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Microarchitecture of the Radial Head and Its Changes in Aging

Matthias Gebauer · Florian Barvencik · Marcus Mumme · Frank Timo Beil · Eik Vettorazzi · Johannes M. Rueger · Klaus Pueschel · Michael Amling

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Abstract Fractures of the radial head are common; however, it remains to be determined whether the radial head has to be considered as a typical location for fractures associated with osteoporosis. To investigate whether the human radial head shows structural changes during aging, we analyzed 30 left and 30 right human radial heads taken from 30 individuals. The specimens taken from the left side were analyzed by peripheral quantitative computed tomography (pQCT) and micro-CT. The specimens taken from the right elbow joint were analyzed by radiography and histomorphometry. In these specimens pQCT revealed a significant decrease of total and cortical bone mineral density (BMD_{to} BMD_{co}) with aging, regardless of sex. Histomorphometry revealed a significant reduction of cortical thickness (Ct.Th), bone volume per tissue volume (BV/TV), and trabecular thickness (Tb.Th) in male and female specimens. In this context, mean BV/TV and mean trabecular number (Tb.N) values were significantly lower and, accordingly, mean trabecular separation (Tb.Sp) was significantly higher in female samples. The presented study demonstrates that the radial head is a skeletal site where different age- and sex-related changes of the bone structure become manifest. These microarchitectural changes might contribute to the pathogenesis of radial head fractures, especially in aged female patients where trabecular parameters (BMD_{tr} and Tb.Sp) change significantly for the worse compared to male patients.

Keywords Bone architecture/structure · Bone density · Quantitative computed tomography · Osteoporosis · Epidemiology · Aging

Matthias Gebauer, Florian Barvencik and Marcus Mumme contributed equally to this work.

M. Gebauer (✉) · F. Barvencik · M. Mumme · F. T. Beil · J. M. Rueger · M. Amling
Department of Trauma, Hand, and Reconstructive Surgery, University Medical Center Hamburg-Eppendorf, Martinistr. 52, 20246 Hamburg, Germany
e-mail: mgebauer@uke.uni-hamburg.de

M. Gebauer · F. Barvencik · M. Mumme · F. T. Beil · M. Amling
Center for Biomechanics and Skeletal Biology, University Medical Center Hamburg-Eppendorf, Martinistr. 52, 20246 Hamburg, Germany

E. Vettorazzi
Department of Medical Biometry and Epidemiology, University Medical Center Hamburg-Eppendorf, Martinistr. 52, 20246 Hamburg, Germany

K. Pueschel
Institute of Forensic Medicine, University Medical Center Hamburg-Eppendorf, Martinistr. 52, 20246 Hamburg, Germany

Fractures of the radial head or neck account for about 1.5–4% of all fractures and for 26% of all elbow fractures [1, 2]. Radial head fractures are classified according to Mason [3], who introduced three clinical types: type I fractures are fissure fractures or marginal sector fractures without displacement, type II fractures are dislocated marginal sector fractures, and type III fractures are comminuted fractures of the whole radial head. Undisplaced fractures usually result in minimal residual deficits independent of treatment, whereas displaced fractures have been described as having the risk of an unfavorable outcome [4].

Based on biomechanical and clinical evidence, radial head fractures are caused by a fall on the extended forearm or a direct trauma to the elbow [5]. While it is recognized that the trauma energy and the position of the elbow at the time of injury are important factors in the pathogenesis and severity of radial head fractures, the possible role of age- and sex-related changes in the radial head remains largely undefined.

In a retrospective analysis of 426 patients (235 females, 191 males) who were treated in our department with a fracture of the radial head, we observed a significant ($P <$ 0.001) difference of the average age at trauma between female (mean 55.8 ± 21.4 years, 48% of injured patients older than 60 years) and male (mean 39.2 ± 15.6 years, 9.4% of injured patients older than 60 years) patients [6].

Based on this epidemiologic observation, it is fair to assume that age- and sex-related bone loss occurs within the radial head and thereby might constitute a structural risk factor for fracture independent of the trauma mechanism. However, age- and sex-related structural changes within the radial head have never been studied in detail.

In addition, osteoporosis is the most frequent bone disease and constitutes a major health concern in the aging population in the Western Hemisphere [7]. It is characterized by a low bone mass caused by an imbalance between osteoblastic bone formation and osteoclastic bone resorption, a physiologically balanced process called "remodeling" that normally maintains bone mass almost constant [8].

