

# Implications of local osteoporosis on the efficacy of anti-resorptive drug treatment: a 3-year follow-up finite element study in risedronate-treated women

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## Abstract

**Summary** The existence of local osteoporosis necessitates patient-specific analysis. Lower and higher ranges of local buckling ratio were found at femoral necks for adequate and inadequate drug response groups, respectively (grouped based on fracture loads). Management of hip fracture risk should be targeted at local geometric abnormalities causing instability.

**Introduction** Hip fracture amongst the elderly is a growing concern especially with improvements in living standards and increasing lifespan. Approximately half of the total hip fractures result from those without osteoporosis. This escalates the need to observe local osteoporosis. By observing the local buckling ratio (BR) in the femoral neck in ten risedronate-treated subjects over 3 years, we discovered that subjects with improved fracture loads, as predicted by finite element (FE) analysis, were associated with lower local BR and vice versa.

**Methods** The 3D models of the left proximal femurs were generated, and local BR values at 30° intervals were obtained from femoral neck slices by measuring the respective mean cortical thickness and mean outer radius. Following geometric analysis, structural strength was examined with FE analysis where critical fracture loads ( $F_{cr}$ ) were acquired from sideways fall load simulations.

**Results** We classified subjects in three groups according to the change in  $F_{cr}$ : adequate (+20 %), inadequate (−22 %) and indefinite (−2 %) drug response groups. A common striking

feature was that lower and higher ranges of local BR values (baseline year) were found for adequate (min=2.14, max=8.04) and inadequate (min=1.72, max=11.38) drug response groups, respectively.

**Conclusions** Subjects in the inadequate drug response group exhibited high local BR at the supero-anterior and supero-posterior regions. These high local BR values coincided with FE-predicted critical strain regions, whereas subjects from the adequate drug response group showed significantly reduced strain regions. The superiority of coupling geometry (BR) with structure ( $F_{cr}$ ) over bone mineral density measurements alone by monitoring local osteoporosis has been illustrated.

**Keywords** Bone mineral density · Bone strength · Buckling ratio · Finite element analysis · Osteoporosis · Prediction of hip fracture

## Introduction

Hip fracture often results in injury and loss in mobility in the elderly and is a growing concern especially with increasing life expectancy and heavy socio-economic costs [1–3]. The incidence of hip fractures increases exponentially with age [4] and has a higher probability of occurring in the elderly diagnosed with osteoporosis by bone mineral density (BMD) from dual X-ray absorptiometry (DXA) [5]. Osteoporosis is a skeletal disease characterized by low bone mass and micro-architectural deterioration of the bone, consequently leading to macroscopic decline in bone strength [6]. Although hip fracture risk can be reduced with the aid of drugs, treated patients still face considerable risk as most people who sustain hip fracture do not have osteoporosis [7]. Attention needs to be given to the local distribution of bone mass which gives rise to the problem of local osteoporosis, making each patient unique in terms of rate and site of bone mass

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deterioration [8]. This necessitates a study of the local distribution of bone mass which contributes to the geometry and consequently the bone strength.

The diagnosis of osteoporosis is expressed as the number of standard deviations below the average BMD of young adult men and women and is associated with a T-score less than or equal to  $-2.5$ , according to the World Health Organization. Although BMD can only predict fractures with a detection rate of 30–50 % [9], the ease of acquirement from DXA renders it favourable in clinical diagnosis [10]. Amongst patients who were diagnosed osteoporotic by BMD, 48 % of the Epidemiology of Osteoporosis study [11] experienced hip fractures. In the Study of Osteoporotic Fractures, 46 % experienced hip fractures [12]. This indicates that BMD is only capable of partially predicting hip fracture risk.

While the inability of BMD to predict fractures accurately is acknowledged, the current treatment available to prevent hip fractures is via drugs that affect bone metabolism. These drugs have been shown to reduce hip fracture risk in patients with low BMD, but not in patients without proven low BMD and/or prior fractures [13–15]. In a study assessing the effect of risedronate, hip fracture risk decreased by 30 % in patients older than 70 years and by 40 % in osteoporotic patients [16]. This proves that categorization with the use of BMD is still valuable clinically but raises the question of why more than half the group of patients had not benefited from drug treatment. This can be attributed to the fact that most people with fractures do not have osteoporosis nor do people diagnosed with osteoporosis incur fractures [17]. Thus, we hypothesize that due to the pathogenic existence of local osteoporosis, an individual faces a higher risk of femoral neck fracture.

