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Commonality in the microarchitecture of trabecular bone: A preliminary study

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ABSTRACT

Understanding the relationship between the microstructure and mechanical function of trabecular bone is critical for prediction and prevention of bone fragility fractures. However, a detailed understanding of the structural design of trabecular microarchitecture is still missing. This study hypothesized that there exists a commonality in the underlying probabilistic distributions of microstructural features of trabecular bones, whereas the microstructural differences among individuals are primarily describe by a set of scalar parameters. To test the hypothesis, twenty-three trabecular bone specimens were obtained from two anatomic locations (*i.e.*, femoral neck and vertebral body) and a diverse group of seventeen donors of different age and sex. The number, size, spatial location, and orientation of individual plates and rods in the trabecular bone specimens were determined *via* volumetric decomposition of 3D μCT images using the Individual Trabecula Segmentation (ITS) technique. Then, *m*/*n* bootstrap Kolmogorov-Smirnov tests were performed to compare the normalized distributions of size, orientation, and spatial arrangement of trabecular plates and rods in the specimens. The results showed that 100% of the twenty-three normalized distributions of each microstructural feature were statistically equivalent irrespective of individual differences among the bone specimens, except the distributions of rod spatial arrangement (<100%). On the other hand, nonparametric Mann-Whitney *U* tests showed that a set of scalar parameters (*i.e.*, the number, average size, and average nearest neighbor distance of trabecular plates and rods) were statistically different among the individual specimens ($p < 0.05$). Due to the commonality of the underlying distributions, the individual differences in the trabecular microstructure among the specimens seemed to be reflected primarily by changes in the scalar parameters. The above results strongly support the hypothesis of this study and may shed more light on understanding the natural design of trabecular bone microstructures.

1. Introduction

Trabecular bone is highly porous (from 30 to 95% porosity), characterized by a foam-like cellular microstructure of interconnected plates and rods [1]. Biomechanically, trabecular bone contributes to the bulk mechanical competency of bone at various anatomic locations [2], *e.g.*, the proximal femur, distal radius/ulna, and vertebral bodies [3], at which it comprises up to 50–75% of the bone mass fraction [4–6]. In fact, recent numerical studies using μCT-based finite element analysis show that trabecular bone carries 40–70% of the load in the femoral neck [7], and as much as 76–89% of the load in the vertebrae [8].

Currently, bone mineral density (BMD) measured *via* Dual-energy X-ray Absorptiometry (DXA) is commonly used for diagnosing osteoporosis and predicting the risk of bone fragility fractures [9]. However, studies have shown that patients who experience a fragility fracture and those who do not, have a large overlap in BMD [10]. For example, a clinical study on a large cohort of patients shows that only 44% of women and 21% of men, among the patients who had a fragility fracture, were considered at risk based on BMD measurements [11]. Thus, BMD alone is not a reliable predictor of fragility fractures without taking into account microstructural changes in bone [2,9,11,12].

The complexity and seemingly random variations of trabecular microstructures among individuals have made it very challenging to characterize the microstructure [13,14]. Using μCT and μMRI imaging

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techniques, three-dimensional morphological parameters have been developed to quantitatively describe trabecular microarchitecture, such as structural model index (SMI), trabecular separation (Tb.Sp), total trabecular number (Tb.N), trabecular thickness (Tb.Th), trabecular connectivity, *etc.* [15–19]. However, these measurements only reflect global averages of some trabecular features. The other detailed information, such as spatial/orientation heterogeneity and area/length distributions of individual trabeculae (*i.e.*, plates and rods), is still missing. In fact, these microstructural features may also significantly contribute to the mechanical properties of trabecular bone [20,21].

Recent advances in image processing techniques (*e.g.*, skeletonization and volumetric spatial decomposition) have made it possible to obtain a complete segmentation of individual plates and rods in trabecular bones [15,22,23]. Using these advanced techniques, the size and orientation distributions of individual trabecular plates and rods have been analyzed [15,24–26]. Interestingly, previous results indicated that the underlying size distribution of trabeculae might follow a similar pattern among bone specimens from different anatomic locations (*e.g.*, femoral neck, vertebral body, and distal tibia) [15]. This observation raises an interesting scientific question: do the microstructural features of trabecular bone have common underlying distributions, regardless of individual differences in age, sex, and anatomical locations? Apparently, trabecular bone is a natural structure adapted to meet its functional requirements [27,28]. Since the functional requirements of trabecular bone are in general similar for all people, it is reasonable to presume that commonality may exist in trabecular microstructures. On the other hand, the individual differences observed among trabecular microstructures may be differentiated by a set of parameters that vary with individuals but are independent of the underlying commonality.

To this end, the overall hypothesis of this study is that there exists a commonality in the underlying probabilistic distributions of microstructural features of trabecular bones, whereas the microstructural differences among individuals are primarily captured by a set of scalar parameters. In this preliminary study, we intended to investigate whether such microstructural commonality in trabecular bone exists using a relatively small but diverse group of bone specimens obtained at two anatomic locations, femoral neck and lumbar vertebral body, and from donors of different age, sex, and bone volume fraction.

