



## Research Article

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# Complications of Intravenous Therapy in The Context of Sports: A Literature Review and Strategies for Prevention and Treatment

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## Abstract

**Purpose:** There is a scarcity of reports on the effectiveness of short-term whole-body vibration (WBV) training on bone mineral density (BMD) and bone mineral content (BMC) in young active adults. The purpose of the pilot study was to determine the effectiveness of a short-term (4 weeks) WBV training with 1) 1 session of 20 min/day and 3 days/week of WBV training or 2) 2 sessions of 10 min/day and 3 days/week on BMD, BMC and Hip Structural Analysis parameters in physically active young women and men.

**Method:** Physically active women and men (n= 42, F=31), age 20-31 yr volunteered as study subjects. Subjects were randomly assigned to 1) WBV training 1 session/day of 20 min/day, 3 days/week for 4 weeks (G1, n=21), or 2) WBV training 2 sessions/day with 5 bouts of 2 min on and 1 min off the vibration platform for recovery rest, 3 days/week for 4 weeks (G2, n=21). A vibration platform with a vibration frequency = 40 Hz, and magnitude = 4 g was used for WBV training. Study outcome measurements include BMD and BMC of femoral head, total hip, lumbar spine L1-L4, lower leg, forearm, and Hip Structural Analysis (HSA) parameters assessed with a dual-energy X-ray absorptiometry (DXA).

**Results:** show that 4 weeks of WBV training induced changes in total hip BMD (2.28%, p=0.02) and BMC (4.42%, p=0.004). Significant results obtained from HSA parameters were 1) femoral shaft cross-sectional moment of inertia (FSCSMI) (p=0.02), 2) narrow neck cross-sectional moment of inertia (NNCSMI) (p<0.000), and 3) femoral shaft cortical thickness (FSCORT) (p<0.03).

**Conclusion:** Four-week of WBV training using a high-frequency and low-magnitude protocol is effective for inducing osteogenic response in total hip BMD and BMC and the HSA parameters: FSCSMI, NNCSMI and FSCORT.

**Keywords:** Dual-Energy X-Ray Absorptiometry (DXA); Bone Mineral Density (BMD); Bone Mineral Content (BMC); Hip Structural Analysis (HAS); Osteoporosis; Women and Men

## Introduction

Bone is a metabolically active tissue with complex physiological roles [1]. To ensure that sufficient skeletal mass is appropriately developed to withstand the rigors of human locomotive activities, bone tissue can rapidly accommodate changes in its mechanical environment [1]. This adaptive potential of increased bone mass

has been consistently shown in long-term musculoskeletal impact-loaded exercise training [2-6]. The mechanical signals responsible for regulating bone adaptation are those associated with the most vigorous locomotion of high-impact activity [1]. Rubin et al. (2002) and [2] reported that a strain of 2000–3000  $\mu\epsilon$  mediates bone mass and morphology through regulation of osteoclast and

osteoblast activity within the targeted bone tissue. [7] suggested that mechanical loading on bone is most effective when the loads are applied in discrete bouts, separated by recovery periods. Furthermore, the observed new bone formation was localized to the most biomechanically relevant sites and the newly enhanced structural integrity and fracture resistance bones, appears to spatially optimize the new bone formation [7].