Since there is a need for a holistic analysis to identify the prediction of hip fractures more accurately in osteoporotic patients and to incorporate it into current clinical screening protocols [9], bone geometry and structural strength together with BMD changes can be analyzed for better characterization of bone properties. Accompanied with normal aging, the proximal femur undergoes remodelling as compensation for declining mass so that its bending strength is maintained [18]. However, this redistribution to preserve bone strength reaches a threshold where excessive cortical thinning ultimately initiates. These local changes can be captured with a geometrical parameter termed as buckling ratio (BR), which is the ratio of the mean outer radius to the mean cortical thickness, quantifies the distribution of bone tissue and is reflective of cortical instability [19, 20].

Currently, it is not possible to obtain structural strength of the bone non-invasively [21]. Thus, finite element (FE) analysis seems to provide a better alternative to obtain information on bone morphology and mechanical properties in vivo [22, 23]. Predicted fracture loads from FE analysis explains at least 20% more of the variance in strength of the

proximal femur than BMD [24] and can be used directly to predict hip fracture risk just like how BMD is used [25]. Such an analysis of the proximal femur generated from CT scans has been studied as a tool to assess bone strength since it is inherently dependent upon both the density and geometric parameters [25, 26].

While BMD may be sufficient as an indicator of osteoporosis in the elderly, it is certainly not adequate to monitor the progression of this skeletal disease since BMD characterizes the general distribution of bone mass and excludes the underlying information on the local bone mass distribution. Thus, an increase in BMD due to drug treatment does not necessarily translate into improved geometry or structure. Therefore, we observed the localized bone mass distribution in the femoral necks of ten risedronate-treated subjects over 3 years. The question that this study aims to answer is to what extent risedronate drug treatment effectively reduces hip fracture risk. This is the first study of its kind to complement local buckling ratio obtained from radiological scans with FE-predicted fracture load to observe the condition of local osteoporosis. We hypothesize that due to the existence of local osteoporosis, effectiveness of risedronate treatment could be compromised in alleviating the condition of bone mass deterioration.

## Materials and methods

This study used data from quantitative computed tomography (QCT) scans obtained from the year 2008 to 2010 of females who are 50 years of age or older. QCT scans were generated using a GE Medical Systems Scanner (General Electric, Milwaukee, WI, USA) with settings as follows: 120 kVp, 219 mAs, contiguous, 2.5-mm-thick slices, 0.703-mm pixels,  $512 \times 512$  matrix and standard reconstruction. The femoral neck BMD values were first obtained from QCT scans and were categorized into three main groups (osteopenic, osteoporotic and normal) in accordance to respective T-scores. We have used femoral neck BMD for this study as we are focusing on buckling at the femoral neck region. Following the extraction of BMD, geometric and structural analysis was performed for 3 years (2008–2010) for each subject. In this preliminary study, ten subjects, who had been administered the same dosage of risedronate regularly over 3 years, were analyzed.

### Geometric analysis

The QCT scans were imported into the commercial software, Mimics (Materialise, Harislee, Belgium). After the generation of 3D model of the left proximal femur, cutting planes were positioned at the base of the femoral head and neck–trochanter junction of the femoral neck as in Fig. 1.

Following which, re-slicing, perpendicular to the plane of the femoral neck, was performed. Profile rays were drawn at 30° intervals, measured from the centroid of the femoral neck slice, totalling up to 12 rays as illustrated in Fig. 1. From each profile ray, cortical thickness was approximated to be twice the measured value of the distance from the peak Hounsfield unit (HU) value to half the peak value [27]. Radius was then taken as the distance between the centroid and the trough Hounsfield unit value. Instead of obtaining an average BR by averaging all the profile ray values, we analyzed 12 BR values individually for each patient for each year to evaluate the local BR changes. A BR value was calculated for each profile ray (at 30° intervals) by the following formula:

