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Predicting the Biomechanical Strength of Proximal Femur Specimens through High Dimensional Geometric Features and Support Vector Regression

Chien-Chun Yang^{*,1}, Mahesh B. Nagarajan¹, Markus B. Huber¹, Julio Carballido-Gamio², Jan S. Bauer³, Thomas Baum³, Felix Eckstein⁴, Eva Lochmüller⁴, Sharmila Majumdar², Thomas M. Link², and Axel Wismüller^{1,5}

¹Departments of Imaging Sciences & Biomedical Engineering, University of Rochester, New York, United States

²Musculoskeletal and Quantitative Imaging Research, Department of Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, United States

³Institut Für Röntgendiagnostik, Technische Universität München, Munich, Germany

⁴Institute of Anatomy and Musculoskeletal Research, Paracelsus Medical University Salzburg, Salzburg, Austria

⁵Department of Radiology, University of Munich, Germany

Abstract

Estimating local trabecular bone quality for purposes of femoral bone strength prediction is important for improving the clinical assessment of osteoporotic hip fracture risk. In this study, we explore the ability of geometric features derived from the Scaling Index Method (SIM) in predicting the biomechanical strength of proximal femur specimens as visualized on multi-detector computed tomography (MDCT) images. MDCT scans were acquired for 50 proximal femur specimens harvested from human cadavers. An automated volume of interest (VOI)-fitting algorithm was used to define a consistent volume in the femoral head of each specimen. In these VOIs, the non-linear micro-structure of the trabecular bone was characterized by statistical moments of its BMD distribution and by local scaling properties derived from SIM. Linear multi-regression analysis and support vector regression with a linear kernel (SVRLin) were used to predict the failure load (FL) from the feature sets; the predicted FL was compared to the FL values determined through biomechanical testing. The prediction performance was measured by the root mean square error (RMSE) for each image feature on independent test set. The best prediction result was obtained from the SIM feature set with SVRLin, which had the lowest prediction error (RMSE = 0.842 ± 0.209) and which was significantly lower than the conventionally used mean BMD (RMSE = 1.103 ± 0.262 , $p < 0.005$). Our results indicate that the biomechanical strength prediction can be significantly improved in proximal femur specimens on MDCT images by using high-dimensional geometric features derived from SIM with support vector regression.

* cyang@bme.rochester.edu; phone 585-276-4775; University of Rochester, NY.

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Keywords

trabecular bone; biomechanical strength; MDCT imaging; bone mineral density; supervised learning

1. PURPOSE

Variations in trabecular bone density and structure are directly related to variations in bone strength, and as a consequence, reduced bone density and a deteriorated bone structure can drastically increase the fracture risk. Changes in the overall bone quality are evident in several musculoskeletal disorders like osteoporosis, which is characterized by an imbalance in bone resorption and apposition. Although reduced bone density is the key clinical finding to predict fracture risk, bone density does not fully describe either the bone quality or the individual fracture risk. Current computer-aided diagnosis systems extract image features that look beyond the bone density and analyze trabecular bone architecture. One objective of these systems is the prediction of local bone strength, which is useful to monitor and diagnose osteoporotic bone changes [1].

We propose a system that utilizes high dimensional geometric features derived from Scaling Index Method which are capable of describing the micro-structure of trabecular bone. Such features can serve as input for supervised learning algorithms such as multi-regression, support vector regression etc, and enable the construction of models for future bone strength prediction. Therefore, the purpose of this study was to evaluate whether high dimensional geometric features extracted from MDCT images of proximal femur specimens in combination with support vector regression provides a better prediction of biomechanical strength than the standard approach of using mean BMD alone. This work is embedded in our group's endeavor to expedite 'big data' analysis in biomedical imaging by means of advanced pattern recognition and machine learning methods for computational radiology, e.g. [2–18].

2. METHODS**Femur Specimens**

Fifty left femoral specimens were harvested from fixed human cadavers over a time period of four years [19]. The surrounding soft tissue was removed before subsequent MDCT scan and failure load test. The specimens were placed in plastic bags filled with 4% formalin/water solution. Air was removed with a vacuum pump and plastic bags were sealed.

