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Estimating the mechanical competence parameter of the trabecular bone: a neural network approach

Érica Regina Filletti*, Waldir Leite Roque

Abstract **Introduction:** The mechanical competence parameter (MCP) of the trabecular bone is a parameter that merges the volume fraction, connectivity, tortuosity and Young modulus of elasticity, to provide a single measure of the trabecular bone structural quality. **Methods:** As the MCP is estimated for 3D images and the Young modulus simulations are quite consuming, in this paper, an alternative approach to estimate the MCP based on artificial neural network (ANN) is discussed considering as the training set a group of 23 *in vitro* vertebrae and 12 distal radius samples obtained by microcomputed tomography (μCT), and 83 *in vivo* distal radius magnetic resonance image samples (MRI). **Results:** It is shown that the ANN was able to predict with very high accuracy the MCP for 29 new samples, being 6 vertebrae and 3 distal radius bones by μCT and 20 distal radius bone by MRI. **Conclusion:** There is a strong correlation ($R^2 = 0.97$) between both techniques and, despite the small number of testing samples, the Bland-Altman analysis shows that ANN is within the limits of agreement to estimate the MCP.

Keywords: Osteoporosis, Trabecular bone, Mechanical competence, Artificial neural network, Machine learning.

Introduction

Osteoporosis is a prevalent disease among the elderly population and due to the increase in life expectancy it is becoming a public health problem with very high cost to both public and private health systems (Dimai et al., 2012). Osteoporosis causes a remarkable bone mass loss and trabecular bone degradation, which normally leads to an increase in bone fragility and an augmented fracture risk. One of the main functions of the bone is to support or bear loads applied on it. For this reason, it should be strong enough to avoid breakage and keep its stiffness. Therefore, it is important to known about bone strength and stiffness, particularly when investigating the effect of different external stimuli.

It is now known that the trabecular microarchitecture degradation impacts the fragility fracture risk. The trabecular bone structure is organized as a network of rod-like and plate-like struts forming a tortuous grid, which influences the mechanical behavior of the structure. Recently, in (Roque et al., 2013a; Roque et al., 2013b) it was shown that the trabecular bone volume fraction (BV/TV), the network connectivity (EPC), the trabecular tortuosity (τ) and the elasticity (E) are relevant parameters to establish the trabecular bone mechanical competence. Using these four parameters, by means of the principal component analysis (PCA), a mechanical competence parameter (MCP) was defined and applied to grade trabecular bone fragility for three different cohorts.

Principal component analysis (PCA) is a technique that reduces a complex data set to a lower dimension to reveal the sometimes hidden, simplified structure that often underlie it. The variable reduction is applicable only when there is a strong correlation between the data sets (Jolliffe, 2002). The linear correlation analysis of the parameters BV/TV, EPC, τ and E, has shown to be very high. When the PCA is applied to these four trabecular bone parameters, it merges morphological, geometrical and mechanical information about the trabecular bone structure into a unique parameter. The MCP was defined as the principal component in the PCA.

Artificial neural network (ANN) is a technique that has attracted much attention as an approach to estimate quantities when there are complex relationships between input and output variables, particularly when no links are known among them *a priori*. Amongst several advantages of neural network models, it can be emphasized that they are easy to use and to update, possess large degree of freedom and give accurate prediction at high speed (Nafey, 2009; Niemi et al., 1995). The main one is the ability to generalize, i.e., to learn from examples. In this regard, after an ANN has been satisfactorily trained and tested, it is able to

*e-mail: erica@iq.unesp.br
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predict the output of new input data in the domain covered by the training examples. In addition, ANNs can also include available theoretical knowledge about the process. As a consequence, some researchers have devoted their time to study the application of neural networks models to the trabecular bone characterization and strength analysis.

