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Spatial Differences in the Distribution of Bone between Femoral Neck and Trochanteric Fractures

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Abstract

There is little knowledge about the spatial distribution differences in volumetric bone mineral density and cortical bone structure at the proximal femur between femoral neck fractures and trochanteric fractures. In this case-control study, a total of 93 women with fragility hip fractures, 72 with femoral neck fractures (mean±SD age: 70.6±12.7 years) and 21 with trochanteric fractures (75.6±9.3 years), and 50 control subjects (63.7±7.0 years) were included for the comparisons. Differences in the spatial distributions of volumetric bone mineral density, cortical bone thickness, cortical volumetric bone mineral density and volumetric bone mineral density in a layer adjacent to the endosteal surface were investigated using voxel-based morphometry (VBM) and surface-based statistical parametric mapping (SPM). We compared these spatial distributions between controls and both types of fracture, and between the two types of fracture. Using VBM, we found spatially heterogeneous volumetric bone mineral density differences between control subjects and subjects with hip fracture, that varied by fracture type. Interestingly, femoral neck fracture subjects, but not subjects with trochanteric fracture, showed significantly lower volumetric bone mineral density in the superior aspect of the femoral neck compared to controls. Using surface-

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Disclosures

All authors state that they have no conflicts of interest.

Authors' contributions

AY is the primary author and contributed to the manuscript in the following ways: conception and design, patient selection, analysis and interpretation of data, manuscript drafting and revision. JCG and AY contributed equally. JCG participated in the design of the study, implemented the image analysis tools to perform VBM and SPM, analyzed data, interpreted results, wrote and revised the manuscript. The following authors contributed as described: LW (patient selection, manuscript drafting, interpretation of data, and revision), YS (patient selection and revision), XW, JX, CY and MW (patient selection), TFL (designed the study, interpreted results, and revision) and XC (study supervisor, conception and design, data analysis and interpretation, manuscript revision).

Competing interests

The authors declare that they have no competing interests.

based SPM, we found that compared to controls both fracture types showed thinner cortices in regions in agreement with the type of fracture. Most outcomes of cortical and endocortical volumetric bone mineral density comparisons were consistent with VBM results. Our results suggest: 1) that the spatial distribution of trabecular volumetric bone mineral density might play a significant role in hip fracture; 2) that focal cortical bone thinning might be more relevant in femoral neck fractures; and 3) that areas of reduced cortical and endocortical volumetric bone mineral density might be more relevant for trochanteric fractures in Chinese women.

Keywords

Osteoporosis; proximal femur; quantitative computed tomography (QCT); voxel-based morphometry (VBM); statistical parametric mapping (SPM); femoral neck fracture; trochanteric fracture; bone mineral density (BMD); cortical bone thickness

Introduction

Osteoporosis constitutes a major public health problem with age-related fractures(1). Osteoporotic hip fracture is the most severe clinical outcome of osteoporosis, with a high degree of morbidity and mortality in the elderly(2). Therefore, it is important to identify subjects at risk for hip fracture. The World Health Organization (WHO) definition of osteoporosis highlighted areal bone mineral density (aBMD) derived from dual x-ray absorptiometry (DXA) as a surrogate parameter for the risk of osteoporotic fractures(3). However, low aBMD measures alone are not sufficient to explain all osteoporotic fractures(4, 5). This is due to the fact that aBMD provides no insight into how the three-dimensional (3D) variation of bone geometry, bone size, and cortical and trabecular bone compartments contribute to bone strength(6, 7).

Computational Anatomy techniques–borrowed from the neuroimaging community–enable local multi-parametric assessments of the spatial distribution of volumetric bone mineral density (vBMD) and structural features of the proximal femur from quantitative computed tomography (QCT) images at the population level. Techniques such as voxel-based morphometry (VBM) for the spatial assessment of vBMD and surface-based statistical parametric mapping (SPM) for the spatial assessment of cortical bone properties, including cortical bone thickness (Ct.Th) and cortical vBMD (Ct.vBMD), have been validated and successfully applied in previous studies(8–14). These advanced image analysis techniques generate cohort-based spatial parametric atlases by registering individual subject images to a common coordinate system, thus enabling point-by-point statistical tests at corresponding anatomic locations. These statistical atlases provide an opportunity to visualize a physical parameter of interest, such as vBMD or Ct.Th in relation to a variable of interest(15). For example, Li et al. and Carballido-Gamio et al. applied VBM to identify regions in the proximal femur where vBMD was significantly associated with acute and incident hip fractures, respectively(8, 10); while Poole and colleagues applied surface-based SPM to identify regions where Ct.Th(12) and cortical and endocortical trabecular density parameters were significantly associated with acute hip fractures(16). These four studies demonstrated

biological relevance by showing significant bone differences between fracture cases and controls in regions commonly involved with hip fracture(10).

Although many studies have grouped hip fractures as a single entity, hip fractures are divided into two major anatomic-based types: femoral neck fractures (intracapsular) and trochanteric fractures (extracapsular)(17). As the two anatomic locations have different amounts and distributions of bone, the etiology and biomechanics of each fracture type may differ. In fact, several studies have shown that risk factors differ between neck and trochanteric fractures of the proximal femur(8, 14, 17–20). However, the potential differences in vBMD and bone structure between femoral neck and trochanteric fractures are currently unclear. To our knowledge, three studies have used statistical atlases to identify differences between the two types of fracture, one using VBM(8) and two applying SPM of cortical bone properties(14, 16). There have not been any studies integrating these different mapping approaches into the same subjects in relation to fracture type.

The goal of this work was to identify spatial differences in proximal femoral vBMD and cortical bone properties between femoral neck and trochanteric fractures in elderly females. For this purpose, we applied statistical multi-parametric mapping to a study of acute hip fracture of 143 subjects, with 50 controls and 93 cases with low-energy fractures that occurred within 48 hours before acquisition of QCT images.

