CHARLES UNIVERSITY IN PRAGUE, FACULTY OF PHYSICAL EDUCATION AND SPORT, DEPARTMENT OF GYMNASTICS<sup>1</sup> DEPARTMENT OF PHYSIOLOGY AND BIOCHEMISTRY<sup>2</sup> DEPARTMENT OF ANATOMY AND BIOMECHANICS, LAB. OF BIOMECHANICS OF EXTREME LOADING<sup>3</sup>

# RISKS AND BENEFITS OF HYPO/HYPERKINETIC LOADING OF HUMAN MUSCULOSKELETAL SYSTEM AND ITS GENETIC PREDISPOSITIONS – RHYTHMIC GYMNASTIC

ŠÁRKA PANSKÁ<sup>1</sup>, MIROSLAV PETR<sup>2</sup>, KAREL JELEN<sup>3</sup>

### SUMMARY

Many studies show that the higher up the high intensity and volume of training load has a positive effect on e.g. bone adaptation especially for children and adolescents. Skeletal response to load is dependent on many different factors related to mechanical loading (training) as well as factors that relate directly to the athlete himself, such as nutritional and hormonal factors and especially age when the training interventions started.

Besides the influence of load on bone adaptation, our initial review study will be based on potential genetic factors involved in the quality of the bone system, namely the density of bone (BMD), bone structure and ability of mineralization.

Key words: hypokinesia, hyperkinesia, training load, bone mineral density (BMD), genetics factors

## INTRODUCTION

Human hyperkinetic musculoskeletal load is in many cases caused by work activity, as well as non-work activity, including sports training and performance. Loads are then in terms of thermodynamics of different types – impact, frequency, long-term, short term, energy, heat as well as describing the chemical kinetics of nutrition. High load of human musculoskeletal system can lead to exhaustion of functional reserves, the loss of the required rheological properties of e.g. soft and hard tissue (ligament, tendon, muscle, cartilage or bone), or even mechanical and functional disorders. At this level it is about changes in thermo-viscous-elastic properties of these biomaterials. Furthermore, it may also weaken the regulatory mechanisms of the organism, noise signals may appear at the management level as well as metabolic regime disorders. Similar effects can be seen also in hypokinetic modes though. Our work enters the extreme hypo-hyperkinetic load modes at the level of needed critical review in the segment of *bone mineral density* (BMD) and its possible influence with the application in rhythmic gymnastic (RG).

Many studies show that the higher up the high intensity and volume of training load has a positive effect on e.g. bone adaptation especially for children and adolescents. Skeletal response to load is dependent on many different factors related to mechanical loading (training) as well as factors that relate directly to the athlete himself, such as nutritional and hormonal factors and especially age when the training interventions started. Hypo kinesis in the sports environment can be understood as a relaxation, regeneration scheme which will have positive implications for local or short-overloaded biological structure.

The aim of this work is to assess the used methods and identifiers of bone mineral density (BMD, vBMD – volumetric bone mineral density or aBMD – areal bone mineral density) and analyse the influence of hypo-hyperkinetic load on BMD (vBMD, aBMD).

The evaluated methods for the detection of bone density include:

DEXA (DXA) - Dual Energy X-ray Absorptiometry,

QCT - Quantitative Computer Tomography,

pQCT - peripheral Quantitative Computer Tomography,

QUS - Quantitative Ultrasound densitometer.

Besides the influence of load on bone adaptation, our initial review study will be based on potential genetic factors involved in the quality of the bone system, namely the density of bone (BMD), bone structure and ability of mineralization. An example might be a gene for the VDR (vitamin D receptor) gene ESR1 (estrogen receptor 1) or the COL1A1 gene (collagen receptor 1, alpha 1).

## CRITICAL REVIEW - BMD

In the cited studies the contributions conclusions are the original conclusions of the individual authors. If these works are commented by the critical review authors, they are highlighted in italics.

Cross-sectional study Wu, Ishizaka, Kato et al. (1998) analyses differences in bone mineral density (BMD) at the right and left proximal femur at RG (Wu, Ishizaka, Kato, Kuroda, & Fukashiro, 1998). Hypotheses on which the study is based assume that gymnasts use a different foot for take-off (left foot) and another for landing (right foot), and therefore the load of left and right legs varies. Gymnasts were divided to two groups: competition group of 15 gymnasts who regularly practiced 28 hours a week, and substitution group of 8 gymnasts who trained 12 hours a week. The control group consisted of 10 non-sporting female college students which did not participate in any regular sports activities. BMD  $[gcm^{-2}]$  was detected in three areas of the hip using XR-26 dual energy X-ray scanner. Muscle strength of knee extensors (EXT) and flexors (FLX) was detected by isokinetic dynamometer (CYBEX6000) and vertical reaction force was measured on the Kistler force plate during a take-off and landing. For the group of more training gymnasts values of BMDs of the left leg were significantly higher than the right leg at the femoral neck, greater trochanter and Ward's triangle (p < 0.01-0.005). Differences were 4.7 to 9.6%. Regarding the power parameters, the left side was significantly larger than the right side for the knee extensors at  $60^{s-1}$  (p < 0.01). For the group of less training gymnasts the BMDs for these three places was also higher on the left leg than the right, but the difference was statistically significant only at the Ward



Figure 1. A curve of vertical ground reaction force components for take-off and landing conditions during the performance of a leap by a RG on the force platform (regular players), (Wu, Ishizaka et. al. 1998)

triangle (9.3%, p < 0.05). The difference in the strength was not significant in this group. In the control group the differences were small between left and right leg with BMDs ranging from -1.8 to 0.5% which was significantly lower than in the more training group. The overall average force was measured bigger on the right leg, except for speed of  $120^{\circ} \text{ s}^{-1}$ . The left and right side difference was statistically significant at EXT  $30^{\circ} \text{ s}^{-1}$ ,  $60^{\circ} \text{ s}^{-1}$  (p < 0.05). Maximum force was higher during take-off than during landing and power per unit of time during take-off was statistically significantly higher than during landing (p < 0.001). In contrast, power impulse was statistically significantly higher when landing than during take-off (p < 0.005). (Fig. 1)

Table 1.	Comparison	of Vertical g	ground reaction	force and	contact t	ime during	take-of	and I	landing	of
the leap	measured in	RG (regula	r players)							

	Peak Force [N]		Impulse [Ns]		Unit time force *[N]		Contact time [ms]	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Take Off	2090.84	213.68	12.25	11.99	60.02+	5.97	204	14
Landing	1925.97	278.39	16.94+	24.79	52.11	6.85	325++	43

Unit time force: impulse per contact time

+ p < 0.001 (take-off > landing); ++ p < 0.005 (take-off < landing), (Wu, Ishizaka et. al. 1998)

As for the difference in BMD of the left and right proximal femur, study results show that the left take-off leg had higher values than the landing leg in both groups of gymnasts, which can be attributed to the vertical reaction force of the pad during take-off, which is higher than during the landing. Higher differences in competition gymnasts group than in the substitution gymnasts group can be explained by the fact that one group is training much more than the other and there were no differences in BMD between the left and right proximal femur in the control group.



