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Regional characteristics of cortical bone quality in the proximal humerus of postmenopausal women: a preliminary study

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Background: Proximal humeral fractures represent the third most common fragility fracture treated in osteoporotic populations, after hip and distal radial fractures. The purpose of this study was to characterize the spatial variability in cortical geometry in the proximal humerus in postmenopausal women.
Methods: The proximal humeri in 43 healthy postmenopausal women were imaged by computed tomography. Cortical bone mapping was applied to create color 3-dimensional thickness maps for each proximal humerus. Cortical parameters, including the cortical thickness (CTh), cortical mass surface density (CM), and endocortical trabecular density, were measured over the humeral head and metaphyseal region after 15 regions of interest (ROIs) were defined.
Results: In the humeral head region, significant differences in CTh and CM values were detected between the anterior, lateral, and posterior walls ($P < .05$). The highest CTh and CM were found in the anterior wall in each plane ($P < .05$). Regarding the endocortical trabecular density, no significant findings were noted in the 3 planes ($P > .05$). In the metaphyseal region, the cortical structure in the medial column had higher CTh and CM values in ROI 10 compared with the lateral column ($P < .05$). The highest CTh and CM values of compact bone were seen in ROI 10 of the medial column (ROIs 10-12) ($P < .05$).
Conclusion: Our results showed significant regional variation of cortical bone in the humeral head region in postmenopausal women. Similar conditions were seen in the medial column in the metaphyseal region. This finding provides discriminatory information for stronger fixation of implants.
Level of evidence: Anatomy Study; Imaging

Keywords: Regional variations; cortical bone; postmenopausal women; proximal humerus; cortical bone mapping; medial column

Proximal humeral fractures, the third most common geriatric fracture after distal radius and hip fractures, account for approximately 10% of all fractures. They affect predominantly postmenopausal women presenting with additional osteopenia or osteoporosis.[5,11] No consensus has been reached on the treatment of proximal humeral fractures in elderly patients. Treatment options range from nonoperative to operative modalities. The popularity of locking-plate fixation has

All procedures performed in this study involving human participants were in accordance with the ethical standards of the Tianjin Hospital research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards (No. 20160300012).

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increased rapidly compared with other methods, without clear evidence of its superiority.[9,11] Although locking-plate fixation provides increased osseous anchorage and higher failure loads with mainly good functional results, surgical complications, such as fracture re-displacement, postoperative implant loosening, and impaired fracture healing, have frequently been reported.[10,21] In a meta-analysis of 514 proximal humeral fractures treated with locking plates in 12 studies, the overall rate of complications was 49% and the reoperation rate was 14%.[21] One important reason for failure is osteoporotic changes in elderly patients, which may compromise satisfactory implant purchase, resulting in limited primary stability.

Previous studies investigated the relation between the stability of screws and areal bone mineral density (BMD) in different regions of the proximal humerus. Tingart et al[23] found a significant correlation between trabecular BMD and the pullout strength of cancellous screws. Barvencik et al[1] showed that the superior and medial part of the humeral head had the highest bone mass and could be considered the best location for screw placement. In fact, cortical bone strength is critical to skeletal integrity, particularly at appendicular sites where the cortex is responsible for the majority of axial load transfer.[2,9] Biomechanical studies clearly showed that both the gross geometric and microstructural properties of cortical bone are determinant factors of fracture risk. However, until now, it has not been shown whether there are age-related changes in the cortical structure in the proximal humerus, especially in a population of postmenopausal women.

Over the past 2 decades, quantitative computed tomography (CT) has been used to identify how the hip changes with aging and its association with fracture risk.[17,18] Cortical bone mapping (CBM) is a new technique that allows measurement of cortical variables from quantitative CT data. It provides several thousand independent measurements across each proximal femur and sufficient sensitivity to detect even small changes.[16,17] In this study, we applied CBM to describe the spatial variability in cortical geometry in the proximal humerus in a sample of postmenopausal women.

