



Review

# The Use of Vibration as Physical Exercise and Therapy

Giuseppe Musumeci <sup>1,2</sup>

<sup>1</sup> Department of Biomedical and Biotechnological Sciences, Human Anatomy and Histology Section, School of Medicine, University of Catania, Via S. Sofia 87, 95123 Catania, Italy; g.musumeci@unict.it; Tel./Fax: +39-095-378-2043

<sup>2</sup> Department of Health, Institut des Etudes Universitaires, UniPoliSI, Route de Miège, 29 CH-3968 Veyras, Switzerland

Academic Editor: Olivier Hue

Received: 23 April 2017; Accepted: 17 May 2017; Published: 19 May 2017

**Abstract:** Musculoskeletal vibration stimulation is the topic chosen for this review. The aim is to discuss this interesting, but poorly analyzed topic in the current literature in order to explain and help readers to better understand the effects of vibration used as an exercise intervention and therapy for muscle, bone, and cartilage tissues. The use of vibration stimulation for enhancing athletic performance and therapeutic use is considered an important matter of medical biology that has developed in the last three decades. Current evidence suggests that vibration is effective in enhancing musculoskeletal strength and power capacity and improving physical conditions in patients with related disorders such as osteoporosis and osteoarthritis, although the mechanisms mediating these effects are still not well known.

**Keywords:** vibration plate; neuromuscular adaptations; bone; cartilage; muscle; osteoporosis; osteoarthritis

## 1. Introduction

Vibration is a mechanical incitement characterized by an oscillatory wave. The biomechanical factors determining its intensity are amplitude, frequency, and magnitude of the fluctuations. The amount of the oscillatory movement regulates the amplitude of the vibration, the replication rate of the cycles of fluctuation indicates the incidence of the vibration, and the acceleration specifies the magnitude of the vibration [1]. Low-amplitude, low-frequency mechanical stimulation of the human body is a safe and active method to improve muscle strength, bone remodeling, and cartilage preservation [2]. The effects of whole-body vibration (WBV) have been considered with subjects exercising on vibrating plates [3,4] that produce sinusoidal vibrations. Low frequency vibration has also been applied locally by means of vibrating cables and vibrating dumbbells [5]. Vibration offers a perturbation of the gravitational arena during the time-course of the involvement. The aim of this short report is to review the present knowledge on the effects of vibration stimulus and to highlight the potential mechanisms that cause the improvement of strength and power production in muscles and its therapeutic effects in bone and cartilage tissues. Furthermore, with a brief note at the end of the review, I am pleased to commemorate the pioneer of vibration studies, Prof. Carmelo Bosco.

## 2. Anatomy of the Muscle (Short Overview)

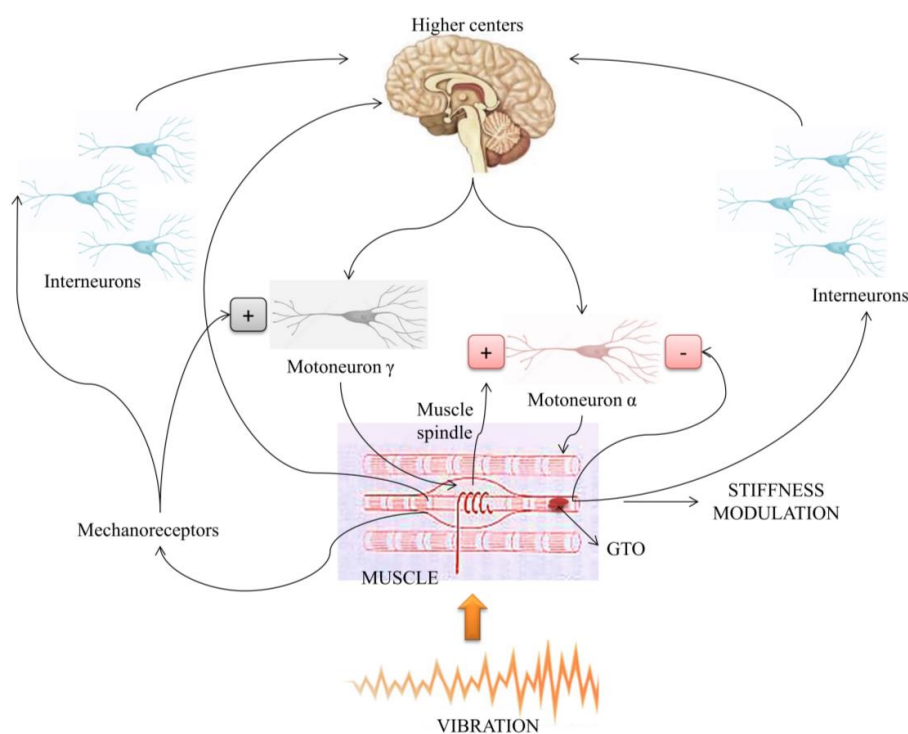
Skeletal muscle or voluntary muscle represents the most abundant of human muscle tissues, as opposed to smooth muscle or “involuntary muscle”, and cardiac muscle (myocardium) [6]. Skeletal muscle has many functions; it makes up the muscles of the locomotor system, and is present in some organs of the digestive and respiratory system (tongue, palate, pharynx, larynx). This type of muscle