Whole-body vibration exercise has been popularized for enhancing bone mass and structural strength in the past decade and is currently drawing interest from the scientific community. For example, researchers have shown that whole-body vibration (WBV) training can induce favorable results on bone mineral density (BMD) in humans and animal models [8-11]. Vibration is a mechanical oscillation by alteration of force, acceleration and displacement over time and the mechanical vibration signals do not need to apply for long duration to induce osteogenic response [12,13]. Note that vibration exercise is a forced oscillation where energy is transferred from the actuator (the vibration platform) to a resonator (the human body). The vibration exercise device produces oscillations sinusoidal waves described by amplitude (A), frequency (f), and phase angle ( $\phi$ ) [14,15]. Several animal and human studies have shown that the application of low-intensity and high vibration frequency to the muscular skeleton can enhance bone mass and BMD, as well as bone formation rate and mineral apposition rate [11,17,12,18]. In clinical studies it has been reported that high frequency and low-magnitude vibration stimulus can improve BMD in trabecular bone and muscular strength in postmenopausal women and in children with disabling ambulatory conditions [19]. [20] and [16] reported that WBV training has a greater effect on trabecular bone than cortical bone using low-magnitude, high-frequency stimulation. This non-pharmacological, noninvasive WBV intervention modality is safe, well-tolerated and potentially effective for young women to gain bone mass [15], and for persons with senile osteoporosis to strengthen the musculoskeletal system and reduce the risk of fracture during aging [19]. Although WBV is a promising non-drug intervention modality for inducing osteogenic response in humans, there are conflicting reports for young premenopausal and postmenopausal women [21-25]. Sitja-Rabert et al. (2012) concluded that the reason WBV training was ineffective for inducing osteogenic effects at the hip or lumbar spine is related to variability in the applied peak acceleration (vibration frequency in terms of Hz), magnitude of the induced peak acceleration (from 0.1 to 30 g, "g" is the Earth's gravitational force), experimental duration (length of the study), duration of the loading bout, and frequency of loading (number of loading session/day or number of day/week). Other factors that may result in non-significant change in bone mass are age, gender, health history, and physical activity levels [24]. Little is known about the individual roles of these variables for orchestrating the osteogenic response in humans. The purpose of this pilot study is to determine the effectiveness of a 4-week WBV training using two different WBV training protocols consisting of 1) one continuous session of 20 min/day, 3 days/week, and 2) two sessions/day with five intermittent bouts/session consisted of 2-min on and 1-min off the vibration platform for recovery period, 3 days/week on BMD

and BMC as well as Hip Structural Analysis parameters in physically active young women and men. The study hypotheses were 1) two sessions/day with five intermittent bouts/session of 2-min on and 1-min off the vibration platform for recovery period for 20 min/day, 3 days/week for 4 weeks will induce significant increase in BMD and BMC as well as Hip Structural Analyses parameters, and 2) one session/day with a continuous bout/session of WBV training for 20 min/day, 3 days/week for 4 weeks will not induce significant increase in BMD and BMC as well as Hip Structural Analysis parameters.

## Materials and Methods

**Subjects:** A total of 50 physically active women and men, age 20-31 years volunteered as study subjects. The subject inclusion criteria include 1) must be physically active without participated in resistance or strength training for the past 2 years, 2) have a body mass index (BMI) between 18.0 and 32.0 kg/m<sup>2</sup>, 3) females must have normal menstrual cycle (i.e., 9-12 menstrual cycle per year), 4) currently not using any tobacco product or drink alcohol more than 2 drinks a day, and 5) not have participated in WBV exercise or training within the past 12 months. The "physically active" status is defined as participation in only endurance type of physical training, 3-4 days a week for the past 12 months. The exclusion criteria are current or chronic use of any bone antiresorptive, corticosteroid or proton-pump inhibiting drugs, and have had or have any of the following health conditions: 1) a diagnosed cardiovascular, pulmonary, orthopedic, gastrointestinal, liver, and/or kidney disease, 2) pregnant (female subjects, verified by a urine pregnancy test), and 3) any metal implant at the region of interest for the bone densitometry (DXA) scan. Women who use contraceptive drug were accepted as study subjects to encourage and increase participation. Subjects who meet the eligibility requirements as determined by an initial telephone interview were scheduled for a personal face-to-face interview. During the personal interview, written information regarding the purpose of the study, study requirements and potential risks of injury as well as the WBV training protocol (i.e., training frequency and duration) were explained. A written informed consent was obtained from each subject before scheduling for the research study outcome measurements. The informed consent was previously approved by the Institutional Review Board of California State Polytechnic University, Pomona (IRB Cal Poly Pomona). The procedures used in this study adhere to the principles of the Declaration of Helsinki. The subject's health and exercise history information were obtained using a Health and Exercise History Questionnaire (HEHQ). Subjects were randomly assigned to 1) one session/day for a total of 20 min, 3 days a week (G1, N = 21, F=12), or 2) two separated sessions/day with each session include 5 bouts of 2 min on and 1 min off the vibration platform for recovery rest, 3 days a week (G2, n = 21, F= 12). The duration of the WBV training was 4 weeks.

