# Physical activity and bone: The importance of the various mechanical stimuli for bone mineral density. A review

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## ABSTRACT

Numerous studies have reported benefits of regular physical activity on bone mineral density (BMD). The effects of physical activity on BMD are primarily linked to the mechanisms of mechanical loading, but the understanding of the precise mechanism behind the association is incomplete. The aim of this paper was to review the main findings concerning sources and types of mechanical stimuli in relation to BMD. Mechanical forces that act on bone are generated from impact with the ground (ground-reaction forces) and from skeletal muscle contractions (muscle forces or muscle-joint forces), but the relative importance of these two sources has not been elucidated. Both muscle-joint forces and gravitational forces seem to be able to induce bone adaptation independently, and there may be differences in the importance of loading sources at different skeletal sites. The nature of the stimuli is affected by the type, intensity, frequency, and duration of the activity. The activity should be dynamic, not static, and the magnitude and rate of the stimuli should be high. In accordance with this, cross-sectional studies report highest BMD in athletes of high-impact activities such as dancing, soccer, volleyball, basketball, squash, speed skating, gymnastics, hockey, and step-aerobics. Endurance activities such as orienteering, skiing, and triathlon seem to be beneficial to a lesser degree, whereas low-impact activities such as swimming and cycling are associated with lower BMD than controls. Both the intensity and frequency of the activity should be varied and increased beyond the habitual level. Duration of the activity seems to be less important, and a few loading cycles seem to be sufficient.

## INTRODUCTION

Osteoporotic fractures constitute a substantial health problem, particularly in the elderly, causing more disability than most other diseases [1]. Among many risk factors, physical inactivity has been related to a higher risk of osteoporotic fracture [2]. Physical activity may postpone the age-related decline in bone mineral density (BMD), and by that reduce the risk of fracture. BMD is at present the most common single measure of bone strength [3] and also a major predictor of fracture risk [4-7]. The effects of physical activity on BMD are primarily linked to the mechanisms of mechanical loading [8-10]. Knowledge about the importance of various types and sources of loading stimuli will have implications for the design of physical activity programs aimed at preventing osteoporosis.

The aim of this paper was to review the literature concerning mechanical loading in relation to BMD, with focus on which types of stimuli and sources of loading that are most effective.

## BONE REMODELING AND MECHANICAL LOADING

Bone is a highly dynamic tissue that adapts its mass and architecture to the physiological and mechanical environment [11]. Bone is constantly renewed during adulthood, when bone mass and architecture are maintained by bone remodeling [12]. Remodeling involves bone resorption and bone formation, a continuous process of bone cells removing and replacing bone tissue, and an imbalance in the remodeling process can cause osteoporosis. The bone cells involved in remodeling are osteoclasts (which remove bone) and osteoblasts (which produce new bone), forming the "basic multicellular unit" [12]. Remodeling can occur at four surfaces; the periosteal, endocortical, trabecular, and intracortical (Haversian) [12], although the turnover is higher in trabecular than in cortical bone.

As early as in 1892, Wolff stated that bone tissue accommodates to stress that is imposed on it [13], and later research on the topic has been founded on this contention. Several theories have been proposed to explain the loading mechanism, and one of the most recognized is the “Mechanostat theory” by Harold Frost [14-16]. Frost proposed that local deformation from mechanical loading stimulates bone cells, resulting in bone adaptation, under the influence of parameters such as age, sex, environment, genes, nutrition, and systemic biochemical factors [11,17]. Today, it is generally acknowledged that loads applied to bone affect bone mass [9] and morphology (e.g. cross-sectional area and thickness of cortical bone) [18,19] through a mechanism called "mechanotransduction”. Mechanotransduction involves conversion of a mechanical force into a cellular response. The process is not yet fully understood, but seems to include osteocytes, which detect mechanical strain and transduce the applied strain to the cells (osteoblasts and osteoclasts) on the surface, where bone remodeling (formation and resorption) occurs [8,10,20]. Details of the cellular processes of mechanical loading have been reviewed previously [20-22] and will not be further elaborated here.

