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Effect of Whole Body Vibration on Muscular Performance, Balance, and Bone

ACADEMIC DISSERTATION

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for public discussion in the small auditorium of Building K,
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This thesis is based on the following original publications, referred to as I-IV in the text:

I Torvinen S, Kannus P, Sievänen H, Järvinen TAH, Pasanen M, Kontulainen S, Järvinen TLN, Järvinen M, Oja P, Vuori I (2002): Effect of a vibration exposure on muscular performance and body balance. Randomized cross-over study. Clin Physiol & Func Im 22, 145-152.

II Torvinen S, Sievänen H, Järvinen TAH, Pasanen M, Kontulainen S, Kannus P (2002): Effect of 4-min vertical whole body vibration on muscle performance and body balance: A randomized cross-over study. Int J Sports Med 23: 374-379.

III Torvinen S, Kannus P, Sievänen H, Järvinen TAH, Pasanen M, Kontulainen S, Järvinen TLN, Järvinen M, Oja P, Vuori I (2002): Effect of four-month vertical whole body vibration on performance and balance. Med Sci Sports Exerc 34:1523-1528.

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ABBREVIATIONS

ANCOVA	analysis of covariance
ANOVA	analysis of variance
BMC	bone mineral content
BMD	bone mineral density
BMU	basic multicellular unit
BSI	bone strength index
CI	confidence interval
CoA	cortical area
CoD	cortical density
CSMI	cross-sectional moment of inertia
CTx	carboxyterminal telopeptide of type I collagen
CV_{rms}	average root-mean-square coefficient of variation
DXA	dual energy X-ray absorptiometry
EMG	electromyography
MES	minimal effective strain
MPF	mean power frequency
MRI	magnetic resonance imaging
OC	osteocalcin
OVX	ovariectomy
PINP	aminoterminal procollagen propeptide
pQCT	peripheral quantitative computed tomography
RMS	root mean square voltage
SD	standard deviation
TRAP-5b	type 5 tartrate-resistant acid phosphatase
TrD	trabecular density
TVR	tonic vibration reflex
VWF	vibration-induced white finger
WBV	whole body vibration

INTRODUCTION

Falls, osteoporosis, and related fractures are a major public health problem worldwide, and aging of populations, especially in Western societies, will accentuate the burden of these injuries on both the health care system and national economy (Cummings et al. 1985, Riggs and Melton 1988, Jones et al. 1994, Kannus 1995a, 1996c,d, 1999a,b, 2002). In the 1990s, there were 1.7 million hip fractures in the world, and this figure is estimated to increase to over 6 million by the year 2050 (Cooper et al. 1992). If the estimations on the continuous growth in the incidence of osteoporotic fractures hold in the future the total number of hip fractures in Finland will increase from 7120 in 1997 to about 19 000 in 2030 (Kannus et al. 1999c). Financially, this means an increase in the annual total costs of hip fracture from the about e 143 million to about e 390 million, respectively.

Due to the alarming prospects for the future, many different prevention and treatment regimens have been developed to resolve the increasing problem of the osteoporotic fractures. The solution is not, however, simple, because these injuries are not only due to the fragility of bone tissue (osteoporosis) but a complex interplay of trauma (typically a fall), and compromised bone strength (Thorngren 1995, Cummings and Nevitt 1989, Nevitt 1994). Today, physical activity or exercise has been shown to be the only method, which can positively influence on both of these risk factors by improving and maintaining bone mass and strength, and enhancing muscle strength, reaction time, balance, and coordination (Suominen 1993, Smith et al. 1994, Province et al. 1995, Kannus et al. 1996d, 1999a, Campbell et al. 1997, Henderson 1998, Taaffe 1999, 2001, Carter et al. 2001, Cochrane Review 2002). In addition, regular physical activity also provides other beneficial and physiological effects for participants: e.g. enhances overall health and physical fitness, increases opportunities for social contacts, has advantageous effects on blood pressure, hyperlipidemia, obesity, diabetes, and impaired glucose tolerance, and thus, cardiovascular events and cerebrovascular disease, and improves the quality of life in elderly populations by reducing the risk of deterioration of functional capacity (Daley and Spinks 2000, Vuori 2001).

It is known that different training regimens load the skeleton at different anatomic sites, and the osteogenic effects of exercise are clearly site specific (Kannus et al. 1995b, Heinonen et al. 1996, Haapasalo et al. 1998). In general, it seems that endurance training not including impact-type movements, has not resulted in significant bone gain (Suominen 1993). Thus, current knowledge suggests that impact type exercise that creates versatile strain distributions throughout the bone structure can best improve bone strength at the loaded skeletal site (Heinonen et al. 1996). The starting age of activity is crucial: the benefit is doubled if the activity is started before or at puberty rather than after it (Kannus et al. 1995b, Haapasalo et al. 1998). Bone tissue responds to exercise in adulthood, too, but this serves to preserve bone rather than stimulate new bone (Nelson et al. 1994, Lohman et al. 1995, Heinonen et al. 1996).

The specific neuromuscular adaptations to training regimen seem to depend much on the training program employed (Sale 1988, Carroll et al. 2001). For example, if particular attention is paid to strength and balance training, as was done in the study of older adults by Campbell et al. (1997), the annual falling rate of these persons reduced significantly and the effect also sustained after cessation of the intervention (Campbell et al. 1999). Thus, exercise regimens, which consist of muscle strengthening and balance training, are effective in preventing falls in elderly people (Cochrane Review 2002). Although the above noted positive effects of physical activity on osteoporotic fractures are mediated through mechanisms irrespective of the bone tissue, it has, however, also been suggested that physical activity-induced muscle action may create and mediate bony effects, too (Hawkins et al. 1999, Turner 2000). The type, frequency, intensity and duration of the most beneficial exercises for bone and fall prevention are, however, not yet well determined (Kannus et al. 1996 d, 1999 a, Lanyon 1996, Skerry et al. 1997).

Bone's ability to adapt to altered functional demands was recognized over a century ago (Wolff 1892), and the loading-induced deformations in bone tissue (*strains)* are believed to cause or mediate the adaptation in bone architecture and mass (Rubin et al. 1985, Frost1987 a). The strain-related osteogenic stimulus is, however, associated with different specific components in the mechanical milieu, that is, peak strain magnitude, strain distribution, strain cycles, and strain rate (Lanyon and Rubin 1984, Rubin and Lanyon 1984, 1985). The predominant perception of biophysical modulation of bone physiology is that the strains must be large to have any morphologic impact (Frost 1990 a). Several studies have, however, shown that if mechanical loading contains high strain rates distributed in an uncustomary way, the strain magnitude does not need to be abnormally high (Lanyon and Rubin 1984, Rubin and Lanyon 1984, 1985, Järvinen et al. 1998). Furthermore, recent experimental studies have suggested, that extremely low-magnitude (several orders of magnitude below those that arise from vigorous activity) but high-frequency mechanical stimulus (vibration) can also be a strong determinant of bone morphology (Rubin et al. 2001 a,b; 2002 a,b).

Recent clinical studies have suggested that mechanical vibration may also improve muscular performance (Bosco et al. 1998, 1999 a, 1999 b, Rittweger et al. 2000, Runge et al. 2000), and thus, it is not surprising that vibration stimulus has aroused great interest among osteoporosis researchers as a very promising method to prevent fractures. Randomized controlled clinical trials are, however, lacking, and the purpose of this thesis was, therefore, to investigate the effects of vibration loading on bone mass and strength, physical performance and balance. The safety issues of vibration were also carefully examined, since vibration loading may also result in adverse reactions (e.g. , low back pain).

REVIEW OF THE LITERATURE

1. Bone Properties

Bone is a vital, rigid form of connective tissue with four major functions: It provides a lever system and mechanical integrity for body motion, protects soft tissues of internal organs and bone marrow, takes part in mineral, especially calcium, homeostasis, and is the primary site of hematopoiesis (hematopoietic bone marrow).

The skeleton can be devided into two parts: The axial skeleton includes the vertebrae, pelvis, and other flat bones, i.e. skull and sternum, and the appendicular skeleton includes the long bones of the extremities. Anatomically, long bones can be distinguished into three different components. Epiphysis is the part at the both ends of a long bone, and in a growing skeleton it is separated by a growth plate from the rest of the bone. Metaphysis, in turn, is the part between the epiphysis and a central portion of the bone shaft called diaphysis.

Bone tissue is organized into cortical (compact) and trabecular (cancellous) bone. Cortical bone is a dense, solid mass covering the external part of the bones. The inner surface of the cortical bone is in contact with bone marrow and is called endosteum, while the outer side of the cortical bone faces the surrounding tissues and is known as periosteum. Trabecular bone, which locates primarily internal to cortical bone and particularly at the ends of the long bones, is cancellous, and consists of arches, plates, and lattice of rods, which are oriented along the lines of principal stresses. Trabecular bone is metabolically more active than cortical bone, but as a structure, it is less stiff and thus weaker than the cortex (Currey 1984, Buckwalter 1995).

Bone tissue consists of 70 % inorganic or mineral salts, 5-8 % water, and 22-25 % organic matrix. Inorganic phase composes mainly (95%) specific crystalline hydroxyapatite and calcium phosphate, whereas 98% of the organic matrix is composed of Type I collagen fibers, usually oriented in preferential directions, and noncollagenous proteins (Currey 1984, Baron 1993, Buckwalter 1995, Einhorn 1996). Cells account for the remaining 2 % of the organic matrix.

Three types of bone cells are responsible for bone metabolism and turnover (responding to various environmental signals, such as mechanical loads). Osteoblasts are bone formation cells, and they synthesize the osteoid, protein component of the bone matrix. Once this synthesized osteoid has been mineralized, osteoblasts will become osteocytes, which consist more than 90 % of the bone cells in the mineralized bone matrix. The function of the osteocytes is poorly understood, but it has been suggested that osteocytes receive mechanical input signals and transmit these signals to the other cells in bone, thus taking part in mechanical regulation of bone tissue (Cowin 1991, Lanyon 1993, Mullender and Huiskes 1995, 1997). The third type of bone cells are called osteoclasts, which act as bone resorption cells.

1.1. Bone Modeling and Remodeling

Two biological mechanisms are involved in bone turnover at tissue level. Modeling is a mechanism providing purposeful size and shape to bone tissue to suit both the genetic plan and the demands of current mechanical usage, and thus, determining the bone mass and strength during growth, or in response to increased mechanical loading. Modeling process adjusts skeletal strength through strategically placed, nonadjacent activity of formation and resorption: A formation drift adds new bone over broad regions of bone's surface (without preceding resorption), and a resorption drift removes bone from another surface (without associated formation). Modeling process can be further divided into micromodeling, which organizes cells and collagen and thus, determine the type of tissue, and macromodeling, which controls the shape, size, strength and anatomy of the bones. On trabeculae, these drift patterns are called minimodeling (Frost 1990a).

Remodeling, in turn, is defined as a lifelong renewal process of the skeleton as being the main process of bone turnover after the completion of skeletal growth. Remodeling is associated with a complex coupled activity of resorption (osteoclasts) and formation (osteoblasts), which removes and replaces bone at or near the same bone location without affecting the macroscopic bone shape or density. Basic multicellular units (BMUs; i.e. small packets of osteoclasts and osteoblasts) are responsible for the remodeling process (Frost 1987a, 1987b, 1990b) (Figure 1).

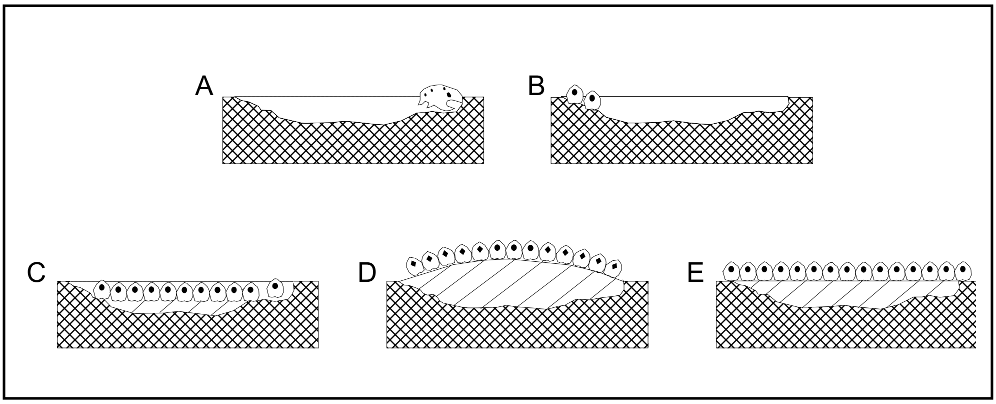


Figure 1. Remodeling process begins when the osteoclasts first attach to a quiescent bone surface and dissolve the bone beneath (A). After that, osteoblasts will become activated and replacement of the resorbed bone will begin (B). BMU-based remodeling occurs throughout life on the periosteal, haversian, cortical-endosteal, and trabecular bone surfaces, and depending on the existing physical stimuli (e.g. mechanical loading), resorption can exceed formation and bone loss will occur (as on endosteal and trabecular surfaces) (C), or, vice versa, formation can exceed resorption and new bone will be gained (as on periosteal surface) (D). In normal or balanced remodeling cycle, the amount of bone resorption and formation is equal (as on haversian surface) (E).

