**Abstract:**

Introduction Using a longitudinal observational study with two evaluations and a one year follow-up interval, we investigated the influence of physical activity (PA) and skeletal geometry in bone mineral density (BMD) and bone mass distribution at the proximal femur (PF) in 96 girls and 81 boys (10-12 yr). It is plausible that the geometry of the pelvis-PF structure moderates mechanical forces exerted at the hip and therefore creates different degrees of mineralization among PF sub-regions.

Methods Whole body and left hip DXA scans were used to derive geometric measures of the pelvis - inter acetabular distance (IAD) - and PF - abductor lever arm (ALA). BMD was measured at the integral, superolateral (SL), and inferomedial (IM) femoral neck (FN), and at the trochanter (TR). These sub-regions were used to represent bone mass distribution via three BMD ratios-FN:PF, IM:SL, and TR:PF. PA was measured using accelerometry and a bone-specific PA questionnaire (BPAQ).

Results A longitudinal panel data approach revealed BPAQ as a positive predictor for all BMD variables (p<0.05) except TR BMD in girls and FN BMD in boys. Comparing the most active with the less active participants, the greatest benefits of PA were observed at the FN of the girls with the lowest IAD (p<0.001), at the FN of the boys with the highest IAD (p<0.001) and at the trochanter of the boys with the lowest ALA (p<0.01).

Conclusion Geometric measures of IAD and ALA seem to moderate the effect of PA role in the relative mineralization of the PF regions. On the other hand, absolute BMD levels appear to be determined by mechanical loading.

**Corresponding Author:**

Fátima Baptista, Ph.D  
Faculty of Human Kinetics, University of Lisbon  
Cruz-Quebrada, PORTUGAL

**First Author:**

Graça Cardadeiro

**Order of Authors:**

Graça Cardadeiro  
Fátima Baptista, Ph.D  
Nicoletta Rosati  
Vera Zymbal  
Kathleen F Janz  
Luís B Sardinha

**Author Comments:**

Dear Editor

My co-authors and I would like to thank you for reviewing the manuscript entitled "Influence of Physical Activity and Skeleton Geometry on Bone Mass at the Proximal Femur in 10-12 Year Old Children - A Longitudinal Study" that was submitted for
publication in the Osteoporosis International. All comments and changes suggested were incorporated on the manuscript and table/figure documents.

Enclosed are the responses to the reviewer's comments that were raised. My co-authors and I hope that now the manuscript is acceptable for publication in the Osteoporosis International.

This manuscript was re-submitted to Osteoporos Int in November 27th (deadline for re-submission after revision) with track changes. However after the submission, we thought it would be better for reviewers to eliminate what was deleted and keep only the new text inserted. The article has been unsubmitted by the editorial board and since that time we cannot upload the new version of the file.

Once again, thank you for reviewing our manuscript.

### Suggested Reviewers:

<table>
<thead>
<tr>
<th>Suggested Reviewers</th>
<th>Email</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>aaaaaaaa bbbbbbb</td>
<td><a href="mailto:fbaptista@fmh.utl.pt">fbaptista@fmh.utl.pt</a></td>
<td>A reviewer was not added because the manuscript was reviewed previously by someone</td>
</tr>
<tr>
<td>cccccc ddddd</td>
<td><a href="mailto:fbaptista@fmh.utl.pt">fbaptista@fmh.utl.pt</a></td>
<td>A reviewer was not added because the manuscript was reviewed previously by someone</td>
</tr>
</tbody>
</table>
Influence of Physical Activity and Skeleton Geometry on Bone Mass at the Proximal Femur in 10-12 Year Old Children – A Longitudinal Study

Graça Cardadeiro\textsuperscript{a}, Fátima Baptista\textsuperscript{a}, Nicoletta Rosati\textsuperscript{b}, Vera Zymbal\textsuperscript{a}, Kathleen F. Janz\textsuperscript{c}, Luís B. Sardinha\textsuperscript{a}

\textsuperscript{a} Exercise and Health Laboratory, Interdisciplinary Centre for the Study of Human Performance, Faculty of Human Kinetics, Technical University of Lisbon, Portugal
\textsuperscript{b} CEMAPRE and Department of Mathematics, ISEG, Technical University of Lisbon, Portugal
\textsuperscript{c} Department of Health and Human Physiology; Department of Epidemiology, University of Iowa, Iowa, US.

Address for correspondence:

Corresponding author: Fátima Baptista

Exercise & Health Laboratory

Faculty of Human Kinetics, Technical University of Lisbon

Estrada da Costa, 1495-688 Cruz Quebrada, Portugal

e-mail: fbaptista@fmh.utl.pt

Tel: 351 214149198

No Competing Interests
Abstract

Introduction Using a longitudinal observational study with two evaluations and a one year follow-up interval, we investigated the influence of physical activity (PA) and skeletal geometry in bone mineral density (BMD) and bone mass distribution at the proximal femur (PF) in 96 girls and 81 boys (10-12 yr). It is plausible that the geometry of the pelvis-PF structure moderates mechanical forces exerted at the hip and therefore creates different degrees of mineralization among PF sub-regions.

Methods Whole body and left hip DXA scans were used to derive geometric measures of the pelvis – inter acetabular distance (IAD) – and PF – abductor lever arm (ALA). BMD was measured at the integral, superolateral (SL), and inferomedial (IM) femoral neck (FN), and at the trochanter (TR). These sub-regions were used to represent bone mass distribution via three BMD ratios-FN:PF, IM:SL, and TR:PF. PA was measured using accelerometry and a bone-specific PA questionnaire (BPAQ).

Results A longitudinal panel data approach revealed BPAQ as a positive predictor for all BMD variables (p<0.05) except TR BMD in girls and FN BMD in boys. Comparing the most active with the less active participants, the greatest benefits of PA were observed at the FN of the girls with the lowest IAD (p<0.001), at the FN of the boys with the highest IAD (p<0.001) and at the trochanter of the boys with the lowest ALA (p<0.01).

Conclusion Geometric measures of IAD and ALA seem to moderate the effect of PA role in the relative mineralization of the PF regions. On the other hand, absolute BMD levels appear to be determined by mechanical loading.