tissue is not only intended to produce body movements and maintain posture, but it also supports the weight of the viscera, protects them from external trauma (abdominal muscles), controls defecation and urination (muscle sphincters of the anus and urethra), and plays a key role in breathing (diaphragm). Furthermore, the muscle is an important endocrine organ that is able to influence metabolic control. Muscles are distinguished in relation to their position as being superficial (or fur muscles) or deep (or under-muscular) muscles. Muscle tissue has the ability to transform chemical energy into mechanical energy, consequently producing movement. Skeletal muscle is composed of a different number of muscle fibers and is surrounded by connective tissue, the epimysium, which is connected to tendons, the structures responsible for the insertion of the muscles to the bone segments [7]. Connective tissue septa originate from epimysium and surrounding groups of muscle fibers, forming the perimysium. Each muscle fiber is surrounded by reticular connective tissue, which constitutes the endomysium [8]. Skeletal muscles can be distinguished based on their shape: short muscles, long, wide, pennated; based on their origin or insertion: biceps, bicaudates, biarticular, and based on their function: flexors, extensors.

### 3. Adaptive Responses of Skeletal Muscle to Vibration Exposure

Skeletal muscle is a particular tissue that modifies its general functional ability in reaction to varied stimuli [6]. Very important is the influence of gravitational load on muscular performance. Ordinarily, the daily action of gravity is enough to enable muscles to maintain their performance capabilities. However, with less gravitational load (microgravity), we have a clear reduction in both muscle mass and force-generating skill. Conversely, a growth in gravitational load (hypergravity) will increase in the cross-sectional area and force-generating aptitude of muscle [5]. Exercise programs planned to increase strength and powers are considered by performing exercises with an increase in gravitational load. These forms of exercise have been revealed to generate particular adaptive responses in skeletal muscles concerning both morphological and neural factors [9]. Exhaustive protracted strength training is known to stimulate a specific neuromuscular and hormonal adaptive reaction in the human body in little time [5]. Even less knowledge is accessible in respect to fatigue, relative strength loss, and hormonal changes during one severe session of exercises [4]. It should be remembered that detailed packages for strength and explosive power training are based on exercises performed with fast and intense variation of gravitational acceleration [5]. In this connection, Prof. Bosco and coauthors discovered that mechanical vibrations applied to the whole body could create modifications in gravitational conditions. Whole-body vibration applied for ten minutes during a ten-day treatment stimulated an improvement in explosive power performances in physically active subjects and it was observed how human skeletal muscle reacted to a single session of ten minutes application of whole-body vibration in athletes [4]. The use of vibrations with exercise is quite a recent innovation. The first use of vibration as an exercise was conducted by Russian scientists, who found that vibration was effective in enhancing strength in athletes [5]. Subsequently, the effects of vibration application have been studied after acute and chronic exposure using different treatment protocols. Acute enhancement of mechanical power has been validated after vibration treatment applied with vibrating cables during bilateral biceps curl on a pulley machine [10]. The experimental procedure consisted of vibration delivered to the subjects by means of vibrating cables producing oscillations at 44 Hz and 3-mm amplitude [10]. In this experiment, both elite and amateur athletes demonstrated improvement, respectively; at 10.4% and 7.9% in maximal power measured during the bilateral biceps curl exercise. Whole-body vibration (WBV) administered through vibrating plates has been revealed to improve vertical jumping ability by 3.8%. In the same study, mechanical power output by the legs during horizontal leg press increased by 7% [11]. Some applications of WBV at a frequency of 26 Hz lasting 60 s with 60-s rest in athletes resulted in a shift to the right of the force velocity and power-velocity curves as measured by a dynamometer during the leg press exercise [12]. Vibration applied for five min with vibrating dumbbells (30 Hz, 6-mm amplitude) created an increase of 13% in average power in the elbow flexor muscles of elite boxers [12]. The increase in mechanical power during arm flexion was associated with a decrease in the electromyography EMG root mean

square activity in biceps brachii. Regular non-pharmacological treatments have also proved to produce improvement in neuromuscular properties of human skeletal muscle. WVB at a low frequency administered for ten days to active subjects was capable of enhancing vertical jump height by 12% [4]. These findings recommend that vibrations can effectively enhance neuromuscular performance. The mechanical action of vibration is to create fast and short changes in the length of the muscle-tendon complex. This perturbation is detected by the sensory receptors that modulate muscle stiffness through reflex muscular activity and attempt to dampen the vibratory waves. To understand the mechanisms responsible for vibration-induced enhancement of performance, it is crucial to differentiate between the effects of vibration on an active muscle from those occurring after an application of vibration [5]. Mechanical vibrations applied to the muscle itself or the tendon can provoke a reflex muscle contraction named “Tonic Vibration Reflex” [13]. The deformation of the soft tissues produced by vibration is capable of activating muscle spindles and leading to an enhancement of the stretch-reflex loop. Thus, the excitatory inflow throughout vibration stimulus is mostly connected to the reflex activation of the motor neuron. Intensification in EMG activity is usually observed during vibration action, with values higher than those observed during voluntary muscular activity. Therefore, authors found the root mean square EMG of biceps brachii muscle to be 200% higher in boxers exercising with a vibrating dumbbell matched with performing a voluntary arm flexion with a load equal to 5% of the subjects’ body mass [14]. This result could be associated with an amplified synchronization of motor units due to the application of vibration. Reflex muscle action represents the response of the neuromuscular system to a strong perturbation triggered by mechanical vibration (Figure 1). This response can be regulated not only by monosynaptic but also by polysynaptic pathways. The primary endings of the muscle spindle are more sensitive to vibration than are the secondary endings and Golgi tendon organs. It is not only the neuromuscular spindles that recognize vibration but so too do the skin, the joints, and secondary endings [15]. Therefore, these sensory structures probably facilitate the system during vibration, whether it is whole-body or locally applied, enhancing the sensitivity of the primary endings.