If, however, the radial head is a skeletal region that is prone to display the characteristic changes of osteoporosis in its microarchitecture, then one has to consider that radial head fractures can occur as osteoporotic fractures as it is the case for fractures of the distal radius, the proximal femur, the proximal humerus, and the spine. Furthermore, as due to the demographic changes in developed countries osteoporotic fractures will double within the next 25 years, this means that fractures of the radial head will gain even more clinical relevance in aged patients.

Therefore, the aim of this study was to determine whether the bone structure of the radial head shows age- and sex-related changes. The question was addressed by analysis of 30 left and 30 right human radial heads taken from 30 individuals at autopsy. The specimens were subjected to morphologic, radiographic, and histologic analyses or micro-computed tomographic (μCT) and peripheral quantitative CT (pQCT) analyses.

Materials and Methods

Specimens

Radial heads, 30 left and 30 right, were harvested from 30 patients at autopsy (15 females, 15 males, five females and five males per age group; age groups 20–40 [32.5 ± 5.37], 41–60 [51.3 ± 5.03], 61–80 [69.2 ± 5.58] years). This study was carried out according to the existing rules and regulations of Hamburg University School of Medicine. All patients had died in accidents or of acute disease without known prolonged periods of immobilization. Iliac crest biopsies were obtained from all autopsy cases to exclude any metabolic diseases known to affect the skeleton, i.e., chronic kidney disease, hyperparathyroidism, Cushing disease, malignancy, or chronic liver disease. Also, donors on drugs known to affect calcium metabolism were excluded.

pQCT

The 30 left radial heads were measured by pQCT, using a micro-computer-controlled, translation-rotation tomographic device with an X-ray source [9] (voxel size 0.2 mm, XCT-2000; Stratec, Pforzheim, Germany). Following generation of a scout view, pQCT sectional images of every analyzed specimen were performed 5 mm below a tangent adjacent to the lowest point of the radial joint cavity (Fig. 1). On the basis of the measurement scan of the radial head, total (BMC_{to}), trabecular (BMC_{tr}), and cortical (BMC_{co}) bone mineral content values were analyzed. Furthermore, total (BMD_{to}), trabecular (BMD_{tr}), and cortical (BMD_{co}) bone mineral density values were calculated. Therefore, the cortical bone area (CBA) was defined through a threshold algorithm detecting bone with high density in a defined region of interest (ROI). All voxels with a lower attenuation coefficient than the given threshold were eliminated. The threshold levels were kept constant for all patients (Fig. 2; trabecular bone 200–600 mg/cm^3, cortical bone >600 mg/cm^3).

μCT Analysis

To visualize the trabecular microarchitecture of the 30 left radial heads, μCT was performed, using a μCT40 scanner

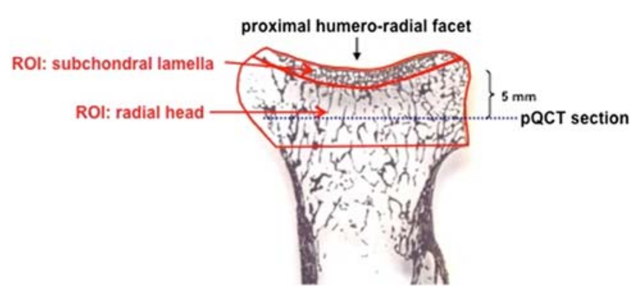

Fig. 1 von Kossa–stained grinding of a radial head specimen. For histomorphometric analysis of the radial head, a 5-mm-thin section was cut out of the center of the radial head in the frontal plane, ground to a thickness of 1 mm, and stained using a modification of the von Kossa method. On the macroscopic view of the radial head, the ROI for histomorphometric analysis were defined. The subchondral lamella adjacent to the proximal humeroradial facet is marked by a *thick line*. The second ROI encircled by a *thin line* shows the area underneath the subchondral lamella passing into the radial column. The distal end of this region is represented by the transition from the radial head to its neck. For pQCT analysis the measurement scan was performed in the axial plane 5 mm distal from the proximal humeroradial facet

