

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

Open access books available

186,000

International authors and editors

200M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



Neurological Osteoporosis in Disabilities

Yannis Dionyssiotis

*Physical and Social Rehabilitation Center Amyntæo
University of Athens, Laboratory for Research of the Musculoskeletal System
Greece*

1. Introduction

Osteoporosis is characterized by low bone mass and destruction of the micro architecture of bone tissue, resulting in increased bone fragility and susceptibility to fractures (NIH 2001). The clinical usefulness of T-score at disabled people on the recognition of people with low BMD remains unclear according to ranking system of the World Health Organization (WHO 1994). Despite the increased number of risk factors in people with disabilities no guidelines are available on BMD measurements; so it would be more appropriate to use the term low bone mass instead of osteoporosis or osteopenia and also take into account the Z-score obtained from the measurement of bone densitometry which is the number of standard deviations above or below that normally expected for someone of similar age, sex, weight and race in question (Dionyssiotis, 2011c, 2011d).

In disabled subjects there are differences according to the type of injury (i.e. lesion with a level of injury vs. upper motor neuron pyramidal lesion), the type of lesion; complete (an absence of sensory or motor function below the neurological level, including the lowest sacral segment) vs. incomplete lesion (partial preservation of motor and/or sensory function below the neurological level, including the lowest sacral segment), the progression or not of the disease (i.e. progressive multiple sclerosis vs. complete paraplegia), life expectancy, the residual mobility and functionality, the ability to walk and stand (i.e. incomplete paraplegia vs. quadriplegia vs. high-low paraplegia), drug treatment (i.e. frequent corticosteroid therapy in multiple sclerosis vs. long-term therapy with anticoagulants in paraplegia), the degree of spasticity (i.e. flaccid vs. spastic paralysis) and it is necessary to take into account the issue of fatigue and muscle weakness. Depression in these subjects is usual; complicates the proposed treatments and limits mobility. Complete and incomplete disabled differ also in physical abilities. Moreover, subjects with complete injuries have greater bone loss than those with an incomplete injury (Garland et al., 1994) and as has already been shown in Brown-Sequard subjects (incomplete spinal cord lesion) where BMD of the more paretic knee was lower than that of the stronger knee (Lazo et al., 2001).

However, there are also similarities; for example the clinical equivalence of diseases with different physiopathology, location, evolution, etc. A severe form of multiple sclerosis (MS) can result in a wheelchair bound patient having a clinical figure equivalent to spinal cord injury paraplegia. One patient with MS may have better walking gait pattern in comparison with a patient with incomplete paraplegia but may also be unable to walk, bedridden and vice versa (Dionyssiotis, 2011c, 2011d).

In addition the role of factors which do not change, i.e.: race or gender is inadequately clarified. Studies in disabled women debate that bones are more affected compared to disabled men. In chronic spinal cord injured women a tendency to have lower bone mass than men (Coupaud et al., 2009) and higher rates of lower bone mass with lower T-scores compared to women with other disabilities have been reported (Smeltzer et al., 2005).

2. Spinal cord injury

Bone loss in spinal cord injury (SCI) is a multifactorial disease in acute and chronic phase and can be enhanced by the lack of weight bearing, muscular tension on bone or other neural factors associated with the injury. Moreover, differentiation of the sympathetic nervous system after SCI is leading to venous and capillary vascular stasis. Some additional non-mechanical factors to stimulate bone loss include poor nutritional adequacy, gonadal changes and other endocrine disorders (Chantraine 1978; Chantraine et al., 1979b; Jiang et al., 2007; Maimoun et al., 2006).

2.1 Bone mineral density

In individuals with SCI bone loss begins immediately after injury (Bauman et al., 1997; Uebelhart et al., 1995). SCI related bone impairment below the level of injury is much greater compared with other conditions (i.e. age, immobilization, bed rest, lack of gravity environment). A reduction of bone mineral content (BMC) during the first years after the injury of 4% per month in regions rich in cancellous bone, and 2% per month on sites containing mainly cortical bone is reported (Wilmet et al., 1995). According to another study 25 out of 41 patients with SCI (61%) met WHO's criteria for osteoporosis, eight (19.5%) were osteopenic and only eight (19.5%) showed normal values (Lazo et al., 2001). In SCI children (boys and girls) values for bone mineral density (BMD) at the hip were approximately 60% of normal, or had a Z-score that indicated a 1.6-1.8 SD reduction in BMD compared with age- and sex-matched peers (Lauer et al., 2007).