1.2. Biomechanical Properties of Bone

1.2.1. Stress and Strain

The concepts of stress and strain are fundamental to bone biomechanics. Stress can be considered as an intensity of force that is applied to a material per unit area. In other words, stress is an internal resistance in bone generated to counter the applied external force (equal in magnitude, but opposite in direction), and is measured by force per unit area. A basic unit of stress is called a pascal (Pa), a force of one Newton acting over an area of one square meter.

Stress can be classified to three basic types: compressive, tensile, and shear. Compressive stress is produced when two forces are directed toward each other along the same line (i.e. the material shortens). Tensile stress, in turn, is produced when two forces are directed along the same line but away from each other (i.e. the material is stretched), and shear stress arises when two forces are parallel to each other, but not along the same line (one region of a material slides relative to adjacent region). In nature, these three basic types of stress can act alone or in combination, and produce different stress patterns as a result of different types of externally applied loads: compression (Figure 2A), tension (Figure 2B), bending (a combination of tensile, and compressive forces, Figure 2C), and torsion (shear stresses along the entire length of the bone, Figure 2D). In addition to the forces which arise during functional activity, the skeleton may be subjected to impact forces which result from collisions, falls and other accidents.

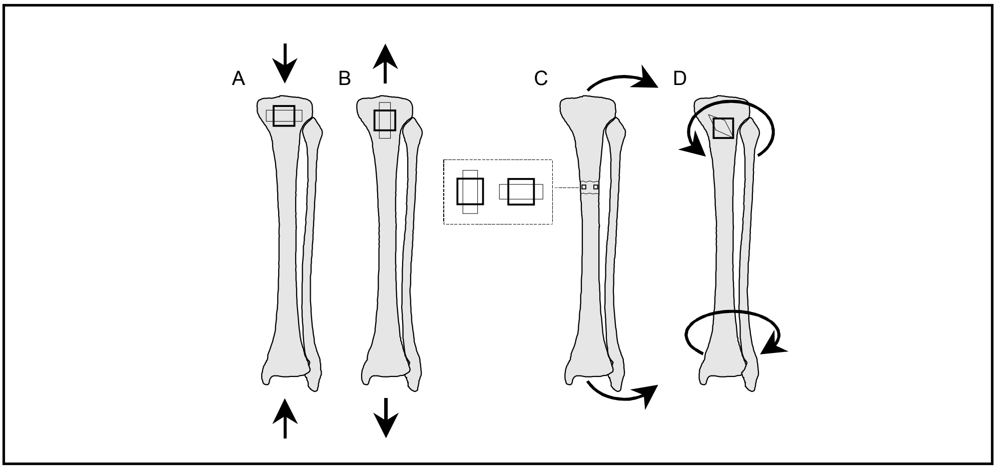


Figure 2. Stress can be classified to three basic types: compressive, tensile, and shear. In nature, these three basic types of stress can act alone or in combination, and produce different stress patterns as a result of different types of externally applied loads: compression (A), tension (B), bending (C), and torsion producing shear (2 D). The boxes on the bones present the deformation of the bone structure during the load application (the bold box presents the original shape, and the regular box the deformation).

Strain, in turn, describes the deformation in shape and size of which bone experiences under the influence of an applied load. Strain is a dimensionless ratio, which is reported as the change in length of a material divided by the original length of the material (Einhorn 1992, Turner and Burr 1993, Currey 2001).

1.2.2. Material and Structural Properties of Bone

The biomechanical properties of bone can be divided into material and structural properties (Einhorn 1992, Turner and Burr 1993). The material properties are the qualities of the bone at tissue level, irrespective of size, structure or geometry, and they can be defined by performing standardized mechanical tests on uniform, machined specimens taken from an intact bone. The relationship between stress applied to a bone structure and strain of bone tissue in response to this load is expressed as a *stress/strain* curve (Figure 3). There is a linear relationship between stress and strain until the *yield point* of the curve is reached. After this point, the curve becomes nonlinear and the slope decreases. The *stiffness* or rigidity of the bone is determined as the linear slope of the stress/strain curve and is called *elastic modulus or Young's modulus*. The linear part of the curve is also known as the *elastic region*, and load applied to bone in that region will only deform the bone temporarily; after the load is removed, the bone will return to its original shape. Increasing the load over the yield point, the permanent deformation begins to accumulate in the bone tissue, and finally, the bone will break (the *ultimate stress* and *strain*). This postyield part of the curve is known as the *plastic region*. The area under the stress/strain curve (i.e. the area of the elastic strain region plus the area of the plastic strain region) is a measure of the *strain energy*, and the amount of energy a bone can absorb before failure determines the *toughness* of the bone (Einhorn 1992, Turner and Burr 1993).

When the bone is considered as a whole functional unit with intact size and shape, the structural properties of bone can be determined. Now, the relationship between applied load and deformation is described by *load/deformation curve* (Figure 3). This curve can, consistently with stress/strain curve, be divided into the *elastic and plastic deformation regions. Extrinsic stiffness* of the structure is defined as the slope of the linear curve in the *elastic deformation* region. In this region, the applied force results in nonpermanent deformation of the bone structure. After the *yield point*, in the *plastic deformation region*, the slope of the load/deformation curve decreases and permanent damage will be caused. The whole area under the load/deformation curve determines the amount of energy needed to cause the failure of the given bone, and the amount of load and deformation to cause the failure is known as the *failure load* and *failure deformation*, respectively (Einhorn 1992, Turner and Burr 1993).

The mechanical properties of bones are governed by the same principles as those of man-made load-bearing structures, but the bone as a living organ is capable to adapt its structure to changes in loading environment. Generally speaking, the structural strength and stiffness of the whole bone is a combination of its size, geometry, mass distribution, and internal architecture. During normal activities, the highest stresses experienced in the bone diaphysis are caused by bending and torsional loadings. In resisting these loads, the cross-sectional area and geometry of the bone can be more important than is its mass or density. Ideally, in bending and torsion, bone should be distributed as far away from the neutral axis of the load as possible. The geometric parameter used to describe this phenomenon in bending (i.e. the distribution of the bone material around the neutral axis and thus, the resistance of the structure to bending) is the *cross-sectional moment of inertia* (CSMI*)*. Structures with a large CSMI have more resistance to bending. In torsion, deformation is also resisted more efficiently if bone is distributed far away from the neutral torsional axis, and this property is known as the *polar moment of inertia* (Einhorn 1992, Turner and Burr 1993).

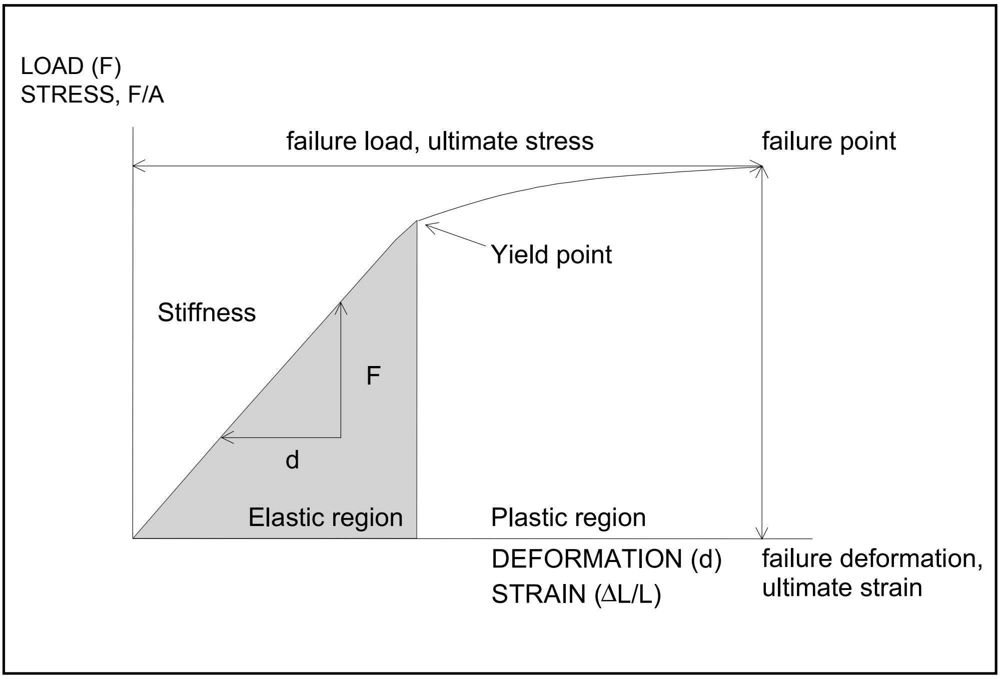


Figure 3. Load-deformation (stress-strain) curve of a bone.

2. Mechanical Adaptation of Bone

Healthy bone is constantly adapting to changes in its loading environment, and thus accommodating the structural competence of the skeleton to the mechanical demands placed upon it (Wolff 1892). The presence of such purposeful bone structure is achieved via above mentioned modeling and remodeling, which remove bone from the site where mechanical demands are minimal, and form bone at the site where the demands are increased.

According to the Frost's "*mechanostat*" theory (Frost 1964), bone cells form sensor and effector systems that adjust skeletal strength by sensing mechanical usage (peak bone strains) and effecting meaningful changes in skeletal mass, and geometric and material properties. The capability of bone to respond to mechanical loading is determined by strain setpoints (*minimal effective strains, MES*), which provide a dual system in which bone modeling adapts the bone mass to gross overloading, and remodeling adapts the bone mass to gross underloading. Peak bone strains above the 1500-3000 microstrains range cause bone modeling to increase cortical bone mass, while strains below the 100-300 microstrains range release BMU-based remodeling, which then removes existing cortical-endosteal and trabecular bone. Bone modeling stops, and bone remodeling is greatly reduced, when skeletal homeostasis (steady-state) is achieved; i.e., the bone adaptation has returned peak strains within the physiological mechanical usage range. Factors, such as hormones, nutrition, age, and diseases can further modulate the above described feedback control system for bone structure (Frost 1987 a,b, Kimmel 1993).

In addition to MES, it has been suggested that three other fundamental rules govern bone adaptation (Turner 1998): (1) Bone adaptation is driven by dynamic, rather than static, loading; (2) Only a short duration of loading is necessary to initiate an adaptive bone response; and (3) Bone cells accommodate to a customary mechanical loading environment, making them less responsive to routine loading signals (thus, strains applied to the skeleton have to be abnormal to drive structural change).

Today, it is generally believed that fluid flow through interstices of bone, either directly by local deformation or by some electrical effect related to streaming potentials, mediates the *mechanotransduction* (the transfer of mechanical stimulus into chemical signals and eventually to cell and tissue response), although it has also been proposed that bone cells could directly detect small deformations of bone tissue that are induced by external forces (Weinbaum et al. 1993, Hsieh and Turner 2001). Osteocytes has been proposed to be the best candidates for mechanosensors in bone, due to their perfect location within the bone matrix, interconnections by which they communicate with each other and with cells at the bone surface, and their sensitivity to fluid flow across their cell membranes (Cowin 1991, Lanyon 1993, Mullender and Huiskes 1995, 1997). Also, bone lining cells might be more involved than generally assummed (mechanical loading appears to activate bone lining cells with a temporal sequence that correlates with bone matrix production) (Chow et al. 1998).

Although loading-induced strains, and the above noted three rules, are widely believed to govern the adaptation of bone tissue (Rubin 1985, Frost1987a), the primary mechanical signal behind the adaptation is, however, not known. Several studies have shown that not only the magnitude, but also the strain distribution (Lanyon 1984, 1996, Rubin and Lanyon 1985, 1987), number of strain cycles (Rubin and Lanyon 1984), strain rate (O'Connor et al. 1982, Turner et al. 1995, 1998, Mosley and Lanyon 1998), and strain gradients (Frost 1993, Gross et al. 1997, Judex et al. 1997) can act as a primary mechanical variables associated with the regulation of bone mass. In addition, very recent experimental studies have also suggested that even extremely low-magnitude strains may strongly determine skeletal morphology, if they are just applied at high frequency (Rubin 2001 a and b, 2002 a and b).

2.1. Strain Magnitude

A traditional conception is that strain magnitude is the primary mechanical signal for the adaptation of bone tissue. The above noted Frost's mechanostat theory specifies the level of the minimum effective strain (MES), which is necessary for the maintenance of the bone tissue. Bone structure is maintained if the customary mechanical strains remain between 200-2500 microstrains (Lanyon 1987, Frost 1990 a, 1992, Cowin et al. 1991, Turner 1991, 1994 b). If loading-induced local strains, in turn, exceed the MES, the modeling will be induced and bone mass will increased. But if customary bone loading is decreased or bone is subjected to disuse, its peak strains fall and the remodeling process will be released. Rubin and Lanyon (1985) showed that functional isolation results in a significant reduction in the cross-sectional area at the midshaft of the turkey ulna, and the cross-sectional bone area is not maintained until the peak strain is increased to 1000 microstrains. On the other hand, strains above this level were associated with a proportional increase in new bone formation.