## PHYSICAL ACTIVITY AND BMD

Data from numerous cross-sectional studies demonstrate a positive association between BMD and physical activity [23-25]. Generally, athletes have higher BMD than age-matched sedentary controls [26-30]. The most extensive evidence from human studies supporting the effect of exercise on bone mass has been obtained from studies of unilateral loading, as in tennis players, where the dominant arm has thicker cortices and up to 22% higher BMD than the non-dominant arm [31-34].

Intervention studies in pre- and peripubertal children confirm the findings from cross-sectional studies that high-impact physical activity [35-37] and regular physical activity increases BMD [38,39]. In adults, the effect of physical activity is smaller and less consistent. Findings from intervention studies in premenopausal women indicate that young women who exercise continue to increase bone mass compared to non-exercising controls [40-42]. In postmenopausal women, systematic reviews indicate that physical activity may slow the rate of bone loss on weight-bearing sites with an effect of approximately 1% per year [40,41]. This finding has been confirmed in two other reviews, which concluded that there is strong evidence of the effect of daily walking on the femoral neck bone mass in postmenopausal women [43,44]. The results seen in women are also present in the few existing studies in men [45-47].

Taken together, most results indicate that physical activity has an effect on BMD. Nevertheless, the exact type and amount of physical activity that may increase BMD and reduce the risk of fracture is still uncertain due to lack of randomized, controlled studies (particularly on fracture risk), a large number of confounders to control for, as well as an incomplete understanding of the precise mechanism behind the association between physical activity and BMD [48,49].

## WHICH TYPES OF STRAIN ARE MOST EFFECTIVE TO INCREASE BMD?

A load that is applied to bone is called stress, defined as force divided by area [50]. The applied load causes a mechanical deformation of bone tissue, and this deformation can be measured as strain [11,51]. Strain is the ratio of the amount of shortening ($\Delta l$) divided by the original length ($l$), typically expressed as microstrain, $10^{-6}$ (i.e. a bone of length 500 mm experiencing 0.5 mm deformation gives a strain of 0.001 or 0.1%, equal to 1000 microstrain) [11,20,51]. Strains may be compressive, tensile (when the bone is stretched), or torsional (shear) (when the bone is twisted), and in most situations, they affect bone in a combined way [11,50], i.e. a deformation can create 2500 microstrain in compression on the concave side of a bending diaphysis, while creating 2000 microstrain in tension on the other side [51].

In humans, an in vivo study of the tibia has shown that running produced larger strains and higher strain rate on the tibia than walking, while bicycling produced lower strains than walking [52]. Step and leg press did not induce larger strain or strain rate than walking. Strain magnitude ranged from 271 to 5027 microstrain and strain rate from 1258 to 38 164 microstrain/s. In accordance with these findings, Burr et al. [53] showed that strains during running were 2-3 times higher than during walking.

Frost's mechanostat theory [54] indicates that there is a lower and an upper strain threshold, creating a range where strain stimuli maintains homeostasis of the remodeling process and bone mass, called the physiological loading zone. Below the lower threshold (200 microstrain), called the "minimum effective strain for remodeling", the stimuli is insufficient to maintain formation, and resorption will be the overriding process, resulting in bone loss. Above the upper threshold (2000 microstrain), the "minimum effective strain for modeling", formation is dominant, resulting in bone gain. These thresholds may be relative to the individual's habitual loads [11].

The mechanostat theory mainly relies on the magnitude of the strain [51], and animal studies support that strain magnitude is an important driving force for bone remodeling [55,56]. However, several animal studies have demonstrated that dynamic, but not static strains (strain rate = 0), induce bone formation [56-59]. In the animal studies, jumping was more osteogenic than running, and strain rate was higher in jumping than running at similar strain magnitude [60,61]. Translated to humans, this would imply that high-impact activities are more effective than running and walking [62]. Moreover, studies of the effect of low-magnitude, high-frequent vibrations indicate that the magnitude may be less important than strain rate and frequency [48,51,58,59]. An important implication of this is that an increase in rate or frequency, not only magnitude, may represent overload and bone formation [11,51].

