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Original Article

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Vibration platform for mice to deliver precise, low intensity mechanical signals to the musculoskeleton

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Abstract

Objective: Low intensity vibration as a therapeutic and training modality has received increased attention despite the lack of clear mechanistic pathways. Thus, to determine mechanisms underpinning vibration-induced musculoskeletal adaptations, a vibration platform for mice was designed, constructed, and validated. **Methods:** Critical aspects of the platform include use of off-the-shelf components to (1) tailor individual parameter selection (acceleration and frequency), (2) produce low error across the plate's surface and throughout the range of vibration parameters, and (3) utilize accelerometer feedback to ensure fidelity within and between bouts of vibration. The vibration device is controlled by a centrally-mounted linear actuator on the underside of the platform that is modulated by accelerometer feedback. **Results:** Triaxial accelerometers confirmed that vibrations were purely vertical and acceleration responses were within 5% of target stimuli for all accelerations (0.2-1.0 *g*) and frequencies (25-90 Hz). The platform produced acceleration responses with ≤4% error between 25-90 Hz. Vibration modes were not detected indicating that the circular plate produced uniform stimuli across the platform (error ≤1.1%, P≥0.23) and mouse body mass did not affect the platform's performance (P≥0.43). **Conclusions:** Our vibration device for mice improves upon existing devices and enables precise, low intensity mechanical signals to be applied with confidence.

Keywords: Acceleration, Bone, Equipment Design, Muscle, Whole Body Vibration

Introduction

The use of low intensity vibration has received increasing attention in recent years as a possible non-invasive therapeutic tool to improve musculoskeletal health. Chronic exposure to short bouts of low-acceleration, high-frequency vibration has been shown to improve muscle power and strength[1], thwart bone loss[2-4], provoke an anabolic bone response[5], and enhance bone strength as well as reduce fracture risk[6]. Despite these beneficial effects, the overall efficacy of low intensity vibration has been challenged due to inconsistent findings across studies or the lack of clinically-meaningful results across various populations (see meta-analysis[7]). This lack of efficacy may be the result of applying sub-optimal vibration parameters, such as frequency and acceleration, to the model of interest.

The magnitude of acceleration used in vibration studies span between 0.1 and 20 *g* (where 1 *g* is equivalent to the Earth's gravitational field or 9.8 $m \cdot s^{-2}$ [8-11]. High intensity vibration (i.e., accelerations that are >1 *g*) has been associated with the development of pain and other contraindications[12-15] and consequently, the International Organization for Standardization (ISO) has established an exposure limit of 1.15 $m \cdot s^{-2}$ RMS (ISO 2631[16]). Thus, the use of high intensity vibration should be done with extreme caution. Low intensity vibration (i.e., accelerations that are ≤1.0 *g* in magnitude), on the other hand, has been shown to be anabolic to bone, especially in trabecular bone regions and improves muscle function[5,17-20]. Despite the safety and efficacy of low intensity vibration, it appears that many devices are limited to fixed parameters. This does not permit investigators to find the optimal parameters of vibration for the clinical population investigated. In addition, selection

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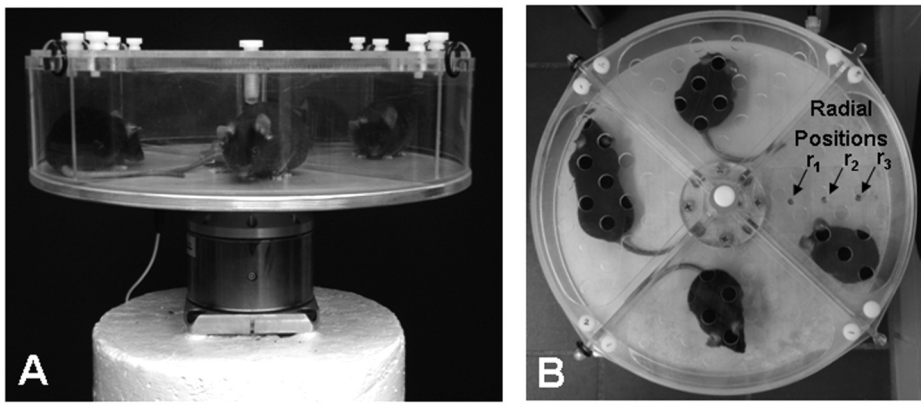

Figure 1. Custom-designed vibration platform specific for mice. (**A**) This picture shows the concrete base in white with the linear actuator attached between it and the aluminum platform with center mounted Plexiglas cage for the mice. Notice the low ceiling height (6.3 cm) which limits rearing and jumping by the mice and facilitates vibration to all four limbs. (**B**) This picture shows four mice within the cage and denotes the three positions of radial testing for the detection of modes in the uniformity of loading experiments.

of the fixed parameters is not always justified by evidence in the literature, and therefore parameters appear to be used somewhat arbitrarily.

