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**Title:** Accelerometer-based osteogenic indices, moderate-to-vigorous and vigorous physical activity, and bone traits in adolescents

**Year:** 2022

**Version:** Published version

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**Please cite the original version:**

Haapala, Eero, A., Rantalainen, Timo, Hesketh, Kylie D., Rodda, Christine P., Duckham, Rachel L. (2022). Accelerometer-based osteogenic indices, moderate-to-vigorous and vigorous physical activity, and bone traits in adolescents. *Journal of Musculoskeletal and Neuronal Interactions*, 22(4), 514-523. [https://www.ismni.org/jmni/pdf/90/jmni\\_22\\_514.pdf](https://www.ismni.org/jmni/pdf/90/jmni_22_514.pdf)

## Original Article

# Accelerometer-based osteogenic indices, moderate-to-vigorous and vigorous physical activity, and bone traits in adolescents

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## Abstract

**Objectives:** We investigated the associations of accelerometry-derived osteogenic indices (OIs), moderate-to-vigorous (MVPA), and vigorous intensity physical activity (VPA) with peripheral quantitative computed tomography (pQCT) parameters in 99 adolescents aged 10–13 years. **Methods:** Bone parameters were assessed at the distal (4%) and shaft (66%) of the tibia using pQCT. Accelerometers were worn on the right hip for 7 consecutive days. OIs were calculated based on acceleration peak histograms either using all of the peaks (OI) or peaks with acceleration  $\geq 5.2$  g (HOI). MVPA and VPA were defined using previously published cut-points. **Results:** HOI was positively associated with total area (Partial correlation= 0.22, 95% CI=0.01 to 0.41), cortical area (CoA) (0.33, 95% CI=0.13 to 0.50), and stress strain index (SSI) (0.29, 95% CI=0.09 to 0.47) of tibial shaft and with total density at the distal tibia (0.23, 95% CI=0.02 to 0.42). OI was positively associated with CoA (0.31, 95% CI=0.11 to 0.49) and SSI (0.26, 95% CI=0.05 to 0.44) of tibial shaft. MVPA was positively associated with CoA (0.28, 95% CI=0.07 to 0.46) of the tibial shaft. **Conclusions:** OI and HOI were positively associated with pQCT parameters while MVPA and VPA demonstrated less consistent associations with them.

**Keywords:** Accelerometer, Children, Exercise, Paediatric, Skeletal

## Introduction

Adequate skeletal loading and a healthy diet during childhood and adolescence together with the sufficient sex-hormone concentrations in adolescence are required to optimise bone health and to minimise the risk of developing

osteoporosis and associated fractures later in life<sup>1</sup>. The adolescent growth spurt, occurring in early puberty in girls and late puberty in boys, in particular has been identified as a window of opportunity to improve bone strength with appropriate skeletal loading such as high-impact exercise<sup>2,3</sup>. Bone response to mechanical loading through exercise depends on the magnitude and rate of a single loading cycle, the number of loading cycles in a bout, and the recovery between loading bouts<sup>4</sup>. Bone also responds more dynamically to atypical loading such as through multi-directional movement patterns. However, loading direction is typically ignored when considering osteogenicity of an exercise regimen<sup>5-7</sup>, presumably due to the practical difficulty in establishing the loading direction of a given exercise<sup>8,9</sup>.

Previous studies on the associations of accelerometry-derived measures of physical activity (PA) have reported mixed findings, with both positive and null associations

The authors have no conflict of interest.

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Edited by: G. Lyrītis

Accepted 13 June 2022



observed between PA and bone traits assessed by peripheral quantitative computed tomography (pQCT) and dual-energy x-ray absorptiometry (DXA) in children and adolescents<sup>10</sup>. The results of previous studies suggest that the amount of moderate-to-vigorous PA (MVPA), or vigorous-intensity PA (VPA) is positively associated with skeletal robustness<sup>11,12</sup> but the evidence is equivocal<sup>4</sup>. The reason for these mixed findings may be that the cut-points for MVPA and VPA in previous studies have been created with the metabolic cost of PA in mind rather than mechanical loading required to produce physiological bone adaptations<sup>13-15</sup>. Therefore, the role of PA intensity and the most appropriate analysis method for accelerometry data in relation to pQCT parameters in observational studies remains unclear.