**WBV training protocol:** This study employed an oscillatory alternating displacement vibration platform (DNK Inc. Alhambra, CA) with a vibration frequency = 40 Hz/sec (e.g., high frequency), peak-to-peak displacement of 1.3 mm and aPeak (also known as amplitude) = 4 g (e.g., low magnitude). During the vibration

training, subjects in a natural standing posture stood on the vibration platform with knees bent at about 40° angle, back straight with both feet contacting the platform. All subjects performed the WBV training with athletic shoes. For keeping balance on the vibration platform, subjects are allowed to place their hands on the front railings of the vibration machine. During each WBV training session, G1 subjects performed the WBV training continuously for 20 min without recovery rest period, once a day. G2 subjects performed five bouts of 2 min training on the vibration platform with 1 min off vibration platform for recovery rest, twice a day. For G2, the second session met after at least 2 hours rest between each session. G1 and G2 subjects were allowed 1-2 sessions of vibration practices before WBV training began. All subjects were required to verbally report their daily physical activity for the investigator to ensure that they were not engaging in any extra aerobic exercise or resistance training. To control the effect of dietary calcium placed on bones, subjects were asked not to take any calcium and vitamin D supplements for the entire study period. To promote better compliance and prevent subject drop-out from the study, all subjects were verbally encouraged to full compliance by using weekly personal contact or via personal email message.

**The whole-body vibration device:** Several types of sinusoidal vibration devices are currently available for studying the effect on bone mass and BMD. For the present study, the researchers followed the CONSORT guidelines for reporting whole body vibration treatments [14]. The terms commonly used to describe vibration include frequency and extent of the sinusoidal vibration, which can be given as the displacement from peak-to-peak or the maximum displacement from equilibrium (e.g., peak acceleration). The term “peak-to-peak displacement” is used to indicate the extent of the vibration. Note that vibration or peak acceleration can be mathematically derived from the frequency ( $f$ ) = Hz/sec and  $1 \text{ Hz} = 1/\text{sec}$ . Peak acceleration (m/s) is the maximal rate of change and is expressed as  $a_{\text{Peak}}$ . Most study reports frequency, peak acceleration and peak-to-peak displacement. To facilitate comparisons between studies we provide acceleration levels associated with the vibration as peak acceleration ( $a_{\text{Peak}}$ ) in multiples of Earth's gravity ( $g$ ) and  $g = 9.81 \text{ ms}^{-2}$ . The formula used to calculate  $a_{\text{Peak}} = 2 \times \pi^2 \times f^2 \times D$ , where  $f$  = frequency and  $D$  = peak-to-peak displacement. Example for calculating peak acceleration ( $a_{\text{Peak}}$ ) when vibration with a frequency ( $f$ ) of 40 Hz/sec and a peak-to-peak displacement ( $D$ ) of 1.3 mm is:  $a_{\text{Peak}} = 2 \times \pi^2 \times 1600 \text{ s}^{-2} \times 0.0013 \text{ m} = 41 \text{ ms}^{-2}$ . Expressed as multiple of standard Earth's gravity,  $a_{\text{Peak}}$  (also known as magnitude) in this calculation is  $41 / 9.81 \text{ g} = 4.1 \text{ g}$ . In the present study, we used a vibration device with a frequency = 40 Hz/sec and peak-to-peak displacement of 1.3 mm. The calculated  $a_{\text{Peak}} = 4.1 \text{ g}$ . It should be noted that the actual oscillations generated by the WBV device may significantly deviate from a pure sine waveform. It is possible that the frequency and amplitude generated by the WBV device differ from the preset values or from the values provided by the manufacturer. Another factor that causes device deviation is when the participant is moving his/her body from side to side or swing forward and backward while standing on the WBV vibration platform.

## Study Outcome Measurements

The following outcome measurements were performed at baseline and at the conclusion of the 4-week study.

