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Age-Related Changes and Regional Variations in Three-Dimensional Microstructural Properties of Human Proximal Femoral Trabecular Bone

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崔文權

Age-Related Changes and Regional Variations in Three-Dimensional Microstructural Properties of Human Proximal Femoral Trabecular Bone

by
Wen Quan Cui

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Supervised by
Ye Yeon Won, M.D., Ph.D.

Department of Medical Sciences
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최문권의 의학 박사학위 논문을 인준함.

심사위원장	조 재 호 인
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심사위원	민 병 현 인
심사위원	송 주 현 인
심사위원	원 예 연 인

아주대학교 대학원

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- ABSTRACT -

Age-Related Changes and Regional Variations in Three-Dimensional Microstructural Properties of Male Proximal Femoral Trabecular Bone

Purpose: The purpose of this study was therefore to explore regional variations in the 3D microstructure of trabecular bone in human proximal femur, with respect to aging.

Materials and Methods: A total of 162 trabecular bone cores were obtained from six regions (femoral head, superior and inferior regions of the neck, and superior/middle and inferior regions of the trochanter) of twenty-seven normal femora of Korean male cadaver donors, aged 40-90 years. These specimens were scanned using high-resolution micro-computed tomography (micro-CT). The following 3D microstructural parameters were calculated: bone volume fraction (BV/TV), trabecular thickness (Tb.Th), separation (Tb.Sp) and number (Tb.N), structure model index (SMI) and degree of anisotropy (DOA).

Results: The results showed that the trabecular microstructure changed significantly with age, as well as varied from different regions of the proximal femur. There was a significant decrease in bone volume fraction and an almost identical decrease in trabecular thickness associated with aging at any region. Regional analysis demonstrated a significant difference not only in BV/TV, Tb.Th, Tb.Sp, Tb.N, DOA between superior and inferior neck, but also difference in BV/TV, Tb.Sp, Tb.N, SMI, DOA between superior and inferior trochanter.

Conclusions: Age-related changes in bone loss and trabecular microstructure within the male proximal femur are not uniform in this Korean cadaveric population. As a result of mechanical and age-related adaptation, significant regional variations in microstructural properties of trabecular bone are likely to be an important factor affecting the mechanical properties of the proximal femur.

Key Words: Aging; Microstructure; Trabeculae; Proximal femur.

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ABBREVIATION

μCT: microcomputed tomography

BV/TV: bone volume fraction

Tb.Th: trabecular thickness

Tb.Sp: trabecular separation

Tb.N: trabecular number

SMI: structure model index

DOA: degree of anisotropy

FH: femoral head

NS: superior region of the neck

NI: inferior region of the neck

TS: superior region of the trochanter

TM: middle region of the trochnater

TI: inferior region of the trochanter

Ⅰ. INTRODUCTION

Hip fractures are one of the most common outcomes of age-related and postmenopausal osteoporosis and often result in high rates of morbidity and mortality in the elderly population (Dubey et al., 1999; Riggs et al., 1995). It has been reported that 50% of patients are unable to walk without assistance and 25% required long-term domiciliary care, and 20% died within 6 months (Riggs et al., 1995). It represents a serious socioeconomic health problem with a rapidly increasing proportion of elderly in the world. While osteoporosis is primarily a disease of postmenopausal women, at least 20% of people with osteoporosis are men (International Osteoporosis Foundation, 2000c). Almost one-third of all hip fractures that occur worldwide are suffered by men (Siddiqui et al., 1999) and the incidence of hip fractures rises exponentially with aging in men as in women (Eastell, 1998). An estimate has been done by Gullberg et al. (Gullberg et al., 1997) that 1.25 million hip fractures (338,000 in men and 917,000 in women) occurred worldwide and that the number of hip fractures will increase by 3.1 time in men and 2.4 time in women by 2025. Furthermore, many studies also show that in the general population, mean age at the first hip fracture is usually younger in men than in women, (Dahl et al., 1980; Holmberg et al., 1987; Nydegger et al., 1991) but the rate of mortality after a hip fracture is twice as high for men as it is for women (Seeman, 1999). Moreover, men that sustain a hip fracture have a 3.2-fold increase in the risk of subsequent hip fracture and a relative risk of 6.3 for any subsequent fracture (Colon-Emeric et al., 2000). Even so, it is surprising that in contrast to postmenopausal osteoporosis in women, the mechanism of age-related bone loss in men has been less studied.

Numerous studies have been performed to examine the potential causes and risk factors for fractures of the proximal femur. Despite significant relationship between hip fracture and both low bone mineral density (BMD) and falling, especially falls to the side, neither BMD nor falling is sufficient to definitively categorize risk group of the fracture. Previous clinical studies have also demonstrated that patients with / without fracture risk have overlapped BMD values (Cummings et al., 1995; Ross et al., 1990). A recent long-term study on Caucasian women, 65 to 84 years of age also showed that only 28% of hip fracture cases can be attributed to low hip BMD (Stone et al., 2003). In addition, it is estimated that 90% of hip fractures result from a fall, but only 5% of falls result in a hip fracture (Greenspan et al., 1994). Thus it seems evident that several factors other than bone mass and falls are important for predicting hip fracture risk. Recently, a statement from NIH emphasizes that bone strength reflects the integration of two main features: bone quantity as assessed by bone mineral density (BMD), and bone quality referring to bone architecture, turnover, damage accumulation, collagen cross-linking, and mineralization (NIH Consens Statement, 2000). As for trabecular bone, it has been shown that the trabecular microarchitecture is closely associated with biomechanically determined bone strength, which has a substantial effect on the aging-induced fracture risk. (Cooper, 1993; Dempster et al., 1993). Therefore, the concept with respect to “microstructural deterioration” of trabecular bone was also included into the current definition of osteoporosis by the World Health Organization (WHO).

Traditionally, trabecular structure has been assessed using two-dimensional (2D) analysis of histomorphometry sections. While measures of trabecular number and thickness can be quantified from histological sections, the anisotropy of trabecular orientation, the plate- or rod-like structure and connectivity of trabecular bone, which is a three-dimensional (3D) quantity, cannot be determined. These 3-D microarchitectures are likely to play an important role in determining bone strength and provide better information for understanding bone quality (Ulrich et al., 1999; Ciarelli et al., 2000; Sugita et al., 1999; Gong et al., 2005). For this reason, age-related studies on trabecular structure have performed on vertebral trabecular bone (Gong et al, 2005), and tibia (Ding et al., 2002) and radius bone (Khosla et al., 2006). To our knowledge, nevertheless, no direct examination of age-related changes in 3-D microstructure of trabecular bone of the proximal femur has been published.