2.2. Strain Distribution

Unusual strain distribution has been suggested to be an efficient modulator between the peak strain magnitude and change in the bone's cross-sectional area. Thus, if mechanical strains are applied in an unusual direction, they do not have to be abnormally high or exceed the MES to stimulate new bone formation (Rubin and Lanyon 1985, 1987). The required strain magnitude can actually be lower than normal to elicit an adaptive response in bone if the mechanical loading pattern differs from the usual. In other words, the more unusual is the strain distribution in the bone, the more osteogenic is the stimulus (Lanyon 1984 b, 1996).

2.3. Strain Cycles

The number of loading cycles is also considered to be a determinant of the adaptive process. Although it is believed to be less important than the strain magnitude, a minimum number of loading cycles are still required for a response (Rubin and Lanyon 1984, Lanyon 1987). Rubin and Lanyon (1984) showed that the osteogenic response to loading (2000 microstrains) became saturated after as few as 36 consecutive loading cycles (lasting only a total of 72 s per day). No additional new bone formation resulted from increased number of loading cycles, and only four cycles per day were sufficient to prevent bone resorption. Thus, only a few loading cycles (<50) at high magnitudes are needed at each distribution, and only a short duration of mechanical stimulus is necessary to initiate an adaptive response (Lanyon 1996). On the other hand, it has been concluded that if the number of loading cycles is increased, the magnitude of the strain stimulus can be decreased for similar adaptive response of bone, and thus, strain rate or frequency associated with the loading stimulus may also play a critical role in the mechanism by which bone responds to mechanical strain (Qin et al. 1998, Cullen et al. 2001).

2.4. Strain Rate

As mentioned above, the rate of strain change has also been suggested to be an important determinant of bone adaptation (O'Connor et al. 1982, Turner et al. 1995, 1998, Mosley and Lanyon 1998, Qin et al. 1998). Turner et al. (1995) concluded that relatively large strains alone are not sufficient to activate bone cells, but high strain rates and possibly the stress-generated fluid flow are required to stimulate new bone formation (stress-induced fluid flow is dependent on the rate of change in bone strain). Also O'Connor et al. (1982) showed that peak strain rate consistently correlated most highly with remodeling, and similar peak strains imposed at high strain rates were associated with greater amounts of new bone formation, and low strain rates were either less osteogenic or resulted in resorption. The suggestion that dynamic load, rather than static loading, initiates an adaptive response (Hert 1978, Lanyon and Rubin 1984), supports also the contention that strain rate is an important factor in the adaptation process of bone (if only the strain magnitude or strain distribution were pertinent, static loading would be able to cause adaptation).

2.5 Strain Gradients

Frost (1993) have also proposed that strain gradients could be the specific osteogenic component of the mechanical stimulus, and this notion has recently supported by Gross et al. (1997) and Judex et al. (1997). They found that loading-induced peak circumferential strain gradients, not the peak strain magnitude or the peak strain rate, correlated highly with the specific sites of bone formation.

Strain gradients reflect differential deformations across a volume of bone tissue in a given direction. Physiologically, strain gradients are relevant as they generate pressure differentials within bone and, thereby, it has been suggested that they may contribute to the fluid flow in bone, which in turn, is proposed to be integral to the process by which bone perceives and responds to mechanical stimuli (Judex et al. 1997).

2.6. Strain Frequency

Also loading frequency is considered to be one of the most important mechanical factors that affects bone adaptation (Rubin and McLeod 1994, Turner et al. 1994 b). Studies suggest that the anabolic potential of mechanical strain is strongly frequency dependent: whereas 1 Hz loads must exceed 1000 microstrains to stimulate cortical bone formation (Rubin and Lanyon 1987), loads applied at 30 Hz necessitate only strains on the order of 50 microstrains to achieve the same result (Qin et al. 1998). Also Hsieh and Turner (2001) have demonstrated that the loading frequency modulates the anabolic effect of mechanical loading on bone tissue in a dose-response manner, and the most recent studies by Rubin et al. (2001 a,b, 2002 a,b) showed that in trabecular bone strain signals as low as 5 microstrains can be strongly anabolic if applied at 30 Hz.

3. Vibration Loading, Bone and Muscular Performance

3.1. Effects of Vibration on Bone

Using the turkey ulna model of bone adaptation, Rubin and McLeod demonstrated in 1994 the sensitivity of bone tissue to the frequency of the applied stimulus. One year later, Rubin et al. (1995) presented that low-magnitude, high frequency mechanical vibration can efficiently enhance trabecular bone formation: Skeletally mature turkeys stood on a vibrating platform, oscillating at 30 Hz (peak-to-peak accelerations of 0.3g) and causing peak strains of approximately 50 microstrains in the cortex of the tibia, for five minutes per day, and following the 30-day intervention, the dynamic indices of new bone formation (mineral apposition rate and labeled surface) were significantly stimulated in the trabeculae of the distal tibia (by 2.3 mm/ day and by 51 %, respectively).

In recent years, Rubin and coworkers have continued their work with vibration, and their new animal studies (2001 a,b, 2002 a,b) have given additional evidence for the efficacy of vibration loading to improve mass and mechanical competence of bone. Using adult female sheep as the test animals, Rubin et al. determined the effects of long-term (12 months) vibration loading on bone tissue in the proximal (2001 a) and distal (2002 a) femur, and in the tibia (2002 b). During these experiments, the hind limbs of experimental sheep were subjected to a vertical vibration, oscillating at 30 Hz (peak-to-peak accelerations of 0.3 g, amplitude 0.1 mm) and causing the peak strains only of about 5 microstrains in the surface of the animal's tibia, for 20 minutes per day, for five days per week.

Following the 12-month vibration stimulation, the DXA-derived bone mineral density (BMD) of the proximal femur in stimulated animals was 5.4 % greater than in controls, but this difference was not statistically significant. Also pQCT failed to demonstrate a significant difference in the total density of the proximal femur (between-group difference 6.5 %, NS), but, when this assay was used to selectively evaluate cortical and trabecular bone at the lesser trochanter, a 34.2 % increase in bone density was observed in the trabecular bone of the vibrated sheep (Rubin et al. 2001 a,c). An increase in trabecular density was also substantiated by undecalcified bone histology, which revealed a 32 % increase in trabecular bone volume, a 45 % increase in trabecular mesh number, and a 36 % reduction in mesh spacing indicating an improvement in the quality of trabecular bone. Also the histomorphometric studies of bone turnover suggested an increase in bone formation and mineralization rate (more than 2-fold increase), although these changes were not statistically significant. The anabolic effect of vibration stimulus was, however, highly specific to trabecular bone, and there were no significant changes in any of the cortical bone parameters (Rubin et al. 2001 a, 2002 b).

Also in the distal femur, trabecular bone was stimulated: trabecular bone mineral content (BMC) was 10.6 % greater, and the trabecular number 8.3 % higher in the experimental animals than controls (evaluated by microcomputed tomography), while trabecular spacing was decreased by 11.3 % after the 12-month vibration loading (Rubin et al. 2002 a). In addition, material testings performed by microcomputed tomography scanning (high-resolution three-dimensional models from the 1-cm bone cubes harvested from the medial condyle of the femur) demonstrated increased stiffness and strength in the plane of weightbearing. DXA measurements did not demonstrate BMD differences between vibration and control group in this study either.

In the tibiae, the pQCT measurements were not performed, despite the very trabecular specific findings in the proximal and distal femur (Rubin et al. 2002 b). During the one-year intervention, the mean change of DXA-derived BMD was slightly greater in the vibrated sheep compared with the controls at all timepoints, but the group difference reached statistical significance at one timepoint only (at 29 weeks, %-unit difference between the vibration and control groups 0.044, $p=0.05$).

Rubin et al. (2001 b) also evaluated the ability of vibration loading to block disuse-induced osteoporosis. They subjected adult female rats to hind limb suspension for 28 days, and, for ten minutes per day, the disuse was interrupted either by vibration stimulus or by normal load bearing. After the 28-day protocol, histomorphometric studies were assessed, and they showed that vibration loading (0.25 g equivalent to < 10 microstrains at 90 Hz vibrations) for 10 minutes per day for 5 days per week had blocked completely the adverse effects of hind-limb tail suspension on bone formation rate at the proximal tibia, whereas a similar period of normal load bearing had only a minimal effect on disuse-induced changes.

In 1998, Flieger et al., in turn, demonstrated that vibration (50 Hz, acceleration of 2 g, 30 min/day for 5 days/week for 12 weeks) is capable to prevent ovariectomy-induced bone loss in rats. In this study, the vibration loading had, however, no effect on the bone mineral density of the nonovariectomized rats.

Several theories have been proposed to explain the influence of loading frequency on osteogenesis. Most notably, it has been suggested that loading induces perturbations of intramedullary pressure, which in turn, induces fluid flow through the extracellular spaces in bony canaliculi and lacunae, and this fluid movement is enhanced by higher loading frequencies. Fluid flow causes shearing stresses on the cell membranes, which, in turn, are well established to stimulate bone cells in culture (Weinbaum et al. 1993, Hsieh and Turner 2001). Also the loading induced "stress-generated" electric potentials have been suggested to enhance extracellular fluid flow and thus stimulate bone cells (Hsieh and Turner 2001). Several potential mechanisms for converting extracellular fluid forces into cellular responses have also been proposed, e.g. membrane mechanoreceptors, focal adhesion proteins, cytoskeletal signaling, and extracellular fiber bowing. In many cases, mechanotransduction begins when fluid flow or shear stress cause deformations of cells or cell membranes. Viscoelasticity of the cell or extracellular matrix will, however, affect the amount of cellular deformation resulting from the fluid forces (Hsieh and Turner 2001). From the biological side, osteogenic mechanical signals that form bone (and prevent bone loss) may also influence the activity of molecules that ultimately stimulate both bone formation and resorption; for example, bone formation rate and RANKL (NFkB ligand, a cytokine involved in osteoclastogenesis) expression level has been shown to have an inverse correlation (Rubin et al. 2001 c).

Because low magnitude (< 5 microstrains), high frequency (10-50 Hz) strain signals also arise through muscular activity (essentially at all times during which muscle contraction is involved including standing), and thus, continually barrage the skeleton, it has been suggested that these persistent, low magnitude strains, when summed, could be at least as important determinants of bone mass and morphology during lifetime as the seldom occurring high magnitude strain events that arise from vigorous activity (Fritton et al. 2000, Huang et al. 1999, Rubin et al. 2002 b). And while the EMG (electromyographic) recordings from soleus muscle have demonstrated a significant decrease in muscle activity in the frequency range above 20 Hz in elderly people, it has been proposed that this decline in muscle activity would be the cause of age-related bone loss, i.e., bone mass declines with advancing age partly because these muscle-based strongly anabolic signals will attenuate (Huang et al. 1999, Rubin et al. 2001 a,b,c, 2002 a,b).

3.2. Effects of Vibration on Muscular Performance

It has long been noticed that vibration of muscles and tendons has an effect on their normal function (Griffin 1990), and thus, mechanical vibration has aroused interest, not only in bone research but also in exercise physiology, as a potentially very efficient training method for skeletal muscles.

In 1999, Bosco et al. showed that a single vibration training (26 Hz, amplitude 10 mm, acceleration 5.5 g, for 10 min in 60 s intervals) resulted in a significant temporary increase in muscle strength and speed of strength production in the lower extremities of female volleyball players (1999b). They also studied the effects of vibration on arm flexor muscles of male boxers (30 Hz, amplitude 6 mm, acceleration 3.5 g, for 5 min in 60 s intervals), and on jumping performance and extension strength of lower extremities of physically active men (26 Hz, displacement +/- 4 mm, 17 g, for 10 min in 60 s intervals), and the results were similar: muscle strength in vibrated arm and lower extremities increased significantly after a single vibration stimulus (Bosco et al. 1999 a, Bosco et al. 2000). The similar increase in maximal and explosive strength of arm and leg muscles has also been demonstrated by Issurin et al. (1994) and Issurin and Tenenbaum (1999).

Also some studies of the effects of longer term vibration loading exist. Bosco et al. demonstrated in 1998, that a 10-day vibration regimen (26 Hz, amplitude 10 mm, acceleration 2.8 g, 10 min/day in 2 min intervals) enhanced significantly the explosive power of lower extremities (height of the best jump and mechanical power of the best jump) in physically active subjects. Runge et al. (2000), in turn, studied the effects of a 2-month vibration regimen (27 Hz, amplitude 7-14 mm, 3x2 min, 3x/week) on physical performance in geriatric patients, and observed an 18 % enhancement in the chair rising time in the vibration group compared to the constant values of the controls.

Rittweger and coworkers (2000) studied the effects of exhaustive whole-body vibration, and demonstrated that heart rate, blood pressure, lactate consentration and oxygen uptake increased after the vibration stimulus (at the frequency of 26 Hz until exhaustion, amplitude 10.5 mm, acceleration 147 m/s^2 or 15 g), but not as much as after bicycling. In addition, immediately after the exhaustive whole-body vibration the jump height and the maximal voluntary force in knee extension was decreased, although the force of the 10-second maximal voluntary contraction test (MVC) decreased less than in the controls, and reduction of jump height was basically recovered within 20 seconds. EMG frequency, in turn, did not change much during MVC test, which means that less force was produced at a higher median frequency, but with less tendency to decline during sustained contraction.