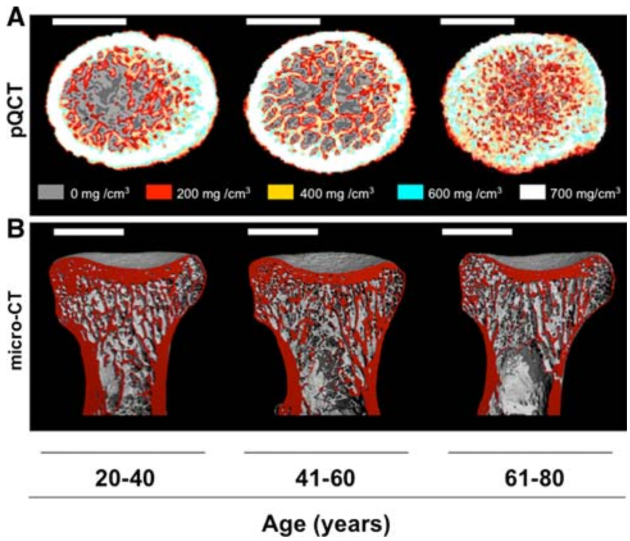

Fig. 2 Representative axial pQCT scans of female radial heads from the three age groups (*upper panels*). Notice the loss of mineralized bone with age. Corresponding structural analysis of the three radial heads by µCT, which demonstrates the loss of cortical and trabecular bone volume with age (*lower panels*). Scale bar = 1 cm

(Scanco-Medical, Bassersdorf, Switzerland). The samples were placed in alcohol and scanned at 55 keV and 145 µA, a field of vision of 36.8 mm, and a matrix of 1,024 × 1,024 × 808 at a nominal resolution of 37 µm with an isotropic voxel size. The 3-D reconstruction was visualized using Scanco Image Processing Software (Scanco-Medical) (Fig. 2).

Sample Preparation and Contact Radiography

From the 30 samples taken from the right elbow of the individuals a 5-mm-thin section was cut out of the center of the radial head in the frontal plane with a diamond saw. Bone marrow was rinsed out thoroughly, and the specimens were macerated in hydrogen peroxide solution for 72 hours, followed by the generation of contact radiographs from each section using a Faxitron X-ray (Wheeling, IL) cabinet. After removing adhering fat tissue, the specimens were dehydrated, embedded in plastic, ground to a thickness of 1 mm, polished, and attached to slides. The surface of this preparation of the radial head was then stained using a modification of the von Kossa method [10]. The high contrast yielded by this silver staining enabled subsequent morphologic evaluation by an automatic computer-assisted analyzing system. Histomorphometric evaluation of the trabecular architecture was performed for every right radial head as follows.

Qualitative and Quantitative Histomorphometry

Two-dimensional analysis was carried out by dark and light field microscopy using a stereomicroscope (Zeiss, Göttingen, Germany). Standard histomorphometry was performed using the Osteoquant workstation (Bioquant Image Analysis, Nashville, TN) on an axioscope II microscope (Zeiss). Histomorphometric analysis was carried out according to the standards of the ASBMR histomorphometric standardization committee [11] as previously described [12]. Analysis was carried out for each radial head from the right elbow of the individuals and included the following parameters: bone volume per tissue volume (BV/TV, %), trabecular number (Tb.N, mm^{-1}), trabecular thickness (Tb.Th, µm), trabecular separation (Tb.Sp, µm), subchondral lamellar bone volume per tissue volume (Subch.Lam BV/TV, %), and mean cortical thickness 15 mm below the lowest point of the radial head joint facet (Ct.Th, µm). Histomorphometric analysis was performed for two different ROI as depicted in Fig. 1.

Statistical Methods

Statistical evaluation was performed using SPSS software for Windows (SPSS, Inc., Chicago, IL). Results are presented as means ± standard deviations of the measurements. Changes of morphometric parameters correlated with age or gender were assessed by ANCOVA. $P < 0.05$ was considered significant.

Results

pQCT of the 30 left radial head specimens revealed a significant decrease of BMD_{to} with age for men and women (Figs. 2, 3 and Table 1) ($P = 0.039$). This was mainly caused by a loss of cortical bone mass (BMD_{co}) during aging ($P = 0.024$). Furthermore, the mean values of BMC_{to} were significantly lower in female compared to male individuals ($P = 0.0004$). Regarding the analysis of trabecular bone parameters, pQCT revealed a significant age-dependent decrease of BMD_{tr} in women ($P = 0.011$), which could not be confirmed for male samples. A significant loss of cortical bone mass with aging was monitored by pQCT as BMD_{co} ($P = 0.024$) and BMC_{co} ($P = 0.03$) likewise decreased with age regardless of gender. In summary,

Fig. 3 Plotting of the age- and sex-related changes of the pQCT data. ▶ BMD_{to} and BMD_{co} were significantly reduced in aging regardless of sex (BMD_{to}, $P = 0.039$; BMD_{co}, $P = 0.024$). The mean values of BMC_{to} were significantly lower in female compared to male patients ($P = 0.0004$) but showed only a slight but not significant reduction with age. Whereas BMC_{co} was significantly reduced in aging regardless of sex ($P = 0.03$). Interestingly, mean values for BMD_{tr} in female specimens were significantly lower ($P = 0.0014$) and significantly decreased with age ($P = 0.011$) compared to males. BMC_{tr} was significantly lower in female samples than in male samples ($P = 0.0004$), and there was a slight but significant increase with age regardless of sex ($P = 0.04$)