Recently, high-resolution microcomputed tomography (μCT) reconstruction of trabecular bone has been introduced that allow assessment of the bone microarchitecture in three dimensions (Hildebrand et al., 1999; Muller et al., 1998). With these techniques, the microstructure of the bone is reconstructed in a computer by stacking the images in a 3D voxel grid. The 3D voxel grid can be used to assess structural indices characterizing the 3D microarchitecture of cancellous bone. Moreover, morphological studies showed a high correlation between uCT-assessed microarchitecture and conventional histomorphometry, using a spatial uCT resolution of 20-26 um, suggesting that the mciroarchitecture can be assessed accurately by uCT (Muller et al., 1996; Uchiyama et al., 1997). It is understood that the bone structure is region-dependent. To determine if architecture has a role in osteoporotic fracture, systematic, regionally specific three-dimensional architectural measurements made at the site of the high fracture risk are needed. Lundeen et al. have investigated the age-related intrafemoral variations in cancellous bone density at 6 specific anatomic subregions (the femoral neck and trochanter) in the proximal femur of Caucasian females, they demonstrated that the distribution of age-related cancellous bone loss within the proximal femur is not uniform (Lundeen et al., 2000). Hereby, we further hypothesize that the age-related changes in trabecular bone microstructure appear to be varied from specific anatomic subregions of the proximal femur followed by non-uniform bone loss.

Thus, with reference to the discussion above, the aim of this experimental study therefore was to explore regional variations in three-dimensional trabecular bone microstructure of the proximal femur in males with aging.

Ⅱ. MATERIALS AND METHODS

Specimen selection and preparation

27 human right proximal femurs were obtained from male cadaver donors aged 40-90 years (mean 61.8 years, S.D. 13.5), without macroscopic pathological changes or a history of musculoskeletal diseases. All of these donors were Korean. They were not immobilized for more than 3 weeks before they died rather suddenly either due to trauma or due to acute disease, i.e. they had been active at a normal level until two weeks before death. The individuals with metabolic bone disease, on pharmaceutical regimens, or with other pathologies that might affect the skeletal system were excluded from this study in accordance with standard bone banking procedures. Other medical history was not available from these donors. And then the bone specimens were examined again, using fluoroscopy to rule out potential pathological changes affecting bone structural evaluation. Femora were selected following standard bone banking procedures (Bloebaum et al., 1993). Typically donors died of cardiac arrest, motor vehicle accidents, or other sudden, traumatic injuries. Each femur was stored in 70% ethyl alcohol for a minimum of 2 weeks, after which it was manually cleaned of adherent soft tissue with a scalpel. All the specimens were wrapped in saline-soaked gauze and shipped to the imaging facility.

Using osteometric techniques previously described by Lundeen (Lundeen et al., 2000), each intact femur was measured and marked to identify three locations which were comparable between all specimens: the base of the head, the neck-trochanter junction (base of the neck), and through the base of the lesser and greater trochanters (Fig.1-A).

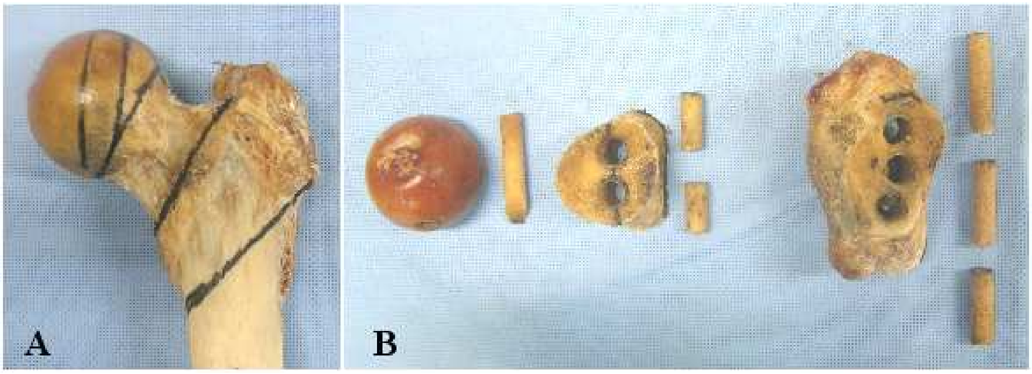


Fig. 1. A) The proximal femur was marked to identify three locations: base of the head, the neck-trochanter junction, and the base of the lesser and greater trochanters. B) The specimens were cut to provide three sections per femur, and trabecular cores were obtained from these three bone sections.

The subchondral principal compressive region and trabecular trajectory direction within femoral head were marked on antero-posterior and lateral views of the fluoroscopic images (Fig.1-A). The specimens were then cut at the specified locations using a reciprocating hand saw, providing three sections per femur: a head section, a neck section and a trochanter section (Fig.1-B). Trabeular bone cores were obtained from the principal compressive region of each femoral head, the superior and inferior aspects of each neck and superior/middle and inferior regions of trochanter segment using a cylindrical saw with an inner diameter of 8mm (Fig. 1-B). The specimens were drilled along the marked trabecular trajectory direction on the femoral head, parallel to the cortical axis avoiding cortical bone within the neck and trochanter sections (Fig.1-B). Thus a total of 27 head and 54 neck and 81 trochanter core specimens were obtained from the 27 proximal femurs. The distal end of each trabecular column was marked. All bone cores were put into tube plastic filled with 70% ethyl alcohol.

