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Predicting the Biomechanical Strength of Proximal Femur Specimens with Minkowski Functionals and Support Vector Regression

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Abstract

Regional trabecular bone quality estimation for purposes of femoral bone strength prediction is important for improving the clinical assessment of osteoporotic fracture risk. In this study, we explore the ability of 3D Minkowski Functionals derived from multi-detector computed tomography (MDCT) images of proximal femur specimens in predicting their corresponding biomechanical strength. 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 trabecular bone micro-architecture was characterized by statistical moments of its BMD distribution and by topological features derived from Minkowski Functionals. A linear multi-regression analysis and a support vector regression (SVR) algorithm with a linear kernel were used to predict the failure load (FL) from the feature sets; the predicted FL was compared to the true FL determined through biomechanical testing. The prediction performance was measured by the root mean square error (RMSE) for each feature set. The best prediction result was obtained from the Minkowski Functional surface used in combination with SVR, which had the lowest prediction error (RMSE = 0.939 ± 0.345) and which was significantly lower than mean BMD (RMSE = 1.075 ± 0.279 , $p < 0.005$). Our results indicate that the biomechanical strength prediction can be significantly improved in proximal femur specimens with Minkowski Functionals extracted from on MDCT images used in conjunction with support vector regression.

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Keywords

trabecular bone; biomechanical strength prediction; multi-detector computed tomography; bone mineral density; Minkowski Functionals; support vector regression

1. MOTIVATION/PURPOSE

Osteoporosis is one of the most common age related diseases amongst the elderly population, and is usually characterized by an imbalance in bone resorption and apposition. A direct consequence of the progression of osteoporosis are the occurrence of osteoporotic fractures, which can adversely affect the quality of life for the patient and increase the mortality rate. This highlights the need for accurate prediction of osteoporotic fracture risks in clinical assessment and management of osteoporosis.

Currently, dual-energy X-ray absorptiometry (DXA) is the standard technique for measuring bone quality in terms of bone mineral density (BMD) for purposes of fracture risk estimation [1–2]. Such BMD measurements, when performed at the proximal femur, have been shown to be predictive of bone fractures when compared to other anatomical sites [1–3]. To address several shortcomings of DXA-derived BMD measurements, quantitative computer tomography (QCT) has recently been proposed for extracting BMD measurements exclusively from the trabecular compartment [4–6]. 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. 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 in the trabecular compartment can drastically increase the fracture risk.

Current computer-aided diagnosis systems are designed to 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 for diagnosis and monitoring of osteoporotic bone changes [7]. We propose a system where Minkowski Functionals derived from integral geometry are utilized for purposes of capturing topological properties of trabecular bone micro-architecture. Such features can serve as inputs for supervised learning algorithms like Multi-Regression and Support Vector Regression to construct models for future bone strength prediction. Therefore, the purpose of this study is to evaluate whether such Minkowski Functional-derived topological features extracted from MDCT images of proximal femur specimens provide a better prediction of bone strength than using mean BMD values, as discussed in the following sections. 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. [8–28].

2. DATA

Femur Specimens

50 left femora were harvested from fixed human specimens over a time period of four years at the Institute of Anatomy at the Ludwig Maximilians University, Munich, Germany. The donors had granted their body to the institute for educational and research purposes, in compliance with local institutional and legislative requirements [29]. The bones were removed from the specimens; the surrounding soft tissues were removed prior to the 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 before scanning.

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. Voxel size was $0.19 \times 0.19 \times 0.5 \text{ mm}^3$. For calibration purposes, a reference phantom with a bone-like and a water-like phase (Osteo Phantom, Siemens Medical Solutions) was placed in the scanner below the specimens.

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). Further details regarding this automated algorithm can be found in [30].

BMD Measurements

The mean BMD of each VOI was calculated by converting pixel attenuations on MDCT (Hounsfield units) into BMD values (mg/cm^3) using a linear relationship proposed in [31]. BMD was calculated as

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

where HA_W ($0 \text{ mg}/\text{cm}^3$) and HA_B ($200 \text{ mg}/\text{cm}^3$) were the densities of the water-like and bone-like parts of the hydroxyapatite calibration phantom respectively, while HU_W and HU_B were their corresponding attenuations on MDCT. Following the transformation, the

range of BMD values within the ROI was restricted to $[-200 \ 1200]$ to emphasize bone content. Examples of ROIs converted to BMD are shown in Figure 1.