$$BR_{\theta} = \frac{R_{\theta}}{CT_{\theta}},$$

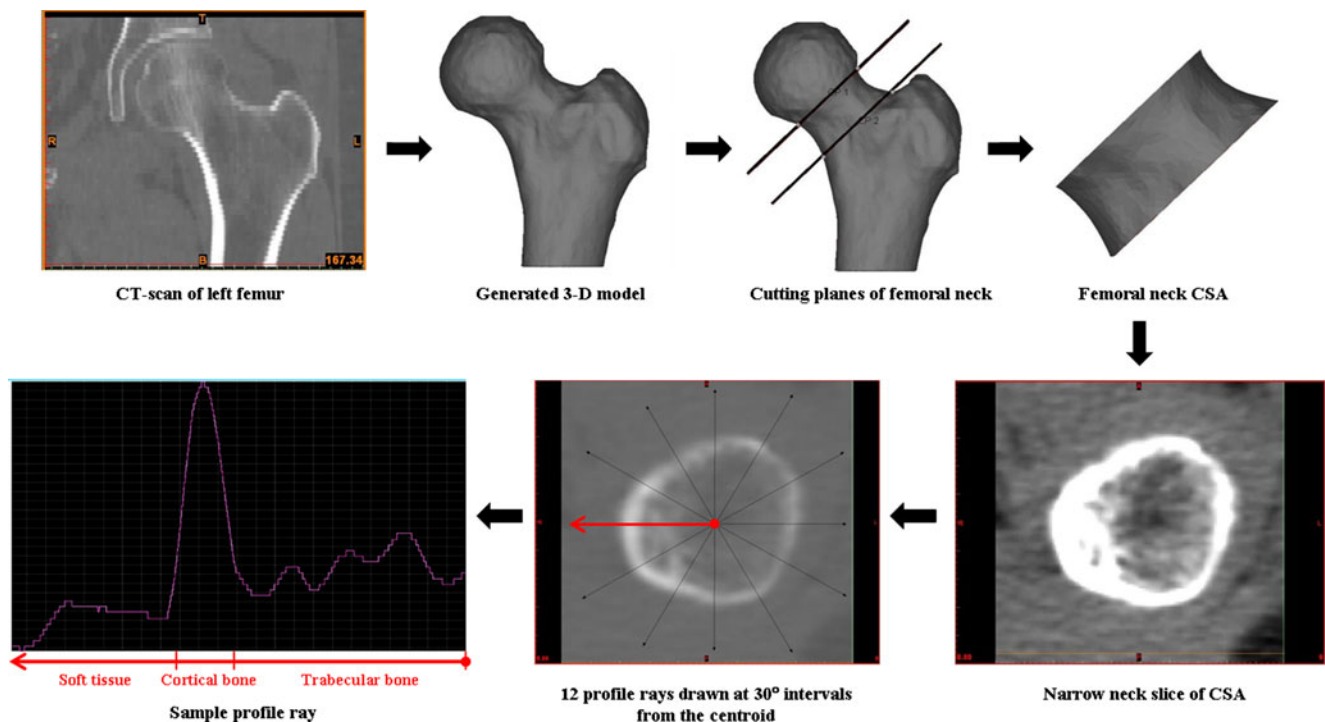
where  $\theta$  is the angle of profile ray.

### Structural analysis

A 3D model using heterogeneous, linear isotropic mechanical properties was generated for each femur. The FE models consisted of an average of 50,000 nodes and 15,000 elements. The elastic modulus and strength of each element

were computed as follows. Two discrete sets of material properties were assigned using two averaged cortical and trabecular HU values. The apparent density ( $\rho_{app}$ ) was computed by reported correlation as follows:  $\rho_{app}=0.001$  HU [28]. The ash density ( $\rho_{ash}$ ) for each CT scan pixel was then derived from the  $\rho_{app}$  ( $\rho_{ash}=\rho_{app}\times 0.6$ ) [29]. An average elastic modulus ( $E$ ) and material strength ( $S$ ) were defined for each material based on its mean  $\rho_{ash}$  using correlations, as described previously [30, 31]:  $E=10,500 \rho_{ash}^{2.29}$ ,  $S=137 \rho_{ash}^{1.88}$  for  $\rho_{ash}<0.317$  g/cm<sup>3</sup> and  $S=114 \rho_{ash}^{1.72}$  for  $\rho_{ash}>0.317$  g/cm<sup>3</sup>. Material yield and ultimate failure were assumed to coincide, and a non-linear isotropic post-yield material behaviour was adopted [25, 32]. A constant Poisson's ratio of 0.3 was assumed.

FE analysis was performed using ABAQUS version 6.12 (Hibbitt, Karlsson and Sorensen, Inc., Pawtucket, RI, USA). A specific sideways fall load configuration was tested at 10° to the horizontal in the frontal plane (Fig. 2). Although, this fall configuration is less probable to occur physiologically [33], for the purpose of comparative analysis, a simplified fall configuration was assumed. Boundary conditions were applied to mimic the mechanical testing performed by Keyak et al. in 2001. The mechanical testing was modelled by applying displacements incrementally to nodes on the femoral head over an approximate 3-cm-diameter region [25].



**Fig. 1** Flow chart of geometric analysis. After acquisition of CT scans of the left femur, a 3D model was generated. Cutting planes were positioned at the base of the femoral head and neck–trochanter junction of the femoral neck. Mid-neck slice of the femoral neck was chosen, and

12 profile rays were drawn at 30° intervals from the centroid. A typical profile ray is shown, where the initial region from the centroid is the trabecular bone, and the region involving the peak represents the cortical bone and soft tissue thereafter

The distal end of the femur was fully constrained, and the greater trochanter region in contact with the ground during fall configuration was constrained in the direction of the applied load. This constrained distal end condition assumes that the inertial effects of the lower extremity are dominant at the point of impact. The elements loaded on the femoral head were identified and assigned an elastic modulus of 20 GPa and a yield strength of 200 MPa to prevent element distortion [25].

