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Muscle weakness, spasticity and disuse contribute to demineralization and geometric changes in the radius following chronic stroke

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Abstract

Following a stroke, demineralization and geometric changes occur in bone as a result of disuse and residual impairments and these can contribute to an increased risk of fragility fractures. This study used peripheral quantitative computed tomography (pQCT) to evaluate volumetric bone mineral density and geometry at the midshaft radius in people living with chronic stroke. Older individuals with chronic stroke were recruited. Each subject underwent a pQCT scan of the midshaft radius at the 30% site on both upper limbs. Muscle strength, motor function, spasticity, and chronic disuse were also evaluated. Data from 47 subjects (19 women) were assessed. A significant difference was found between the two limbs for cortical bone mineral content, cortical bone mineral density, cortical thickness, and polar stress-strain index. There was no significant side-to-side difference in total bone area. Percent side-to-side difference in muscle strength, spasticity, and chronic disuse were significant determinants of percent side-to-side difference in cortical bone mineral content and cortical thickness. The findings suggest that following chronic stroke, endosteal resorption of the midshaft radius occurred with a preservation of total bone area. Muscle weakness, spasticity, chronic disuse significantly contributed to demineralization and geometric changes in the radius following chronic stroke.

Keywords

Bone density; cerebrovascular accident; osteoporosis; rehabilitation

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INTRODUCTION

Residual physical impairments such as poor motor control, muscle weakness and spasticity can occur in the upper extremity after a stroke leading to chronic disuse of the limb [1]. One of the secondary complications arising from chronic disuse is bone demineralization [2–5], contributing to an increased risk of fragility fractures [6]. Indeed, upper extremity fractures account for 27–36% of all fractures in the stroke population [7,8], posing a serious health threat to this group of individuals and placing a tremendous fiscal burden on the health care system [9].

Previous evidence suggests a negative relationship between upper extremity bone mineral density (BMD) and length of time since stroke event [3,4], that is, bone health tends to deteriorate as time since stroke increases. It has been previously reported that those with severe impairment in the paretic arm had as much as 25% reduction in proximal humerus areal BMD within the first year post-stroke [10]; it is likely that this progressive deterioration in upper extremity bone health may continue beyond 1 year post-stroke. Other evidence highlights that the majority of fractures occur in the chronic stage of recovery, with the median time of the first fracture at approximately 2.4 years post-stroke [7]. Therefore, upper extremity bone health is an important concern among chronic stroke survivors.

Only a few studies have examined upper extremity bone health in the chronic stroke population [2,3,11–14]. A number of these studies have found a significant side-to-side difference in areal BMD at different skeletal sites in the upper extremity, indicating substantial bone demineralization on the paretic side [2,3,11]. However, these studies did not provide any information on bone geometry, which is a determinant of bone strength in addition to bone density [15,16]. It is therefore important to evaluate the bone geometric adaptations that could occur in conjunction with demineralization following stroke. Peripheral quantitative computed tomography (pQCT) can separate cortical and trabecular bone compartments and is a useful instrument to evaluate volumetric BMD and geometric parameters.

To date, only one study has examined upper extremity bone status in the stroke population using pQCT [17]. Based on a sample of 15 subjects, significant differences in certain parameters (e.g. total and cortical bone mineral content, cortical BMD, Stress-Strain Index) were found at the 30% radius site between the paretic and non-paretic side. However, the study was limited by inadequate statistical power due to the small sample size. This may explain why no significant differences were found in some pQCT parameters (e.g. cortical thickness, total bone area). In addition, multivariate analysis could not be performed with a small sample. Second, bone structural adaptations may differ between the two sexes [18]. Data from male and female subjects with stroke have not previously been analyzed separately. Finally, the influence of the extent of disuse of the affected upper extremity on bone health has not been quantified.

In summary, there is limited research on studying bone geometric changes in the upper extremity following chronic stroke. In this study, we examined bone density and geometry of the midshaft radius in older individuals with chronic stroke using pQCT. The primary

purpose of this study was two-fold: to (1) compare the densitometric and geometric parameters in the midshaft radius between the paretic and non-paretic sides, and (2) examine the relationship between the pQCT parameters and stroke impairments (muscle weakness, motor function, spasticity, and chronic disuse).

METHODS

Subjects

Subjects were originally recruited to participate in a clinical trial examining the effects of an exercise program on physical fitness, balance and muscle strength [19]. All subjects were recruited from a local rehabilitation hospital database, community stroke clubs and local newspaper advertisements. Inclusion criteria were: (1) sustained a single stroke ≥1 year onset, (2) age ≥50 years, (3) ability to walk >10 meters independently (with or without walking aids), (4) living at home, and (5) Mini-mental state examination score >22 [20]. In addition, to ensure exercise safety, each individual was required to raise heart rate to at least 60% age-predicted heart rate maximum without any cardiac signs and symptoms using cycle ergometry. Heterogeneity in upper extremity function within the study sample was desired and therefore individuals with different levels of impairment were included. Exclusion criteria included: (1) history of serious cardiac disease (i.e. myocardial infarction), (2) uncontrolled blood pressure (systolic blood pressure >140, diastolic blood pressure >90), (3) pain while walking, (4) neurological conditions in addition to stroke, (5) other serious diseases that preclude the individual from participating in the study, and (6) metal implants within the imaging field.