In studies with peripheral quantitative computed tomography (p QCT) in spinal cord injured subjects bone loss in the epiphyses was 50% in the femur and 60% in the tibia, while in the diaphyses of these bones was 35% and 25%, respectively, meaning that bone loss in the epiphyses almost doubled the loss in the diaphyses (Eser et al., 2004). This study also showed that bone loss between trabecular and cortical bone compartment differs in mechanism, i.e. in the epiphyses bone is lost due to the decrease in trabecular, while in diaphysis, the cortical bone density is maintained and bone is lost due to endocortical resorption. In line with the previous study another p QCT study, performed in complete paraplegics with high (thoracic 4-7) and low (thoracic 8-12) neurological level of injury at the tibia, found a loss of trabecular (57.5% vs. 51%, in high vs. low paraplegics, respectively) and cortical bone (3.6% and 6.5%, respectively), suggesting that trabecular bone is more affected during the years of paralysis in comparison with cortical bone (Dionyssiatis et al., 2007). In the same study both paraplegic groups had a similar loss of total BMD (46.90% vs. 45.15%, in high vs. low paraplegics, respectively) suggesting that a homogeneously deficit pattern occurs in the epiphyseal area, especially in the group of low paraplegics because the central and the peripheral of the cross sectional area of bone were similarly affected. On the contrary, in high paraplegics' group trabecular bone loss was higher suggesting an increasing endocortical remodeling keeping the total BMD similar. Concerning cortical geometric properties the results had shown an increased endosteal circumference between

both paraplegic groups vs. controls leading to reduction of cortical thickness, 19.78% vs. 16.98% in paraplegic groups respectively, whereas periosteal circumference was comparable to controls (Fig. 1).