Christopher and Ramakrishnan (2007) evaluated the mechanical strength of the trabecular structure of the human femur using digital processing of images obtained by radiographs and artificial neural networks to classify normal or abnormal bone structure. The results have shown that the method is able to provide useful information about the strength of the femur trabecular structure. Gregory et al. (1999) have used the Fourier transform and neural networks to identify changes in the structure of the trabecular bone. Hambli (2011) developed an approach based on finite element methods and neural networks to estimate the density and length of cracks in trabecular bone. The results have shown a good qualitative agreement compared with experimental results published previously.

In this regard, in a previous study (Filletti and Roque, 2015), the authors investigated the application of an ANN to predict the MCP for 20 magnetic resonance image (MRI) samples based on a training set of 83 *in vivo* distal radius MRI samples. The ANN was able to predict the MCP of the test samples with a relative average error of 6.5%. As the ANN was applied to a set of *in vivo* distal radius MRI samples, in this paper an investigation on how the ANN responds to a set of samples from different bone sites, vertebrae and distal radius, using MRI and μCT as two different imagery techniques is carried out. The results obtained by the ANN have shown to be very satisfactory, with a relative average error of 11%, when considering as the training set both bone samples merged in a unique set. Therefore, while the paper Filletti and Roque (2015) had only distal radius bone samples with MRI, in this paper it is shown that the ANN can estimate the MCP for a more general case, including samples that originate from different bone sites and different imaging techniques.

Thus, this paper shows that the ANN technique can be extended to estimate the MCP for the trabecular bone from different sites and imaging devices without appealing to calculate it through PCA. Once the ANN is trained, it will provide a simple, accurate and faster method to estimate the MCP, thus avoiding PCA, which is a much more laborious technique.

Methods

To investigate the potentiality of the ANN, the current work considers three different cohorts. Two *in vitro* μCT sets of trabecular bone 3D image samples: one set from distal radius containing 15 images and another containing 29 L3 vertebral samples. The final isotropic resolution was 34μm and the analyzed direction was craniocaudal to the vertebrae and distal-proximal to the radius. These two set of trabecular bone samples were obtained from human cadavers following all the technical procedure requirements. Additional details can be found in Roque and Alberich-Bayarri (2015), Arcaro (2013) and references therein.

The third cohort was composed of 103 MRI radius samples from *in vivo* human subjects, captured from the distal metaphysis and from a cohort including healthy subjects and a mix of bone mineral density stages, which includes osteopenic and osteoporotic subjects. The MRI acquisitions were performed in a 3 Tesla system, scanned in 3D using a T1-weighted gradient echo sequence (TE/TR/a=5 ms/16 ms/25 Å) and with a nominal isotropic resolution of 180 μm. Full details about all these samples can be found in (Roque et al., 2013b).

Figure 1 shows 3D images of two pair of trabecular bone samples, vertebral bodies at the top and distal radius at the bottom. On the left side, for both, it can be noticed that the structures are more disrupted than those on the right side, due to the advanced osteoporosis. Figure 2 shows 3D images of two distal radius trabecular bone samples, with the image on the right side more disrupted.

Mechanical competence parameter

Principal component analysis (PCA) technique for variable reduction is applicable only when there is a strong correlation between these variables (Jolliffe, 2002). In (Roque et al., 2013a) the mechanical competence parameter (MCP) was defined to grade the trabecular bone fragility by means of four trabecular bone fundamental quantities: volume fraction (*BV/TV*), network connectivity via the volumetric Euler-Poincaré characteristic (EPC_V), tortuosity (τ) and the Young modulus of elasticity (*E*).