Informed and written consent were first obtained from all eligible individuals. In addition, the primary care physician was required to provide written information on the clinical history of the individual and make recommendations about the individual's participation in the study. The study was approved by the local university and hospital ethics committees. The experiments were conducted in accordance with the Helsinki Declaration.

For each subject, height (to the nearest millimeter) and weight (to the nearest 0.1kg) was measured using the Health O Meter (Continental Scale Corp., Bridgeview, IL, USA). The functional classification level of the American Heart Association Stroke Outcome Classification was used to measure residual disability in basic (e.g. dressing, bathing) and instrumental activities of daily living (e.g. shopping, preparing meals) (BADL and IADL) [level I = as independent as before the stroke; level V = completely dependent in BADL and IADL] [21].

Peripheral quantitative computed tomography

Peripheral QCT was used to measure the midshaft radius on both the paretic side and non-paretic side (Stratec Medizintecnik XCT 2000; software version 5.50; Pforzheim, Germany). All subjects were seated comfortably in a chair adjacent to the pQCT gantry with the upper extremity supported by a custom-built tray. We obtained a scout view and positioned the anatomical reference line at the distal medial edge of the radius. The length of the radius (mm) was measured according to the recommendation by the manufacturer and one 2.5 mm

scan of the midshaft radius at the 30% site (measured from the distal end) was obtained on each side. We specifically chose the 30% site (midshaft) for measurement because of its anatomical proximity to the origin/insertion of many muscle groups (e.g. Abductor pollicis longus, extensor pollicis brevis, pronator teres, etc.), and the polar Stress-Strain Index (pSSI) at this site is a measure of bone strength in torsion. As a result, muscle weakness and spasticity following stroke may have a more significant impact on the cortical bone sites.

An in-plane pixel size of 300 microns and slice thickness of 2.5 mm were used for all scans. All pQCT scans were acquired by the same technician who was trained to perform the scanning procedures and had 3 years of experience. The outcome variables of interest were total bone area ($Area_{total}$, mm^2), total BMC (BMC_{total}, mg/mm), total BMD (BMD_{total}, mg/cm^3), cortical bone area ($Area_{cort}$, mm^2), cortical bone mineral content (BMC_{cort}, mg/mm), cortical bone mineral density (BMD_{cort}, mg/cm^3), cortical thickness (mm), and p-SSI, mm^3.

XCT v.5.50 software was used for analysis. CALCB Contour (Mode 3 and Peel Mode 2) was used for total bone analysis whereas CORTBD Mode 4 was used for cortical bone analysis. For edge detection and cortical bone analysis, we analyzed all scans using 710\710 mg/cm^3 thresholds. These particular thresholds were chosen based on the experiences drawn from our previous research [17,22], the default thresholding recommended by the manufacturer and consultation with an independent pQCT technician. Regarding the precision of the scanner, the coefficient of variation varied from 0.4% to 1.85% (with repositioning), and 0.20% to 1.83% (without repositioning) [23]. Each scan was reviewed independently by two investigators to determine whether the scan should be accepted for analysis based on its quality.

Arm muscle strength

Mechanical force influences bone outcomes and the greatest force acting on bone is generated by muscle. Muscle weakness may thus be a key factor affecting bone demineralization in the stroke population. Isometric strength of 5 different upper extremity movements was tested with the subject sitting upright in a chair: (1) shoulder flexion, (2) shoulder abduction, (3) elbow flexion (4) elbow extension, and (5) hand grip. A hand-held dynamometer (Nicholas MMT, Lafayette Instruments, Lafayette, IN, USA) was used to assess muscle strength in the first four muscle groups whereas hand grip strength was measured by using the Jamar dynamometer (Sammons Preston, Mississauga, Ontario, Canada).

The testing positions were the same for all subjects. For testing shoulder flexion and abduction, the arm was held straight by the side of the trunk with 0 degrees of shoulder flexion and abduction. For testing elbow flexion, the shoulder position remained unchanged but the elbow was flexed at 90 degrees. For testing elbow extension, the arm was placed horizontally in front of the subject with both the shoulder and elbow joints flexed at 90 degrees. The testing position for hand grip strength was based on the recommendation by the American Society of Hand Therapists [24]. The shoulder was adducted and neutrally rotated. The elbow was flexed at 90 degrees with neutral supination and pronation, and wrist in a neutral position. Three maximal isometric contractions of each of the five muscle groups

were performed on each side with a brief rest between contractions. The data were averaged and the mean force values of the 5 muscle groups on one side were summed to obtain the composite muscle strength score for each upper extremity. We have previously reported isometric strength in stroke and found similar average range and magnitude values of these upper extremity muscles in the paretic limb [25]; thus, one muscle group should not have undue weighting on the composite score. Hand-held dynamometry has been shown to be a reliable method of testing muscle strength [26,27].

Recovery of upper extremity function

The Wolf Motor Function Test (WMFT) was used to assess upper extremity function [28]. It is a 15-item assessment and quantifies upper extremity movement through timed joint-segment movements and functional tasks. A score from 0 to 5 was given for each task (0: does not attempt with upper extremity being tested; 3: movement is influenced to some degree by synergy or is performed slowly or with effort; 5: movement appears to be normal). The scores for the 15 tasks were summed and then averaged to yield the mean functional ability score, with a higher score indicating better recovery of upper extremity motor function. WMFT has been shown to have high interrater reliability [intraclass correlation coefficients (ICC)≥0.88], internal consistency (Cronbach's $\alpha \geq 0.86$) and test-retest reliability ($r \geq 0.90$) in people with stroke [28,29].