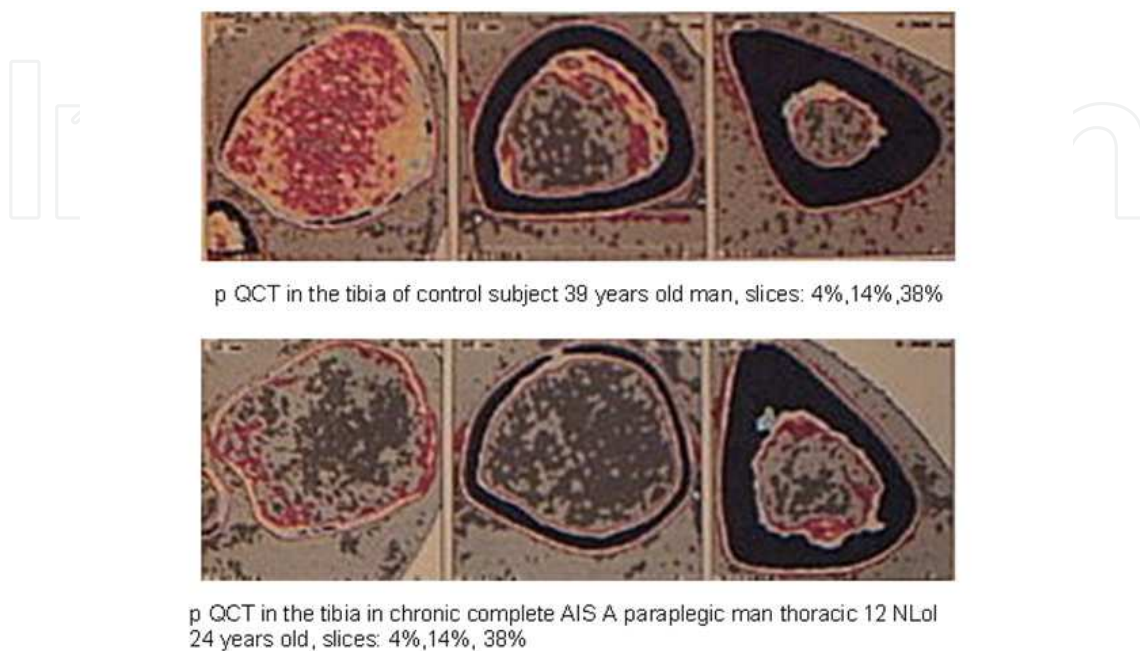


Fig. 1. Peripheral quantitative computed tomography (p QCT) tibia slices in control (a) and paraplegic subject (b), (scanner XCT 3000 Stratec, Medizintechnik, Pforzheim, Germany). Areas in red represent trabecular bone, while areas in grey represent fat; pQCT allows the measurements of true volumetric densities at a minimum exposure to X-rays, assess cortical and trabecular bone density separately as well as to evaluate the geometrical properties of long bones non-invasively, adapted from Dionyssiotis, 2011c, 2011d, with permission.

Regarding tetraplegic patients statistically significant differences were found in BMD of the spine, trochanteric region and upper limbs between paraplegic and tetraplegic patients but not in the femoral neck, pelvis, and lower extremities (Tzuzuku et al., 1999). Indeed, the effects on spinal BMD differed from previously published work in which the investigation was mainly focused in paraplegics (Biering-Sorensen et al., 1988, 1991; Leslie & Nance, 1993).

The importance of mechanical loading and site specificity to maintain or increase BMD is already shown (Lanyon, 1986). According to bone loss there are some interesting features in spinal cord injured subjects; demineralization is area dependent, occurs exclusively in the areas below the level of injury (Dauty et al., 2000), affecting mainly paralyzed extremities and increasing from proximal to distal regions i.e. in paraplegics weight bearing skeleton regions, as the distal end of femur and proximal tibia, which are rich in cancellous bone, while region of the diaphysis of the femur and tibia, rich in cortical bone is reserved (Eser et al., 2004; Kiratli et al., 2000; Dionyssiotis et al., 2007). Moreover, bone loss between trabecular and cortical bone compartment differs in mechanism, i.e. in the epiphyses is due to decrease in trabecular but in diaphysis cortical bone is maintained and bone is lost through endocortical resorption by reducing cortical wall thickness (Dionyssiotis et al., 2007; Eser et al., 2004).

Women with disabilities have a higher risk of losing bone mass compared to men because of the inevitable reduction in estrogen levels that occurs at menopause. Findings that women with serious disabilities have low bone density are not surprising and are probably related to the lack of activity (reduced mobility, reduced loading on bone) and worsening of the disability. Regarding women with complete SCI, the initial bone loss in the lumbar spine is negligible. Post injury over a period of years BMD in SCI women is maintained or increases compared with non-injured age-matched women, in whom BMD decreases during aging (Dionyssiatis, 2011c).

2.2 Duration of paralysis and bone steady state

The duration of paralysis affects the degree of bone loss in regions below the level of injury. A study of 21 men with SCI with an average duration of 10.6 years, using dual-energy X-ray absorptiometry (DXA), expressed at various levels of injury an inverse relationship between BMD in the legs and the duration of the lesion (Clasey et al., 2004), while others found a weaker relationship regarding the microarchitecture of the distal end of tibia (Modlesky et al., 2004).

In a study which included paraplegics with duration of paralysis of 14 ± 11.5 years a positive correlation between the duration of paralysis and the degree of bone loss was found (Eser et al., 2004). The length of immobilization in the acute posttraumatic period increased bone loss in the legs, particularly in the proximal tibia; over 50% of bone mass was lost (in the affected areas) in the period of ten years after the injury (Dauty et al., 2000). When subjects categorized depending on the length of the lesion (0-1, 1-5, 6-9, 10-19, 20-29, 30-39, 40-49, and 50-59 years after the injury), in all age groups bone loss to the hip area occurs a year after the injury (Szollar et al., 1998).