Materials and methods

Subjects and study design

A cohort of 43 postmenopausal women was included in our study to assess cortical bone quality in the proximal humerus in the dominant upper extremity. The subjects ranged in age from 51 to 86 years (mean, 65.51 ± 7.21 years). All subjects were Han Chinese. There were 8 women in their 50s, 24 in their 60s, 9 in their 70s, and 2 in their 80s. Arm dominance was determined as the arm with which subjects would throw a ball. There were no BMD requirements for inclusion. We excluded (1) women with a history or evidence of metabolic bone disease; (2) women with a history of receiving chronic treatment that may affect bone metabolism; (3) women with a previous fracture of the humerus or shoulder surgery; (4) women who underwent hysterectomy and/or bilateral oophorectomy or early menopausal women whose age at menopause was less than 40 years; and (5) women with a history of smoking. All subjects provided written informed consent prior to participation.

Cortical bone mapping

CT scanning (Mx 8000 IDT; Philips Medical Systems, Best, The Netherlands) was performed at 120 kV (peak) and 168 milliampere-seconds. CT images were created in slice increments of 2.00 mm, at a resolution of 0.566×0.566 mm/pixel, with a field of view of 29×29 cm.

The cortical parameter measurement and mapping technique has been described previously.[16,18] Cortical thickness (CTh) measurement was performed using CBM, implemented by a freely available in-house program called Stradwin (http://mi.eng.cam.ac.uk/~rwp/stradwin/). By use of this software, the CT data were sampled at each vertex of the mesh using 18-mm lines perpendicular to and passing through the femoral cortex and trabeculae.[17] Stradwin is able to accurately estimate the CTh (in millimeters) and cortical mass surface density (CM) (ie, cortical mass per unit cortical surface area), as well as the endocortical trabecular density (ECTD), which is the trabecular density directly adjacent to the cortex.

Definition of regions of interest for cortical bone distribution assessment

Humeral head region

For evaluation of bone morphometric analysis, specific regions of interest (ROIs) were defined within the proximal end of the humerus. The cortical bone in the humeral head region was defined as the anterior, lateral, and posterior walls. From an anatomic perspective, the anterior wall is roughly equivalent to the lesser tuberosity. The lateral and posterior parts of the greater tuberosity corresponded to the lateral and posterior walls in this study. After creation of a single 3-dimensional thickness map, the humeral head height was determined by measuring the distance between the most distal margin of the articular surface and the highest point of the humeral head (Fig. 1). The humeral head was then subdivided into 4 regions of

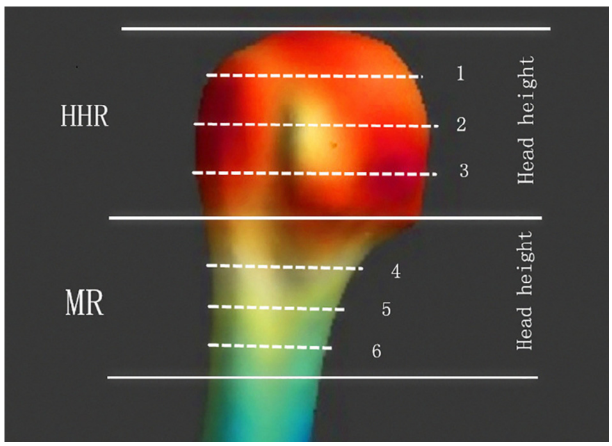

Figure 1 Area of exploration in humeral head region (*HHR*). The humeral head height was quartered by axial planes 1-3. Similarly, the medial and lateral walls in the metaphyseal region (*MR*) were divided by planes 4-6 using the humeral head height as the reference distance. Cortical parameters were determined at 6 different levels.

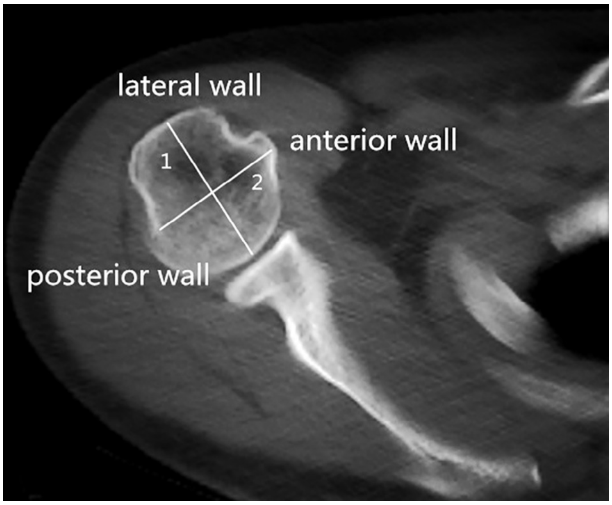

Figure 2 Locations of measurement points in humeral head region. Line *1* is the longest diameter between the glenoid side and greater tuberosity. *Line 2* is the bisection of line 1 at a right angle.