Keywords: Pelvis; Proximal Femur; BMD; Bone Geometry; Physical Activity; Children; Sex
Mini Abstract

Physical activity have long been identified as a determining factor of the mineralization of the skeletal, particularly in children. Our research supports the hypothesis that the geometry of the pelvis and proximal femur might moderate the effect of physical activity in the relative mineralization of the proximal femur sub-regions.
1. Introduction

Osteoporosis is an underlying etiological factor in most hip fractures in elderly people with sex distinction in hip fracture risk attributed largely to a lower peak adult bone mass in females and women’s accelerated bone loss following the menopause [1]. However sex-specificities in bone morphology and mechanical competence may also contribute to rate differences in two main types of hip fracture. Until age 70 yr, femoral neck (cervical) fractures are more common than trochanteric fractures in women, when compared to men, while men are at greater risk for trochanteric fractures [2, 3]. After age 70 yr, both women and men are more likely to incur trochanteric fractures (rather than femoral neck fractures) [2, 3]. Some research suggests that these two types of fractures reveal dissimilar etiologies, i.e., trochanteric fractures are associated with bone fragility or reduced bone mineral density (BMD) [4, 5], and femoral neck fractures are determined by proximal femur geometry [6, 7]. BMD and proximal femur geometry might, therefore, play distinctive roles as risk factors for hip fractures.

Geometric measures of the proximal femur, particularly the proximal femur axis length [6-8] and the neck shaft angle [9], and geometric measures of the pelvis structure have been associated with hip fracture risk in adults [9-11]. These observations suggest the anatomy of the proximal femur and the pelvis are potential determinants of the type of hip fracture. For example, geometry influences the combination of bending and axial compression at the proximal femur in the event of a (side) fall in elderly people [12]. Geometry may also influence the distribution of bone mass throughout the life course and especially during growth.

The geometry of the pelvis–hip and mechanical forces caused by abductor muscles during physical activity (PA) create stresses at different regions of the proximal femur [13, 14]. The
abductor lever arm (ALA), the hip offset, and the length of the femoral neck are determinants of the abductors’ contraction forces that stabilize the pelvis during single leg stance. This stance is essential for locomotion as it allows the other leg to swing while the body weight is balanced (on the contra lateral leg) [15]. The body weight lever arm is linearly related to the pelvis width [15]; therefore it is plausible that the inter-acetabular distance (IAD) also plays a role in the forces exerted on the proximal femur during locomotion. Concerning the geometry of the pelvis-hip system, dissimilarities between sexes are well documented, in particular the wider female pelvis and the female pro-valgus hip type [16-18], compared to male individuals. This sex-specific morphology of the pelvis and thigh, observable as early as the gestation period [19], along with the sex discrepancies in muscle activity during locomotion may contribute to different motion patterns [20]. As clear sex differences in hip kinematics and muscle activity during walking and running have been observed [21, 22], and as PA (including locomotion) is one of the determinants of the loads exerted on the proximal femur, it is reasonable to formulate the hypothesis that the geometry of the pelvis and the hip may be associated to sex-specific mineralization patterns of the proximal femur.

It has been widely accepted that entering adulthood with greater bone mass may reduce fractures experienced in old age [23]. Nearly 40% of total young adult bone mass is achieved during the four years around peak height velocity (approximately 11-12 yr for girls and 13-14 yr for boys) [24]. This peri-pubertal period is considered crucial for skeletal mineralization and a time when bone adapts in a particularly efficient way to loading [25]. This is also an opportune period during which physical activities that generate impact to the skeleton are naturally integrated into day-to-day life. Recent studies have suggested that sex moderates the association between mechanical loading from PA and bone accrual at some weight-bearing bones [26-28]. The studies report that boys’ proximal femur appears to be more sensitive to mechanical loading than girls’ [27, 28]. The hypothesis of a higher responsiveness of the
proximal femur to PA in boys (when compared to girls) has mainly been based on studies focused only on the femoral neck and not on other sub-regions of the proximal femur (i.e., trochanter and intertrochanter). In addition, these studies have not been designed to specifically analyse sex differences.

Using a longitudinal design with boys and girls aged 10 to 12 yr, the aims of our study were to: a) analyse the effects of PA and pelvis - proximal femur geometry on bone mass distribution at the proximal femur; and b) investigate whether sex distinctive geometric variables influence sex-specific bone mass distribution patterns. We hypothesized that higher responsiveness might be an artefact of sex-related biomechanical differences that influence loading at different regions of the proximal femur.

2 Materials and methods

2.1 Sample

Participants were 10 to 12 yr children recruited from schools in Oeiras municipality, in the greater Lisbon area, Portugal. DXA scans, PA, and maturity measures were obtained twice at baseline and one-year follow-up. All participants were healthy Caucasian students not taking any medication known to influence bone metabolism. The Ethics Committee of the Faculty of Human Kinetics, Technical University of Lisbon approved the study and parents or legal guardians of each child provided written informed consent.

2.2 Proximal femur bone mass distribution

Using standard measurement routines, integral BMD of the left proximal femur and BMD of each proximal femur sub-region were evaluated using dual x-ray absorptiometry (DXA) (QDR Explorer, Hologic, Waltham, MA, USA). The region of interest was adjusted to each...
participant following the procedures defined in QDR Reference Manual and covers the entire proximal femur of each individual.

Three BMD ratios were calculated as indicators of bone mass distribution of the proximal femur, following previous literature [29, 30, 31]:

\[
FN:PF = \frac{\text{Femoral neck BMD}}{\text{Proximal femur BMD}};\quad TR:PF = \frac{\text{Trochanter BMD}}{\text{Proximal femur BMD}};\quad IM:SL = \frac{\text{Inferomedial femoral neck BMD}}{\text{Superolateral femoral neck BMD}}
\]

where FN:PF is the femoral neck to proximal femur BMD ratio, TR:PF is the trochanter to proximal femur BMD ratio, and IM:SL is the inferomedial to superolateral femoral neck BMD ratio. These ratios were used to overcome inter and intra individual variability resulting from bone size differences among the participants and measurement periods, respectively.

All measurements were made by the same technician and a spine phantom was scanned daily to maintain quality assurance. The coefficients of variation of the femoral neck and the trochanter BMDs, estimated from 2 measurements by repositioning and scanning 28 subjects, were 1.6% and 1.7%, respectively, in the baseline evaluation. In the follow-up evaluation, they were 1.5% and 1.6%, respectively. After verification and saving of the results of the standard regions of interest, a manual analysis of each hip scan was performed. We reused every image to reanalyze the femoral neck region. In order to get the superolateral femoral neck BMD, we dragged the inferomedial neck box line towards the proximal femur axis length (which is defined automatically by the DXA analysis software and represent the midline midway between the two sides of the femoral neck) (Fig.1A). A symmetric procedure, using the DXA-defined superolateral box line, was followed to determine the inferomedial femoral neck BMD (Fig.1B).