**Figure 1.** Schematic graph illustrating stiffness modulation following vibration stimuli. There is a quick change in muscle length due to the stimulation of both  $\alpha$  and  $\gamma$  motoneurons and mechanoreceptors. In addition, the higher centers are involved. GTO; Golgi Tendon Organ.

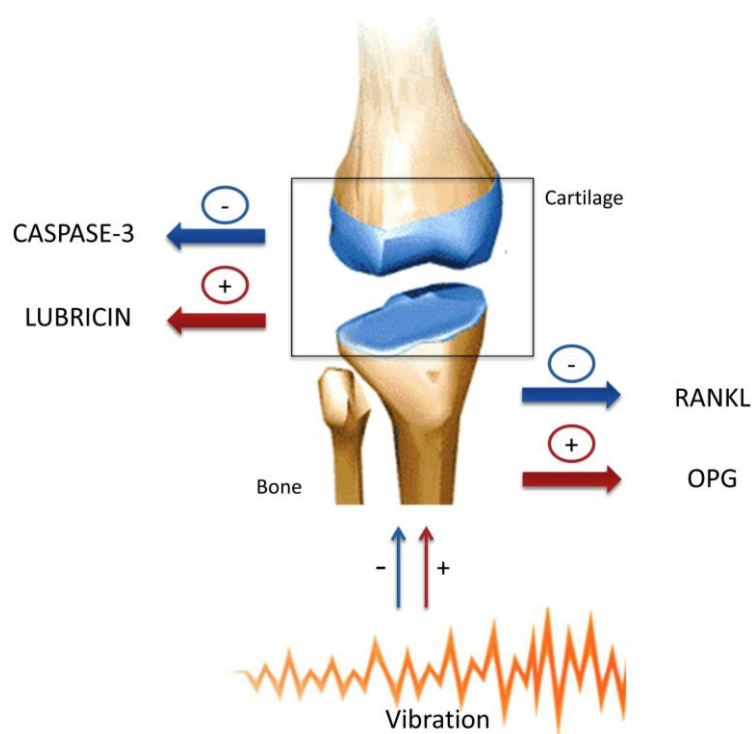
#### 4. Anatomy of the Bone and Cartilage (Short Overview)

Bone tissue is the main structural connective tissue of the body. Bone tissue forms the rigid portion of the bones that make up the skeleton [16]. Bones are organs constituted of bone tissue as well as bone marrow, small blood vessels, epithelium, and nerves. Bone tissue refers specifically to the bone mineral matrix that forms the rigid segments of the organ, and the bone cells inside it. The two kinds of bone tissue are cortical bone and cancellous bone. There is another type of bone tissue called subchondral bone, which is underneath the articular cartilage, and is a multilayer connective tissue that covers the epiphysis of long bones [17]. Articular cartilage is divided into different layers of chondrocytes: superficial zone, middle zone, deep zone, tidemark, and calcified zone [17]. The bone cells develop and remodel bone tissue, maintaining the bones and the regulation of minerals in the body [18]. Bone cells include osteoclasts, which break down bone tissue; osteoblasts, which build new bone tissue; osteocytes, which hold and protect the bone. Lower or no mechanical stimulation is important for maintaining the bone function, which could induce bone resorption and restrain bone formation and remodeling [19]. The skeleton is a metabolically active organ that experiences several remodeling's during the life. Bone remodeling includes removal of mineralized bone by osteoclasts and formation of bone matrix through osteoblasts. This remodeling is affected by a variety of pathologic conditions such as osteoporosis, which appears when the formation of bone does not keep up with removal of bone [19].