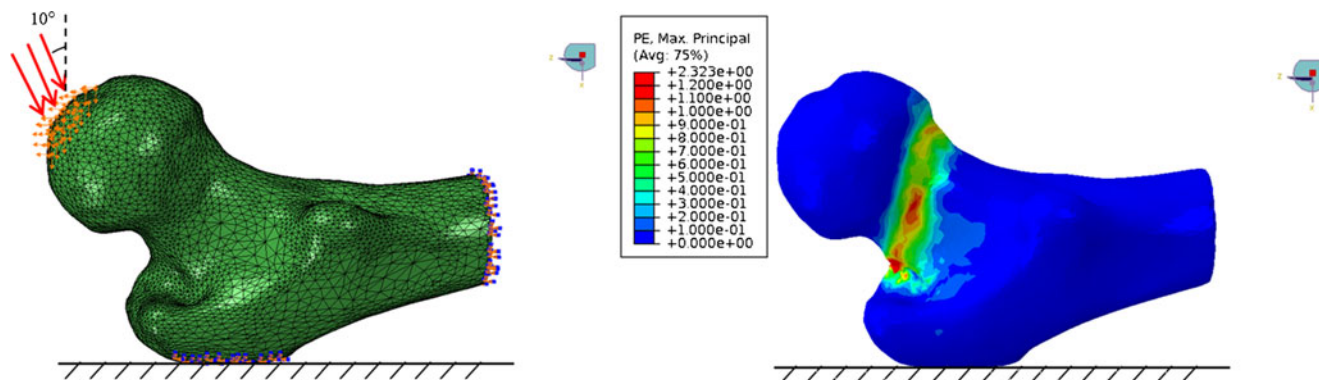
The reaction force at each node was obtained at each displacement increment, and subsequently, the reaction forces were summed to obtain the total reaction force at each displacement increment. The critical fracture load ( $F_{cr}$ ) was obtained from the summed force–displacement curve as the peak total reaction force achieved over the displacement increments. Furthermore, stiffness was also calculated as the maximum slope of the curve and was determined by dividing the total reaction force with the first displacement increment [25].

## Results

Subjects were grouped according to an increase in  $F_{cr}$ , decrease in  $F_{cr}$  or negligible change in  $F_{cr}$ . Since these subjects were treated with risedronate, assuming they were compliant with therapy and that anti-resorptive drug treatment directly influences structural properties of bone, we termed these groups as adequate ( $n=4$ ), inadequate ( $n=3$ ) and indefinite ( $n=3$ ) drug response groups, respectively. These classifying terms were used in reference to the responses of the individual subjects to their drug treatments. As such, the average changes from baseline (2008) to final (2010) year in subperiosteal diameter ( $D_{sp}$ ), endocortical diameter ( $D_{ec}$ ), cortical thickness (CT), overall BR, femoral neck (FN) BMD and  $F_{cr}$  were tabulated (Table 1). It can be noted that CT showed the most drastic change compared to the other geometrical parameters. Significant cortical thickening of

the bone (14.5 %), attributed to a decrease in mean endocortical diameter (−1.3 %) as well as an increase in periosteal diameter (+3 %) (Table 1), accompanied a 19.5 % increase in  $F_{cr}$  in the adequate drug response group. Similarly, an 8.7 % of cortical thinning, attributed to a small increase in the mean endocortical diameter (+0.3 %) and a small increase in mean periosteal diameter (+0.7 %), resulted in a 22 % decline in  $F_{cr}$  in the inadequate drug response group.

A closer look at two subjects, each from the adequate and inadequate groups, with similar age (73 and 75 years) and BMI (26.1 and 26.0), respectively, shed light on the effect of local osteoporosis on the geometry and structure of the bone. With reference to Fig. 3, which illustrates the angles corresponding to its respective regions, the geometric and structural changes were observed. Figure 4 shows the CT scans, digitized annular representations (radar plots) and FE images of the smallest cross section of femoral necks of both subjects. For subject 1 from the adequate drug response group, BR decreased by 5 %, which is mainly attributed to a periosteal apposition of 8 % with a small decline (−1 %) in the inner diameter. With a slight decline in FN BMD of 2 %, the  $F_{cr}$  increased by 23 %, suggesting an improvement in the structural strength of bone despite a small reduction in bone mass. In contrast, the BR of subject 5 from the inadequate drug response group declined by 12 %, and the  $F_{cr}$  declined by 22 % with little change in her FN BMD. Despite the decline in overall BR, the structural strength of the bone unexpectedly degraded. A look at the local BR values showed that at the supero-anterior region (30°), local BR increased from 6.80 to 10.07 from baseline to final year which is an increase by 48 % (Fig. 4). Similarly, subject 6 and subject 7 from the inadequate drug response group exhibited a significant increase in local BR by 50 and 67 % at the supero-posterior region (150°), respectively. The changes in local BR values were also consistent with changes in critical strains found in common fracture-prone regions in the femurs. Due to local buckling, critical strain