**Figure 1** about here…
2.3 Inter-acetabular distance and abductor lever arm

Images of whole body and left hip were obtained for all children using DXA to determine the IAD and ALA, respectively. Since the accuracy of DXA images to determine geometric measures of the skeleton is quite sensitive to the patient’s position during scanning, strict protocols for positioning and analysis of DXA scans were followed. From images, linear measures of the IAD and the ALA were made for each subject using the CorelDRAW X6 software (Coral Corporation, Ottawa, Ontario, Canada). All measurements were performed by the same technician. Linear geometric measures of the pelvis included: the lower IAD (LIAD), defined as the distance between the left and the right lower points of the acetabular opening \( CD \) in Fig. 2A; the upper IAD (UIAD), defined as the distance between the left and the right upper points of the acetabular opening \( AB \) in Fig. 2A; and the IAD, calculated as the distance between left and right middle points of the previous references \( EF \) in Fig. 2A.

**Figure 2** about here…

The path of the abductor muscles was represented by drawing a tangential line to the lateral margin of the greater trochanter which was parallel to the line between the highest point of great trochanter (point J in Fig. 2B) and the inferior limit of this sub-region (point K in Fig. 2B). The ALA \( IL \) in Fig. 2B is represented by the perpendicular distance between tangent of the greater trochanter and the center of rotation of the femoral head [32].

All parameters were measured three times in a random sub-sample of fifteen participants in order to determine measurement precision. The root mean square of coefficient of variations was 0.8%, 0.6%, 0.5% and 0.8% for IAD, UIAD, LID and ALA, respectively.

2.4 Physical Activity

2.4.1 Accelerometry
PA was assessed at baseline and follow-up using the GT1M accelerometer (Actigraph, Fort Walton Beach, Florida, USA) with 15 second epochs. Children were instructed to wear the accelerometers for four consecutive days (two weekdays and two weekend days) providing at least 600 minutes per day of accelerometer data. Those not complying with these requirements were excluded from the sample. The accelerometer was secured on the right hip and the children were asked to wear the accelerometer all day, except during water activities and sleeping. They were also asked to put them on as soon as they got out of bed in the morning and take them off when they went to bed at night. Accelerometers were programmed to start recording in the morning of the first day and measure continuously for 4 days. Time with over 30 min of continuous zero values was assumed to represent non-wear time.

Activity data were analyzed and processed using the MAHUffe analysis program (www.mrc-epid.cam.ac.uk). The output from the program included accumulated time spent at sedentary-, light-, moderate-, and vigorous-intensity PA in minutes per day. The intensity of PA was defined according to the counts per minute (cpm) as follows: sedentary activity, up to 100 cpm; light-intensity (LPA) from 101 to 2295 cpm; moderate-intensity (MPA) from 2296 to 4011 cpm; and vigorous-intensity (VPA) over 4012 cpm [33]. MVPA was calculated as the sum of moderate and vigorous activity.

2.4.2 Bone-specific physical activity questionnaire

The Bone-Specific Physical Activity Questionnaire (BPAQ) was used to quantify current and historical PA participation relevant to the musculoskeletal system [34]. This questionnaire uses ground reaction forces (GRF) loading reference values. An algorithm was developed to weight the factors of load intensity, years of participation, and frequency of current and historical activity according to the principles of the osteogenic index [35]. This algorithm was used to convert the raw BPAQ data into a score that reflects total bone-relevant PA history. The original BPAQ was validated for young adults, however, it was designed to be applied to
a wide age range (including children) via a specific age weighting factor in the algorithm. Recent analyses indicate that, in contrast of the inability of traditional measures of PA to reflect bone loading history, BPAQ score predicts up to 60% of the variance in indices of bone strength at the femoral neck and lumbar spine [36]. The questionnaire was administered to each participant by a trained interviewer. Participants were asked to record (a) all regular physical activities performed throughout their life and the approximate number of years of participation; and (b) all activities practiced on a regular basis over the previous 12 months, including frequency of participation. A PA score was derived for each individual. We assumed the following GRF equivalences for popular sports reported that were not included in GRF original database [33]. Handball ≈ Basketball; Canoeing ≈ Rowing; Rhythmic gymnastics ≈ Dance.

2.5 Body size and body composition

Hip bone mineral content (g), bone area (cm²), and areal BMD (g/cm²) were derived from the scan images. Quality control scans were performed daily using the Hologic phantom. To minimize operator-related variability, all measurements were conducted by the same technician. Our error for BMC measurements is low, with a coefficient of variation < 1% for quality control scans.

Standing and sitting height were measured to the nearest 0.1 cm using a stadiometer (Secca 770, Hamburg, Germany) with children in underwear and barefoot. Body mass (kg), total fat (kg), and total lean mass without bone (kg) were determined from a total-body scan using DXA (QDR Explorer; Hologic, Waltham, MA, USA) with children in a fasting state. Body mass index (BMI) was calculated as body mass in kilograms divided by height (in meters) squared.
2.6 Maturity and calcium intake

Maturity was estimated as the years of distance positive or negative from the age of peak height velocity using sex-specific prediction equations that include age, body height, and sitting height [37]. Calcium intake (mg) was calculated from a semi-quantitative Food Frequency Questionnaire, assessing regular intake of a wide set of a typical Portuguese foods.

2.7 Statistical Analysis

Data were analysed using the STATA statistics and data analysis software package (Version 12.0 for Windows; StataCorp LP, Texas, USA). The sample distribution of the survey variables was examined using appropriate measures of central tendency and variability. Differences between girls and boys, within a specific year of observation, were analysed by comparing sample means of the two groups for that year using independent-samples t-tests when variables were normally distributed and Mann-Whitney nonparametric tests when not. Parametric t-tests for proportions were used in the case of variables expressed in percentage.

A longitudinal data approach was adopted to control for unobservable individual effects, which reflect heterogeneity between subjects related to genetics, environment, family, etc. Several linear regression models were considered to analyse the effect of the explanatory variables of PA and geometry on proximal femur sub-regional BMDs and each of the three BMD ratios (response variables). Models were adjusted for maturity, body height, and body lean mass.

The F-test for overall significance of the regression was used to confirm the joint significance of the chosen explanatory variables. A test for the presence of unobservable individual effects confirmed significant heterogeneity across individuals, which was accounted for.
of the regression parameters was performed under the hypothesis of random effects (i.e., supposing that the unobservable individual effects are not correlated with the observed explanatory variables), and the Hausman test was used to confirm that hypothesis. All models were initially estimated for boys and girls together and then repeated separately.