Spasticity

The Modified Ashworth Scale (MAS) was used to assess resistance to passive movements in the elbow and hand on the paretic side (0: no increase in muscle tone, 4: affected part rigid in flexion and extension). The scores for the elbow and hand were averaged. The Modified Ashworth Scale is a reliable tool to assess upper extremity muscle tone in individuals with stroke [30].

Assessment of Disuse

The amount of use scale in the Motor Activity Log (MAL) was used to evaluate how much a person used the affected upper extremity in daily activities and may provide important information on disuse [31]. MAL consists of 30 functional tasks (e.g. putting on shoes, opening a refrigerator) and was administered as a semi-structured interview (van der Lee et al. 2004). A score, based on a 6-point scale, was given for each item (0: paretic arm not used; 3: paretic arm used about half as much as before the stroke; 5: paretic arm used as much as before the stroke). The scores for the 30 items were averaged to obtain a mean score. The MAL has been shown to have high internal consistency (Cronbach's $\alpha \geq 0.88$), and reasonable construct validity (Spearman's $\rho = 0.63$) in persons with stroke [31].

Statistical Analysis

Descriptive statistics were used to report the subject characteristics. Data from men and women were analyzed separately first. Paired t-tests were used to compare the pQCT parameters between the paretic and non-paretic sides. The percent side-to-side difference in the pQCT parameters was established by calculating the difference of values between the two sides (non-paretic - paretic) divided by the value obtained from the non-paretic side and

then multiplying it by a factor of 100. Thus, a positive side-to-side difference indicates a higher value on the non-paretic side when compared with the paretic side. Independent t-tests were then used to determine whether there was a significant difference in percent side-to-side difference in pQCT parameters between the two sexes. If no significant difference was found, the data would be pooled for subsequent analyses.

Pearson's correlation coefficient was used to assess the association between pQCT parameters and stroke impairments (percent side-to-side difference in muscle strength, WMFT, MAS, and MAL scores). Multiple linear regression analyses were then performed to identify the determinants of percent side-to-side difference in BMC_{cort}, BMD_{cort}, cortical thickness, and p-SSI. First, demographics such as age, sex, BMI, and post-stroke duration were forced into the regression model. Upper extremity impairments that were significantly associated with any of the aforementioned pQCT parameters in the bivariate correlational analysis were then entered into the regression model. All statistical analyses were conducted using SPSS 14.0 software. A significance level was set at 0.05.

RESULTS

Subject characteristics

Sixty-three subjects were originally enrolled in the trial. Peripheral QCT scans could not be acquired for one subject because she had such severe flexor spasticity that the affected arm could not fit into the supporting tray. Another 15 scans were excluded for analysis because there were obvious artifacts due to movement/tremor/spasticity. As a result, scans from 47 subjects were analyzed. The 16 individuals who were excluded from analysis did not have any significant difference in percent side-to-side muscle strength (independent t-test, p=0.990), WMFT (p=0.706), MAS (p=0.853), and MAL scores (p=0.980) when compared with the 47 individuals who were included. Subject characteristics are described in Table 1. On average, the paretic upper extremity was 38.5 % weaker than the non-paretic upper extremity. Seven (15%) subjects had very poor motor function in the affected upper extremity, with a WMFT score ≤1. Fifteen subjects (32%) had a MAL score ≤1, indicating severe disuse. The majority of the subjects did not have severe spasticity in the affected upper extremity, however, with only 2 individuals (4%) obtaining a MAS score ≥3. Five subjects (4 women) were on osteoporosis medications (i.e. Alendronate, Etidronate). On average, they had been taking osteoporosis medications for 2.7 years at the time of the study (range: 5 months to 6 years). The duration between the time they started the osteoporosis medications and stroke onset varied, ranging from 0.7 years before stroke to 4.6 years after stroke. None of the subjects had a history of forearm fracture.

pQCT analysis

Our results showed significant differences in pQCT parameters between the paretic and non-paretic limbs (Table 2). For men there were significant differences for BMC_{total} ($p<0.001$), BMD_{total} ($p<0.001$), $Area_{cort}$ ($p<0.001$), BMC_{cort} ($p<0.001$), BMD_{cort} ($p=0.003$), cortical thickness ($p<0.001$), and p-SSI ($p=0.005$). For women, significant differences were found in BMC_{total} ($p=0.019$), BMD_{total} ($p=0.013$), $Area_{cort}$ ($p=0.025$), BMC_{cort} ($p=0.020$), and cortical thickness ($p=0.018$). There was a trend for a lower p-SSI on the paretic side for

women, but it did not reach statistical significance (p=0.073), probably due to the reduced statistical power related to the smaller number of women in our sample. Interestingly, $Area_{total}$ did not show any significant difference between the two sides for both male (p=0.877) and female subjects (p=0.963).

Percent side-to-side differences in all pQCT parameters were computed (Table 2). Independent t-tests revealed no significant differences between the two sexes in all of the parameters measured (p>0.2), indicating that hemiparesis exerted similar influences on bone demineralization and geometry in the midshaft radius for both our male and female subjects.