#### 5. Adaptive Responses of Bone and Cartilage to Vibration Exposure

Spaceflight has proved to cause a loss of bone mass and strength, especially in the lower limbs [20]. The weightlessness-induced bone loss during spaceflight seriously affects astronauts' health. Treadmill, resistance exercise, and bicycle ergometer are three main training exercises to prevent musculoskeletal system degeneration in the International Space Station (ISS) [21]. Astronauts spent approximately 2.5 h doing exercises every day, but bone loss and muscle atrophy still persisted [22,23]. In general, exercise countermeasures adopted in space to resist bone loss have had only limited success [21]. More effective exercise training against bone loss is required to minimize the negative effects of space on astronauts' musculoskeletal system. Some studies demonstrated that there was less energy consumption of exercise in space flight than on the ground when doing the same exercise [24–26]. These studies indicated that exercise trainings in space might be different from on the ground. Studies demonstrated that WBV had a positive effect on countering age-related and disuse-induced bone loss [27,28]. WBV could restrain bone resorption, promote bone formation, increase the amount of bone alkaline phosphatase, and enhance muscle strength [29,30]. Local vibration loaded on hind limbs of rats was shown to be able to improve the function of the musculoskeletal system [31,32]. Passive exercise could increase the expression of bone nerve growth factor gene to enhance the performance of bone [33]. Vibration is a mechanical stimulus characterized by a cyclic motion back and forth in the same pattern. When an athlete stands on a vibrating platform, the cyclic movement gives a strong stimulus to musculoskeletal structure, resulting in changes in muscle stiffness in response to the vibration, as physiological adaptations to accommodate the vibratory waves [5]. Vibration exercise is a new and effective measure to prevent muscular atrophy and osteoporosis [34]. Osteoporosis is a disorder described by low bone mass and structural deterioration of bone tissue leading to bone fragility and an increased risk of hip, spine, and wrist fractures [35]. The latter could be associated with osteoarthritis leading to several histopathological changes and determining an endogenous cellular response [2,36]. Yearly, in the USA, about 1.5 million osteoporosis-related fractures occur, and there is expected to be an increase of 50% by 2025 [37]. Three common risk factors for osteoporosis are age, immobility, and low body weight, especially in postmenopausal women. Prevention has been suggested as an important approach to reduce the incidence of osteoporosis. Physical activity increases energy metabolism, contributes to a healthy energy balance, and can be used to increase lean mass and bone mass. Physical activity is also beneficial in attenuating or improving chronic disease conditions [36,38,39]. To reach these goals, aging people with diabetes use physical exercise

regimes to reduce the risk of osteoporosis and fractures [40]. However, immobility, age, and other weaknesses may prevent optimal participation in exercise regimes designed for osteoporosis patients. A scientific study indicated that a mechanical stimulus in the form of vibration, traveling from the sole of the foot through the skeleton, is anabolic for bone [41]. Studies have shown that current vibration devices induce beneficial increases in bone mineral density (BMD), although diminished functional loading has been shown to decrease bone quantity in the case of bed rest patients or astronauts under microgravity conditions [21–24]. In a recent study, Pichler et al. suggested that it might be possible, through mechanical stimulation, to inhibit the activity of receptor activator of nuclear factor  $\kappa$ B ligand (RANKL) through the RANKL/RANK/OPG system in bone modeling and remodeling [42]. Mechanical stimulation could release inhibitors of RANKL such as osteoprotegerin (OPG) that are capable of inhibiting RANKL activity, preventing osteoblast differentiation into mature osteoclasts and thus inhibiting bone destruction (Figure 2). The balance between RANKL and OPG production establishes the level of osteoclastogenesis [42]. So, in certain diseases, such as osteoporosis, mechanical stimulation could be a possible therapeutic treatment, through lowering the RANKL level, thereby increasing bone formation and preventing fractures in osteoporotic bone [42]. The majority of clinical trials in postmenopausal women suggest the utility of WBV training in improving bone mass, and thus better outcomes in osteoporosis condition, but few indications exist on the treatment by WBV of senile osteoporosis in men, so further studies are needed in order to confirm the same for the male sex. At any rate, from the above reported scientific data it is highlighted that low intensities and low amplitudes are more suitable for individuals with a higher risk of fractures such as patients with osteoporosis [43]. Physical activity could also be used as therapeutic action for cartilage diseases such as osteoarthritis [44,45]. Physical activity should have the primary goal of preventing overloading and misuse of the joints. Regular exercise, correctly performed (mild adapted physical activity), strengthens the joints, decreases bone loss, and may be useful in the control of pain [38–40]. In overheavy arthritis patients, sports additionally contribute to decreasing body weight and diabetes, thus limiting the overload of the joints [46,47]. The often-held perception that joints affected by osteoarthritis should be used as little as possible must be absolutely invalidated [36,38–40]. In a recent research study, Musumeci et al. studied the beneficial effect of physical activity (treadmill and vibration stimulation training) on articular cartilage [2]. These results suggest that mechanical stimulation is able to release lubricin in articular cartilage and to inhibit caspase-3 activity (Figure 2), preventing chondrocyte death and favoring cartilage preservation thanks to the effects of lubricin lubricants and nutrients [2]. To date, vibration training is considered complementary to pharmacological and dietary treatments of osteoporosis. The limit of this kind of training is that it is not always suitable for patients with osteoporosis, who are often elderly people [40]. In order to improve bone mineral density (BMD), bone parameters, and metabolism, many clinical trials show that a multi-component training regime, including aerobic activity and other types of training (resistance and/or strength exercises) seems much more useful. This improves bone mass and bone metabolism in older adults and particularly osteopenic and osteoporotic women. Moreover, WBV training seems to be a valid alternative to existing approaches due to its greater adaptability to patients. It has similar effects to strength training and it also has other benefits, improving balance and, consequently, reducing the risk of falls. Such mechanical stimulation could therefore be a possible therapy in osteoporosis and in preservation of bone tissue as well as prevention of further bone and cartilage damage [48–50]. Further findings are needed to better understand the interactions between the molecular signals induced by physical/vibration activity and the pathways involved in bone and cartilage metabolism in order to define the best treatment for the development and progression of osteoporosis and osteoarthritis in medical therapy to preserve tissue function and prevent bone and cartilage damage.