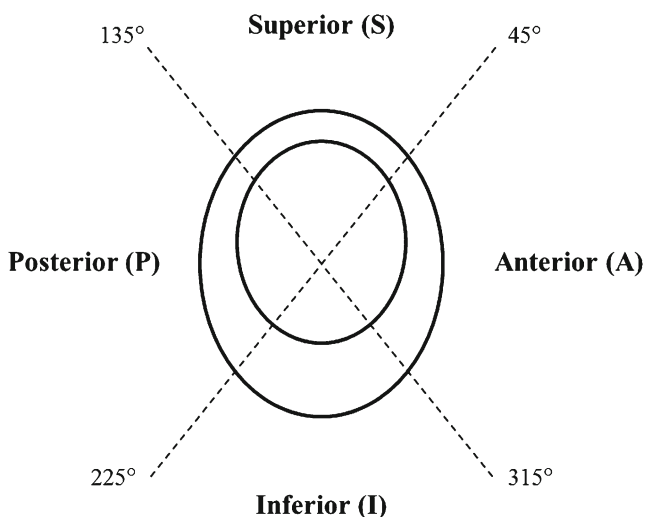
**Fig. 2** A typical FE model of the proximal femur with boundary conditions with arrows indicating load applied at 10° to vertical axis (*left*) and post-FE analysis (*right*)

**Table 1** Mean geometrical properties, femoral neck BMD and critical fracture load ( $F_{cr}$ ) of subjects ( $n=10$ ) classified according to increase (adequate drug response), decrease (inadequate drug response) or negligible change (indefinite drug response) in  $F_{cr}$

	Adequate ( $\uparrow F_{cr}$ ) (%)	Inadequate ( $\downarrow F_{cr}$ ) (%)	Indefinite ( $\approx F_{cr}$ ) (%)
Subperiosteal diameter ( $D_{sp}$ )	+3	+0.7	-8
Endocortical diameter ( $D_{ec}$ )	-1.3	+0.3	+1
Cortical thickness (CT)	+14.5	-8.7	-1
Overall buckling ratio (BR)	-3	-3.7	+2.7
Femoral neck BMD	-2	-4	-2.7
Critical fracture load ( $F_{cr}$ )	+19.5	-22	-2

regions had become more severe from baseline year to the final year although subject 5 had been under drug response. This region of buckling coincided with thin regions observed in the supero-anterior region in the radar plot (Fig. 4). On the other hand, structural strength of subject 1 had improved, and this is denoted by the disappearance of critical strain region at the supero-anterior region. This is again further substantiated by a general increase in cortical thickness in that region.

Since average changes in overall geometrical parameters ( $D_{sp}$ ,  $D_{ec}$  and BR) were small, the local changes in geometry were required to get a clearer perspective of the response of the bone to drug treatment. Plots of local BR versus angle showed that lower and higher ranges of local BR values (final year, 2010) were found for adequate (min=2.14, max=8.04) and inadequate (min=1.72, max=11.38) drug response groups, respectively (Fig. 5). All six plots exhibited two distinct peaks at the supero-anterior ( $30^\circ$ ) and supero-posterior ( $150^\circ$ – $180^\circ$ ) regions. Adjusting the local BR values



**Fig. 3** Illustration of angles corresponding to respective superior (S), anterior (A), inferior (I) or posterior (P) region

with age and/or BMI did not result in significant differences to the observations. The observations for each group were as follows:

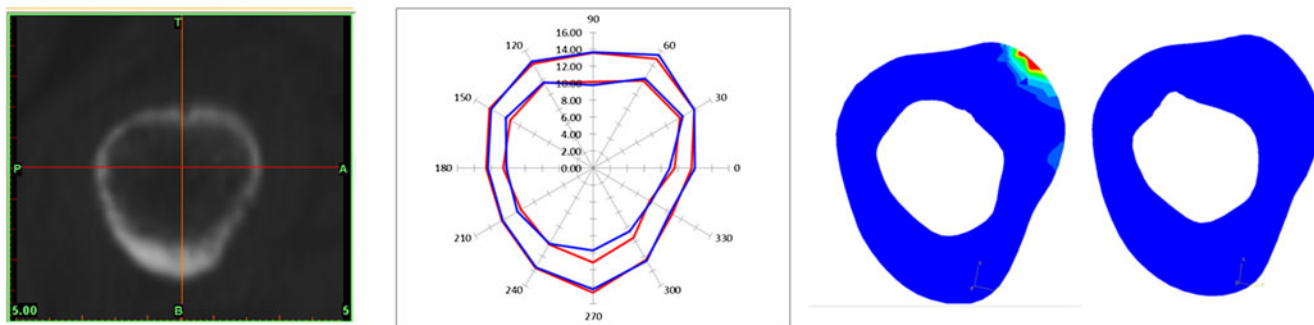
1. *Adequate drug response group.* The local BR values remained well below the critical BR value of 10, and the standard deviation of the local BR values at the supero-posterior peak reduced significantly in the final year as compared to the baseline year (Fig. 5).
2. *Inadequate drug response group.* It exhibited higher local BR values tending towards the critical BR value of 10, especially at the two peaks aforementioned, with its means reaching local BR values of 8.33 and 8.05, respectively (Fig. 5). Compared to baseline year, we can observe a shift in peak from  $180^\circ$ – $210^\circ$  to  $150^\circ$ – $180^\circ$  in the final year. Despite the reduction in standard deviation of local BR values at  $210^\circ$ , the acutely high local BR region at  $210^\circ$  (max=13.49, min=2.19 in baseline year) with a mean of 7.84 transformed into a more widespread region from  $150^\circ$  to  $210^\circ$  (max=9.45, min=4.96 in the final year) with a mean of 7.20. In addition, the mean of the local BR value at the supero-anterior region increased from 6.95 to 8.33, tending towards instability.
3. *Indefinite drug response group.* The peak at the supero-anterior region reduced from a mean local BR value from 9.86 to 8.95, while the remaining local BR values remain relatively low with the peak at the supero-posterior region being relatively less distinct than the other two groups (Fig. 5).

## Discussion

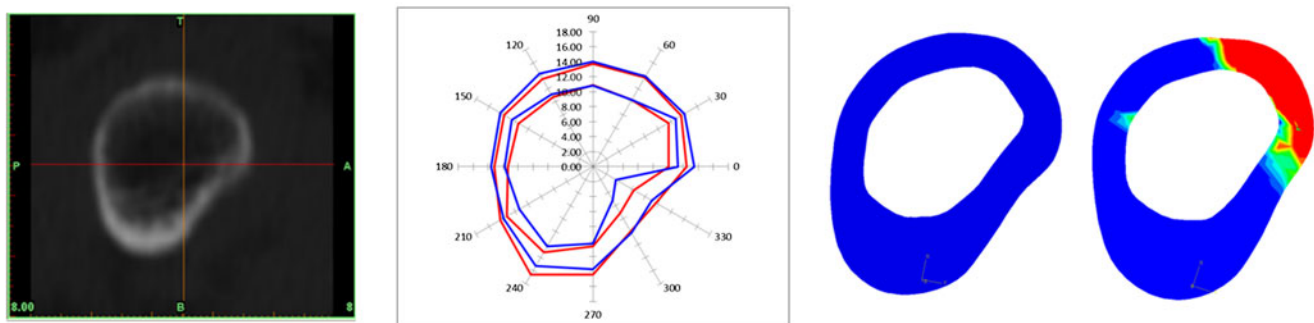
In this study, we observed the localized bone mass distribution in the femoral necks of ten subjects diagnosed with osteopenia or osteoporosis by DXA-obtained BMD. Geometry with the use of BR and structural strength with the use of numerically obtained  $F_{cr}$  were analyzed since the use of BMD alone is not sufficient to predict hip fracture risk. In light of this current limitation, we explored the existence of local osteoporosis which produced differentiated effects within a femoral neck cross section. We believe that these localized reactions to drug treatment ultimately affect the efficacy of drug treatment and consequently influence the geometry and structural strength.

The presence of local osteoporosis raises an uncertainty on how the effects of aging and osteoporosis respond to the effects of anti-resorptive drug treatment. The effect of aging has been known to influence cortical thickness and geometry where subperiosteal diameter increases to counteract cortical bone loss to maintain bending strength [18, 34]. However, excessive bone loss results in cortical thinning and increases the risk of local buckling. Thus, the effect of osteoporosis

**Subject #1 (Adequate Drug Response)**



**Subject #5 (Inadequate Drug Response)**



CT scan (baseline year, 2008)      Mid-neck (baseline year, 2008)      FE mid-neck (baseline year, 2008)      FE mid-neck (final year, 2010)  
 Mid-neck (final year, 2010)

**Fig. 4** CT scans, radar plots and FE cross sections of mid-necks of two subjects. Critical strain region has disappeared from baseline to final year for subject 1, while the opposite occurs for subject 5. A decrease in