Beyond issues related to the selection of vibration parameters, the design of the vibration platform system itself is another important factor. The initial low-acceleration, high-frequency platforms described in the literature utilized square or rectangular platforms (e.g. [21,22]). This design introduces the possibility for an additional mode to be created during wave transmission, which can either add to, or subtract from, the target vibratory environment; this may be minimized with a radially symmetric design. In addition, few studies have utilized accelerometers to provide feedback to control the vibration stimulus[21-25]. Our objective was to create a vertical vibration platform specifically for mice that produces a uniform stimulus with low error across a range of frequencies (25-90 Hz) and accelerations (0.2-1.0 *g*) to allow the user to optimize the parameters of vibration specific to their disease model or tissue of interest.

Methods

Vibration platform design and fabrication

A vertical vibration platform was designed after the work of Fritton et al.[21], to provide a low-acceleration, high-frequency tunable device for mice. The device was constructed on a vibration-isolation base composed of concrete (Figure 1A). Mounted directly into the isolation base was an electromagnetic linear actuator (SA5 V30, CSA Engineering, Mountain View, CA) with an operational bandwidth of 20-1000 Hz and a force output of 22 N. The acceleration and frequency of the actuator were driven by a sinusoidal voltage signal. A 6061-T6 aluminum circular "loading platform" (256.0 mm diameter, 6.7 mm thick), upon which mice stood, was directly coupled with the center of the actuator. A uniaxial feedback accelerometer (Model 352C42; PCB Piezotronics, Depew, NY) was mounted to the underside of this platform to monitor the magnitude of both acceleration and frequency of vertical vibration (Figure 1A). The top of the loading platform was fit with a center-mounted Plexiglas cage (mass of cage is 553 g), designed to individually house four mice (Figure 1B).

The vibration platform was controlled by a custom virtual instrument in LabVIEW (National Instruments, Austin, TX) that utilized uniaxial accelerometer feedback with proportional gain control to modulate the signal applied to the actuator producing the vibration stimulus. The ±3 V sinusoidal signal output from the virtual instrument was conditioned through an analog amplifier (AD620, Analog Devices Inc., Norwood, MA) with a gain of 100 and then power amplified using a linear high-speed amplifier (Model BOP 100-4M 400 Watt Linear High-Speed Amplifier, Kepco, Inc., Flushing, NY). A relationship that governed the range of frequencies between 25 to 90 Hz and accelerations between 0.2 *g* and 1.0 *g* was determined in the absence of mice and fed back into the control system.

Vibration platform characterization and fidelity

To characterize the vibration platform's performance and fidelity, three separate experiments were performed using data collected for a minimum of 30 seconds for each experiment. The first experiment characterized vertical vibration versus the two other orthogonal axes and the platform's ability to match target vibration specifications. A triaxial accelerometer (Model 339A30; PCB Piezotronics, Depew, NY) was mounted to the platform at radial position two (i.e., r_2 in Figure 1B). Data were collected at 10 kHz s at increments of 10 Hz from 5-125 Hz and at 0.2 *g* between 0.2 *g* and 1 *g*. Ratios of acceleration comparing the actual accelerations along the primary axis (z-direction) to acceleration along both the x and y axes were calculated. Output acceleration was normalized by target acceleration to illustrate the system's error function.

Next, two separate experiments were performed to: 1) characterize the acceleration profile across the loading platform