Uneven distribution of the strain seems to have a higher potential for increasing osteogenesis than the habitual loading pattern [62-65], indicating that the intensity and type of activity should be increased or changed beyond the habitual level. Moreover, after a few loading cycles, the adaptive response decreases [56,66]. Inserting a rest period after each loading cycle can increase the osteogenic response [55,58,67,68].

In conclusion, animal studies and a small number of studies of humans indicate that the stimuli from high-impact activities (e.g., jumping) is more effective than running and walking, as jumping has a higher strain rate than running even at the same strain magnitude. The activity should be dynamic, not static, and the load should be increased or changed beyond the habitual level. Moreover, a few loading cycles seems sufficient, and a rest period after each loading cycle can increase the osteogenic response.

## WHICH SOURCES OF MECHANICAL LOADING ARE MOST IMPORTANT TO BMD?

During physical activity, mechanical forces that act on bone are generated mainly from two sources; loads from impact with the ground (ground-reaction forces) and loads from skeletal muscle contractions (muscle forces or muscle-joint forces) [69,70]. Ground-reaction forces are generated from contact between the body and a surface due to gravitation, whereas muscle loads result from muscle contractions creating a force that is transmitted to the bone through the tendons [49]. The relative importance of these two sources for stimulation of bone is under debate and was recently the center of attention in four symposium reviews [48,49,69,71].

In support of his mechanostat theory, Frost asserted that ''*Bone strength and mass normally adapt to the largest voluntary loads on bones. The loads come from muscles, not body weight*'' [48]. From a theoretical view, the magnitude of muscle loading on bone is larger than the gravitational loading, at least during simple static movements, because of differences in lever arm length [48,49]. In a static exercise, *ground-reaction forces x lever A* should equal *muscle force x lever B* to maintain equilibrium at the joint. Thus, if lever A is longer than lever B, the muscle forces must be equally larger than ground-reaction forces [49]. However, many factors must be considered in more complex, dynamic exercises; varying lever arm lengths, body mass, acceleration (or deceleration), and eccentric muscle contractions [49]. Thus, only simple loading situations are easily measurable because most movements are complex [49]. Experimental research has shown that peak ground-reaction forces are approximately 1.5 times body weight during walking (3.6-10.8 km/h) and 2-3 times body weight during running (5.4-21 km/h) [72], whereas peak muscle force is 2.8-4.8 times body weight during walking (1-5 km/h) and 5-6 times body weight during jogging and stair walking [73]. For more complex activities, less experimental evidence exists, and the discussion must be based on research of associations between disuse, loading, muscle mass, and bone mass.

Space flight studies are particularly suitable because astronauts are subject to weightlessness, while at the same time, they are required to perform exercise while being in space [49]. During long-duration spaceflight, severe loss of both trabecular and cortical bone mass has been observed, particularly in the lower skeleton, despite daily exercise routines [74-76]. In paraplegic patients, bone loss continues several years longer than muscle loss [77]. These findings indicate that gravitational loading is essential for bone homeostasis [49,78].

Papers in the field of mechanical loading during exercise often refer to weight-bearing and weight-supported (non-weight-bearing) activities. Kohrt et al. [69] has suggested that the terms "impact" (ground-reaction forces) and "no-impact" (joint-reaction forces or muscle-joint forces) activities are better suitable to describe the source of loading.

*Impact activities* generate gravitational loads on the skeleton; thus, impact activities are weight-bearing (e.g. jumping) [69]. However, most impact activities also involve muscle forces [49,69], and the individual effect of the ground-reaction forces can be difficult to separate. Impact activities primarily involve the lower skeleton and are often divided into high-impact and low-impact activities.

In contrast, *no-impact activities* influence bone mostly through muscle loading [49,69]. No-impact activities can be weight-bearing (e.g. weight lifting) or weight-supported (e.g. swimming, cycling) [49,69].

The understanding of the effects and importance of various strains and loading sources in humans is challenging, and much of the knowledge comes from exercise studies [49]. To differentiate between sources of reaction force, it may be useful to study whether the activity involves primarily impact/ground-reaction loads or not.