Although bone responds to the product of load magnitude and rate, Turner and Robling proposed that it suffices to measure just the load magnitude to capture specific osteogenic loads in free-living humans<sup>7</sup>. This is presumably because high load magnitudes are difficult to achieve in the absence of a high loading rate. Moreover, defining 'bouts' of loading is difficult in free-living data, and recovery between loading bouts tends to be ignored when evaluating osteogenicity from accelerometry. With the above in mind, Ahola and colleagues developed and validated a bone physiology-based loading estimate assessed from free-living accelerometry in premenopausal women (referred to by these authors as "Daily Impact Score" but we will refer to it as osteogenic index [OI] keeping with Turner and Robling's<sup>7</sup> terminology)<sup>4,16</sup>. OI takes the magnitude and number of acceleration peaks into account, thereby presenting a more specific evaluation of the osteogenic stimulus compared to the other accelerometry-based load estimates mentioned above, namely, looking at minutes spent in moderate- to vigorous- or vigorous-intensity physical activities<sup>11,17</sup>. This OI has been shown to be associated with the bone responses (femoral neck assessed with DXA) in two independent year-long randomised controlled trials, one in pre-<sup>4,16</sup> and the other in postmenopausal women<sup>5</sup>. Deere and colleagues further simplified the approach by considering any local maxima in the acceleration signal as opposed to identifying continuous peaks above a given threshold<sup>18-20</sup>. They showed that this approach is associated with bone traits in a cross-sectional dataset of older adults, but utilised a histogram-based approach rather than describing the load with an index<sup>20</sup>. Based on this strong evidence from adults it could be assumed that OIs will also be positively associated with bone traits among adolescents<sup>21,22</sup> and that the associations between OIs and pQCT parameters will be stronger than the associations of MVPA and VPA with pQCT parameters. As approximately 90% of adult bone<sup>23</sup> is developed during the adolescent period, the positive associations of OI may be further impacted by the rapid changes in bone physiology observed during this critical growth period.

Considering the strong link to the underlying bone physiology<sup>4,16</sup>, Ahola's OI is seemingly a promising method to be used as an osteogenic load monitoring tool. However, its validity has not been established among adolescents, who

have the capacity to derive a robust skeletal response from an osteogenic loading intervention<sup>2</sup>. Therefore, the purpose of the present study was to evaluate the criterion validity of accelerometer assessed OI in adolescents by exploring the association between OI and pQCT parameters. A secondary purpose was to evaluate whether accelerometry-derived OIs, MVPA, and VPA were differentially associated with pQCT parameters in adolescents.

## Materials and methods

### Participants

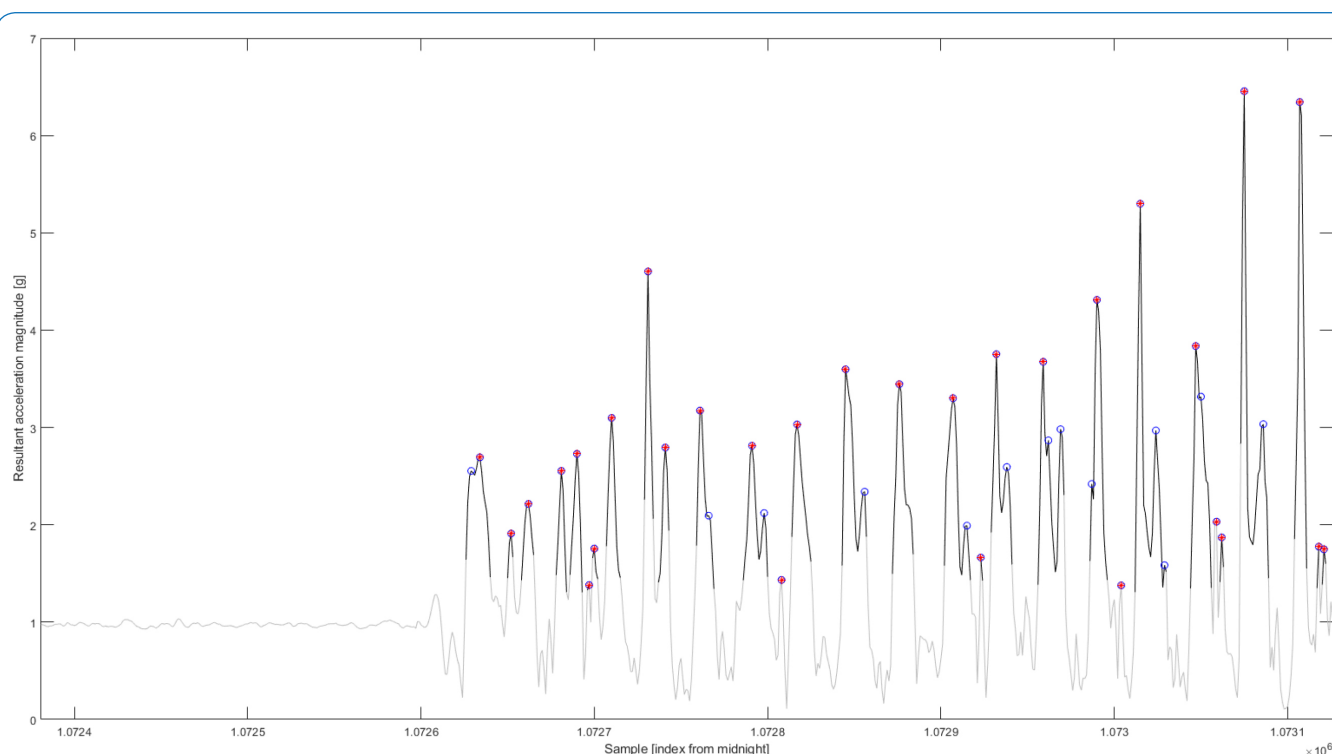
Adolescents aged 10-13 years from the longitudinal Healthy, Active Preschool & Primary Years (HAPPY) study cohort<sup>24</sup> were invited to participate in the present study. Of the 450 who participated in the study in 2016, a subsample of 208 with consistently low or high sedentary behaviour over the past three to six years were invited to participate in the bone health sub study to assess bone and muscle health<sup>24,25</sup>. Out of the 208 invited to take part, 118 indicated interest and after excluding individuals with past bone fractures a total of N=99 (girls N=45, boys N=54) participated. The children with bone fractures were excluded because recovery from bone fractures cause significant changes in bone geometry that are more marked than that of loading-induced adaptations<sup>26</sup>. The study protocol was approved by the Deakin University Human Research Ethics Committee (HEAG-H 88\_2016), and conducted in accordance with the Declaration of Helsinki. Prior to participating written informed consent was provided by the parent/guardian and verbal assent by the child.