Mciro-CT imaging

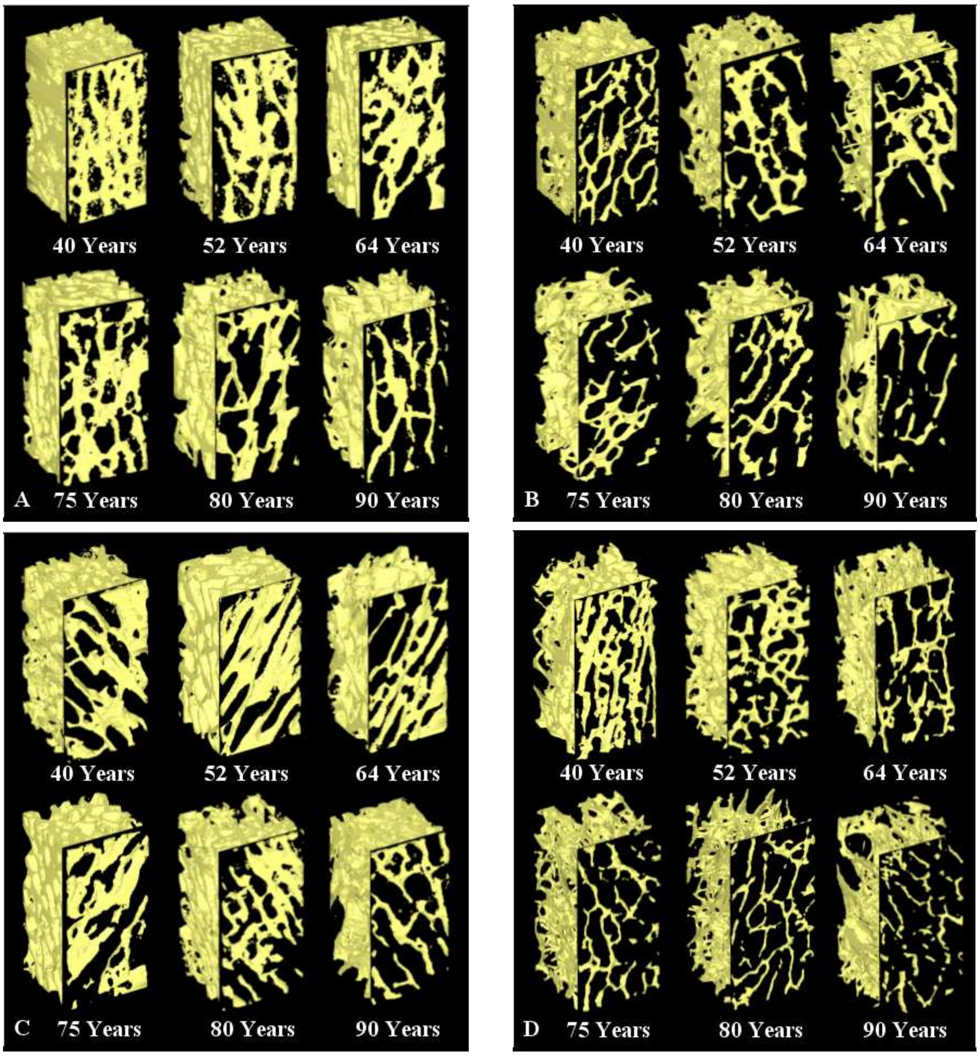
A mciro-CT system was used to evaluate the microstructure of trabecular columns. All bone cores were scanned with a high-resolution micro-computed tomography (μCT) system (Skyscan 1072, Belgium) at an isotropic voxel resolution of 21 μm. Each column was attached on a sample holder with a consistent superior-inferior orientation. The spatial resolution for specimen scanning was set to 21 um. From the resulting voxel data, the volume of interest (VOI) was selected as a central region with a side length of 5mm and height of 10 mm at 3 mm level below the proximal cutting surface of trabecular column, to exclude boundary artifacts. Trabecular bone tissue was segmented from marrow using an optimally global thresholding procedure. After scanning, 2D image data were transferred to the image software, and 3D reconstructions were made for visualization and display. With the μCT scanner's built-in software, the following three-dimensional structural parameters were calculated: bone volume fraction (BV/TV), trabecular number (Tb.N), thickness (Tb.Th) and separation (Tb.Sp), structure model index (SMI), and degree of anisotropy (DA). These structural parameters were assessed from the 3D μCT images using direct structural analysis techniques. Tb.Th, Tb.Sp and Tb.N were assessed using the distance transformation method described by Hildebrand et al. (Hildebrand et al., 1997)i.e. Tb.Th was calculated as the mean diameter of spheres filling the trabecular structure, while similarly Tb.Sp was calculated as the mean diameter of spheres filling the marrow phase. Inversing the mean diameter of spheres filling the skeletonized structure resulted in the Tb.N. The Structure Model Indes (SMI), a parameter describing the general shape of the structure, was calculated using the method described by Hildebrand and Ruegsegger (Hildebrand et al., 1997). BV (bone volume) is calculated from a surface generated by a triangle meshing technique. Total tissue volume was the volume of the entire scanned sample. The normalized indices, trabecular bone volume fraction (BV/TV) were then calculated from these values. The degree of anisotropy (DA) was determined from the ratio between the maximal and minimal radii of the mean intercept length (MIL) ellipsoid.

Statistical analysis

Linear regression analyses were used to assess the relationship between age and the microstructural parameters overall from 6 regions of the proximal femur. And then, the data were divided into three age groups: young (40-59 years), old (60-79 years), and elderly age (80-90 years) groups, and further divided into decades of life. Thus, 9, 11, 7 proximal femurs were included into young, old and elderly group, respectively. 4, 5, 5, 6, 4 and 3 proximal femurs were contained into 40, 50, 60, 70, 80 and 90 decades of life. One-way analysis of variance (ANOVA) was used to compare the structural parameters in the three different age groups.

Ⅲ. RESULTS

The trabecular histomorphometry from micro-CT showed significant changes with age, as well as varied from different regions of the proximal femur. Typical 3D reconstructions of trabecular microarchitecture from FH, NS, NI, TS, TM and TI of the proximal femur are shown for different age stages in Fig2. A-F.