**Figure 2.** Schematic graph illustrating the effects of vibration stimulation on bone and cartilage. Its effects on bone determine modulation of RANKL/OPG system by inhibiting RANKL activity through the increased production of OPG. Its effects on cartilage include the increased expression of lubricin and reduced apoptosis represented by the decreased expression of Caspase-3. RANKL, receptor activator of nuclear factor  $\kappa$ B ligand; OPG, osteoprotegerin. Red arrows indicate activation. Blue arrows indicate inhibition.

## 6. Memory of Prof. Carmelo Bosco

Prof. Carmelo Bosco (Figure 3) is considered to be the most important Italian researcher in Sports Science. Born in Catania (Militello 1943–Roma 2003), after graduating in 1968 Istituto Superiore di Educazione Fisica (ISEF) of Turin, he moved to Finland, where he graduated in Biology of Physical Activity at the University of Jyväskylä, where he completed one of the most prestigious Ph.D.'s in Physiology and Biomechanics of sport, writing a doctoral thesis on muscle elasticity. He worked at the same university for many years as a teacher. In 1994, he was awarded an Honorary Degree from the University of Budapest. He was a member of several associations and International Academies of Science. He worked with many European laboratories, including Freiburg, Lyon, Barcelona, the Institute of Sports Science Comitato Olimpico Nazionale Italiano (CONI) and with many Italian Sports Federations (Winter Sports, Volleyball). He significantly improved knowledge in this field in Italy. He was Scientific Advisor and Coordinator of Scientific Studies & Research Centers for many years. Many collaborators participated in his research, studying elasticity and strength conditioning, including Prof. Marco Cardinale (Head of Sports Physiology Aspire Academy, Doha, Qatar). However, his name is linked to the invention of equipment known throughout the world for the brilliance and simplicity of its use. Those involved in physical education and sports undoubtedly know the ERGO-JUMP and MUSCLE-LAB (Bosco-System), which have now become indispensable tools for the evaluation of muscle capacity and therefore also for training methodology in sports. The practical result of this fascinating study was the creation of a special vibrating platform, the N.E.M.E.S. (Neuro Muscular Mechanical Stimulation), created exclusively with medical and scientific criteria. The “Muscle-Lab” has been adopted by National Aeronautics and Space Administration (NASA) for physiology studies on astronauts. His most recent studies were directed on muscle vibration and overload stress prevention.

Back in Italy, he worked as an Associate Professor at the University of Rome—Tor Vergata and Adjunct Professor at the University of Catania, where he was a professor for the Sports Science degree course. His articles in scientific journals worldwide are countless. His books have been translated into many languages worldwide.



**Figure 3.** Photograph of Prof. Bosco during a lecture.

## 7. Conclusions

This review highlights the beneficial effects of vibration in muscles, bone, and cartilage tissues. Musculoskeletal structures respond to vibration because of the need to modulate muscle stiffness rapidly so as to accommodate the vibratory waves. This reaction is regulated by monosynaptic and polysynaptic afferent pathways, which are capable of generating specific hormonal responses. These findings suggest that vibration could represent an effective exercise intervention for improving neuromuscular performance in sedentary and trained people. The possible effect of vibration on hormonal activity also opens exciting viewpoints for its application in training and rehabilitation programs for distinctive pathologies. Due to the huge abilities of vibration exercise treatments, it is also important to study the effects of long-term vibration exercise packages or non-pharmacological vibration therapy treatment on different physiological and pathological parameters and define safe exercise protocols based on individual responses. In conclusion, I can suggest that vibration of musculoskeletal structures could be an effective exercise intervention for reducing the effects of aging and other related disorders, but the type of vibration treatment (amplitude, frequency, and magnitude of the oscillations) should be personalized because the effect of vibration stimulus is very subjective, otherwise, this treatment would have no effect. This is due to the fact that we are all different from each other, both physically and molecularly; for this reason a standard protocol cannot exist for all individuals. Finally, the effects of vibration exercise on musculoskeletal interactions need to be better analyzed in order to verify its effectiveness on muscle strength, bone remodeling, and cartilage preservation including the potential effects on osteoporosis and osteoarthritis. We hope that in the next future we will be able to study specific initial evaluations in order to individually customize this therapy to make it even more effective.

**Acknowledgments:** This study was supported by a Grant-in-Aid provided by Finanziamento della Ricerca d'Ateneo (FIR) 2014–2016, (cod. 314509), University of Catania, Italy. I would like to thank Iain Halliday for reviewing the manuscript and providing feedback for language corrections and Marta Anna Szychlinska for providing illustration materials.