Materials and Methods

Subjects

A total of 93 women with fragility hip fractures were included in this case-control study between 2012 and 2014. Seventy-two of these women had femoral neck fractures and 21 had trochanteric fractures. All cases were recruited from the emergency room, Department of Traumatology and Orthopedic Surgery, Beijing Jishuitan Hospital. The enrollment process of cases was as follows: clinically-suspected hip fracture subjects were referred to the emergency room CT scanning service by orthopedic surgeons. Then the radiologist on call in the emergency radiology service explained the nature of the study to the subjects. If the subjects agreed to participate, they would be asked to sign a consent form, fill out a questionnaire about the circumstances of the fall and other information regarding metabolic bone disease. The questionnaire permitted exclusion of those subjects with known health conditions affecting the bone mineral status of the hip, including metabolic bone disease, fixation of the proximal femur, previous bone fracture, and previous use of drugs that have an influence on bone metabolism. Prior to the hip fracture, all subjects were community-dwelling adults. Further, only those who fractured within 48 hours before hip CT scans were recruited into the study, in order to minimize changes in vBMD and body composition factors due to hip fractures. The definition of low-energy fracture was reported in a previous study(6). Fracture type was sub-grouped as: femoral neck (FN), trochanteric (TR), or other based on X-rays and CT images.

For comparison with the fracture cases, 50 female controls in good health were invited by advertisement from communities near Beijing Jishuitan Hospital to participate in the study. All women were living independently in the community. Participants who had used or were

using drugs that have an influence on bone metabolism were excluded. The exclusion criteria also included thyroid, parathyroid disease and metabolic bone diseases other than age-related osteoporosis and postmenopausal osteoporosis (achieved from the same questionnaire).

The sample described above was a subset of a larger number of subjects acquired in the study. Based on availability of computing and manpower resources at the analytic site (UCSF), we analyzed those study images acquired prior to 11/19/2013. This data set included 72 women with FN fractures, 21 with TR fractures and 50 control subjects. The whole dataset included 293 women with FN fractures, 175 with TR fractures and 429 control subjects.

QCT image acquisition

For each fracture subject, bilateral hip QCT scans were obtained with a Toshiba Aquilion 16-slices CT scanner (Toshiba Medical Systems Corp., Tokyo, Japan) in the emergency service with a calibration phantom (Mindways Software Inc., Austin, TX, USA) beneath the hip.

For each control subject, QCT scans were acquired using a Toshiba Aquilion 64-slices CT scanner (Toshiba Medical Systems Corp., Tokyo, Japan) in the outpatient service also with a calibration phantom (Mindways Software Inc., Austin, TX, USA) beneath the hip.

Both hips were scanned in the supine position from the top of the acetabulum to 3 cm below the lesser trochanter. Scan parameters for both CT scanners were 120 kVp, 125 mAs, 1mm slice thickness, 50 cm field of view, and 512×512 matrix in spiral and standard reconstructions.

To correct for the effect of inter-scanner differences, a European spine phantom (ESP; QRM, Erlangen, Germany) was scanned in both CT scanners for cross-calibration between the scanners. Based on the BMD measured on each scanner in the different ESP regions, we applied phantom-derived corrections to in-vivo images, and QCT vBMD voxel values on the 16-slice scanner were mapped to equivalent values in the 64-slice scanner.

Image processing

For subjects with hip fracture, the contralateral proximal femur was analyzed. For control subjects, the left hip was analyzed.

Using the calibration phantom, Hounsfield units were converted to equivalent concentrations of liquid K_2HPO_4 in mg/cm^3. QCT scans were then processed using the pipeline described by Carballido-Gamio and colleagues yielding segmented calibrated proximal femora suitable for VBM of vBMD, and surface-based maps of Ct.Th, Ct.vBMD and vBMD in a layer adjacent to the endosteal surface (EndoTb.vBMD), all suitable for SPM of cortical bone properties(11).

In order to perform VBM, all calibrated scans in the population were spatially normalized to a common template as previously described by Carballido-Gamio and colleagues(10).

Briefly, proximal femora were registered to a femoral template(10) using the bone segmentations and 3D affine (3 translations, 3 rotations and 3 scalings) and nonlinear registrations. The calculated transformations were then applied to the calibrated scans effectively bringing all vBMD maps into anatomical correspondence. Spatially-normalized vBMD maps were then smoothed with a Gaussian filter before spatial comparisons.

In order to perform SPM of cortical bone properties, the surface-based maps were spatially normalized to a triangulated surface representing the periosteal surface of the femoral template. Spatial normalization was completed with the previously computed VBM transformations, thus effectively bringing all surface-based Ct.Th, Ct.vBMD, and EndoTb.vBMD maps into anatomical correspondence. Spatially-normalized surface-based maps were also smoothed before spatial comparisons.

Statistical analysis

In order to confirm that this subset was representative of the entire study, we used ANOVA to compute differences in age, height, weight and hip BMD between the controls reported in this paper and those in the entire study, as well as between the subgroups of FN and TR subjects and their counterparts in the whole study.

Statistical significance of differences in subject characteristics (age, height and weight) between controls and subjects with femoral neck fracture, controls and subjects with trochanteric fracture, and subjects with femoral neck fracture and subjects with trochanteric fracture was established using analysis of variance. Differences were considered significant at $P<0.016$ to correct for multiple comparisons using the Bonferroni method.

VBM was performed in the form of voxel-wise general linear models. The vBMD values at each voxel location of the spatially-normalized and smoothed vBMD maps were used as the dependent variable and group membership (control or femoral neck fracture, control or trochanteric fracture, femoral neck fracture or trochanteric fracture) as the independent variable. Age, height and weight were included as covariates in the comparisons. False discovery rate (FDR)(21) correction was used to correct for multiple comparisons ($q=0.05$).