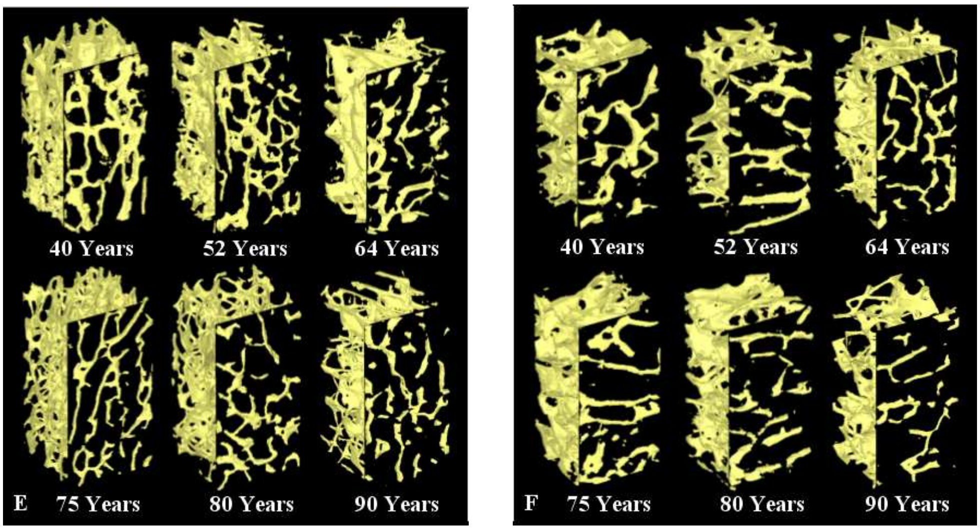
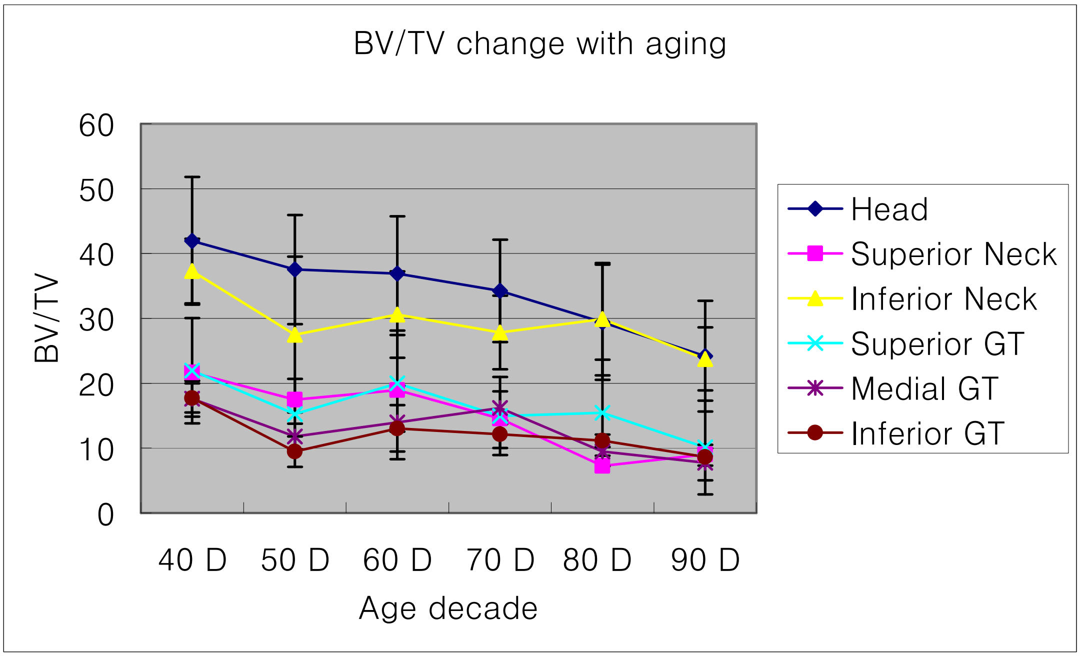
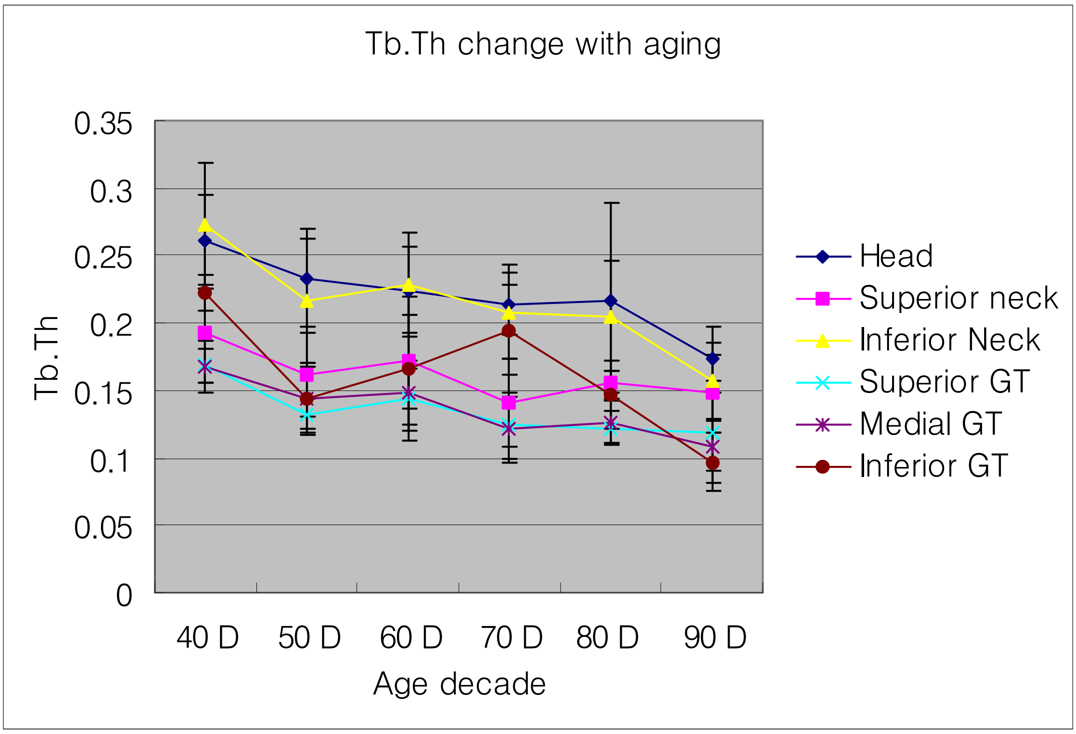
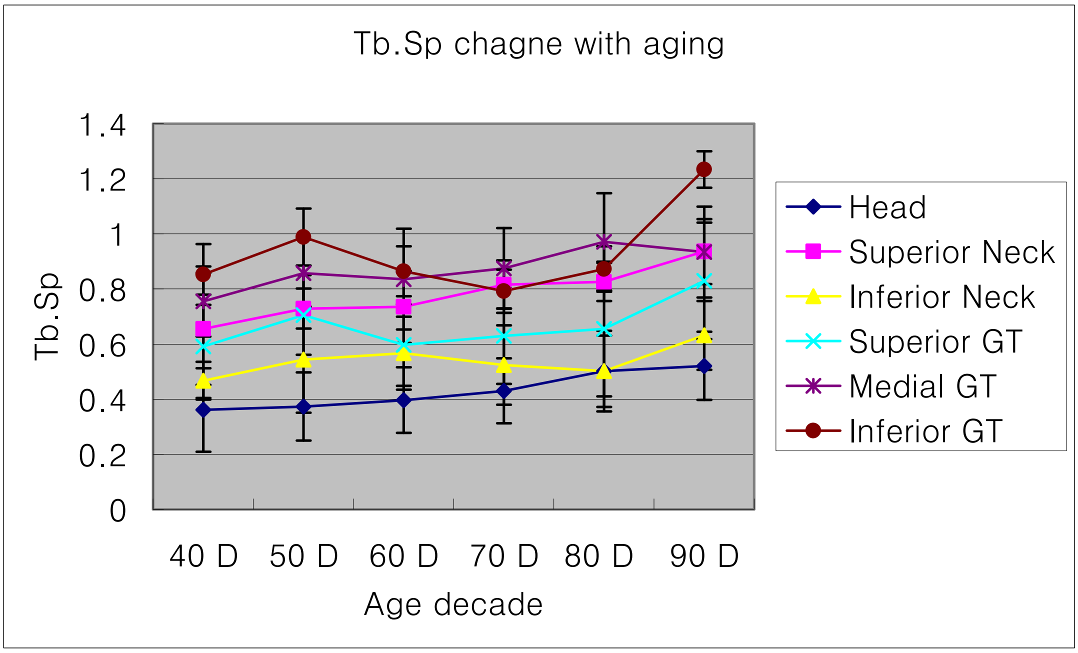
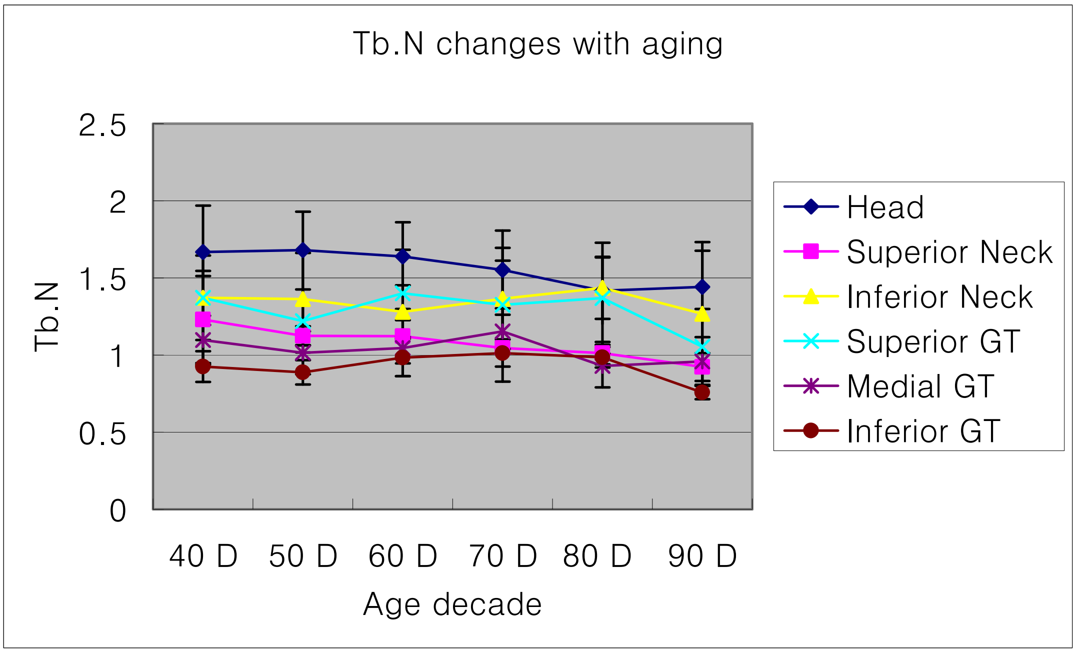