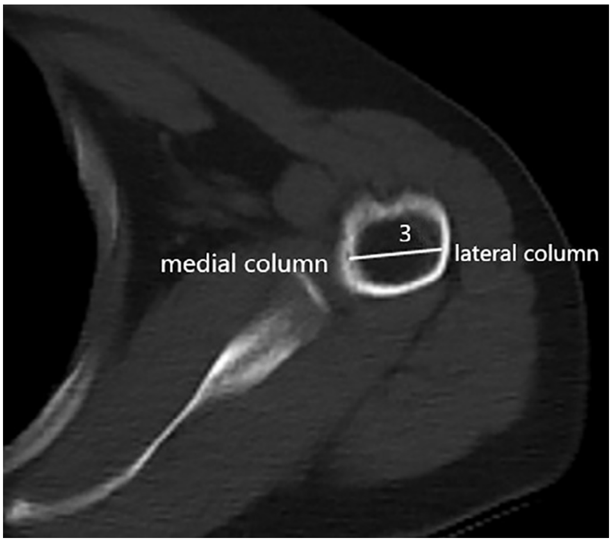

Figure 3 Locations of measurement points in metaphyseal region. *Line 3* is the longest line between the medial and lateral columns.

equal height by axial planes 1-3. In each slice, the longest line (line 1) between the joint surface and greater tuberosity was drawn. This line was divided into medial and lateral segments by line 2 (Fig. 2). ROIs 1-9 were defined as cortical bone measurement points. The data collected from these ROIs were analyzed to describe the regional difference between the anterior, lateral, and posterior walls.

Metaphyseal region

By use of the humeral head height as the reference distance, the medial and lateral columns in the metaphyseal region were divided into 4 segments of equal length by axial planes 4-6. In each plane, the longest line (line 3) between the medial and lateral columns was drawn. The individual geometry of the medial and lateral compact bone lamella was obtained at 3 points on each side (Fig. 3). ROIs 10-15 were defined as well (Fig. 4). Regional variations in the medial and lateral columns were analyzed after data collection.

Statistical analysis

All statistical analysis was performed using SPSS software (version 16; IBM, Armonk, NY, USA). The significance level was set at $P < .05$ for all statistical tests. For detection of normally distributed values, the Kolmogorov-Smirnov test was used. The results of the different sites in the humeral head and metaphyseal region regarding CTh, CM, and ECTD were compared using 1-way analysis of variance for normally distributed values and the Kruskal-Wallis test for non-normally distributed values. Similarly, the Student *t* test or Mann-Whitney *U* test was used to determine differences in cortical parameters between the lateral and medial columns in the metaphyseal region depending on whether the data were normally distributed.

Results

Humeral head region

When the CTh and CM values of the anterior, lateral, and posterior walls were compared in planes 1-3, there was a significant difference between each side ($P < .05$). The highest CTh and CM values were found in the anterior wall in each plane, whereas the lowest values were found in the posterior wall in planes 1 and 2 and the lateral wall in plane 3. Regarding ECTD, no differences were found in the 3 planes ($P > .05$) (Table I).

Overall, these results suggested that statistically significant differences in cortical parameters were apparent in defined locations of the humeral head region. The anterior walls had the thickest and highest density of the cortex with higher bone quality, whereas the lateral and posterior walls had relatively lower bone quality.

Metaphyseal region

The cortical structure in the medial column had higher CTh and CM values in ROI 10 compared with the lateral column ($P < .05$), whereas the ECTD values were approximately equivalent on the 2 sides ($P > .05$) (Table II). Notably, the highest CTh and CM values of the compact bone were found in ROI 10 of the medial column (ROIs 10-12) ($P < .001$ and $P = .064$, respectively). The ECTD values of the ROIs in the medial column were comparable ($P = .06$) (Figs. 5 and 6).

Discussion

Implant failure is a serious complication after surgical treatment of proximal humeral fractures.[10,21] Although bone quality in the humeral head is the most important determining factor for the final fixation strength of inserted implants, only a few studies have investigated areal BMD of the humeral head,[13,22,23] and to our knowledge, none has investigated the 3-dimensional distribution of cortical bone in the humeral head.