In this paper, the MCP was applied to grade the TB fragility of the three cohorts (Roque and Alberich-Bayarri, 2015), with the distal radius μCT samples given by

$$MCP_{DR} = 0.52 \times BV/TV - 0.49 \times EPC_V + 0.51 \times E - 0.48 \times \tau, \quad (1)$$

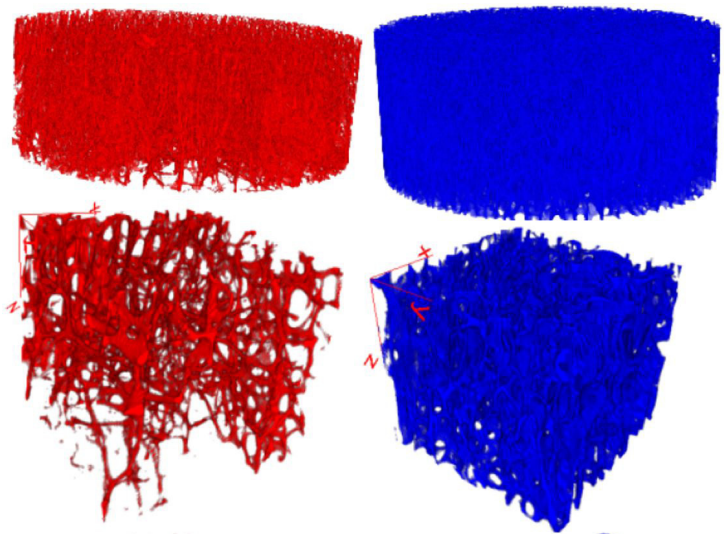

Figure 1. 3D visualization of two μCT distal radius and vertebra trabecular bone samples.

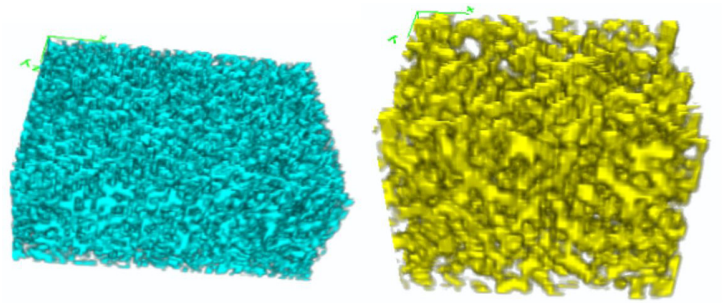

Figure 2. 3D visualization of two MRI distal radius trabecular bone samples.

MCP for the vertebrae μCT samples is given by

$$MCP_V = 0.55 \times BV/TV - 0.48 \times EPC_V + 0.50 \times E - 0.47 \times \tau, \quad (2)$$

and MCP for the MRI distal radius samples is given by

$$MCP_{MRDR} = 0.53 \times BV/TV - 0.50 \times EPC_V + 0.51 \times E - 0.45 \times \tau. \quad (3)$$

Once the four parameters are provided in Equations 1, 2 and 3, the MCP for each set of samples can be determined. To set the range of the MCP in the interval [0, 1], a normalization procedure is defined as

$$MCP_N = \frac{MCP_k - MCP_{MIN}}{MCP_{MAX} - MCP_{MIN}} \quad (4)$$

where MCP_k is sample k MCP value, MCP_{max} and MCP_{min} are the maximum and minimum MCP values, respectively. In a cohort, the worst trabecular structure has $MCP_N = 0$ and the best $MCP_N = 1$. The MCP_N for the three cohorts can be found in Arcaro (2013).

Neural network algorithm implementation

In this work it is used a feed forward network, i.e., the input of a specific layer is formed only by the values of the preceding layer. The architecture of such a network is composed of an input layer, a certain number of hidden layers and an output layer in forward connections. Each neuron in the input layer represents just a single input parameter. These values are directly transmitted to the subsequent neurons of the hidden layers. The neurons of the last layer represent the ANN outputs.

