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Published in:
Journal of sports sciences

DOI:
10.1080/02640414.2018.1537173

Publication date:
2019

Upper Extremity Bone Mineral Content Asymmetries in Tennis Players: a Systematic Review and Meta-Analysis.

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Funding details: this manuscript did not benefit from any grant.

Manuscript word count: 3993

Abstract word count: 195

Number of tables: 3

Number of figures: 6

Conflict of interest: none.

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Abstract

The aim of this study was to examine the magnitude of upper extremity bone mineral content (BMC) asymmetries in tennis players. Furthermore, the influence of sex (male versus female versus mixed), chronological age (juniors: <18 years; adults: 18 – 39 years and seniors: ≥40 years) and starting age (early starters: < 14 years and late starters: >18 years) on these asymmetries were examined. Two databases were searched for scientific articles that examined upper extremity BMC in tennis players. Pooling of the individual study effect sizes was conducted using the random-effects model. Three subgroup analyses were performed based on sex, chronological age and starting age. Out of the 15 included studies 24 effect sizes were extracted resulting in a significant difference in BMC value between the dominant and nondominant upper extremity of the tennis players (Standardised Mean Difference: 0.85 [95% CI: 0.67 – 1.03]). The three subgroup analyses all showed medium to strong effect sizes and significant intergroup differences. To conclude, BMC was significantly higher in the dominant upper extremity compared to the nondominant upper extremity in tennis players. Nevertheless, the influence of training volume and playing experience on these asymmetries are yet to be examined.

Key words: Tennis; Bone Mineral Content; Asymmetry.

Introduction

The process of lateralisation results in the preferred use of one extremity (i.e. left or right upper and/or lower extremity) during voluntary motor actions (Carpes, Mota, & Faria, 2010). The repetitive use of a specific extremity for a longer period of time while performing these motor actions will induce morphological adaptations to the dominant side of the body such as an increased bone or lean mass (Krzykala & Leszczynski, 2015; Palmer & Strobeck, 1986). The associated gradual development of morphological asymmetries within an individual may be further reinforced by intensive practice of a unilateral sport due to the uneven training loads to the body sides (Krzykala & Leszczynski, 2015). Tennis is a typical example of such a unilateral sport (Pluim, Staal, Windler, & Jayanthi, 2006). As one of the most popular sports worldwide, tennis is ideally suited to closely examine the effects of systematic (chronic) unilateral loading since both sides of the body are subject to similar intrinsic factors (including genetic, nutritional and neurohormonal aspects), while only the dominant upper extremity is exposed to intensive and repetitive asymmetric loading (Sanchis-Moysi et al., 2016).

Wolff's law implies that bone tissue adapts to mechanical loading through the process of mechanotransduction (Clarke, 2008). Consequently, persistent unilateral loading will increase bone mass and bone size in the dominant upper extremity of tennis players, resulting in asymmetry between both arms, which is quantifiable by measuring bone mineral content (BMC) (Heaney, 2003; Taylor et al., 2009). BMC responses to chronic unilateral loading are well documented in tennis players of different ages and competition levels using Dual X-ray Absorptiometry (DXA) and peripheral Quantitative Computed Tomography (pQCT). Nevertheless, the influence of sex (i.e. male versus female tennis players) on these BMC asymmetries is less evident. Several studies reported

significantly greater BMC asymmetries in males compared to females both in a young (Ireland et al., 2013) and adult population (Ducher et al., 2005a), whilst other studies reported no significant sex differences in BMC asymmetries in an adult (Ducher, Jaffre, Arlettaz, Benhamou, & Courteix, 2005b) and senior population (Ireland, Maden-Wilkinson, Ganse, Degens, & Rittweger, 2014). Similarly, it is unclear to what extent BMC asymmetries differently occur in young (< 18 years), adult (18 – 39 years) and senior (≥ 40 years) tennis players. Finally, it has been suggested that the starting age of playing tennis considerably influences the development of BMC asymmetry since prepubertal players (< 14 years) are reported to be more responsive to mechanical loading changing their bone mass when compared to their more mature counterparts (> 18 years) (Ducher, Tournaire, Meddahi-Pelle, Benhamou, & Courteix, 2006; Haapasalo et al., 1996).