Using DXA and QUS (quantitative ultrasound) measurements in 100 men with SCI, aged 18 to 60 years, it was found that bone density decreases over time in all measured points, while bone loss followed a linear pattern in the femoral neck and distal epiphysis, stabilized within three years after the injury. On the contrary, Z-scores of the distal region of the diaphysis of the tibia continued to decrease even beyond ten years after the injury (Zehnder et al., 2004). Duration of paralysis related bone loss in the legs of monozygotic twins with chronic paraplegia in comparison with their able-bodied co-twins has been also reported (Bauman et al., 1999).

The results of a comparison of chronic complete paraplegic men vs. controls in another study found a reduction of BMD in paraplegics' legs independent of the neurological level of lesion. BMD of the legs was negatively correlated with the duration of paralysis in the total paraplegic group, but after investigation according to the neurological level this correlation was due to the strong correlation of high paraplegics' legs BMD with the duration of paralysis, suggesting a possible influence of the neurological level of injury on the extent of bone loss (Dionyssiatis et al., 2008). A significant inverse relationship between percentage-matched in BMD leg, arm and trunk values and time since injury was found when varying levels of SCI were analyzed (Clasey et al., 2004).

Studies are supporting the concept of a new bone steady state at 16-24 months after injury, especially for bone metabolic process (Bauman WA 1997; Demirel et al., 1998; Szollar et al., 1998), but BMD decreases over the years at different areas and is inversely related to the time of the injury, which means continuous bone loss beyond the first two years after the injury (Coupaud et al., 2009; Dionyssiatis et al., 2008; Eser et al., 2004) (Fig. 2).