1. Anthropometry measurements. Participants' standing height (cm) and weight (kg) were measured barefoot in light indoor clothing (T-shirt and shorts). Height was measured using a stadiometer scale and weight (kg) was measured with a calibrated Physician Scale (Detecto, Webb City, MO, USA). Body mass index (BMI, kg/m<sup>2</sup>) was calculated as body mass divided by height squared.
2. Bone densitometry scans. All participants were scanned in the supine position using a dual-energy X-ray absorptiometry (DXA) scanner (Hologic Discovery-QDR, Bedford, MA, USA) for obtaining BMD and Hip Structural Analysis parameters for each subject at the Musculoskeletal Research Laboratory (MRL). The DXA device was calibrated each day using a lumbar spine phantom. One scan was performed for each subject prior to WBV training, and one scan was performed following the conclusion of the WBV training to obtain BMD (g/cm<sup>2</sup>), and BMC (g) of femoral neck (FN), total hip (TH), lumbar spine L1-L4 (LS L1-4), lower leg (LL), forearm (FA) and whole body (WB). The whole-body scan was used to obtain data for fat mass (kg), lean mass (kg) and percentage body fat (%BF). All DXA scans were performed on the non-dominant arm. Analyses were performed using the Hologic software. A single trained and certified DXA operator (MTCL) performed all DXA scans and is blind to the subject's group identity. The participant positioning and analyses of the scanned results were done according to International Society of Clinical Densitometry. A DXA-BMD test-retest reliability study was performed for obtaining coefficient of variance (%CV) which was between 1.0% and 2.9% for lumbar spine and femoral neck, respectively.
3. Hip structural analysis (HSA) parameters were obtained using the Hip Strength Analysis software provided by the Hologic Discovery-QDR densitometer company (Bedford, MA, USA). The HSA software obtained the following hip strength parameters: 1) mineralized hip bone surface cross-sectional area (CSA) (mm<sup>2</sup>) which is equivalent to the cortical area, 2) mineralized hip bone surface cross-sectional moment of inertia (CSMI) (mm<sup>4</sup>) which is an index of structural rigidity, 3) hip section modulus (Z) (mm<sup>3</sup>) which is an indicator of bending strength for maximum bending stress in the direction of the image plane, 4) bucking ratio (BR), 5) cortical thickness (CORT) for narrow femoral neck region (NN), 6) intertrochanteric region (IT), and 7) the proximal femoral shaft (FS). It was recommended that from the HSA parameters, the values of CSMI and Z are the predictive strength of the bone in bending (Beck, 2003; Bonnicksen 2007). The short-term precision percentage coefficient of variance of these variables has been reported to be between 2.4 and 10.1% [28].

## Statistical Analysis

Descriptive data are presented as mean ± standard deviation.

Data was analyzed using SPSS Statistical software (version 20, IBM Corporation, Armonk, NY, USA). Descriptive statistics were run to determine normal distribution using the Kolmogorov-Smirnov test. The significant differences between the mean values of variables in two independent groups (Group 1 and Group 2), and time factors (pre-test and post-test) were determined using two-way ANCOVA. The covariates are age, gender, weight, height, body mass index (kg/m<sup>2</sup>), body fat (kg), lean mass (kg), and percent body fat. All data obtained for BMD, BMC and Hip Structural Analysis parameters were normally distributed. Statistical significance was set at alpha < 0.05.

### Power Analysis for Sample Size Determination

The sample size for a directional hypothesis with a desired power of 0.80 and a significance level at 0.05 were estimated to be 42 participants [29]. The sample size was comparable to that of [22,21] for WBV studies. The use of a sample size of 42 subjects (G1 = 21 and G2 = 21) was needed to detect a training effect of 2.0%

and 0.98% difference in BMD in femoral neck and lumbar spine L1-L4, respectively. We recruited a total of 50 women and men for the study with an anticipated drop-out rate of 15% (n=42).

### Results

Baseline anthropometrics measurements of subjects in G1 and G2 were similar about subject's age (yr) and height (cm), but not their weight ( $p = 0.0001$ ), body mass index (BMI) ( $p = 0.0001$ ), body fat ( $p = 0.0001$ ), lean mass ( $p = 0.0001$ ), and percent body fat ( $p = 0.002$ ) (Table 1). Results show that WBV training induced significant changes between pre-test and post-test in total hip MBD and BMC in G2 subjects, but not in G1. The pre-test to post-test difference in total hip for G2 in BMD of total hip was 1.27% ( $p = 0.02$ ) and BMC of total hip was 4.42% ( $p = 0.004$ ) (Table 2). No statistical differences were observed between pre-test and post-test for G2 in BMD and BMC for femoral neck, trochanter, lumbar spine L1-L4, forearm, lower leg, and whole body.

