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Original Article

Hylonome

Feasibility, compliance, and efficacy of a randomized controlled trial using vibration in pre-pubertal children

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Abstract

Objective: Interventions utilizing vibration may increase bone mass and size which may reduce forearm fractures in children. This randomized controlled pilot trial tested the feasibility, compliance and efficacy of forearm loading regimes in an after-school program in pre-pubertal children aged 6-10 years. **Methods:** A 12-week randomized controlled trial incorporated high (HMMS; N=10) and low (LMMS; N=10) magnitude mechanical stimulation vibration, floor exercises (N=9), and controls (N=10). Radial bone measures by DXA and pQCT were compared at the end of intervention (12-weeks) and 4-months post-intervention (4-months post). **Results:** Percent changes were significantly greater in floor vs. control for ultra-distal areal BMD by DXA at 12-weeks (1%[-2,5] vs.-5%[-8,-2] respectively, p=0.02) and 4-months post (5%[1,8] vs -2%[-5,2], p=0.03) and in HMMS vs. controls for trabecular vBMD by pQCT at 12-weeks (4%[0, 8], vs. -8% [-14, -2], p=0.02). Children exposed to HMMS showed positive changes in cortical BMC, area, and cortical vBMD after 12 weeks that remained 4 months post-intervention. Children exposed to floor exercise showed positive changes in cortical BMC, area, and periosteal circumference 4-months post-intervention. Controls had decreased trabecular BMD, but increased bone area and periosteal circumference. **Conclusions:** Exposure to floor exercise and HMMS increased trabecular aBMD and vBMD in the radius.

Keywords: BMC, BMD, High-intensity Vibration, Low-intensity Vibration, DXA, pQCT

Introduction

The forearm is the most common site of fracture in children. Low bone mineral density (BMD) with smaller cortical area at the radius have been associated with increased forearm fracture risk[1,2]. Forearm fracture incidence peaks between 8 and 12 years of age in girls and 11 and 14 years in boys[3,4]. The incidence of forearm fractures has increased by 56% in females and 32% in males between 1970 and 2000[3]. Childhood forearm fractures in boys have been associated with increased risk for fractures in adulthood[5]. Since only about half of children remain fracture free during childhood[6], it is wise to consider interventions that may increase bone density and cortical area, possibly reducing forearm fracture risk in otherwise healthy children.

Vibration devices used to load the forearm may be a method to increase bone mass and size during growth. Platforms that move up and down (synchronous vibration) or in a side-to-side tilting manner about an axis (side-altering vibration) create mechanical oscillations or vibrations[7]. By changing the amplitude and frequency of the wave patterns set up by vibrating platforms, higher or lower g-forces (1 g= normal force of gravity) can be produced. Platforms that deliver less than 1 g are considered low intensity, while those that deliver more than 1 g are considered high intensity[8]. Though the mechanisms are not fully understood, there is substantial evidence that bone tissue contains mechanosensitive cells that respond to loading by mechanical stimulation as summarized in a recent review[9].

Studies utilizing vibrating devices with the intent to increase BMD and/or muscle function have been conducted in unique populations of children with limited mobility[10-12]. Although aBMD was decreased at the distal femoral diaphysis in children with cerebral palsy, increases in trabecular aBMD, grip strength of the upper body, and walking speed also were noted in these studies. The effects of vibration on healthy populations of children have not been studied. The objective of this pilot randomized controlled trial was to assess the feasibility, compliance

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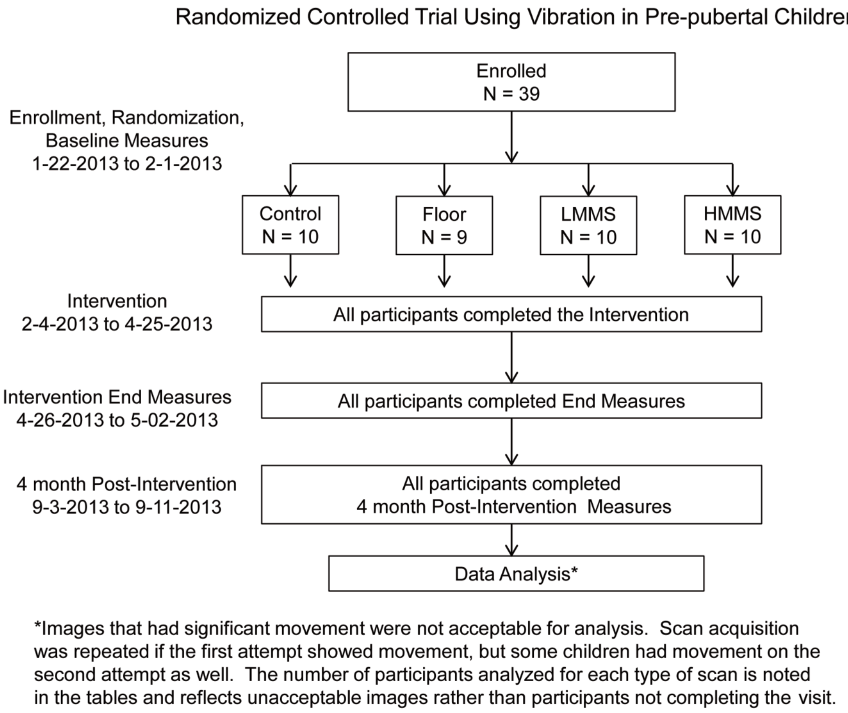

Figure 1. Study design.

and efficacy of a 12-week weight-bearing exercise program utilizing both high- and low-magnitude vibration and targeting the forearm of healthy children 6-10 years of age. The primary outcomes were percent change in trabecular BMD measured as areal bone mineral density (aBMD) by DXA and volumetric BMD (vBMD) by pQCT. The main hypothesis was that percent changes in trabecular BMD would increase more in the treatment groups than in the control group and that the vibration groups would have the greatest increases. Secondary outcomes were percent changes in cortical bone mineral content (Crt BMC) and bone size (cortical area and periosteal circumference). The hypothesis was that exercise with vibration would alter the bone response by increasing BMC and bone size.