In the animal study of Falempin and In-Albon (1999), vibration stimulus (120 Hz, amplitude 0.3 mm, 192 s/day for 14-day period) applied directly to the Achilles tendon of an unloaded soleus muscle (tail-suspension experiment) attenuated significantly, but not completely prevented, the disuse-induced muscle loss. They also studied the contractile properties of the soleus muscle by EMG recordings during the vibration stimulus plus passive stretching, and found an attenuation in the decrease of the maximal twitch and tetanic tensions and half relaxation time. They suggested that vibration-induced activation of Ia afferent impulses of muscle spindle recruited more motor units in the soleus muscle, and thus enhanced the force development.

The vibration-induced enhancements in the muscular performance (Bosco et al. 1998, 2000) have been suggested to be similar than those after several weeks of explosive power training (Coyle et al. 1981, Häkkinen and Komi 1985, Bosco et al. 1999 a). Because the first adaptation mechanism of a skeletal muscle to resistance training is neural (Moritani and DeVries 1979, Sale 1988, Carroll et al. 2001), and changes in the neural factors occur within a few weeks and months, the enhancements of physical performance in above mentioned studies are proposed to be mainly caused by neural adaptation. Several explanations have been presented to cause this adaptation; e.g., increase in motor unit synchronization, co-contraction of the synergist muscles, and increased inhibition of the antagonist muscles. In addition, an increase in the ability of motor units to fire briefly at very high rates, and thus induce an increase in the rate of force development even if the peak force does not necessarily increase, has been proposed to correspond to enhancement (Moritani and DeVries 1979, Sale 1988, Carroll et al. 2001). However, the exact mechanism by which the explosive power training can enhance neuromuscular adaptation is still unknown. Adaptations to specific training depend much on the training program employed. Conventionally, strength and explosive power training are based on exercises performed with rapid and violent variation of the gravitational acceleration, and these changes in the gravitational conditions have also been suggested to be produced by whole body vibration (Rubin et al. 1994, Bosco 1998, 1999 a).

Mechanical vibration has been reported to exert a tonic excitatory influence on the muscles exposed to it, and the reflexive reaction of skeletal muscles to whole body vibration is a chain of a small and rapid involuntary muscle contractions. In the spinal cord, the activation of Ia afferents by muscle vibration initiates impulses in a polysynaptic excitatory pathway, which evokes the response called "tonic vibration reflex" (TVR; tonic contraction of muscles in response to vibration-induced stretching force). TVR has been suggested to increase with vibration frequency up to 100-150 Hz but decrease beyond. Whether the TVR is produced only by vibration of an individual muscle-tendon, or could it be evoked also by whole-body vibration is, however, not known (Hagbarth 1973, Desmedt and Godaux 1978, Griffin 1990, Romaiguere et al. 1991). Also skin mechanoceptors (as Meissner and Pacinian corpusles) have been indicated to trigger muscle spindle activation, may be via a long loop, and induce a flexion reflex during the vibration stimulus (Kodachi et al. 1987, Hollins and Roy 1996).

Vibration-induced TVR includes excitation of muscle spindles, mediation of neural signal by 1 a afferents to alpha-motoneurons, and finally, activation of muscle fibers. It may also recruit more motor units via activation of muscle spindles and polysynaptic pathways (De Gail et al., 1966, (Hagbarth 1973, Falempin and In-Albon 1999), and if the corresponding muscle is under a high pre-tension (stretched), it can be argued that the response of the primary sensory endings of the muscle spindle could be even greater (Burke et al. 1976, Matthews and Wattson 1981, Roll and Vedel 1982). On the other hand, preceding muscle exercise may also accentuate the TVR (Bongiovanni et al. 1990).

TVR is capable to re-recruit motor units and sustain motor unit firing rates even in fatigued muscles, which is seen as a temporary increase in the muscle activity (Martin and Park 1997, Griffin et al. 2001). However, if muscle-spindles are irritated by long-term vibration, muscles will ultimately become fatigued (Bongiovanni et al. 1990, Martin and Park 1997). On the other hand, vibration-induced synchronization process has also been proposed to influence muscle fatigue, since it forces the driving of motor units, and thus leads to a decrease in contraction efficiency. Muscle fatigue is seen, besides as a reduction of force output, also as a reduction of EMG activity and motor unit firing rates.

There may be one-to-one correspondence between muscle spindle discharges and the mechanical vibration stimulus in low frequencies (Seidel 1986, Roll et al. 1989, Wierzbicka et al. 1998). Roll et al. (1989) demonstrated that most of the muscle spindles of the peroneus muscle fired harmonically with the tendon vibration up to 80 Hz and then discharged in a subharmonic manner (1/2-1/3) with increasing vibration frequencies.

Vibration-induced activation of Ia afferents may, however, also initiate impulses in a presynaptic inhibitory pathway, which, in turn, is responsible for the vibration-induced reflex inhibition (Desmedt 1978, 1983, Ashby 1987, Romaiguere et al. 1991). Already in 1966, De Gail et al. demonstrated that spinal reflexes, such as the Achilles tendon reflex, were reduced while a tonic contraction developed in a vibrated muscle. Later, Roll et al. (1980) reported that this inhibition of tendon reflexes lasts throughout the whole-body vibration exposure (18 Hz, 15 min) and continues for several minutes after the end of the exposure. A presynaptic inhibition, a trasmitter depletion and a fatigue of the Ia afferents, have been postulated (Bongiovanni et al. 1990). This dichomotous effect of muscle vibration on spinal interneuronal pathways (excitatory pathway and inhibitory pathway) is known as the vibration paradox (Desmedt 1983).

3.3. Other Physiological Responses to Vibration

Knowledge of the chronic effects of whole-body vibration is largely based on retrospective or cross-sectional studies of persons exposed to vibration during their work, e.g. in industrial machinery, and many forms of industrial illness are thought to result from the effects of vibration on the human body. It has to, however, be kept in mind, that pysiological and also pathological responses in working environment are not predominantly whole-body vibration-specific, while related to the totality of working conditions (i.e. to common environmental stresses), and human responses to whole-body vibration depend on many variables in the working environment, e.g. on the frequency, magnitude, and duration of vibration, posture of body, and attitude, experience and susceptibility of the subject. Thus, reliable conclusions of exposure-response relationships of vibration for different symptoms and injuries are difficult to be drawn (Griffin 1990). Recommendations of the daily dose of whole-body vibration point, however, towards a continuous dose reduction. Directive of the European Parliament and of the Council (Article 16(1) of Directive 89/391/EEC) determines that continuous, daily whole-body vibration exposure limit is 2.3 m/s^2 (0.2 g) for an 2-hour reference period for industry workers. For hand-arm vibration, the limit is 10 m/s^2 (1 g). Temporary or short-term vibration may naturally exceed these limits, although the directive does not give any precise exposure limit for short-term accelerations.

In contrary to those above mentioned positive effects on musculoskeletal system, epidemiologic studies have indicated that there is an increased risk for various disadvantageous symptoms and changes in musculoskeletal system, including neck and low back pain, and degenerative and mineralization changes in bones and spinal system, among the occupational groups (e.g., crane operators, and bus and tractor drivers) exposed to whole body vibration (WBV) (Fialova et al. 1995, Bovenzi and Hulshof 1999). In the review article of Bovenzi and Hulshof (1999), the mean WBV exposure time for the low back pain and lumbar disc disorders varied between 7 and 21 years, and the vibration magnitude from 0.25 to 1.45 m/s^2 in cranes, busses, and tractors. Vibration-induced muscle fatigue, related latency to a sudden load, and microfractures at the end plates of the bones has proposed to cause these changes (Griffin 1990, Pope et al. 1998). In animal studies, changes in muscle fibres' size has also been demonstrated as a sign of vibration-induced (80 Hz, 32 m/s^2, 5 hours/day for 5 days) muscle injury (Necking et al. 1992). On the other hand, the vibration of limb muscles have been used in therapeutic applications, such as in spastic disorders and orthopedic and geriatric patients with musculoskeletal problems (Griffin 1990).

Increased occurance of digital vasospastic disorders [called vibration-induced white finger (VWF)], sensorineural problems, and structural changes in peripheral nerves (demyelination, fibrosis, edema) are injuries related to occupational exposure to hand-held high-frequency vibrating tools (Stromberg et al. 1997, Bovenzi 1998, Bovenzi et al. 1998, 2000 a,b). Vibration with frequencies 31-250 Hz has been shown to induce significant reductions in finger blood flow (5.5 m/s^2, 15 min) (Bovenzi et al. 2000 b). Sensorineural problems were found to increase with increasing daily vibration exposure, especially if acceleration exceeded 6 m/s^2 for a 8-hour period/day (Bovenzi et al. 1998). In these patients, in whom the structural nerve changes were observed, the median exposure time for vibration was 25.5 years (1-8 hours/day) (Stromberg et al. 1997). Daily, 8-hour exposure to 5 m/s^2 hand-vibration, has been estimated to cause white finger disease for 30 % of forestry workers after the 30 years of exposure (Bovenzi 1998) Raynaud's syndrome (according to French physician, who described the phenomenon of finger blanching on exposure to cold) is one of the best known ill-effect of vibration, and sympathetic hyperactivity as well as damage in vaso-regulatory structures and functions in the skin of fingers has been postulated to account for vibration-induced white fingers (Gemne 1994). Interestingly, contrary to high-frequency exposure, low-frequency (26 Hz, 9 min) whole body vibration has, however, been shown to enhance muscular blood circulation after exercise (Kerschan-Schindl et a. 2001). Ribot-Cisar et al. (1996) demonstrated that vibration (amplitude 0.5 mm, 100 Hz, 10 min) may also alter human cutaneous afferent discharges, and consequently at least partly account for the alterations in sensorimotor performance (e.g. depressed sensitivity to simultaneous skin stroking) that have been reported to occur in humans after exposure to vibration.

Vibration exposure (e.g., tendon vibration at 80 Hz, amplitude 0.2 mm) may induce illusions of limb position, evoke a spatially oriented postural response, and cause problems with body balance. The evoked illusory movement occurs in a direction that would produce stretching of the stimulated muscle if the actual movement were made. Direction of the vibration-induced sway, in turn, is dependent on the vibration side (Griffin 1990, Wierzbicka et al. 1998, Kavounoudias et al. 1999). Kavounoudias et al. (1999) showed that when stimulating each zones of human plantar soles separately, the direction of the body tilt was always opposite to the plantar site vibrated. When two zones of plantar soles were, in turn, co-stimulated at different frequencies, the parameters of the postural responses depended on the frequency difference. When this frequency difference was zero, no clearly oriented body tilts occurred, and they concluded that the change in the relative pressures evoked by differently co-vibrating zones of foot sole give rise to regulative postural adjustments able to cancel the simulated body deviation.

Vibration-induced excitation of sensory systems and degeradation of the information received from sensory system has, in turn, been proposed to cause disorders in postural functions (Griffin 1990, Wierzbicka et al. 1998). Manninen and Ekblom (1984), in turn, concluded that increased sway of standing person exposed to high frequency vibration may, besides to be attributable to interference with somatosensory feedback, also arise from the response at the vestibular system. Also, vibration-produced sympathetic vasoconstriction in the cochlea has been suggested to cause the balance and hearing disorders related to vibration. The role of noise exposure has, however, to be remembered, when considering the vibration-related hearing disorders (Pyykkö et al. 1981, Griffin 1990, Seidel 1993).

In cardiovascular system, moderate to high magnitudes of vertical vibration (2 - 20 Hz) have been reported to induce responses similar to that normally occurring during moderate exercise: heart rate, respiration rate, cardiac output, mean arterial blood pressure, pulmonary ventilation and oxygen uptake all increase. Findings have been explained by psychological stress or raised metabolic activity caused by increased muscular activity (Griffin 1990, Rittweger et al. 2002). Also fetal heart rate can increase if vibration is applied to the maternal abdomen, and various fetal responses to vibration, and fetal habituation to vibration, are being investigated as diagnostic indicators of fetal health (Jammes et al. 1981, Griffin 1990, Rittweger et al. 2001). Some vibration studies have also demonstrated changes in blood (e.g. testosterone, growth hormone, adrenaline, hematocrit, endothelin, plasma red cell transit), and urine (e.g. hydroxyproline) constituents due to vibration but there is no widespread agreement on the significance or repeatability of these findings (Kasamatsu et al. 1982, Motoba et al. 1985, Griffin 1990, Palmer and Mason 1996, Greenstein and Kester 1997, Bosco et al. 2000).

Vibration-induced reduction in visual acuity, perturbations of oculo-manual co-ordination, changes in the electroencephalogram and decreases in the amplitude of auditory brain potentials as a sign of effect of vibration on central nervous information processing are also reported (Ullsperger and Seidel 1980, Griffin 1990, Martin et al. 1991, Ishitake et al. 1998, Schwarzer et al. 2000). Itching erythema, oedema of the skin over the activated muscles, and thermal sensory impairment are also mentioned. Gastrointestinal problems, e.g. suppression of gastric motility has been proposed to result from resonance of vibration frequency as a mechanical factor and stomach contents, or from increase regulation of neurohumoral factors due to vibration stress (Ishitake et al. 1999, Rittweger et al. 2000, Miyazaki 2000, Nilson and Lundstrom 2001). Long-term whole-body vibration exposure may also contribute to the pathogenesis of disorders of female reproductive organs (menstrual disturbances, anomalies of position) and disturbances of pregnancy (abortions, stillbirths). Animal experiments suggest harmful effects on fetus (Griffin 1990).