Furthermore, and to the best of our knowledge, meta-analyses to quantify the magnitude of these upper extremity BMC asymmetries as wells as the influence of sex, chronological age and, in lesser extent, starting age on BMC asymmetries in tennis players are still lacking. Therefore, the objectives of this systematic review and quantitative meta-analysis were twofold. The first objective was to quantify upper extremity BMC asymmetries in tennis players. The second objective was to examine the influence of sex, chronological age and starting age on the magnitude of these BMC asymmetries in tennis players.

Methods

This systematic review and meta-analysis was conducted following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines

(Moher, Liberati, Tetzlaff, & Altman, 2009). The review protocol was registered a priori and can be accessed on the online PROSPERO database (registration number: 52594).

Systematic search strategy

The article searches were performed by two independent researchers (LC and NR) between April and July 2017. This search was updated in August 2018. The Pubmed and Web of Science databases were searched using the following *a priori* determined search terms: tennis , tennis player*, asymmetr*, structural asymmetr*, imbalance*, body composition, unilateral body composition, Bone Mineral Content or BMC. Furthermore, both researchers hand searched the references of the eligible articles previously identified. A consensus meeting between the two researchers was organised following the completion of the independent searches. In case of disagreement a third researcher (PC) would be contacted to clarify the disagreement.

Screening process

Inclusion and exclusion criteria were determined *a priori*. As we intend to provide a highly sensitive systematic review and meta-analysis regarding all the research examining BMC asymmetries in tennis players, there was no age, language or study design restriction. To be included, the study population had to consist of tennis players who played at least one hour a week and BMC had to be determined and reported (in g or in g/mm) for both the dominant and non-dominant upper extremity. Studies reporting only side-to-side differences in percentages were accordingly excluded. These criteria were used to independently determine the inclusion or exclusion of the studies by screening through the title, abstract and, finally, the full article text.

Data Extraction and risk of bias assessment

The first author's name and publication year, assessment method, number of participants, chronological age, sex, starting age, playing experience, training volume, assessed location as well as the BMC values for the dominant and non-dominant upper extremity were extracted and tabulated by two independent researchers (LC and NR). If a study examined BMC in several upper extremity locations one average value was calculated. A pre-tested standardised electronic reporting sheet was used and a consensus meeting was organised following the completion of the data extraction. In case of disagreement a third researcher (PC) would have been contacted to clarify the disagreement. If standard error means (SEM) were reported they were converted into standard deviations (SD) by multiplying the SEM with the square root of the sample size. Several effect sizes were extracted when studies reported data stratified by sex or chronological age. Only the baseline values were extracted if the included study implemented a longitudinal design. A symmetry index (SI) was used to calculate the difference, expressed as a percentage, between the extracted dominant and non-dominant upper extremity BMC values using the following formula: SI = ((dominant BMC/ non-dominant BMC) -1) x 100 (Rogowski et al., 2016). Two researchers (LC and NR) independently assessed risk of bias using the Joanna Briggs Institute (JBI) critical appraisal tool for Analytical Cross-sectional or Cohort Studies (Moola et al., 2017). Item 4 and 3 of the JBI critical appraisal tool for Analytical Cross-sectional and cohort studies respectively was not applicable since all the included studies either used a DXA or pQCT scan to determine BMC. Cohen's Kappa value was calculated as a measure of agreement for the screening process, data extraction and risk of bias assessment between the two independent researchers (Altman, 1990).

****Figure 1 near here****

Statistical analysis and Meta-Analyses

All individual study effect sizes of the cross-sectional designed studies were calculated and reported as standardised mean differences (SMD) using the following formula: SMD = (mean BMC (dominant side) – mean BMC (non-dominant side)) / pooled standard deviation. Their corresponding 95% confidence intervals (95% CI) were calculated. As dominant extremity data and non-dominant extremity data are clearly matched data, the pooled standard deviation was calculated based on the standard deviation of the differences and, hence, a Pearson correlation was needed. To protect against a possible underestimation of the variability, a very conservative r was set at 0.5. To account for the fact that this r was set arbitrary, a sensitivity analysis was run. Cohen's d benchmarking was used for the interpretation of the effect sizes: 0.00 - 0.19 (trivial), 0.20 – 0.49 (small), 0.50 – 0.79 (medium) and > 0.80 (large) (Cohen, 1992). Pooling of the individual study effect sizes was conducted using the random-effects model based on the inversed-variance method to calculate the individual studies' weighting factors.