Materials and methods

Subjects

This 12-week randomized controlled pilot trial was conducted with participants recruited from an afterschool program. The study design is shown in Figure 1. Eligible children were aged 6-10 years, without conditions affecting bone metabolism, and attended the program at least 3 days per week. Participants were stratified by gender and randomized in sets of 4 to one of four parallel groups using random numbers generated prior to recruitment. Study personnel gave a brief presentation about the study to the children at the after-school program and letters describing study details were sent home with the children. Signed forms, assents from the child and consents from the parent, were returned to the center. Out of approximately 80 children who attended the center, 39 (24 male) returned signed consents. Phone calls to the parents were made to answer questions they had about the study and to obtain information on their child's health history and dietary patterns. All 39 children were determined to be eligible. None of the parents were aware of any pubertal changes in their child and therefore the participants were considered to be pre-pubertal (age range= 6.1 to 9.7 years). The study protocol and materials were approved by the South Dakota State University Institutional Review Board.

Covariate measures

Anthropometric measures: Height was measured to the nearest 0.5 cm in duplicate using a portable stadiometer (Seca Model 225, Hanover, MD), and was repeated if measurements differed by more than 0.5 cm. Weight was recorded to the nearest 0.1 kilogram using a digital scale (SECA, Model 770, Hanover, MD) while participants wore light clothing with shoes removed. Forearm length was measured with the child resting their elbow at a 90° angle on a flat counter surface and holding their forearm perpendicular to the counter surface. The wrist area was palpitated to locate the most distal end of the ulnar styloid process and a light pen-mark was made. One end-plate of the segmometer (Segmometer 4, Rosscraft, Vancouver, Canada) was placed flat on the counter surface and the tape was stretched to the pen-mark. Arm length was recorded to the nearest millimeter.

Food frequency questionnaire (FFQ) and accelerometers: Dietary patterns were assessed using a calcium and vitamin D questionnaire[13] implemented via a phone interview with the parent or guardian at baseline. Activity levels were assessed during the 10th week of the study using the GT3X ActiGraph accelerometer (ActiGraph, Pensacola, FL). This device is capable of recording the amount and intensity of physical activity over a period of days. The accelerometer was attached to a belt and distributed to and collected from the children during the after-school program. Participants were instructed by study staff to wear the belt for 7 days with the device positioned at the level of the iliac crest toward the front of the hip. Instruction letters for the parents were sent home with the child. The accelerometers were set to record activity in 10-second epochs and cut points were used for determining moderate and vigorous activity as discussed by Puyay et al.[14] and Trost et al.[15]. The percent of moderate plus vigorous activity per day was calculated and the mean percent was used for analysis.

Strength measures: The non-dominant arm was used in all strength and bone measures. The child was asked to write their name and the hand used for this task was noted. The opposite side was considered the non-dominant arm. Grip strength was measured using a hand-held dynamometer (GRIP-D, Takei Scientific Instruments Co., Tokyo, Japan) and recorded to the nearest 0.1 kg as indicated by the device digital read-out.

Outcome measures

Bone measures of the non-dominant arm were obtained at three time points; baseline, end of exercise intervention (12-weeks), and 4 months post-intervention (4-months post) using DXA (Discovery, Hologic, Inc., Bedford, MA) and pQCT (XCT 2000, Orthometric Inc., White Plains, NY). The forearm DXA image was obtained and analyzed for ultra- and 1/3-distal radius bone outcomes using APEX 3.3 software supplied by the manufacturer. The ultra-distal radius is predominately trabecular bone while the 1/3-distal site is cortical bone. pQCT slice images were obtained using a scout view to reference the most proximal end of the growth plate and slices were obtained at 4% (trabecular bone) and 20% (cortical bone) of the forearm length. Settings to acquire the image were 0.4 mm voxel and scan speed of 20 mm/s. Analysis was completed by a certified bone densitometry technician using XCT6.00B software (Ortometric Inc, White Plains, NY) with contour mode and peel mode set at 2, a threshold density of 400 mg/mm^3 to define trabecular bone, 710 mg/mm^3 to define cortical bone, and 480 mg/mm^3 for the strength strain indices as suggested by the manufacturer.

Primary bone outcome measures were percent change in ultra-distal (UD) aBMD by DXA and trabecular vBMD by pQCT. Secondary bone outcome measures were UD and 1/3-distal bone area and bone mineral content (BMC) by DXA and cortical BMC (Crt BMC), volumetric BMD (Crt vBMD), area (Crt Area), and periosteal circumference (Peri C) by pQCT. Coefficients of variation (CVs) at our institution based on 9 children 5-11 years of age (mean age= 8 years) range from 0.36% for Crt vBMD to 2.46% for Crt BMC.

