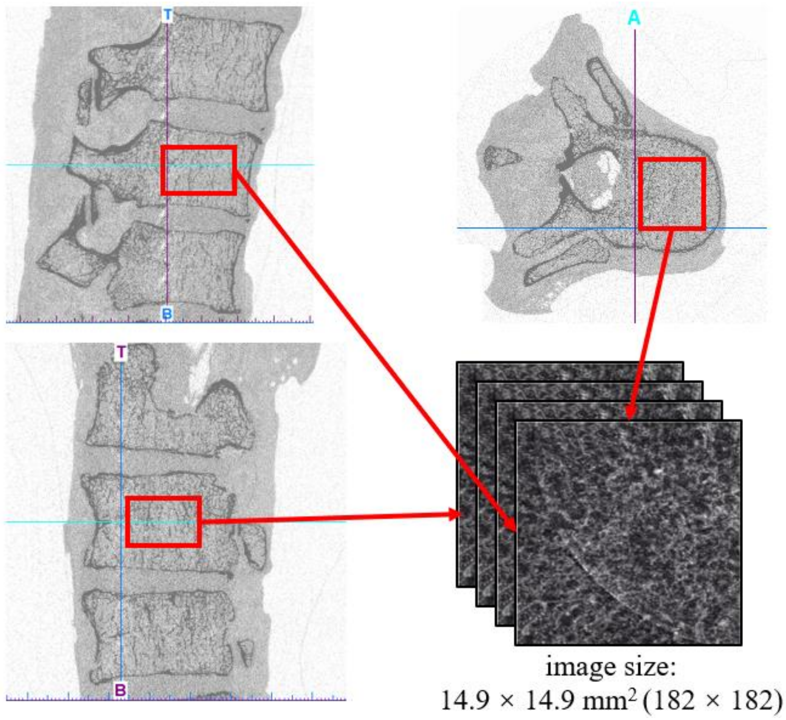
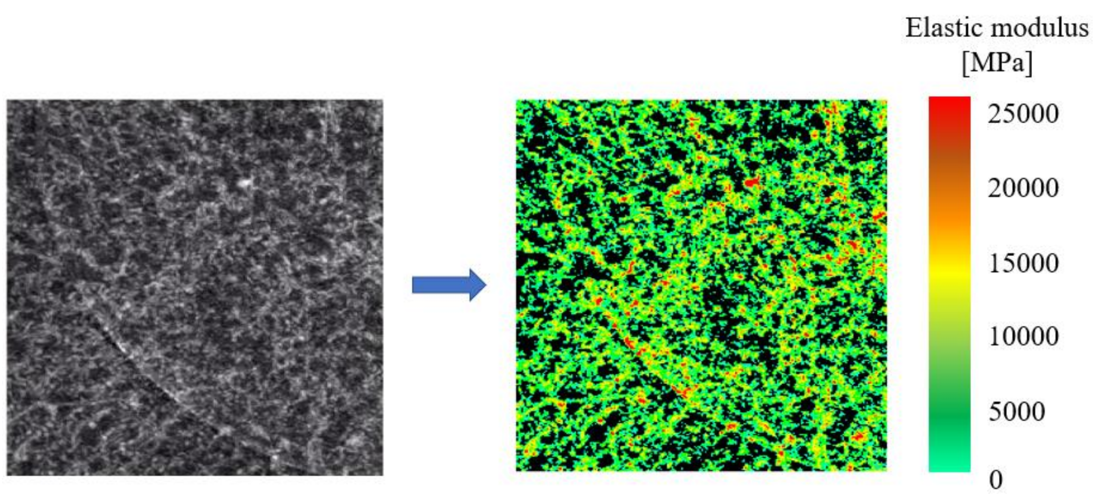


Figure 1. Extraction of the CT data of the human cancellous bone for the construction of the convolutional neural network model.



(a) **(b)**

Figure 2. Establishment of the heterogeneous finite element model for calculating the effective elastic modulus of bone tissues.