Although the substantial side-to-side difference in BMC_{cort} and BMD_{cort} observed in our study could be explained by the effect of hand dominance, (i.e. the non-paretic arm was the dominant hand prior to the stroke), our results suggest that it is highly unlikely. The percent side-to-side difference in BMC_{cort} and BMD_{cort} for those with the dominant hand affected (n=18) was not significantly different from those with the non-dominant side affected (n=29) (independent t-tests, p> 0.05). This suggests hand dominance alone could not account for the paretic side-to-side difference in pQCT parameters and our results point to the potent influence of hemiparesis on bone density and geometry.

Relationship between pQCT parameters and upper extremity impairment

High correlations were found among all the measures of upper extremity impairment (Table 3). The associations between pQCT parameters and various measures of upper extremity impairment are shown in Table 4. Percent side-to-side difference in BMC_{cort} and cortical thickness had positive correlations with percent side-to-side difference in upper extremity muscle strength and spasticity. On the other hand, less upper extremity motor function (WMFT) and more disuse (MAL) were related to greater side-to-side differences in BMC_{cort} and cortical thickness. BMD_{cort} and p-SSI had no significant correlation with any of the measures of upper extremity impairment.

Predictors of pQCT parameters

Multiple regression analyses were performed to identify the determinants of the percent side-to-side difference in BMC_{cort} and cortical thickness. We did not enter all of the upper extremity impairment measures into a single regression model due to concerns of collinearity, since high correlations exist among these variables (Table 3). First, we selected percent side-to-side difference in muscle strength to be the independent variable in the regression analysis because muscle strength is a common outcome measure used in the clinical setting and previous DXA studies have highlighted a close muscle-bone relationship in different populations [11,32,33]. We also chose spasticity as the independent variable because spasticity impairs arm function and could be easily evaluated in a daily clinical practice. It would be of value if we could use spasticity to predict bone mineralization and geometric changes. Finally, we also entered the MAL score into the regression models, as it provides a unique measure of paretic arm use in the real world setting. WMFT was not selected due to its extremely high correlation with percent side-to-side difference in muscle strength (Table 3).

In the first set of regression models (Table 5), we used percent side-to-side difference in muscle strength, spasticity and MAL scores, respectively, to predict percent side-to-side difference in BMC_{cort}. We first accounted for demographics such as age, sex, BMI and post-stroke duration. We then found that percent side-to-side difference in upper extremity muscle strength (model 1), spasticity (model 2), and MAL scores (model 3) were all significant predictors of percent side-to-side difference in BMC_{cort}, accounting for 22.9%, 20.2, and 16.3% of its variance, respectively.

In the next set of regression models (Table 5), we used the same measures of upper extremity impairment to predict percent side-to-side difference in cortical thickness. Our results revealed that percent side-to-side difference in upper extremity muscle strength (model 4), spasticity (model 5) and MAL scores (model 6) were all independently associated with percent side-to-side difference in cortical thickness, accounting for 25.9%, 23.2% and 14.9% of its variance, respectively.

DISCUSSION

Several previous studies have examined upper extremity bone health in individuals with chronic stroke. One common limitation of these studies is the lack of information on bone geometry [2,3,11,13], which is another important determinant of bone strength besides bone density [15,16]. This novel study provides important information on bone volumetric density, size, and geometry in the midshaft radius among individuals with chronic stroke.

Demineralization and endosteal resorption in midshaft radius after chronic stroke

Our results showed that BMC_{cort} and BMD_{cort} in the midshaft radius on the paretic side are on average 7.6% and 1.6% lower, respectively, than the non-paretic side (Table 2). This difference is comparable to a previous small study in which a significant 8% and 3% side-to-side difference in BMC_{cort} and BMD_{cort} were identified at the same radial site in a different group of 15 chronic stroke survivors [17]. Our findings thus extend the previous work from our laboratory and others using DXA or single-photon absorptiometry, showing compromised areal BMD in the paretic upper extremity [2,11].

The midshaft radius on the paretic side had a significantly lower p-SSI than the non-paretic side, indicating compromised bone strength. Several deleterious stroke-related bone changes that may contribute to the reduction in bone strength. First, the paretic side had significantly lower BMC_{cort} and BMD_{cort}, which reflects loss of bone mineral and increased porosity of bone tissue [18]. Second, the cortical wall on the paretic side was also significantly thinner than the non-paretic side, whereas no side-to-side difference in $Area_{total}$ was found. Together, the findings suggest endosteal resorption, a phenomenon reported previously in people living with a spinal cord injury [34]. Endosteal resorption without compensatory periosteal apposition in our subjects contributes to a significantly lower bone strength index value (p-SSI) on the paretic side.

On the other hand, our findings are in contrast with the age-related bone changes observed in different skeletal sites. With aging, besides bone demineralization, endosteal resorption is coupled with periosteal apposition [18,35,36]. This leads to increased total bone cross-

sectional area and outward displacement of the cortex [18,35,36]. This phenomenon may be a compensatory response to age-related demineralization for maintaining bone strength, since adding bone to the periosteal surface will increase the cross-sectional moment of inertia [16] and helps to offset some of the deleterious effects of endosteal resorption on bone strength [18]. Our findings do not support such a compensatory structural adaptation in response to stroke-induced demineralization.