**Table 1:** Subjects' baseline anthropometry, BMD and BMC data.

Variable		Group 1 (N = 21)	Group 2 (N = 21)	T-test p value*
Age (yr)	mean	22.1	21.5	0.37
	SD	2.3	1.7	
Weight (kg)	mean	44.98	59.87	0.0001
	SD	5.59	7.6	
Height (cm)	mean	159.01	162.45	0.109
	SD	5.88	6.21	
Body Mass index (kg/m <sup>2</sup> )	mean	17.72	22.61	0.0001
	SD	1.26	1.78	
Training History (yr)	mean	2.1	1.8	0.634
	SD	1.2	0.78	
Exercise status (yr)	mean	2.13	1.67	0.115
	SD	0.95	0.66	
Body fat (kg)	mean	11.27	17.89	0.0001
	SD	2.7	4.1	
Lean mass (kg)	mean	32.9	40.46	0.0001
	SD	3.01	4.95	
Percent body fat (%)	mean	25.2	30.4	0.002
	SD	3.9	4.7	
BMD femoral neck (g/cm <sup>2</sup> )	mean	0.7484	0.9718	0.007
	SD	0.136	0.128	
BMC femoral neck (g)	mean	3.2762	4.1094	0.002
	SD	0.792	0.636	
BMD total hip (g/cm <sup>2</sup> )	mean	0.8461	1.0693	0.005
	SD	0.145	0.122	
BMC total hip (g)	mean	24.7493	38.5	0.002
	SD	5.056	10.54	
BMD Lumbar L1-L4 (g/cm <sup>2</sup> )	mean	0.9261	1.0764	0.019
	SD	0.142	0.133	



<b>BMC Lumbar L1-L4 (g)</b>	mean	51.7506	60.0383	0.019
	SD	10.207	9.432	
Abbreviation: BMD, bone mineral density; BMC, bone mineral content;				
*Independent sample T test (2-tailed)				

**Table 2:** Anthropometry and Bone mineral density (BMD) and mineral content (BMC) between pre-test and post-test in group 2.

Gender	N	Pre-test N =21 (F=12)	Post-test N = 21 (F=12)	Paired T-test p value*
Age (yr)	Mean ± SD	22.52 ± 2.14	22.5 ± 2.10	NS
Weight (kg)	Mean ± SD	59.87 ± 7.6	61.13 ± 10.06	0.56
Height (cm)	Mean ± SD	162.45 ± 7.26	162.85 ± 7.20	0.51
Body mass index (kg/m <sup>2</sup> )	Mean ± SD	22.61 ± 1.78	23.8 ± 2.7	0.51
BMD femoral neck	Mean ± SD	0.9718 ± 0.141	0.9674 ± 0.144	0.25
BMD total hip	Mean ± SD	1.0693 ± 0.136	1.0818 ± 0.134	0.02
BMC total hip (g)	Mean ± SD	38.50 ± 10.54	40.20 ± 11.65	0.004
BMD trochanter	Mean ± SD	0.8064 ± 0.119	0.8074 ± 0.110	0.86
BMD lumbar L1-L4	Mean ± SD	1.0764 ± 0.133	1.0878 ± 0.122	0.16
BMD forearm	Mean ± SD	0.8013 ± 0.106	0.7945 ± 0.103	0.29
BMD lower leg	Mean ± SD	1.2383 ± 0.167	1.2405 ± 0.173	0.76
BMD whole body	Mean ± SD	1.2139 ± 0.117	1.2169 ± 0.118	0.46
*Group 2 Pre-test vs Post-test comparison using paired T-test				

**Table 3:** Hip Structural Analysis for narrow neck and femoral shaft parameters between pre-test and post-test in group 2.