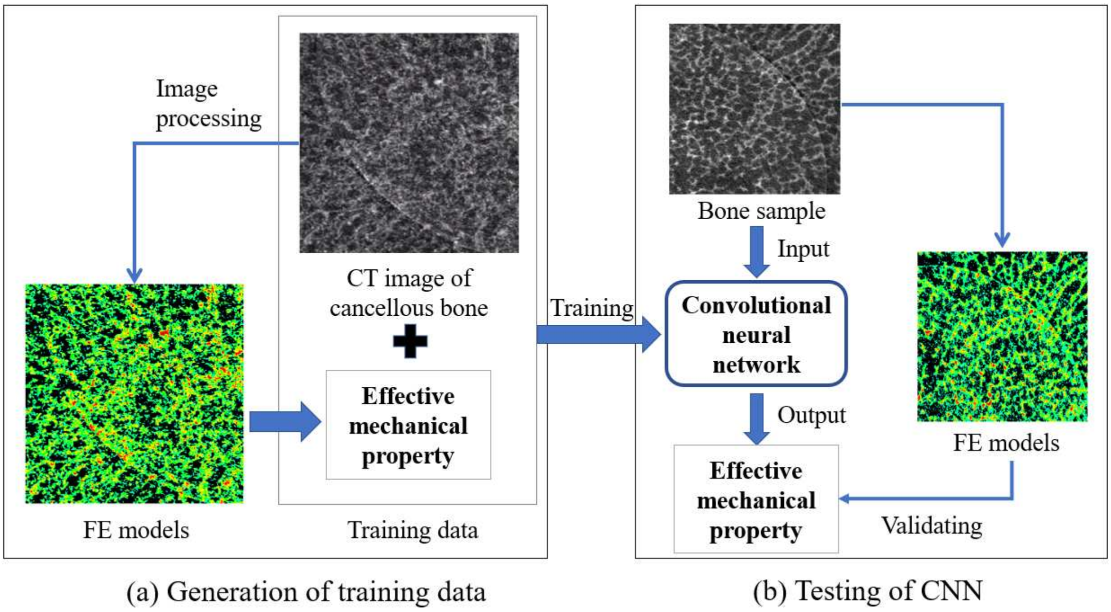


Figure 3. The workflow for the training and testing of the convolutional neural network (CNN) model.

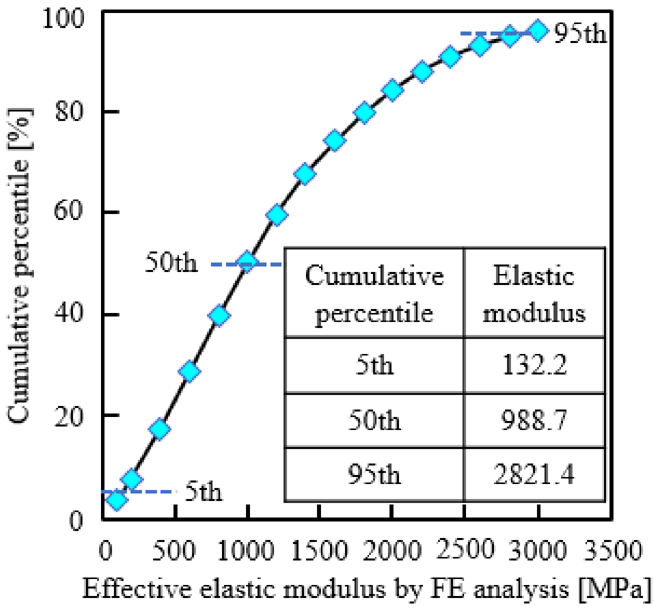


Figure 4. Distribution of the effective elastic moduli of bone samples used in the present study (all the bone samples, N = 10636).