Figure 2. Position of the participant using the LMMS plate. Position on the HMMS plate and exercise mat was similar.

Exercise intervention

The Soloflex WBV Platform (Soloflex, Inc., Hillsboro, OR) a synchronous vibration device, produces low magnitude mechanical signals (LMMS, ~1 g) while the VibraFlex®450S (VibraFlex LLC, Naples, FL), a side-altering device, produces high magnitude mechanical signals (HMMS, >1 g). The two levels of vibration were compared to floor exercises targeting the arms but with no vibration, and a control group. The study was scheduled around the school calendar since our intent was to test the feasibility of the intervention during an after-school program. The exercise sessions were scheduled to be every day the after-school program was in session for a 12-week period starting the first week of February and finishing the end of April. The school calendar had 4 scheduled holidays during this time, leaving 55 exercise sessions. School was cancelled on six days due to inclement weather (excessive snow and blizzard conditions). There were two days when staff were unavailable to supervise the interventions, one day was needed to distribute activity monitors, and one day was needed to test children who would be absent on the end-intervention testing days. This left 45 possible exercise sessions. Compliance was recorded for each child assigned to an intervention group as to whether they came to their exercise group (attended), were at the center but refused to come to their exercise group (non-compliant), or not at the center (absent). The control group did not have any compliance data collected.

The first six weeks were planned to be an acclimation period while the children in all treatment groups became accustomed to the exercises. Exercises were done with the children's hands on the vibrating platform or exercise mat and knees on the floor with elbows straight, but not locked (Figure 2). This position allowed the forearm to be loaded with minimal damping and a vibration dose considered safe according to the National Institute for Occupational Safety and Health (NIOSH) and American National Standards Institute (ANSI) in the United

States and similar institutions in the European Union[16-18]. Study staff asked and encouraged the children to report any soreness, prolonged tingling, or stiffness in the hands or arms. Stretches were done before and after exercise sessions in an effort to reduce any injuries or muscle aches. No soreness, prolonged tingling, or stiffness were reported.

The formula for peak acceleration[7] was used to define the settings for the HMMS and LMMS vibration platforms. Since the HMMS and LMMS plates differ in the peak acceleration (g-force) they generate, our intent was to have each group receive the same g*minutes (g*min) of vibration per exercise session. Therefore, the HMMS plate delivered a higher g-force for a shorter time and the LMMS plate delivered a lower g-force for a longer time. Due to space and time limits at the after-school program and the limitation of only one HMMS device, HMMS intervention was limited to 2 minutes per participant. The HMMS device required the frequency (f) to be entered and was set at 13.5 Hertz (Hz) with hands placed at the 1mm position (2 mm displacement) for 2 minutes, calculated to be approximately 0.75 g for 2 minutes or 1.5 g*min per session. The HMMS participants completed the 2-minute session with one supervisor instructing them to keep their hands on the plate with elbows straight but not locked. The LMMS device had a dial that read in g units and the dial was set at 0.3 g (the lowest setting) and exercises lasted 5 minutes to equal 1.5 g*min. According to the manufacturer, 0.3 g on the dial is approximately 29 Hz and the average amplitude is approximately 0.1 mm. We had five LMMS platforms and therefore completed these exercise sessions in two groups with 5 LMMS participants in each group. Participants in the floor exercise group completed exercise interventions alongside the LMMS group with all of the children doing the same exercise movements for 5 minutes each day throughout the study. The children in the floor and LMMS groups were on all fours with hands on a yoga mat, elbows straight, but not locked. Dots were marked across both the LMMS plates and the yoga mats and the exercises/games were done to music or rhymes using the dots to indicate hand placement (Figure 2). Since these sessions lasted for 5 minutes, one instructor led the sessions and encouraged the participants to move the hands from dot-to-dot sideways, cross the hands over each other to move side to side, have one hand on the plate or mat with the other raised, "hand marching", and push-ups from the knee position. A second instructor monitored the room and encouraged children to remain in the proper position to load the arms. The control group completed measures at Base, End, and Post time points but had no exercise intervention.

To optimize the training effect in the last 6 weeks, we intended to increase the vibration dose for each group to 5 g*min which was the maximum amount of vibration the LMMS plate could deliver in the time allotted at the after-school program (dial set at 1 g ~55 Hz, 0.1 mm amplitude, for 5 minutes). However, this meant increasing the HMMS frequency to 24.9 Hz to reach 5 g*min in the allotted 2 minute time period. This amount of vibration was considered cautionary or "above action values" according to ANSI guidelines. Alternatively, the hands were moved to the 2 mm position (4mm displacement) with the frequency remaining at 13.5 Hz for a calculation of approximately 3 g*min, which was double the initial HMMS dose. None of the children reported soreness, prolonged tingling, or stiffness in their hands or arms at these settings.

Statistical analysis

Statistical analysis was completed using JMP software (version 10, SAS Institute, Cary, NC). Sample size was estimated using data from the study by Ward et al[12] based on the difference in trabecular vBMD in the proximal tibia of disabled children who stood on low magnitude vibrating platforms. With 10 participants in each group, a net benefit of 15.72 mg/ml ($p=0.003$) was found between active and placebo groups using an intervention of 10 minutes/day, 5 days/week, for 6 months.