### Assessment of bone traits

Bone traits were evaluated in the University Clinic with pQCT from the non-dominant lower leg (tibia and fibula). Two scans (slice thickness 2.3 mm, in-plane voxel size 0.4 x 0.4 mm, scanning speed 30 mm/s, XCT 3000, Stratec Medizintechnik GmbH, Pforzheim, Germany) were obtained from the lower limb at 4% and 66% of tibial from the distal joint cleft towards the proximal end, respectively. If excessive movement was noticed during scanning one re-scan attempt was made. We used the subjective classification scheme based on visual cues caused by motion artefact (e.g., streaking, discontinuity of cortical shell) which have been described and presented previously by Rantalainen et al.<sup>27</sup>, to classify the scans into acceptable/failed and only acceptable scans were considered further. At the 66% bone sites stress-strain index (SSI [mm<sup>3</sup>]), cortical area (CoA [mm<sup>2</sup>]), and total area (ToA [mm<sup>2</sup>]) were calculated using a threshold of 480 mg/cm<sup>3</sup><sup>28</sup>. Cortical density (CoD [mg/cm<sup>3</sup>]) was calculated using a threshold of 710 mg/cm<sup>3</sup><sup>28,29</sup>. SSI was calculated as:

$$\sum_{i=1}^n \frac{r_i^2 \times D_i \times dA}{r_{\max} \times 1200 \text{ mg/cm}^3}$$

where where  $i$  is the index of voxel,  $n$  is the number of voxels,  $D_i$  is the density of voxel  $i$  (in mg/cm<sup>3</sup>),  $dA$  is the area of voxel (=0.25 mm<sup>2</sup>),  $r_i$  is the distance of voxel  $i$  from the area center of mass (in mm), and  $r_{\max}$  is the distance of the furthest voxel



**Figure 1.** Accelerometry processing strategy. Note: Grey, resultant magnitude; black, the continuous acceleration peaks above 1.3 g with the peak value indicated with the red dots, as per the Ahola et al.<sup>4</sup>; blue dots, >1.3 g local maxima per the Hannam et al.<sup>20</sup>.

from the area center of mass (in mm)<sup>30</sup>. At the 4% bone sites compressive bone strength index (BSI<sub>d</sub> [g/cm<sup>4</sup>]), total area (ToA [mm<sup>2</sup>]) and total density (ToD [mg/cm<sup>3</sup>]) were calculated using a threshold of 169 mg/cm<sup>3</sup><sup>31</sup>. Bone analyses were completed using the BoneJ<sup>32,33</sup> ImageJ<sup>34</sup> plug-in. For this analysis tibial bone shaft SSI was considered the primary outcome variable<sup>35</sup> as it is indicated that mechanical loading through PA has the greatest impact on bone strength traits. Secondary outcome measures CoA and COD are also reported in this analysis due to their strong determinant of strength.