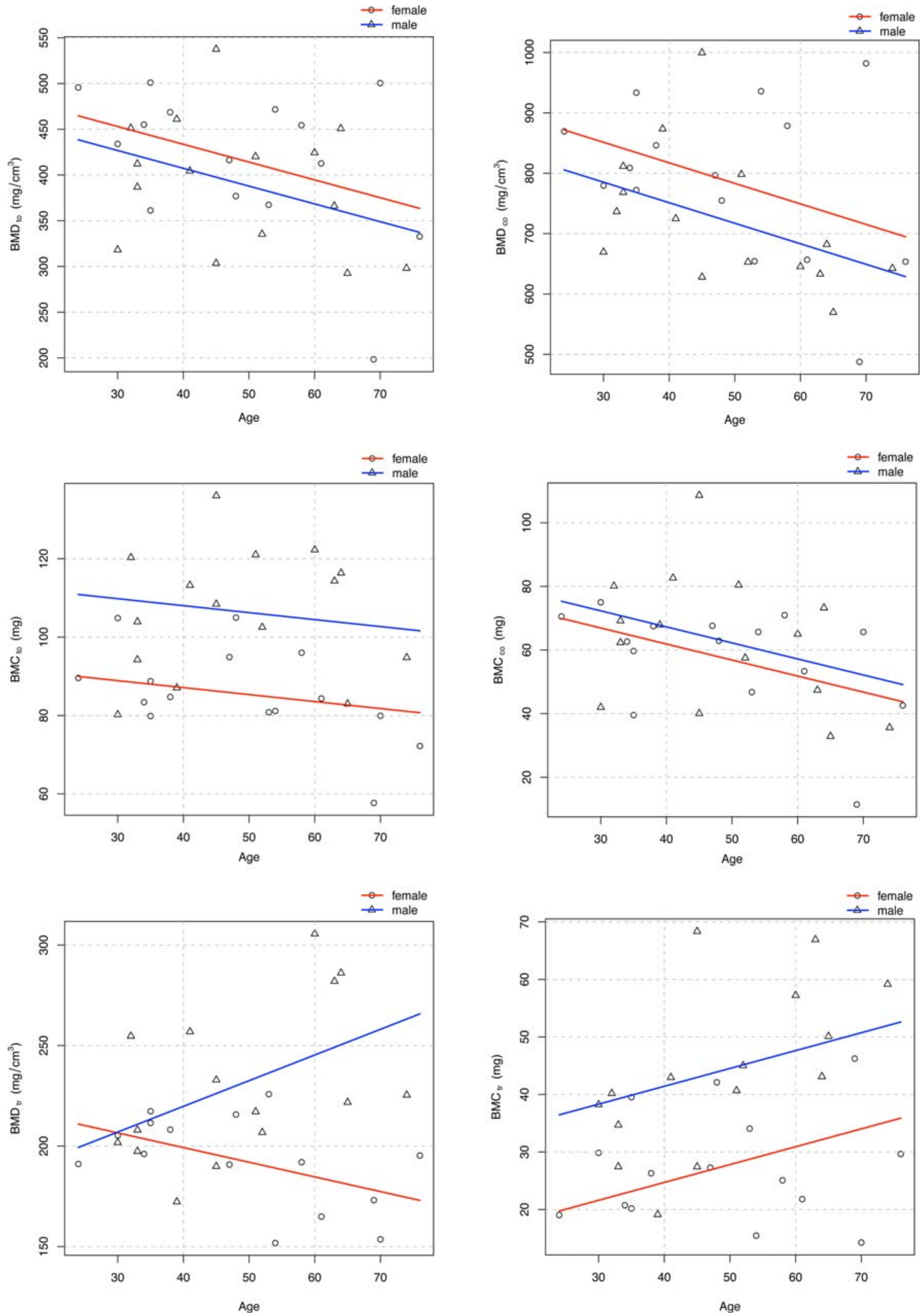
female
male
BMD to (mg/cm3)
BMD co (mg/cm3)
BMC to (mg)
BMC co (mg)
BMD tr (mg/cm3)
BMC tr (mg)
Age

Table 1 Quantitative data (mean ± SD) resulting from pQCT scans of the radial head related to sex and age (20–40, 41–60, 61–80 years)