Biomechanical Tests

The failure load was assessed using a side-impact test, simulating a lateral fall on the greater trochanter as described previously [32]. 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.

3. METHODS

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 19 evenly distributed quantiles (BMD.p19).

MF Features

In addition to BMD features, 3D Minkowski Functionals [33] were used to quantitatively represent the topological properties of trabecular bone. For this purpose, the VOIs were binarized at 15 thresholds selected at equal intervals between the minimum and maximum BMD values. For each binarized VOI, four Minkowski Functionals i.e. volume, surface area, mean breadth and Euler characteristic were calculated from binary images as follows –

$$\text{MF.volume} = n_c \quad (2)$$

$$\text{MF.surface} = -6n_c + 2n_f, \quad (3)$$

$$\text{MF.mean_breadth} = (3/2)n_c - n_f + (1/2)n_e, \quad (4)$$

$$\text{MF.Euler} = -n_c + n_f - n_e + n_v, \quad (5)$$

where " n_c " is the total number of cubes, " n_f " is the total number of faces, " n_e " is the total number of edges and " n_v " is the number of vertices. The volume feature records the number of white voxels in the binary image, the surface measures the surface area of the 3D binary structure, and the Euler characteristic is a measure of connectivity (topology) between the

white voxel regions. The Minkowski Functionals computed at each threshold were then combined to yield four 15-D feature vectors.

Function Approximation

After the computation of different trabecular bone characterizing features sets, their ability to predict the biomechanical strength of the femur specimens (measured by failure load) was evaluated. Standard multi-regression analysis was used for each feature set to assess a linear prediction. In addition, support vector regression (SVR) [34] with a linear kernel was used. SVR is an extension of support vector machines (SVM), which is a supervised learning model that is widely used in the literature for different data analysis and pattern recognition tasks. The SVR implementation was taken from the libSVM library [35].

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,

$$RMSE_{T_i} = \sqrt{\langle (FL_{pred} - FL_{true})^2 \rangle_{T_i}}. \quad (6)$$

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. In addition, the coefficient of determination R^2 was calculated to evaluate the correlation between different feature sets and FL_{true} for each iteration. A Wilcoxon signed-rank test was used to compare two RMSE distributions and test for statistical significant differences in performance. The statistical analysis, feature extraction, function approximation, performance evaluation and significance testing were performed in MATLAB, version R2010a (MathWorks, Natick, MA).

4. RESULTS

The prediction performance of different feature sets with multi-regression and SVR in terms of RMSE and R^2 are presented in Table 1. The best prediction performance was observed with Minkowski Functional surface ($RMSE = 0.939 \pm 0.345$, $R^2 = 0.544 \pm 0.265$), while comparable performance was noted with Minkowski Functionals breadth ($RMSE = 0.954 \pm 0.304$, $R^2 = 0.537 \pm 0.245$) and volume ($RMSE = 1.003 \pm 0.378$, $R^2 = 0.517 \pm 0.277$). All of these feature sets yielded a significantly improved prediction performance over MDCT-derived mean BMD ($RMSE = 1.075 \pm 0.279$, $R^2 = 0.417 \pm 0.228$) ($p < 0.005$). We also note that for smaller feature sets such as mean BMD, there was no significant difference in prediction performance when used in conjunction with multi-regression and SVR machine learning algorithms. However, for larger feature sets such as those derived from Minkowski

Functionals, feature sets used in conjunction with SVR significantly outperformed those processed with standard multi-regression analysis.