		Pre-test	Post-test	Paired T-test p value*
N, Gender		21 (F=12)	21 (F=12)	
Narrow neck cross sectional area (NNCSA)	Mean ± SD	3.2262 ± 0.639	3.2167 ± 0.660	0.836
Narrow neck cross sectional moment of inertia (NNCSMI)	Mean ± SD	2.1810 ± 0.807	6.8519 ± 3.074	0.0001
Narrow neck z	Mean ± SD	1.3795 ± 0.431	1.3800 ± 0.448	0.988
Narrow neck cortical thickness (NNCORT)	Mean ± SD	0.2257 ± 0.042	0.2262 ± 0.040	0.89
Femoral shaft cross sectional area (FSCSA)	Mean ± SD	2.8871 ± 0.536	2.9100 ± 0.552	0.383
Femoral shaft cross sectional moment of inertia (FSCSMI)	Mean ± SD	0.9252 ± 0.300	0.8619 ± 0.254	0.024
Femoral shaft z	Mean ± SD	4.8920 ± 18.127	0.9386 ± 0.292	0.33
Femoral Shaft cortical thickness (FSCORT)	Mean ± SD	0.6305 ± 0.104	0.5843 ± 0.132	0.036
*Group 2 Pre-test vs Post-test comparison using paired T-test				

### Whole-body vibration training effects on Hip Structural Analysis (HSA) outcomes

For the G2 between pre-test and post-test comparison, significant results obtained from the HSA parameters were 1) femoral shaft cross-sectional moment of inertia (FSCSMI) ( $p = 0.024$ ), 2) narrow neck cross-sectional moment of inertia (NNCSMI) ( $p < 0.0001$ ), and 3) femoral shaft cortical thickness (FSCORT) ( $p < 0.036$ ) (Table 3).

These changes in HSA outcomes were not observed in G1. Subjects' compliance with WBV training was excellent (i.e., 96%). G1 and G2 subjects completed all required WBV training sessions and reported without any adverse effects. The drop-out of the study includes 3 from G1, and 4 from G2. The reasons reported from the dropouts include training induced lower-back pain ( $n=2$  in G2) and conflict with training schedule ( $n=5$ ; G1 = 2 and G2 = 3). The overall drop-out rate was 14% which is considered "satisfactory".

## Discussion

The novel finding of this pilot study is that this is the first study to report short-term (4 weeks) WBV study using multiple bouts of work-rest intervals with WBV training that increased total hip BMD and BMC as well as Hip Structural Analysis parameters in femoral shaft cross-sectional moment of inertia (FSCSMI), narrow neck cross-sectional moment of inertia (NNCSMI), and 3) femoral neck cortical thickness (CORT). There was a lack of osteogenic response using the present WBV training regimen on BMD in femoral neck, trochanter, lumbar L1-L4, lower leg, forearm and whole body. The present WBV training regimen followed the training recommendations of [7] that mechanical loading on bone is most effective if the loads are applied in discrete bouts, separated by recovery rest periods. In addition, [7] suggested that mechanical loading presents a potent osteogenic stimulus to bone cells, and that bone cells desensitize rapidly to continuous repeated mechanical stimulation. Thus, resensitization of new stimulus must occur before the cell can effectively transduce new mechanical signals [7]. Note that the present study WBV stimulus did not achieve resensitization of new stimulus in bone cells at the femoral neck, trochanter, lumbar L1-L4, forearm, lower leg, and whole body. The reason for this lack of osteogenic responses is unknown. The only positive osteogenic response observed in this pilot study is at the femoral neck BMD and BMC. Earlier literature showed positive results with various durations of WBV training include [23] who observed in young untrained women with graded WBV or WBV plus resistance training significant improvements in BMD of the femoral neck and lumbar spine. [19] who reported that high- frequency and low-magnitude vibration stimulus improves BMD and muscular strength in children with disabling ambulatory conditions, especially on trabecular bone. [22] reported improvements in BMD of femoral neck in premenopausal women using a 16-week WBV training protocol with resistance training. [20] and [16] observed greater effects on trabecular bone using high frequency and low-magnitude vibration stimulation. Note that in long bone (i.e., the femur, tibia and ulna) the magnitude of the deflection in bending and therefore the resistance to deflection in bending is typically decreased by increasing the cross-sectional moment of inertia (CSMI). The decrease in FSCSMI in G2 reflects bone's ability to resist decreased bending forces [26,27]. This suggests the measurement of geometric contributions to bone bending strength in the femoral neck decreases. Other bone outcome measurements (i.e., BMD and BMC of lumbar spine L1-L4, lower leg, forearm and whole body) did not show any osteogenic response. According to subjects' post training verbal report that most subjects experienced or felt greater vibration stimuli at the lower limb and near the hip region, not at bone sites near the lumbar spine and forearms. The possible mechanism for the site-specific response with four weeks of WBV stimulus is unclear. The possible mechanism(s) for inducing osteogenic response at the vibration site of long bone may be associated with increased fluid flow to extracellular space of the canaliculi and lacunae system of bone which is proportional to the mechanical load and loading frequency [30]. The increased fluid flow to extracellular space of the canaliculi and lacunae system suggested that micro-fluid flow