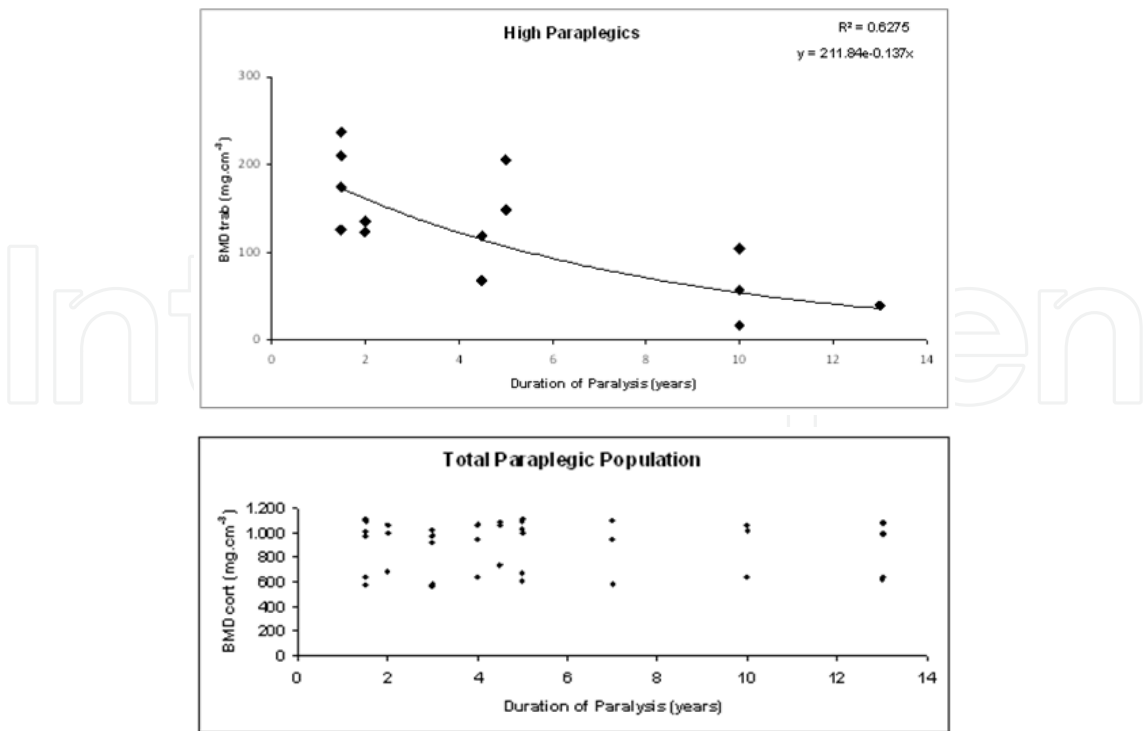


Fig. 2. The duration of paralysis was inversely related with trabecular bone loss in spinal cord injured subjects. Exponential correlation between volumetric trabecular bone mineral density BMD trab and duration of paralysis in high paraplegics was found to fit best. On the contrary no significant decrease in BMD cort of the diaphyses was found in total paraplegic group. BMD parameters were measured by pQCT in 31 paraplegic men in chronic stage (>1.5 years of injury). Spinal cord injury paraplegic men were allocated into 2 subgroups based on the neurological level of injury; subgroup A (n=16, Thoracic (T)4-T7 neurological level of injury) and subgroup B (n=15, T8-T12 neurological level of injury). BMDtrab: BMD trabecular; BMDcort: BMD cortical; (adapted from Dionyssiotis et al., 2011a, with permission).

The role played by factors such as race or gender of patients is not yet clear documented, but studies indicated more loss in women than men (Garland et al., 2001). Loss of bone is closing fracture threshold from 1 to 5 years after injury (Szollar et al., 1998) and risk factors for fractures after spinal cord injury are gender (women are more at risk than men), age and duration of injury (increasing age and duration of injury increases the risk of fracture with a statistically significant increase in 10 years after injury), the type of injury (complete SCI subjects have more fractures than incomplete), low body mass index (BMI) and low bone density in the tibia (Garland et al., 2004a,b; Garland et al., 1992; Lazo et al., 2001).

2.3. The role of central nervous system

2.3.1 Sympathetic denervation in SCI

Spinal cord injury is a dynamic process that is related to alterations in both the central and peripheral sympathetic nervous system (SNS). Sympathetic denervation in SCI may cause arteriovenous shunts and a slowdown of intraosseous blood flow, thus increasing bone resorption (Chantraine et al., 1979). With high-level spinal cord lesions the SNS is disproportionately involved when compared with the parasympathetic nervous system. In a complete high-level SCI, functioning in the isolated spinal cord below the lesion becomes

independent of supraspinal control and has been termed “decentralization” of the SNS (Karlsson et al., 1998).

Loss of supraspinal control leads to dysregulation of those homeostatic mechanisms normally influenced by the SNS through loss of facilitation or lack of inhibition (Teasell et al., 2000). Today there is clinical evidence that the sympathetic regulation of bone does exist in humans and plays a clinically important role in diseases characterized by excessive sympathetic activity (Schwartzman, 2000). The scientific finding about sympathetic innervations of bone tissue (Takeda et al., 2002; Kondo et al., 2005) and its role in the regulation of bone remodelling is of major interest in situations where uncoupling between osteoclasts and osteoblasts occurs (Levasseur et al., 2003).

2.3.2 Spasticity

Controversial results have also been reported regarding the effect of spasticity on BMD in SCI paraplegics. A cross-sectional study of 41 SCI paraplegics reported less reduction of BMD in the spastic paraplegics SCI patients compared to the flaccid paraplegic SCI patients (Demirel et al., 1998). Others reported that spasticity may be protective against bone loss in SCI patients, however, without any preserving effect in the tibia (Dionyssiatis et al., 2011; Eser et al., 2005). A possible explanation for that could lie in the fact that in the present study all paraplegics were above thoracic (T)12 level with various degrees of spasticity according to the Ashworth scale. In addition, muscle spasms affecting the lower leg would mainly be extension spasms resulting in plantar flexion thus creating little resistance to the contracting muscles. Furthermore, the measuring sites of the tibia did not include any muscle insertions of either the knee or the ankle extensor muscles (Dionyssiatis et al., 2011a; Dionyssiatis, 2011c). Other investigators also have not been able to establish a correlation between BMD and muscle spasticity (Lofvenmark et al., 2009).

3. Multiple sclerosis

Reduced mobility has been implicated as an important factor in bone loss in patients suffering from multiple sclerosis (MS) and it seems to greatly influence the BMD of the femur. However, the high proportion of ambulatory patients with bone loss suggest additional non-mechanical factors (Cosman et al., 1998; Dionyssiatis, 2011b).