The output $y_{i,j}$ of neuron i in a layer j is calculated as

$$y_{i,j} = f(v_{i,j}) \quad (5)$$

$$v_{i,j} = \sum_{k=1}^{L} w_{k,i,j-1} y_{k,j-1} + b_{i,j} \quad (6)$$

where f is the activation function, L is the number of connections to the previous layer, $w_{k,i,j-1}$ corresponds to the weights of each connection and $b_{i,j}$ is the bias. In this work, the activation functions used in the neural

network were the tangent sigmoid in the hidden layers and a linear function in the output layer, expressed respectively as

$$f(v_{i,j}) = \frac{2}{(1+\exp(-2v_{i,j}))} - 1 \quad (7)$$

$$f(v_{i,j}) = v_{i,j} \quad (8)$$

The training process in the ANNs involves presenting a set of examples (input patterns) with known outputs (target output) (Jenkins, 1997). The system adjusts the weights $w_{k,i,j}$ of the internal connections to minimize errors between the network output and target output. The knowledge is represented and stored by the weights of the connections between the neurons.

Back propagation is probably the most used training algorithm and it is particularly well adapted to feed-forward architecture of the multi-layer network. It is based on the iterative application of a discrete gradient descent algorithm, designed to compute the connection weights so minimizing the total mean-square error between the actual output of the network and the target output. In general, the back propagation algorithm, which is implemented in this work, can be summarized as follows (Haykin, 1999):

1. Initialize the ANNs parameters $b_{i,j}$ and $w_{k,i,j}$ with random numbers;
2. Calculate the outputs of all the neurons layer by layer, starting with the input layer until the output layer using Equations 5-8;
3. Calculate the mean square error by:

$$MSE = \frac{1}{2}\sum_{i=1}^{N}(d_i - y_i)^2 \quad (9)$$

where y_i is the actual output of the i-th output node, d_i is the corresponding desired output and N is the number of output nodes;

4. Calculate the derivatives of the error with respect to $b_{i,j}$ and $w_{k,i,j}$;
5. Update the weights and bias along the negative gradient of the *MSE* and a specified learning rate γ

$$b_{i,j} \leftarrow b_{i,j} - \gamma\frac{\partial(MSE)}{\partial b_{i,j}} \quad (10)$$

$$w_{i,j} \leftarrow w_{i,k,j} - \gamma\frac{\partial(MSE)}{\partial w_{i,k,j}} \quad (11)$$

6. Repeat by going back to step 2, successively modifying $b_{i,j}$ and $w_{k,i,j}$, up to a certain number of epochs to be achieved or until *MSE* is sufficiently small.

The neural network implemented here has four inputs and one output. Various architectures were trained and tested. The neural model that had the best performance, obtained by trial and error, has two hidden layers with twelve and six neurons, respectively.

The training procedure comprehended the acquisition of the volume fraction, connectivity, tortuosity and Young modulus of elasticity (input patterns) obtained as described in the previous section. In total, 118 examples of data were considered to construct a database applied to artificial neural network parameters that could be adjusted. From those examples, 23 were from vertebrae by μCT, 12 from distal radius by μCT and 83 from distal radius by MRI samples. The neuron of the output layer is responsible for estimating the MCP.

To determine the values of the learning rate, the number of epochs as well as the number of neurons in the intermediate layers of the neural networks, an optimization of the parameters of the neural networks was performed by trial and error, in order to diminish the error within a reasonable time. The learning rate used in the neural network was 0.1 and the training time was 35 minutes, in a processor Intel Xeon CPU E-3 1225 V2 with 3.2 GHz and 16 GB of RAM. The error of the training was the order of 10^{-4}, as shown in Figure 3. One method to avoid over-training is to follow the performance of the neural network on a test set not presented in the training. The optimal parameters of the ANN were chosen empirically observing the minimum error and reached the capacity of maximum possible generalization. In this work, the training stopped at 300000 epochs when the error of the test set reached 11%, avoiding over-training.

For the generalization, 29 data different from those used in the training set were presented to the neural network, being 6 vertebrae by μCT, 3 from distal radius by μCT and 20 from distal radius by MRI. The division of the examples in training and test sets was made randomly and a good correlation among the data was obtained, as shown in Figure 4.