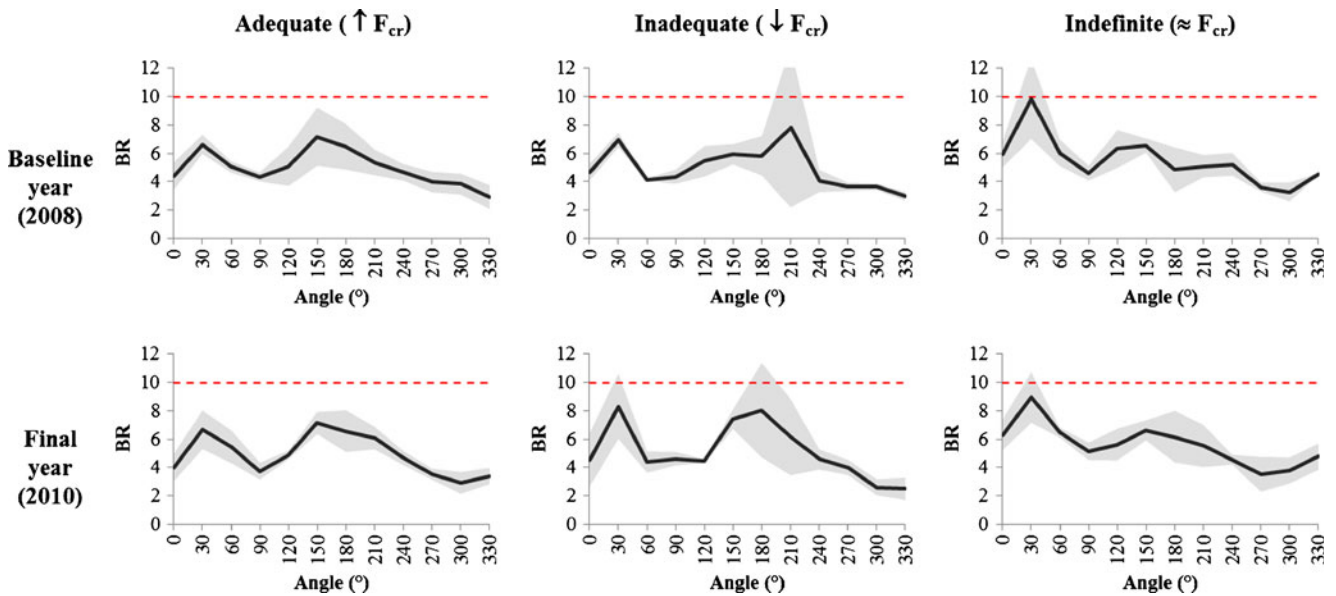
cortical thickness and a consequent increase (48 %) in local buckling ratio at the supero-anterior region (30°) for subject 5 was accurately predicted by FE analysis

affects the bending resistance and the stability of the bone [35]. Anti-resorptive drug treatment opposes the effect of osteoporosis by reducing bone resorption and bone turnover. With regard to periosteal apposition, it is not yet clear as to whether bisphosphonates play a role and if apposition on the periosteal surface is modelling or remodelling driven [36]. A positive effect of risedronate is reflected in the adequate drug response group with a reduction in resorption and a possible modelling-driven apposition. The increased rate of periosteal apposition could have been transient and occurred early during treatment [36] since anti-resorptive drugs induce a faster decrease of resorption markers (3 months) than formation markers (6–12 months) [37]. In the inadequate drug response group, resorption at the endosteal surface and formation at the periosteal surface increased slightly. This indicates that risedronate did not have a positive effect on this group since there was an increase in resorption and a possible remodelling-driven apposition.

Consequently, changes in CT were significantly different amongst the three groups and indicated a positive correlation with  $F_{cr}$ . This is concomitant with the literature where reduced thickness of the cortical bone has been related to increased risk of fracture initiation [38], and it has been

suggested that the cortical bone supports 50 % of the stresses associated with normal gait at the mid-neck [39, 40]. However, whether one can predict hip fracture using only mean cortical thickness is questionable. A prospective study ( $n=143$ ) showed that the cortical thickness estimates from the supero-anterior region were the most sensitive to femoral neck fractures, while the estimates from other regions did not vary significantly between cases and controls [41]. Again, this compels us to look at the local changes in geometry rather than observing the average values.