Figure 2. Maximal muscle strength artistic gymnasts, rhythmic gymnasts compared to control (Helge & Kanstrup, 2002)

Authors of another study investigated the BMD of top Danish gymnasts in relation to the maximum muscle strength, concentration of sex hormones and status of the menstrual activity and evaluated whether mechanical stimuli of gymnastics training could compensate for the expected low concentrations of sex hormones (Helge & Kanstrup, 2002). There were six artistic gymnasts, five rhythmic gymnasts and six control subjects aged 15–20 years tested. Load of the gymnasts was represented by more than 15 hours of training per week with an undisclosed, but a similar body load. The control group of girls underwent physical load (walking, cycling and one hour of compulsory physical education) less than 4 hours per week. Using absorptiometry (DXA) was measured BMD [gcm<sup>2</sup>] at the lumbar spine, proximal femur, distal radius and whole body. Maximum muscle strength was isokinetically measured at speed of  $60^{\circ}$  s<sup>-1</sup> in extension and flexion of the trunk and knee extension at maximum torque.

Maximum trunk force was significantly higher in artistic and rhythmic gymnasts than in the control group. The highest values were in the artistic gymnasts (Fig. 2). When the maximum strength of the trunk was linked to body weight, the difference between the gymnasts and the control sample was even much greater (38–56%). Compared with the control group, the maximum muscle strength in artistic gymnasts was larger in extension of the right (30%, P < 0.001) and left (18%, P < 0.01) knee, compared with the rhythmic gymnasts in the right knee extension (14%, P < 0.05).

For artistic gymnasts the BMD was higher than in the control group in all aspects except WBBMD (P < 0.05), while rhythmic gymnasts had higher BMD in all aspects except the distal radius (P < 0.05) (Fig. 3). Artistic gymnasts had higher BMD than the rhythmic gymnasts at the right (30%, P < 0.01) and left (50%, P < 0.001) distal radius, which may be indicative of a significant number of impacts on the bones of the arms and hands (for example jumps over the gymnastic equipment using arms, acrobatic exercises using arms and hands). This corresponds to the theory of bone remodelling, resp. paradigm of bone physiology (Frost, 2000).



Figure 3. BMD artistic gymnasts, rhythmic gymnasts compared to control (Helge & Kanstrup, 2002)

Published differences in rhythmic and artistic gymnasts stem primarily from differences in training methods and their own physical characteristics.

The authors did not demonstrate the significance of the relationship between BMD and menarche. However, in artistic gymnasts and gymnasts competing in the multi-event was a significant association between WBBMD (r = 0.93), LFBMD (r = 0.92) and BMD L2–L4 (r = 0.89) and the concentration of progesterone in the follicular phase; in rhythmic gymnasts was a relationship between the BMD L2–L4 (r = 0.99) and estrogen levels in the luteal phase. These correlations could indicate that the concentration of sex hormones affects BMD in gymnasts with menstrual disorders.

There was a strong correlation between maximal muscle strength and appendicular and axial BMD in gymnast, which was in the range between 0.60 and 0.90. The above mentioned correlation could indicate that the current exercise which represents the load on bones and / or muscle activity are the most important factors affecting BMD of the top athletes in this age. When the rhythmic and artistic gymnasts were investigated separately, the results of the second group tended to have a closer relationship between BMD and maximal muscle strength. The positive correlation between BMD and maximal muscle strength was not evident in the control sample, indicating that high pressure is needed in order to osteogenous effect to appear that would have an impact on positive bone remodelling.

Although diagnosed with oligomenorrhea or amenorrhea, it is possible for the gymnasts to maintain a high BMD in the axial (L2–L4) and the appendicular skeleton. Correlations between BMD, maximal muscle strength and concentrations of progesterone may indicate in the gymnasts that within a single sport group, the concentration of progesterone has a permissive role in bone remodelling, which positively affects muscle strength.

Other literature data deal with the relationship between construction and remodelling of bone tissue and sex hormones, whose importance should be mainly in the reproductive function of women. Questions regarding the onset of menstrual cycle and related issues, such as oligomenorrhoea, amenorrhoea or contraception significantly influence the modelling ability of bones. It is therefore necessary to map the information from the submitted study about the connection between levels of sex hormones and their effects on BMD with muscle strength. It is also necessary to take into account the permissive role of concentrations of progesterone in bone remodelling, since we are talking about the age group that is in terms of modelling and remodelling of bone tissue at the boundary of both processes.

Subsequent study dealt with the change in bone density and bone indicators (markers) at RG and ballet dancers as a consequence of puberty and leptin levels (Muñoz, de la Piedra, Barrios, Garrido, & Argente, 2004). The aim of this study was to compare physical activity and biochemical indicators (markers) of bone mineral gain of the gymnasts, ballet dancers and age and sex-matched control group as well as analysis of indicators of bone formation and resorption in adolescents and to determine whether the degree of osteopenia correlated with bone indicators and leptin levels in these adolescent girls.

The subjects were 35 healthy girls - nine rhythmic gymnasts (RG), twelve ballet dancers and fourteen girls of control group of the same age. RG and ballet dancers were devoted to intense training at least 20 hours a week with previous 5-years' experience with intense training. Adolescents in the control group performed less than 3 hours of physical activity per week. Nutritional status was determined by anthropometric measuring of weight, height and BMI. The monitored subjects were further analysed for food intake, bone age and menstrual history. Bone mineral density (BMD) was assessed using dual energy X-ray absorptiometry (DXA) at the lumbar spine, hip and forearm. By collecting blood samples were measured bone alkaline phosphatase (bAP) and amino-terminal propeptide of procollagen I (PNIP), from urine samples was measured  $\alpha$  - isomer of carboxy-terminal telopeptide of collagen I ( $\alpha$ -CTX).