	Female			Male		
	20–40	41–60	61–80	20–40	41–60	61–80
Age (mean)	30.0 ± 5.49	52.0 ± 4.27	73.0 ± 3.33	35.0 ± 4.05	50.6 ± 5.83	65.4 ± 4.74
BMD_{to} (mg/cm^3)	443.87 ± 50.02	389.80 ± 53.72	355.0 ± 99.45	417.70 ± 64.55	463.07 ± 43.75	346.42 ± 60.67
BMC_{to} (mg)	88.39 ± 8.42	107.93 ± 8.91	76.58 ± 14.78	92.03 ± 15.84	108.36 ± 16.65	85.21 ± 20.20
BMD_{tr} (mg/cm^3)	200.13 ± 11.73	236.55 ± 40.0	202.78 ± 38.40	211.87 ± 25.72	193.78 ± 13.35	225.38 ± 34.67
BMC_{tr} (mg)	25.52 ± 7.52	48.20 ± 15.35	35.60 ± 13.29	31.09 ± 8.71	28.68 ± 5.81	40.90 ± 14.00
BMD_{co} (mg/cm^3)	1,020.30 ± 55.71	958.35 ± 76.04	935.15 ± 103.27	1,003.00 ± 80.20	1,057.21 ± 53.57	864.72 ± 39.57
BMC_{co} (mg)	46.83 ± 6.97	36.09 ± 12.67	26.55 ± 18.57	42.38 ± 12.31	63.54 ± 16.20	21.58 ± 9.76

changes of BMC_{co} and BMD_{co} are age-dependent and changes of BMD_{tr} are age- and sex-dependent.

The loss of trabecular bone volume with aging in women was qualitatively confirmed by 3-D reconstruction after micro-CT of the left radial head specimens (Fig. 2). These age-related structural changes in the proximal radius of the left side were also observed by contact X-ray analysis and on surface-stained grindings (Fig. 4) of the radial head specimens taken from the contralateral right elbow joint. Qualitatively, the highest radiodensity was found in the subchondral and cortical–subcortical regions in female and male specimens under the age of 60 years, whereas the central and cortical–subcortical regions in female specimens over 60 years appeared as radiolucent zones. The changes in radiolucency with aging monitored by contact X-ray were quantitatively confirmed by histomorphometric analysis (Fig. 5 and Table 2). In line with pQCT, histomorphometric analysis detected significant age-related changes of several trabecular bone parameters. In male and female specimens BV/TV ($P = 0.011$) and Tb.Th ($P = 0.0006$) significantly decreased with age. Tb.Sp significantly increased with age within the radial head from female individuals, corresponding to the decrease of BMD_{tr} ($P = 0.037$). Interestingly, Tb.N was significantly higher in males compared to females regardless of age ($P = 0.002$), and there was only a slight but not significant age-related decrease ($P = 0.21$).

A significant age-related decrease in Subch.Lam BV/TV was observed for female as well as male specimens ($P = 0.009$). Interestingly, throughout all ages Subch.Lam BV/TV was at least fourfold higher than the corresponding BV/TV of the entire preparation. Analogous to pQCT, histomorphometry of the radial head 15 mm below the lowest point of the radial head joint facet confirmed a significant reduction of cortical bone mass (Ct.Th) with aging, regardless of sex ($P = 0.0009$) (Fig. 5 and Table 2).

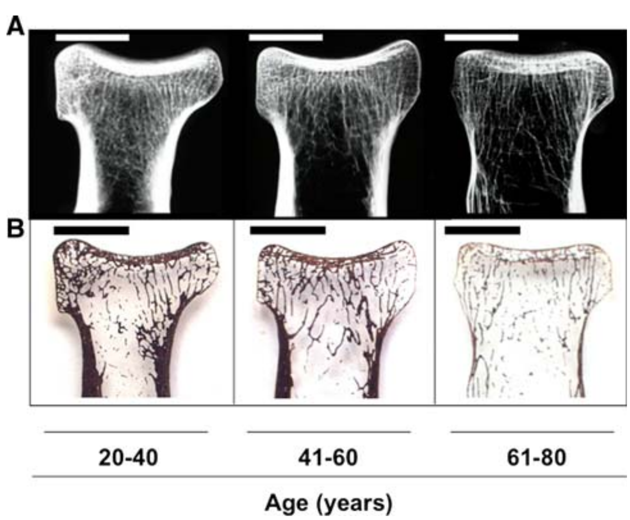

Fig. 4 Contact radiographs (*upper panels*) and corresponding surface-stained grindings (*lower panels*) (thickness 1 mm, von Kossa staining) of three radial head preparations. In contrast to the low sensitivity of conventional X-ray analysis, contact X-ray demonstrates an increase in radiolucency with aging; this bone loss is confirmed in the block-grindings at the structural level. Scale bar = 1 cm