The critical regions, mainly the supero-anterior and supero-posterior regions, predicted by both the geometry and structural analyses coincided with common fracture prone regions in the femur. The main physical activity of the elderly, walking, results in a thin superolateral cortex and a thick inferomedial cortex [40]. As such, in a sideways fall on the trochanter, the superior cortex undergoes excessive compression load which increases the risk of local buckling. Therefore, in our FE analysis, we are able to observe the local buckling of the superior cortex as a compression load was applied, simulating a sideways fall in the frontal plane. In fact, due to the thin superolateral cortex, we observed peaks at the supero-anterior and supero-posterior regions,



**Fig. 5** Plots of local BR against angle in the baseline and final years for the adequate ( $\uparrow F_{cr}$ ), inadequate ( $\downarrow F_{cr}$ ) and indefinite ( $\approx F_{cr}$ ) drug response groups. In the adequate drug response group, the local BR values remained well below the critical BR value of 10, and the standard deviation at the supero-posterior peak reduced significantly in the final year as compared to the baseline year. The inadequate drug response

group exhibited higher local BR values tending towards the critical value of 10 at the supero-posterior and supero-anterior peaks. In the indefinite drug response group, the peak at the supero-anterior region reduced, while the remaining local BR values remain relatively low with the peak at the supero-posterior region being relatively less distinct than the other two groups

indicating high buckling risk (Fig. 5). We found that the inadequate drug response group showed an approximate mean BR value of 8 and a maximum value of 10 corresponding to these peaks, where a value of 10 and above indicates increasing susceptibility to local buckling and instability [42]. Future work may include establishing a critical buckling ratio, specific for long bones such as the femur.

With local variations in CT and BR, it is not surprising that the effects of local osteoporosis at specific regions will play a more influential role than in other regions. Of note is that average geometrical parameters such as  $D_{sp}$ ,  $D_{ec}$  and overall BR did not show significant differences between the adequate, inadequate and indefinite drug response groups. Averaging the geometrical parameters may not accurately reflect local changes because critical regions (i.e. cortical thinning regions) would be concealed by averaging the local values. Thus, this key finding emphasizes the presence of underlying structural changes (i.e.  $F_{cr}$ ) that are masked by averaged measurements [43]. By observing each subject's local BR individually, we were able to relate spikes in local BR in the supero-anterior and supero-posterior regions to the fall in  $F_{cr}$  amongst the subjects from the inadequate drug response group. This indicates that these subjects either require a revision of their anti-resorptive drug treatment or a more well-targeted exercise that would provide sufficient loading to the superior section of the femur.

Lots and Hayes in 1990 had showed that the combination of cross-sectional area and density at the site of fracture produced a significant correlation to fracture load when

tested in a fall configuration ( $n=12$ ,  $r^2=0.93$ ). Pulkkinen et al. in 2004 reported that BMD measurements are biased by the thickness of the cortical shell meaning that BMD is influenced by the geometry of bone and concluded that the combination of BMD and radiological upper femur geometric properties improved the evaluation of bone strength. Since bone strength is influenced by the spatial distribution of bone mass [18], we believe that FE-predicted  $F_{cr}$  can be better characterized by BR. As such, our work combined the use of geometric analysis with FE analysis to compare the changes in local BR with the macroscopic change in  $F_{cr}$ . Changes in cortical thickness, among other factors such as neck shaft length, femoral neck axis length and femoral neck width, were found to be highly sensitive to BMD and 3D FE analysis in a simulation study [24]. This is in line with our finding where CT was most sensitive to changes in  $F_{cr}$ . However, for more accurate fracture prediction, local changes in BR and CT have to be monitored. Few studies have worked on local osteoporosis. For example, Poole et al. [8] had recently utilized cortical thickness mapping to explore local osteoporosis in the cortical structure of the femoral neck in patients with and without hip fractures. In this study, we incorporated the use of local BR to illustrate the phenomenon of local osteoporosis and its implications.

This work has several limitations, primarily the lack of FE validation in this study. Direct experimental validation is important in determining the level of accuracy in FE modeling [22]. Also, the assignment of two discrete set of material properties could limit the accuracy of the FE results obtained.

Only one fall configuration was simulated in this FE study. Different fall configurations may give rise to varying  $F_{cr}$  values that could alter the observations obtained [33]. More sophisticated boundary conditions such as the simulation of other fall configurations and contributions of complex muscular segments were not considered, but they would be priority for future work. Nevertheless, the equations governing the material properties and boundary conditions used in this study have been established once or more [25]. In addition, FE model provides the best source of information on bone morphology currently, and several studies have already illustrated the predictive ability of FE models against experimental values of surfaces strains [44, 45]. Thus, we believe that this study will serve as a foundation to future studies on the phenomenon of local osteoporosis.

The existence of local osteoporosis aggravates the limitation of using generalized parameters and necessitates patient-specific monitoring of the bone, especially in elderly, osteoporotic patients where the probability of hip fracture is high. We suggest that management of hip fracture risk should be targeted not only with anti-resorptive drug treatment but also at the local geometric abnormalities causing instability. Individuals may need early assessment of their radiological scans complemented with patient-specific finite element analysis to monitor the heterogeneity in bone geometry. By assessing local osteoporosis via a patient-specific analysis, a more suitable anti-resorptive drug treatment can be recommended and could pave the way for an improved diagnosis of osteoporosis and fracture prediction.

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**Conflicts of interest** None.

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