The interpretation of the estimated coefficients for the explanatory variables can be done individually in most cases, with each coefficient representing the direct effect of a specific regressor on the response variable. However, in cases where interactions between variables are considered, the impact of a variable is given by a combination of coefficients, called the partial effect, and should be interpreted accordingly. Specifically, three interactions were considered, the IAD/ALA ratio, and the interactions between physical activity and IAD or ALA, given by total BPAQ*IAD and total BPAQ*ALA, respectively. The corresponding partial effects of IAD, ALA and total BPAQ on a generic response variable $Y$ are given by the following expressions:

$$\frac{\partial Y}{\partial \text{IAD}} = \beta_1 + \frac{1}{\text{ALA}} \beta_3 + \beta_4 \cdot \text{total BPAQ}$$

$$\frac{\partial Y}{\partial \text{ALA}} = \beta_2 - \text{IAD} \cdot \text{ALA}^{-2} \cdot \beta_3 + \beta_5 \cdot \text{total BPAQ}$$

$$\frac{\partial Y}{\partial \text{total BPAQ}} = \beta_6 + \beta_4 \cdot \text{IAD} + \beta_5 \cdot \text{ALA}$$

Here $\beta_1$ represents the estimated coefficient associated to IAD, $\beta_2$ is the coefficient associated to ALA, $\beta_3$ is the coefficient associated to IAD*ALA$^{-1}$, $\beta_4$ is the coefficient associated to total BPAQ*IAD, $\beta_5$ is the coefficient associated to total BPAQ*ALA, and $\beta_6$ is the coefficient associated to total BPAQ. Therefore, the sign and size of the partial effect on a specific variable $Y$ depend not only on the estimated coefficients but also on the values of ALA, IAD and total BPAQ.
3. Results

Participant characteristics are provided in table 1. The maturity offset, peak height velocity and body fat mass differ significantly between boys and girls in both periods of observation. On the other hand, the mean body height, body mass index, and BMI were similar between boys and girls at baseline and follow-up. Body mass and the percentage of body fat mass were comparable at baseline, but girls presented higher values for these variables at follow-up.

The PA variables did not show differences between girls and boys at baseline. At follow-up, the PA levels as assessed by accelerometer decreased for girls while boys became more active. In contrast, the PA variables estimated through BPAQ continued to be similar between boys and girls at follow-up. Concerning the average measurements of bone density, boys had higher BMD values at the integral proximal femur and at the neck region when compared to girls at baseline, but not at follow-up.

The bone mass distribution expressed by the ratios did not differ at the neck region, neither at baseline nor at follow-up. However, girls’ TR:PF ratio was greater than that of boys’ at both occasions. Regarding geometric parameters girls revealed wider IAD and greater ALA than boys at both measurement periods.

Table 1 about here

Table 2 shows the estimated parameters for the random effects GLS regression models for the BMD outcomes. In girls, the models for the BMD of the three neck regions show similar explanatory variables, namely lean mass and total BPAQ both with a positive effect of comparable magnitude across regions. In the cases of the integral and inferomedial femoral neck, body height was also significant, with a negative effect. The trochanter BMD was positively influenced by lean mass and maturity. In boys, lean mass was the only variable
influencing positively BMD at all bone regions. PA (moderate PA and total BPAQ) also explained positively the variance of the trochanter BMD while body height revealed a negative effect in the BMD of both the trochanter and inferomedial neck.

Table 2 about here

The estimated parameters for the random effects GLS regression models for the BMD ratios are showed in table 3. In girls, lean mass affected positively the variation of the FN:PF and negatively the IM:SL while maturity influenced negatively the FN:PF. IAD was a positive predictor of the TR:PF and ALA predicted negatively the FN:PF; the effect of the ratio of IAD to ALA was positive in the IM:SL. Thus, the effect of IAD was positive on BMD ratios while the effect of ALA was negative. The interaction of total BPAQ*IAD influenced positively the FN:PF.

In boys, the lean mass influenced positively the TR:PF while maturity determined negatively the FN:PF variation. Modification of the IM:SL BMD ratio was influenced positively by IAD and negatively by ALA. In the model for the TR:PF ratio, both total BPAQ and ALA showed negative coefficients. The partial effects of IAD and total BPAQ on FN:PF and the partial effects of total BPAQ on TR:PF were all positive. Despite the negative signal of the interaction of the IAD/ALA for the FN:PF model, the partial effects of the IAD and ALA were computed according to the expressions given in the statistics section.

Table 3 about here

Comparing the most active with the less active participants, the greatest benefits of PA were observed at the femoral neck of the girls with the lowest IAD, at the femoral neck of boys with highest IAD, and at the trochanter of the boys with the lowest ALA (Fig. 3).

Figure 3 about here
4. Discussion

This longitudinal observational study examined the effect of PA and geometric-related variables of the pelvis and hip on proximal femur regional BMDs and proximal femur relative mineralization. Differences in relative mineralization are important since it provides insight to risk for two main hip fracture types (cervical and trochanteric fractures) [11]. The femoral neck was differentiated between the superolateral and the inferomedial femoral bone areas to provide additional insight of the risk for cervical fracture [7].

The results showed a positive influence of PA on the regional neck BMDs for girls as well as on the TR BMD for boys; PA also revealed a significant interaction with geometrical variables in the BMD ratio models. As expected, the body lean mass was significant in every BMD model, as well as other control variables such as body height and maturity in some of them. Lean mass is frequently entered in models for proximal femur bone mass and its high explanatory power is occasionally referred as a cause for reduced contribution of other variables in the same models [38]. But above all, the geometric variables IAD and ALA were not significant in the BMD models. This was somehow surprising since locomotion involves a single leg stance that is supported by the joint action of ALA and the abductor muscles. The seminal model of Pauwels [39] for the biomechanics of the pelvis-hip system suggests that since the length of the ALA is smaller than the bodyweight lever arm, the abductors must generate a force that is higher than the body weight (without the weight of the stance leg) to maintain the pelvis leveled [40]. Therefore, all other factors equal, an increase of the ALA, or the hip offset, will reduce the required force of the abduction muscles, while an opposite consequence is obtained with the increase of body weight lever arm indicators, such as IAD. This model of counterbalancing forces has been used to explain abduction muscles activity [13] and inform surgical strategies for total hip arthroplasty [41], using different variables as indicators of the body weight lever arm: the IAD; half of the distance measured between the
centers of the femoral heads; or the bi-trochanteric width [20]. All these variables are linearly related to the body weight lever arm. However, we did not find any significant influence of either the IAD or the ALA on the BMD variations of the studied regions of the proximal femur.

Unlike the BMD models, IAD, ALA, IAD ALA\(^{-1}\) or their interaction with PA were significant in the relative mineralization models. In these models, the estimated coefficients suggest a positive partial effect of larger IADs on the relative mineralization of the neck regions (boys) and the trochanteric region (girls), whereas the partial effect of larger ALAs seems to be negative on the femoral neck region (girls) and trochanter region (boys), i.e., opposite effects between boys and girls. Regarding the IM:SL ratio, the results would mean that the narrower the IAD and the wider the ALA, as expressed by IAD ALA\(^{-1}\), the more homogeneous the bone mass distribution at the proximal femur neck tends to be in girls but less homogeneous in boys with greater BMD at the inferomedial than at the superolateral neck. Additionally, the effects of PA (total BPAQ) in the relative mineralization of the neck region in both sexes, and of the trochanteric region in boys seem to be moderated by IAD and ALA, respectively. High level of PA promotes greater BMD at the femoral neck than at other proximal femur region especially in boys and girls with very high and very low IAD, respectively. The advantage of high level of PA at the trochanter seems to be particularly relevant in boys with the lowest ALA.