5. NEW AND BREAKTHROUGH WORK

Measurements of BMD through multi-detector CT or DXA do no account for a complete characterization of trabecular bone health in terms of quality or structure. This limits the accuracy of such BMD measurements in bone strength prediction and subsequent diagnosis of osteoporosis. To address this shortcoming, we pursue a more sophisticated global characterization of trabecular bone micro-architecture in this study for improving bone strength prediction in the proximal femur. Specifically, we used topological features derived from Minkowski Functionals for characterizing bone structure in the femoral trabecular compartment. In addition, we also investigate the use of a sophisticated machine learning algorithm, i.e. SVR, to construct the bone strength predicting model. The performance of FL prediction in the femoral using such topological features with SVR was compared with a baseline approach which used mean MDCT-derived BMD in conjunction with conventionally used multi-regression. Our results show that such Minkowski Functional-derived topological texture features, when used in combination with support vector regression, can contribute to improvements in biomechanical strength prediction, especially when compared to more conventional BMD measures.

We specifically focus on characterization of trabecular bone micro-architecture in the femoral head; features extracted from this anatomical region have shown better correlation to specimen failure load over those extracted from other regions such as the neck or trochanter [30]. Of the feature sets investigated in this study, the best prediction performance was noted with Minkowski Functionals volume, surface and mean breadth (curvature). The global characterization provided by these feature sets accounts for both the density and the geometry of trabecular bone micro-architecture which likely explains their superior prediction of femoral bone strength over MDCT-derived mean BMD. We also note that the best prediction performance with such large feature sets (15-D feature vectors in this case) is achieved only when used in conjunction with SVR. This suggests that standard multi-regression analysis does not properly handle feature sets of large sizes. However, when the size of the feature set is small (less than 4 in this study), both multi-regression and SVR yield comparable results. Thus, the choice of machine learning algorithm used plays an important role in the overall bone strength prediction performance achieved.

6. CONCLUSION

In conclusion, the results presented in this work indicate that topological features derived from Minkowski Functionals used in combination with support vector regression can significantly improve the prediction of biomechanical strength in proximal femur specimen when compared to conventional approaches. The automated and non-subjective manner in which the trabecular bone micro-architecture is analyzed and the prediction performance achieved suggest tremendous potential in serving as imaging markers for diagnosis of osteoporosis, monitoring disease progression and evaluating responses to therapeutic intervention.

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Figure 1. The center slice of the head VOI of proximal femurs with the highest failure load (left), medium FL (center), and the lowest FL (right). The images are scaled to a bone mineral density window of $[-200, 1200]$ mg/cm³.

Figure 2.

Comparison of prediction performance (RMSE) for trabecular bone characterizing features extracted from the femoral head on MDCT, i.e. mean BMD and Minkowski Functionals, when processed with multi-regression (red circle) and SVR (blue square). For each RMSE distribution, the central mark corresponds to the median and the edges are the 25th and 75th percentile.

Figure 3.

Comparison of prediction performance (R^2) for trabecular bone characterizing features extracted from the femoral head on MDCT. i.e. mean BMD and Minkowski Functionals, when processed with multi-regression (red circle) and SVR (blue square). For each RMSE distribution, the central mark corresponds to the median and the edges are the 25th and 75th percentile.

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 baseline for comparison, i.e. mean BMD with multi-regression. As seen here, Minkowski Functional surface yields the best prediction result.

Feature Groups	Multi-Regression		SVR	
	RMSE (sth)	R^2 (sth)	RMSE (sth)	R^2 (sth)
<u>BMD.mean</u>	<u>1.075 (0.279)</u>	<u>0.417 (0.228)</u>	1.100 (0.292)	0.417 (0.228)
BMD.m2	1.099 (0.268)	0.394 (0.226)	1.129 (0.284)	0.389 (0.225)
BMD.m4	1.223 (0.306)	0.332 (0.236)	1.215 (0.317)	0.339 (0.229)
BMD.p19	1.707 (0.402)	0.152 (0.151)	1.138 (0.276)	0.371 (0.212)
MF.volume	1.619 (0.778)	0.293 (0.253)	1.003 (0.378)	0.517 (0.277)
MF.surface	1.536 (0.875)	0.320 (0.250)	0.939 (0.345)	0.544 (0.265)
MF.breadth	1.416 (0.585)	0.372 (0.255)	0.954 (0.304)	0.537 (0.245)
MEuler	1.247 (0.402)	0.372 (0.265)	1.042 (0.310)	0.501 (0.239)