Serum bAP concentrations were quantified by immunoradiometric test (Tandem-R Ostase, Hybritech, Lie'ge, Belgium). Levels of urinary  $\alpha$ -CTX were determined using RIA ( $\alpha$ -Crosslaps, Osteometer Biotech, Austin, TX, USA) as well as leptin levels (Linco, St. Charles, Missouri, USA).

	Ballet dancers	Gymnasts	Controls	
Age (years)	16.4 ± 2 16.2 ± 2		16.9 ± 1	
Weight (kg)	48.8 ± 4	48 ± 7	58.8 ± 8	
Height (cm)	162.4 ± 4	161.8 ± 6	161.5 ± 6	
BMI** (S.D.)	$-0.6 \pm 0.7$	$-0.5 \pm 0.9$	$0.2 \pm 0.9$	
Menarche(years)	13.7 ± 1*	15 ± 1*	12.8 ± 1	
Bone age (years)	14 ± 0.5	14 ± 0.5	16 ± 1	
Dietary calcium (mg/day)	933 ± 312	730 ± 173	700.7 ± 255	

Table 2. Physical and dietary characteristics of the three experimental groups. Values are means  $\pm$  S.D. (Muñoz et al., 200).

\* P < 0.01 vs. controls

\*\* The values for BMI mean deviation from the population of Spain by age and sex (Hernandez et al., 1988)

The results showed that the bone age of the gymnasts and ballet dancers was delayed by 2 years and the average age of menstruation was  $15 \pm 0.9$  year in the gymnasts and  $13.7 \pm 1$  in the ballet dancers, compared with  $12.5 \pm 1$  year in the control group. Possible causes of delay in bone age the authors attribute primarily to nutritional deficiency in the groups of both gymnasts and ballerinas. Nutritional regimes as well as genetic factors play an important role in the onset of menstrual cycles in these age groups of girls.

BMD of trochanter and femoral neck was significantly higher in rhythmic gymnasts compared with ballet dancers and control group. BMD of the right forearm (unloaded zone) was significantly lower in rhythmic gymnasts and ballet dancers compared with the control group.

Site of measurements	Ballet dancers	Gymnasts	Control
Lumbal spine	0.970 ± 0.10	1.010 ± 0.16	1.033 ± 0.09
Femoral neck	0.922 ± 0.09	1.030 ± 0.190*	0.730 ± 0.090
Trochanter	0.755 ± 0.77**	$0.870 \pm 0.120^{*}$	0.730 ± 0.090
mid-radius	0.471 ± 0.033*	0.462 ± 0.051*	0.533 ± 0.036

Table 3. BMD measurements [gcm  $^{\rm 2}$ ] in the three experimental groups. Values are means ± S.D. (Muñoz et al., 2004)

\* P < 0.05, \*\* P < 0.05 vs. gymnasts

All subjects had normal levels of bAP and PNIP but  $\alpha$ -CTX/creatinine (Cr) ratio was increased in rhythmic gymnasts (P < 0.001) with inverse correlation between BMD of the right forearm and ration of  $\alpha$ -CTX/Cr (r = -0.74, P < 0.001). The level of leptin serum was reduced in rhythmic gymnasts and ballet dancers. Rhythmic gymnasts had a positive correlation between BMD of the right forearm and leptin level (r = 0.85, P < 0.001).

Table 4. Biochemical analyses of the three groups, Values are means ± S.D. (Muñoz et al., 2004).

	Ballet dancers	Gymnasts	Control
bAP (μg/l)	56.9 ± 13	64.3 ± 11	49 ± 9
PNIP (µg/l)	132 ± 11	175 ± 11	200 ± 48
α-CTX/Cr (µg/l/mM)	1900 ± 350	3220 ± 339*	1416 ± 185
Leptin (ng/ml)	5.7 ± 3**	5.1 ± 2**	15 ± 8

\* P < 0.05, \*\* P < 0.01 vs. controls



Figure 4. a-CTX serum levels and BMD vs. ballet dancers, gymnasts and controls. (Muñoz et al., 2004)



Figure 5. Leptin levels and BMD correlation vs. ballet dancers, gymnasts and controls. (Munoz et al., 2004)

Finally, it can be stated that the reduction of bone mass in the RG can be partly explained by the increase in bone resorption introduced by increased levels of  $\alpha$ -CTX. Leptin serum levels appear to be a suitable indicator of bone mass in these objects and could contribute to delay puberty.

According to the authors of the study it is possible that higher levels of  $\alpha$ -CTX in RG are a result of increased changes in bone tissue including resorption of newly formed bone. Increased bone resorption without changing bone formation may explain the findings of osteopenia in the radius of observed girls. *Changes of leptin levels are correlated with BMD, but it is not clear whether this is caused by reduced food intake or anorexia nervosa.* 

Ward, Roberts et al. (2005) have dealt with bone geometry and bone density of prepubertal gymnasts and school children (Ward, Roberts, Adams, & Mughal, 2005).

The aim of this study was to monitor the differences between the construction of peripheral and axial skeleton of pre-pubertal gymnasts and school children of the same age. The authors hypothesized that, compared with others, gymnasts will have bigger and stronger shaft radius and tibia with higher bone mineral content and greater cross-sectional area of muscle. In the distal metaphyseal radius and tibia the gymnasts should have a greater cross-sectional area and overall larger volume bone mineral density (vBMD). Differences were also monitored in the lumbar spine and total body composition of gymnasts and control group. To measure bone geometry and bone and muscle density of peripheral skeleton computer tomography (pQCT) was used, overall bone density was detected by X-ray absorptiometry (DXA).

Subjects were 86 prepubertal children, 44 gymnasts (average age 9 years, range 5.4 to 11.9) and 42 children in control group (mean age 8.8 years, range from 5.6 to 11.9). Differences were also tested in effect rates between the sexes.