In general the geometric variables seem to better explain the variance of the BMD ratios within the individuals (changes over time) than between them (variations between individuals), which highlights the importance of longitudinal approaches when examining these effects.

Should there be a biomechanical reasoning behind the effects of IAD and ALA, as the theory suggests, one would expect to find similar effects on models for both sexes, being sex-
specificities given by the significant differences in the IAD and ALA. These geometric differences were observed in our children sample, but sex-specific morphology of the pelvis and hip are also well documented in the literature for men and women, namely the hip offset and some pelvis width related variables [43-45]. Our results are compatible with the theoretical importance of the geometric variables in the relative mineralization of the studied regions of the proximal femur. However, a deeper understanding of the effects reported in this study require more complex biomechanics models to estimate the resultant forces exerted in each of the proximal femur regions as consequence of physical activity engagement.

This study has some limitations, mostly intrinsic to the technology used to assess physical activity, body composition and bone. The ability to accurately measure physical activity in a free-living environment is among the many overarching strengths of accelerometry, but our use of a short time period (four days) may not be representative of the activity level during last months. To minimize this limitation, we applied the accelerometry in a regular week of the school calendar and explained to the subjects the importance of keeping their usual standards. The bone-specific questionnaire (BPAQ) may have provided more complete description of children's activity, as well as yearlong information and physical activity history. However, assessing physical activity through self-report questionnaires in children has a drawback associated with the children's recall skills. In order to mitigate this limitation, the interviews were carefully standardized and we contacted the parents whenever the responses provided did not seem to be valid. The use of DXA created additional limitations. Areal BMD does not represent a volumetric density; therefore the densitometric image provides no direct information about strength and bone material composition. However, the alternative use of pQCT also presents limitations including movement challenges and scans that are not clinically relevant. In general, DXA is preferable for pediatric application because it scans large regions of interest (ROIs) rapidly at low radiation doses and is robust to movement and...
positional variation. The latter factors improve scan quality and congruence of repeated measures within subjects—a critical issue in longitudinal pediatric applications.

Our use of DXA images for geometric measures, rather than radiographic images, provided important insights without exposing the children to additional radiation, a critical issue in a pediatric research.

In conclusion, we made use of the commonly applied DXA technique and appropriate procedures to mitigate known limitation, to examine the potential importance of the hip and pelvis geometric features on the mineralization of the proximal femur. Our results suggest that the IAD and ALA, as indicators of the main lever arms of the biomechanics of the hip, may moderate the effect of PA in the relative mineralization of the proximal femur in peripubertal boys and girls. However unlike total lean body mass and PA, the same geometric variables don’t seem to influence the absolute BMD levels at the proximal femur neck and trochanter. Further research is needed to better understand the effects of geometric variables on the relative mineralization of the proximal femur regions including the development of a specific biomechanical model to simulate the vector forces exerted on these regions.

Acknowledgements

This work was funded by Portuguese Science and Technology Foundation (SFRH/BD/38671/2007 and PTDC/DES/115607/2009).

References


assessment, implications for preoperative templating and hip arthroplasty. Orthop Traumatol Sur 95(3):210-219


LEGENDS

**Table 1** Descriptive characteristics of the participants at baseline and one-year follow-up.

**Table 2** Estimation results of regression models for femoral neck (total, superolateral, and inferomedial) and trochanter BMDs, testing for the effects of physical activity and geometric parameters of the pelvis and hip, controlling for maturity, body height and body lean mass.

**Table 3** Estimation results of regression models for proximal femur BMD ratios, testing for the effects of physical activity and geometric parameters of the pelvis and hip, controlling for maturity, body height and body lean mass.

**Figure 1** Hip image from Hologic DXA scanner showing the region of interest of the superolateral femoral neck (A) and the inferomedial femoral neck (B).

**Figure 2** Panel A - Geometric measures of the pelvic bone: [AB] – upper inter-acetabular distance (UIAD); [CD] - lower inter-acetabular distance (LIAD); [EF] – inter-acetabular distance (IAD). Panel B - DXA image illustrating the abductor lever arm determination: [IL] – abductor lever arm (ALA); [JK] - line between the higher point of great trochanter and the inferior limit of this sub-region; mn – tangential line to the lateral margin of the greater trochanter.