The presence of heterogeneity was tested using a Q-test, its corresponding degrees of freedom (df) and p-value. Because the Q-test is in fact a chi-square test, which has a low statistical power, the alpha level was set at 0.10. Higgins' I^2 statistic was calculated to express the amount of the total variance that could be explained by the true between-study variance. For the interpretation of this true between-studies heterogeneity, Higgins' benchmarking was used: I^2 values around 25% were interpreted as low heterogeneity, around 50% as moderate and around 75% or more as high heterogeneity (Higgins & Thompson, 2002). Tau^2 and its squared root Tau were calculated as the variance and standard deviation of the distribution of the true effect sizes and allowed for the

calculation of 95% prediction intervals (95% PI). The latter were calculated to express a possible range of true effect sizes on the level of most populations (Borenstein, Hedges, Higgins & Rothstein, 2009).

In case of high observed heterogeneity (I^2 around 75% or more), subgroup meta-analyses were conducted to assess the possible confounding effect of sex, chronological age and starting age on upper extremity BMC asymmetries in the tennis players. Because of the relatively low number of studies within the subgroups, a pooled Tau^2 was used across the subgroups. The participants of the included studies were categorised based on their reported mean chronological age as junior (< 18 years), adult (18 – 39 years) or senior (≥ 40 years) tennis players. Where mean starting age was reported participants were categorised as early (< 14 years; before puberty) or late (> 18 years; after puberty) starters based on their reported mean starting age. No studies with the participants' mean starting age between 14 and 18 years were found. All analyses and forest plots were conducted and prepared using the Comprehensive Meta-Analysis software (CMA-II, Biostat Inc., Englewood, USA).

Table 1 near here

Results

Study characteristics

The systematic search identified a total of 1,349 records. After screening of the title, abstract and full text, a total of 15 studies (totalling 690 tennis players) were included in this meta-analysis (Figure 1). Although study design was not a selection process criterion,

only one study performed by Kontulainen et al. (1999) used a longitudinal design whereas all of the other studies implemented a cross-sectional design. All included studies either used a DXA scan or a pQCT to determine upper extremity BMC values. Table 1 depicts the characteristics of the eligible studies. The risk of bias assessment of the included cross-sectional studies resulted in JBI scores that ranged from 3 to 6 out of 7 (Table 2). The JBI score of the included cohort study was 7 out of 10 (Table 3). Out of the 15 included studies, 9 were not able to measure the exposure in a valid and reliable way, 12 did not identify confounding factors, 9 did not implement strategies to deal with these confounding factors and 1 did not implement strategies to address incomplete follow up leading to a high risk of performance, detection and attrition bias (Figure 2). The agreement between the two independent researchers was very good for both the systematic search (Cohen's kappa = 0.93) and data extraction (Cohen's kappa = 1.00) and also good for the study quality assessment (Cohen's kappa = 0.74). For both the selection and data extraction process the two independent reviewers could always agree and an involvement of a third reviewer was not needed. The sensitivity analysis revealed that setting r at 0.5, 0.7 and 0.9 yielded an overall weighted estimate of 0.85 [95% CI: 0.67 – 1.03], 0.86 [95% CI: 0.69 – 1.04] and 0.85 [95% CI: 0.69 – 1.01], respectively indicating that the overall weighted estimate was robust against changes in r.

****Table 2 near here****

****Figure 2 near here****

Main meta-analysis

Out of the 15 included cross-sectional studies, 24 effect sizes could be extracted. Figure 3 shows that BMC was significantly higher in the dominant upper extremity compared to the non-dominant upper extremity (SMD = 0.85; 95% CI: 0.67 – 1.03). Heterogeneity across studies was high and statistically significant (Q = 86.95; df(Q) = 23; $p < 0.001$; $I^2 = 73.55$ %). The 95% PI showed that the possible true effect size values in most populations ranged from 0.08 to 1.63.