The overall compliance in our study was calculated based on the 29 exercise participants and 45 exercise sessions. Sessions attended divided by the number of sessions possible are reported as percent compliance overall and for each exercise group. Primary and secondary outcome variables are mentioned above. Covariates were gender, percent time in moderate plus vigorous activity, and baseline measures of age, height, weight, arm length, calcium and vitamin D intake, and grip strength. These covariates were tested for correlations with baseline bone measures and compared among groups at baseline using ANOVA and post-hoc Tukey test to control for multiple comparisons. Covariates showing correlations with outcome variables or a difference among groups at baseline were included to evaluate regression models. Changes in height, weight, forearm length and grip strength were calculated from Base to End and Base to Post and were tested for differences among groups. Percent compliance and group-by-gender and group-by-age-interactions also were tested for significance in models to determine if the bone response to the different loading interventions varied by compliance, gender or age. Final regression models controlled for the baseline bone measure, age, height, weight, forearm length, grip strength, and change in forearm length. Marginal means for outcome measures were tested for differences among groups by post-hoc Tukey and for significant change using 95% confidence intervals (CI; CI not including zero considered significant change). Differences in treatment groups vs. control group were tested post-hoc using Dunnett's test for multiple comparisons.

Results

We found the after-school program to be a favorable environment to conduct this study. Children attended the exercise sessions 84±11% (mean±SD) overall and compliance did not differ among exercise groups. Non-compliance was 3±5% and children were absent from the intervention 13±11% of the time. Absences recorded for two participants in the LMMS group and one participant in the floor group were due to prescheduled recurring after-school activities one day every week. Also one participant in the LMMS group was only scheduled to be at the program 3 days per week. There were 19 recorded

	Control	Floor	LMMS	HMMS	p-value
Gender [Male/Female]	6 / 4	6 / 3	6 / 4	6 / 4	—
Age [yr]	7.8±1.1	7.9±0.9	6.8±1.0	7.0±1.0	0.04*
Height Baseline [cm]	127.0±8.0	130.0±3.5[A]	121.0±7.0[A]	124.0±5.5	0.03
Δ Height [cm, End – Base]	1.7 [1.0, 2.4]	1.3 [0.7, 1.8]	1.3 [-0.1, 2.6]	2.4 [1.6, 3.2]	—
Δ Height [cm, Post – Base]	3.8 [2.7, 4.9]	2.8 [1.6, 4.1]	3.4 [2.1, 4.6]	4.2 [3.2, 5.2]	—
Weight [kg]	28.6±5.5	29.5±4.1	23.7±5.8	25.7±6.1	0.10
Δ Weight [kg, End – Base]	0.9 [0.4, 1.4]	1.1 [0.0, 2.1]	0.6 [0.2, 1.1]	0.6 [0.2, 1.0]	—
Δ Weight [kg, Post – Base]	2.3 [1.2, 3.3]	2.4 [1.2, 3.6]	1.9 [1.4, 2.3]	2.2 [1.2, 3.1]	—
Forearm Length [mm]	200±14[A]	204±9[B]	183±13[AB]	192±11	0.003
Δ Forearm Length [mm, End – Base]	0.0 [-1.3, 1.3]	0.0 [-1.7, 1.0]	2.9 [1.6, 4.2]	0.0 [-1.3, 1.3]	<0.01
Δ Forearm Length [mm, Post – Base]	2.8 [0.0, 5.6]	1.7 [-1.3, 4.6]	3.6 [0.8, 6.4]	4.2 [1.4, 7.0]	—
Grip Strength [kg]	14.3±3.8[A]	14.2±1.9[B]	10.0±2.1[AB]	11.1±4.6	0.01
Δ Grip [kg, End – Base]	0.0 [-1.7, 1.7]	-0.9 [-2.7, 0.9]	0.4 [-1.3, 2.1]	0.1 [-1.6, 1.8]	—
Δ Grip [kg, Post – Base]	1.4 [-0.4, 3.2]	0.5 [-1.4, 2.4]	2.6 [0.8, 4.4]	1.6 [-0.2, 3.4]	—
Calcium Intake [mg/d]	1672±507	1324±259	1407±503	1455±525	—
Vitamin D Intake [IU/d]	504±291	451±195	373±202	701±515	—
Mod + Vig Activity [%]	19.9±5.3	18.0±6.5	20.6±5.7	18.8±4.7	—
[N]	(6)	(8)	(9)	(10)	
Compliance [%]	—	78±10	82±13	88±10	—
[NC, ABS]		(5, 15)	(2, 15)	(2, 8)	

Data are Mean ± SD for baseline and Mean [95% CI] for changes. p-values ≤0.10 are shown.
*Indicates significant ANOVA but no difference among groups by post-hoc Tukey test at p<0.05.
Groups with the same letter are different by post-hoc Tukey test at p<0.05.
Base – baseline measure; End – end of intervention measure; Post – 4 month post-intervention measure;
LMMS – Low Magnitude Mechanical Signals; HMMS – High Magnitude Mechanical Signals; NC – non-compliant; ABS – Absent.

Table 1. Covariate measures by intervention group.

non-compliances with 8 of those in one participant who was challenged with behavior issues and who followed a special disciplinary plan at the program. Other reasons for non-compliance were a preference for a special activity in the after-school program or not feeling well. There were no reports of discomfort, soreness, prolonged tingling, or stiffness with the exercise regimes.