In this study, we assessed the cortical structure quantitatively in the humeral head and metaphyseal regions in a sample of postmenopausal women using CBM. Heterogeneity of the

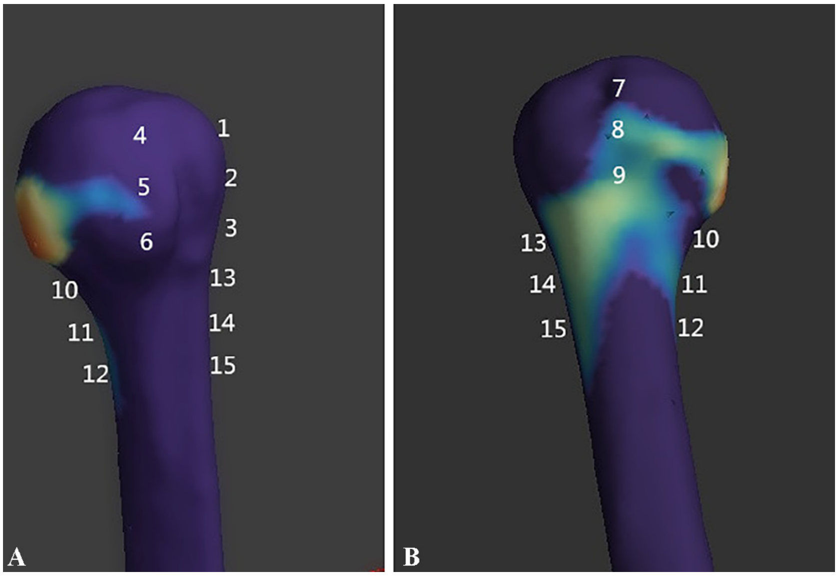

Figure 4 Fifteen regions of interest were defined in the humeral head and metaphyseal regions. **(A)** Anterior view. **(B)** Posterior view.

Table I Values of cortical parameters of specific ROIs in humeral head region

	CTh, mm	CM, HUmm	ECTD, HU
Plane 1			
ROI 1	3.27 ± 1.72	37,421.36 ± 20,555.09	10,023.87 ± 223.48
ROI 4	3.71 ± 1.52	39,579.88 ± 18,284.84	9945.44 ± 596.67
ROI 7	2.99 ± 1.58	31,468.22 ± 15,857.19	10,027.25 ± 204.31
P value	<.001	.11	.54
Plane 2			
ROI 2	2.40 ± 1.45	28,044.39 ± 16,627.94	9983.98 ± 3126.33
ROI 5	3.49 ± 1.72	37,782.57 ± 19,116.15	10,000.71 ± 210.99
ROI 8	2.05 ± 0.89	23,491.80 ± 10,061.50	10,003.05 ± 217.65
P value	<.001	<.001	.94
Plane 3			
ROI 3	2.23 ± 1.06	25,859.67 ± 11,801.51	9961.30 ± 217.43
ROI 6	3.43 ± 1.77	38,340.93 ± 20,503.10	10,004.13 ± 215.31
ROI 9	2.67 ± 1.14	30,795.39 ± 13,870.09	9978.58 ± 222.85
P value	<.001	<.001	.66

ROI, region of interest; *CTh*, cortical thickness; *CM*, cortical mass surface density (cortical mass per unit cortical surface area); *ECTD*, endocortical trabecular density; *HU*, Hounsfield units.
Data are presented as mean ± standard deviation.

cortical bone structure within the humeral head region was found after menopause. The CTh and CM values were highest in the anterior walls. Cortical thinning was seen in the lateral and posterior walls. Moreover, in the metaphyseal region, higher CTh and CM values were found in the proximal part of the medial column than in the lateral column.

The gross properties of cortical bone change substantially after the withdrawal of estrogen.[2,16,17] Previous studies showed that the cortical geometry and microarchitecture of the femoral neck display marked regional heterogeneity.[3,4,14,19] During normal gait, the compressive stresses were concentrated in the inferior part of the femoral neck and small-magnitude tensile stresses occurred in the superior part. Accordingly, the CTh of the inferior region was known to be greater than that of the superior region.[24] Moreover, the relative bone decrement with aging was 3-fold greater superiorly than inferiorly, especially in elderly women.[4,8] However, the morphologic changes of cortical bone varied greatly at different anatomic sites. The proximal humerus may be particularly vulnerable to rapid bone loss after menopause because the humerus is not a weight-bearing element.[1,6,22,23] Several studies investigated the areal BMD and the trabecular microstructure of the proximal humerus.[1,22,23] Although the definition of specific ROIs was not the same, significant regional variance in the trabecular microarchitecture or BMD was found.[1,22] Tingart et al[22] showed that higher trabecular and cortical BMD values were found in the proximal half of the humeral head. In our study, there were obvious cortical