****Figure 3 near here****

Subgroup meta-analyses

Due to the high heterogeneity observed in the main meta-analysis ($I^2 = 73.55\%$), three subgroup meta-analyses were conducted based on sex, chronological age and starting age of playing tennis. The first subgroup meta-analysis showed large effect sizes in the male (SMD = 1.07; 95% CI: 0.80 – 1.34; 95% PI: 0.31 – 1.63) subgroup, whilst the effect sizes in the female (SMD = 0.78; 95% CI: 0.49 – 1.07; 95% PI: -0.73 – 1.80) and mixed (SMD = 0.58; 95% CI: 0.24 – 0.92; 95% PI: 0.35 – 0.84) subgroups were medium (figure 4). The differences between the subgroup means were statistically different ($p < 0.001$). Heterogeneity became lower in the male ($I^2 = 51.98\%$) and mixed ($I^2 = 0.00\%$) subgroups but remained high in the female ($I^2 = 84.27\%$) subgroup.

****Figure 4 near here****

The second subgroup meta-analysis found large effect sizes for the adult (SMD = 0.98; 95% CI: 0.71 – 1.25; 95% PI: 0.09 – 1.51) subgroup and medium effect sizes for the junior (SMD = 0.73; 95% CI: 0.42 – 1.05; 95% PI: 0.23 – 1.70) and senior (SMD = 0.76; 95% CI: 0.35 – 1.17; 95% PI: -2.07 – 3.06) subgroups (figure 5). The between-subgroup differences were statistically different ($p = 0.011$). Heterogeneity decreased in the junior ($I^2 = 31.58\%$) and adult ($I^2 = 63.97\%$) subgroups but remained high for the senior ($I^2 = 91.95\%$) subgroup.

****Figure 5 near here****

Finally, large effect sizes were found in the early starter (SMD = 0.92; 95% CI: 0.69 – 1.50; 95% PI: 0.15 – 1.43) subgroup, whilst medium effect sizes were found in the late starter (SMD = 0.76; 95% CI: 0.33 – 1.19; 95% PI: -2.07 – 3.06) subgroup (figure 6). The difference between both subgroups was statistically significant ($p = 0.003$). Heterogeneity became lower for the early starter ($I^2 = 59.40\%$) subgroup but remained high for the late starter ($I^2 = 91.95\%$) subgroup.

****Figure 6 near here****

Discussion

The first objectives of this meta-analysis was to quantify the magnitude of upper extremity BMC asymmetries in tennis players. The overall meta-analysis showed a large and statistically significant effect of upper extremity dominance on BMC (SMD = 0.85) in tennis players, with higher BMC values for the dominant compared to the non-dominant arm. These BMC asymmetries result from mechanical loading being imposed

on the dominant upper extremity provoked by muscle contractions, torsional forces and racket vibrations during the execution of the different tennis strokes (Ducher et al., 2005b). The mechanically loaded bones adapt by locally increasing BMC resulting in an increased cortical thickness. Mechanical loading will also result in an increased mineral apposition and endosteal bone resorption which will displace the bone's centre of the cortex further away from the neutral axis. This mechanism is known as Frost's "mechanostat theory" and will result in stronger bones, showing greater resistance to torsion and breaking (Ruff & Hayes, 1988).

The second objective of this meta-analysis was to examine the influence of sex, chronological age and starting age on the magnitude of BMC asymmetry in tennis players. The three subgroup meta-analyses were also performed in an attempt to explain part of the observed high heterogeneity of the main analysis since an I^2 value of 73% indicated that about 73% of the observed variance results from the true between-study variance. Hence, around 27% of the resulting variance is due to random error or sampling error and would probably disappear if very large sample sizes were used. The first subgroup meta-analysis indicated large effect sizes within the male subgroup but medium effect sizes in both the female and mixed subgroup, while between-group differences were statistically significant. Interestingly, several included studies reported a more pronounced upper extremity BMC asymmetry in males compared to females (Ducher et al., 2005b; Ducher et al., 2006; Ireland et al., 2014). Several possible explanations are reported in the literature. Firstly, males tend to have more lean mass compared to females which will, in turn, influence the "mechanostat theory" and increase BMC (Tyrovola, 2015). Secondly, male tennis players are inclined to have a higher training intensity and achieve higher ball speeds leading to more mechanical loading being imposed on the dominant upper extremity (0'Donoghue & Ingram, 2001). And finally, periosteal apposition is stimulated

297 in males during puberty, whilst it is inhibited in females by oestrogen at the onset of
298 menarche (Nieves et al., 2005). As a result, female tennis players seem to adapt less
299 effectively to mechanical loading (Nieves et al., 2005). Heterogeneity decreased in the
300 male and mixed subgroup, whilst it remained high in the female subgroup. The latter
301 finding may result from the low degree of consistency of the individual studies' outcomes
302 related to the female subgroup. On the contrary, consistency was high in the male
303 subgroup (i.e. every study reported significant upper extremity BMC asymmetries
304 favouring the dominant upper extremity).