Covariates by group are presented in Table 1 for baseline and for changes in the covariates from baseline to the two time points. There was a significant difference in age at baseline among the groups by one-way ANOVA, but no difference by post-hoc Tukey test. Visits were scheduled for all groups at the same time, so there was no difference in the change in age among groups. Children randomized to the LMMS group were shorter than those randomized to the floor group at baseline, but not different from the Control or HMMS groups. This difference remained throughout the study with no difference in change in height among groups. Weight was not different among the groups at any visit. Children in the LMMS group had shorter arm lengths and less grip strength than those in the control and floor group at baseline. The change in arm length during the intervention was greater in the LMMS group than other groups however, the greater change did not make up for the difference seen at baseline and arm length remained shorter at 12-weeks (LMMS 186±12 mm vs. Control 200±14 mm and Floor 204±9 mm; p=0.01) and 4-months post-intervention (LMMS 186±12 mm vs. Control 203±14 mm and Floor 206±10 mm; p<0.01). There was no difference in grip strength among groups by post-Hoc Tukey at 12-weeks (LMMS 10.4±3.1 kg vs. Control 14.3±4.8 kg and Floor 13.3±1.6 kg; p=0.05) or 4-months post (LMMS 12.7±2.4 kg vs. Control 15.7±4.1 kg and Floor 14.7±2.6 kg; p=0.09). There were no differences among groups in the change in grip strength over the study period, but the LMMS group showed a significant increase in grip strength by 4-months post-intervention. Calcium and vitamin D intakes did not differ among groups. Accelerometer data were used if the child had at least 6 hours of counts on at least three days over the 7-day period (N=33, 85%). Moderate plus vigorous activity was calculated as a percent of the day spent at this level of activity and the mean was used for analysis. Percent time in moderate plus vigorous activity did not differ among groups (Table 1). Baseline bone measures are shown in Table 2. After controlling for covariates, differences among groups in UD aBMD and Trab vBMD remained at baseline. UD aBMD was lower in the control and LMMS group compared to the HMMS group. Trab vBMD

	Control	Floor	LMMS	HMMS	p-value
DXA Forearm	**N=10**	**N=9**	**N=10**	**N=10**	
UD aBMD (g/cm²)	0.299±0.028[A]	0.323±0.038	0.289±0.017[B]	0.324±0.041[AB]	0.05[†]
UD Area (cm²)	2.2±0.3	2.1±0.1	2.0±0.3	1.9±0.3	0.09
UD BMC (g)	0.65±0.08	0.68±0.09	0.57±0.06	0.62±0.12	0.07
1/3 aBMD (g/cm²)	0.470±0.044	0.492±0.046	0.446±0.031	0.472±0.439	—
1/3 Area (cm2)	2.1±0.2	2.1±0.2	1.9±0.2	1.9±0.2	—
1/3 BMC (g)	0.98±0.14	1.04±0.13	0.86±0.13	0.92±0.18	0.06
pQCT 4% Site	**N=10**	**N=8**	**N=10**	**N=10**	
Trab vBMD (mg/mm²)	192±21[AB]	231±21[A]	207±14	226±30[B]	0.002[†]
pQCT 20% Site	**N=10**	**N=8**	**N=10**	**N=10**	
Crt Area (mm²)	38±4[A]	41±5[B]	31±3[AB]	35±9	0.005
Crt BMC (mg)	38±5	42±5[A]	31±4[A]	35±10	0.005
Crt vBMD (mg/mm²)	1003±42	1031±15	1005±50	997±32	—
Peri C (mm)	28±2	28±1	26±3	26±4	—

Data are Mean ± SD. p-values ≤0.10 are shown.
[†]Indicates differences among groups remained after controlling for age, gender, weight, height, grip strength, and arm length.
Groups with the same letter are different by post-hoc Tukey test at p<0.05.
LMMS – Low Magnitude Mechanical Signals; HMMS – High Magnitude Mechanical Signals
UD – ultra distal forearm; 1/3 – 1/3 distal forearm; BMC – bone mineral content; aBMD – areal bone mineral density; vBMD – volumetric bone mineral density; Trab – trabecular bone; Crt – cortical; Peri C – periosteal circumference.

Table 2. Baseline bone measures by group.

	Baseline to end of intervention					Baseline to 4 months post intervention				
	Control	Floor	LMMS	HMMS	p	Control	Floor	LMMS	HMMS	p
DXA Outcomes	N=10	N=8	N=10	N=10		N=9	N=9	N=10	N=10	
Δ UD aBMD [%]	**-5 [-8, -2][A]**	1 [-2, 5][A]	-2 [-5, 2]	-2 [-5, 1]	0.02	-2, [-5, 2][A]	**5 [1, 8][A]**	4 [0, 7]	2 [-1, 5]	0.03
Δ UD Area [%]	**5 [2, 8]**	0 [-4, 3][A]	0 [-4, 4]	**7 [3, 10][A]**	0.01	4 [0, 7]	3 [0, 7]	1 [-3, 5]	**5 [2, 9]**	—
Δ UD BMC [%]	0 [-3, 3]	1 [-2, 4]	-2 [-5, 2]	**3 [1, 6]**	—	3 [-1, 6]	**7 [3, 11]**	**6 [2, 10]**	**6 [3, 10]**	—
Δ 1/3 aBMD [%]	2 [0, 4]	2 [-1, 4]	0 [-2, 2]	-1 [-3, 2]	—	**3 [1, 6]**	**5 [3, 7]**	2 [0, 4]	1 [-1, 3]	—
Δ 1/3 Area [%]	0 [-3, 3]	1 [-2, 4]	-2 [-5, 2]	2 [-1, 5]	—	1 [-1, 4]	**4 [1, 7]**	2 [-1, 5]	**3 [1, 6]**	—
Δ 1/3 BMC [%]	2 [0, 5]	3 [0,6]	-1 [-4, 2]	1 [-2, 3]	—	**5 [3, 8]**	**9 [6, 12][A]**	**4 [1, 8]**	**4 [1, 6][A]**	0.05
pQCT Outcomes	N=10	N=7	N=9	N=10		N=9	N=8	N=10	N=10	
Δ Trab vBMD [%]	**-8 [-14, -2][A]**	3 [-3, 9]	-3 [-9, 3]	4 [0, 8][A]	0.02	-3 [-8, 3]	5 [-1, 12]	4 [-2, 9]	4 [-1, 8]	—