### Accelerometry

All participants were asked to wear Actigraph accelerometer (sampling tri-axial accelerations at 100 Hz with  $\pm 6$  g range and 12 bit analog-to-digital conversion; ActiGraph LLC, Pensacola, FL, USA) on an elastic belt on their waist in line with the right thigh. Accelerometers were worn for a period of 7 consecutive days during every waking hour excluding water-based activities (e.g., swimming, bathing). The accelerometers were pre-calibrated according to the manufacturer's instructions before the participants were fitted with the accelerometers. Waist-worn accelerometer-measured accelerations have been shown to correspond to force plate-measured ground reaction forces during normal everyday tasks such as walking, running, and skipping<sup>36</sup>.

The waist-worn accelerometer was therefore considered to provide a reasonable estimate of lower body skeletal loads produced when exercising. During the clinical visit participants were fitted and instructed how to wear the accelerometers, and provided with a reply-paid padded envelope to mail the accelerometers back on the eighth day after visiting the University premises.

Resultant acceleration was used in all analyses, and no filtering was applied. Data were analysed in non-overlapping 24-hour epochs. The accelerometer-recorded time stamps were used to identify midnight, and the first seven midnights were used as a starting point for the seven epochs included for each participant. Any data prior to the first midnight (that is the data accumulated on the day of visiting the clinic), and past the eighth midnight (i.e. the 7<sup>th</sup> 24-hour epoch) were discarded. Each 24-hour epoch was analysed independently.

Non-wear time was defined as any 60 minute epoch with a standard deviation less than 0.024 g (Gravitational acceleration)<sup>37</sup>. Non-wear time analysis was based on 4<sup>th</sup> order zero-lag Butterworth 2 Hz high-pass filtered data using one minute overlapping epochs<sup>38</sup>. Three days with at least 10 hours of wear-time per day has been shown to produce a reliable estimate of physical activity behaviour among children<sup>39</sup> and therefore all days with less than 10 hours of wear-time, and any participants with less than 3 included days were excluded from analyses.

**Table 1.** Descriptive characteristics, physical activity, and osteogenic index.

	Mean (SD)		Between sexes p-value
	Girls (n=45)	Boys (n=54)	
<b>Descriptive characteristics</b>			
Age [year]	12.2 (0.9)	12.2 (0.8)	0.591
Maturity offset [year]	0.42 (1.06)	-1.34 (1.00)	< 0.001
Body mass [kg]	44.0 (11.0)	46.0 (12.5)	0.336
Height [cm]	154 (9)	156 (10)	0.535
Tibial length [mm]	357 (34)	364 (31)	0.247
<b>Physical Activity Intensity</b>			
Moderate- to vigorous [min/day]	100 (34)	136 (44)	< 0.001
Vigorous [min/day]	5.0 (4.3)	11.4 (12.1)	< 0.001
<b>OI</b>			
100 Hz	389 (85)	446 (110)	0.007
<i>P-value reported for main effect of analysis of variance with sex as the between-groups factor; OI = osteogenic index.</i>			

### Osteogenic indices

We implemented three potential ways to define an OI: 1) by utilising the maximum value of each continuous acceleration peak above 1.3 g as per the Ahola et al. approach<sup>4</sup> (OI), 2) utilising local maxima >1.3 g (a local maxima was defined as datum  $x_n$  where  $x_{n-1} < x_n > x_{n+1}$ ) as per the Deere et al. approach<sup>12,18,19</sup> (OI<sub>l</sub>), and 3) utilising only peaks higher than or equal to 5.2 g as per the results of Ahola et al.<sup>4,40</sup>, Deere et al.<sup>41</sup>, and Hannam et al.<sup>20</sup> i.e. OI based on high intensity accelerations (HOI) and HOI defined using the Deere et al. approach (HOI<sub>d</sub>). Accelerometry processing is depicted in Figure 1, where the definition of an impact peak used in the three analytical approaches is visualized. All of these studies reported that only the higher acceleration peaks contribute significantly towards predicting bone traits.

Following the approach presented by Ahola et al.<sup>4</sup> the maximum value of each continuous peak above 1.3 g was recorded, and a histogram with 32 bins from 1.3 to 10.3 g was then calculated in all of the approaches. The histogram bin thresholds were incremented into five thresholds: 1) 0.2 g until 4.29 g, 2) 0.3 g until 6.69 g, 3) 0.4 until 8.29 g, 4) 0.5 g until 10.29 g and 5)  $\geq 10.3$  g. The osteogenic index was calculated as:

$$OI = \sum_{i=threshold}^{32} a_i \ln(N_i + 1)$$

where  $i$  = the index of the histogram bin,  $threshold=1$  for approaches 1 and 2, and 20 (bins  $\geq 5.2$  g) for approach 3,  $a_i$  = the lower threshold of the  $i^{\text{th}}$  histogram bin and  $N_i$  = the number of peaks within the  $i^{\text{th}}$  histogram bin<sup>4</sup>. The mean of all days is reported as the result.