Vibration technique has also been used in detection of prosthetic loosening in hip replacements and in assessing the progress of bone fracture healing in animal models (Usui et al. 1989, Li et al. 1995, 1996, Wolf et al. 2001). Chest wall vibration, in turn, has been used to enhance pulmonary hemodynamics and 0_2-saturation in patients with chronic obstructive pulmonary disease (Nakayama et al. 1998, Oermann et al. 2001).

AIMS OF THE STUDY

The aims of this thesis were:

1. To investigate the effects of a single, 4-min whole body vibration bout on muscle performance and body balance in young healthy adults with two different vibration stimuli (studies I-II).

2. To assess the effects of 4-month vertical whole-body vibration on muscle performance and body balance (study III).

3. To study the effects of an 8-month whole body vibration intervention on bone, muscular performance, and body balance in healthy, young volunteers, and also to address the safety issues of the long-term vibration loading (study IV).

4. To study the maintenance of the possible changes in the bone, and muscular performance on the basis of the results of the study IV.

MATERIALS AND METHODS

1. Subjects and Design

Young (18-38 years of age), healthy volunteers participated in the studies I-V. They were recruited from the local university. Written informed consent was obtained from all participants. None of the subjects had any chronic diseases or contraindications with vibration exposure. Neither did they use medication that might have affected bone or participate in impact-type exercises more than three times a week. The subjects were asked not to change their current diet or physical activity during the intervention.

The basic characteristics of the subjects are presented in Table 1. Detailed information on the exclusion criteria of the subjects and study designs are given in the original reports.

	n	**Age** (years)	**Weight** (kg)	**Height** (cm)
	Vibration/control	**Vibration/control**	**Vibration/control**	**Vibration/control**
Study I Women Men	16 / 16 8 / 8 8 / 8	28.1 (2.5) / 28.1 (2.5)	67.3 (9.0) / 67.3 (9.0)	175.6 (9.4) / 175.6 (9.4)
Study II Women Men	16 / 16 8 / 8 8 / 8	28.3 (2.0) / 28.3 (2.0)	68.2 (9.4) / 68.2 (9.4)	175.4 (7.8) / 175.4 (7.8)
Study III Women Men	26 / 26 17 / 16 9 / 10	23.2 (4.4) / 25.5 (5.8)	71.6 (13.3) / 71.1 (12.8)	174.4 (8.0) / 174.0 (7.7)
Study IV Women Men	27 / 26 18 / 16 9 / 10	23.1 (4.3) / 25.5 (5.8)	71.6 (13.1) / 71.1 (12.8)	174.4 (7.8) / 174.0 (7.7)
Study V Women Men	25 / 25 16 / 15 9 / 10	24.6 (4.3) / 26.4 (5.4)	71.7 (11.4) / 71.6 (13.1)	174.5 (8.1) / 174.3 (7.7)

Table 1. Characteristics of the subjects in the studies (I-V), means (standard deviations).

1.1 Study I-II

Studies I-II were randomized cross-over studies and investigated the effects of a single, 4-min vibration bout on muscular performance and body balance. 16 volunteers participated in the studies. All participants received both the vibration- and sham-exposure and were randomly assigned to start with either the vibration- or shamregimen. Both interventions were carried out in a standing position on the vibration platform, with (vibration-intervention) or without (sham-intervention) the whole body vibration. Vibration exposures were different in the study I and II (see section 2. "Vibration loading regimens"). Six performance tests were done 10 minutes before (baseline), and 2 and 60 minutes after, the intervention (see section "3. Measurements"). The performance tests were shared between two days to avoid potential contamination of results due to the fatigue. The study procedure is presented in the Figure 1.

The effects of vibration on the muscle activity of lower extremity and back were investigated during the vibration exposure by surface electromyography (EMG) (see section 3. "Measurements").

1.2. Study III

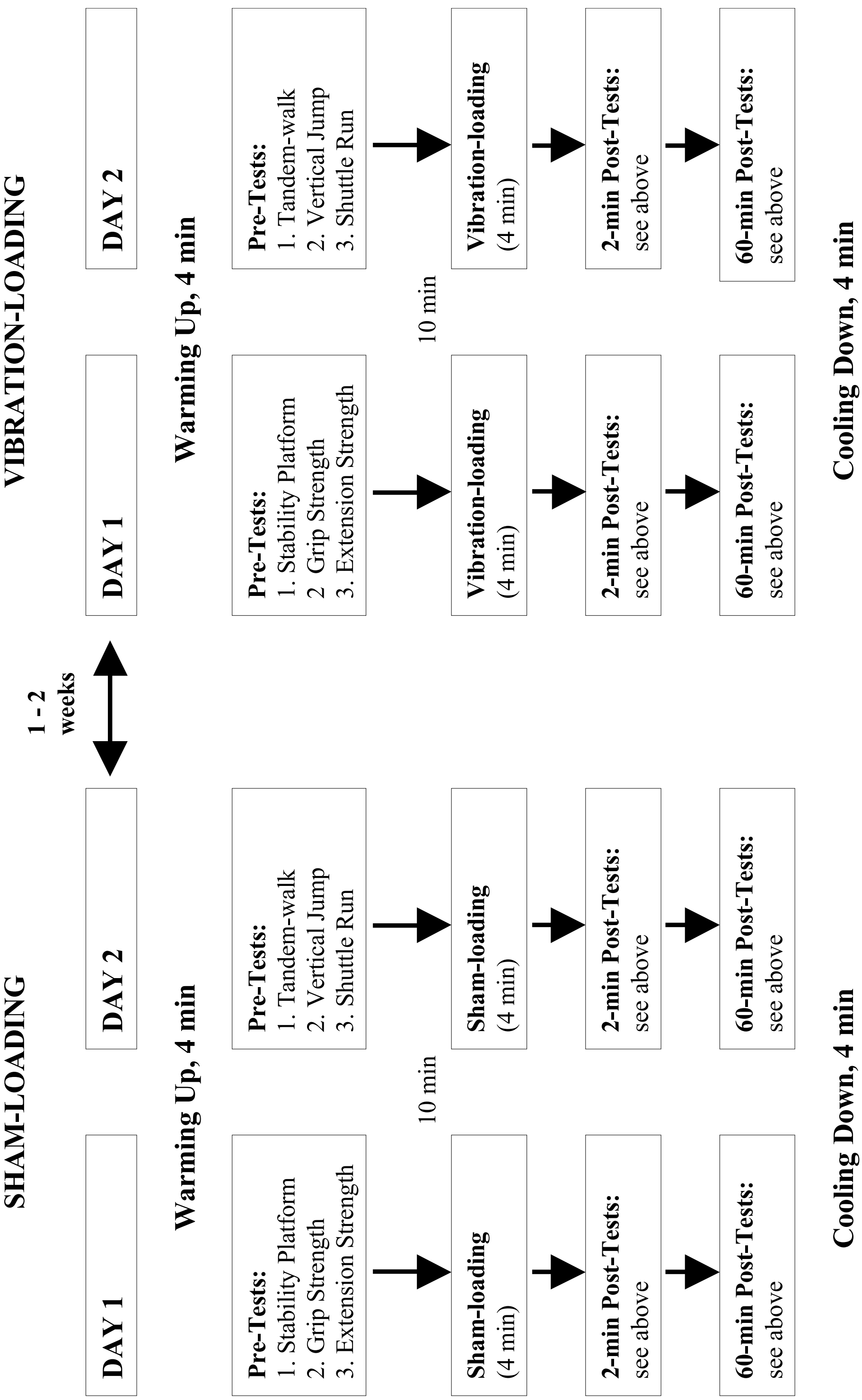
Study III was a randomized controlled intervention trial and assessed the effects of a 4-month whole body vibration-intervention on muscular performance and body balance. 56 volunteers participated in the study. Half of the subjects were randomized to the vibration group and half to the control group. The men and women were randomized separately into the groups so that number of men and women would be approximately equal in both groups. The vibration protocol consisted of a 4-month whole body vibration training (see section 2. "Vibration loading"). Five performance tests were performed initially (before randomization) and at 2 months and 4 months (see section 3. "Measurements").

During the 4-month intervention, two participants in the control group withdrew from the study because of loss of interest, and two participants of vibration group withdrew because of musculoskeletal problems (independent of the vibration-loading).

1.3. Study IV

Study IV was a randomized controlled intervention trial and investigated the effects of an 8-month whole body vibration-intervention on bone, muscular performance, and body balance. The study IV was a direct continuation of the study III. Thus, the above mentioned volunteers (56), men and women were randomly assigned to the vibration group or control group as described above. The vibration protocol consisted of an 8-month whole body vibration training (see section 2. "Vibration loading regimen"). Bone measurements, as well as five performance tests, were assessed at baseline and after the 8-month intervention. Serum markers of bone turnover were determined at baseline and after 3, 6, and 8 months. All baseline measurements were done before the randomization (see section 3. "Measurements").

Figure 1.



SHAM-LOADING
DAY 1
DAY 2
Warming Up, 4 min
Pre-Tests:
1. Stability Platform
2. Grip Strength
3. Extension Strength
Pre-Tests:
1. Tandem-walk
2. Vertical Jump
3. Shuttle Run
10 min
Sham-loading
(4 min)
Sham-loading
(4 min)
2-min Post-Tests:
see above
2-min Post-Tests:
see above
60-min Post-Tests:
see above
60-min Post-Tests:
see above
Cooling Down, 4 min
1 - 2
weeks
VIBRATION-LOADING
DAY 1
DAY 2
Warming Up, 4 min
Pre-Tests:
1. Stability Platform
2 Grip Strength
3. Extension Strength
Pre-Tests:
1. Tandem-walk
2. Vertical Jump
3. Shuttle Run
10 min
Vibration-loading
(4 min)
Vibration-loading
(4 min)
2-min Post-Tests:
see above
2-min Post-Tests:
see above
60-min Post-Tests:
see above
60-min Post-Tests:
see above
Cooling Down, 4 min

During the 8-month intervention, two participants in the control group withdrew from the study because of loss of interest and one participant in the vibration group because of a musculoskeletal problem (independent of the vibration-loading).

1.4. Study V

The study V was a follow-up study performed 8 months after the cessation of the study IV (16 months after the baseline) and assessed the maintenance of the possible changes obtained in the bone and physical performance in the study IV. The bone and physical performance measurements were the same in both the study IV and V (see section 3. "Measurements"). Fifty subjects participated in the 16-month follow-up study.

2. Vibration Loading Regimens

Vibration exposures were carried out in the standing position on the vibrating platform [(a prototype of Galileo 2000, Novotec Maschinen GmbH, Pforzheim, Germany (study I) or Kuntotäry, Erka Oy, Kerava, Finland (studies II-IV), Figs. 2 and 3]. In the Galileo 2000 the platform vibrates around a horizontal rotation axis, while the Kuntotäry-platform vibrates vertically. The duration of the vibration exposure was 4 minutes in all four studies (I-IV) and the vibration frequency increased in one-minute intervals during the exposure: In the study I (prototype of Galileo 2000) from 15 Hz to 30 Hz, and in the studies II and III (Kuntotäry), from 25 Hz to 40 Hz. Estimated (mathematically calculated) accelerations (g-values) are given in the Table 2). In the study IV (Kuntotäry), during the first 4 months the frequency of the vibration increased also from 25 Hz to 40 Hz during the 4-min exposure, but then the starting level was increased so that during the remaining four months of the 8-month intervention, the frequency increased from 30 Hz to 45 Hz during the exposure (Table 2). While standing on the platform, the subjects repeated four times a 60 s light exercise program: Light squatting (0 s – 10 s), standing in the erect position (10 s – 20 s), standing in a relaxed position the knees in a slight flexion (20 s – 30 s), light jumping (30 s – 40 s), alternating the body weight from one leg to another (40 s – 50 s), and standing on the heels (50 s – 60 s).

In the studies III and IV, there was a practice period of the vibration exposure at the beginning of the intervention, i.e. during the first two weeks, the duration of the vibration loading was 2 minutes. During next 1.5 months, the duration was 3 minutes, and during the remaining intervention (2 months in the study III, and 6 months in the study IV), the duration of the vibration loading was 4 minutes. The subjects were asked to train with vibration platform 3 to 5 times a week.

Characteristics of the vibration loading regimens are presented in the Table 2, and detailed information in the original reports.

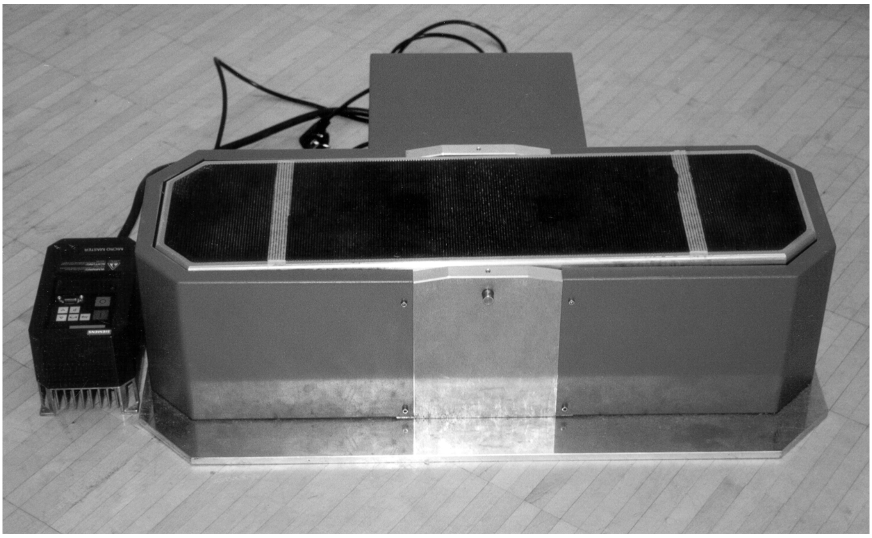


Figure 2. A prototype of the Galileo 2000 vibrates around a horizontal rotation axis (study I).