There exists a possibility that the cortical thinning reported in this study may contribute to underestimation of BMD_{cort} due to the partial volume effect. However, this artifact should be minimal. First, we sought to address this issue a priori by scanning at a higher resolution (in-plane pixel size =300microns). Second, cortical thickness of 2mm or greater should improve accuracy of bone evaluation [37] and 91% of our subjects have a cortical thickness >2mm on the paretic side.

Determinants of pQCT parameters and clinical implications

Another important finding of this study is that various measures of upper extremity impairment (i.e. muscle weakness, spasticity, and disuse) are independently associated with BMC_{cort} and cortical thickness. Percent side-to-side difference in muscle strength has the highest correlation with the aforementioned pQCT parameters. It points to the powerful influence of muscle strength on bone mass and geometry. The close relationship between muscle strength and bone health in the upper extremity observed in this study is consistent with previous studies in chronic stroke and other populations using DXA [11,32,33].

As muscle weakness is a major determinant of bone mass and geometry in the midshaft radius among chronic stroke survivors, improving muscle strength may be a potentially effective method to enhance bone density and geometry in this group. There is some evidence that muscle strengthening exercise can enhance upper extremity bone density and geometry in postmenopausal women (i.e. corticalization of trabecular bone at endosteal surface combined with periosteal apposition) [38]. To date, no study has investigated the effect of strength training on upper extremity bone density and geometry in individuals with stroke. However, the beneficial effects of exercise on lower extremity bone density and geometry in chronic stroke have been demonstrated [19,22]. Whether upper extremity muscle strengthening would produce similar gains in bone density and geometry awaits further research.

It is the first study to demonstrate that spasticity as measured by MAS is also a significant determinant of bone health. A previous study in stroke failed to find such a relationship between spasticity and DXA parameters in the upper extremity [11]. The different skeletal sites measures, the different bone parameters used may account for the difference in findings. The relationship between spasticity and bone health may be a complex one. Severe spasticity may adversely affect bone health through its high influence on upper extremity function and muscle strength (Table 3). On the other hand, the tonic muscle activity associated with spasticity may have some protective effect on the bone as opposed to flaccid paralysis, as seen in spinal cord injury [39]. However, our study does not seem to support this latter point as we found that greater demineralization is associated with greater levels of

spasticity. Clinically, it would be valuable to investigate the effects of different spasticity management strategies on bone health.

We demonstrated the new finding that disuse is related to upper extremity bone health in people with chronic stroke. Its correlation with the pQCT parameters is not as high when compared with the correlation between muscle strength and pQCT parameters (Table 3). It is probably due to that fact that MAL does not quantify the effort of arm use (e.g. lifting heavy versus light objects). Stroke patients often develop learned non-use of the paretic upper extremity despite the presence of motor ability [1], which may in turn lead to further decline in upper extremity function and compromise in bone health. Our results suggest that one could potentially improve bone health by simply increasing the use of the paretic upper extremity in functional activities. Exercise therapy such as the constraint-induced movement therapy, is particularly designed to reduce the learned non-use of the paretic upper extremity [1,40]. Further study is required to investigate the effects of these treatment approaches to upper extremity bone health.

It is intriguing that p-SSI is not significantly correlated with any of the upper extremity impairment measures (Table 3). Several factors may contribute to this finding. First, the sample size in this study may be too small to detect a significant correlation. Second, although we did not observe any significant periosteal apposition, the $Area_{total}$ was nevertheless well maintained on the paretic side. This may explain why side-to-side difference in p-SSI (4.8%) is relatively modest when compared with that in BMC_{cort} (7.6%) and cortical thickness (9.8%), and a weak correlation between muscle strength and p-SSI (0.224).

Limitations of study

There are some limitations to this study. First, the study could not assess the temporal changes of pQCT parameters within subjects due to the cross-sectional study design. Second, we assessed the influence of stroke on upper extremity bone health by comparing the paretic and non-paretic sides. While this method may allow us to study the effects of stroke on bone health while providing some control for the different cofactors (i.e. environmental, genetic) which may affect bone metabolism in different subjects, the non-paretic side may not provide the ideal control. For example, some individuals, especially for those with more severe impairment of the paretic upper extremity, may compensate by using the non-paretic upper extremity to perform most daily activities. This increased activity performed by the non-paretic upper extremity may in turn induce specific changes in bone density and geometry [5]. Alternatively, the well-known sedentary lifestyle of stroke survivors could reduce bone density on both paretic and non-paretic sides.

Conclusion

This novel study provides important information on bone volumetric density, size, and geometry in the midshaft radius among individuals with chronic stroke. We found a significantly lower BMC_{cort}, BMD_{cort}, cortical thickness and p-SSI on the paretic side when compared with the non-paretic side. The $Area_{total}$, however, shows no significant side-to-side difference. The findings indicate endosteal resorption on the paretic side, without any

evident periosteal apposition. This is the first study to show that muscle strength, spasticity and disuse after a stroke are all significant determinants of bone demineralization and geometry in the midshaft radius.