**Conflicts of Interest:** The author declares no conflict of interest.

## References

1. Bosco, C. Adaptive responses of human skeletal muscle to simulated hypergravity condition. *Acta Physiol. Scand.* **1985**, *124*, 507–513. [[CrossRef](#)] [[PubMed](#)]

2. Musumeci, G.; Loreto, C.; Leonardi, R.; Castorina, S.; Giunta, S.; Carnazza, M.L.; Trovato, F.M.; Pichler, K.; Weinberg, A.M. The effects of physical activity on apoptosis and lubricin expression in articular cartilage in rats with glucocorticoid-induced osteoporosis. *J. Bone Miner. Metab.* **2013**, *31*, 274–284. [[CrossRef](#)] [[PubMed](#)]
3. Bosco, C.; Belli, A.; Astrua, M.; Tihanyi, J.; Pozzo, R.; Kellis, S.; Tsarpela, O.; Foti, C.; Manno, R.; Tran-Quilli, C. Dynamometer for evaluation of dynamic muscle work. *Eur. J. Appl. Physiol.* **1995**, *70*, 379–386. [[CrossRef](#)]
4. Bosco, C.; Cardinale, M.; Colli, R.; Tihanyi, J.; von Duvillard, S.P.; Viru, A. The influence of whole body vibration on jumping ability. *Biol. Sport* **1998**, *15*, 157–164.
5. Cardinale, M.; Bosco, C. The use of vibration as an exercise intervention. *Exerc. Sport Sci. Rev.* **2003**, *31*, 3–7. [[CrossRef](#)] [[PubMed](#)]
6. Trovato, F.M.; Imbesi, R.; Conway, N.; Castrogiovanni, P. Morphological and functional aspects of human skeletal muscle. *J. Funct. Morphol. Kinesiol.* **2016**, *1*, 289–302. [[CrossRef](#)]
7. Musumeci, G.; Castrogiovanni, P.; Coleman, R.; Szychlinska, M.A.; Salvatorelli, L.; Parenti, R.; Magro, G.; Imbesi, R. Somitogenesis: From somite to skeletal muscle. *Acta Histochem.* **2015**, *117*, 313–328. [[CrossRef](#)] [[PubMed](#)]
8. Imbesi, R.; D'Agata, V.; Musumeci, G.; Castrogiovanni, P. Skeletal muscle: From development to function. *Clin. Ter.* **2014**, *165*, 47–56. [[PubMed](#)]
9. Duchateau, J.; Enoka, R.M. Neural adaptations with chronic activity patterns in able-bodied humans. *Am. J. Phys. Med. Rehab.* **2002**, *81*, 17–27. [[CrossRef](#)]
10. Issurin, V.B.; Tenenbaum, G. Acute and residual effects of vibratory stimulation on explosive strength in elite and amateur athletes. *J. Sports Sci.* **1999**, *17*, 177–182. [[CrossRef](#)] [[PubMed](#)]
11. Bosco, C.; Iacovelli, M.; Tsarpela, O.; Cardinale, M.; Bonifazi, M.; Tihanyi, J.; Viru, M.; de Lorenzo, A.; Viru, A. Hormonal responses to whole body vibrations in man. *Eur. J. Appl. Physiol.* **2000**, *81*, 449–454. [[CrossRef](#)] [[PubMed](#)]
12. Bosco, C.; Colli, R.; Introini, E.; Cardinale, M.; Tsarpela, O.; Madella, A.; Tihanyi, J.; von Duvillard, S.P.; Viru, A. Adaptive responses of human skeletal muscle to vibration exposure. *Clin. Physiol.* **1999**, *19*, 183–187. [[CrossRef](#)] [[PubMed](#)]
13. Hagbarth, K.E.; Eklund, G. Motor effects of vibratory stimuli in man. In *Muscular Afferent and Motor Control*; Granit, R., Ed.; Almqvist and Wiksell: Stockholm, Sweden, 1965; pp. 177–186.
14. Bosco, C.; Cardinale, M.; Tsarpela, O. The influence of vibration on arm flexors mechanical power and EMG activity of *Biceps brachii*. *Eur. J. Appl. Physiol.* **1999**, *79*, 306–311. [[CrossRef](#)] [[PubMed](#)]
15. Ribot-Ciscar, E.; Vedel, J.P.; Roll, J.P. Vibration sensitivity of slowly and rapidly adapting cutaneous mechanoreceptors in the human foot and leg. *Neurosci. Lett.* **1989**, *104*, 130–135. [[CrossRef](#)]
16. Musumeci, G.; Loreto, C.; Clementi, G.; Fiore, C.E.; Martinez, G. An in vivo experimental study on osteopenia in diabetic rats. *Acta Histochem.* **2011**, *113*, 619–625. [[CrossRef](#)] [[PubMed](#)]
17. Pichler, K.; Musumeci, G.; Vielgut, I.; Martinelli, E.; Sadoghi, P.; Loreto, C.; Weinberg, A.M. Towards a better understanding of bone bridge formation in the growth plate—An immunohistochemical approach. *Connect. Tissue Res.* **2013**, *54*, 408–415. [[CrossRef](#)] [[PubMed](#)]
18. Pichler, K.; Kraus, T.; Martinelli, E.; Sadoghi, P.; Musumeci, G.; Uggowitz, P.J.; Weinberg, A.M. Cellular reactions to biodegradable magnesium alloys on human growth plate chondrocytes and osteoblasts. *Int. Orthop.* **2014**, *38*, 881–889. [[CrossRef](#)] [[PubMed](#)]
19. Boyce, B.F.; Xing, L. Functions of RANKL/RANK/OPG in bone modeling and remodeling. *Arch. Biochem. Biophys.* **2008**, *473*, 139–146. [[CrossRef](#)] [[PubMed](#)]
20. Vico, L.; Collet, P.; Guignandon, A.; Lafage-Proust, M.H.; Thomas, T.; Rehaillia, M.; Alexandre, C. Effects of long-term microgravity exposure on cancellous and cortical weight-bearing bones of cosmonauts. *Lancet.* **2000**, *355*, 1607–1611. [[CrossRef](#)]
21. Smith, S.M.; Heer, M.A.; Shackelford, L.C.; Sibonga, J.D.; Ploutz-Snyder, L.; Zwart, S.R. Benefits for bone from resistance exercise and nutrition in long-duration spaceflight: Evidence from biochemistry and densitometry. *J. Bone Miner. Res.* **2012**, *27*, 1896–1906. [[CrossRef](#)] [[PubMed](#)]
22. Cavanagh, P.R.; Genc, K.O.; Gopalakrishnan, R.; Kuklis, M.M.; Maender, C.C.; Rice, A.J. Foot forces during typical days on the international space station. *J. Biomech.* **2010**, *43*, 2182–2188. [[CrossRef](#)] [[PubMed](#)]
23. Trappe, S.; Costill, D.; Gallagher, P.; Creer, A.; Peters, J.R.; Evans, H.; Riley, D.A.; Fitts, R.H. Exercise in space: Human skeletal muscle after 6 months aboard the international space station. *J. Appl. Physiol.* **2009**, *106*, 1159–1168. [[CrossRef](#)] [[PubMed](#)]