Results

Tables 1, 2 and 3 present the MCP_N computed from Equations 1, 2 and 3 with data provided in Arcaro (2013), and the response of the ANN for the 29 data contained in the test set. As it can be noticed, the results of the ANN for the test samples are quite satisfactory, with a Pearson correlation r = 0.9848; the two-tailed P value equals to 0.9563, considered to be

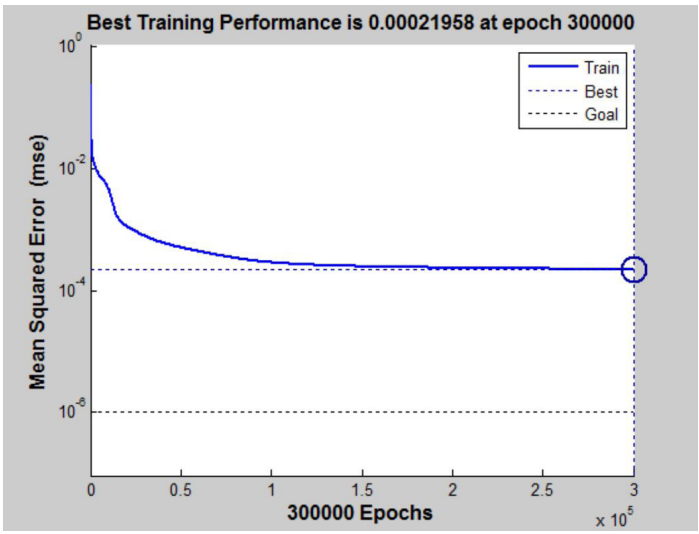

Figure 3. Decrease of the error during the training of the neural network to estimate the MCP_N.

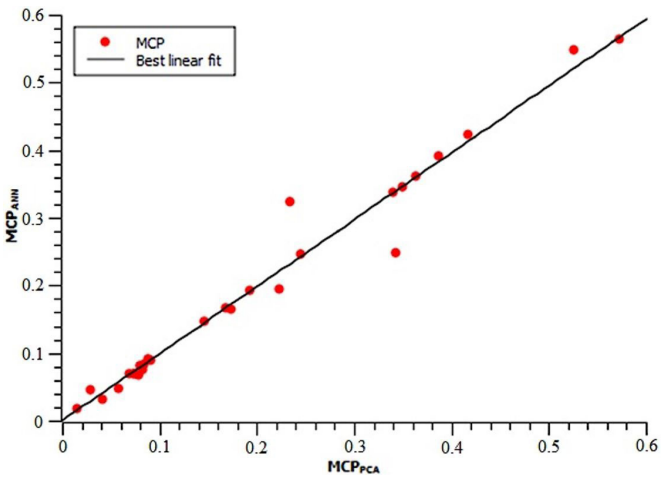

Figure 4. MCP correlation between the PCA and ANN for the test samples.

Table 1. MCP_N obtained by PCA and ANN algorithm for the 3 distal radius samples by µCT.

Sample	MCP_{PCA}	MCP_{ANN}
07	0.3247	0.2335
08	0.1951	0.2224
09	0.0450	0.0288

Table 2. MCP_N obtained by PCA and ANN algorithm for the 6 vertebra samples by µCT.

Sample	MCP_{PCA}	MCP_{ANN}
01	0.2475	0.3433
02	0.1655	0.1731
03	0.5487	0.5250
04	0.3908	0.3871
05	0.3617	0.3629
06	0.4223	0.4176

not statistically significant within a 95% confidence interval ranging from [-0.084444, 0.079927].

To compare ANN and PCA techniques to estimate the MCP_N, the Bland-Altman plot was considered and presented in Figure 5. From that, it can be inferred that the two methods of measurement agree sufficiently close and that only three points were outside the 95% confidence interval, while most of them are near the line of equality.

Discussion

MCP is a parameter introduced by Roque et al. (2013a) to provide a way to grade the trabecular bone fragility based on volume fraction, connectivity, tortuosity and elasticity, four fundamental quantities

Table 3. MCP_N obtained by PCA and ANN algorithm for the 20 distal radius samples by MRI.