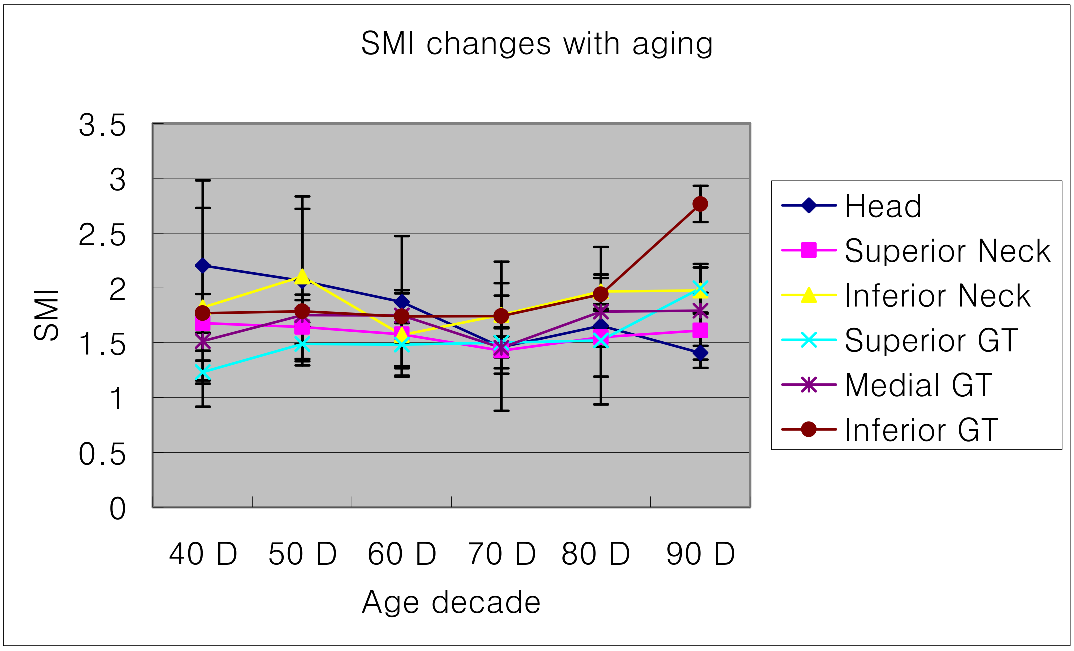
Fig. 2. A-F: Variations in 3D trabecular microstructure in the femoral head (A), the neck superior (B) and inferior regions (C), and the trochanteric superior (D), middle (E) and inferior regions (F) with aging.




Tb.Th change with aging
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
Tb.Th
40 D
50 D
60 D
70 D
80 D
90 D
Age decade
Head
Superior neck
Inferior Neck
Superior GT
Medial GT
Inferior GT


Tb.Sp chagne with aging
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Tb.Sp
40 D
50 D
60 D
70 D
80 D
90 D
Age decade
Head
Superior Neck
Inferior Neck
Superior GT
Medial GT
Inferior GT


Tb.N changes with aging
Tb.N
2.5
2
1.5
1
0.5
0
40 D
50 D
60 D
70 D
80 D
90 D
Age decade
Head
Superior Neck
Inferior Neck
Superior GT
Medial GT
Inferior GT


SMI changes with aging
SMI
3.5
3
2.5
2
1.5
1
0.5
0
40 D
50 D
60 D
70 D
80 D
90 D
Age decade
Head
Superior Neck
Inferior Neck
Superior GT
Medial GT
Inferior GT