**Figure 3** Comparison of FN: PF and TR:PF BMD ratios between very low and very high active participants with very low and very high inter acetabular distance (girls, boys) and with very low and very high abductor lever arm (boys). TBPAQ, total BPAQ.
<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th></th>
<th>One-year follow-up</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Girls</td>
<td></td>
<td>Boys</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Age, y</td>
<td>10.7 (0.4)</td>
<td>10.7 (0.3)</td>
<td>11.8 (0.4)</td>
<td>11.8 (0.3)</td>
</tr>
<tr>
<td>Maturity Offset, y</td>
<td>-1.26 (0.05)</td>
<td>-2.87 (0.05)</td>
<td>-0.03 (0.06)</td>
<td>-1.88 (0.07)</td>
</tr>
<tr>
<td>Peak Height Velocity, y</td>
<td>11.5 (0.5)</td>
<td>13.1 (0.7)</td>
<td>11.8 (0.5)</td>
<td>13.6 (0.7)</td>
</tr>
<tr>
<td>Body Height, cm</td>
<td>145.1 (6.8)</td>
<td>143.5 (6.8)</td>
<td>152.4 (6.9)</td>
<td>149.9 (8.1)</td>
</tr>
<tr>
<td>Body Mass, kg</td>
<td>39.9 (8.1)</td>
<td>38.2 (8.6)</td>
<td>45.8 (8.9)</td>
<td>43.0 (9.8)</td>
</tr>
<tr>
<td>Body Mass Index, kg/m²</td>
<td>18.9 (3.3)</td>
<td>18.4 (3.2)</td>
<td>19.6 (3.0)</td>
<td>19.0 (3.2)</td>
</tr>
<tr>
<td>Body Fat Mass, kg</td>
<td>11.8 (4.7)</td>
<td>9.92 (5.1)</td>
<td>13.53 (5.2)</td>
<td>11.0 (5.3)</td>
</tr>
<tr>
<td>Body Lean Mass, kg</td>
<td>26.9 (4.2)</td>
<td>27.1 (4.1)</td>
<td>30.7 (4.9)</td>
<td>30.6 (5.5)</td>
</tr>
<tr>
<td>Body Fat, %</td>
<td>28.8 (6.8)</td>
<td>24.73 (7.3)</td>
<td>28.9 (6.6)</td>
<td>24.7 (6.8)</td>
</tr>
<tr>
<td><strong>Physical activity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate PA, min/d</td>
<td>32.5 (11.5)</td>
<td>31.0 (10.9)</td>
<td>28.5 (11.3)</td>
<td>39.7 (11.2)</td>
</tr>
<tr>
<td>Vigorous PA, min/d</td>
<td>13.7 (8.5)</td>
<td>13.3 (7.5)</td>
<td>11.6 (7.4)</td>
<td>18.9 (9.7)</td>
</tr>
<tr>
<td>Moderate and Vigorous PA, min/d</td>
<td>46.1 (18.3)</td>
<td>44.3 (17.5)</td>
<td>40.1 (17.2)</td>
<td>58.6 (19.2)</td>
</tr>
<tr>
<td>PA Average Intensity, count/min/d</td>
<td>441.1 (109.2)</td>
<td>419.6 (111.0)</td>
<td>387.9 (117.2)</td>
<td>481.3 (118.6)</td>
</tr>
<tr>
<td>Past BPAQ</td>
<td>9.0 (14.1)</td>
<td>6.6 (14.2)</td>
<td>12.8 (19.2)</td>
<td>8.1 (15.4)</td>
</tr>
<tr>
<td>Current BPAQ</td>
<td>18.6 (34.2)</td>
<td>16.1 (20.4)</td>
<td>17.1 (28.5)</td>
<td>17.2 (18.8)</td>
</tr>
<tr>
<td>Total BPAQ</td>
<td>27.7 (41.2)</td>
<td>22.7 (31.8)</td>
<td>29.9 (42.7)</td>
<td>25.3 (25.5)</td>
</tr>
<tr>
<td><strong>Bone Mineral Density</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal Femur BMD, g/cm²</td>
<td>0.729 (0.009)</td>
<td>0.774 (0.008)</td>
<td>0.801 (0.011)</td>
<td>0.807 (0.010)</td>
</tr>
<tr>
<td>Neck BMD, g/cm²</td>
<td>0.699 (0.009)</td>
<td>0.744 (0.009)</td>
<td>0.754 (0.011)</td>
<td>0.771 (0.010)</td>
</tr>
<tr>
<td>Trochanter BMD, g/cm²</td>
<td>0.592 (0.008)</td>
<td>0.609 (0.008)</td>
<td>0.655 (0.010)</td>
<td>0.638 (0.009)</td>
</tr>
<tr>
<td>SL Neck BMD, g/cm²</td>
<td>0.602 (0.010)</td>
<td>0.638 (0.009)</td>
<td>0.665 (0.012)</td>
<td>0.678 (0.011)</td>
</tr>
<tr>
<td>IM Neck BMD, g/cm²</td>
<td>0.775 (0.09)</td>
<td>0.831 (0.09)</td>
<td>0.825 (0.11)</td>
<td>0.845 (0.10)</td>
</tr>
<tr>
<td><strong>Bone Mineral Density Ratios</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neck/Proximal Femur BMD</td>
<td>0.96 (0.05)</td>
<td>0.96 (0.05)</td>
<td>0.94 (0.05)</td>
<td>0.95 (0.04)</td>
</tr>
<tr>
<td>Trochanter/Proximal Femur BMD</td>
<td>0.81 (0.04)</td>
<td>0.79 (0.04)</td>
<td>0.82 (0.04)</td>
<td>0.79 (0.03)</td>
</tr>
<tr>
<td>IM Neck BMD/SL Neck BMD</td>
<td>1.297 (0.010)</td>
<td>1.308 (0.010)</td>
<td>1.253 (0.012)</td>
<td>1.255 (0.011)</td>
</tr>
<tr>
<td><strong>Geometric Parameters</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inter-Acetabulum Distance, cm</td>
<td>12.59 (0.09)</td>
<td>12.31 (0.07)</td>
<td>13.49 (0.11)</td>
<td>12.77 (0.09)</td>
</tr>
<tr>
<td>Abductor Lever Arm, cm</td>
<td>4.20 (0.04)</td>
<td>3.68 (0.05)</td>
<td>4.66 (0.03)</td>
<td>4.22 (0.05)</td>
</tr>
</tbody>
</table>

*Significant difference at p < 0.05.
PA, physical activity; BPAQ, bone physical activity questionnaire; BMD, bone mineral density; SL, superolateral; IM, inferomedial; * p < 0.05 difference between boys and girls within each examination
Table 2

<table>
<thead>
<tr>
<th></th>
<th>Femoral Neck BMD</th>
<th>Superolateral Femoral Neck BMD</th>
<th>Interomediol Femoral Neck BMD</th>
<th>Trochanter BMD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Coef. estimate</td>
<td>Robust SE</td>
<td>Coef. estimate</td>
<td>Robust SE</td>
</tr>
<tr>
<td>Girls</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height, cm</td>
<td>-0.0017</td>
<td>0.0006 b</td>
<td>-0.0030</td>
<td>0.0010 b</td>
</tr>
<tr>
<td>Lean mass, kg</td>
<td>0.0170</td>
<td>0.0016 a</td>
<td>0.00154</td>
<td>0.001 a</td>
</tr>
<tr>
<td>Maturity, yr</td>
<td></td>
<td></td>
<td>0.00185</td>
<td>0.002 a</td>
</tr>
<tr>
<td>Total BPAQ</td>
<td>0.0003</td>
<td>0.0001 c</td>
<td>0.0004</td>
<td>0.0002 c</td>
</tr>
<tr>
<td>Constant</td>
<td>0.4790</td>
<td>0.0616 a</td>
<td>0.1776</td>
<td>0.0294 a</td>
</tr>
<tr>
<td>Model R²</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>within</td>
<td>0.74</td>
<td>0.73</td>
<td>0.61</td>
<td>0.87</td>
</tr>
<tr>
<td>between</td>
<td>0.59</td>
<td>0.48</td>
<td>0.56</td>
<td>0.56</td>
</tr>
<tr>
<td>overall</td>
<td>0.61</td>
<td>0.51</td>
<td>0.56</td>
<td>0.61</td>
</tr>
<tr>
<td>Boys</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height, cm</td>
<td></td>
<td></td>
<td>0.0031</td>
<td>0.0013 c</td>
</tr>
<tr>
<td>Lean mass, kg</td>
<td>0.0081</td>
<td>0.0009 a</td>
<td>0.0101</td>
<td>0.0011 a</td>
</tr>
<tr>
<td>Moderate PA</td>
<td></td>
<td></td>
<td>0.0113</td>
<td>0.0021 a</td>
</tr>
<tr>
<td>Total BPAQ</td>
<td></td>
<td></td>
<td>0.0005</td>
<td>0.0002 c</td>
</tr>
<tr>
<td>Constant</td>
<td>0.5241</td>
<td>0.0274 a</td>
<td>0.3665</td>
<td>0.0328 a</td>
</tr>
<tr>
<td>Model R²</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>within</td>
<td>0.56</td>
<td>0.59</td>
<td>0.30</td>
<td>0.67</td>
</tr>
<tr>
<td>between</td>
<td>0.23</td>
<td>0.11</td>
<td>0.32</td>
<td>0.24</td>
</tr>
<tr>
<td>overall</td>
<td>0.25</td>
<td>0.15</td>
<td>0.31</td>
<td>0.28</td>
</tr>
</tbody>
</table>