### Moderate and vigorous physical activity

Mean amplitude deviation (MAD)<sup>42</sup> a method previously validated in both children and adults<sup>13,42,45,47,53</sup> was calculated from the resultant acceleration in non-overlapping 5

second epochs, and any epochs falling into the non-wear time were assigned a value of 0. The 5 second epochs were summarised as one minute means (mean of 12 consecutive 5 second epochs)<sup>43</sup> and any one minute values including non-wear time were assigned a value of 0. The number of the one minute values above 0.091 g was recorded as the minutes of MVPA, while the number of minutes above 0.414 g is given as VPA<sup>13</sup>. The mean of all included days is reported as the result. Numerical analyses of the accelerometry signals were conducted with custom-written Matlab (version 8.6.0.267246, R2015B, MathWorks Inc., USA) scripts.

### Other assessments

Height (Holtain limited, Crymych, Pembs., U.K. stadiometer to nearest 0.1 cm), sitting height (Harpenden sitting height stadiometer to nearest 0.1 cm, Holtain limited, Crymych, Pembs., U.K.) and weight (UC-321 A&D Co., Ltd., Tokyo, Japan electronic scales to nearest 0.1 kg) were recorded at the Deakin University Burwood campus clinical laboratory using standardised procedures. An estimation of age at peak height velocity (APHV) was predicted using the method described by Mirwald et al.<sup>44</sup>. The APHV is estimated based on the persons date of birth, height, weight, sitting height, and sex on the day of on the day of assessment<sup>44</sup>. An estimate of the child' maturity offset was then calculated as age minus APHV.

### Statistical analyses

Differences in descriptive characteristics between girls and boys were investigated using analysis of variance with sex as the between-groups factor. Associations of OI, MVPA, and VPA with pQCT parameters were evaluated with partial correlation after accounting for sex and maturity offset. Some data were not normally distributed (particularly MVPA and

**Table 2.** Bone characteristics measured with peripheral quantitative computed tomography.

	Girls	Boys	Between sexes p-value
<b>Tibia 66%</b>	N = 40	N = 49	
SSI [mm <sup>3</sup> ]	1710 (500)	1880 (560)	0.128
CoA [mm <sup>2</sup> ]	266 (48)	290 (60)	0.05
CoD [mg/cm <sup>3</sup> ]	1010 (50)	970 (30)	< 0.001
ToA [mm <sup>2</sup> ]	520 (120)	577 (117)	0.025
<b>Tibia 4%</b>	N = 37	N = 50	
BSId [g/cm <sup>4</sup> ]	0.711 (0.24)	0.819 (0.271)	0.058
ToA [mm <sup>2</sup> ]	843 (197)	865 (212)	0.630
ToD [mg/cm <sup>3</sup> ]	288 (35)	306 (29)	0.0120
<b>Fibula 66%</b>	N = 40	N = 49	
SSI [mm <sup>3</sup> ]	87.9 (31.8)	92.2 (42.7)	0.597
CoA [mm <sup>2</sup> ]	52.5 (10)	52.5 (14.2)	0.991
CoD [mg/cm <sup>3</sup> ]	986 (49)	954 (47)	0.003
ToA [mm <sup>2</sup> ]	64.2 (15.9)	68.2 (21.1)	0.325
<b>Fibula 4%</b>	N = 38	N = 50	
BSId [g/cm <sup>4</sup> ]	0.272 (0.085)	0.282 (0.087)	0.593
ToA [mm <sup>2</sup> ]	116 (29)	121 (36)	0.453
ToD [mg/cm <sup>3</sup> ]	488 (84)	487 (73)	0.982
<b>Radius 66%</b>	N = 42	N = 46	
SSI [mm <sup>3</sup> ]	194 (55)	203 (61)	0.476
CoA [mm <sup>2</sup> ]	69.3 (11.5)	70.1 (14.2)	0.784
CoD [mg/cm <sup>3</sup> ]	1020 (50)	1000 (50)	0.042
ToA [mm <sup>2</sup> ]	100 (23)	111 (30)	0.080
<b>Radius 4%</b>	N = 41	N = 50	
BSId [g/cm <sup>4</sup> ]	0.221 (0.061)	0.224 (0.064)	0.797
ToA [mm <sup>2</sup> ]	238 (78)	249 (64)	0.479
ToD [mg/cm <sup>3</sup> ]	313 (68)	304 (52)	0.460
<b>Ulna 66%</b>	N = 41	N = 46	
SSI [mm <sup>3</sup> ]	257 (83)	283 (88)	0.162
CoA [mm <sup>2</sup> ]	88.5 (16.8)	91.5 (17.8)	0.412
CoD [mg/cm <sup>3</sup> ]	1040 (50)	1000 (50)	< 0.001
ToA [mm <sup>2</sup> ]	127 (29)	145 (40)	0.015
<b>Ulna 4%</b>	N = 42	N = 50	
BSId [g/cm <sup>4</sup> ]	0.12 (0.033)	0.126 (0.031)	0.329
ToA [mm <sup>2</sup> ]	105 (26)	106 (23)	0.822
ToD [mg/cm <sup>3</sup> ]	343 (67)	349 (55)	0.650