At 50% of radius diaphysis the gymnasts had larger bones (9.2%, p = 0, 0054) with greater cortical area (8.2%, p = 0.022) and SSI (13.6%, p = 0.015) than the control group. The difference between the sexes (in all observed groups) was in the size of cortical thickness (p = 0.03). At 65% of tibia diaphysis the gymnasts had greater cortical area (5.3%, p = 0.057) and thickness (6.2%, p = 0.068) than the control group, bone density was 5.4% higher (p = 0.14). No significant differences between groups were detected in



Figure 6. Clustered box-plots that ilustrate interaction between Sex and activity at the peripheral skeleton (Ward et al., 2005)

 A) Radius cortical thickness, (B) Tibia muscle cross-sectional area (unfilled boxes = controls, filled = gymnasts).

cortical volumetric density (vBMD) at radio or tibia diaphysis. The differences were in size of muscle cross-sectional area of tibia between sexes (p = 0.035). At distal radio and tibia the total and trabecular vBMD was larger (total: radius 17%, p < 0.0001, tibia: 5.7%, p = 0, 0053; trabecular: radius 21%, p < 0.0001, tibia 4.5%, p = 0.11). The size of the bones was not different between gymnasts and control group.

BMC of lumbar spine (12.3%, p = 0.0007), areal bone mineral density (aBMD) (9.1%, p = 0.0006) and bone mineral apparent density (BMAD) (7.6%, p = 0.0047) were greater in gymnasts, but no significant differences were found in the size of the vertebrae. Total body BMD (3.5%, p = 0.0057) and BMC (4.78%, p = 0.085) were greater in gymnasts, but no significant differences were found in geometric parameters of the skeleton.

The results suggest specific differences in the development of prepubescent skeleton depending on the repeated load of regular exercise. The study showed differences in bone parameters between gymnasts and control group. The differences appear to be specific with regard to sex. In diaphysis areas these differences are mainly in bone and muscle geometry and not in bone density. On the contrary, at the trabecular sites there are larger differences in density than in geometry.

Tournis et al. (2010) investigated the effect of RG on the density of bone mineral density and bone geometry in the premenstrual age of gymnasts. The aim was to test the hypothesis that the peak load in the RG has positive effects on bone mineral density, volume and geometry and to determine whether an exercise-induced bone adaptation is associated with increased formation of periosteum or medullar contractions (Tournis et al., 2010).

In this study, the authors evaluated selected physiological, biomechanical and geometric parameters of the bones of 49 premenstrual girls aged from 9 to 13 years. Twenty-six girls were in the top group of rhythmic gymnasts training at least two years with a training load of at least 24 h/week. 23 girls attended school physical education only. For each of the girls volumetric bone density (vBMD), bone mineral content (BMC), cortical thickness (CRTHK outer packaging, bone), cortical and trabecular bone area and strength through SSip was measured using DEXA and pQCT.

Cross-sectional study was performed on the left tibia from proximal to distal metaphysis at 14% (trabecular density), at 38% length of tibia (cortical density), and 66% length of the tibia from the distal end (muscle mass), including changes in bone parameters.

The main findings were:

- 1) RG was associated with positive bone adaptation especially in cortical areas, marked by an increased rate of mineralization and area, while vBMD remained unchanged;
- 2) increased geometric parameters as well as CRTHK, periosteal circumference and eventually even increased bone strength index provide evidence that intensive and long-term RG in the growth period can be beneficial for bone metabolism;
- 3) muscle area is associated with a positive response of both quantitative and qualitative parameters of bone while training age showed a similar context, independent of chronological age.

Distance		RG	Control	Р
38.00%				
	Total BMC [mg]	272.72 ± 5.57	218.19 ± 5.9	<0.001
	Cortical BMC [mg]	243.82 ± 5.45	187.17 ± 5.88	<0.001
	Cortical CSA [mm <sup>2</sup> ]	233.85 ± 5.28	179.78 ± 5.70	<0.001
	CRTHK [mm <sup>3</sup> ]	4.53 ± 0.09	3.60 ± 0.10	<0.001
	SSip [mm <sup>3</sup> ]	1129.74 ± 38.01	858.92 ± 40.98	<0.001
14.00%				
	Total BMC [mg]	187.77 ± 3.58	162.27 ± 3.86	<0.001
	Cortical BMC [mg]	123.64 ± 2.98	104.79 ± 3.21	<0.001
	Cortical CSA [mm <sup>2</sup> ]	125.63 ± 31.70	107.71 ± 2.99	<0.001
	SSip [mm <sup>3</sup> ]	964.57 ± 31.70	810.68 ± 34.18	0.005
66.00%				
	Muscle area [mm <sup>2</sup> ]	4551.06 ± 85.76	4094.89 ± 92.46	0.002

Table 5. BMC and selected bone geometry characteristics tested using pQCT. (Tournis et al., 2010)

Effect of stress exercises on vBMD and bone geometry was assessed in a relatively small number of studies that differed in terms of methodology (e.g. DXA with or without hip structural analysis, quantitative computer tomography, magnetic resonance or pQCT), areas of evaluation (humerus, radius, femur, tibia and vertebrae), type (cross-sectional study using inactive volunteers as a control group) and more extensive study of a population differing in age, gender, race, pubertal maturation and the type and intensity of exercise (Daly, 2007).

The available literature suggests that in prepubertal age the long bones react to increased load by increasing the periosteal layer, while the distal areas increase density of tissue rather than size. No studies have tested the long-term impact of top level RG on bone geometry by pQCT on the tibia, along with a detailed evaluation of maturation stages, dietary habits, and bone changes.

In this study, the authors observed the greatest effect of RG on the cortical area, subject to bending and torsion forces. On relevant 38% of tibia the area and BMC were increased by 30% compared with the control group, whereas cortical vBMD was comparable. This difference was caused by the deposition of bone on the surface of the periosteum, leading to a significant increase in bone strength assessed by SSIp (bone strength index). Subsequent analysis showed that the study (n = 49) had at least 90% of the informative value and 30% intergroup difference in SSIp on the confidence level 0.005.

Data on the effects of RG on the trabecular areas by axial and compression forces show that bones react through increased BMC rather than scaling, leading to relatively higher tissue density. At the distal end of the tibia at 14% the trabecular BMC was higher by 26.80% resp. 39.80%, while the corresponding area increased by 12.70% and 10.90% leads to higher trabecular vBMD. Taking into account the inherent limitations of pQCT for estimating trabecular structure due to low resolution, it can be assumed that more sensitive methods such as magnetic resonance imaging could provide more information concerning the influence of load on the trabecular bone. However, it seems that in the distal skeletal regions the stress exercises increase the density of tissues by more effective transfer of the load across the articular surface.