in bone is to facilitate mechanotransduction signals to bone cells (both osteoblastic and osteoclastic cells) for remodeling [31,32]. [33] elaborated that via pulsating fluid flow to extracellular space on the canaliculi and lacunae system of bone induced by mechanical stimulation that initiates intracellular nitric oxide production of the cell body. Nitric oxide (NO) plays a critical role in bone mass regulation [34,35]. During WBV training, the release of NO from the cell body is a known mediator of the osteocytes to mechanical loading [36, 37]. NO has been shown to have many osteogenic effects on bone, it reduces osteoclast motility and increases some cytokine actions on osteoblasts [36,37]. The other possible mechanism of WBV stimulus for inducing osteogenic response is that WBV stimulus can influence the regulation of bone remodeling and bone cell expression via the endocrine system by elevating serum testosterone and growth hormone [38]. Although WBV training is a promising non-drug intervention modality for inducing osteogenic responses in humans, there are conflicting reports for premenopausal and postmenopausal women. For example, [24] did not find significant changes in any bone site measurements in WBV trained subjects compared with subjects with no WBV treatment.

We applied WBV training regimens suggested by [7] and that comprised of 5 repeated bouts of 2-min on and 1-min off the vibration platform for recover period, 2 sessions/day for a total of 20 min/day, 3 days/week for 4 weeks. We compared the above training regimen with one continuous bout of 20- min vibration training without rest interval, 1 session/day for a total of 20 min/day, 3 days/week for 4 weeks. We employed a high frequency vibration (i.e., 40 Hz/sec) and low amplitude (i.e., 4 g) for WBV training and observed changes in only total hip BMD and BMC as well as FSCSMI, NNCSMI and FSCORT from the Hip Strength Analysis. It should be noted that earlier studies have shown the ability of WBV training to induce osteogenic effects on trabecular bone (i.e., lumbar spine, femoral neck) but not cortical bone (i.e., lower leg, forearm) [9]. The reason is that the trabecular bone is highly porous, its vascularity and containing bone marrow all of which allow for better transmissibility of the mechanical signals from the vibrating platform to the bone cells. Our data did not show osteogenic response in femoral neck, trochanter, lumbar spine L1-L4, forearm, lower leg, and whole-body BMD and BMC. The present study has limitations that must be addressed. First, the sample size for G1 = 21 and G2 =21 subjects is considered small. Second, our samples included both physically active young female and male subjects. All of which may limit our study for drawing any conclusion on causal relationships. Note that our initial sample size calculation using 50 subjects with 21 subjects for the two experimental groups was considered adequate to detect significant changes in femoral neck and lumbar spine L1-L4 with  $\beta$  (power) = .8 and an  $\alpha$  = 0.05. It is reasonable to speculate that the length of the WBV training (i.e., 4 weeks) might be ineffective to induce osteogenic responses on bone. Lastly, with its inherent shortfalls, the health and exercise history data were obtained using a self-reported questionnaire.

In conclusion, four weeks of WBV training using a high-frequency and low-magnitude protocol was shown to be effective for inducing significant osteogenic response in total hip BMD and BMC and Hip Structural Analyses parameters such as femoral

shaft cross-sectional moment of inertia (FSCSMI), femoral shaft cortical thickness (FSCORT), and narrow neck cross-sectional moment of inertia (NNCSMI) [39-42]. Further study is warranted to elucidate osteogenic response in cortical and trabecular bone with high-frequency and low magnitude WBV training in untrained or physically inactive premenopausal women using a WBV training protocol with more intermittent bouts per session of WBV training for longer duration. We recommend the application of 10 bouts of 2-min on and 1-min off the vibration platform for recovery interval, 2 sessions/day and 2 days/week for 16 weeks using a sample size of 30 per group.

## Acknowledgement

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## Conflict of Interest

No Conflict of Interest.

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