2. Materials and methods

2.1. Specimen preparation

Twelve proximal femurs and eight lumbar 1 (L1) vertebral bodies were acquired from ten male (67.5 ± 12.8 years of age) and seven female donors (70.8 ± 13.4 years of age) (Table 1). A total number of twenty-three specimens (N = 23) were prepared from the bones. Among them, twelve were prepared from femoral neck, and eleven were prepared from vertebral bodies. Of the twelve femoral neck specimens, nine were obtained each from nine different donors, with the three additional specimens acquired from the contralateral femurs of three of the donors. Of the eleven vertebral body specimens, eight were obtained each from eight different donors, with the three additional specimens acquired from the same vertebral body of three of the donors (Table 1). Despite the limited number of specimens, the group of specimens were considerably diverse in terms of anatomic location, donor sex, donor age, and bone volume fraction (BV/TV), which was required for testing the hypothesis of this study. Regarding specimen preparation, cylindrical specimens (8.7 ± 0.1 mm in diameter and 8.1 ± 0.2 mm long) were cored from the center portion of femoral neck and vertebral body, with the axis of the cored specimen being aligned as much as possible with the principal trabecular orientation, according to an established protocol in the literature [29–32]. Using the samples, only local trabecular bone microstructures were examined in this study, without considering regional variations of microstructure in whole femurs and vertebral bodies.

2.2. Extraction of key microstructural features

The bone specimens were scanned using μCT (ViVaCT 40, Scanco Medical) following the protocol reported elsewhere [15]. A 3D image of each specimen was rendered at a voxel size of 21 μm, which had a good resolution to capture microstructural features of the bone specimens. The size, spatial location, and orientation of individual plates and rods in the trabecular bone specimens were determined using the 'Individual Trabecula Segmentation' (ITS) software [15]. The output information generated from ITS included the total number of plates and

Table 1
General information about human donors from which bone samples were prepared and scalar factors used to normalize the histogram of structural parameters of trabecular bone.

Age (yrs.)	Sex	Anatomic location[a]	BV/TV[b]	Number of plates	Number of rods	No. density of plates (#/mm^3)	No. density of rods (#/mm^3)	μ_{PA} (mm^2)	μ_{PT} (μm)	μ_{PS} (μm)	μ_{RL} (mm)	μ_{RD} (μm)	μ_{RS} (μm)
73	M	FN	0.122	4911	1388	10.2	2.88	0.100	106	232	0.403	98.8	304
80	M	FN	0.132	5754	2172	11.9	4.51	0.090	102	218	0.385	87.7	255
90	F	FN	0.143	5293	1118	11.0	2.32	0.104	110	214	0.381	93.7	305
90	F	FN	0.153	5512	1213	11.4	2.52	0.106	110	215	0.379	88.7	293
40	M	FN	0.193	10,132	3945	21.0	8.19	0.072	104	194	0.371	93.3	217
73	M	FN	0.208	7576	2251	15.7	4.67	0.093	122	213	0.379	100	252
85	M	FN	0.356	14,157	4895	29.4	10.17	0.081	128	189	0.364	92.8	198
85	M	FN	0.36	14,700	5305	30.5	11.02	0.079	127	186	0.363	93.1	186
64	F	FN	0.377	11,146	3924	23.1	8.15	0.100	137	202	0.378	91.4	194
51	F	FN	0.382	11,829	4210	24.6	8.74	0.091	139	193	0.382	97.4	207
64	F	FN	0.429	11,359	3840	23.6	7.97	0.107	140	199	0.39	90.7	194
80	F	FN	0.443	10,656	5370	22.1	11.15	0.104	150	192	0.397	93.3	185
76	M	VB	0.093	3635	1832	7.5	3.80	0.091	115	232	0.453	104	284
72	F	VB	0.057	1794	1191	3.7	2.47	0.091	125	236	0.502	115	300
69	M	VB	0.077	2773	1397	5.8	2.90	0.105	112	250	0.494	112	321
70	M	VB	0.088	3461	1785	7.2	3.71	0.087	116	229	0.48	106	296
68	F	VB	0.093	3330	2231	6.9	4.63	0.084	119	233	0.463	114	273
66	M	VB	0.096	5068	2962	10.5	6.15	0.073	100	220	0.459	99.4	269
70	M	VB	0.104	3982	1326	8.3	2.75	0.105	108	238	0.462	95.7	301
48	M	VB	0.104	4277	2286	8.9	4.75	0.087	110	228	0.496	103	297
60	M	VB	0.108	5105	1835	10.6	3.81	0.093	100	227	0.447	94.2	285
48	M	VB	0.111	4674	2578	9.7	5.35	0.081	114	219	0.48	103	273
68	F	VB	0.157	4920	4269	10.2	8.87	0.082	136	218	0.428	114	209

μ_{PA}: Mean plate area; μ_{PT}: Mean plate thickness; μ_{PS}. Mean nearest neighbor distance of plates; μ_{RL}: Mean rod length; μ_{RD}: Mean rod diameter; μ_{RS}: Mean nearest neighbor distance of rods.
[a] Anatomic Location: Femoral Neck (FN) and Lumbar 1 Vertebral Body (VB).
[b] BV/TV: Ratio of bone volume *vs.* tissue volume.