The study is the first work comparing indices of bone strength in athletes, along with a detailed evaluation of calcium homeostasis and BTMs (changes in bone indicators). The data are identical with the findings of previous studies in children, whose obesity is associated with lower levels of 25 (OH)D (serum 25 – hydroxyvitamin D), (Reinehr, de Sousa, Alex, Kersting, & Andler, 2007). Although all the tested subjects had levels of vitamin D higher than 50nmol/litre, this difference was associated with higher iPTH and lower levels of calcium in the control group and was completely abolished after normalization of weight. Given the fact that vitamin D intake and day time of physical activity in the test groups were comparable, the only possible explanation could less sun exposure due to reduced mobilization of vitamin D from fat stores. The reported data suggest that long-term top level training of girls in premenstrual age insignificantly modifies BTMs (Lehtonen-Veromaa et al., 2000; Nickols-Richardson, O'Connor, Shapses, & Lewis, 1999).

Complete results show that the intense workload in the RG in premenstrual age girls is associated with positive effects on the skeleton, especially on the cortical bone, characterized by increased bone mass and improved geometric properties.

### GENETIC FACTORS

It is generally assumed that the quality of bone tissue is strongly genetically determined (Kelly et al., 1991; Slemenda, Christian, Williams, Norton, & Johnston, 1991). Results of studies on twins and families indicate that up to 50–85% variance in bone tissue is genetically conditioned (Gueguen et al., 1995, Krall, & Dawson-Hughes, 1993). Genetic factors play an important role in regulating bone growth and impact its phenotypic characteristics such as geometry and tissue turnover, thereby contributing to the possible pathogenesis of osteoporosis and possible risk of fractures (Albagha, & Ralston, 2003).

BMD achieved during adolescence is one of the major determinants for the risk of osteoporotic fracture in later life. Currently used methods for determining BMD, including taking other risk factors into account are not sufficient to accurately and in advance be able to identify individuals who are at higher risk of fractures. Influence of genetic polymorphisms and their interaction with the environment is therefore intensively studied. The candidate genes affecting the quality of bone tissue influencing the risk of osteoporosis, fractures and lower BMD include:

## VDR gene (vitamin D receptor)

Osteocalcin, the most abundant noncollagenous protein in bone, is a marker of bone turnover in normal and disease states. Its synthesis is induced by calcitriol, the active hormonal form of vitamin D, through the vitamin D receptor and a specific vitamin D-responsive element in the osteocalcin gene promoter. The studies on twins have shown that the levels of serum osteocalcin are strongly genetically determined (Kelly et al., 1991) and strongly correlated with the genetic diversity of bone density (Pocock et al., 1987). Furthermore they are an important macro of bone tissue turnover in both healthy and diseased (Morrison et al., 1992). Induction of calcitriol is mediated by binding specific responsible element for vitamin D on osteocalcin gene promoter.

It was presented that polymorphisms in the VDR gene may influence serum osteocalcin levels (Morrison et al., 1992), may lead to reduced BMD and increased risk of fractures in pre-and postmenopausal women (Garner, Muñoz, Borel, Sornay-Rendu, & Delmas, 2005; Gennari et al., 1998, Houston, Grant Reid, & Ralston, 1996) and men (Chatzipapas et al., 2009). In this context, the most frequently studied polymorphisms were BsmI, ApaI, TagI and FokI. Although the vast majority of studies devote to associations with the risk of fractures in the elderly and postmenopausal women, which are most at risk in this respect, several studies have evaluated these relationships in younger populations. For example, in U.S. pre-pubertal girls with Mexican origin was found that aa (ApaI) and bb (BsmI) genotypes had by 2 to 3% higher femoral BMD and vertebrae BMD from 8 to 10% than girls with AA and BB genotypes. There was, however, not found an association between cross-sectional sizes of vertebrae and femur cortical area and the genotypes of vitamin D receptor (Sainz et al., 1997). In Australian Caucasian prepubertal children aged 7 years was found that girls tt for TaqI allele had lower BMD than the TT homozygotes but not in all parts of the bone analysed. Carriers of TT genotype were also about 3.9kg heavier and 4.1 cm higher than the tt genotype, with this variability associated with genotypes was not present after birth. For the male part of studied population these relationships were not observed (Tao et al., 1998). Weak association of BsmI polymorphism with body height were confirmed in another study of Australian adolescents (MacGregor et al., 2008). Interesting results are also provided by studies evaluating the influence of genotypes in conjunction with lifestyle factors such as calcium intake (Ferrari, 2001; Garner, Borel, Sornay-Rendu, Arlot, & Delmas, 1996), caffeine intake (Rapuri, Gallagher, Kinyamu, & Ryschon, 2001) or physical activity (Gentil et al., 2009). Many studies, including several meta-analyses, however, have not found any statistically significant association between polymorphisms in the VDR gene and bone quality or level of risk of fracture (Fang et al., 2006, Guo et al., 2006).

# COL1A1 gene (Collagen Type 1 Alpha 1)

COL1A1 gene encodes the alpha 1 chain of type I collagen, which is the main protein of bone tissue and, moreover, is located in almost all connective tissues, including cartilage, tendons, skin and sclera. It is one of the most intensively studied genes influencing susceptibility to developing osteoporosis.

Substitution Sp1 polymorphism increases transcription of COL1A1, which as a result is manifested as an imbalance of the ratio between the alpha 1 and alpha 2 type I collagen chains and a slight influence on bone mineralization (Stewart et al., 2005). This polymorphism was associated with reduced BMD and increased susceptibility to osteoporotic fractures of especially vertebrae (Mann & Ralston, 2003, Uitterlinden et al., 1998). Girls aged 10 to 13 years with this polymorphism had significantly lower BMD and lower bone tissue mineral content especially of the lumbar spine vertebrae and proximal femur compared to girls who did not carry this gene variant. The authors of the study suggest evaluating Sp1 polymorphism in COL1A1 gene in young girls, because they regard it as an early indicator of suboptimal development of bones, allowing an early start of osteoporosis prevention (Suuriniemi et al., 2006). Similar results occur in other studies of Caucasian children and young individuals (van der Sluis et al., 2002). Chinese study evaluated geometrical structure of bones in Caucasian and Chinese families with the result that the COL1A1 gene is in this regard a significant association (Jiang et al., 2007).