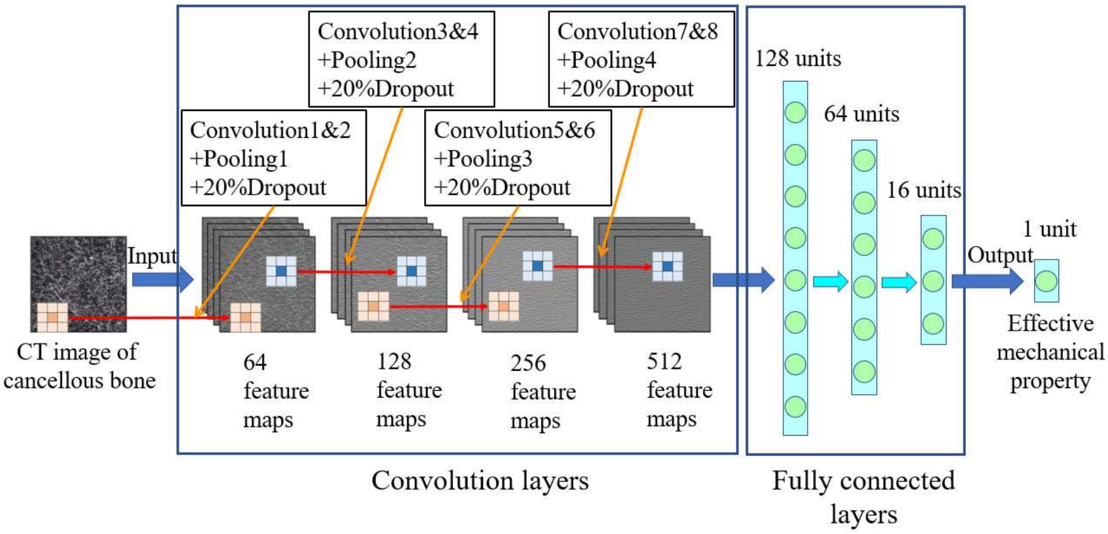


Figure 5. The convolutional neural network model constructed in the present study.

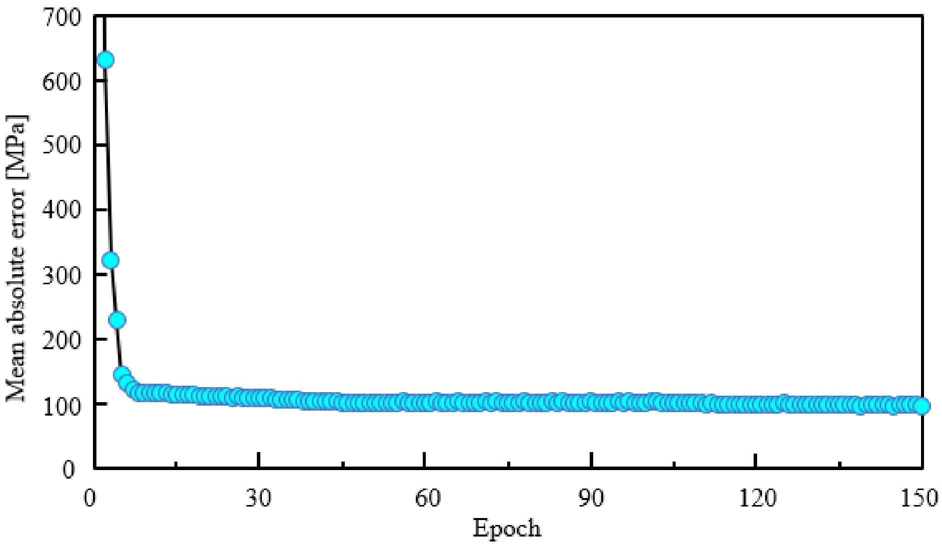


Figure 6. The relationship between the mean absolute error and the Epoch.