305 The subgroup meta-analysis of junior, adult and senior tennis players showed large
306 and medium pooled within-group effect sizes with statistically significant between-group
307 differences. Interestingly, heterogeneity remained high for the senior subgroup, whilst it
308 decreased for the junior and adult subgroup. A possible explanation is the low number of
309 studies ($n = 4$) included in the senior subgroup. Furthermore, Nara-Ashizawa et al. (2002)
310 reported no significant difference in BMC between the dominant and non-dominant
311 radius in senior female tennis players. However, it should be noted that these participants
312 only started to play tennis in their adulthood as the reported mean starting age was 35
313 years. The smaller upper extremity BMC asymmetries in senior tennis players may
314 partially be explained by the reduced osteogenic response to mechanical loading starting
315 from the third decade of life. Furthermore, BMC is known to decrease with age (Riggs et
316 al., 2004). This is especially the case in senior women since a decrease in oestrogen levels
317 following the onset of menopause is associated with an even further decrease in BMC
318 (Ireland et al., 2014). Specifically for the junior tennis player subgroup, two effect sizes
319 reported no significant BMC asymmetries in young, prepubertal, tennis players (Bass et
320 al., 2002; Ducher et al., 2006). Interestingly, the population in these studies were either
321 mixed or exclusively female.

The early starter subgroup showed large effect sizes, whilst the late starter subgroup showed medium effect sizes with a statistically significant between-group difference. Early starters (i.e. those who started playing tennis before puberty onset) are known to have a higher bone responsiveness to mechanical loading (Ducher et al., 2005a). Hence, in early starters bone mass and geometry adapt more easily to mechanical loading compared to older starters. Accordingly, Ducher et al. (2005a) reported a negative correlation between starting age and upper extremity BMC asymmetries. Furthermore, 50 to 75% of the interlimb asymmetries are likely to develop before or during puberty, whilst even a decrease in activity cannot diminish these adaptations (Kontulainen et al., 1999; Sanchis-Moysi, Dorado, Olmedillas, Serrano-Sanchez, & Calbet, 2010b). Similarly, Kannus et al. (1995) reported that upper extremity BMC asymmetries in female tennis (and squash) players were two times greater if play began before the onset of menarche compared to after menarche. In the present study, heterogeneity remained high for the late starters only. A possible explanation is that only four effect sizes could be included in the late starter subgroup, whilst 19 effect sizes could be included in the early starter subgroup. It should also be noted that the cut-off values to divide the tennis players in early or late starters based on their mean reported starting age were arbitrary.

Due to the observed large variability reported in the included studies for playing experience or training volume, it was decided to omit these factors for further subgroup analyses. Nevertheless, it could be hypothesised that a longer playing experience and higher training volume will elicit higher mechanical loading on the dominant upper extremity and, therefore, greater upper extremity BMC asymmetries. However, in the study performed by Ducher et al. (2005a) playing experience did not correlate with side-to-side differences in upper extremity bone mass parameters. A higher training volume, on the other hand, was indeed associated with greater BMC asymmetries in previously

performed studies (Ducher, Daly, & Bass, 2009; Ireland et al., 2013; Sanchis-Moysi, Olmedillas, Serrano-Sanchez, & Calbet, 2010a). As such, Sanchis-Moysi et al. (2010a) reported that the BMC asymmetry magnitudes depend on the tennis players' training frequency. Similarly, the young male participants in the Ireland et al. (2013) study displayed a greater BMC asymmetry (i.e. S.I. was 30.2%) compared to previously performed studies. The authors attributed this finding to the relatively high training volume (i.e. 10.8 ± 3.7 training hours per week) of the participants. Future research is needed, however, to further clarify the influence of playing experience and training volume on upper extremity BMC asymmetries in tennis players.