In addition to Sp1 polymorphism the polymorphisms in the promoter region – 1997G/T and 1663indelT have been frequently investigated. Haplotypes of these two options together with the Sp1 polymorphism (in these studies often referred to as the +1245 G/T) were often associated with the risk of fracture of the femoral neck (Jin et al., 2009) and the risk of fractures (Selezneva et al., 2008). These polymorphisms are in strong "linkage disequilibrium" and three haplotypes accounted for more than 95% of alleles for COL1A1 locus (Stewart et al., 2006). In elderly women a collaborating TaqI polymorphism influence in the gene for the VDR and Sp1 in the COL1A1 gene to the risk of hip fractures (Nguyen et al., 2005) was found. A combined effect was also confirmed on the risk of osteoporosis in the genotype between haplotype AABBtt and Sp1 in the gene for the VDR (Gennari et al., 1998).

# ESR1 gene (Estrogen Receptor Alpha)

ESR1 gene encodes core receptors for estrogens. Estrogens and their receptors are important for proper sexual development and reproduction, but also affect the structure and formation of bone. ESR1 is one of the candidate genes associated with the risk of osteoporosis (JP Ioannidis et al., 2002), as reduced activity of this gene is associated with lower BMD.

Among the most examined polymorphisms in this gene are XbaI and PvuII in intron 1, which are spaced 46 bases and are also in a strong "linkage disequilibrium" with the TA-variable number of tandem repeats (VNTR) polymorphism, located 2.1 kilobytes upstream in promoter region of the gene for ESR1 (JPA Ioannidis et al., 2004). On a group of 205 Polish children treated with oncological complications and on a group of 70 healthy children the presence of XbaI and PvuII polymorphisms increased the risk of osteoporosis, especially in individuals with only a minimal share of physical activity

(Anna et al., 2008). TA (n) repeat allelic variants were then associated with lumbar spine BMD in postmenopausal women (Becherini et al., 2000). Recent large association study conducted on Caucasian and African premenopausal women associated the region of C6 orf 97 gene and ESR1 with BMD of femoral neck and lumbar spine vertebrae (Ichikawa et al., 2010).

## CONCLUSION

There are a very limited number of studies that deal with bone metabolism and its dependency on the load in top level sports, specifically the RG or other gymnastic sports. The above studies suggest that the influence of a certain intensity of impact loads in hyperkinetic regime leads to increases in BMD, while in hypokinetic regime the BMD was at lower levels. Along with inadequate or inappropriate dietary habits the reduced BMD can result in predicted osteoporosis in later life. In relation to power properties, we can say that with an increase in muscle power output the BMD increases with the size of load forces based on muscle power output as the muscles spanning the reference bone segment. Unlike monogenic diseases, where a single gene mutation can lead to clinical consequences, the examples of polymorphic sites in the genes mentioned in this review are of only minor importance. Susceptibility to health complications, as is the risk of bone fractures in this case, is also the result of many genes. Together with other external factors (physical activity, quantity and quality of diet) it significantly increases the susceptibility to osteoporotic fractures, especially in genetically predisposed individuals.

### ACKNOWLEDGEMENTS

This project is supported by grant GAČR P407/10/1624 and by the grant SVV-2011-263601.

### REFERENCES

- ALBAGHA, O. M., & RALSTON, S. H. (2003). Genetic determinants of susceptibility to osteoporosis. *Endocrinology and metabolism clinics of North America*, 32(1), pp. 65–81, VI.
- ANNA, P., KATARZYNA, M. R., MARYNA, K. R., ANNA, G., ANDRZEJ, R., & MALGORZATA, S. Z. (2008). Puvll and Xbal gene polymorphisms of estrogen receptor alpha in children and young adults with cancer from north-eastern region of Poland. *Polski merkuriusz lekarski: organ Polskiego Towarzystwa Lekarskiego*, 25(146), pp. 137–140.
- BECHERINI, L., GENNARI, L., MASI, L., MANSANI, R., MASSART, F., MORELLI, A., et al. (2000). Evidence of a linkage disequilibrium between polymorphisms in the human estrogen receptor alpha gene and their relationship to bone mass variation in postmenopausal Italian women. *Hum Mol Genet*, 9(13), pp. 2043–2050.
- DALY, R. M. (2007). The effect of exercise on bone mass and structural geometry during growth. Medicine and sport science, 51, pp. 33–49.
- FANG, Y., RIVADENEIRA, F., VAN MEURS, J. B., POLS, H. A., IOANNIDIS, J. P., & UITTERLINDEN, A. G. (2006). Vitamin D receptor gene BsmI and TaqI polymorphisms and fracture risk: a meta-analysis. *Bone*, 39(4), pp. 938–945.