Multi-detector Computed Tomography (MDCT)

Cross-sectional images of the femora were acquired using a 16-row multi-detector (MD)-CT scanner (Sensation 16; Siemens Medical Solutions, Erlangen, Germany). The specimens were positioned in the scanner as in an in-vivo exam of the pelvis and proximal femur, with mild internal rotation of the femur. Each specimen was scanned with a protocol using a collimation and a table feed of 0.75 mm and a reconstruction index of 0.5 mm. A high resolution reconstruction algorithm (kernel U70u) was used, resulting in an in-plane

resolution of $0.29 \times 0.29 \text{ mm}^2$. The image matrix was 512×512 pixels, with a field of view of 100 mm.

Image Processing and Volume of Interest (VOI) Selection

The outer surface of the cortical shell of the femur was segmented by using bone attenuations of the phantom in each image. By analyzing the size and shape of the contours and the center of mass of the contours of consecutive slices, the superior part of the femoral head was detected. A sphere was fitted to the superior surface points of the femoral head using a Gaussian Newton Least Squares technique. The fitted sphere was scaled down to 75% of its original size to account for cortical bone and shape irregularities like the fovea capitis, and then saved as the femoral head volume of interest (VOI).

BMD Measurements

The mean BMD of each VOI was calculated by converting the pixel attenuations in Hounsfield units (HUs) into BMD values (mg/cm^3) using the calibration phantom which corresponds to $\text{HA}_W = 0 \text{ mg}/\text{cm}^3$ and $\text{HA}_B = 200 \text{ mg}/\text{cm}^3$ hydroxyapatite for the water-like and the bone-like phase, respectively. Besides these constants, the HUs of the sections in the reference phantom were measured in each image, which resulted in the Hounsfield units HA_W and HA_B for the water-like and bone-like phantom part, respectively. Assuming a linear relation between BMD and HU, BMD values were calculated for every voxel based on the following equation proposed by Bauer et al., and the resulting BMD image in the VOI is shown (Figure 1).

$$\text{BMD} = [\text{HA}_B - \text{HA}_W / (\text{HU}_B - \text{HU}_W)] * (\text{HU} - \text{HU}_W)$$

Biomechanical Tests

The failure load was assessed using a side-impact test, simulating a lateral fall on the greater trochanter as described previously [20]. Briefly, the femoral shaft and head faced downward and could be moved independently of one another while the load was applied on the greater trochanter using a universal materials testing machine (Zwick 1445, Ulm, Germany) with a 10 kN force sensor and dedicated software. The failure load was defined as the peak of the load-deformation curve.

BMD Features

The BMD distributions within VOIs were represented by their statistical moments and percentiles: the mean (BMD.mean); mean and standard deviation (BMD.m2); a set of mean, standard deviation, skewness, and kurtosis (BMD.m4); and 9 evenly distributed percentiles (BMD.p9).

SIM Features

In addition to BMD features, Scaling Index Method (SIM) [21,22] can be used to quantitatively represent the local geometric properties. The SIM extracts nonlinear information from multidimensional, arbitrary point distributions by assessing local dimensions of each data point.

Consider N pixels in a ROI represented by a 3-D vector $x_i = (x_i, y_i, g_i)$, $i = \{1, \dots, N\}$, where x_i and y_i are the spatial dimensions and g_i is the gray-level intensity of the i^{th} pixel, i.e. $g_i = g(x_i, y_i)$. The application of SIM for a given scale r can be regarded as an image transformation where each pixel of the original ROI is assigned a local scaling property $\alpha_i = \alpha(x_i, r)$ resulting in a transformed image (SIM image) that depends on the neighboring pixels N weighted by a given radius r

$$\alpha(x_i, r) = \frac{2 \sum_{j=1}^N (d_{ij}/r)^2 \exp[-(d_{ij}/r)^2]}{\sum_{j=1}^N \exp[-(d_{ij}/r)^2]}$$

where $d_{ij} = |x_i - x_j|$ is the Euclidean distance between two pixels. Pixels that are located in a cluster-like pixel neighborhood obtain a SIM value $\alpha \sim 0$, pixels in a line-like element a SIM value $\alpha \sim 1$, pixels in a plane-like structure a SIM $\alpha \sim 2$, and pixels in a uniformly distributed neighborhood a SIM value $\alpha \sim 3$.