Sample	MCP_{PCA}	MCP_{ANN}
10	0.0679	0.0783
11	0.0697	0.0688
12	0.0477	0.0581
13	0.1660	0.1678
14	0.0912	0.0885
15	0.0809	0.0800
16	0.0185	0.0151
17	0.0892	0.0905
18	0.5648	0.5731
19	0.0308	0.0406
20	0.1930	0.1924
21	0.1462	0.1460
22	0.0761	0.0832
23	0.3457	0.3494
24	0.0698	0.0731
25	0.0702	0.0746
26	0.2459	0.2453
27	0.0689	0.0867
28	0.3370	0.3397
29	0.0826	0.0840

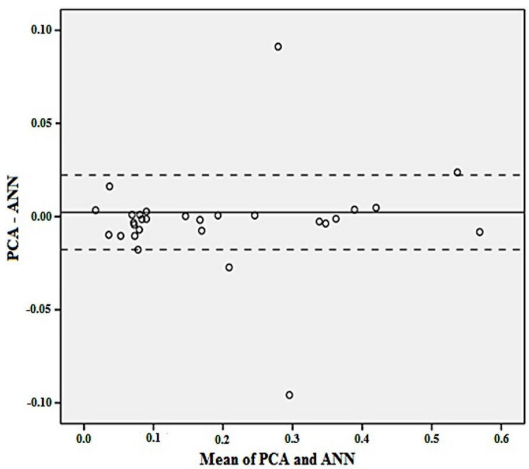

Figure 5. Bland-Altman plot of the MCP_N values presented in Tables 1, 2 and 3.

that characterize the bone mechanical structure. In Roque et al. (2013a), Roque et al. (2013b) it has been shown that the MCP can suitably be defined for different trabecular bone sites using distinct image scanning devices and distinct mechanical test procedures.

The approach used in Roque et al. (2013a) is based on the principal component analysis whose principal component defines the MCP equation. In this paper an artificial neural network approach was applied to estimate the MCP based on two sets of *in vitro* images samples from two distinct bone sites, L3 vertebrae and distal radius, and one set of *in vivo* MRI distal radius samples. The results presented here have shown the potentiality of the ANN to estimate the MCP taking into account different bone sample sites, distinct imagery devices and the subject form as *in vivo* or *in vitro*.

The normalized MCP was estimated by both approaches and the results were compared by means of the Bland-Altman plot, which has shown that these techniques provide very similar results. In other words, the ANN performs essentially as good as the PCA to estimate the MCP_N, within the limits of agreement. Of course, as neither is considered the gold standard technique to estimate the MCP_N, as much as the results are concerned, the ANN can suitably be used to estimate the MCP.

Overall, in this paper an ANN was used to estimate the mechanical competence parameter based on μCT and MRI image samples of vertebrae and distal radius bones, together. The ANN predicted very well the MCP for a set of 38 test data composed of 6 vertebrae and 32 distal radius samples. The correlation between the MCP evaluated by the PCA and ANN is quite high ($R^2 = 0.97$) and the Bland-Altman analysis indicates that both approaches are comparable within 95% confidence interval.

The ANN technique has shown to be a good alternative to estimate the MCP, avoiding the cost of the PCA, which requires the individual computation of the MCP for each cohort. Of course, further studies are required to investigate whether a unique ANN can be applied to estimate the MCP_N from any trabecular bone site, as in this paper only two sites were investigated, and also independently of the imagery technique.

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Authors

Érica Regina Filletti[1]*, Waldir Leite Roque[2]

[1] Departamento de Físico-Química, Instituto de Química, Universidade Estadual Paulista – UNESP, Rua Prof. Francisco Degni, 55, Bairro Quitandinha, CEP 14800-900, Araraquara, SP, Brazil.

[2] Departamento de Computação Científica, Centro de Informática, Universidade Federal da Paraíba – UFPB, João Pessoa, PB, Brazil.