- FERRARI, S. L. (2001). Osteoporosis, vitamin D receptor gene polymorphisms and response to diet. World Rev Nutr Diet, 89, pp. 83–92.
- FROST, H. M. (2000). The Utah paradigm of skeletal physiology: an overview of its insights for bone, cartilage and collagenous tissue organs. *Journal of bone and mineral metabolism*, 18(6), pp. 305–316.
- GARNERO, P., BOREL, O., SORNAY-RENDU, E., ARLOT, M. E., & DELMAS, P. D. (1996). Vitamin D receptor gene polymorphisms are not related to bone turnover, rate of bone loss, and bone mass in postmenopausal women: the OFELY Study. J Bone Miner Res, 11(6), pp. 827–834.
- GARNERO, P., MUNOZ, F., BOREL, O., SORNAY-RENDU, E., & DELMAS, P. D. (2005). Vitamin D receptor gene polymorphisms are associated with the risk of fractures in postmenopausal women, independently of bone mineral density. J Clin Endocrinol Metab, 90(8), pp. 4829–4835.
- GENNARI, L., BECHERINI, L., MASI, L., MANSANI, R., GONNELLI, S., CEPOLLARO, C., et al. (1998). Vitamin D and estrogen receptor allelic variants in Italian postmenopausal women: evidence of multiple gene contribution to bone mineral density. J Clin Endocrinol Metab, 83(3), pp. 939–944.
- GENTIL, P., DE LIMA LINS, T. C., LIMA, R. M., DE ABREU, B. S., GRATTAPAGLIA, D., BOTTARO, M., et al. (2009). Vitamin-d-receptor genotypes and bone-mineral density in postmenopausal women: interaction with physical activity. J Aging Phys Act, 17(1), pp. 31–45.
- GUEGUEN, R., JOUANNY, P., GUILLEMIN, F., KUNTZ, C., POUREL, J., & SIEST, G. (1995). Segregation analysis and variance components analysis of bone mineral density in healthy families. [Comparative Study Research Support, Non-U.S. Gov't]. Journal of bone and mineral research: the official journal of the American Society for Bone and Mineral Research, 10(12), pp. 2017–2022.
- GUO, S. W., MAGNUSON, V. L., SCHILLER, J. J., WANG, X., WU, Y., & GHOSH, S. (2006). Meta-analysis of vitamin D receptor polymorphisms and type 1 diabetes: a HuGE review of genetic association studies. *Am J Epidemiol*, 164(8), pp. 711–724.
- HELGE, E. W., & KANSTRUP, I. L. (2002). Bone density in female elite gymnasts: impact of muscle strength and sex hormones. [Clinical Trial Controlled Clinical Trial]. *Med Sci Sports Exerc*, 34(1), pp. 174–180.
- HERNÁNDEZ, M., CASTELLET, J., NARVAÍZA, J. L., RINCÓN, J. M., RUIZ, I., SÁNCHEZ, E., et al. (1988). Instituto de Investigación sobre Crecimiento y Desarrollo. Fundación Faustino Orbegozo. In Curvas y Tabla de Crecimiento.
- HOUSTON, L. A., GRANT, S. F., REID, D. M., & RALSTON, S. H. (1996). Vitamin D receptor polymorphism, bone mineral density, and osteoporotic vertebral fracture: studies in a UK population. *Bone*, 18(3), pp. 249–252.
- CHATZIPAPAS, C., BOIKOS, S., DROSOS, G. I., KAZAKOS, K., TRIPSIANIS, G., SERBIS, A., et al. (2009). Polymorphisms of the vitamin D receptor gene and stress fractures. *Horm Metab Res*, 41(8), pp. 635–640.
- ICHIKAWA, S., KOLLER, D. L., PADGETT, L. R., LAI, D., HUI, S. L., PEACOCK, M., et al. (2010). Replication of previous genome-wide association studies of bone mineral density in premenopausal American women. [Research Support, N. I. H., Extramural]. Journal of bone and mineral research: the official journal of the American Society for Bone and Mineral Research, 25(8), pp. 1821–1829.
- IOANNIDIS, J. P., STAVROU, I., TRIKALINOS, T. A., ZOIS, C., BRANDI, M. L., GENNARI, L., et al. (2002). Association of polymorphisms of the estrogen receptor alpha gene with bone mineral density and fracture risk in women: a meta-analysis. [Meta-Analysis]. Journal of bone and mineral research: the official journal of the American Society for Bone and Mineral Research, 17(11), pp. 2048–2060.
- IOANNIDIS, J. P. A., RALSTON, S. H., BENNETT, S. T., BRANDI, M. L., GRINBERG, D., KARASSA, F. B., et al. (2004). Differential Genetic Effects of ESR1 Gene Polymorphisms on Osteoporosis Outcomes. JAMA: *The Journal of the American Medical Association*, 292(17), pp. 2105–2114.
- JIANG, H., LEI, S. F., XIAO, S. M., CHEN, Y., SUN, X., YANG, F., et al. (2007). Association and linkage analysis of COL1A1 and AHSG gene polymorphisms with femoral neck bone geometric parameters in both Caucasian and Chinese nuclear families. *Acta Pharmacol Sin*, 28(3), pp. 375–381.
- JIN, H., STEWART, T. L., HOF, R. V., REID, D. M., ASPDEN, R. M., & RALSTON, S. (2009). A rare haplotype in the upstream regulatory region of COL1A1 is associated with reduced bone quality and hip fracture. *J Bone Miner Res*, 24(3), pp. 448–454.
- KELLY, P. J., HOPPER, J. L., MACASKILL, G. T., POCOCK, N. A., SAMBROOK, P. N., & EISMAN, J. A. (1991). Genetic factors in bone turnover. *J Clin Endocrinol Metab*, 72(4), pp. 808–813.
- KRALL, E. A., & DAWSON-HUGHES, B. (1993). Heritable and life-style determinants of bone mineral density. [Research Support, Non-U.S. Gov't, Research Support, U.S. Gov't, Non-P. H. S.]. Journal of bone and mineral research: the official journal of the American Society for Bone and Mineral Research, 8(1), pp. 1–9.