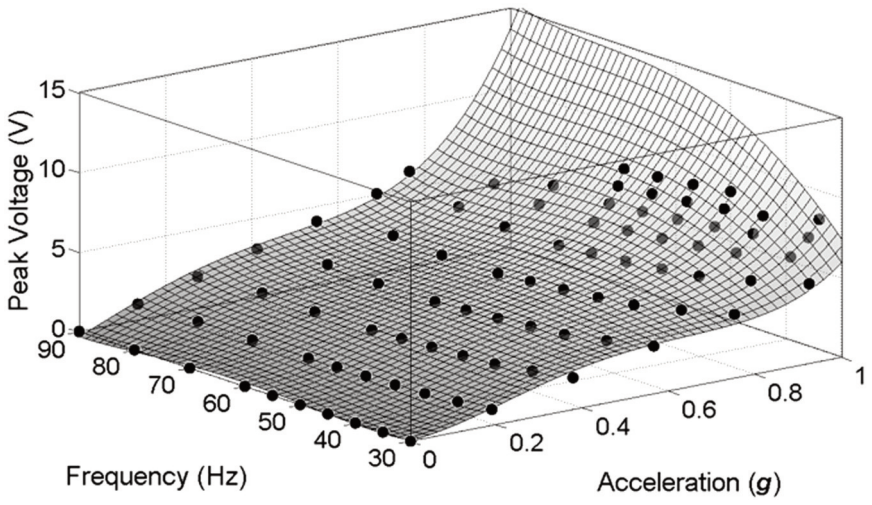

Figure 2. Surface function governing the actuator performance. This surface plot describes the relationship between output voltage to the actuator, frequency, and acceleration and is described by Equation 1. The points indicate the experimental data that were used to describe the function.

surface, and 2) ensure that the vibration platform was capable of meeting vibration parameters accurately, irrespective of mouse body mass. A single uniaxial accelerometer was placed at three radial positions (position r_1=50.8 mm, r_2=76.2 mm, and r_3=101.6 mm from the center, Figure 1B). Acceleration errors were compared between the positions as a function of frequency. Finally, different sized mice were placed on the vibration loading platform to examine accuracy with different loads. Comparisons were made between 3- and 16-week old, C57Bl/6 mice of mixed gender with mean body mass of 8.8 g and 28.8 g, respectively (n=4 per group). The acceleration and frequency data were collected using a uniaxial accelerometer at each combination of accelerations (0.3, 0.6, or 0.9 *g*) and frequencies (30, 45, 60 or 90 Hz). All procedures were approved by the Institutional Animal Care and Use Committee at the University of Minnesota.

Statistical analysis

Statistics were performed in SPSS (IBM SPSS, IBM Corp., Somers, NY). Significance was set at P<0.05. Two-way analysis of variance (ANOVA) with Tukey post-hoc tests were used.

Results

The resonant frequency of the actuator is 32 Hz; however the addition of mass due to the plate and mounted cage change the overall resonant frequency of the system to 240 Hz. A three-dimensional surface function (Equation 1) describes the relationship between acceleration, frequency, and actuator input voltage (Figure 2). This relationship governs the control of the actuator to provide a vibration from 0.2 *g* to 1.0 *g* accelerations across a frequency range of 25 to 90 Hz.

Equation 1. 4th order polynomial model:

$$V(A,F) = \langle \sum_{i=1}^{4} (P[i,0] * A^i) + (P[0,i] * F^i) \rangle + \langle \sum_{j=1}^{3} (P[j,1] * A^j F) \rangle + \langle \sum_{k=2}^{3} (P[1,k] * AF^k) \rangle + (P[2,2] * A^2F^2 + (P[0,0]) \quad (1)$$

Where the actuator voltage (V) is defined as a function of the acceleration (A) and frequency (F) with the following constants: p00=3.586; p10=2.016; p01=-0.021; p20=0.421; p11=0.088; p02=-0.383; p30=1.044; p21=0.625; p12=-0.443; p03=0.0475; p40=0.470; p31=0.280; p22=-0.223; p13=0.128; p04=0.0840 (R-square: 0.987).

Acceleration errors above 5% were corrected by feedback within 3 seconds. Loading was confirmed in the vertical direction and acceleration had minimal error within the determined range of fidelity (25-90 Hz). Accelerations in the horizontal plane were less than 0.08% of the vertical accelerations. Within the range of fidelity the maximal error between actual and target acceleration was 3.81% and the average error was ±0.37% (Figure 3). No vibration modes were found between the radial positions on the circular platform within the range of fidelity (P=0.226); the vibration environment was consistent across the three radial positions with a maximum error between r_2 and r_3 to be ±0.94% (Figure 4) and greatest at 1.0 *g*. Mouse body mass had no effect on the loading environment (P=0.434); accelerations were on average 1.3% different across the entire range of fidelity.