In this study, 5 SIM images were generated from each BMD image for 5 different pixel radii settings, R_i , $i = \{1, \dots, 5\}$. After SIM images were generated, 9 evenly distributed percentile features, denoted as SIM.p9Ri, $i = \{1, 2, 3, 4, 5\}$, were extracted from scaling index images for each radius setting to characterize the non-linear microstructure organization of BMD images (Fig. 1.).

Function Approximation

After the calculation of the features sets, their ability in predicting the biomechanical strength as measured by the failure load was evaluated. Standard multi-regression analysis (MultiReg) was used for each feature set to assess a linear prediction. In addition, support vector regression [23] with a linear kernel (SVRLin) was also used. The SVRLin implementation was taken from the libSVM library [24].

Prediction Performance

In order to generalize the prediction performance of the image features, the set of VOIs was divided into training and test sets. In one iteration, a randomly selected training set of VOIs (80%) was used to approximate the target function (failure load). The resulting model was used to predict the failure load of the remaining, independent test set. The average residual error between the predicted failure load FL_{pred} and the true failure load FL_{true} for the VOIs in this test set T_i , $i = 1, \dots, N_{iter}$, was measured by the root-mean-square error,

$RMSE_{T_i} = \sqrt{\langle (FL_{pred} - FL_{true})^2 \rangle_{T_i}}$. This iteration was repeated $N_{iter} = 50$ times resulting in a RMSE distribution for each bone feature set. In addition, R^2 was calculated for each iteration. A Wilcoxon signed-rank test was used to compare two RMSE distributions and test for statistical significant differences in performance.

3. RESULTS

Different feature groups were used to construct the models for bone strength prediction. Among these feature groups, conventional BMD statistical features such as standard

deviation, skewness, kurtosis and 9 quantiles do not show improvement in prediction performance when compared with mean of BMD regardless of which regression algorithm was used. However, with our proposed feature extraction method, i.e. scaling index method, the performance of predicting bone strength is significantly improved.

Figure 2 shows the prediction performance results indicated by RMSE by using different feature groups with MultiReg and SVRlin. The red horizontal dash line indicates the prediction performance of the clinical standard, which uses mean of BMD and MultiReg; whereas, the blue horizontal dash line indicates the best prediction performance achieved by using SIM feature with SVRlin. The RMSE is significantly reduced ($p < 0.005$) when comparing with the clinical standard.

Figure 3 shows the prediction performance results indicated by R^2 by using different feature groups with MultiReg and SVRlin. The red horizontal dash line indicates the prediction performance of the clinical standard, which uses mean of BMD and MultiReg; whereas, the blue horizontal dash line indicates the best prediction performance achieved by using SIM feature with SVRlin. The RMSE is significantly reduced ($p < 0.005$) when comparing with the clinical standard.

In Table 1, the numerical results of prediction performance from different feature groups with MultiReg and SVRlin are presented in terms of RMSE and R^2 . The lowest RMSE (0.842) and highest R^2 (0.62) values were noted with SIM features processed with SVRlin, which significantly outperformed the standard FL prediction approach of using BMD.mean with MultiReg ($\text{RMSE} = 1.103 \pm 0.262$, $R^2 = 0.395$, $p < 0.005$).

4. DISCUSSION

Current bone strength estimation has relied on the measurement of bone mineral density through DXA or quantitative CT; however, previous studies have shown that BMD measurement alone does not fully describe nor accurately estimate the biomechanical strength of the bone [25–32]; therefore, its subsequent use in osteoporosis diagnosis is limited. Moreover, studies have shown that the changes in trabecular bone are also significantly related to the bone strength. Huber et al. have shown that incorporating the texture feature analysis such as GLCM to characterize the trabecular bone texture can significantly improve the biomechanical strength prediction [33].