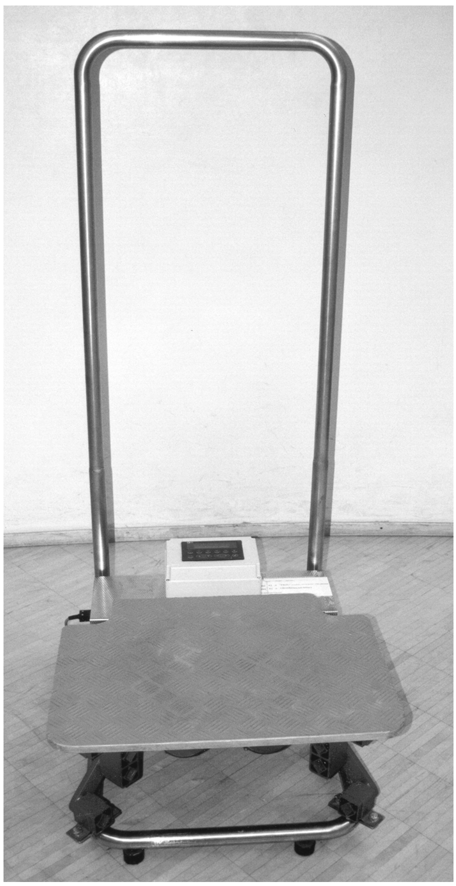


Figure 3. Kuntotäry-platform vibrates vertically (studies II-IV).

	Platform	Loading type	Frequency (Hz)	Amplitude (peak-to-peak, mm)	Acceleration, (theoretical maximum, g**)
Study I	prototype of Galileo 2000	tilting platform (vibration around a horizontal axis)	1. minute: 15 Hz 2. minute: 20 Hz 3. minute: 25 Hz 4. minute: 30 Hz	10	3.5 6.5 10 14
Study II	Kuntotäry	vertically vibrating platform	1. minute: 25 Hz 2. minute: 30 Hz 3. minute: 35 Hz 4. minute: 40 Hz	2	2.5 3.6 4.9 6.4
Study III	Kuntotäry	vertically vibrating platform	1. minute: 25 Hz 2. minute: 30 Hz 3. minute: 35 Hz 4. minute: 40 Hz	2	2.5 3.6 4.9 6.4
Study IV	Kuntotäry	vertically vibrating platform	1. minute: 25 Hz 2. minute: 30 Hz 3. minute: 35 Hz 4. minute: 40 Hz 4. minute: 45 Hz*	2	2.5 3.6 4.9 6.4 8.2

* During the final 4 months, the starting level of frequency was increased: The frequency during the first minute was 30 Hz, during the second 35 Hz, during the third 40 Hz, and during the fourth 45 Hz.

** g= =9.81 ms^{-2}

Table 2. Characteristics of the vibration loading regimens in the studies I-IV.

3. Measurements

The outcome measurements and their timetables of the studies are listed in the Table 3. Detailed information on the measurements is given in the original reports.

3.1. Questionnaires

Information on living habits, health status, training history, physical activity, injuries, medication, diseases and possible contraindications, menstrual status, diet and vitamin or mineral supplementation (I-V), calcium intake (III-V), and the consumption of alcohol and cigarettes was assessed with detailed questionnaires (I-V) at the beginning of the study, and in 2-month intervals thereafter in the long-term intervention studies (III and IV). Possible side-effects or adverse reactions were asked by the questionnaire in the studies I and II immediately after the single bout of vibration, and in the long-term interventions (studies III and IV), monthly from the subjects of the vibration group and in 2-month intervals from the control group.

3.2. Bone Measurements

Dual-energy X-ray absorptiometry (DXA) and peripheral quantitative computed tomography (pQCT) were used to evaluate the effects of vibration loading on bone. DXA technique is currently considered the method of choice for clinical practice and research. It offers a rapid, precise, relatively inexpensive, and low radiative measurement for bone mineral content (BMC) and areal bone mineral density (aBMD) at almost any part of the skeleton (Sievänen et al. 1994). PQCT, in turn, provides an accurate measurement of cross-sectional geometry of a bone section in a appendicular bone, its composition (cortical / trabecular), and apparent densities, in addition to quantification of BMC (Genant et al. 1996, Sievänen et al. 1998).

Bone measurements were done in the studies IV and V. BMC (g) was measured with the DXA (Norland XR-26, Norland Inc., Fort Atkinson, WI, USA) from the lumbar spine (L2-L4), femoral neck, trochanter, calcaneus, and distal radius according to our standard procedures (Sievänen et al. 1996). In our laboratory, the in vivo day-to-day precision of the DXA-measurements (coefficient of variation, CV%) is less than 2.6 % (Sievänen et al. 1996). The pQCT measurements (XCT 3000, Stratec GmbH, Germany) were, in turn, done at the distal site (trabecular bone) and midshaft (cortical bone) of the tibia. The analyzed variable for the distal tibia was the trabecular density (TrD, g/cm^3), and for the tibial shaft, the cortical density (CoD, g/cm^3), cortical area (CoA, mm^2), and bone strength index (BSI, mm^3). BSI is defined as the density weighed polar section modulus of given bone cross-section. In our laboratory, the in vivo CV % in different pQCT variables for the tibia ranges from 0.9% to 4.2% (Sievänen et al. 1998).

Both DXA and pQCT measurements were done at baseline, after the 8-month intervention (study IV), and after the 8-month follow-up period (study V).

3.3. Serum Markers of Bone Turnover

Various biochemical markers, which appear in the circulation or are excreted in the urine, are used to reflect bone turnover in osteoporosis and in monitoring the bone response to treatment (Risteli and Risteli 1999, Halleen et al. 2001). Serum osteocalcin (OC), and aminoterminal (PINP) procollagen propeptides are today among the most commonly used serum markers of bone formation, and serum carboxyterminal telopeptide of type I collagen (CTx), and type 5 tartrate-resistant acid phosphatase (TRAP-5b), in turn, among the markers of bone resorption. These four markers were used in the study IV and were determined at baseline and at 3, 6, and 8 months.

Osteocalcin is a small, noncollagenous protein, which is synthesized by osteoblast, and thus, considered as a specific marker of osteblast function, as its levels correlate with bone formation rates. In this thesis, osteocalcin was assessed by the electrochemiluminescence immunoassay for N-MID osteocalcin (Elecsys Systems

1010, Roche Ltd., Basel, Switzerland). PINP, in turn, is an extension peptide cleaved from the aminoterminus of type I procollagen during type I collagen formation. PINP was analyzed by radioimmunoassay (Orion Diagnostica, Espoo, Finland) (Tähtelä et al. 1997, Risteli and Risteli 1999, Delmas et al. 2000).

Serum CTx (CrossLaps) is a recently developed new assay to measure the degradation of type I collagen, and because it has relatively low spontaneous day-to-day variation but very great responsiveness to antiresorptive therapy, it is considered a very useful assay to measure bone resorption. In this thesis, beta-CTx was determined by electrochemiluminescence immunossay (beta-CrossLaps/serum, Elecsys System 1010, Roche Ltd.) (Risteli and Risteli 1999, Rosen et al. 2000). TRAP-5b, in turn, is secreted into the circulation by osteoclasts thus providing a useful method to assess osteoclast activity and bone resorption. TRAP-5b determinations were performed by solid phase immunofixed-enzyme activity assay (BoneTRAPâ, SBA, Turku, Finland).

3.4. Performance and Balance Tests

Effects of exercise on physical performance and fall risk can be evaluated by different performance and balance tests, which may range from simple field tests (e.g. jumps and sprints) to laboratory techniques (e.g. treadmill running, vertical jumping, cycle ergometry). In order to evaluate the strength of lower extremities, leg press dynamometer is one of the most used test methods to measure the maximal isometric strength of lower limbs (Heinonen et al. 1994). Recently, however, lower limb explosive strength and performance capacity have been suggested to be perhaps even more important factors in fall prevention than maximal isometric strength and thus, also better methods to assess the risk of falling (Skelton et al. 2002). The leg extensor power or lower limb expolosive performance capacity is normally evaluated using a vertical counter-movements jump test while various test methods has been used to evaluate body balance, both static (e.g. different postural sway platforms) and dynamic (e.g. tandem walk test), as well as agility of subject (e.g. shuttle run test) (Baker et al. 1993, Nelson et al 1994, Schmitz and Arnold 1998). These tests also are important methods in predicting physical performance and risk of falling. The tests used in different studies are given below.

3.4.1. Study I-II

Six physical performance and balance tests were done 10 minutes before (baseline), and 2 and 60 minutes after the sham- and vibration-exposure. As mentioned above, the tests were shared between two days to avoid potential contamination of the results due to fatigue (Figure 1).

Maximal isometric strength of the leg extensors was assessed with a standard leg press dynamometer (Tamtron, Tampere, Finland) (Heinonen et al. 1994), and grip strength (which was considered as a reference test) was measured using a standard grip strength meter (Digitest, Muurame, Finland). The leg extensor power or lower limb explosive performance capacity, in turn, was evaluated using a vertical countermovement jump test, which was performed on a contact platform (Newtest, Oulu, Finland) (Bosco et al. 1983).

Body balance was assessed with a postural sway platform (Biodex Stability System, New York, NY) (Schmitz and Arnold 1998), and with the tandem walk (Nelson et al. 1994) and shuttle run tests (Baker et al. 1993).

3.4.2. Study III-V

In the study III, five performance and balance tests (leg press, grip strength, vertical jump, postural sway, and shuttle run), were done at baseline, and at 2 and 4 months. In the study IV, the same tests were done at baseline and after 8-month intervention, and in the study V, also after the eight-month follow-up period.

3.5. Electromyographic Measurements

Surface electromyography (EMG) provides a noninvasive technique to investigate indirectly the neuromuscular activity of a contracting muscle. In the study I, we investigated the effects of vibration on the muscle activity of soleus, gastrocnemius, and vastus lateralis (of the quadriceps) during the vibration exposure by surface EMG (Myosystem 1008, Noraxon, Oulu Finland). In the study II, the recorded muscles were soleus, vastus lateralis, gluteus medius, and paravertebralis muscles. Four separate frequency spectra were determined in 1-second intervals over some 4-second period in the middle of the relaxed standing phase, and the average of these spectra was determined. From this average spectrum, a representative mean power frequency (MPF, in Hz) and root mean square voltage (RMS, in mV) of the EMG signal were calculated for each minute of intervention and these variables were used as test outcomes.

Measurements	Study I	Study II	Study III	Study IV	Study V
Anthropometry Age Height Weight	At baseline	At baseline	At 0, 2, and 4 months	At 0, 3, 6, and 8 months	After the 8-month follow-up
Questionnaires (living habits, health status, physical activity, injuries, medication, diseases, diet, consumption of alcohol and cigarettes)	At baseline	At baseline	At 0, 2, and 4 months	At 0, 3, 6, and 8 months	After the 8-month follow-up
Calcium intake	–	–	At 0, 2, and 4 months	At 0, 3, 6, and 8 months	After the 8-month follow-up
Side-effects, adverse ractions	After the exposure	After the exposure	Monthly/2-month intervals	Monthly/2-month intervals	After the 8-month follow-up
EMG-measurements (surface-electrode; during the vibration exposure)	Soleus, gastrocnemius, and vastus lateralis muscles.	Soleus, vastus lateralis, gluteus medius, and paravertebralis muscles.	–	–	–
Physical performance Isometric strength Leg press Grip strength Explosive strength Vertical jump Static balance Postural sway Dynamic balance Tandem walk Dynamic balance and agility Shuttle run	10 min before, and 2 and 60 min after the exposure *	10 min before, and 2 and 60 min after the exposure *	At 0, 2, and 4 months	At 0 and 8 months	After the 8-month follow-up
Bone Measurements DXA Bone mineral content Lumbar spine Femoral neck Trochanter Calcaneus Distal radius pQCT Distal tibia Trabecular density Tibial shaft Cortical density Cortical area Bone strength index	–	–	–	At 0 and 8 months	After the 8-month follow-up
Serum markers Bone formation Osteocalcin PINP Bone resorption CTx TRAP-5b	–	–	–	At 0, 3, 6, and 8 months	–

*= Tandem walk was performed in the studies I and II only.

Table 3. Measurements and timetables of the studies I-V.

3.6. Safety Issues

Possible side-effects or adverse reactions were assessed by the questionnaire in the studies I and II immediately after the exposure to vibration, and in studies III and IV monthly from the subjects of vibration group and in 2-month intervals from the control group. In the long-term interventions (studies III and IV), the subjects also had a possibility to consult the responsible physician whenever needed.