There is a high incidence of vitamin D deficiency in MS patients and is determined by levels of 25-hydroxy vitamin D <20ng/ml (Nieves et al., 1994). The reasons might be due to a combination of low dietary vitamin D intake and avoiding of sun exposure, and that because of MS symptoms may worsen after sun exposure (fatigue-related heat) leading these patients to avoid sun. Low testosterone alone in these populations does not explain bone loss and no clear effect of smoking or alcohol abuse to decreased bone mass could be established (Weinstock-Guttman et al., 2004).

Glucocorticoid (GC)-induced osteoporosis (OP-GC) is the main type of secondary osteoporosis (Canalis et al., 2004; Canalis et al., 2007; Lakatos et al., 2000; Mazziotti et al., 2006; Schwid et al., 1996; Shuhaibar et al., 2009). The mechanism is that excess GC causes a rapid and significant damage to bone quality. Now days we know that GCs act direct on bone mainly to the stromalosteoblastic lineage and at high concentrations alter differentiation, survival, and function of them causing a shift from osteoblastic to adipocytic differentiation of precursors; inducing apoptosis of mature osteoblasts; and inhibition of

synthesis and secretion of bone components (Manolagas, 2000; Pereira et al., 2002). Finally, GCs promote osteoclasts and stimulate bone resorption (Weinstein et al., 2002). The mechanisms of GCs action in bone has been studied extensively. In patients receiving chronic per os GC, bone loss is admitted rapidly and is evident within 6 or even 3 months (Cosman et al., 1998). A study investigated the effect of intravenously (i.v.) administration of glucocorticoids in MS patients found no clear effect on bone loss: on the contrary they reported an increase in BMD of the lumbar spine (Schwid et al., 1996). Prolonged treatment with glucocorticoids results in increased risk of fractures, evident at 3 months, regardless of changes in BMD. High dose, short-term i.v. treatment with GCs leads directly to reduction of bone formation and increased bone resorption, as indicated by markers of bone turnover (De Vries et al. 2007; Van Staa et al., 2000). Osteopenia not osteoporosis was significantly more frequent in patients with MS compared with controls, especially in women who received high dose methylprednisolone pulses (HDMP) in relapses period making important the regularly monitoring of BMD in these patients. The authors concluded that disability and the subsequent immobilization osteoporosis is the more serious factor in this group and treatment with repeated HDMP pulses did not cause osteoporosis in MS subjects followed-up for almost 8 years unlike chronic corticosteroid therapy which induces osteoporosis and/or recovery of BMD is permitted without permanent skeletal damage (Zorzon et al., 2005). The lack of physical activity exacerbates osteoporosis. All MS patients should be considered high risk for osteoporosis. Prevention with calcium rich foods and dietary supplements containing vitamin D and antiosteoporotic drugs is necessary for these patients. Particular attention should be paid to transfers and falls prevention in this population to prevent fractures which occur easily and heal slowly (Cattaneo et al., 2007; Dionyssiotis, 2011b).

In osteoporosis molecular mechanisms leading to bone loss are inadequately explained. There is evidence of interaction between bone and immune system. T cells' activity could stimulate bone loss under certain circumstances such as estrogen deficiency. Women with post-menopausal osteoporosis have higher T cell activity than healthy post-menopausal subjects which could be also the case in inflammatory or autoimmune disorders like MS: receptor activator of nuclear factor kappa B ligand (RANKL) stimulates osteoclastogenesis and the same do cytokines, such as TNF- α , IL-1, or IL-11, all produced by T-cells activation, leading to bone destruction. On the contrary osteoprotegerin (OPG) is an osteoclastogenesis inhibitory factor preventing the function from RANKL. A balanced system of RANKL/OPG regulates bone metabolism. In MS this system is disturbed in favour of RANKL (Zhao et al., 2008; Kurban et al., 2009).