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References

1. Wolf SL, Lecraw DE, Barton LA, et al. Forced use of hemiplegic upper extremities to reverse the effect of learned nonuse among chronic stroke and head-injured patients. Exp Neurology. 1989; 104:125–32.
2. Hamdy RC, Krishnaswamy G, Cancellaro V, et al. Changes in bone mineral content and density after stroke. Am J Phys Med Rehabil. 1993; 72:188–91. [PubMed: 8363812]
3. Prince RL, Price RI, Ho S. Forearm bone loss in hemiplegia: a model for the study of immobilization osteoporosis. J Bone Miner Res. 1988; 3:305–10. [PubMed: 3213623]
4. Liu M, Tsuji T, Higuchi Y, et al. Osteoporosis in hemiplegic stroke patients as studied with dual-energy X-ray absorptiometry. Arch Phys Med Rehabil. 1999; 80:1219–26. [PubMed: 10527077]
5. Ramnemark A, Nyberg L, Lorentzon R, et al. Progressive hemiosteoporosis on the paretic side and increased bone mineral density in the nonparetic arm the first year after severe stroke. Osteoporos Int. 1999; 9:269–75. [PubMed: 10450417]
6. Kanis J, Oden A, Johnell O. Acute and long-term increase in fracture risk after hospitalization for stroke. Stroke. 2001; 32:702–6. [PubMed: 11239190]
7. Ramnemark A, Nyberg L, Borssen B, et al. Fractures after stroke. Osteoporos Int. 1998; 8:92–5. [PubMed: 9692083]
8. Dennis MS, Lo KM, McDowall M, et al. Fractures after stroke. Frequency, types and associations. Stroke. 2002; 33:728–34. [PubMed: 11872896]
9. Garrett NA, Brasure M, Schmitz KH, et al. Physical inactivity. Direct cost to a Health Plan. Am J Prev Med. 2004; 27:304–9. [PubMed: 15488360]
10. Jorgensen L, Jacobsen BK. Functional status of the paretic arm affects the loss of bone mineral in the proximal humerus after stroke: a 1-year prospective study. Calcif Tissue Int. 2001; 68:11–5. [PubMed: 12037618]
11. Pang MYC, Eng JJ. Muscle strength is a determinant of bone mineral content in the hemiparetic upper extremity: implications for stroke rehabilitation. Bone. 2005; 37:103–11. [PubMed: 15869927]
12. Iwamoto J, Takeda T, Ichimura S. Relationships between physical activity and metacarpal cortical bone mass and bone resorption in hemiplegic patients. J Orthop Sci. 2001; 6:227–33. [PubMed: 11484115]
13. Sahin L, Ozoran K, Gunduz OH, et al. Bone mineral density in patients with stroke. Am J Phys Med Rehabil. 2001; 80:592–6. [PubMed: 11475480]
14. Sato Y, Fujimatsu Y, Kikuyama M, et al. Influence of immobilization on bone mass and bone metabolism in hemiplegic elderly patients with long-standing stroke. J Neurol Sci. 1998; 156:205–10. [PubMed: 9588859]
15. Frost HM. Absorptiometry and “osteoporosis”: problems. J Bone Miner Metab. 2003; 21:255–60. [PubMed: 12928825]

16. Burr, DB., Turner, Ch. Biomechanics of Bone. In: Favus, MJ., editor. Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism. 5. American Society for Bone and Mineral Research; Washington DC: 2003. p. 58-64.
17. Ashe MC, Fehling P, Eng JJ, et al. Bone Structural Changes to Chronic Disuse following Stroke. Journal of Musculoskel and Neuron Interact. (in press).
18. Riggs LB, Melton LJ, Robb RA, et al. A population-based study of age and sex differences in bone volumetric density, size, geometry and structure at different skeletal sites. J Bone Miner Res. 2004; 19:1945–54. [PubMed: 15537436]
19. Pang MYC, Eng JJ, Dawson AS, et al. A community-based Fitness and Mobility Exercise program for older adults with chronic stroke: a randomized controlled trial. J Am Geriatr Soc. 2005; 53:1667–74. [PubMed: 16181164]
20. Folstein MF, Folstein SE, McHugh PR. Mini-Mental State: A practical method for grading the state of patients for the clinician. J Psychiat Res. 1975; 12:189–98. [PubMed: 1202204]
21. Kelly-Hayes M, Robertson JT, Broderick JP, et al. The American Heart Association Stroke Outcome Classification: executive summary. Circulation. 1998; 97:2474–8. [PubMed: 9641702]
22. Liu-Ambrose TY, Khan KM, Eng JJ, et al. Both resistance and agility training increase cortical bone density in 75- to 85-year-old women with low bone mass: a 6-month randomized controlled trial. J Clin Densitom. 2004; 7:390–8. [PubMed: 15618599]
23. Pang MYC, Ashe MC, Eng JJ, et al. A 19-week exercise program for people with chronic stroke enhances bone geometry at the tibia: a peripheral quantitative computed tomography study. Osteoporos Int. 2006; 17:1615–25. [PubMed: 16896509]
24. Fess, EE. Grip strength. In: Casanova, JS., editor. Clinical assessment recommendations. 2. American Society of Hand Therapists; Chicago: 1992. p. 41-45.
25. McCrea PH, Eng JJ, Hodgson AJ. Time and magnitude of torque generation is impaired in both arms following stroke. Muscle Nerve. 2003; 28:46–53. [PubMed: 12811772]
26. Bohannon RW. Measurement and nature of muscle strength in patients with stroke. J Neuro Rehabil. 1997; 11:115–25.
27. Mathiowetz V. Comparison of Rolyan and Jamar dynamometers for measuring grip strength. Occup Ther Int. 2002; 9:201–9. [PubMed: 12374997]
28. Wolf SL, Catlin PA, Ellis M, et al. Assessing Wolf Motor Function Test as outcome measure for research in patients after stroke. Stroke. 2001; 32:1635–9. [PubMed: 11441212]
29. Morris DM, Uswatte G, Crago JE, et al. The reliability of the Wolf Motor Function Test for assessing upper extremity function after stroke. Arch Phys Med Rehabil. 2001; 82:750–5. [PubMed: 11387578]
30. Bohannon BW, Smith MB. Interrater reliability of a Modified Ashworth Scale of muscle spasticity. Phys Ther. 1987; 67:206–7. [PubMed: 3809245]
31. van der Lee JH, Beckerman H, Knol DL, et al. Clinimetric properties of the Motor Activity Log for the assessment of arm use in hemiparetic patients. Stroke. 2004; 35:1410–4. [PubMed: 15087552]
32. Hughes VA, Frontera WR, Dallal GE, et al. Muscle strength and body composition: associations with bone density in older subjects. Med Sci Sports Exerc. 1995; 27:967–74. [PubMed: 7564983]
33. Di Monaco M, Di Monaco R, Manca M, et al. Handgrip strength is an independent predictor of distal radius bone mineral density in postmenopausal women. Clin Rheumatol. 2000; 19:473–6. [PubMed: 11147759]
34. Eser P, Schiessl H, Willnecker J. Bone loss and steady state after spinal cord injury: a cross-sectional study using pQCT. J Musculoskel Neuron Interact. 2004; 4:197–8.
35. Russo CR, Laurentani F, Bandinelli S, et al. Aging bone in men and women: beyond changes in bone mineral density. Osteoporos Int. 2003; 14:531–8. [PubMed: 12827220]
36. Ahlborg HG, Johnell O, Turner CH, et al. Bone loss and bone size after menopause. New Engl J Med. 2003; 349:327–34. [PubMed: 12878739]
37. Hangartner TN, Gilsanz V. Evaluation of cortical bone by computed tomography. J Bone Miner Res. 1996; 11:1518–25. [PubMed: 8889852]