Due to the ability of magnetic resonance imaging (MRI) to visualize the articular cartilage (Lawrence et al. 1999), MRI technique (Artoscan, Esaote s.p.a., Genova, Italy) was also used to evaluate the safety of the long-term vibration loading on the cartilage of the ankle joint (study IV).

3.7. Statistical Analysis

3.7.1. Studies I-II

The 2-minute and 60-minute effects of whole body vibration on individual physical performance were defined as relative differences between the changes in the given test outcome observed after the vibration- and sham-exposure. The relative differences were achieved through log-transformation of the variables. The time-effect at 2 and 60 minutes was determined by one-way analysis of variance (ANOVA) with repeated measures. Repeated measures ANOVA was also used to estimate the time-effect on EMG variables (MPF and RMS) during vibration-interventions.

The day-to-day reproducibility (expressed as a root-mean-square coefficient of variation $CV\%_{rms}$) of the performance tests was determined using the duplicate baseline data measured before the vibration-and sham-interventions. The associations between the mean power frequency and root mean square voltage minute-values were analyzed by the Pearson's correlation coefficients (study I).

3.7.2. Studies III-V

In study III, the 2-month and 4-month effects of the whole body vibration on physical performance and balance were defined as absolute and relative mean differences [with 95 % confidence intervals (CI)] between the vibration and control groups. The relative differences were achieved through log-transformation of the variables. The time-effect at 2 and 4 months was determined by one-way analysis of covariance (ANCOVA), using the baseline values as the covariate.

In study IV, the DXA- and pQCT-derived bone variables, along with the muscular performance and balance tests, were the primary outcome measures of the study all the remaining measures being secondary outcomes. The analyses were first done by intention-to-treat and then by an active-treatment approach (efficacy-analysis).

The 8-month effects of the whole body vibration on individual physical performance were defined as relative differences between the vibration and control groups (log-transformation). The one-way analysis of covariance (ANCOVA) with the baseline measurements as the covariate was used to analyze the effect of vibration at 8 months.

In the study V, the effects of 8-month detraining on bone and performance variables were also defined as relative differences (log-transformation), and the ANCOVA (with the baseline measurements as the covariate) was used to analyze the effect of detraining.

In all five studies, p-value less than 5 % (<0.05) was considered statistically significant.

RESULTS

In general, vibration loadings had a statistically significant positive effect on jump height (visible in both short-term and long-term studies). Enhancements could also been seen in the isometric strength of lower extremities and body balance, but these changes were not so obvious. On bone mass, structure or strength, or serum markers of bone turnover, the vibration loading had, in turn, no effect.

In the study III, the reported mean vibration-training frequency was 3.1 (SD 0.9) times per week, and in the study IV, 2.8 (SD 0.8) times per week. Physical activity or calcium intake did not change during the interventions.

Because there were no gender differences in the time-effect at any time point during the interventions, the data of women and men were pooled and analyzed together in all five studies.

The results of the individual studies are reported briefly below. More detailed information on the results is given in the original reports.

1. Effects of a Single Vibration Bout on Muscular Performance and Body Balance

The single, 4-minute bout of vibration-loading, based on a tilting platform (a prototype of Galileo 2000), induced a transient (significant at the 2-min test) net benefit in the jump height (2.5%), in the isometric extension strength of lower extremities (3.2%) and in the body balance (15.7%) (study I). In the EMG measurements, the MPF of all recorded muscles (soleus, gastrocnemius, vastus lateralis) decreased during the vibration exposure, while the RMS voltage of EMG signal increased in calf muscles (soleus and gastrocnemius).

The 4-min vertical vibration-loading (Kuntotäry) did not induce any statistically significant changes in the performance- or balance-tests at the 2 or 60 min tests (study II). The MPF of the vastus lateralis and gluteus medius muscles, in turn, decreased during the vibration exposure, and the RMS voltage of EMG signal increased in the gluteus medius muscle.

2. Effects of Long-term Vibration Loading on Bone

The 8-month vibration-intervention had no effect on bone mass, structure or strength at any measured skeletal site. Serum markers of bone turnover did not changed during the vibration intervention either (study IV).

3. Effects of Long-term Vibration Loading on Physical Performance and Body Balance

The 4-month vibration-intervention induced a statistically significant net improvement in the jump height (8.5%) (study III). Lower limb extension strength increased after the 2-month vibration-intervention (a 3.7% net benefit for the vibration), but this benefit diminished by the end of the 4-month intervention. In the grip strength, shuttle run, or balance tests, the long-term vibration-intervention showed no effect.

The 8-month vibration-intervention had a beneficial effect on the vertical jump height (a 7.8 % net benefit) (study IV). On the other performance or balance variables, the vibration-intervention had, in turn, no effect.

4. 8-month Follow-up of the 8-month Vibration-intervention

After the 8-month follow-up period of the 8-month vibration-intervention, the between-group difference in jump height was decreased from 8.5 % (between-group difference after the 8-month vibration intervention) to 3.0 % (study V). This difference was not statistically significant. As expected, in the other performance or balance tests, or in the bone measurements, there were no between-group differences at the follow-up (Table 4, 5, and 6, Figure 4).

5. Safety of the Vibration Loading

The vibration-interventions succeeded well and were safe to perform. No vibration related side-effects or adverse reactions were reported or observed in the short-term or long-term studies (I-V). Further, the MRI examinations failed to reveal any changes in the articular cartilage or bone tissue of the ankle joint during the long-term intervention (study IV).

Variables	Baseline Mean	Baseline SD	Between-groups difference for the relative change by the 8-month intervention Mean	95 % CI	p-value	Between-groups difference for the relative change by the 8-month follow-up Mean	95 % CI	p-value
Lumbar spine (g)			0.4	-1.0 to 1.9	0.564	-1.4	-3.2 to 0.5	0.152
Vibration group	52.3	(9.9)						
Control group	51.7	(10.6)						
Femoral neck (g)			0.1	-1.7 to 1.9	0.898	0.5	-1.5 to 2.6	0.613
Vibration group	3.7	(0.7)						
Control group	3.7	(0.8)						
Trochanter (g)			0.1	-2.7 to 2.9	0.968	0.5	-1.5 to 2.6	0.230
Vibration group	7.2	(1.4)						
Control group	7.3	(1.4)						
Calcaneus (g)*			0.5	-2.9 to 4.1	0.759	1.6	-2.1 to 5.5	0.387
Vibration group	10.2	(2.6)						
Control group	10.7	(3.0)						
Distal radius (g)**			-0.4	-2.9 to 2.3	0.783	-0.4	-4.1 to 3.4	0.828
Vibration group	1.8	(0.4)						
Control group	1.7	(0.4)						

* n=24 in the vibration group and n=25 in the control group
* * n=21 in the vibration group and n=20 in the control group

Table 4. BMC values at baseline, after the 8-month whole body vibration intervention, and after 8-month follow-up. Mean (SD) and mean between-groups difference for the relative change by time (percentage, 95 % CI, and p-value). n=25 in both the vibration group and control group.

Variables	Baseline Mean	Baseline SD	Between-groups difference for the relative change by the 8-month intervention Mean	95 % CI	p-value	Between-groups difference for the relative change by the 8-month follow-up Mean	95 % CI	p-value
Distal tibia								
Trabecular density (mg/cm3)								
Vibration group	250.4	(26.4)						
Control group	238.8	(31.4)	-0.2	-1.3 to 0.9	0.697	-0.5	-1.8 to 0.9	0.482
Tibial shaft*								
Cortical density (mg/cm3)								
Vibration group	1103.2	(23.7)						
Control group	1105.6	(23.4)	0.4	-0.6 to 1.4	0.422	-0.2	-0.7 to 0.3	0.361
Cortical area (mm2)								
Vibration group	318.5	(41.7)						
Control group	318.5	(59.9)	0.0	-0.8 to 0.9	0.978	-0.2	-1.3 to 1.0	0.769
Bone strength index (mm3)								
Vibration group	1917.7	(342.0)						
Control group	1900.7	(442.7)	0.4	-1.0 to 1.9	0.548	-0.1	-1.7 to 1.4	0.849

* n=23 in the vibration group and n=23 in the control group

Table 5. pQCT values at baseline, after the 8-month whole body vibration intervention, and after 8-month follow-up. Mean (SD) and mean between-groups difference for the relative change by time (percentage, 95 % CI, and p-value). n=25 in both the vibration group and control group.

Variables	Baseline Mean	SD	Between-groups difference for the relative change by the 8-month intervention Mean	95 % CI	p-value	Between-groups difference for the relative change by the 8-month follow-up Mean	95 % CI	p-value
Vertical jump (cm)								
Vibration group	27.8	(7.8)						
Control group	28.9	(8.4)	8.5	3.5 to 13.6	0.001	3.0	-1.6 to 7.8	0.199
Extension strength of the lower extremities (kg)								
Vibration group	198.4	(63.9)						
Control group	219.1	(104.6)	2.1	-2.5 to 6.9	0.368	0.8	-3.6 to 5.3	0.732
Grip strength (kg)								
Vibration group	31.8	(8.3)						
Control group	32.7	(9.6)	2.0	-0.6 to 4.7	0.132	1.8	-0.5 to 4.1	0.128
Postural sway (index)								
Vibration group	3.1	(1.7)						
Control group	3.5	(1.2)	-2.6	-15.5 to 12.3	0.711	-2.2	-15.9 to 13.7	0.767
Shuttle run (s)								
Vibration group	11.0	(1.3)						
Control group	11.1	(1.4)	-0.7	-2.5 to 1.2	0.302	-1.1	-3.2 to 1.0	0.302

Table 6. The performance and balance test parameters at baseline, after the 8-month whole body vibration intervention, and after the 8-month follow-up. Mean (SD) and mean between-groups difference for the relative change by time (percentage, 95 % CI, and p-value). n=25 in both the vibration group and control group.

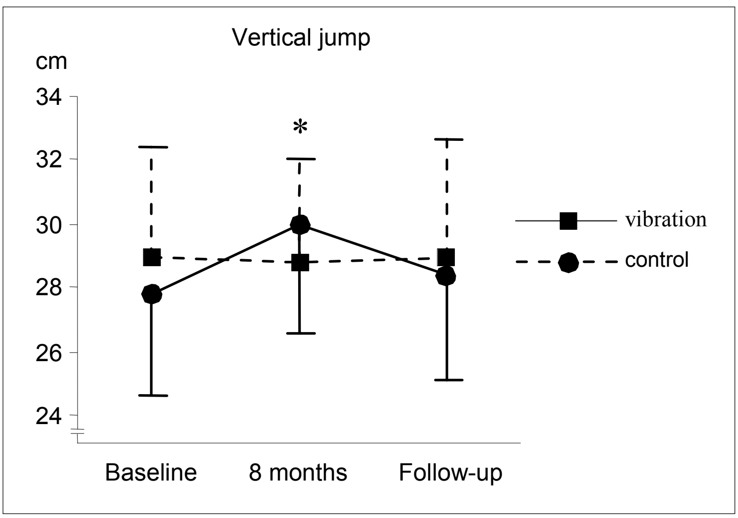


Figure 4. Mean values (cm, 95 % CI) in vertical jump at baseline, and 8 months, and after the 8-month follow-up period. CI of the vibration group are presented downwards, and upwards in the control group.

DISCUSSION

In general, whole body vibration loadings of this thesis generated both Galileo and Kuntotäry platforms improved jump height, which suggests a vibration-induced enhancement in the explosive performance capacity of the lower extremities. This enhancement could already be seen after the single, 4-min tilting type vibration stimulus (Galileo). The 4-min vertical vibration (Kuntotäry), in turn, was not capable to enhance jump height, but long-term training (4 and 8 months) with this vertically vibrating platform had, however, a similarly enhancing effect. After the 8-month follow-up period, jump height has decreased from the 8-month intervention value, but still demonstrated a small, beneficial trend for vibration.

Single, 4-min bout of tilting type vibration improved transiently lower limb isometric extension strength and body balance. The EMG-recordings during the 4-minute vibration exposures demonstrated that the tilting type vibration changed muscle activity especially in the calf's area, while the vertical vibration influenced in the hip region. An increase in lower limb isometric extension strength could be seen after the 2-month vertical vibration, but this increase, however, diminished by the end of the 4-month intervention. On the other performance or balance tests (except jump height), or on bone mass, structure or strength, the vibration loading had no effect, and neither changed the serum markers of bone turnover due to vibration.

This thesis is the first randomized controlled clinical trial evaluating the effects of long-term whole body vibration on both the physical performance and bone. Adherence of the subjects to the vibration loading protocol was good and just a few participants withdrew from the study during the 8-month intervention. In addition to the very few drop-outs, the compliance of the participants to training with the platform was also high (mean training frequency 2.8 times a week).