*P*-value reported for main effect of analysis of variance with sex as the between-groups factor; SSI = stress strain index; CoA = cortical area; CoD = cortical density; ToA = total area, BSId = compressive bone strength index; \*Some scans were excluded from the analysis due to excessive motion artefact.

VPA minutes) but no normality correction was applied, and the parametric statistical approaches were applied to this data as well because non-parametric methods do not allow adjustments for co-variates. Repeated measures ANOVA with two within-subject factors (sampling rate or peak detection method, and histogram bin) was used to evaluate the effects of sampling rate and peak detection method on detected acceleration peaks. Missing data were excluded in a pairwise manner per analysis. Statistical significance was set at  $p \leq 0.05$ , and the analyses were executed using project R

(64-bit version 3.4.3, www.r-project.org) and IBM SPSS (64-bit version 24.0.0.2, IBM corp., Armonk, NY, USA).

## Results

### *Characteristics of participants and agreement between methods*

Descriptive characteristics, physical activity, and OI are shown in Table 1. Girls had a higher maturity offset, lower PA levels, and lower OI compared to boys ( $P < 0.001$  to  $P = 0.007$ ).

**Table 3.** Partial correlations controlled for sex and maturity offset (95% confidence interval) between OI, HOI, moderate- to vigorous- and vigorous intensity physical activity minutes, and bone traits of the bone shafts and distal bone sites.

	OI	HOI	Moderate- to vigorous-intensity physical activity	Vigorous-intensity physical activity
<b>Tibia 66%</b>				
ToA	0.19 (-0.02 to 0.38), P=0.092	<b>0.22 (0.01 to 0.41), P=0.045</b>	0.18 (-0.02 to 0.38), P=0.095	0.10 (-0.11 to 0.30), P=0.388
CoA	<b>0.31 (0.11 to 0.49), P=0.004</b>	<b>0.33 (0.13 to 0.50), P=0.003</b>	<b>0.28 (0.07 to 0.46), P=0.011</b>	0.20 (-0.01 to 0.39), P=0.073
CoD	-0.08 (-0.28 to 0.13), P=0.473	-0.06 (-0.27 to 0.15), P=0.574	-0.09 (-0.30 to 0.12), P=0.404	-0.01 (-0.22 to 0.19), P=0.899
SSI	<b>0.26 (0.05 to 0.44), P=0.019</b>	<b>0.29 (0.09 to 0.47), P=0.007</b>	0.21 (0.00 to 0.40), P=0.058	0.15 (-0.06 to 0.34), P=0.185
<b>Fibula 66%</b>				
ToA	0.04 (-0.17 to 0.24), P=0.739	0.09 (-0.12 to 0.30), P=0.394	-0.03 (-0.24 to 0.18), P=0.776	0.03 (-0.18 to 0.24), P=0.794
CoA	0.00 (-0.20 to 0.21), P=0.975	0.06 (-0.15 to 0.27), P=0.562	-0.09 (-0.29 to 0.12), P=0.435	-0.01 (-0.22 to 0.20), P=0.941
CoD	-0.17 (-0.36 to 0.04), P=0.128	-0.16 (-0.36 to 0.05), P=0.138	-0.12 (-0.32 to 0.09), P=0.271	-0.06 (-0.27 to 0.15), P=0.579
SSI	0.01 (-0.20 to 0.22), P=0.942	0.07 (-0.14 to 0.27), P=0.532	-0.07 (-0.27 to 0.14), P=0.551	-0.01 (-0.22 to 0.19), P=0.898
<b>Tibia 4%</b>				
ToA	0.01 (-0.20 to 0.22), P=0.938	0.05 (-0.17 to 0.26), P=0.677	-0.01 (-0.22 to 0.20), P=0.925	-0.00 (-0.21 to 0.21), P=0.979
ToD	0.19 (-0.02 to 0.38), P=0.095	<b>0.23 (0.02 to 0.42), P=0.043</b>	0.16 (-0.05 to 0.36), P=0.142	0.15 (-0.07 to 0.35), P=0.190
BSId	0.10 (-0.11 to 0.31), P=0.356	0.16 (-0.06 to 0.36), P=0.164	0.08 (-0.13 to 0.29), P=0.472	0.06 (-0.15 to 0.27), P=0.584
<b>Fibula 4%</b>				
ToA	0.03 (-0.18 to 0.23), P=0.820	0.08 (-0.13 to 0.29), P=0.457	-0.05 (-0.26 to 0.16), P=0.653	-0.07 (-0.28 to 0.14), P=0.520
ToD	0.03 (-0.18 to 0.24), P=0.770	0.02 (-0.19 to 0.23), P=0.825	0.08 (-0.14 to 0.28), P=0.494	0.14 (-0.07 to 0.34), P=0.217
BSId	0.03 (-0.18 to 0.24), P=0.759	0.08 (-0.13 to 0.28), P=0.489	0.01 (-0.20 to 0.22), P=0.928	0.08 (-0.13 to 0.28), P=0.488