To the authors' knowledge this is the first systematic review and meta-analysis, which was conducted using the PRISMA guidelines, to examine the magnitude of BMC asymmetries in tennis players. Furthermore, the influence of sex, chronological age and starting age of playing tennis on these asymmetries was examined. Nevertheless, several limitations can be identified that should be addressed in future research. Firstly, the results of the subgroup analyses in the context of this meta-analysis should be discussed with caution since randomisation was broken in the subgroup analyses and causality can, therefore, not be discussed. Secondly, the risk of bias assessment indicated the inability of a lot of studies to measure the exposure in a valid and reliable way, to identify confounding factors and to implement strategies to deal with these confounding factors. This led to high risk of performance (i.e. systematic differences between groups), detection (i.e. differences in how outcomes were assessed) and attrition bias (i.e. systematic differences in withdrawal) which could, in turn, explain why heterogeneity in several subgroup analyses remained high (Moola et al., 2017). Thirdly, the included studies either examined the whole upper extremity or only several parts of it. Responses to chronic unilateral loading are, however, reported to be site specific due to differences

372 in bone composition (i.e. trabecular versus cortical bone) and loading conditions
373 (Haapasalo et al., 2000). Nevertheless, this meta-analysis calculated an average value if
374 a study examined several skeletal sites and, therefore, was unable to differentiate between
375 the different sites since the percentage of cortical versus trabecular bone as well as the
376 different behaviour from bone type was not taken into account. Further, it was not
377 possible to examine the influence of playing experience and training volume on the
378 magnitude of BMC asymmetries due to the high reported variation. Therefore, to examine
379 the influence of playing experience and training volume on BMC asymmetries future
380 research should have less variation regarding these parameters. Finally, in case of using
381 mixed groups, the authors should always mention the exact number of males and females
382 (i.e. sex ratio) or report sex-specific results.

383 Only one included study reported BMC values of the lower extremities alongside
384 those of the upper extremities in tennis players (Sanchis-Moysi et al., 2010b). Although
385 this study did not report significant lower extremity BMC asymmetries, it should be noted
386 that the participants of that particular study were quite young (10.6 ± 1.0 years).
387 Interestingly, a study reported that bone mineral density showed a tendency to be greater
388 in the left leg (i.e. the tennis players are right-handed) compared to the right suggesting
389 that the left leg supports more mechanical stress, perhaps due to its role in
390 counterbalancing the rotational torques generated when hitting the ball with the right arm
391 (Calbet, Moysi, Dorado, & Rodriguez, 1998). Nevertheless, future research should
392 examine if BMC asymmetries occur in the lower extremity of tennis players as well.

393 **Conclusion**

394 In tennis players, BMC was found to be significantly higher in the dominant upper
395 extremity compared to the nondominant upper extremity showing a large effect size. The

three subgroup analyses, which examined the influence of sex (i.e. males versus females), chronological age (i.e. junior versus adult versus senior tennis players) and starting age (i.e. early versus late starters), all showed medium to large effect sizes and statistically significant between-group differences. Nevertheless, future research is warranted to determine the influence of training load and playing experience on these BMC asymmetries. Furthermore, possible BMC asymmetries in the lower extremity of tennis players should be examined as well.

Disclosure of interest

The authors report no conflict of interest

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524

525 Table 1. Overview of the included studies (n = 15).

526 Table 2. Overview of the results from the risk of bias assessment using the Johanna
527 Briggs Institute critical appraisal tool for Analytical Cross-sectional Studies.

528 Table 3. Overview of the results from the risk of bias assessment using the Johanna
529 Briggs Institute critical appraisal tool for Cohort Studies.

530

531 Figure 1. flow chart of the screening process.

532 Figure 2. Risk of bias of the included studies.

533 Figure 3. Forrest plot of the upper extremity bone mineral content asymmetries in tennis
534 players. The diamond at the bottom represents the overall weighted Standardised Mean
535 Difference (SMD = 0.85) and its 95% CI [0.67 – 1.03]. *Bone mineral content was
536 measured using peripheral Quantitative Computed Tomography.

537 Figure 4. Subgroup analysis based on sex (males versus females versus mixed tennis
538 players). *Bone mineral content was measured using peripheral Quantitative Computed
539 Tomography.

540 Figure 5. Subgroup analysis based on chronological age (junior versus adult versus
541 senior tennis players). *Bone mineral content was measured using peripheral
542 Quantitative Computed Tomography.

543 Figure 6. Subgroup analysis based on starting age (early versus late starters). *Bone
544 mineral content was measured using peripheral Quantitative Computed Tomography.