38. Adami S, Gatti D, Braga V, et al. Site-specific effects of strength training on bone structure and geometry of ultradistal radius in postmenopausal women. J Bone Miner Res. 1999; 14:120–4. [PubMed: 9893073]

39. Wilmet E, Ismail AA, Heilporn A, et al. Longitudinal study of the bone mineral content and of soft tissue composition after spinal cord section. 1995; 33:674–7.

40. Taub E, Miller NE, Novack TA, et al. Technique to improve chronic motor deficit after stroke. Arch Phys Med Rehabil. 1993; 74:347–54. [PubMed: 8466415]

Table 1

Subject characteristics

Demographics	**Male (n=28)**	**Female (n=19)**	**All (n=47)**
Age (years)	62.1±8.6	68.0±7.4	64.5±8.6
Height (cm)	176.7±7.5	160.1±8.1	170.0±11.2
Weight (kg)	84.8±14.3	64.9±12.2	76.7±16.6
Body mass index (m/kg^2)	27.2±4.7	25.2±3.7	26.4±14.4
Mini Mental Status Examination (0–30)	27.6±2.1	28.3±1.7	27.9±2.0
Stroke characteristics			
Post-stroke duration (years)	5.1±3.3	5.6±5.1	5.3±8.6
Paretic side (right) (n)	11	8	19
Paretic side (dominant side) (n)	11	7	18
Hemorrhagic stroke (n)	17	11	28
American Heart Association Stroke Functional Classification (I/II/III/IV/V)	3/15/8/2/0	4/12/3/0/0	7/27/11/2/0
Outcome Measures (Upper extremity impairment)			
Muscle strength (Paretic side) (N)	584.7±440.7	500.4±214.2	550.6±365.6
Muscle strength (Non-paretic side) (N)	1167.3±275.0	643.3±128.8	955.5±344.1
Percent side-to-side difference in muscle strength (%)	50.0±34.1	21.4±30.3	38.5±35.2
Wolf Motor Function Test Score (0–5)	2.7±1.8	4.1±1.2	3.3±1.7
Modified Ashworth Scale of Spasticity Score (0–4) Median (interquartile range)	0.5(1.9)	0.0(1.0)	0.25(1.3)
Motor Activity Log Score (0–5)	2.0±1.8	3.3±1.6	2.5±1.9