4. Stroke

Disuse has been suggested as the main cause for loss of bone mass in patients immobilized because of stroke (Takamoto et al., 1995). However, this was not confirmed in a prospective study, in which only weak associations between bone loss and motor function, activities of daily living (ADL), or ambulation were found (Ramnemark et al., 1999a). This could be explained by the selected severely affected patients, but it does raise questions about other risk factors for the development of hemiosteoporosis apart from paresis and immobilization (Ramnemark et al., 1999b).

The critical role in pathogenesis of osteoporosis is attributed to hormonal processes and osteoporosis itself is often defined as generalized skeletal disorder. Findings of tibial bone

changes in hemiplegic patients are not compatible with this view. The adaptations are found in trabecular bone in the epiphysis as well as in cortical bone in the diaphysis. They represent an individually different distribution of local changes which can be explained by the feedback principles of the muscle-bone-unit, in which bone strength is controlled by the muscle forces that act upon the bone. Muscle forces acting habitually on the paretic limb are considerably less than on the opposite side. This reduction of forces reduces the strain on bones. This leads to loss of bone mass and bone strength (Runge et al., 2004).

Determinants of bone mineral loss have been identified as duration of hemiplegia-induced immobilization and severity of palsy (Sato, 1996). A rapid and pronounced loss of BMD in the paretic extremities that progressed during the first year after stroke (Ramnemark et al., 1999a) more pronounced during the first few months after stroke onset (Hamdy et al., 1993). The lower extremities lost BMD bilaterally, but the losses were significant after 12 months in the affected femur, proximal femur and trochanter. In immobile patients, this could explain the loss of BMD in the nonaffected leg as compared with the nonaffected arm, which even increased in BMD, probably due to increased compensatory activity (Ramnemark et al., 1999a).

Hemioosteoporosis has previously been described as being caused by disuse and vitamin D deficiency (Sato et al., 1996), and in a randomized study a significant decrease in the rate of bone loss in stroke patients with a mean duration of 4.8 years after stroke when supplemental vitamin D was given (Sato et al., 1997). Bone mineral loss was more pronounced in the upper than in lower limbs, and the difference between sides was more marked in long-standing poststroke hemiparesis. The upper versus lower difference may reflect that hemiparesis from stroke is commonly more severe in the upper limb. Notably, BMD on the nonhemiplegic side is intermediate between that for the hemiplegic side and that in control subjects. The decrease in mobility of the intact limb, resulting from stroke-related need for assistance with activities of daily living, presumably results in mild osteoporosis paralleling the patient's overall degree of immobilization (Sato et al., 1998, 2000).

5. Myelomeningocele and cerebral palsy

Previous studies suggest that the level of neurological injury and mobility affect BMD in myelomeningocele (MMC). Studies concluded that loading of the lower limbs rather than child's potential ability to walk because of the level of neurological lesion or residual motor capacity of lower limbs is a prognostic criterion for the BMD (Apkon et al., 2009; Ausili et al., 2008; Quan et al., 1998). This theory is probably challenged by other studies that revealed low values of forearm BMD in individuals and indicate that in this patient osteoporosis can be caused by neurogenic and metabolic mechanisms. The fact is that these patients are loading the arms through the use of crutches and wheelchairs and BMD values in the upper extremities are expected to be higher in relation to immobilized people (Quan et al., 1998). Subjects with MMC may have hypercalciuria associated with immobilization and an additional risk factor for osteoporosis in these patients group (Quan et al., 2003). Others support that low-energetic fractures in MMC children may result from metabolic disturbances that are a consequence of excessive renal calcium loss or excessive fatty tissue content (Okurowska-Zawada et al., 2009).

Children with cerebral palsy (CP) are growing slowly. The impact of this altered growth on skeletal development and bone density is a difference in linear growth which becomes more accentuated over time compared with their typically growing peers. In addition, as growth slows, the bone mineral density also falls further outside the normal range (Houlihan et al., 2009). Significantly decreased bone density is virtually universal in non-ambulatory children with moderate to severe CP after the age of 10 years (Henderson et al., 2002); Bone-mineral content and density were measured in a study by dual energy X-ray absorptiometry in the proximal femur, femoral neck, and total body of nutritionally adequate children (n=17; 11 girls, six boys; aged 7.6 to 13.8 years) with spastic cerebral palsy (CP) and found that non-independent ambulators had lower z scores for total body BMD, femoral neck BMD, and BMC than independent ambulators (Chad et al., 2000). The potential causes of deficient bone mineralization in this population are multiple, including poor nutrition and abnormal vitamin D metabolism. Findings from recent studies (Shaw et al. 1994, Henderson et al. 1995, Wilmhurst et al. 1996) suggest that non-nutritional factors, such as ambulation, may contribute to the alterations in body composition observed in children with CP.