SPM was performed in the form of vertex-wise general linear models. The cortical bone property (Ct.Th, Ct.vBMD or EndoTb.vBMD) at each vertex location of the spatially normalized and smoothed surface-based maps was used as the dependent variable and group membership (control or femoral neck fracture, control or trochanteric fracture, femoral neck fracture or trochanteric fracture) as the independent variable. Age, height and weight were also included as covariates in the comparisons, and FDR correction was used to correct for multiple comparisons ($q=0.05$). The femoral head was excluded in these statistical tests due its thin cortical bone.

In both VBM and surface-based SPM, we allowed for shape in the comparisons to minimize systematic misregistration effects as previously shown by Gee and Treece(22). We allowed for 5 components (14), however, femoral size was not part of the first component since anisotropic scaling was used for the generation of the statistical shape model.

In light of a recent publication by Eklund et al. (23) addressing inflated false-positive rates in functional magnetic resonance imaging studies – based on SPM – we evaluated the specificity of VBM and surface-based SPM. For this purpose, the set of 50 controls was randomly partitioned 10 times into two sub-groups of 25 subjects each. Each time, vBMD, Ct.Th, Ct.vBMD and EndoTb.vBMD were compared between the two groups using VBM and surface-based SPM allowing for age, height, weight and shape (5 components); and using FDR to correct for multiple comparisons.

Results

Characteristics of the study participants are shown in Table 1. Significant differences in age were observed between controls and subjects with both types of fracture (femoral neck and trochanteric fracture); in height between subjects with femoral neck fracture and controls, and between subjects with femoral neck fracture and trochanteric fracture; and in weight between controls and subjects with trochanteric fracture.

For the TR cases, there were significant age and height differences between the analyzed sample and the whole sample ($p=0.048$ for age, $p=0.049$ for height), but weight and hip aBMD comparisons showed no significant differences. For the FN cases, there were no significant differences for age, height, weight and hip aBMD between the analyzed sample and the whole sample. And for the controls, there was only significant age difference between the two samples($p=0.033$).

Different proximal femoral views of the VBM Student's t-test statistical map – which we refer as T-Map – from the vBMD comparisons between controls and women with femoral neck fracture are shown in Figure 1A. Positive T-values indicate higher vBMD in controls than in fracture cases. In order to facilitate the 3D visualization in this figure, transparency was applied to each voxel according to its individual T-value. Non-significant voxels were rendered fully transparent, and voxels with maximum T-values were rendered fully opaque. Significant differences in vBMD between these groups were primarily observed in the superior and inferior aspects of the femoral neck, the inter-trochanteric region, and the calcar femorale. Differences were primarily seen in the trabecular compartment with involvement of the endosteal layer of the cortical bone.

Figure 1B shows the VBM T-Map from the vBMD comparisons between controls and women with trochanteric fracture. As in Figure 1A, positive T-values indicate higher vBMD in controls than in fracture cases, and transparency was also applied to each voxel according to its individual T-value. Significant vBMD differences between these groups were primarily observed in the inferior aspect of the femoral neck, the greater trochanter, the intertrochanteric region, and the calcar femorale. No significant differences were observed at the superior aspect of the femoral neck. As in the comparison between controls and women with femoral neck fracture, most of the significant vBMD differences were observed in the trabecular compartment and the endosteal layer of the cortical bone. The color-coding of Figures 1A and 1B was set to a standardized dynamic range of T-values based on the comparisons between controls and women with femoral neck fracture: 2.4 – 6.0 (controls vs. women with trochanteric fracture: 2.4 – 5.0).

The spatial vBMD comparisons of proximal femora between women with femoral neck fracture and women with trochanteric fracture yielded the VBM T-Map of Figure 1C. In the different views of this T-Map it is clear that women with femoral neck fracture demonstrated higher vBMD than women with trochanteric fracture (positive T-values) primarily in the greater trochanter.

Different femoral views of the SPM T-Map from the Ct.Th comparisons between controls and women with femoral neck fracture are shown in Figure 2A. In this figure, positive T-values indicate thicker cortices in controls than in fracture cases. Figure 2A shows global Ct.Th differences anteriorly, medially and around the femoral neck. Clear focal differences can be observed in the superior-anterior aspect of the femoral neck, the inferior aspect of the femoral neck, and the anterior aspect of the inter-trochanteric region. Non-significant vertices were rendered white in this figure.

Figure 2B shows similar proximal femoral views as in Figure 2A, but for the SPM T-map of the Ct.Th comparisons between controls and women with trochanteric fracture. As in Figure 2A, positive T-values indicate thicker cortices in controls than in fracture cases. Significant Ct.Th differences were mainly observed medially. Similar to Figure 2A, non-significant vertices were rendered white. The color-coding of Figures 2A and 2B was set to a standardized dynamic range of T-values from 3.0 to 7.2 (controls vs. women with femoral neck fracture: 2.4 – 7.2; controls vs. women with trochanteric fracture: 3.0 – 5.3).

The SPM T-Map of the comparisons of Ct.Th between women with femoral neck fracture and women with trochanteric fracture is shown in Figure 2C. This figure clearly shows thinner cortices (negative T-values) in women with femoral neck fracture than in women with trochanteric fracture in the superior aspect of the femoral neck. As in Figures 2A and 2B, non-significant vertices were rendered white in Figure 2C.

SPM comparisons of Ct.vBMD between controls and women with both types of fracture yielded very small regions where women with fracture had significantly lower Ct.vBMD than controls (positive T-values) as can be appreciated in the SPM T-Maps of Figures 3A and 3B. In these figures, the color-coding was set to a standardized dynamic range of T-values from 3.5 to 5.2 (controls vs. women with femoral neck fracture: 3.5 – 4.6; controls vs. women with trochanteric fracture: 3.4 – 5.2).