Mean±SD unless otherwise indicated

Table 2

pQCT parameters at the 30% radial site

pQCT parameter		Paretic side	Non-paretic side	P*	Percent difference
Total area ($Area_{total}$, mm^2)	Male	116.6±18.3	116.9±18.7	0.877	−0.2±8.3
	Female	76.1±12.9	76.1±12.9	0.963	−0.1±5.8
	All	**100.2±25.8**	**100.4±26.1**	**0.871**	**−0.2±7.3**
Cortical area ($Area_{cort}$, mm^2)	Male	94.2±15.7	100.4±13.3	<0.001	6.3±7.7
	Female	59.0±11.4	63.1±11.0	0.025	6.0±11.5
	All	**1182.4±42.4**	**85.3±22.2**	**<0.001**	**6.2±9.3**
Cortical bone mineral content (BMC_{cort}, mg/mm)	Male	111.3±20.0	121.0±17.2	<0.001	8.2±8.1
	Female	70.2±15.1	76.0±15.6	0.020	6.7±13.0
	All	**84.7±27.2**	**102.8±27.7**	**<0.001**	**7.6±10.2**
Cortical bone mineral density (BMD_{cort}, mg/cm^3)	Male	1179.8±40.4	1204.2±33.2	0.003	2.0±3.3
	Female	1186.2±46.0	1198.5±59.9	0.192	0.9±3.4
	All	**1182.4±42.4**	**1201.9±45.4**	**0.001**	**1.6±3.3**
Cortical thickness (mm)	Male	3.6±0.8	4.0±0.7	<0.001	10.1±12.2
	Female	2.9±1.0	3.2±0.9	0.018	9.2±16.5
	All	**3.3±0.9**	**3.7±0.9**	**<0.001**	**9.8±14.0**
Polar Stress-strain Index (p-SSI, mm^3)	Male	313.1±62.5	331.1±64.6	0.005	5.1±8.9
	Female	165.9±29.5	175.8±35.8	0.073	4.5±11.7
	All	**253.6±89.2**	**268.3±94.2**	**0.001**	**4.8±10.0**

*Paired t-test to compare between the paretic and non-paretic sides.

Table 3

Correlations among various measures of upper extremity impairment

	Percent side-to-side difference in muscle strength	WMFT	MAS	MAL
Percent side-to-side difference in muscle strength	-	−0.929	0.770	−0.818
WMFT	−0.929	-	−0.785	0.857
MAS	0.770	−0.785	-	−0.698
MAL	−0.818	0.857	−0.698	-

Table 4

Correlations between pQCT parameters and upper extremity impairment

Upper extremity impairment	Percent side-to-side difference			
	Cortical bone mineral content	Cortical bone mineral density	Cortical thickness	P-SSI
Percent side-to-side difference in muscle strength	0.474†	0.273	0.477†	0.224
WMFT	−0.415†	−0.282	−0.412†	−0.150
MAS	0.457†	0.225	0.476†	0.221
MAL	−0.396*	−0.217	−0.365*	−0.246

*p<0.05

†p<0.005

Table 5

Multiple regression analyses to predict pQCT parameters

Model	Predictors	F	R^2 change	B	95%CI	Beta	p
Dependent variable: Percent side-to-side difference in BMC_{cort}							
Model 1	Age	3.869	0.092	−0.103	−0.435, 0.229	−0.086	0.534
	Gender			4.766	−1.531, 11.063	0.231	0.134
	BMI			0.534	−0.104, 1.173	0.227	0.099
	Post-stroke duration			−0.316	−0.981, 0.350	−0.126	0.344
	Percent side-to-side difference in muscle strength		**0.229**	**0.155**	**0.071, 0.240**	**0.534**	**0.001**
Model 2	Age	3.412	0.092	−0.142	−0.479, 0.194	−0.142	0.534
	Gender			2.309	−3.744, 8.361	2.309	0.134
	BMI			0.281	−0.365, 0.928	0.281	0.099
	Post-stroke duration			−0.562	−1.235, 0.110	−0.224	0.344
	MAS scores		**0.202**	**5.010**	**2.054, 7.965**	**0.463**	**0.001**
Model 3	Age	2.812	0.092	−0.122	−0.469, 0.224	−0.103	0.480
	Gender			3.637	−2.847, 10.120	0.176	0.264
	BMI			0.422	−0.241, 1.084	0.179	0.206
	Post-stroke duration			−0.518	−1.208, 0.172	−0.206	0.137
	MAL scores		**0.163**	**−2.410**	**−4.034, −0.787**	**−0.437**	**0.005**
Dependent variable: Percent side-to-side difference in cortical thickness							
Model 4	Age	3.216	0.022	0.013	−0.453, 0.478	0.008	0.956
	Gender			6.496	−2.338, 15.330	0.231	0.145
	BMI			0.484	−0.412, 1.379	0.151	0.282
	Post-stroke duration			−0.123	−1.057, 0.811	−0.036	0.792
	Percent side-to-side difference in muscle strength		**0.259**	**0.226**	**0.107, 0.344**	**0.569**	**<0.001**
Model 5	Age	2.805	0.022	−0.044	−0.517, 0.428	−0.027	0.850
	Gender			2.947	−5.536, 11.429	0.105	0.487
	BMI			0.115	−0.791, 1.020	0.036	0.799
	Post-stroke duration			−0.482	−1.425, 0.461	−0.141	0.308
	MAS score		**0.232**	**7.334**	**3.192, 11.477**	**0.497**	**0.001**
Model 6	Age	1.698	0.022	−0.021	−0.520, 0.478	−0.013	0.932

Model	Predictors	F	R^2 change	B	95%CI	Beta	p
	Gender			4.372	−4.958, 13.702	0.155	0.350
	BMI			0.312	−0.642, 1.265	0.097	0.513
	Post-stroke duration			−0.413	−1.406, 0.579	−0.121	0.405
	MAL score		**0.149**	**−3.142**	**−5.478, −0.806**	**0.417**	**0.010**