BMD, bone mineral density; BPAQ, bone physical activity questionnaire. *p < 0.001; **p < 0.01; ***p < 0.05
### Table 3

<table>
<thead>
<tr>
<th></th>
<th>Femoral neck to proximal femur BMD ratio</th>
<th>Inferomedial FN to superolateral FN BMD ratio</th>
<th>Trochanter to proximal femur BMD ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Coef. estimate</td>
<td>Robust SE</td>
<td>Coef. estimate</td>
</tr>
<tr>
<td><strong>Girls</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lean mass, kg</td>
<td>0.0027</td>
<td>0.0011 b</td>
<td>-0.0071</td>
</tr>
<tr>
<td>Maturity, yr</td>
<td>-0.0156</td>
<td>0.0077 c</td>
<td></td>
</tr>
<tr>
<td>IAD, cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALA, cm</td>
<td>-0.0403</td>
<td>0.0121 a</td>
<td></td>
</tr>
<tr>
<td>IAD.ALA (^1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TotalBPAQ*IAD</td>
<td>0.00002</td>
<td>0.000005 a</td>
<td></td>
</tr>
<tr>
<td><strong>Model R(^2)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>within</td>
<td>0.41</td>
<td>0.25</td>
<td>0.04</td>
</tr>
<tr>
<td>between</td>
<td>0.07</td>
<td>0.06</td>
<td>0.18</td>
</tr>
<tr>
<td>overall</td>
<td>0.12</td>
<td>0.09</td>
<td>0.15</td>
</tr>
</tbody>
</table>

**Boys**

<table>
<thead>
<tr>
<th></th>
<th>Femoral neck to proximal femur BMD ratio</th>
<th>Inferomedial FN to superolateral FN BMD ratio</th>
<th>Trochanter to proximal femur BMD ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Coef. estimate</td>
<td>Robust SE</td>
<td>Coef. estimate</td>
</tr>
<tr>
<td>Lean mass, kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maturity, yr</td>
<td>-0.0243</td>
<td>0.0045 a</td>
<td></td>
</tr>
<tr>
<td>TotalBPAQ</td>
<td>-0.0046</td>
<td>0.0012 a</td>
<td></td>
</tr>
<tr>
<td>IAD, cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALA, cm</td>
<td>-0.0168</td>
<td>0.0054 b</td>
<td></td>
</tr>
<tr>
<td>IAD.ALA (^1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TotalBPAQ*ALA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td>0.9383</td>
<td>0.0167 a</td>
<td>1.8461</td>
</tr>
<tr>
<td><strong>Model R(^2)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>within</td>
<td>0.29</td>
<td>0.39</td>
<td>0.12</td>
</tr>
<tr>
<td>between</td>
<td>0.02</td>
<td>0.01</td>
<td>0.006</td>
</tr>
<tr>
<td>overall</td>
<td>0.04</td>
<td>0.04</td>
<td>0.002</td>
</tr>
</tbody>
</table>

BMD, bone mineral density; BPAQ, bone physical activity questionnaire; IAD, inter-acetabular distance; ALA, abductor lever arm; IAD.ALA \(^1\): inter-acetabular distance to abductor lever arm ratio.

\(^a\) p < 0.001; \(^b\) p < 0.01; \(^c\) p < 0.05
Reviewer #1:

Comments to the Author

In this original and well documented study of physical activity and bone mass in children/adolescents, the authors investigated the contribution of geometrical and biomechanical parameters on aBMD of the hip. Their results suggest that the interacetabular distance (IAD) and abductor level arm (ALA), as derived from DXA images, are positively, respectively negatively, associated with the relative, but not total, BMD of subregions of the hip, and this independently of physical activity. Although interesting, the accuracy and relevance of these findings remains uncertain. Several questions indeed remain to be clarified.

1. Although the hypothesis that IAD and ALA may influence the load, and thereby the distribution of aBMD, in distinct subregions of the hip is sustainable, more common hip geometrical parameters, such as hip axis length and angle could do as well. Hence it is unclear whether the geometrical and biomechanical parameters studied here still play a role once the proper hip geometry is taken into account. Analyses should be performed accordingly.

In fact it is common to find in the literature, namely concerning the risk of fracture, the use of the hip axis length (HAL), the neck-shaft angle (NSA) or the femoral neck with (FNW), but mainly in adults.

However, as these variables were not sex distinctive at these ages in our sample and the aim was to study sex specific responses to mechanic stimuli, these were not primary variables. Furthermore, this type of variables, despite playing a role in the way the forces are exerted on the studied regions of the proximal femur, are not derived from any biomechanic model as is the case of the abductor lever arm and the pelvis width.

Nevertheless, those variables were tested but didn’t turn out to be significant in our models.

2. In the methods it should be clarified whether the ROI area of the total hip region was fixed or variable, i.e. adapted for each patient. In the latter case, what is the influence of a smaller tot hip ROI on the relative aBMD of the Fn or trochanter?

The ROI area was adjusted (“adapted”) to each patient following the procedures defined in QDR Reference Manual and covers the entire proximal femur of each individual. The very same procedures were applied in all cases.

Therefore, smaller or larger total hip ROI are solely a consequence of different bone sizes among individuals and not of the evaluation process. Given that we used the aBMD ratios to study bone mass distribution, our method is not influenced by those differences in bone size.

As suggested by the reviewer, this issue was clarified in the methods section.

3. In the GLS models, it seems that the values recorded at baseline and after one year are both included to minimize individual variations in the measurements? please confirm. In any case, it would also be very interesting to investigate the interaction between physical activity and IAD, respectively ALA. It is suggested to include such an interaction term in the model, if that is not already the case.

In the GLS models, both baseline and after one year values are included for each individual, being a longitudinal study. This allows the study not only the differences across individuals at a specific point in time, but also the “internal” variations for the same individual over time. Therefore, rather than “minimizing individual variations”, the objective of the longitudinal framework is to exploit such variations in order to disentangle across-individuals from within-individual variations.
Following the reviewer’s suggestion, the interaction between physical activity (as measured by Total BPAQ) and IAD or ALA has been studied in an extended model, where these interactions have been added to the set of explanatory variables. While the proposed interactions do not have a statistically significant effect on the absolute BMD measures, they prove to be relevant in some of the models for the relative distribution of BMD, as measured by the ratios. In particular, the interaction between physical activity and IAD is significant in the models for the neck to proximal femur BMD ratio (girls and boys), while the interaction between physical activity and ALA is significant in the boys’ model for the trochanter to proximal femur BMD ratio. In the remaining models for ratios, both interactions are not significant.