The SPM T-Map of the comparisons of Ct.vBMD between women with femoral neck fracture and women with trochanteric fracture is displayed in Figure 3C. In this figure, it is clear that women with femoral neck fracture had higher Ct.vBMD (positive T-values) than women with trochanteric fracture primarily in the greater trochanter. A very small patch of lower Ct.vBMD in women with femoral neck fracture (negative T-values) can also be appreciated in the superior-anterior aspect of the femoral neck.

Consistent with VBM, EndoTb.vBMD comparisons yielded significant differences between controls and both types of fracture. While these differences were more sparse between controls and women with femoral neck fracture, they were more global between controls and women with trochanteric fracture as can be observed in Figures 4A and 4B, respectively. In these figures, positive T-values indicate higher EndoTb.vBMD in controls than in fracture

cases. The color-coding in Figures 4A and 4B was set to a standardized dynamic range of T-values from 2.4 to 6.3 (controls vs. women with femoral neck fracture: 2.4 – 5.3; controls vs. women with trochanteric fracture: 2.1 – 6.3). Similar to all the SPM figures, non-significant vertices were rendered white.

In the last SPM comparison of this case-control study, EndoTb.vBMD was compared between the two fracture types indicating higher EndoTb.vBMD in women with femoral neck fracture than in women with trochanteric fracture mainly in three areas: 1) posterior region of the greater trochanter; 2) lateral region of the greater trochanter; and 3) lesser trochanter, as shown in the SPM T-Map in Figure 4C (positive T-values).

In the assessment of false-positives, the 40 comparisons (4 parameters × 10) between different sub-groups of 25 controls yielded non-significant voxels or vertices indicating robust specificity.

Discussion

In this study, we applied statistical multi-parametric mapping to investigate spatial differences in proximal femoral density and cortical bone properties between two major types of hip fracture – femoral neck and trochanteric fracture – and healthy controls. In contrast to previous studies(10, 14, 16, 24), we identified acute hip fracture related features with both VBM of vBMD and SPM of cortical bone properties, thus providing a more comprehensive QCT assessment of the proximal femur. Investigated features included vBMD, Ct.Th, Ct.vBMD and EndoTb.vBMD. Comparisons were performed between controls and both types of fracture, and between the two types of fracture. VBM results suggest that the spatial distribution of trabecular vBMD might play a significant role in both types of fracture; and SPM results suggest that focal areas of cortical bone thinning might be more relevant in femoral neck fractures, while focal areas of reduced cortical and endocortical vBMD might be more relevant in trochanteric fractures.

VBM results indicated that there are large proximal femoral regions with significant vBMD differences between controls and women with both types of hip fracture (Figures 1A–1B). Consistent with a previous study of incident hip fracture(10), VBM showed lower vBMD in fracture cases compared with controls in the inter-trochanteric region and at the inferomedial aspect of the trabecular compartment, which is a primary load-bearing region that is assumed to preserve bone mass in older subjects. In addition, in agreement with Li et al.(8) in a VBM study with similar characteristics as the presented here, VBM demonstrated that compared with the group of femoral neck fractures, the trochanteric fracture group had lower vBMD in the greater trochanter (Figure 1C). VBM also showed that the trochanteric fracture group did not have vBMD differences compared with controls in the superior aspect of the femoral neck (Figure 1B). It is also interesting to note that the areas of significant vBMD deficits in both fracture groups included regions that match well with the hip fracture sites that are associated with each fracture type. The different anatomical locations of vBMD deficits may help to explain the mechanisms in determining fracture type and might play a critical role in resistance to fractures with falls.

In terms of SPM of Ct.Th, compared to controls, groups of both types of fracture showed thinner cortices in regions in agreement with the type of fracture (Figures 2A–2B). Results were also consistent with those of Poole and colleagues(12), who also performed SPM of Ct.Th in a study of acute femoral neck and trochanteric fracture, and with those of Treece and colleagues in a study of incident hip fracture in men(14). In the three studies, subjects with femoral neck fracture showed a focal patch of cortical bone thinning with respect to controls in the superior-anterior aspect of the femoral neck. When Ct.Th was compared between the two types of fracture, results were remarkable (Figure 2C). Women with femoral neck fracture clearly showed a significant focal patch of thinner cortical bone than women with trochanteric fracture in the superior-anterior aspect of the femoral neck. Women with femoral neck fracture also showed a very small significant focal patch of thicker cortical bone than women with trochanteric fracture at the base of the lateral aspect of the greater trochanter. Consistent with the VBM T-Maps, SPM of Ct.vBMD (mean vBMD along the streamlines used to compute Ct.Th) comparisons yielded very small regions with significant differences between healthy controls and women with both types of fracture (Figures 3A and 3B). In this particular study, VBM and SPM of Ct.vBMD suggest that areas of the deep layer of cortical bone might be more relevant in hip fracture than areas of the superficial layer. Nevertheless, in agreement with VBM, SPM comparisons of Ct.vBMD between the two types of fracture showed that women with trochanteric fracture had significantly lower Ct.vBMD in the greater trochanter (Figure 3C). Also consistent with VBM, EndoTb.vBMD comparisons yielded significant differences between controls and both types of fracture (Figures 4A–4B), and between the two types of fracture (Figure 4C). An interesting outcome was that women with femoral neck fracture showed significantly higher EndoTb.vBMD in the posterior aspect of the proximal femur and in the lateral aspect of the greater trochanter compared with women with trochanteric fractures. These regions are critical for the external forces applied to the proximal femur on a posterolateral fall. Furthermore, the SPM endocortical density results of Poole et al. from a recent acute hip fracture study involving UK and Czech subjects, are actually quite in agreement with those presented here for Chinese women. In that study, the authors confirmed that focal osteoporosis was specific to fracture type by using SPM of cortical and endocortical density parameters associated with targeted biopsies for micro CT measures(16). Unfortunately, the femoral head was not included in our surface-based SPM analyses, thus limiting our visual comparisons to the rest of the proximal femur.

