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VIBRATION AND BONE – AN OPTION FOR LONG-TERM SPACE MISSIONS?

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ABSTRACT

Bone is lost during sojourns in microgravity. In order to prevent fractures in future manned inter-planetary missions, efforts are currently being made to develop effective countermeasures. Bones adapt to mechanical stimuli, and biomechanical analysis suggests that muscle forces play an important role. Thus, resistance training is advocated as a first option for a countermeasure modality. In addition, vibration has certain characteristics (well controllable, rapid stretch-shortening and large number of contractions) that could be of interest. Studies in the past decade have shown that conventional resistive exercise may be sufficient to maintain bone when performed on a daily basis, but not when performed only every other day. Whole body vibration without additional load seems to be ineffective, but it shows good potential, and probably will have a genuine effect upon bone when combined with additional loads in the order of twice the body weight. There is now accumulating evidence to suggest that effective exercises exist to counteract microgravity-related bone loss. At least for bed rest, forceful muscle contractions seem to be a prerequisite. They may be fortified, but probably not replaced, by vibration exposure.

Keywords: *immobilization, human physiology, physical medicine, bed rest*

VIBRACIJA IN KOST – MOŽNOST ZA DOLGOTRAJNE MISIJE V VESOLJE?

IZVLEČEK

Kostna gostota se zmanjšuje med bivanjem v mikrogravitacijskem prostoru. Z namenom, da bi preprečili zlome med prihodnjimi medplanetarnimi misijami, se trenutno vlaga precej truda v razvoj učinkovitih protiukrepov. Kosti se prilagodijo mehaničnim stimulansom, biomehanična analiza tako predvideva, da mišične sile tu igrajo pomembno vlogo. Zato se trening odpornosti priporoča kot prvo možnost med načini protiukrepov. Poleg tega bi nas lahko zanimale tudi določene značilnosti vibracij (dobro nadzorljivo, hitro in neprekinjeno kratko in daljše trajanje kontrakcij). Študije v preteklem desetletju so pokazale, da konvencionalna telovadba za odpornost zadostuje za ohranjanje kostne gostote, če se telovadba izvaja redno, vendar le, če se izvaja vsak drugi dan. Vibracije celotnega telesa brez dodatne obremenitve so očitno neučinkovite, vendar pa kažejo dober potencial oziroma bodo lahko imele dejanski vpliv na kosti, ko jih bomo združili z dodatnimi obremenitvami po načelu dvojne telesne teže. Tako obstaja več dokazov, ki navajajo, da obstajajo učinkovite vaje, ki delujejo proti izgubi kostne gostote, ki je pogojena z mikrogravitacijo. Vsaj v primeru ležanja v postelji je prvi pogoj za to silovito krčenje mišic. Takšne vaje lahko okrepimo, vendar jih najverjetneje ne moremo zamenjati z izpostavljenostjo vibracijam.

Ključne besede: *imobilizacija, človeška fiziologija, fizikalna medicina, ležanje v postelji*

STATEMENT OF THE PROBLEM

It was a surprising result of the Gemini program that astronauts seemed to lose bone tissue from their legs at an astounding rate. The awareness of Space as a particularly ‘hostile’ environment for bone was borne. This connotation has been substantiated during the Skylab era, even though the rate of bone loss found was not as severe as initially feared (Vogel, 1975). Systematic research in the Spacelab, on the Mir station and on board the International Space Station (ISS) has provided us with valuable descriptive information (Lang, Leblanc, Evans, & Lu, 2006; Vico et al., 2000), even though the exact mechanisms of bone loss are still under debate. The existing evidence can be briefly summarised as follows: In humans, bone is lost at a rate of approximately 1% per month from the legs, but not from the arms. Animals, including monkeys, however, lose bone from all extremities. As to the consequences, it is evident that removing tissue from the bone reduces its strength and increases the likelihood of fracture. Given the deleterious consequences of a fracture during manned planetary exploration, development of effective countermeasures is mandatory before embarking on such missions.

Why, then, would one lose bone in microgravity? The initial suspects were hormonal and nutritional alterations, in particular in relation to Vitamin D and calcium metabolism (Globus, Bikle, Halloran, & Morey-Holton, 1986; Halloran et al., 1985). However, this idea did not prevail, and 'immobilisation' of the astronauts' legs is now widely held as the cause. In parallel to research on bone losses in astronauts, and probably stipulated by it, it has been established that bone is also lost in clinical cases of leg immobilization, such as spinal cord injury (Eser et al., 2004; Griffiths, Bushueff, & Zimmermann, 1976), stroke (Jorgensen, Crabtree, Reeve, & Jacobsen, 2000), anterior cruciate ligament injury (Leppala et al., 1999) – and bed rest (LeBlanc, Schneider, Evans, Engelbretson, & Krebs, 1990; Rittweger et al., 2005; Vico et al., 1987). The latter is of particular interest, as experimental bed rest in combination with -6° head-down tilt (HDT) has been proposed as a ground based model for the cardiovascular alterations induced by space flight (Kakurin, Kuzmin, Matsnev, & Mikhailov, 1976; Kakurin, Lobachik, Mikhailov, & Senkevich, 1976), and it is currently also recognized as a model for the musculo-skeletal effects of microgravity (Pavy-Le Traon, Heer, Narici, Rittweger, & Vernikos, 2007).