Data are marginal means [95% CI] controlling for baseline measure, age, height, weight, forearm length, grip strength, and change in forearm length (End of intervention – baseline). Percent changes significantly different from zero are indicated by CI not containing zero and are in **bold type**.
Groups with the same letter are different by post-hoc Tukey test. LMMS – Low Magnitude Mechanical Signals; HMMS – High Magnitude Mechanical Signals ; UD – ultra distal forearm; 1/3 – 1/3 distal forearm; BMC – bone mineral content; aBMD – areal bone mineral density; vBMD – volumetric bone mineral density; Trab – trabecular bone.

Table 3. Percent changes in bone outcomes at end and 4 months post-intervention.

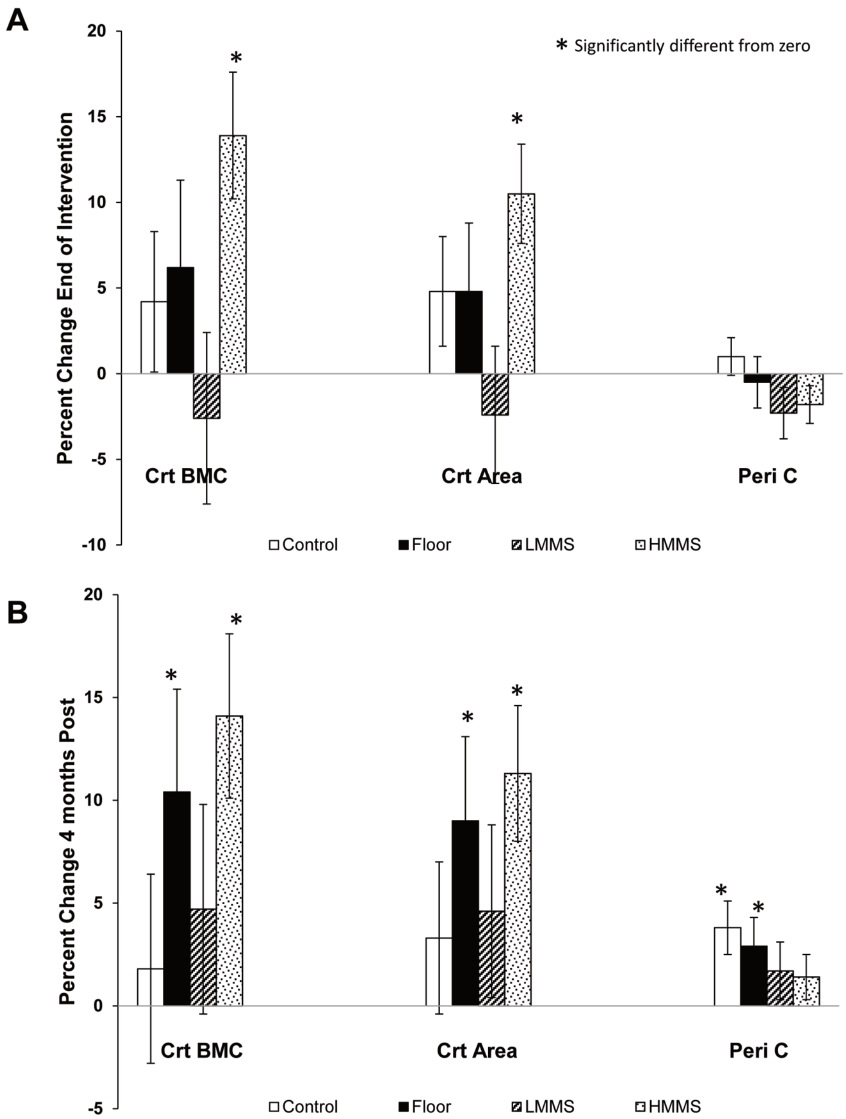

Figure 3. Percent changes in cortical bone outcomes. (A) 12-weeks, End of intervention. (B) 4 months post-intervention. Data are marginal means (with standard error bars) controlling for baseline measure, age, weight, height, arm length, grip strength, and change in forearm length (End – Baseline). *Indicates a change that is significantly different from zero. Crt - cortical, BMC – bone mineral content, Peri C – periosteal circumference.

was lower in controls compared to the floor and HMMS group.

Efficacy of the intervention was based on the percent change in trabecular aBMD and vBMD over the intervention period and at the 4-month post-intervention time point to test for persistent or delayed effects. Table 3 shows the marginal means for percent change in bone outcomes between baseline and both the 12-week and 4-month post visits. Movement during the acquisition of scans caused some scans to be unacceptable; therefore the number of participants in each group is given for each type of scan.