The article was revised with the updated models, which include (when significant) the suggested interactions, and are now presented in the respective Tables, and are commented upon in the Results section.

We are grateful for this suggestion, as it helped improve the explanatory power of some of the proposed models, with especially remarkable improvements in the boys’ case. This suggests that, in the boys’ case, not only the absolute amount of physical activity and the absolute geometric variables itself, but also their interaction is relevant in explaining the BMD distribution.

4. Results p12, the formulae as well as the paragraph about partial effects pertains to the methods. more generally, the results are very hard to read and the tables are crowded and not reader-friendly. Some graph illustrating the relationship between IAL, ALA and aBMD in boys and girls would help to take home some message here.

Following the reviewer’s suggestion the paragraph on partial effects and the formulae has been moved to the methods’ section. Due to the addition of the new interactions between physical activity and geometric measures, the expressions of the partial effects have now changed, and a new partial effect (that of Total BPAQ) has been added.

The tables have been reformatted so as to improve readability. Besides the revision of the titles, column headings and notes, the main change was not to present the results of the models for boys and girls together, as they were not essential for the article and, in fact, contributed for the crowding of the tables. But we found no way of further simplifying the tables.

One figure was added to improve comprehension of physical activity, IADL, and ALA interactions.

5. In the discussion, BMD is misinterpreted as "mineralization", whereas as the authors certainly know it partially represents size. whether or not the relative aBMD calculated here has an influence on the contribution of hip diameter on the measurement should also be clarified.

In the discussion we refer to the relative mineralization because it is a longitudinal study and the main response variables are expressed via three BMD ratios. These ratios were used to overcome inter and intra individual variability resulting from bone size differences among the participants and measurement periods, respectively. This later sentence was introduced in the materials and methods section.

Reviewer #2:

Comments to the Author
The authors present a relatively large, one year follow-up study of 96 girls and 81 boys and suggest that DXA derived geometric measures of inter acetabular distance (IAD) and abductor lever arm
(ALA) play a role in the relative mineralisation of proximal femur sub-regions. Although the design of the study is sound, there are some concerns regarding the results and discussion.

1. The results are presented in three "heavy" tables. The results section is quite difficult to read as well. Condensation of the text and highlighting the most important findings in the tables might help the readers.

   Following the suggestion of both the reviewers, the tables have been reformatted so as to improve readability. Please see above the answer to comment 4 of reviewer 1.

   The results section has been revised in its structure and contents in order to make access to the relevant information more effective, as suggested.

2. The titles of the tables should be more informative. Table 2 do not include the results of the geometric measures.

   Following the suggestion of both the reviewers, the tables have been reformatted so as to improve readability. Please see above the answer to comment 4 of reviewer 1.

3. The authors suggest that physical activity (BPAQ) has a significant effect on BMD but the conclusion that geometric measures play a role in mineralisation of proximal femur is not justified based on their results. Although some BMD ratios were significantly related to ALA and IAD (overall Model R² from 0.01 to 0.15), absolute BMD values were not. The use of certain ratios has not been properly justified by the authors and is questionable.

   The findings of the study point out that geometric measures do not play a role in the absolute level of mineral density of proximal femur, but do play a role in the relative regional BMD, as represented through the ratios of BMD across regions.

   Irrespective of the slight improvement in some models’ R² as a result of the introduction of the interactions of PA with geometric variables (as suggested by reviewer 1), the low levels of the R² in some models shall be interpreted in the context of these panel data type of models, specially having in mind that the models presented passed all types of tests, even assuming the less restrictive assumptions (i.e. random effects option).

   Concerning the choice of the proposed ratios to represent the relative distribution of bone mass across regions it was based on previous studies in the relevant literature:


   The use of the proposed ratios can be justified as they are not biased by individual characteristics affecting the skeletal mineralization, reflecting essentially differences in the relative mineralization of the studied regions. As the ratios were computed from density measures they are not affected by differences in the dimension of the bone.

   The corresponding paragraph in this section was revised to justify the option.
OSTEOPOROSIS INTERNATIONAL
Authorship & Disclosure Form

Influence of Physical Activity and Skeleton Geometry on Bone Mass at the Proximal Femur in 10-12 Year Old Children – A Longitudinal Study

Article Title (first few words)
First Author: Graça Cardado
E-mail: g.cardado@isapo.pt

After submission of this agreement signed by all authors, changes of authorship or in the order of the authors listed will not be accepted by Springer.

AUTHORSHIP
I, the undersigned author(s), certify that:

- I have seen and approved the final version of the manuscript, and all subsequent versions.
- I have made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data;
- I have drafted the article or revised it critically for important intellectual content.

I accept public responsibility for it, and believe it represents valid work. As an author of this article, I also certify that none of the material in the manuscript has been previously published, nor is it included in any other manuscript. I certify that this manuscript is not under consideration for publication elsewhere, nor has it been submitted or accepted in another publication in any form. The rights or interest in the manuscript have not been assigned to any third party.

Moreover, should the editor of Osteoporosis International request the data upon which the manuscript is based, I shall produce it. I also certify that I have read and compiled with the copyright information, as found on the Osteoporosis International home page website.

FINANCIAL DISCLOSURE/CONFLICT OF INTEREST
I certify that any financial interests such as employment, stock ownership, honoraria, paid expert testimony, as well as any personal relationships, academic competition, and intellectual passion which may inappropriately influence my actions, have been disclosed on a separate attachment.

All funding sources supporting the work and all institutional or corporate affiliations of mine are acknowledged in a footnote.

I have had full access to all the data in the study (if applicable) and thereby accept full responsibility for the integrity of the data and the accuracy of the data analysis.

By checking the box next to my signature I assert that there are no conflicts of interest (both personal and institutional) regarding specific financial interests that are relevant to the work conducted or reported in this manuscript.

PLEASE NOTE
1. Every author must sign the Authorship & Disclosure form.
2. It is possible to submit more than one form if the authors are in several locations.
3. All forms must be submitted at the same time.
4. Completed forms must be scanned and included as a pdf file during the online submission process as a supplemental file not for review.

Please email any queries to the appropriate Managing Editor:
European Office: Fina Liu – gi.europe@jofbonehealth.org
USA Office: Adrianne Tewksbury – tewksbury@helenhayeshosp.org

Page 1 of 2- (signatures & dates required on page 2)