Rationale for exercise countermeasures

There is compelling evidence to suggest that mechanical stimuli per se can elicit a so-called 'osteogenic' response, i.e. a reaction by which bone accrual leads to an enhancement of bone rigidity and strength. It is straightforward to regard the immobilization-induced bone losses as the reverse of this, and to integrate bone strengthening and losing reactions into the concept of a self-adaptive system – commonly known as Wolf's Law (Wolff, 1870). But which is the decisive signal within the mechanical environment that drives bone adaptation? Most researchers would currently agree that it is 'strain' (a dimensionless number that quantifies the deformation of bone), or a signal that is related to the generation of strain. The evidence for this view came initially from the striking observation that peak bone strains center around 2000[1] µstrain across a wide range of species the mass of which spans several orders of magnitude. More compellingly, even, Rubin et al. (1987) have demonstrated in the 'isolated-ulna' model in Turkey that daily loading leads to modelling[2] -based bone accrual when the strains are in excess of 1000 µstrain, but that bone will be lost to disuse-mode remodelling when that threshold is not achieved. Viewing strain as the invariant of a feed-back control system makes sense also from an engineering point of view, as it is the strain that is ultimately destructive. The mechanostat theory (Frost, 1987) was the first to conceptualize this relationship between strains, modelling and remodelling as a semi-quantitative model of bone adaptation. It predicts that bone rigidity varies in direct relationship to the peak loads experienced by bones.

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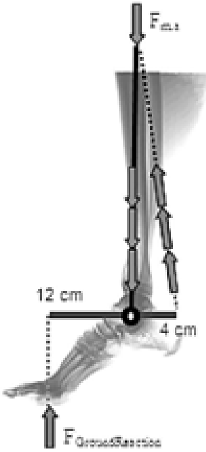
[1] One µstrain means deformation by 10^{-6}, hence 2000 µstrain signify 0.2% of the original length.

[2] Modelling is shapes and strengthens bone structures – here, formation normally outweighs resorption.



	Standing	Hopping
Body Mass [kg]	70	70
Groundreactionforce [kN]	0.7	2.5
Torque [Nm]	84	300
Acceleration [g]	1	3
$Force_{AchillesT}$ [kN]	2.1	7.5
$Force_{Tibia}$ [kN]	2.1	10

Figure 1: Free body diagram of the human ankle. This simplified diagram suggests that loading of the tibia by the mere body weight is only around 700N, whilst a load of 10,000N is achieved when calf muscles accelerate the body, e.g. in hopping. One important aspect herein is the short lever (1:3) against which the calf muscles work. Figure adapted from Maganaris et al. (2011).

So, where do the peak loads arise from? The commonly-used term ‘weight bearing’ bone suggests that, at least in the leg bones, they may arise from the accelerated body mass. Let us remember, though, that weight is defined in physics as mass · gravitational acceleration. Thus, the body weight of a 70 kg person is approximately 700 N on Earth. However, as can be seen from Figure 1, forces more than 10 times greater than body weight can arise from muscle contractions when these muscles accelerate our body mass, as e.g. during hopping. Accordingly, weight-bearing in itself engenders comparatively small forces on the tibia. Countermeasure interventions to prevent bone loss should thus require forceful muscle contractions in order to replicate the bone’s mechanical environment on Earth. Accordingly, resistance training is usually advocated as the first option (Frost, 1997).

Vibration as an exercise modality

Although the mechanostat theory has been the first formal model of bone adaptation, and it continues to be the most popular one, other authors have focused on various aspects not covered by this theory (Schriefer, Warden, Saxon, Robling, & Turner, 2005). One important aspect not covered by that theory is the question of how many strain cycles are required to elicit a response and how many to saturate it, and also whether only supra-threshold cycles contribute to the adaptive process. Moreover, it seems certain nowadays that not only strain magnitude, but also other strain-related entities such as strain energy density, and strain rate have a role to play (Mosley & Lanyon, 1998). This notion has been further elaborated to propose that many small-magnitude strain cycles could be as efficient as few cycles of large strain magnitude – provided the former have greater strain rate than the latter (Qin, Rubin, & McLeod, 1998). It was further proposed that strain rate could be increased with constant amplitude in sinusoidal vibration by increasing the frequency of vibration – which was the birth of vibration as a therapeutic modality for bone (C. Rubin, Turner, Bain, Mallinckrodt, & McLeod, 2001).

The current concepts of vibration exercise have been recently reviewed (Rittweger, 2010). Most vibration devices are meant to be used for 'whole-body vibration', meaning that people usually stand with their feet on a platform. This can be by imposing mechanical oscillations in a synchronous or in a side-alternating fashion (Rauch et al., 2010), as illustrated in Figure 2. Vibration transmission to the trunk and head is more pronounced with synchronous mode vibration (Abercromby et al., 2007). Strictly speaking, ISO norms 2631–1 (for occupational exposure) and 5349 (for hand-held devices) need to be considered, although it is evident that therapeutic (Rittweger, Just, Kautzsch, Reeg, & Felsenberg, 2002) and exercise applications do not strictly fall into their remit (Rittweger, 2010).