Consistent with results of Poole et al., our study shows that lower endosteal bone in sites where fractures are thought to initiate (Fig. 1). In a hip fracture testing in vitro, by using a high speed camera, Helgason et al. showed a superior femoral neck fracture first seen at time=6.99 ms, then followed by anterior neck crack(25). This Fall simulation experiment probing fracture in a sideways fall scenario, not like load being generally increased monotonically until fracture occurs in many studies. In another study simulating sideways falls, de Bakker et al. showed a crack initiate in the superior or anterior femoral neck although most of the proximal femur T-scores derived from DXA could not be diagnosed for osteoporosis(26). Further, Nawathe et al.(27) biomechanically tested 12 cadaver proximal femurs to directly measure strength for a sideways fall and also performed finite element analysis to estimate the initial structural failure sites, and found that just a tiny proportion of

the bone tissue is associated with failure. The results were consistent with our observation, femoral neck fracture is highly focal and disadvantageously concentrated in sites that are going to be subjected to high forces during falls. In order to highlight the contribution of these image analysis techniques towards our understanding of femoral fracture, Figure 5 summarizes the femoral neck fracture results with respect to controls. In this figure, there are four important aspects to be noted: 1) differences in the spatial distribution of bone, 2) the compartmental analyses, 3) the multi-parametric assessments, and 4) the statistical robustness. Although conventional approaches based on statistical analyses of predefined regions of interest provide relevant fracture information, assessments as those on Figure 5 are only possible with Computational Anatomy approaches such as VBM and surface-based SPM. Although inflated false-positive rates have recently been noted in neuroimaging studies(23) using SPM, high specificity has been observed in this and other musculoskeletal studies using VBM and surface-based SPM(28).

In this case-control study, by using statistical multi-parametric mapping we explored spatial differences in the distribution of bone between femoral neck and trochanteric fractures. Our results and results of Poole et al. both suggest focal osteoporosis should be highly valued in clinical practice of osteoporosis, because hip fractures were not uniform with the diagnosis of osteoporosis and the focal defects in bone might get across this problem. What's more, identifying focal defects might help implement appropriate pharmacological or lifestyle interventions in clinical practice.

This study has three major limitations. The first limitation is the lack of a baseline QCT scan previous to the occurrences of the femoral neck and trochanteric fractures. The second major limitation of this study is that neither the FN cases nor the TR cases were age-matched to controls. The age-related variations might reduce the impact of the findings, however, we accounted for variations in age in all VBM and SPM comparisons to minimize age effects. Third, all women were Chinese limiting the interpretation of the results to other ethnicities since there have been studies showing structural differences of the proximal femur between Asian and other ethnicities (29–31). It would be useful to repeat these analyses in non-Chinese populations, since there are particular characteristics of Chinese women with hip fracture that may influence the pathophysiology of their bone loss. However, it is becoming vitally important to understand and intervene to prevent the rapid rise in hip fractures in China, specifically in urbanizing regions. This study also has two main strengths. The first strength of this study is that in addition to VBM which incorporates both trabecular and cortical bone for spatial assessments of vBMD, we applied surface-based SPM for the spatial assessments of cortical bone properties only. Assessing both trabecular and cortical bone properties is essential as the two types of bone differ in their fracture related changes(32). To date, the respective contributions of trabecular and cortical bone to hip fracture risk are not completely understood(33). However, most of the fractures occur at cortical sites and 70% of age-related appendicular bone loss is cortical(34). The second strength of this study is that women who fractured were scanned within 48 hours of the fracture minimizing bone structural changes and lean and adipose tissue variations due to the fracture.

In conclusion, using statistical multi-parametric mapping we explored the differences in proximal femoral density distribution and cortical bone properties between femoral neck and trochanteric fractures in Chinese women. VBM results suggest that the spatial distribution of trabecular vBMD might play a significant role in hip fracture, while SPM results suggest that focal cortical bone thinning might be more relevant in femoral neck fractures, and areas of reduced cortical and endocortical vBMD in trochanteric fractures.