- LEHTONEN-VEROMAA, M., MOTTONEN, T., IRJALA, K., NUOTIO, I., LEINO, A., & VIIKARI, J. (2000). A 1-year prospective study on the relationship between physical activity, markers of bone metabolism, and bone acquisition in peripubertal girls. [Clinical Trial Research Support, Non-U.S. Gov't]. J Clin Endocrinol Metab, 85(10), pp. 3726–3732.
- MACGREGOR, S., HOTTENGA, J. J., LIND, P. A., SUCHIMAN, H. E., WILLEMSEN, G., SLAGBOOM, P. E., et al. (2008). Vitamin D receptor gene polymorphisms have negligible effect on human height. *Twin Res Hum Genet*, 11(5), pp. 488–494.
- MANN, V., & RALSTON, S. H. (2003). Meta-analysis of COL1A1 Sp1 polymorphism in relation to bone mineral density and osteoporotic fracture. *Bone*, 32(6), pp. 711–717.
- MORRISON, N. A., YEOMAN, R., KELLY, P. J., & EISMAN, J. A. (1992). Contribution of trans-acting factor alleles to normal physiological variability: vitamin D receptor gene polymorphism and circulating osteocalcin. *Proc Natl Acad Sci USA*, 89(15), pp. 6665–6669.
- MUÑOZ, M. T., de la Piedra, C., Barrios, V., Garrido, G., & Argente, J. (2004). Changes in bone density and bone markers in rhythmic gymnasts and ballet dancers: implications for puberty and leptin levels. [Comparative Study]. *Eur J Endocrinol*, 151(4), pp. 491–496.
- NGUYEN, T. V., ESTEBAN, L. M., WHITE, C. P., GRANT, S. F., CENTER, J. R., GARDINER, E. M., et al. (2005). Contribution of the collagen I alpha1 and vitamin D receptor genes to the risk of hip fracture in elderly women. J Clin Endocrinol Metab, 90(12), pp. 6575–6579.
- NICKOLS-RICHARDSON, S. M., O'CONNOR, P. J., SHAPSES, S. A., & LEWIS, R. D. (1999). Longitudinal bone mineral density changes in female child artistic gymnasts. [Research Support, Non-U.S. Gov't]. Journal of bone and mineral research: the official journal of the American Society for Bone and Mineral Research, 14(6), pp. 994–1002.
- POCOCK, N. A., EISMAN, J. A., HOPPER, J. L., YEATES, M. G., SAMBROOK, P. N., & EBERL, S. (1987). Genetic determinants of bone mass in adults. A twin study. J Clin Invest, 80(3), pp. 706–710.
- RAPURI, P. B., GALLAGHER, J. C., KINYAMU, H. K., & RYSCHON, K. L. (2001). Caffeine intake increases the rate of bone loss in elderly women and interacts with vitamin D receptor genotypes. *Am J Clin Nutr*, 74(5), pp. 694–700.
- REINEHR, T., DE SOUSA, G., ALEXY, U., KERSTING, M., & ANDLER, W. (2007). Vitamin D status and parathyroid hormone in obese children before and after weight loss. *Eur J Endocrinol*, 157(2), pp. 225–232.
- SAINZ, J., VAN TORNOUT, J. M., LORO, M. L., SAYRE, J., ROE, T. F., & GILSANZ, V. (1997). Vitamin D-receptor gene polymorphisms and bone density in prepubertal American girls of Mexican descent. N Engl J Med, 337(2), pp. 77–82.
- SELEZNEVA, L. I., KHUSAINOVA, R. I., NURLYGAIANOV, R. Z., FAZLYEVA, E. A., USENKO, K. P., LESNIAK, O. M., et al. (2008). [Association of polymorphisms and haplotypes in the 5' region of COLIA1 gene with the risk of osteoporotic fractures in Russian women from Volga-Ural region]. *Genetika*, 44(2), pp. 219–225.
- SLEMENDA, C. W., CHRISTIAN, J. C., WILLIAMS, C. J., NORTON, J. A., & JOHNSTON, C. C., Jr. (1991). Genetic determinants of bone mass in adult women: a reevaluation of the twin model and the potential importance of gene interaction on heritability estimates. [Research Support, Non-U.S. Gov't, Research Support, U.S. Gov't, P. H. S.]. Journal of bone and mineral research: the official journal of the American Society for Bone and Mineral Research, 6(6), pp. 561–567.
- STEWART, T. L., JIN, H., MCGUIGAN, F. E., ALBAGHA, O. M., GARCIA-GIRALT, N., BASSITI, A., et al. (2006). Haplotypes defined by promoter and intron 1 polymorphisms of the COLIA1 gene regulate bone mineral density in women. J Clin Endocrinol Metab, 91(9), pp. 3575–3583.
- STEWART, T. L., ROSCHGER, P., MISOF, B. M., MANN, V., FRATZL, P., KLAUSHOFER, K., et al. (2005). Association of COLIA1 Sp1 alleles with defective bone nodule formation in vitro and abnormal bone mineralization in vivo. *Calcif Tissue Int*, 77(2), pp. 113–118.
- SUURINIEMI, M., KOVANEN, V., MAHONEN, A., ALEN, M., WANG, Q., LYYTIKAINEN, A., et al. (2006). COL1A1 Sp1 polymorphism associates with bone density in early puberty. *Bone*, 39(3), pp. 591–597.
- TAO, C., YU, T., GARNETT, S., BRIODY, J., KNIGHT, J., WOODHEAD, H., et al. (1998). Vitamin D receptor alleles predict growth and bone density in girls. Arch Dis Child, 79(6), pp. 488–493, discussion pp. 493–484.
- TOURNIS, S., MICHOPOULOU, E., FATOUROS, I. G., PASPATI, I., MICHALOPOULOU, M., RAPTOU, P., et al. (2010). Effect of rhythmic gymnastics on volumetric bone mineral density and bone geometry in premenarcheal female athletes and controls. *J Clin Endocrinol Metab*, 95(6), pp. 2755–2762.

- UITTERLINDEN, A. G., BURGER, H., HUANG, Q., YUE, F., MCGUIGAN, F. E., GRANT, S. F., et al. (1998). Relation of alleles of the collagen type Ialpha1 gene to bone density and the risk of osteoporotic fractures in postmenopausal women. *N Engl J Med*, 338(15), pp. 1016–1021.
- Van Der SLUIS, I. M., DE MUINCK KEIZER-SCHRAMA, S. M., POLS, H. A., LEQUIN, M. H., KRENNING, E. P., & UITTERLINDEN, A. G. (2002). Collagen Ialpha1 polymorphism is associated with bone characteristics in Caucasian children and young adults. *Calcif Tissue Int*, 71(5), pp. 393–399.
- WARD, K. A., ROBERTS, S. A., ADAMS, J. E., & MUGHAL, M. Z. (2005). Bone geometry and density in the skeleton of pre-pubertal gymnasts and school children. [Research Support, Non-U.S. Gov't]. Bone, 36(6), pp. 1012–1018.
- WU, J., ISHIZAKI, S., KATO, Y., KURODA, Y., & FUKASHIRO, S. (1998). The side-to-side differences of bone mass at proximal femur in female rhythmic sports gymnasts. *Journal of bone and mineral research:* the official journal of the American Society for Bone and Mineral Research, 13(5), pp. 900–906.

#### RIZIKA A BENEFITY HYPO-HYPER KINETICKÉHO ZATĚŽOVÁNÍ POHYBOVÉHO SYSTÉMU ČLOVĚKA A JEHO GENETICKÉ PŘEDPOKLADY V RYTMICKÉ GYMNASTICE

#### ŠÁRKA PANSKÁ, MIROSLAV PETR, KAREL JELEN

#### SOUHRN

Řada studií prokazuje, že vyšší až vysoká intenzita a objem tréninkového zatížení má pozitivní vliv např. na kostní adaptaci zejména u dětí a dospívající mládeže. Kosterní odezva na zátěž je však závislá na mnoha různých faktorech souvisejících s mechanickým zatěžováním (tréninkem) i na faktorech, které se vztahují přímo na sportovce samého, jako jsou výživové, hormonální faktory a zejména věk, kdy byly tréninkové intervence zahájeny. Kromě vlivu zátěže na kostní adaptaci se naše úvodní review studie opírá o možné potenciální genetické faktory podílející se na kvalitě kostěného sytému, konkrétně pak na hustotě kostní tkáně (BMD), struktuře kostní tkáně či její schopnosti mineralizace.

Klíčová slova: hypokineza, hyperkineza, tréninkové zatížení, kostní minerální hustota (BMD), genetické faktory

Šárka Panská spanska@ftvs.cuni.cz