Because the long-term intervention succeeded well and the participants were well motivated to train with the vibration platform (study IV), we may speculate that one reason for negative findings could be that the subjects who participated in the study were young and their musculoskeletal tissues could cope well with the given vibration stimulus with no need of adaptation. Thus, bone and performance responses (other than jump height) to vibration loading might have been seen if the participants had been older (sheep used in the study of Rubin et al. were aged), or their bone tissue weaker. It might also be argued that the ability of vibration to enhance the skeleton could be achieved primarily in cases where some component of the normal physiology of the regulatory signal is diminished (e.g. muscle activity in disuse) (Rubin et al. 2001b). On the other hand, it has to also be kept in mind that vibration stimulus as a treatment regimen is new, and when we started the long-term trial, convincing evidence of its safety was completely lacking. Thus, it was important to carefully evaluate the possible side effects and adverse reactions of long-term, relatively high-magnitude vibration in young and healthy adults before planning any studies with elderly people.

Another reason for the unchanged bone variables may be the selected type of vibration loading. When we started our long-term trial, it was not clear what kind of vibration stimulus would be the most effective for the musculoskeletal system. For example, the positive results of the animal studies with very low magnitude (0.3g) but high frequency (30Hz) vibration were not available at that time (Rubin et al. 2001a,b, 2002a, b). Thus, we had to rely on the most largely-spread concept of the osteogenic mechanical stimulus, i.e. mechanical stimulus must be of a relatively high-magnitude, provide a multidirectional exposure to the skeleton, and be progressive and long-term by nature (Lanyon and Rubin 1984a, Rubin and Lanyon 1984, Kannus et al. 1996d, Skerry 1997).

We also had to take into consideration the effects of vibration stimulus on physical performance (which is also an important factor in preventing osteoporotic fractures, and another prime outcome of this thesis) and the training compliance of the subjects although these considerations might partly compromise the effect of vibration on bone tissue. Thus, when training on the platform, the subjects repeated a light exercise program, the purpose of which was to be multidirectional and direct the vibration loading not only on bone but also on muscles (e.g. light jumping and alternating the body weight from one leg to another). The exercise also made the standing on the platform less monotonous for the subjects. Four minutes duration of the vibration exposure per day is also a matter of discussion but was considered to be applicable and convenient for the subjects in a long-term trial but still capable to initiate an adaptive response in bone (Rubin and Lanyon 1984, Turner 1998).

The parts of the above noted exercise regimen (performed during the vibration exposure), which were directed to have influence on muscle performance, contained movements in which subjects kept their knees bent (light jumping, standing in a relaxed position, and alternating the body weight from one leg to another), and this might have reduced the transmissibility of the vibration wave through the skeleton, since standing with bent knees on the platform vibrating at 30 Hz has been shown to decrease transmissibility of the vibration wave below 20 % at the femur and spine (as compared if the subject stands in an erect position) (Rubin et al. 1994). In addition, transmissibility of a vibration wave has also been shown to decrease as a function of frequency, so that transmissibility remains above 50 % up to 35 Hz, but when frequency approaches 40 Hz, transmissibility falls off by 60 % at the femur and spine (Rubin et al. 1994). The frequency of the vibration loading of this thesis varied from 25 Hz to 45 Hz, and thus, it can be supposed that transmissibility remained above 50 % at the level of femur and spine at least in the half of the stimulus. In addition, our exercise regimen contained also parts which were particularly directed to have effect on bone tissue (standing in the erect position and on the heels), and during these parts, it was thought that vibration stimulus could easily travel through the skeleton, or at least, had a strong effect on the distal part of the lower limb, e.g. the calcaneus. The eight-month intervention might, however, have been too short to cause any significant changes in the bone tissue of young adults, and thus the bone responses might have required a longer exposure (e.g. one year) to become visible in the DXA- and pQCT-measurements. On the other hand, if vibration loading of this thesis had at least initial effects on bone tissue, they should have become visible in the serum markers of bone turnover.

When comparing our results to those of the animal experiments (Rubin et al. 2001a,b, 2002 a, b), it is also obvious that the lower extremities of animals are very different than those of humans, and thus, the responses of the animals to mechanical loading and vibration can be different, too. For example, sheep have hard and relatively stiff hooves, which may not damp the given loading stimulus to a considerable degree, and thus the mechanical vibration wave can more easily traverse through the hoof to the lower limb skeleton without substantial attenuation. It is also possible that vibration loading waveform may be an important factor in bone formation. Theoretically, a pure sinusoidal waveform is possible only if the maximum acceleration of the platform does not exceed one Earth's gravitational field (g). In the vibration regimens of Rubin et al. (2001a,b, 2002 a, b), the loading waveform was 0.3 g, whereas in our study it was substantially higher than one g (estimated 2 to 8 g). Consequently, in the vibration regimens of Rubin et al. (2001a,b, 2002a,b), the loading waveform remained sinusoidal, whereas in our study, it was apparently distorted. If the pure sinusoidal loading waveform at a certain frequency, not the peak load, is the key factor behind the osteogenic response (as the studies of Rubin et al. indicates), it would be a fundamental observation definitely needing repetition by experimental and clinical studies. The optimal vibration frequency for bone formation is, however, yet unknown, but because the one g-threshold constrains the simultaneous ranges of vibration frequency and amplitude, the search for the most optimal vibration frequency might become a bit easier in the future studies. It may also be speculated that large WBV signals (high g-values) may be the cause for bone's unresponsiveness; e.g. "window" of effective strain signal might have been exceeded in this thesis thus shutting down the sensitive cellular response system in bone.

The EMG-recordings during the 4-min vibration loadings showed that vibration exposure did have influence on muscle activity, although extended interpretations of these findings cannot be made. The 4-min tilting-type vibration decreased the MPF and increased the RMS voltage in the calf area, while the 4-min vertical vibration had the similar influence at the hip region. On the ground of these results, and while the long-term trial was performed only with the vertical type of loading, it is difficult to interpret these different muscle effects of the two loading types. Perhaps, tilting type loading warms up or stimulates the muscles of the lower extremities more effectively than vertical loading. In Galileo, the theoretical maximal acceleration was also higher than that in Kuntotäry (3.5g-14 g versus 2-8g). A reduction in MPF and increase in RMS voltage is generally considered as a sign of muscle fatigue, and it has been speculated that in the initial muscle fatigue, an accumulation of lactic acid causes first the slowed conduction velocity, which in turn, drives the power density spectrum to lower frequencies during fatigue (i.e. MPF decreases). The initial increase in RMS voltage, in turn, compensates the decrease in MPF by synchronization of the motor unit firing patterns, and recruitment of additional motor units, and thus, force output may remain relatively constant (although EMG-recordings show continuously decreasing MPF-value). Ultimately, long term loading also leads, however, to a decrease in the RMS voltage values (Jurell 1998). In this thesis, EMG-recordings also showed the signs of evolving muscle fatigue, but in the results of the performance tests, the signs of the fatigue could not been seen; in fact, the strength tests indicated even improved values immediately after the vibration exposure. Thus, these findings, improved results in the strength tests but the decreased EMG activity, suggest that our 4-min vibration stimulus was long enough to warm or stimulate the muscles of the lower extremities (perhaps due to the additional recruitment of motor units), but too short to induce any significant muscle fatigue. Thus, it can be speculated that since no significant muscle fatigue occurred, the muscle fatigue did not stimulate any positive bone effects (i.e., when a muscle fatigues, a larger proportion of the vibration energy may be directed to bones instead of being absorbed by muscles, as hypothesized in the studies I and II).

When considering the vibration-induced performance effect (increased jump height), it can be speculated that whole-body vibration of this thesis was able to evoke the TVR, which, in turn, excited muscle spindles, activated muscle fibers, recruited more motor units, and thus, enhanced the physical performance. It is, however, still unknown whether the TVR, in general, could be induced by whole-body vibration or is it evoked only by high (>100 Hz) tendon or muscle vibration. In addition, while the subjects performed exercise regimen during the vibration exposure (which have been suggested to accentuate the TVR), and no specific myographic recordings were performed, very strong suggestions about the TVR-induced enhancements in the physical performance can not be made.

When interpreting the quick and clear rise in the vertical jump height, and knowing the effects of resistance and explosive power training on neuromuscular properties of skeletal muscle (Häkkinen and Komi 1985, Sale 1988, Häkkinen 1989, Häkkinen et al. 2000, Carroll et al. 2001), it is likely that neural adaptation did occur in the vibration groups in response to the vibration-intervention. The lower limb extension strength increased after the 2-month vibration loading thus referring to neural potentiation, too. The rate of the strength increase, and the difference between the intervention groups, however, diminished by the end of the 4-month intervention, which could be explained by general muscular adaptation to the vibration program: further improvement in the extension strength might have required a greater progression in the training stimulus.

One may suspect that the above noted improvement in the jump height of the vibration groups was due to exercise regimen performed on the platform. The exercises were, however, very light, and thus it was very unlikely that exercise alone was behind the clear rise in the jump height. Instead, the exercise regimen could direct the vibration stimulus to the muscles in a way, which was beneficial for jumping performance in the long-term interventions (studies III and IV). In the short-term studies (studies I and II), the subjects of the control group performed the same exercise regimen on the platform than the subjects of the vibration group.

On the other hand, we may also speculate whether the positive results, improved jump height and transient enhancement in the extension strength of lower extremities, are specific for vibration stimulus only, or would it have been possible to get a similar effect by other forms of training (such as by conventional plyometric or strength training). Comparative studies on the effects of the vibration loading and conventional training regimens are, however, lacking, and since the contents of the conventional training regimens vary considerably in the different studies, a reliable comparison of the results of this thesis to those of the conventional training studies is impossible.

The osteogenic signal and human biology (30000 genes) are undoubtedly a complex system. Both the vibration stimulus and exercise regimen can also be modified in multiple ways (including type, periodicity, magnitude, frequency, and duration of the vibration, and the type of exercise regimen), and thus, the results of the other interventions can be different than we received in our trial. Since the long-term trial of this thesis was performed only with a vertical vibration loading regimen, it is not known whether tilting-type of loading would have resulted in a different effect on performance and bone. It may be speculated that likewise the muscle effects (or perhaps just due to the different muscle effects), the bone effects of these two devices may also be different. When considering the positive bone effects of the recent animal studies (Rubin et al. 2001 a, b, 2002 a, b), it has to, however, be kept in mind, that since bone strength in many sites of the skeleton is attributable to a composite of trabecular and cortical bone as well as complex aspects of bone geometry, it is not clear that the changes observed in trabecular bone of sheep would necessarily translate into clinically relevant or sustained effects on overall bone strength (Van der Meulen et al. 2001, Eisman 2001). On the other hand, it is also true that if trabecular bone is maintained by the stimulus, it is likely that cortical bone can be preserved too.

Although the results of this thesis were not so positive as suggested by the previous experimental and clinical investigations, vibration loading used in this thesis may be seen as a safe and potentially efficient training and rehabilitation method, not only for athletes, but also for frail elderly, since lower limb explosive strength and performance capacity have been suggested to be even more important determinants of falls than pure maximal strength (Skelton et al. 2002). However, future human studies are definitely needed before any stronger clinical recommendation for vibration exercise. Such studies should vary the type, magnitude, frequency, and duration of the vibration.

On the ground of this thesis and the positive results of previous animal studies, it can be suggested that future vibration studies should perhaps focus to elderly people or people with disabling conditions (i.e., people who have something to improve in their musculoskeletal system, such as bone mass and muscular performance). Also, a decrease in vibration magnitude would be interesting, because just an extremely low magnitude but high frequency stimulus has been shown to be efficient for bone formation in animals.

SUMMARY AND CONCLUSIONS

1. In the study I and II, the short-term effects of a single, 4-min whole body vibration bout on muscle performance and body balance of healthy young adults were evaluated. In the study I, tilting-type of vibration induced transient, moderate improvements in jump height, isometric extension strength of lower extremities, and body balance. EMG-recordings of muscle activity demonstrated initial muscle fatigue, especially in the calf area. In the study II, a vertically-vibrating vibration stimulus did not induce changes in the performance and balance tests, while EMG-measurements showed the vibration exposure activated the muscles particularly in the hip region.

2. In the study III, the effects of the 4-month vertical whole body vibration on muscle performance and body balance were investigated. The results showed a clear enhancement in jumping power suggesting neuromuscular adaptation to the vibration stimulus. The vibration-intervention showed no effect on body balance of the subjects.

3. In the study IV, the effects of 8-month whole body vibration on bone, muscle performance, and body balance were assessed using DXA and pQCT measurements, serum markers of bone turnover, and performance and balance tests. The 8-month vibration intervention was safe to perform, but induced no effect on bone mass, structure or strength at any measured skeletal site. Serum markers of bone turnover changed during the vibration-intervention neither. Vertical jump height in the vibration group, however, improved, while on the other performance or balance tests, the vibration intervention had no effect.

4. In the follow-up study (V), the maintenance of the changes observed in the study IV was evaluated. After the 8-month follow-up period or detraining, the vertical jump height still demonstrated a small net benefit for vibration, but this difference was no more statistically significant.

5. Although the results of this thesis were not so positive as suggested by the previous experimental and clinical investigations, vibration loading used in this thesis may be seen as a safe and potentially efficient training and rehabilitation method, not only for athletes, but also for frail elderly, since lower limb explosive strength and performance capacity have been suggested to be a very important determinant of falling. On the other hand, this thesis left many questions about the effects of long-term vibration on bone and physical performance open. One reason for the nonresponse could be that the subjects participated in this study were young and healthy, and more positive bone and performance effects might have been seen if the participants had been older, their bones weaker, or their basic performance capacity at lower level. Future studies are needed before any clinical recommendations for vibration.

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