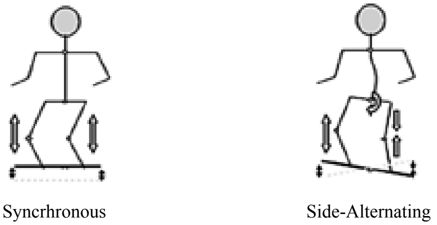


Figure 2: The two principle ways of applying vibration for whole body vibration exercise. The synchronous applies a purely linear acceleration, thus compressing both legs at the same time. In the side-alternating mode, the legs operate anti-phase, which introduces a rotary component to the lumbar spine, and therefore reduces vibration transmission to the trunk. Figure adopted from Rittweger (2010).

Vibration exposure leads to rhythmic elongation and shortening of the musculature (Cochrane, Loram, Stannard, & Rittweger, 2009). Oxygen uptake is moderately enhanced during vibration exposure (Cochrane et al., 2008; Rittweger, Schiessl, & Felsenberg, 2001), and the latter effect can be parametrically controlled by adjustment of frequency and amplitude of vibration (Rittweger et al., 2002). These observations are compatible with the idea of vibration eliciting monosynaptic stretch reflexes, although it has to be considered that the H-reflex, as well as probably the stretch reflex amplitude are mitigated during vibration exposure itself (Ritzmann, Kramer, Gollhofer, & Taube, 2011).

Thus, even though our understanding is not complete, we can outline the following salient features of vibration as an exercise modality in the context of a space-flight countermeasure:

1. Well controllable force and displacement profile
2. Rapid stretch-shortening cycles
3. Large number of muscle contractions per unit time

Evidence from bed rest studies

The scene for a resistive-type of exercise as a countermeasure against bed rest-induced muscle atrophy and bone loss was set by the 90-days HDT Long Term Bed Rest (LTBR) study carried out in Toulouse in 2001 and 2002 (Rittweger et al., 2005). In this study, a gravity-independent ‘flywheel’ ergometer was used as an exercise device 2–3 times per week, resulting in good preservation of the knee extensor, but not of the plantar flexor muscles (Alkner & Tesch, 2004). Bone loss from the tibia was halved in the group that performed the exercise as compared to those who were on bed rest only, which however was not significant because of the huge inter-individual variability (Rittweger et al., 2005). The 17-week study by Shackelford et al. (2004) has been more successful: conventional exercise performed on 6 days per week with a custom-made 'horizontal exercise machine' led to enhanced muscle strength (at least as tested on the horizontal exercise machine), prevented muscle atrophy and bone loss from the heel, and mitigated bone loss from the hip.

Vibration as a countermeasure was first tested at the German Aerospace Centre in Cologne in the 14-day VBR-study, which failed to demonstrate any effect of whole body vibration (twice daily, no additional load) upon muscle atrophy (Zange, Mester, Heer, Kluge, & Liphardt, 2008). Similarly, no effect was observed on bone (Baecker, Frings-Meuthen, Heer, Mester, & Liphardt, 2011). Good results were achieved, however, when whole body vibration was combined with resistive exercise in the 56-day Berlin Bed Rest study, performing exhaustive exercises 11 times per week, with an additional static load equivalent to twice the body weight (Rittweger et al., 2006): atrophy of the calf muscle was prevented and plantar flexor strength maintained (Blottner et al., 2006), and bone loss from the tibia, and probably also from the hip were likewise prevented (Rittweger et al., 2010). A recent study by Wang et al. (2011) in which vibration, albeit with much smaller peak acceleration than in the BBR study, was applied once daily in combination with a static load equivalent to 1.5 times body weight corroborates these findings and shows good efficacy for bone.

The pertinent question, of course, is whether the benefits of these latter two studies were an effect of the vibration (probably not, in the light of results from the VBR study), of the resistive exercise component (possibly, as indicated by Shackelford's study), or a result of both. A case for the latter view can be made on basis of the results from the BBR-2 study. In this 60-day HDT study, the group that performed resistive exercise 3 days per week in combination with whole body vibration depicted a significantly smaller bone loss than the group that performed resistive exercise only (Belavy et al., 2011). Thus, there seems to be a benefit in vibration, although 3 exercise sessions per week may not be sufficient to completely counteract bed-rest induced bone loss.

CONCLUSION

Whilst the exact physiological mechanisms of bone losses induced by space flight and immobilization may still be under scientific debate, the past decade has seen the development of countermeasures that are becoming increasingly effective, at least in a bed rest scenario. Although the recognition of such effective countermeasures cannot invalidate the quest for the establishment of the exact physiological mechanisms behind the bone loss, it will certainly inform and guide future research. In this sense, skeletal forces as induced by muscle contractions should be regarded as an important determinant of bone health. At least for bed rest, the effects of muscle contractions may be fortified, but probably not replaced, by vibration exposure.

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