Table II Values of cortical parameters of specific ROIs in metaphyseal region

	ROI 1 (medial column) or ROI 4 (lateral column)			ROI 2 (medial column) or ROI 5 (lateral column)			ROI 3 (medial column) or ROI 6 (lateral column)		
	CTh, mm	CM, HUmm	ECTD, HU	CTh, mm	CM, HUmm	ECTD, HU	CTh, mm	CM, HUmm	ECTD, HU
Medial column	4.69 ± 1.89	50,244.46 ± 20,850.79	9901.77 ± 641.73	3.68 ± 1.24	40,968.06 ± 13,238.39	9920.24 ± 210.42	3.58 ± 1.09	41,771.21 ± 12,749.56	9917.88 ± 207.04
Lateral column	2.79 ± 1.03	31,318.64 ± 11,745.54	9932.74 ± 210.00	3.17 ± 1.14	35,625.08 ± 12,185.85	9926.85 ± 208.83	3.39 ± 1.15	38,557.37 ± 12,787.16	9925.77 ± 208.63
P value	<.001	<.001	.09	.71	.77	.98	.96	.82	.98

ROI, region of interest; *CTh*, cortical thickness; *CM*, cortical mass surface density (cortical mass per unit cortical surface area); *ECTD*, endocortical trabecular density; *HU*, Hounsfield units.
Data are presented as mean ± standard deviation.

regional variations in the humeral head region, with the highest CTh and CM values in the anterior wall (lesser tuberosity). Meanwhile, we observed that cortical thinning was detected in the posterior (planes 1 and 2) and lateral (plane 3) parts of the greater tuberosity. These results were distinct from those in the corresponding age group.[25] We believe that this pronounced focal osteoporosis in the greater tuberosity might be associated with the higher risk of proximal humeral fracture in postmenopausal women.

Gardner et al[6] and Lee and Shin[12] have emphasized that mechanical support of the medial column is essential for maintaining fracture reduction in locked plating of proximal humeral fractures. Medial comminution and insufficient medial support were proved to be independent risk factors for reduction loss.[15,26] Our results showed that the cortical bone of the medial column adjacent to the humeral head was thicker and denser compared with the lateral column. This finding supports a previous notion that there is greater compressive stress on the medial column than on the lateral side.[13] Histomorphometric analysis of the bone stock in the metaphyseal region showed that the medial column in the osteoporotic specimens exhibited a significant reduction in bone density in comparison with the lateral side.[20] Helfen et al[7] found age-related bone loss of the humeral cortex of the surgical neck in terms of increased cortical porosity and showed that decreased thickness predominantly occurred around the age of 65 years. In this study, the thickest and highest-density bone cortex was seen in the proximal end of the medial calcar. The ECTD values of ROIs in the medial column tended to be comparable. The results were significantly different from those in the corresponding age group (data not shown). The disappearance of anisotropy in cancellous bone in the medial column may be an early sign of the decline of its buttress behavior.

This study has many limitations. Our series had a small number of cases. Despite this limitation, our method has profound significance in terms of allowing for in vivo evaluation of the cortical bone properties of each patient. On the basis of these data, our further investigation measuring the absolute value by using an imaging phantom may help to determine individual variance in bone quality for the creation of personalized surgical protocols. Second, the definition of regions used in this study was arbitrary. However, it was in accord with the gross anatomic system and independent of patient positioning. The measurement location was set with fixed planes regardless of bone length. Finally, our previous work can provide some baseline values about age-related changes within the proximal humerus,[25] although we did not collect the data from premenopausal women as a control to compare bone quality.