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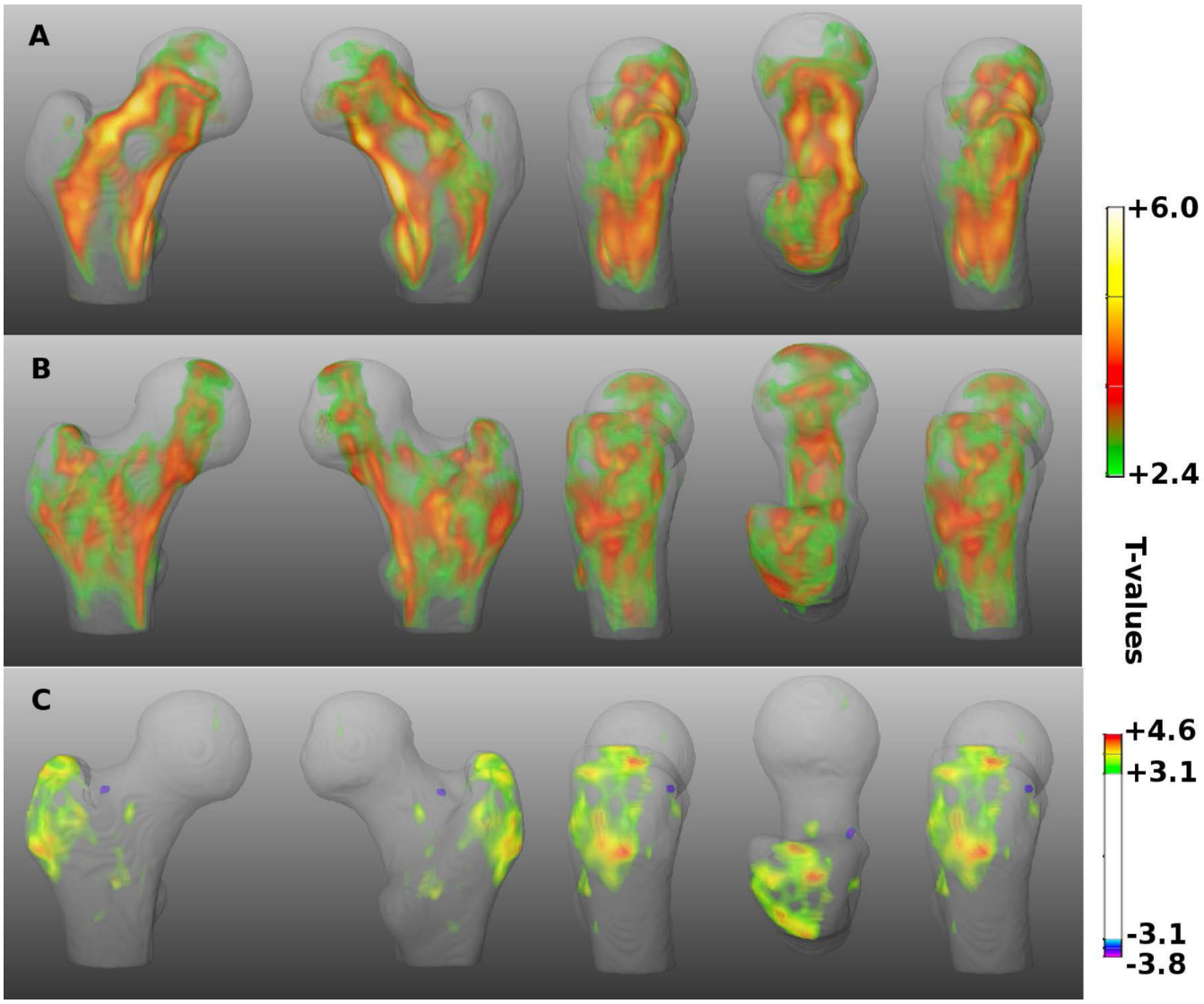

Figure 1.

Different proximal femoral views of VBM T-Maps from vBMD comparisons between: A) controls and women with femoral neck fracture; B) controls and women with trochanteric fracture; and C) women with neck fracture and women with trochanteric fracture.

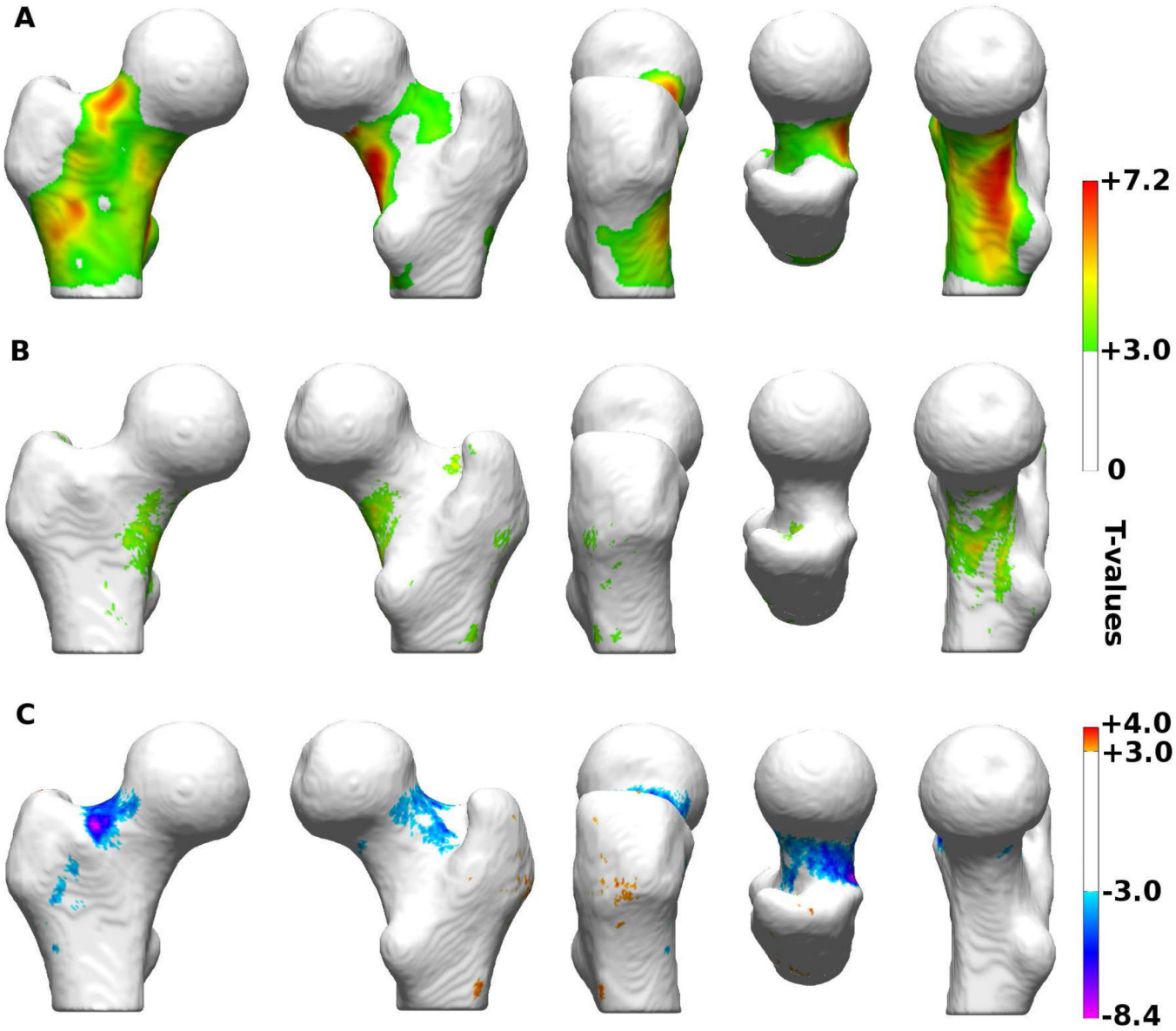

Figure 2.