Discussion

This report details our construction and validation of a vibration device for mice (Figure 1) that enables the effects of low intensity vibration training on musculoskeletal structures and functions to be analyzed. The device was constructed for less than $12,000. Of this total, computer software, hardware, and the data acquisition board were approximately $4,500. The

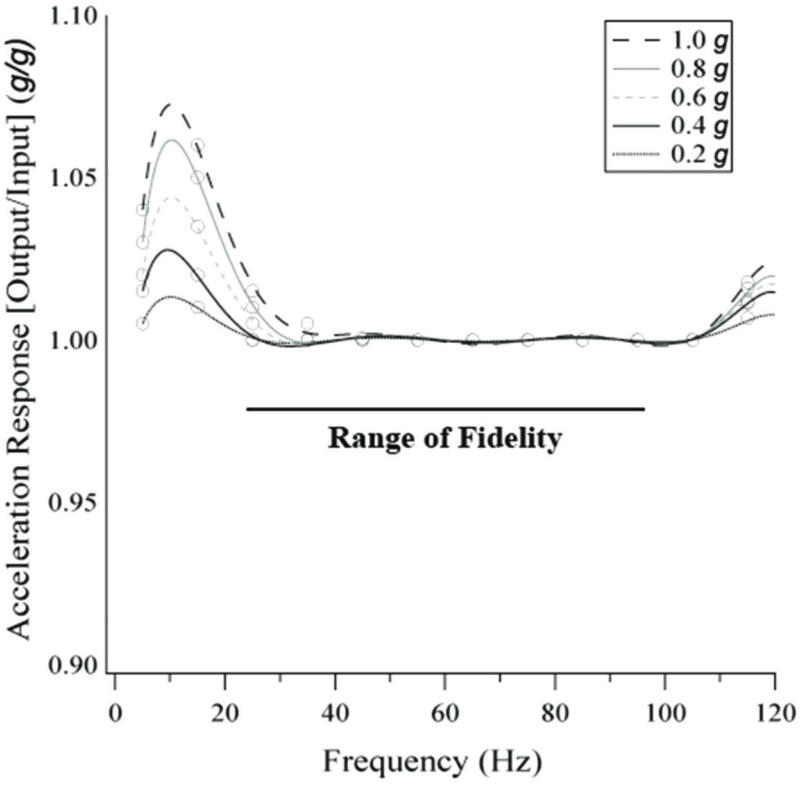

Figure 3. Acceleration response, indicating the error in acceleration as a function of frequency. The actual vertical accelerations were measured across the entire frequency domain and the response (actual acceleration/target acceleration) is reported. Data points represent the mean acceleration response over the 3 minute duration of testing.

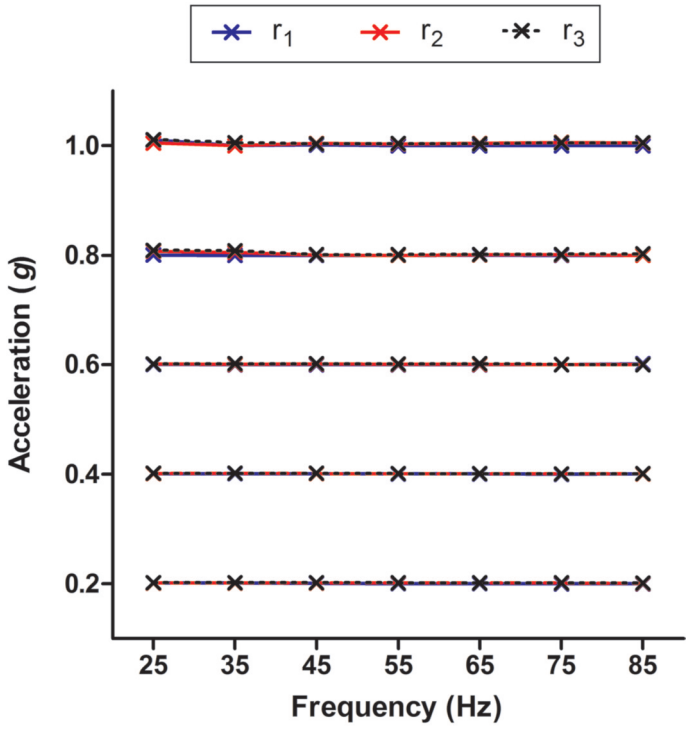

Figure 4. Detection of modes and uniform loading across the platform surface. The actual accelerations at each of the three radial positions on the loading platform surface are plotted against frequency within the range of fidelity. Differences in actual acceleration production at the spatial positions along the platform would indicate the presence of a mode. Position r_1=50.8 mm, r_2=76.2 mm, and r_3=101.6 mm from the center.

actuator and amplifier totaled ~$5,000 and the accelerometers ~$2,000. Small parts were minimal and labor is not included in these estimates.