Cross-sectional studies have typically compared athletes in various sports and sedentary controls [28,29,63,79-83]. As an example, Nikander et al. [29] compared femoral neck BMD in premenopausal female athletes who competed in sports with different types of load. Athletes competing in high-impact sports (volleyball, hurdling, squash-playing, soccer, speed skating, step-aerobics ) had the highest femoral neck BMD, followed by weight-lifters, thereafter orienteering and skiing athletes, while swimmers and cyclists had BMD similar to the non-athletes [29].

Mudd et al. [79] found that swimmers and runners had lower total and site-specific BMD than athletes in sports such as gymnastics, track, soccer, softball and field hockey. In another study, female runners had highest femoral neck BMD, compared to triathletes and cyclists, who had higher BMD than controls, while swimmers had lower BMD than controls [80]. Similar results have been found in other cross-sectional studies of athletes, mostly premenopausal women [63,81-83] and men [28] with impact activities including soccer, dancing, volleyball, basketball, squash, speed skating, weight lifting, and gymnastics compared to swimming as no-impact activity and/or sedentary controls.

In conclusion, cross-sectional studies indicate that a range of high-impact activities are associated with higher BMD, while swimming and cycling are associated with lower BMD, than controls. Endurance activities seem to be beneficial to a lesser degree. These studies indicate that ground-reaction forces are important for site-specific BMD and that muscle contractions are less important but still effective. However, causal conclusions cannot be drawn from cross-sectional studies.

In an intervention study, Kohrt et al. [73] compared the effect of impact load (walking, jogging, stair climbing) and no-impact, weight-bearing load (weight-lifting, rowing) on BMD in postmenopausal women. After 9 months, both types of exercise increased spine and total hip BMD, while only the impact group increased their femoral neck BMD [73]. Impact activities (walking, jogging, star climbing) were associated with the highest increase in BMD, in contrast to controls who did not increase their BMD at all [73]. Likewise, Snow-Harter et al. [42] found that in young women, both weight-training and running produced an increase in spine BMD, whereas only weight-training increased muscle strength. Intervention studies indicate that gravitational forces are essential for BMD of the femoral neck, but not the spine, suggesting that muscle contractions and ground-reaction forces could be efficient at different skeletal sites. However, in other studies, no-impact resistance training have been found to increase or preserve femoral neck BMD in postmenopausal women [84] and elderly men [85], emphasizing the inconsistency of the findings.

Unfortunately, most studies of humans are based on small sample sizes, and epidemiological studies of large cohorts are difficult to implement. Recent meta-analyses by Martyn-St James and Carroll [86-90] studied the effect of different exercise types on BMD in pre- and postmenopausal women. Resistance training alone increased lumbar spine BMD, but not femoral neck BMD [86,87,89], whereas combining impact activities with resistance training significantly increased BMD at both sites [89,90]. In postmenopausal women, low-impact exercise (jogging combined with stair climbing and walking) also increased BMD at the lumbar spine and femoral neck [90], but not walking alone [88]. These meta-analyses suggest that impact forces of a certain magnitude and rate, but not resistance training, were sufficient to increase femoral neck BMD, and that resistance training has strongest effect on lumbar spine BMD.

## CONCLUSION

The existing literature shows that both muscle-joint forces and gravitational forces may be able to induce bone adaptation independently; though in most situations these forces act together. Ground-reaction forces of a certain magnitude and rate seem to be essential for BMD at the hip, but not the spine, whereas resistance training seems to have strongest effect on spine BMD. This suggests that muscle contractions and ground-reaction forces could act differently at different skeletal sites. The nature of the activity should be dynamic, not static, and the magnitude and rate of the stimuli should be high, preferentially involving high-impact activities and resistance training. Endurance activities seem to be beneficial to a lesser degree, whereas low-impact activities are not beneficial. Both the intensity and frequency of the activity should be varied and increased beyond the habitual level. Duration of the activity seems to be less important, as a few loading cycles seem to be sufficient.

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