Different proximal femoral views of SPM T-Maps from Ct.Th comparisons between: A) controls and women with femoral neck fracture; B) controls and women with trochanteric fracture; and C) women with neck fracture and women with trochanteric fracture.

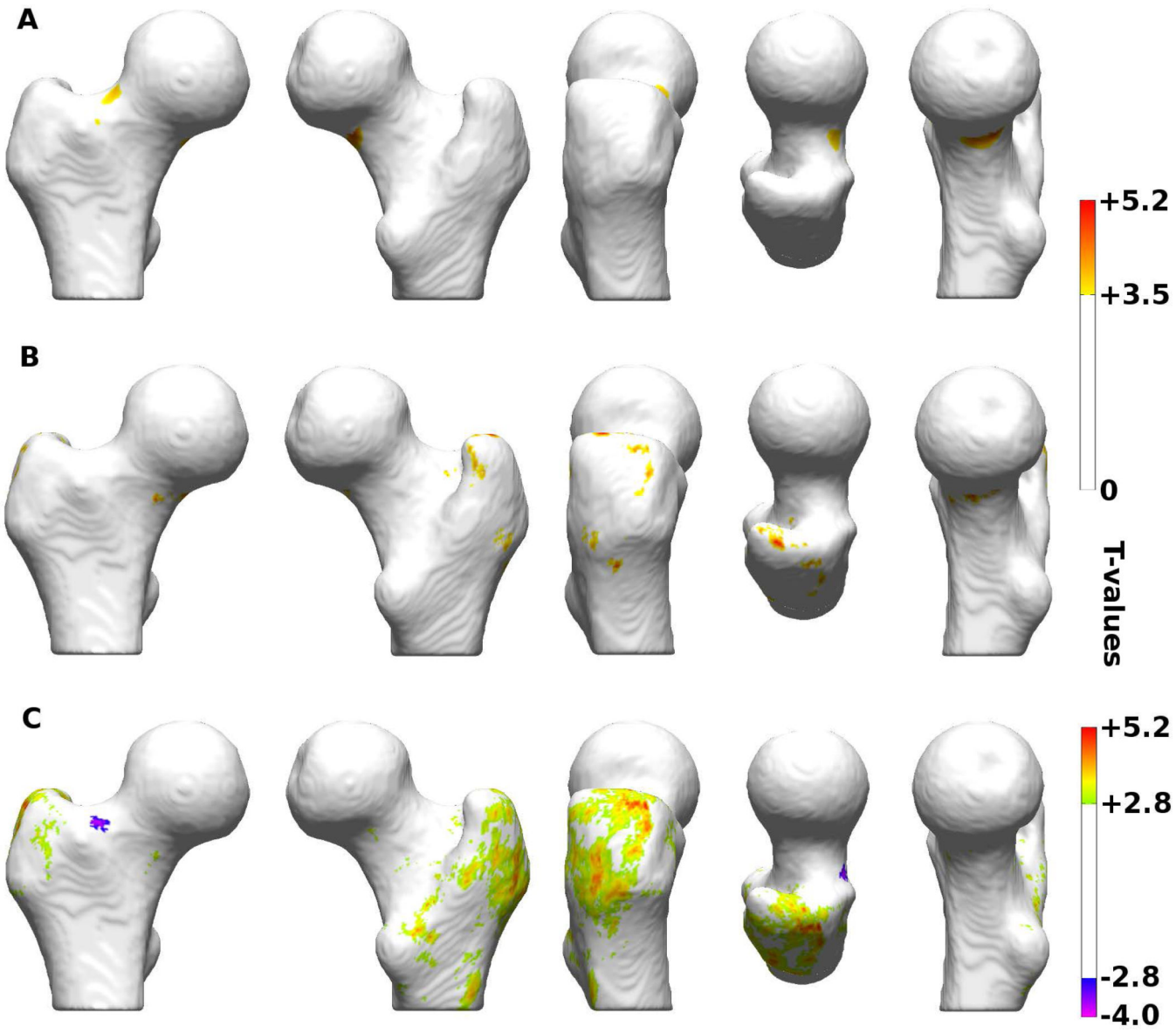

Figure 3.

Different proximal femoral views of SPM T-Maps from Ct.vBMD comparisons between: A) controls and women with trochanteric fracture; B) controls and women with trochanteric fracture; and C) women with neck fracture and women with trochanteric fracture.