Percent change during the intervention in trabecular aBMD and vBMD, the primary outcomes, differed among groups. The Floor group had a greater percent change in UD aBMD than the Control group. The change in trabecular vBMD was greater in the HMMS group than the Control group. The increase in UD bone area without a concomitant increase in BMC resulted in a significant decrease in aBMD and trabecular vBMD in the control group. At the 4-month post visit the percent change in aBMD between the Floor and Control group remained different but there were no differences among groups in the trabecular vBMD.

Secondary outcomes during the intervention showed that the HMMS group had a greater increase in UD area than the floor group (Table 3), but the effect did not persist 4 months post-intervention. Increases in BMC at the 1/3 distal radius were greater in the floor group than the HMMS group 4 months post-intervention. Percent changes in cortical bone measures are shown for Baseline to 12-weeks (Figure 3A) and

Baseline to 4-months post (Figure 3B). There were no differences in the percent change in any cortical outcome measures among the groups. The HMMS group showed significant increases in cortical BMC and area during the intervention which translated to a significant increase in cortical vBMD (2.8% [0.9, 4.6]; mean [95% CI]). No other groups showed significant increases in these measures. Both the HMMS and Floor group showed significant increases in cortical BMC and area from the start of the intervention to 4 months post-intervention, but only the HMMS group showed a significant increase in cortical vBMD (2.3% [0.6, 4.0]); Peri C showed significant increases in the control and floor group.

Discussion

We found the after-school program to be a feasible environment to implement short daily exercise routines to load the forearm of healthy children 6-10 years of age. The main hypothesis that trabecular aBMD and vBMD would increase more in the treatment groups than in the control group was confirmed for the floor and HMMS groups, but not for the LMMS group. At the end of the 12-week intervention, the percent change in ultra-distal aBMD was greater in floor exercise and trabecular vBMD percent change was greater in HMMS compared to the control group. Differences in ultra-distal aBMD between floor and control groups remained 4 months post-intervention, but differences between HMMS and control groups did not persist.

The control group showed a significant decrease during the intervention in UD aBMD and trab vBMD which appears to be due to an increase in bone area without an associated increase in BMC. The phenomenon of a lag between the increase in bone size and the later increase in density during the growth spurt has been outlined by Parfitt[19]. Unlike the control group, the intervention groups did not show a decrease in trabecular aBMD or vBMD. In particular, UD BMC showed significant increases from baseline to 4 months post-intervention in all the treatment groups but not in the controls. Whether or not the increase in BMC at this vulnerable time could reduce fracture risk is not known. Ward et. al found the distal radius to have greater total and trabecular vBMD in pre-pubertal gymnasts compared to controls but no difference in bone area[20]. The authors suggested that an increase in trabecular thickness or primary spongiosa converting to secondary spongiosa caused the increase in trabecular vBMD, allowing loads to be transmitted through the joint more efficiently. The interventions in our study may have caused similar responses.

Changes in cortical bone responses were not different among groups at 12-weeks or 4 months post-intervention. At the 1/3-distal radius site measured by DXA, significant changes were minimal during the intervention, but became more notable post-intervention; in particular, all DXA measures showed significant increases for the floor group. Changes in pQCT cortical bone responses showed significant increases in BMC, area and vBMD during the intervention for the HMMS group only. Changes by 4 months post-intervention included significant increases in cortical BMC, area, and vBMD in HMMS group; increases in cortical BMC, area, and peri C in floor group and peri C in control group. Although the results are not consistent among the intervention groups and interpretation is not straightforward, these results may suggest that the cortical bone response due to loading via floor exercises or HMMS may be delayed during growth.

These results are interpreted with limitations. The small sample size did not allow for a balanced randomization in regard to baseline bone measures. The study is limited by the classification of a pre-pubertal population based on the parents' judgment via responses to the questionnaire. The 12-week intervention resulted in only 45 exercise sessions and this may not have been long enough to initiate a strong bone response. Due to space restrictions at the after-school program, the floor and LMMS groups did exercises side-by-side in the same room with two study staff supervising the sessions. Meanwhile, one HMMS plate was located in an adjacent room and participants exercised one at a time with one study staff supervising. Although there was no difference in compliance among groups, it is possible that the one-to-one participant-to-staff configuration in the HMMS group might have allowed for better adherence to proper positioning during the exercise sessions than the five-to-one ratio in the Floor/LMMS group.

Both the HMMS and the LMMS vibration platforms used in the study were commercial grade. One HMMS plate was used which had a digital readout for settings while the five LMMS plates had rheostat dial-type control knobs for settings. Testing on one LMMS plate at our facility was done using an accelerometer to test the accuracy of the dial reading frequency. It was found that the frequency was 23-50% higher than the manufacturers expected value when the dial was set ≤0.7 g, but was not different from the expected frequency when the dial was set above 0.7 g[21]. We had the children rotate between the five different plates, spending one week on a plate before changing. We did not test all of the LMMS plates nor did we test the HMMS plate to see if the digital setting of the frequency matched accelerometer readings. Although we calculated and used similar g*min for the vibration groups in the first 6 weeks, there were different doses the last 6 weeks with the LMMS plate at 5 g*min and the HMMS at 3 g*min. Whether or not the changes in bone were affected by these issues is not known.