Although GLCM features can be used to characterize the texture features for trabecular bone, the information of local micro-architecture dimensionality is overlooked. In this study, a more sophisticated feature extraction technique, i.e. the Scaling Index Method, was used to extract high dimensional features that characterized the micro-structural organization of trabecular bone through its local scaling properties. A more sophisticated machine learning algorithm, i.e. support vector regression (SVRlin), was used to construct a bone strength predicting model. The performance of FL prediction using these SIM features with SVRlin was compared with the standard clinical approach which used mean BMD values with multi-regression analysis. Our results show that such non-linear geometric features, when used in combination with support vector regression analysis, can contribute to improve the

performance of biomechanical strength prediction when compared to conventional BMD measures.

5. CONCLUSION

In conclusion, scaling index method can be used to extract high dimensional geometric features to characterize the micro-structural organization of trabecular bone. Our results indicate that using such features in combination with support vector regression can significantly improve the performance of predicting biomechanical strength of proximal femur specimen when compared to conventional approaches, which uses only mean BMD with multi-regression. Therefore, our proposed method could play a significant role in bone fracture risk prediction in the context of computer-aided diagnosis for osteoporosis.

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Figure 1.

Left Panel: (Top row) The center slice of the head VOI of proximal femurs with the highest Failure Load (FL) (left), medium FL (center), and the lowest FL (right). The images are scaled to a bone mineral density window of $[-200, 1200]$ mg/cm^3 . (Second row) The corresponding SIM images with radii setting, $R = 5$. **Right Panel:** The percentage of scaling index distribution within the ROIs of different FL cases (Red, blue and green denote high, medium and low FL respectively).

Figure 2.

Prediction performance indicated by RMSE between different feature groups and MultiReg and SVRlin. The red vertical bars are the 25 percent and 75 percent prediction performance distribution based on 50 iterations by using MultiReg. The blue vertical bars are the 25 percent and 75 percent prediction performance distribution based on 50 iterations by using SVRlin.

Figure 3.

Prediction performance indicated by R^2 between different feature groups and MultiReg and SVRlin. The red vertical bars are the 25 percent and 75 percent prediction performance distribution based on 50 iterations by using MultiReg. The blue vertical bars are the 25 percent and 75 percent prediction performance distribution based on 50 iterations by using SVRlin.

Table 1

The prediction performance of different feature groups with Multi-Regression and Support Vector Regression are shown in RMSE and R^2 . The underlined values denote the standard clinical method, i.e. mean BMD with MultiReg. The SIM features computed with R4 (radius = 4) yield the best prediction result (RMSE = 0.842 $\pm$ 0.209, R^2 = 0.62) in contrast with mean BMD (RMSE = 1.103 $\pm$ 0.262, R^2 = 0.395, p < 0.005).

Feature Groups	MultiReg		SVRlin	
	RMSE (std)	R^2 (std)	RMSE (std)	R^2 (std)
<u>BMD.mean</u>	<u>1.103(0.262)</u>	<u>0.395(0.225)</u>	1.142(0.272)	0.395(0.225)
BMD.m2	1.119(0.272)	0.389(0.229)	1.166(0.270)	0.382(0.228)
BMD.m4	1.234(0.315)	0.313(0.235)	1.263(0.308)	0.323(0.241)
BMD.p9	1.541(0.341)	0.098(0.099)	1.336(0.238)	0.074(0.109)
SIM.p9R1	1.068(0.235)	0.530(0.213)	0.941(0.206)	0.579(0.229)
SIM.p9R2	1.096(0.285)	0.517(0.189)	1.047(0.230)	0.520(0.216)
SIM.p9R3	1.036(0.230)	0.530(0.233)	0.870(0.202)	0.614(0.241)
SIM.p9R4	0.947(0.259)	0.561(0.248)	0.842(0.209)	0.620(0.247)
SIM.p9R5	0.972(0.336)	0.561(0.247)	1.078(0.411)	0.529(0.224)