Discussion

Since Mason's fundamental work on fractures of the head of the radius published in the *British Journal of Surgery* in 1954, there is consensus that this injury is mainly caused by an indirect trauma through the long axis of the radius [1–3]. Amis and Miller [13] tested the influence of different angles of force impact on fracture patterns of 40 human elbow specimens. In their series fractures were created by an average indirect impact of 2,900 N along the axis of the radius and in all cases the radial head fracture took a longitudinal path.

Fig. 5 Plotting of the age- and sex-related changes of the histomorphometric data. BV/TV and Tb.Th significantly decreased with age (BV/TV, $P = 0.011$; Tb.Th, $P = 0.0006$), but there was only a slight and insignificant reduction of Tb.N for male and female samples. Mean values for Tb.Sp were significantly higher in female specimens (Tb.Sp, $P = 0.0009$) and significantly increased with age compared to males (Tb.Sp, $P = 0.037$). Subch.Lam BV/TV and Ct.Th (15 mm) significantly decreased with age regardless of sex (Subch.Lam BV/TV, $P = 0.009$; Ct.Th, $P = 0.0009$) ▶

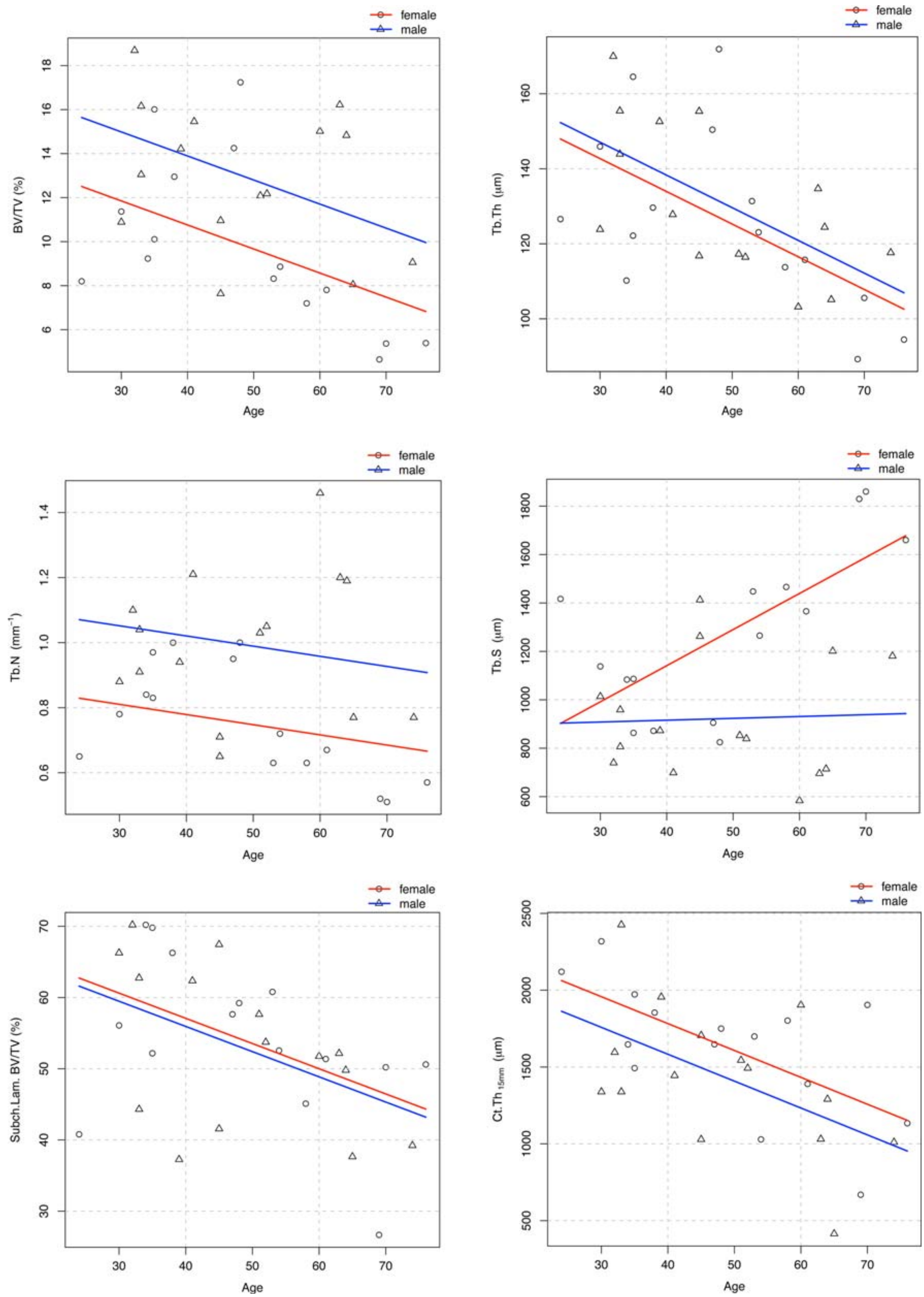
female
male
BV/TV (%)
Age
female
male
Tb.Th (μm)
Age
female
male
Tb.N (mm⁻¹)
Age
female
male
Tb.S (μm)
Age
female
male
Subch.Lam. BV/TV (%)
Age
female
male
Ct.Th 15mm (μm)
Age