Two other low intensity vibration devices for animal models have been described[21,22]. We designed our platform based on those devices. Our device delivers low intensity vibration across a range of accelerations (0.2 *g* to 1.0 *g*) and frequencies (25-90 Hz) with the goal to improve bone and skeletal muscle function as previously shown[22]. We used a circular platform with a centrally-mounted actuator to deliver a uniform vibration across the entire surface of the platform; irrespective of mouse location and mass (Figure 4). The vibration of the platform was continually monitored and modulated by acceleration feedback. This is important because it confirms that vibration signals remain the same during and between bouts of vibration. These validations show that our platform is mechanically functioning as intended.

Our device was made to investigate low intensity vibration training, or accelerations <1 *g*. A limitation of our platform is the inability to deliver higher magnitude accelerations. Thus, comparing "high" to "low" intensity vibration stimuli is not possible. With the growing interest in vibration training, it is important to consider that different types of vibration stimuli may produce different responses. Along these lines, it is also essential that sufficient information about vibration stimuli be accurately reported in animal studies as well as human whole body vibration studies[26]. Failure to report actual vibration exposure (e.g. [27-29]) can lead to ambiguous interpretations and therefore does not provide convincing evidence to progress the field. Another potential limitation of our vibration device for mice is that nonlinearities exist at low frequencies (Figure 3). These nonlinearities are due to the actuator's inability to produce output below 20 Hz. Vibration at these lower frequencies, however, have been contraindicated for humans[30-32].

We constructed and validated a low intensity vibration device specific for mice that improves upon previously described devices. These improvements in the design and functionality of the platform allow the investigator to use off-the-shelf components to tailor the parameters to specific experimental conditions. The stimulus provided is uniform across 25-90 Hz and 0.2 to 1.0 *g* as well as between bouts of vibration. Our short-term objective is to use this device to identify optimal vibration parameters for musculoskeletal adaptations in mouse models of muscular dystrophy (see [33]) in this issue) and then to determine the therapeutic potential of vibration training in muscle diseases such as Duchenne Muscular Dystrophy. An additional long-term goal is to determine mechanisms underlying musculoskeletal adaptations that occur in response to low intensity vibration training[33,34].

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References

1. Marin PJ, Rhea MR. Effects of vibration training on muscle power: a meta-analysis. J Strength Cond Res 2010; 24:871-8.
2. Mikhael M, Orr R, Fiatarone Singh MA. The effect of whole body vibration exposure on muscle or bone morphology and function in older adults: a systematic review of the literature. Maturitas 2010;66:150-7.
3. Prisby RD, Lafage-Proust MH, Malaval L, Belli A, Vico L. Effects of whole body vibration on the skeleton and other organ systems in man and animal models: what we know and what we need to know. Ageing Res Rev 2008; 7:319-29.
4. Slatkovska L, Alibhai SM, Beyene J, Cheung AM. Effect of whole-body vibration on BMD: a systematic review and meta-analysis. Osteoporos Int 2010;21:1969-80.
5. Ozcivici E, Garman R, Judex S. High-frequency oscillatory motions enhance the simulated mechanical properties of non-weight bearing trabecular bone. J Biomech 2007; 40:3404-11.
6. Rubin C, Turner AS, Bain S, Mallinckrodt C, McLeod K. Anabolism. Low mechanical signals strengthen long bones. Nature 2001;412:603-4.
7. Lau RW, Liao LR, Yu F, Teo T, Chung RC, Pang MY. The effects of whole body vibration therapy on bone mineral density and leg muscle strength in older adults: a systematic review and meta-analysis. Clin Rehabil 2011;25:975-88.
8. Yang P, Jia B, Ding C, Wang Z, Qian A, Shang P. Whole-body vibration effects on bone before and after hind-limb unloading in rats. Aviat Space Environ Med 2009;80:88-93.
9. Bautmans I, Van Hees E, Lemper JC, Mets T. The feasibility of Whole Body Vibration in institutionalised elderly persons and its influence on muscle performance, balance and mobility: a randomised controlled trial [ISRCTN 62535013]. BMC Geriatr 2005;5:17.
10. Rees S, Murphy A, Watsford M. Effects of vibration exercise on muscle performance and mobility in an older population. J Aging Phys Act 2007;15:367-81.
11. Rees SS, Murphy AJ, Watsford ML. Effects of whole-body vibration exercise on lower-extremity muscle strength and power in an older population: a randomized clinical trial. Phys Ther 2008;88:462-70.
12. Franchignoni F, Vercelli S, Ozcakar L. Hematuria in a runner after treatment with whole body vibration: A case report. Scand J Med Sci Sports 2012.
13. Jordan MJ, Norris SR, Smith DJ, Herzog W. Vibration training: an overview of the area, training consequences, and future considerations. J Strength Cond Res 2005; 19:459-66.
14. Murfee WL, Hammett LA, Evans C, et al. High-frequency, low-magnitude vibrations suppress the number of blood vessels per muscle fiber in mouse soleus muscle. J Appl Physiol 2005;98:2376-80.
15. Monteleone G, De Lorenzo A, Sgroi M, De Angelis S, Di