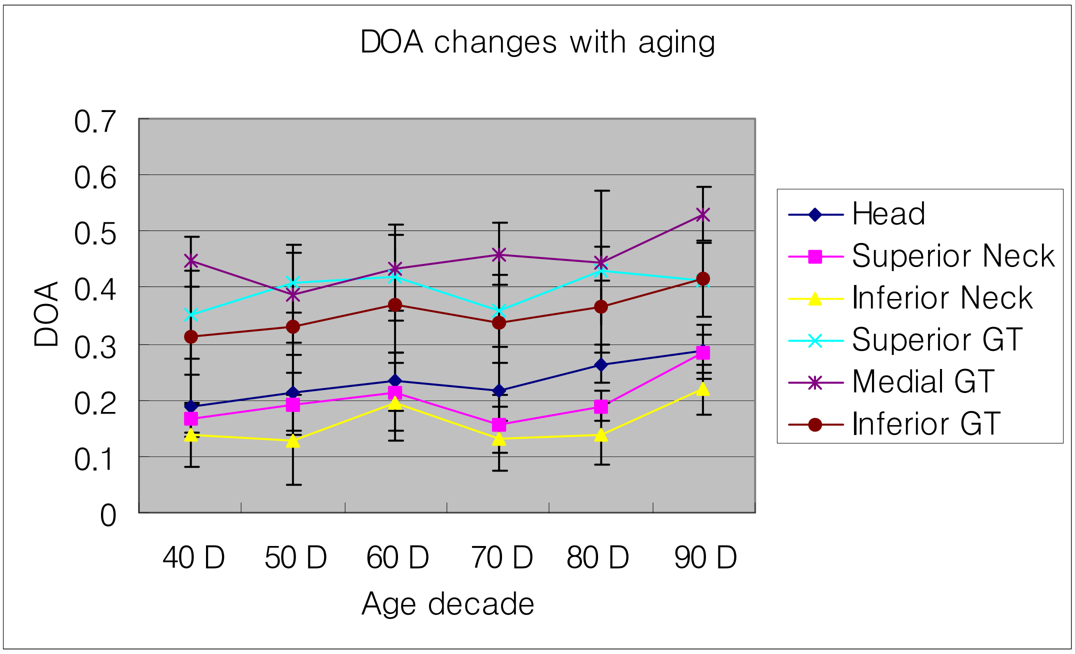


Fig. 3. Changes in microstructural properties of trabecular bone in 6 regions: the femoral head, neck superior and inferior regions, and trochanteric superior, medial and inferior regions.

Bone Volume Fraction

With increasing age, bone volume fraction decreased significantly in all of regions (From FH to TI, r = -0.54, -0.53, -0.39, -0.38, -0.51, -0.43, $p < 0.05$, respectively) as showed in Table I.

Table I

Regression coefficient r values from linear regression analysis for regional variations in 3D microstructural properties of trabecular bone with aging.

Microstructural parameters	FH N = 27	NS N = 27	NI N = 27	TS N = 27	TM N = 27	TI N = 27
BV/TV (%)	-0.54^{*}	-0.53^{*}	-0.39^{*}	-0.38^{*}	-0.51^{*}	-0.43^{*}
Tb.Th (mm)	-0.47^{*}	-0.36	-0.41^{*}	-0.62^{*}	-0.58^{*}	-0.49^{*}
Tb.Sp (mm)	0.43^{*}	0.51^{*}	0.21	0.18	0.33	0.11
Tb.N (/mm)	-0.39^{*}	-0.47^{*}	0.05	-0.08	-0.21	0.15
SMI	-0.35	-0.10	-0.11	0.5^{*}	0.42^{*}	0.46^{*}
DOA	0.45^{*}	0.35^{*}	0.22	0.24	0.21	0.16

Abbreviation: FH; Femoral head. NS; Neck superior region. NI; Neck inferior region. TS; Trochanter superior region. TM; Trochanter middle region. TI; Trochanter inferior region. BV/TV; Bone volume fraction. Tb.Th; Trabecular thickness. Tb.Sp; Trabecular separation. Tb.N; Trabecular number. SMI; Structure model index. DOA; Degree of anisotropy. * Significant correlation between the microstructural indices and age, $p < 0.05$.

This age-related decrease in BV/TV showed a proximate linear fashion in all regions at different baseline (Fig.3A), except for NI that was found to be 10.3%, 24%, 9.6%, 13.8% per decade. The trend was for NI to retain the relative high volume of trabecular bone after 50 years of age (Fig.3A). When the anatomic regional volume fraction data were analyzed for the different age groups, the highest BV/TV for any age groups was found in FH, the lowest BV/TV for both young and old group was in TI, and for elderly was in NS (Table II).

Table II Microstructural parameters derived from 6 regions in the three age groups.

Microstructural Prameters	Regions	Young group N = 9	Old group N = 11	Elderly N = 7
BV/TV (%)	FH	**39.9±9.03**	36.7±8.38	**28.4±8.05***
	NS	**19.7±7.04**	**18.5±7.21**	**7.61±7.17***†
	NI	32.8±9.81	30.3±6.36	27.4±9.35
	TS	18.9±6.31	19.5±6.06	14.4±6.08
	TM	**15.1±3.82**	**14.2±5.43**	**9.15±0.96***†
	TI	**13.9±4.84**	13.5±3.74	**10.6±1.39***
Tb.Th	FH	0.25±0.04	0.22±0.03	0.21±0.07
	NS	**0.18±0.04**	0.17±0.03	**0.15±0.01***
	NI	0.25±0.05	0.23±0.04	0.19±0.04
	TS	0.15±0.02	**0.14±0.02**	**0.12±0.01**†
	TM	**0.16±0.02**	**0.15±0.02**	**0.12±0.02***†
	TI	**0.19±0.05**	0.17±0.05	**0.14±0.03***
Tb.Sp	FH	0.37±0.13	0.40±0.11	0.51±0.13
	NS	**0.69±0.16**	0.74±0.13	**0.85±0.08***
	NI	0.50±0.14	0.56±0.13	0.53±0.13
	TS	0.64±0.17	0.60±0.14	0.69±0.23
	TM	**0.80±0.13**	0.81±0.19	**0.96±0.15***

	TI	0.91±0.12	0.86±0.09	0.94±0.18
Microstructural Parameters	Regions	Young group N = 9	Old group N = 11	Elderly N = 7
Tb.N	FH	**1.67±0.26**	1.63±0.21	**1.42±0.19***
	NS	**1.18±0.21**	1.11±0.17	**0.99±0.07***
	NI	1.37±0.23	1.28±0.16	1.4±0.19
	TS	1.3±0.25	1.39±0.27	1.31±0.34
	TM	1.06±0.15	1.08±0.21	0.93±0.12
	TI	0.91±0.09	0.99±0.11	0.94±0.12
SMI	FH	2.14±0.74	1.83±0.58	1.61±0.63
	NS	1.66±0.41	1.56±0.36	1.56±0.08
	NI	1.95±0.76	**1.53±0.39**	**1.97±0.14**†
	TS	1.35±0.18	1.48±0.19	1.61±0.36
	TM	**1.62±0.14**	1.72±0.26	**1.78±0.08***
	TI	**1.78±0.14**	**1.74±0.23**	**2.1±0.39***†
DOA	FH	**0.2±0.06**	0.23±0.05	**0.27±0.03***
	NS	0.18±0.04	0.21±0.07	0.21±0.05
	NI	0.13±0.06	0.19±0.07	0.16±0.06
	TS	0.38±0.07	0.41±0.08	0.43±0.12
	TM	0.42±0.07	0.44±0.07	0.46±0.05
	TI	0.32±0.11	0.36±0.10	0.38±0.04

Values are means ± standard deviation.

* Significant difference between young group vs. elderly group, $p < 0.05$. † Significant difference between old group and elderly group, $p < 0.05$.