Table 2 Quantitative data (mean ± SD) resulting from histomorphometric analysis of the trabecular and cortical microarchitecture of the radial head related to sex and age (20–40, 41–60, 61–80 years)

	Female			Male		
	20–40	41–60	61–80	20–40	41–60	61–80
Age (mean)	30.0 ± 5.49	52.0 ± 4.27	73.0 ± 3.33	35.0 ± 4.05	50.6 ± 5.83	65.4 ± 4.74
BV/TV (%)	11.76 ± 2.32	9.85 ± 3.10	6.19 ± 1.56	15.37 ± 2.42	13.00 ± 1.72	12.14 ± 2.08
Tb.N (mm^{-1})	0.88 ± 0.08	0.86 ± 0.34	0.61 ± 0.10	1.11 ± 0.20	0.99 ± 0.17	1.00 ± 0.27
Tb.Th (µm)	132.72 ± 18.55	116.18 ± 8.20	101.25 ± 12.82	140.80 ± 25.22	133.46 ± 17.32	126.04 ± 21.51
Tb.Sp (µm)	1,009.43 ± 111.49	1,167.46 ± 364.02	1,585.40 ± 265.70	784.27 ± 140.73	911.69 ± 198.30	911.51 ± 213.70
Subch.Lam BV/TV (%)	59.22 ± 11.14	50.04 ± 6.49	38.51 ± 15.07	61.25 ± 12.96	58.35 ± 6.34	46.08 ± 8.72
Ct.Th (µm)	1,900.83 ± 289.27	1,554.60 ± 292.30	934.80 ± 302.66	1,771.50 ± 406.30	1,464.40 ± 197.24	1,114.16 ± 254.86

However, it is widely accepted that skeletal mass is the one of the three determinants of structural bone strength—besides geometric properties and material quality—which can be measured best and can estimate future fracture risk well [14–17]. For the distal radius, a skeletal site where bone mass changes during aging are of dramatic clinical relevance, the correlations between bone mass and bone strength have been repeatedly reported [18, 19].

Regarding the microarchitecture of the radial head, already Mason observed a "columnar type of dense cancellous bone running in a more or less longitudinal pattern." Mason concluded that "in consequence, fractures of the radial head tend to be oblique or longitudinal in direction" [3]. This longitudinal orientation of trabeculae in the radial head results from modeling and remodeling in the proximal radius. Modeling contributes to skeletal strength homeostasis by adjusting bone mass and geometric properties to withstand loading conditions [14].

In this context, it is somehow surprising that even though Mason's microstructural observation was made half a century ago, up to now a comprehensive morphometric analysis of the microstructure of the radial head is missing. Hence, to characterize the michroarchitecture of the radial head and to answer the question of whether the bone structure of the radial head shows age- and sex-related changes, which might explain the clinically apparent high number of female patients of advanced age sustaining a radial head fracture (48% of injured female patients older than 60 years), we performed the present study. A total of 60 specimens were subjected either to radiography and histology or to µCT and pQCT analyses as described previously [10, 12, 20, 21].

pQCT revealed a significant decrease of BMD_{to} and BMD_{co} with aging, regardless of sex. Histomorphometry revealed a significant reduction of cortical and trabecular parameters (Ct.Th, BV/TV, and Tb.Th) in male and female specimens, although the deterioration of bone mass monitored by changes of BV/TV, Tb.N, and Tb.Sp was significantly more pronounced in female than in male samples.