Renzo L. Contraindications for whole body vibration training: a case of nephrolitiasis. J Sports Med Phys Fitness 2007;47:443-5.
16. Griffin MJ. Minimum health and safety requirements for workers exposed to hand-transmitted vibration and whole-body vibration in the European Union; a review. Occup Environ Med 2004;61:387-97.
17. Muir J, Judex S, Qin YX, Rubin C. Postural instability caused by extended bed rest is alleviated by brief daily exposure to low magnitude mechanical signals. Gait Posture 2011;33:429-35.
18. Reyes ML, Hernandez 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.
19. Ward K, Alsop C, Caulton J, Rubin C, Adams J, Mughal Z. Low magnitude mechanical loading is osteogenic in children with disabling conditions. J Bone Miner Res 2004;19:360-9.
20. Gilsanz V, Wren TA, Sanchez M, Dorey F, Judex S, Rubin C. Low-level, high-frequency mechanical signals enhance musculoskeletal development of young women with low BMD. J Bone Miner Res 2006;21:1464-74.
21. Fritton JC, Rubin CT, Qin YX, McLeod KJ. Whole-body vibration in the skeleton: development of a resonance-based testing device. Ann Biomed Eng 1997;25:831-9.
22. Christiansen BA, Silva MJ. The effect of varying magnitudes of whole-body vibration on several skeletal sites in mice. Ann Biomed Eng 2006;34:1149-56.
23. Rubin C, Turner AS, Muller R, et al. Quantity and quality of trabecular bone in the femur are enhanced by a strongly anabolic, noninvasive mechanical intervention. J Bone Miner Res 2002;17:349-57.
24. Rubin C, Turner AS, Mallinckrodt C, Jerome C, McLeod K, Bain S. Mechanical strain, induced noninvasively in the high-frequency domain, is anabolic to cancellous bone, but not cortical bone. Bone 2002;30:445-52.
25. Rubinacci A, Marenzana M, Cavani F, et al. Ovariectomy sensitizes rat cortical bone to whole-body vibration. Calcif Tissue Int 2008;82:316-26.
26. 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.
27. Christiansen BA. Whole-body vibration and weight loss: truth or consequence? Int J Obes (Lond) 2009;33:384; author reply 2-3.
28. Maddalozzo GF, Iwaniec UT, Turner RT, Rosen CJ, Widrick JJ. Whole-body vibration slows the acquisition of fat in mature female rats. Int J Obes (Lond) 2008; 32:1348-54.
29. Maddalozzo GF, Pavol MJ, Philbrick KA, et al. Whole-body vibration slows the acquisition of fat in mature female rats: a response to BA Christiansen. Int J Obes (Lond) 2009;33:382-3.
30. Magnusson ML, Pope MH, Wilder DG, Areskoug B. Are occupational drivers at an increased risk for developing musculoskeletal disorders? Spine (Phila Pa 1976) 1996; 21:710-7.
31. Anderson JA, Otun EO, Sweetman BJ. Occupational hazards and low back pain. Rev Environ Health 1987;7:121-60.
32. Goel VK, Park H, Kong W. Investigation of vibration characteristics of the ligamentous lumbar spine using the finite element approach. J Biomech Eng 1994;116:377-83.
33. Novotny SA, Eckhoff MD, Eby BC, Call JA, Nuckley DJ, Lowe DA. Musculoskeletal response of dystrophic mice to short term, low intensity, high frequency vibration. J Musculoskelet Neuronal Interact 2013;13:418-429.
34. McKeehen JN, Novotny SA, Baltgalvis KA, Call JA, Nuckley DJ, Lowe DA. Adaptations of mouse skeletal muscle to low-intensity vibration training. Med Sci Sports Exerc 2013;45:1051-9.