24. Michel, E.; Rummel, J.; Sawin, C. Skylab experiment M-171 “metabolic activity”—Results of the first manned mission. *Acta Astronaut.* **1975**, *2*, 351–365. [[CrossRef](#)]
25. Rummel, J.A.; Michel, E.L.; Sawin, C.F.; Buderer, M.C. Medical experiment M-171: Results from the second manned Skylab mission. *Aviat. Space Environ. Med.* **1976**, *47*, 1056–1060. [[PubMed](#)]
26. Lane, H.W.; Feeback, D.L. Water and energy dietary requirements and endocrinology of human space flight. *Nutrition* **2002**, *18*, 820–828. [[CrossRef](#)]
27. 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. [[CrossRef](#)] [[PubMed](#)]
28. Lynch, M.A.; Brodt, M.D.; Silva, M.J. Skeletal effects of whole-body vibration in adult and aged mice. *J. Orthop. Res.* **2010**, *28*, 241–247. [[CrossRef](#)] [[PubMed](#)]
29. Prisby, R.D.; Lafage-Proust, M.H.; 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*, 319–329. [[CrossRef](#)] [[PubMed](#)]
30. Xie, L.; Jacobson, J.M.; Choi, E.S.; Busa, B.; Donahue, L.R.; Miller, L.M.; Rubin, C.T.; Judex, S. Low-level mechanical vibrations can influence bone resorption and bone formation in the growing skeleton. *Bone* **2006**, *39*, 1059–1066. [[CrossRef](#)] [[PubMed](#)]
31. Sonza, A.; Völkel, N.; Zaro, M.A.; Achaval, M.; Hennig, E.M. A whole body vibration perception map and associated acceleration loads at the lower leg, hip and head. *Med. Eng. Phys.* **2015**, *37*, 642–649. [[CrossRef](#)] [[PubMed](#)]
32. Sun, L.W.; Luan, H.Q.; Huang, Y.F.; Wang, Y.; Fan, Y.B. Effects of local vibration on bone loss in -tail-suspended rats. *Int. J. Sports Med.* **2014**, *35*, 615–624. [[CrossRef](#)] [[PubMed](#)]
33. Edwards, J.H.; Reilly, G.C. Vibration stimuli and the differentiation of musculoskeletal progenitor cells: Review of results in vitro and in vivo. *World. J. Stem Cells* **2015**, *7*, 568–582. [[CrossRef](#)] [[PubMed](#)]
34. Rittweger, J.; Ehrig, J.; Just, K.; Mutschelknauss, M.; Kirsch, K.A.; Felsenberg, D. Oxygen uptake in whole-body vibration exercise: Influence of vibration frequency, amplitude, and external load. *Int. J. Sports Med.* **2002**, *23*, 428–432. [[CrossRef](#)] [[PubMed](#)]
35. Fratini, A.; Bonci, T.; Bull, A.M. Whole body vibration treatments in postmenopausal women can improve bone mineral density: Results of a stimulus focussed meta-analysis. *PLoS ONE* **2016**, *11*, e0166774. [[CrossRef](#)] [[PubMed](#)]
36. Musumeci, G. Effects of exercise on physical limitations and fatigue in rheumatic diseases. *World J. Orthop.* **2015**, *6*, 762–769. [[CrossRef](#)] [[PubMed](#)]
37. Adachi, J.D.; Ioannidis, G.; Pickard, L.; Berger, C.; Prior, J.C.; Joseph, L.; Hanley, D.A.; Olszynski, W.P.; Murray, T.M.; Anastassiades, T.; et al. The association between osteoporotic fractures and health-related quality of life as measured by the Health Utilities Index in the Canadian Multicentre Osteoporosis Study (CaMos). *Osteoporos. Int.* **2003**, *14*, 895–904. [[CrossRef](#)] [[PubMed](#)]
38. Castrogiovanni, P.; Musumeci, G. Which is the best physical treatment for osteoarthritis? *J. Funct. Morphol. Kinesiol.* **2016**, *1*, 54–68. [[CrossRef](#)]
39. Musumeci, G.; Loreto, C.; Imbesi, R.; Trovato, F.M.; di Giunta, A.; Lombardo, C.; Castorina, S.; Castrogiovanni, P. Advantages of exercise in rehabilitation, treatment and prevention of altered morphological features in knee osteoarthritis. A narrative review. *Histol. Histopathol.* **2014**, *29*, 707–719. [[PubMed](#)]
40. Castrogiovanni, P.; Trovato, F.M.; Szychlinska, M.A.; Nsir, H.; Imbesi, R.; Musumeci, G. The importance of physical activity in osteoporosis. From the molecular pathways to the clinical evidence. *Histol. Histopathol.* **2016**, *31*, 1183–1194. [[PubMed](#)]
41. Dionello, C.F.; Sá-Caputo, D.; Pereira, H.V.; Sousa-Gonçalves, C.R.; Maiworm, A.I.; Morel, D.S.; Moreira-Marconi, E.; Paineiras-Domingos, L.L.; Bembem, D.; Bernardo-Filho, M. Effects of whole body vibration exercises on bone mineral density of women with postmenopausal osteoporosis without medications: Novel findings and literature review. *J. Musculoskelet. Neuronal Interact.* **2016**, *16*, 193–203. [[PubMed](#)]
42. Pichler, K.; Loreto, C.; Leonardi, R.; Reuber, T.; Weinberg, A.M.; Musumeci, G. RANKL is downregulated in bone cells by physical activity (treadmill and vibration stimulation training) in rat with glucocorticoid-induced osteoporosis. *Histol. Histopathol.* **2013**, *28*, 1185–1196. [[PubMed](#)]