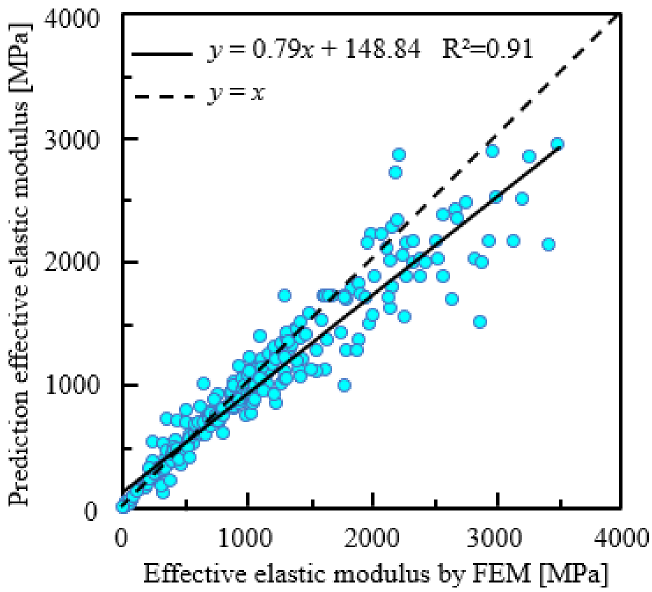


Figure 7. The relationship between the effective elastic moduli predicted from the convolutional neural network (CNN) model and those calculated from the finite element method (FEM)

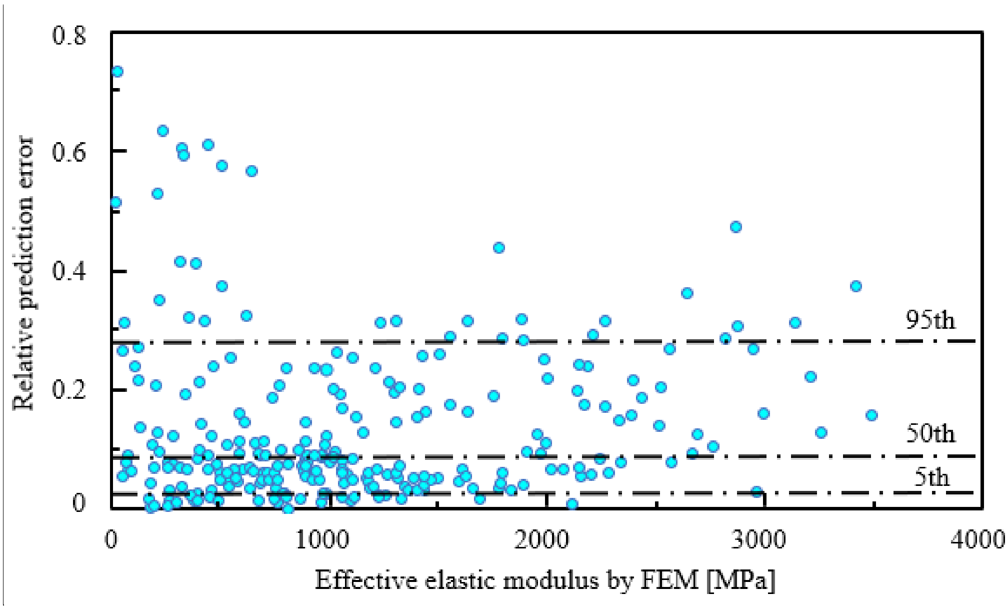


Figure 8. Distribution of the relative prediction errors of the convolutional neural network model

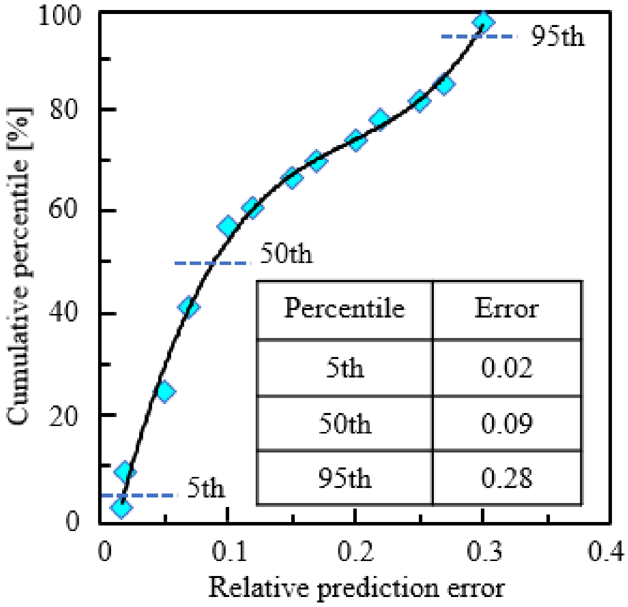


Figure 9. The relationship between the cumulative percentile and the relative prediction error of the convolutional neural network model