There was a statistically significant difference in BV/TV measurements between young group and elderly group in FH, NS, TM and TI, with 28.8%, 61.4%, 39.4%, 23.7% lower in the elderly group compared with the young group, respectively. Significant difference in BV/TV between old group and elderly group was found only in NS and TM region, with a decrease by 58.9% and 35.6% in elderly. No significant difference between young group and old group was found in any regions. The inferior neck region demonstrated the smallest decline in volume fraction among three age groups, with an overall decline of 33.2%. These results are summarized in Table II. BV/TV in the inferior neck was statistically greater than in the superior region for all age groups. ($p < 0.05$). Trabecular BV/TV was significantly greater in the femoral neck than the trochanter in young and old groups. Regional analysis in the trochanter demonstrated no statistical difference between the superior, middle or inferior volume fractions at any age group.

Trabecular Thickness

Similar to BV/TV, Tb.Th decreased significantly with age in all regions, except for NS region ($r= 0.36$, $p < 0.05$; Table I and Fig.7B). With regard to variations in trabecular thickness by region, the greater Tb.Th was found in the compressive stress regions, i.e. FH and NI region, the thinning trabeculae were in the trochanteric region. Regarding changes in Tb.Th for different age groups within a given region of the proximal femur, the NS, TM, TI regions of trabeculae from young group had higher Tb.Th than those from elderly group. TS and TM regions of trabeculae from old group had higher Tb.Th than those from elderly group. There was no significant difference in Tb.Th between young and old group in any regions. These results are summarized in Table II.

Trabecular Separation

BV/TV and Tb.Th decreased with increasing age, while the trend for Tb.Sp was toward to increase in all regions (Fig.7C). But a statistically significant level was reached in FH and NS regions only ($p < 0.05$, Table I). With regard to variations in Tb.Sp by region, the greatest and least Tb.Sp were found in TM and FH for any age groups. There was a significant difference in Tb.Sp measurements between young group and elderly group in NS, TM ($p < 0.05$, Table II). No significant difference in Tb.Sp was found in other regions for any age groups.

Trabecular Number

Only in FH and NS regions Tb.N siginificantly decreased with age (Fig.7D), while the trend For NI and TI was toward to increase, but not reached a significant level (Table I). With regard to variations in Tb.N by region, the greatest and least amount of Tb.N were found in FH and TI regions. Regarding changes in Tb.N for different age groups within a given region, there was a significant difference in Tb.N between young and elderly group in FH and NS regions. No significant difference in Tb.N was found in other regions for any age groups.

Structure Model Index

With increasing age, SMI significantly increased in three regions of the trochanter. For other regions, no age-related changes in SMI were presented. Analysis in decade groups showed that it seemed to increase more dramatically at higher ages (> 70 years, Fig.7E), indicating that more rod-like structure was presented with increasing aging. The SMI was highest in elderly group of TI region, with significant difference between young/old group and elderly group. There was a significant difference in SMI between young group and elderly group in TM region, as well as a significant difference between old group and elderly group in NI region. These results are summarized in Table II.

Degree of Anisotropy

The trend for DOA was toward to increase with aging in all regions, but dramatic increase in DOA was in FH and NS regions, indicating that the aging trabeculae seem to align more strongly to the primary direction followed by bone loss. This parameter was relatively unchanged until the seventh decade, followed by a dramatically increase in the last decade investigated (Table II, Fig.7F). There was a significant difference in DOA between young group and elderly group in FH region. For other regions, no significant difference in DOA was found for any age groups.

Ⅳ. DISCUSSION

This study is the first to investigate regional variations in three-dimensional microstructural properties of proximal femoral trabeculae with aging. To draw a pattern of age-related bone changes, 3-D global morphometric indices were computed from micro-CT images in trabecular bone sampled from 6 sub-regions of the proximal femur of males, representing individuals over five decades of life. The contribution of these microstructural indices of trabecular bone to the mechanical properties of trabecular bone has been also widely accepted. The results of the present study demonstrate that the mechanisms for age-related changes in trabecular loss and microstructure appear to be different in our proposed sub-regions of the proximal femur defined as one of the most common fracture site.

The first and most accepted age-related change in trabecular bone structure is bone loss as expressed in a decrease of calcified bone tissue. It is well accepted that such bone loss is an important factor leading to enhanced bone fragility and fracture risk in the elderly. Such bone loss has been demonstrated in many studies for different anatomical sites, i.e. vertebral bone, the tibial, the radius, and the proximal femur. The results from our study are in line with these findings in overall. Interestingly, the distribution of such age-related bone loss within the male proximal femur is not uniform in this Korean cadaveric population. This finding is similar to a previous report for cancellous bone in selected regions of the proximal femur of Caucasian females. Specifically, with increasing age, there is a significant reduction in BV/TV in all of regions. This reduction displays a typical linear fashion in FH, NS, GM regions at different baseline level. However, the trend was for NI to retain the relative high volume of trabecular bone after 50 years of age. There was a significant difference in reduction in the magnitude of BV/TV between NS and NI, with 61.4%, 33.2% lower in the elderly group compared with the young group, respectively. Thus, NS is believed to undergo the greatest stress during a fall as well as the initiating site of neck fractures (Lotz et al., 1995). Such regional heterogeneity could be explained that various sub-region of the proximal femur are subjected different loading conditions. The trabeculae within the superior region of the femoral neck mainly undergo the tensile stress, called by the “principal tensile system”, while the trabeculae within the inferior region of the femoral neck undergo the compressive stress, called by the “principal compressive system”. It is known that osteocytes are more susceptible to the compression forces. An inhibitory signal is generated by the osteocytes, which is passed through their cell processes to osteoclasts to prevent bone resorption (Marotti et al., 1992). Additionally, Apparent BV/TV is the structure parameter most similar to BMD, and some studies demonstrated a well correlation exists between BMD values as measured by dual energy X-ray absorptiometry (DXA) or peripheral Quantitative computed Tomography (pQCT) and BV/TV values derived from multisection CT scans or micro-CT at a correlation coefficient of 0.67 and 0.94 in the femoral neck, respectively. (Ahi Sema Issever et al, 2002; Lai YM et al, 2005) However, current BMD measurements by DXA provide an averaged value for the entire neck and would not differentiate regional heterogeneity. This would be misleading for predicting the fracture risk of the femoral neck. Our results suggest that the absolute BMD of the superior region would be a useful clinical measurement, as the greatest reduction in BV/TV occurs in NS with aging.

It is well known that an interaction exists among the microstructural parameters. Following BV/TV, Tb.Th decreased significantly with age in all regions, except for NS region. However, regarding changes in Tb.Th for different age groups, a significant difference between young and elderly groups was found in NS. Surprisingly, there was no significant difference in Tb.Th among three groups in FH and NI regions that are subjected to the compressive force. It is intriguing to speculate that, when bone structure deteriorates later in life caused by the loss of bone mass, compensatory mechanisms try to maintain bone strength by increasing trabecular thickness. This is an important function for bone adaptation to mechanical loading. Similar demonstrations have been shown in several animal studies and human vertebral studies (McNamara et al, 2004; Moselilde, 1998; Waarsing et al., 2004). Investigations have also shown a significant age-related decrease in the thickness of horizontal trabeculae, but not in the thickness of vertical trabeculae (Mosekilde et al., 1998).