As it is widely accepted that BMD, bone geometry, and bone microarchitecture are all components that determine bone strength by the bone's ability to withstand loading [22], our findings strongly suggest that the presented structural changes within the radial head might contribute to the pathogenesis of radial head fractures, especially in aged female patients where trabecular parameters (BMD_{tr} and Tb.Sp) change significantly for the worse compared to male patients.

Looking through the recently published literature on the structure and bone mass of the radial head, only a few publications were found. In 2003 Gordon et al [23] presented a study on 13 radial heads (mean age 70.5 ± 9.5 years; seven male, six female) to determine the mechanical properties of subchondral cancellous bone. To detect regional variations in bone stiffness and strength in the radial head, they performed indentation tests on 3-mm-thick slices of the radial heads in four different quadrants (AL, AM, PL, PM). Unfortunately, in that study multiple linear regression tests could not detect a clear influence of the patients' sex and age on bone stiffness and strength of the radial head. Probably this was due to the advanced mean age of 70.5 years of the tested specimens. A young control group was not included in the study.

With regard to the humeroradial joint, Eckstein et al [24] were able to identify a direct influence of loading conditions and geometric configurations of the joint to the pattern of subchondral bone distribution, which again reflects the potential of a mechanobiological adaptation of the bone. Because of these mechanobiological principles of skeletal remodeling, Mason′s microstructural observation fitted exactly with the fracture paths resulting from the biomechanical experiments performed by Amis and Miller [13] 40 years later.

In another study on the subchondral bone density in 36 human elbow specimens by CT osteoabsorptiometry, Eckstein et al [25] described a typical pattern of bone mineralization within the radial head. They found a central density maximum in the fovea, with mineralization falling off concentrically toward the margins of the radial head. The authors concluded that the presence of this central density maximum in the fovea of the radial head indicates a predominantly central pressure transmission in the humeroradial joint. Our findings, that Subch.Lam BV/TV was at least fourfold higher than the corresponding BV/TV of the entire preparation throughout all different groups, are in line with the observations of Eckstein et al [25]. In addition, the significant age-related decrease of Subch.Lam BV/TV in female as well as in male specimens monitored by the present investigation leads to an impaired function of this region of the radial head to withstand transition forces from the articular cartilage to the radial head, resulting in a higher susceptibility to fractures of this skeletal site.

As in Gordon et al [23], in the study by Eckstein et al [25] the average age of the specimens was advanced (76.8 years). Therefore, again the age-related morphological changes in the radial head could not be differentiated.

In a study by Koslowsky et al [26] the subchondral bone density of the radial head was measured with subtraction densitometry. In line with the findings of Eckstein et al [25], an eccentric distribution of the subchondral bone density reflecting an eccentric force transmission through the radiohumeral joint was again detected. Even though a number of 37 specimens with a range of 36–90 years of age were examined, Koslowsky et al did not analyze the influence of age on regional BMD. They found an asymmetric bone density pattern of the radial head with maxima at the ulnar-dorsal and ulnar-ventral areas of the radial head, giving an explanation for the higher incidence of fractures in the lateral area of the radial head.

Concerning the methodology of the present work, one has to evaluate the data resulting from pQCT measurements with caution as several articles have discussed a poor short-term precision of pQCT measurements at the appendicular skeleton, leading to less sensitivity of this technique in discriminating osteoporotic bone mass changes if compared to other techniques (i.e., DXA, SPA) [27, 28]. Furthermore, it has to be considered that pQCT and 2-D histomorphometry are susceptible to sampling errors as the amount of analyzed bone volume per sample is limited. In this context Ashe et al. [29] examined the accuracy of pQCT for evaluating the bone strength of 10 pairs of aged fresh-frozen radial specimens and found that pQCT scans varied systematically as they are affected by analysis mode, resolution, and thresholding. A reason for the imprecise bone mass measurements by pQCT as well as by histomorphometry might be that only thin slices of the whole bone specimen are determined, making them susceptible to sampling errors.

Another limitation concerns the study design. As this is a cross-sectional study, the monitored structural changes of the bone might be rather cohort effects than real age effects, e.g., due to changes in the nutritional status of the oldest subjects born in the late 1930s.

In conclusion, our findings provide evidence that the radial head shows distinct age-related changes in its microarchitecture that affect both the cortical and the trabecular compartments and that are known to reduce the biomechanical stability of the bone. This deterioration of the microarchitecture of the radial head in aging might contribute to the pathogenesis of radial head fractures, especially in aged female patients. This implies that fractures of the radial head are at least in part osteoporotic fractures, which may lead to an increase of the number of radial head fractures in the elderly due to the demographic changes in the Western world.

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