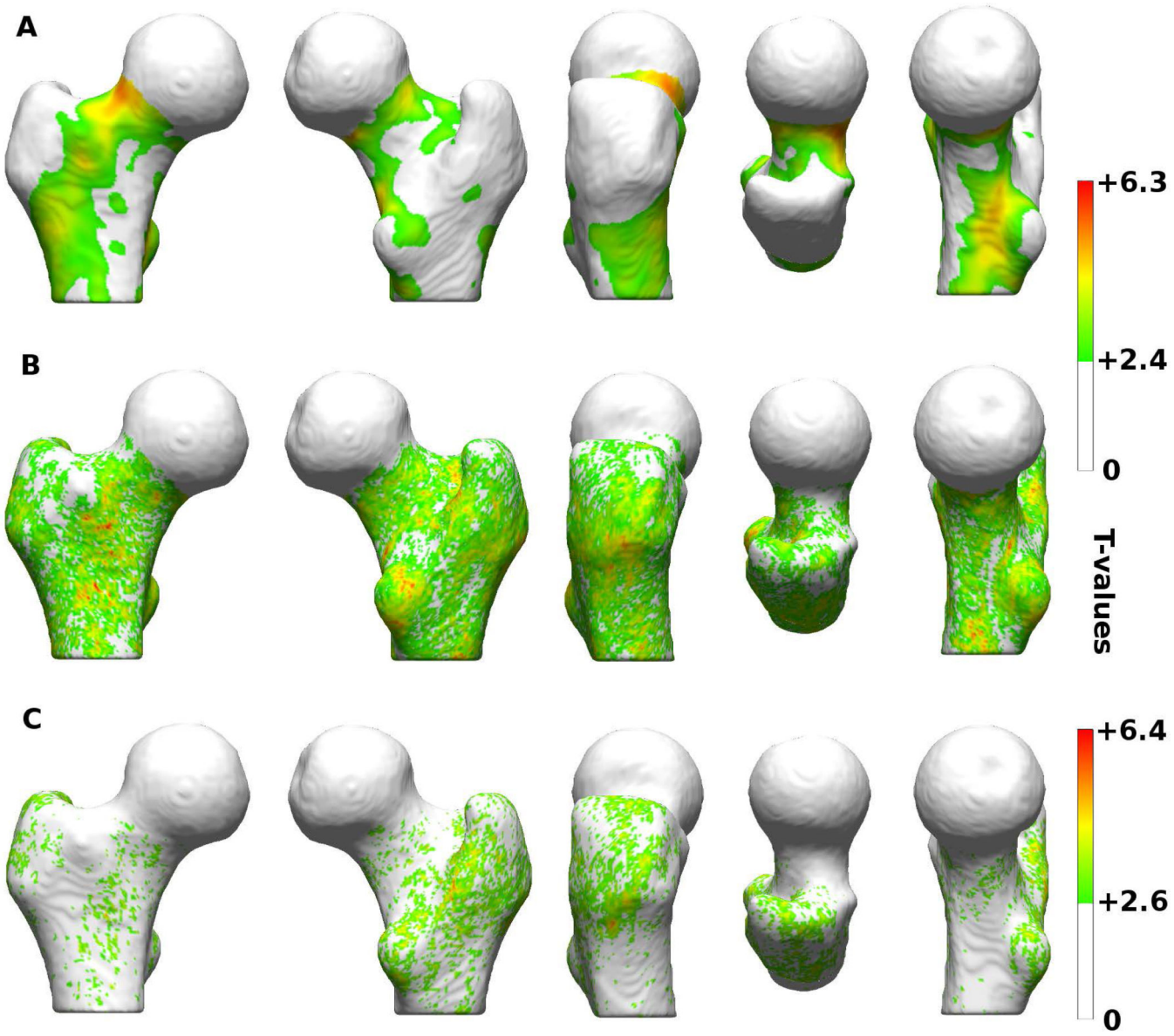

Figure 4.

Different proximal femoral views of SPM T-Maps from EndoTb.vBMD comparisons between: A) controls and women with femoral neck fracture; B) controls and women with trochanteric fracture; and C) women with neck fracture and women with trochanteric fracture.

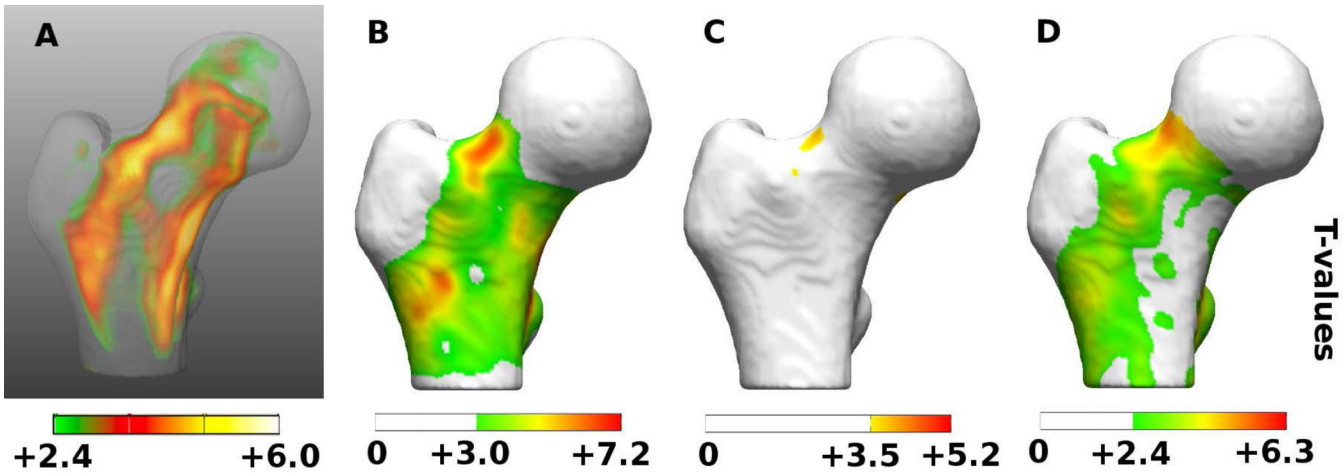

Figure 5.

Comparisons of the femoral neck fracture results with respect to controls from different aspects: A) VBM T-Maps from vBMD comparisons; B) SPM T-Maps from Ct.Th comparisons; C) SPM T-Maps from Ct.vBMD comparisons; D) SPM T-Maps from EndoTb.vBMD comparisons.

Table 1

Characteristics of the study participants – Mean±SD

Group	Age (years)	Height (cm)	Weight (Kg)
Controls (n=50)	63.7±7.0	156.8±6.0 †	63.4±9.1
Femoral neck fracture (n=72)	70.6±12.7 *	160.4±5.3	61±13.0
Trochanteric fracture (n=21)	75.6±9.3 *	154.7±3.6 †	55±12.8 *

* Significantly different than controls: p<0.016

† Significantly different than femoral neck fracture: p<0.016