A number of studies have reported that trabecular bone loss in females is associated with a loss of trabecular elements, resulting in a significant increase in trabecular separation (Parkinson et al., 2002). An increase in Tb.Sp means that the trabecular elements are generally further separated from each other, which can be achieved by a general increase in the intertrabecular distance or by the occurrence of larger areas with no trabecular at all (“wholes”). Both cases clearly reduce bone strength because of a reduction in bone material. Our data also show that BV/TV and Tb.Th decreased with increasing age, while the trend for Tb.Sp was toward to increase in all regions. But a statistically significant level was reached in FH and NS regions only. Moreover, a significant difference in Tb.Sp measurements between young group and elderly group was found in NS, TM only. This finding was similar to a recent study (Tsangari et al., 2007), showing that the trabecular separation was less in aged males than aged females. It suggests a better preservation of the microarchitecture in males.

SMI represents the ratio of plate- and rod-like structures. In a three-dimensional image, we can clearly observe changes from the plate-like structure of trabecular bone to the rod-like structure with aging that we cannot see in a two-dimensional image. In according to our results, SMI significantly increased in three regions of the trochanter with increasing age, indicating that the structure model for trabeculae within trochanteric region represent more rod-like structure. In aging, the reduction in bone volume is mainly caused by a reduction in plate density, where the process of plate removal is initiated by an excessive depth of osteoclastic resorption cavities, leading to focal perforation of plates, followed by progressive enlargement of the perforation with conversion of plates to rods. These changes may cause loss in mechanical strength. A micro-CT study in the tibia by Ming D. et al. (Ding et al., 2002) have shown that the structure model index was the best predictor for Young’s modulus ($R^2=0.45$). Additionally, Cellular solid theory predicts different dominant deformation and failure mechanisms for different architectures (Gibson and Ashby, 1997). For instances, rod-like structures are more susceptible to large deformations such as bending and rotation of trabeculae than are plate-like structures. This theory is supported by the experimental data of Muller et al., who observed large deformations of trabeculae during compression tests in rod-like trabecular specimens but not plate-like specimens (Muller et al., 1998). Our results may help explain the increased incidence of trochanteric fractures in elderly populations. (why the trochanteric fractures are more common in elderly individuals). Interestingly, there was a significant difference in SMI between old and elderly groups in NI, although significant difference in BV/TV among three groups group was not found in NI region, indicating that SMI is more sensitive to age-related changes in trabecular structure. It is also noteworthy that the proposed model only included structural information not directly related to BMD or bone mass.

DOA is an index reflecting the orientation of trabecular bone, isotropy or anisotropy. Thus DOA also reflects trabecular adaptation function for mechanical environment. Our results showed that the trend for DOA was toward to increase with aging in all regions, but dramatic increase in DOA was in FH and NS regions, indicating that the aging trabeculae seem to align more strongly to the primary direction followed by bone loss. One point should be noted that the measurement value of DOA might be affected by the specimen preparation, i.e., trabecular coring orientation aligning the primary compressive or tensile dirction. However, in this study a consistent orientation was applied during coring trabeculr bone in the femoral neck and trochanteric regions. Thus this ensures reliable comparison between specimens. Recently, ciarelli et al. (Ciarelli et al., 2000) examined cancellous bone from age-matched woman with and without femoral neck fractures. Architectural parameters such as trabecular number, connectivity, and thickness were not significantly different between the groups. The maximal elastic modulus and ultimate stress in the inferosuperior direction were also the same. The only difference found was a significantly greater architectural anisotropy in the fracture group. It has demonstrated that degree of anisotropy is important for prediction of the fracture risk. Ming D. et al. have believed that DOA is predominant factor in determining the mechanical properties of cancellous bone of tibia (Ding et al., 2002). Following aging and progression of bone loss, the remodeling occurred in the principal trabecular system of femoral head and subchondral bone of tibia are mainly adapted to compressive mechanical stress. Thus, trabecular orientation becomes more anistropic.

In summary, the greater bone loss occurs in NS compared to NI, whereas Ni maintained a significantly greater bone volume fraction. Such different bone loss pattern within two regions of the femoral neck suggests that the absolute BMD of the superior region would be a useful clinical measurement, as the greatest reduction in BV/TV occurs in NS with aging. Significant changes occur in microstructure of trabecular bone, despite only a slight reduction in bone volume fraction occurs. SMI and DOA are more sensitive to such age-related changes in trabecular structure.

Ⅴ. CONCLUSION

In conclusion, age-related changes in bone loss and trabecular microstructure within the male proximal femur are not uniform in this Korean cadaveric population. As a result of mechanical and age-related adaptation, significant regional variations in microstructural properties of trabecular bone are likely to important factors affecting the mechanical properties of the proximal femur.

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- 국문요약 -

인간 대퇴골 근위부의 3차원적 골소주 미세구조에서 연령에 따른 변화와 부위에 따른 차이

아주대학교 대학원 의학과

최문권

(지도교수: 원 예 연)

목적: 본 연구의 목적은 사람 대퇴골두 근위부 해면골의 3차원 미세구조의 나이와 부위에 따른 변화를 연구하고자 한다.

대상 및 방법: 한국인 사체 27구의 대퇴부에서 해면골 샘플은 6부위에서 162개 채취했다. 나이는 40-90세의 성인 남성이었다. 모든 샘플은 미세단층촬영기를 이용하여 촬영하였다. 촬영된 영상을 바탕으로 골소주 두께, 골소주 거리, 골 체적비, 구조모델지수, 이방성정도 그리고 골소주 개수 등의 형태학적 지수들은 계산되었다.

결과: 근위대퇴부의 형태학적 지수는 부위에 따른 차이 뿐 만 아니라 나이에 따른 중요한 변화를 보여준다. 골 체적비는 6부위 모두에서 나이가 증가함에 따라서 의미있게 감소했으며, 골소주 두께는 5부위에서 의미있게 감소했다. 대퇴경 상부와 하부 사이에서 골소주 두께, 골소주 간격, 골체적 비, 이방성정도 그리고 골소주 개수는 부위에 따라서 의미있는 차이를 보였으며, 대퇴전자 상부와 하부

사이는 골소주 개수, 골 체적비 구조모델지수, 이방성정도 그리고 골소주 개수에서 중요한 차이를 보였다.

결론: 남성 근위 대퇴부의 골 소실과 골소주 미세구조의 나이에 따른 변화는 부위에 따라서 일정하지 않았다. 해면골의 나이에 따른 순응적 적응으로 인해서 부위에 따른 미세구조의 다양한 변화는 근위 대퇴부의 기계적 특성에 영향을 미치는 중요한 인자라고 사료된다.

핵심어: 나이, 미세구조, 골소주, 근위 대퇴부