OI=osteogenic index; HOI=osteogenic index based on peaks with acceleration  $\geq 5.2$  g; SSI=stress strain index; ToA=total area; CoA=cortical area; CoD=cortical density; Bold font indicates  $p \leq 0.05$ .

Bone characteristics were similar between boys and girls with the exception of girls having higher CoD than boys on all bone shaft sites, and a smaller ToA on the tibial and ulnar shaft than the boys ( $P < 0.001$  to  $P = 0.025$ ) (Table 2).

#### Peak detection on the OI and HOI

OI and  $OI_p$  were strongly positively associated with each other, as were HOI and  $HOI_p$  (all  $r = 1.00$ ,  $p < 0.001$ ), although the Deere et al.<sup>41</sup> peak identification method values were systematically higher than the Ahola et al.<sup>4</sup> peak identification method values (repeated measures ANOVA indicated main effects for peak detection method and peak detection method  $\times$  histogram bin interaction, all  $P < 0.001$ ). To limit the number

of statistical tests only results from the Ahola et al.<sup>4</sup> method OI and HOI were used in the analyses.

#### Physical activity and bone characteristics

After controlling for sex and maturity offset in all analyses partial correlation analysis indicated that OI was positively associated with Tibial shaft CoA and SSI. HOI was positively associated with tibial shaft ToA, CoA, and SSI and distal tibia ToD. MVPA, but not VPA was positively associated with tibial shaft CoA. Neither MVPA nor VPA were associated with any of the distal pQCT parameters of the tibia or ulna shaft (Table 3).

## Discussion

The primary finding of this study was that OI and HOI had moderate positive associations with tibial SSI as estimate of bone strength, that was our primary pQCT outcome, and ToA and CoA in adolescent boys and girls after accounting for maturity status and sex. In contrast, MVPA and VPA had very few and weak associations with bone traits. These results suggest that OI and HOI produces a meaningful assessment of osteogenic loads in adolescents during the rapid growth of the bone mass and thus could be used as an efficient osteogenic load monitoring measure.

The present findings in adolescent boys and girls showing a positive association with OI and lower limb bone traits is in line with the previous literature in adult women<sup>4,5</sup> and research indicating that low-intensity peaks are less relevant for overall bone osteogenic load estimation in adults and older adults<sup>4,20,41</sup>. Similarly, our findings also correspond to previous findings from cross-sectional<sup>12,46</sup> and intervention studies<sup>6,48</sup> in children and adolescents showing that particularly high intensity accelerations and high impact exercise are positively associated with bone traits. More precisely, OI and HOI were associated with bone strength, total area, and cortical area, suggesting that high impact exercise could have wide benefits on tibial bone traits. However, in contrast to previous studies reporting the positive associations between MVPA, VPA, and bone traits<sup>10,11,49</sup>, we found weak if any association between them. Nevertheless, the magnitude of the associations of MVPA and VPA with bone traits including SSI in the present study are similar to the ones reported by Kehrig et al.<sup>46</sup>. Cut-points for MVPA and VPA used in the present and previous studies have been created using the metabolic cost of PA<sup>13–15</sup> and therefore it is possible that previous studies have not fully elucidated the role of high-impact osteogenic PA on bone health in youth. Therefore, these results together suggest that high-intensity impacts should be considered when reporting accelerometry data related to bone traits among adolescents.