43. Cerciello, S.; Rossi, S.; Visonà, E.; Corona, K.; Oliva, F. Clinical applications of vibration therapy in orthopaedic practice. *Muscles Ligaments Tendons J.* **2016**, *6*, 147–156. [[CrossRef](#)] [[PubMed](#)]
44. McCann, M.R.; Yeung, C.; Pest, M.A.; Ratneswaran, A.; Pollmann, S.I.; Holdsworth, D.W.; Beier, F.; Dixon, S.J.; Séguin, C.A. Whole-body vibration of mice induces articular cartilage degeneration with minimal changes in subchondral bone. *Osteoarthr. Cartil.* **2016**, *25*, 770–778. [[CrossRef](#)] [[PubMed](#)]
45. Musumeci, G. The effect of mechanical loading on articular cartilage. *J. Funct. Morphol. Kinesiol.* **2016**, *1*, 154–161. [[CrossRef](#)]
46. Aiello, F.C.; Trovato, F.M.; Szychlinska, M.A.; Imbesi, R.; Castrogiovanni, P.; Loreto, C.; Musumeci, G. Molecular links between diabetes and osteoarthritis: The role of physical activity. *Curr. Diabetes Rev.* **2017**, *13*, 50–58. [[CrossRef](#)] [[PubMed](#)]
47. Musumeci, G.; Aiello, F.C.; Szychlinska, M.A.; di Rosa, M.; Castrogiovanni, P.; Mobasheri, A. Osteoarthritis in the XXIst century: Risk factors and behaviours that influence disease onset and progression. *Int. J. Mol. Sci.* **2015**, *16*, 6093–6112. [[CrossRef](#)] [[PubMed](#)]
48. Munakata, M. Dynamic whole-body vibration training: A unique upstream treatment from the muscle to the arterial system and central hemodynamics. *Hypertens. Res.* **2017**, *40*, 436–438. [[CrossRef](#)] [[PubMed](#)]
49. Savage, R.; Billing, D.; Furnell, A.; Netto, K.; Aisbett, B. Whole-body vibration and occupational physical performance: A review. *Int. Arch. Occup. Environ. Health* **2016**, *89*, 181–197. [[CrossRef](#)] [[PubMed](#)]
50. Kiiski, J.; Heinonen, A.; Järvinen, T.L.; Kannus, P.; Sievänen, H. Transmission of vertical whole body vibration to the human body. *J. Bone Miner. Res.* **2008**, *23*, 1318–1325. [[CrossRef](#)] [[PubMed](#)]



© 2017 by the author. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).