Conclusions

CBM was a feasible technique to assess cortical bone quality in the proximal humerus. Our results showed significant regional variation of cortical bone in the humeral

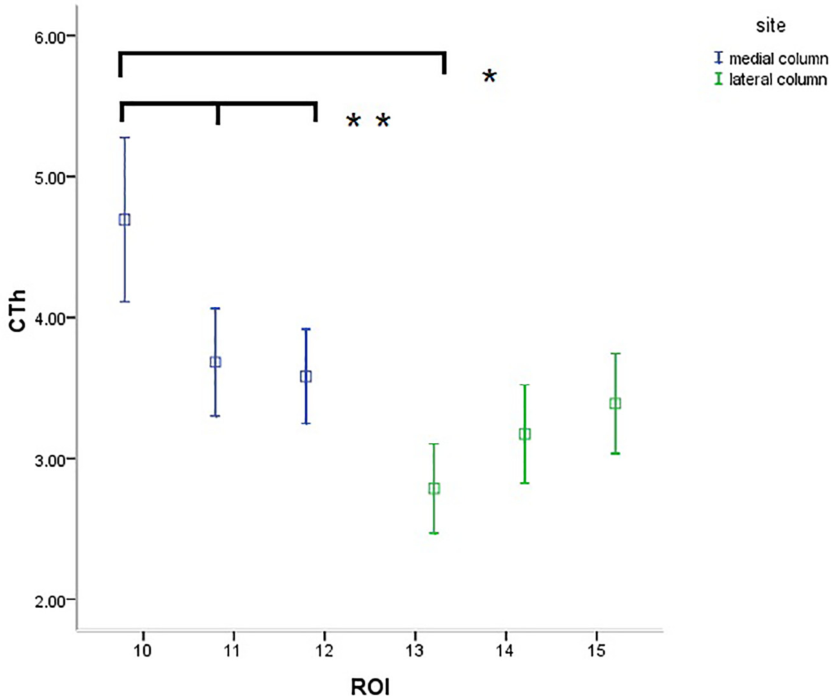

Figure 5 Cortical thickness (*CTh*) in metaphyseal region. The CTh value in region of interest (*ROI*) 10 was significantly higher than that in ROI 13 on the lateral side. The highest CTh value of cortical bone was found in ROI 10 in the medial column. *Differences between medial and lateral columns. **Differences between ROIs 10-12 ($P < .05$).

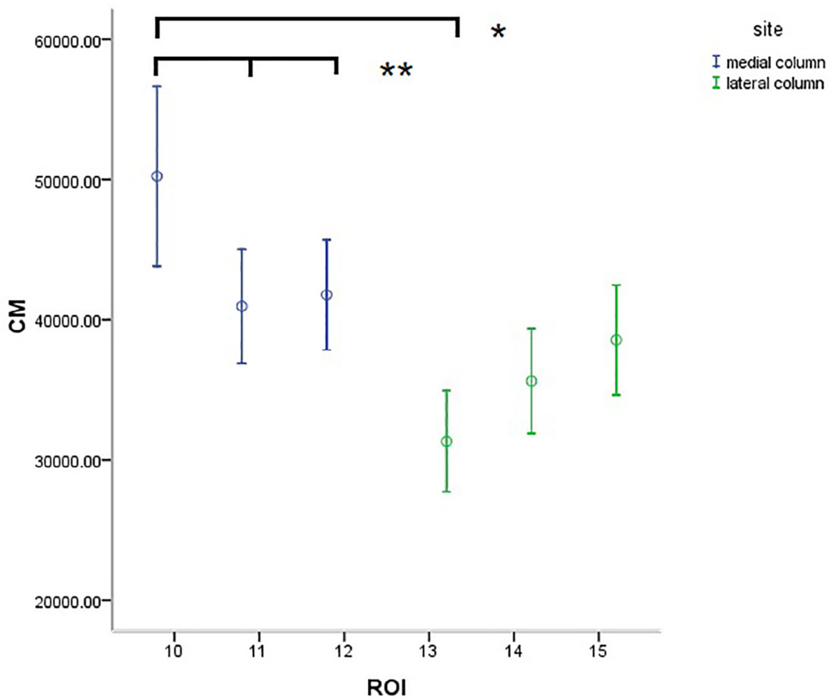

Figure 6 Cortical mass surface density (*CM*) in metaphyseal region. The CM value in region of interest (*ROI*) 10 was significantly higher than that in ROI 13 on the lateral side. The highest CM value of cortical bone was found in ROI 10 in the medial column. *Differences between medial and lateral columns. **Differences between ROIs 10-12 ($P < .05$).

head region in postmenopausal women. Similar conditions were seen in the medial column in the metaphyseal region. Our findings may potentially lead to the development of new fixation techniques for osteoporotic proximal humeral fractures.

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Disclaimer

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