As HOI describes osteogenic loading with a single number, it may be easier to interpret compared to reporting the whole acceleration peak histogram. This makes it more useful in the applied setting, providing unambiguous feedback immediately after a bout of loaded exercise or athletic performance. Based on the present findings we propose that osteogenic loading could be monitored using a hip- or waist-worn accelerometer by utilising HOI (or HOI<sub>g</sub>). Both methods can be computed from raw accelerometry data routinely used to define cut-points for MVPA and VPA, and the measures are computationally simple enough to be used in near real-time applications, for example immediately following an exercise set. OI takes the magnitude and number of acceleration peaks into account, thereby presenting a more specific evaluation of the osteogenic stimulus compared to traditional method to quantify MVPA and VPA<sup>17,50</sup>. OI has been shown to be associated with the bone responses (femoral neck assessed DXA) in two independent year-long

randomised controlled trials, one in pre-<sup>4,16</sup> and the other in postmenopausal women<sup>5</sup>. Therefore, using HOI instead of external load, minutes spent in MVPA or VPA, or number of repetitions completed would enable fully osteogenically informed exercise progression, and dose estimation in adolescents. In addition, although the prevalence of stress fractures are increasing in youth<sup>51</sup>, a safe osteogenic load for adolescents are yet to be established. HOI could be used towards this end by at least monitoring the amount of accumulated osteogenic loading during the optimal growth period to reduce the risk of growth associated bone injury. It is well-established that stress-fractures are associated with the accumulated osteogenic load, e.g., limiting the amount of high loading physical training proved the only effective way to minimise the number of stress-fractures among Israeli military conscripts from eight different interventions (adequate sleep, more comfortable boots, and access to physical therapy had no impact)<sup>52</sup>. Moreover, similar load monitoring during the adolescence with a simple osteogenic monitoring tool may help to identify those adolescence at higher risk of injury.

The strengths of this study include a valid assessment of habitual PA and pQCT parameters and the ability to control the data for maturity. Although there are strengths of this study we do identify a number of limitations which are as follows. First, due to the cross-sectional study design, causality could not be established between the osteogenic loads and pQCT parameters. The rationale of the study rests on the fact that the prudence and validity of accelerometer-based OIs has been rigorously established among adults in prospective studies<sup>4,5,16</sup>. The chosen threshold to define MVPA and VPA could have impacted the associations observed in this study with the pQCT parameters. While available evidence has not firmly indicated an optimal set of intensity cut-offs<sup>53,54</sup>, future studies should consider investigating whether the associations between PA and pQCT parameters are dependent on the chosen intensity cut-offs. Second, no statistical adjustments were made for the multiple partial correlations evaluated in the present study and therefore some statistically significant associations observed could have been occurred by chance. Third, the age-span included in the study was relatively wide, and some of the participants were pre-pubertal, others peri-pubertal, and some post-pubertal. The growth-spurt and sex hormone-related bone changes may mask some of the skeletal loading-related effects in this sort of heterogeneous adolescent population<sup>1</sup>. Nevertheless, an independent association between pQCT parameters and OI was observed, which increases our confidence in the finding. Fourth, it should be noted that not all bones and bone sites exhibited similar associations with the OI. It is not atypical to find that some bone sites are associated with bone load estimates while others are not and it is in fact a topic of contemporary bone research<sup>55</sup>. It is not possible to further clarify this with the present findings. Finally, we knowingly violated the normality assumptions when analysing the partial correlations between physical activity minutes and pQCT parameters. Non-parametric methods do not allow



for effective adjustments for the important covariates that had to be included in the analyses, and therefore we decided to report this data as well for completeness. Even though this decreases the scientific rigour, it does, in our opinion, nevertheless contribute towards demonstrating that HOI is likely a more specific indicator of osteogenic loading compared to other alternatives among adolescents.

In conclusion, OIs and especially HOI calculated from a 7-day accelerometry recording is a reasonable indicator of skeletal loading among adolescents. Furthermore, OIs may be better indicators of skeletal loading during habitual PA than MVPA and VPA. Longitudinal and intervention studies among children and adolescents are warranted to investigate possible causal relationships of OIs to pQCT parameters and the applied application of this skeletal loading monitoring.

#### Funding

The HAPPY study received funding from the Australian Research Council (DP110101434 & DP140100554). This sub-study was funded by a Deakin University Central Research Grant (2016). KDH is supported by an Australian Research Council Future Fellowship (FT130100637) & Honorary National Heart Foundation of Australia Future Leader Fellowship (100370).

#### Author contributions

RLD, TR, CR and KDH participated the conception of the study. EAH conducted the analyses and produced the first draft of the manuscript. All authors participated in drafting and revising the manuscript, and approved the final version of the manuscript. All authors agree to be accountable for the work and to ensure that any questions relating to the accuracy and integrity of the paper are investigated and properly resolved.

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