Post-hoc power analysis from data we collected at the 20% distal radius site indicate a 38% power to detect a difference in cortical BMC and 45% power to detect a difference in cortical area with our sample size. Future studies would need approximately 60 participants per group to detect these differences. In addition, future studies could explore whether or not exercise interventions alone or with vibration can maintain synchronization between bone mineral content and bone area during growth and if this phenomenon could decrease forearm fractures.

The novelty of this study was the use of high and low intensity vibration platforms to target the forearm, a site most commonly fractured in children this age. Both DXA and pQCT densitometry were used so that changes in both areal and volumetric BMD, as well as bone geometry, could be measured. In summary, this study tested the effect of loading by vibration and non-vibration exercise on forearm bone density in healthy children aged 6-10 years. We found that floor exercises and high-magnitude vibration targeting the forearm increased trabecular BMD in the radius.

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References

1. Kalkwarf HJ, Laor T, Bean JA. Fracture risk in children with a forearm injury is associated with volumetric bone density and cortical area (by peripheral QCT) and areal bone density (by DXA). Osteoporosis Int 2011;22:607-16.
2. Goulding A, Cannan R, Williams SM, Gold EJ, Taylor RW, Lewis-Barned NJ. Bone mineral density in girls with forearm fractures. J Bone Miner Res 1998;13:143-8.
3. Khosla S, Melton JL, Dekutoski M, Achenbach S, Oberg A, Riggs BL. Incidence of childhood distal forearm fractures over 30 years. JAMA 2003;290:1479-85.
4. Landin L. Fracture patterns in Children. Acta Orthop Scand Suppl 1983;202:1-109.
5. Amin S, Melton III J, Achenbach S, et al. A distal forearm fracture in childhood is associated with an increased risk for future fragility fracture in adult men, but not women. J Bone Miner Res 2013;28:1751-9.
6. Jones IE, Williams SM, Dow N, Goulding A. How many children remain fracture-free during growth? A longitudinal study of children and adolescents participating in the Dunedin Multidisciplinary Health and Development Study. Osteoporosis Int 2002;13:990-5.
7. Rauch F, Sievanen H, Boonen S, et al. Reporting whole-body vibration intervention studies: recommendations of the International Society of Musculoskeletal and Neuronal Interactions. J Musculoskelet Neuronal Interact 2010;10:193-8.
8. Wysocki A, Butler M, Shamliyan T, Kane R. Whole-body vibration therapy for osteoporosis. (Prepared by the University of Minnesota Evidence-based Practice Center under contract No. HHSA 290 2007 10064 1.) Available at http://www.effectivehealthcare.ahrq.gov/ehc/products/268/836/TechBrief10_Vibration_20111107.pdf. Rockvill, Md 2011:Technical Brief No. 10; pg 6.
9. Ozcivici E, Luu YK, Adler B, et al. Mechanical signals as anabolic agents in bone. Nature 2010;6:50-9.
10. Reyes ML, Hernandex M, Holmgren LJ, Sanhueza E, Escobar RG. High-frequency, low-intensity vibrations increase bone mass and muscle strength in upper limbs, improving autonomy in disabled children. J Bone Miner Res 2011;26:1759-66.
11. Ruck J, Chabot G, Rauch F. Vibration treatment in cerebral palsy: A randomized controlled pilot study. J Musculoskelet Neuronal Interact 2010;10:77-83.
12. Ward K, Alsop C, Caulton J, Rubin C, Adams J, Mughal Z. Low magnitude mechanical loading is osteogenic in children with diabling conditions. J Bone Miner Res 2004;19:360-9.
13. Taylor C, Lamparello B, Kruczek K, Anderson EJ, Hubbard J, Misra M. Validation of a food frequency questionnaire for determining calcium and vitamin D intake by adolescent girls with anorexia nervosa. J Am Diet Assoc 2009;109:479-85, 85.e1-3.
14. Puyau M, Adolph A, Vohra FA, Zakeri I, Butte N. Prediction of activity energy expenditure using accelerometers in children. Med Sci Sport Exer 2004;36:1625-31.
15. Trost s, Loprinzi P, Moore R, Pfeiffer K. Comparison of accelerometer cut points for predicting activity intensity in youth. Med Sci Sport Exer 2011;43:1360-68.
16. American National Standards Institute. ANSI S2.70: Guide for themeasurement and evaluation of human exposure to vibration transmitted to the hand [Revision and replacement of ANSI S3.34-1986]. New York:. available from: Acoustical Society of America, Standards Secretariat, 35 Pinelawn Road, Suite 114E, Melville, NY 2006.
17. Health and Safety Executive. Hand Arm Vibration Exposure Calculator available at www.hse.gov.uk/vibration/hav/vibrationcalc.htm. 2012.
18. National Institute for Occupational Safety and Health. Criteria for a recommended standard; Occupational standard to hand arm vibration. Department of Health and Human Services (NIOSH) Publication No 89-106 1989.
19. Parfitt AM. The two faces of growth: benefits and risks to bone integrity. Osteoporosis Int 1994;4:382-98.
20. Ward K, Roberts S, Adams J, Mughal M. Bone geometry and density in the skeleton of pre-pubertal gymnasts and school children. Bone 2005;36:1012-8.
21. Mattison L, Binkley T, Duan S. Translation of vibration from a vibrational plate to the human body. South Dakota State University Undergraduate Research 2012;10:109-16.