5.1 Interventions to prevent bone loss

5.1.1 Weight bearing activities-cycling-body weight supported treadmill

The effect of standing in bone after SCI has been investigated by many researchers. A beneficial effect on bone mass using passive mechanical loading has been shown on preservation of bone mass in the region of the femoral shaft, but not at the proximal hip of standing and non-standing patients and relatively better-preserved densities in patients standing with braces than in those using a standing frame or standing wheelchair (Goemaere et al., 1994). A slower rate of bone loss in paraplegic subjects who did standing was expressed in a prospective study of 19 patients in acute SCI phase participated in early standing training program showed benefits concerning the reduction of cancellous bone loss compared to immobilized subjects (de Bruin and others 1999; Frey-Rindova and others 2000), while no correlation for passive standing-training to bone status was found in another p QCT study (Eser et al., 2005). Protection afforded by standing in the femoral diaphysis stands in contrast with the loss of bone in the proximal femur. This suggests that the transmission of forces through trabecular and cortical bone varies; so the less effective strain for the initiation of bone remodeling reaches faster cortical bone (Frost, 1992, 2001, 2003). Others also supported the concept of different strain thresholds bone remodeling control (Gutin & Kasper, 1992; LeBlanc et al., 2007; Smith et al., 2009). There is level 2 evidence (from 1 non-randomized prospective controlled trial) that Functional Electrical Stimulation (FES) - cycling did not improve or maintain bone at the tibial midshaft in the acute phase (Eser et al., 2003). Moreover, there is level 4 evidence (from 1 pre-post study) that 6 months of FES cycle ergometry increased regional lower extremity BMD over areas stimulated (Chen et al., 2005). Body weight supported treadmill training (BWSTT) did not alter the expected pattern of change in bone biochemical markers over time and bone density at fracture-prone sites (Giangregorio et al., 2009).

5.1.2 Whole body vibration

At a meeting of the American Society for Bone and Mineral Research results of a small randomised, placebo-controlled study among 20 children with cerebral palsy who used a similar, commercially available vibrating platform for 10 min per day, 5 days per week for 6 months were reported (Ward et al., 2001). A significant increase in tibial, but not lumbar-

spine bone density in the treated group was found despite the simplicity, short duration of the “vibration”, the young age of the children and the poor compliance (Eisman, 2001).



Fig. 3. Weight bearing in disabled subjects; using standing frames, functional walking with orthoses between bars and crutches, even push-ups in the wheelchair (in case of multiple sclerosis with a clinical equivalent like tetraplegia) bone can be loaded and bone loss rate would be slower (unpublished photos of Dionyssiotis Y).

After 6 months of whole body vibration (WBV) therapy in twenty children with cerebral palsy (age 6.2 to 12.3 years; 6 girls) randomized to either continue their school physiotherapy program unchanged or to receive 9 minutes of side-alternating WBV (Vibraflex Home Edition II®, Orthometrix Inc) not effect on areal BMD at the lumbar spine was observed, while areal BMD seemed to decrease somewhat in the cortical region of the femoral diaphysis. Authors explained that mechanical stimulation increases intracortical bone remodeling and thereby cortical porosity; moreover changes occurred in ways that are not reflected by areal BMD, but might be detectable by more sophisticated techniques such as such as peripheral quantitative computed tomography (Ruck et al., 2010). Low-intensity vibration (LIV) has shown to be associated with improvement in bone mineral density in post-menopausal women and children with cerebral palsy. Seven non-ambulatory subjects with SCI and ten able-bodied controls underwent transmission of a plantar-based LIV signal (0.27 ± 0.11 g; 34 Hz) from the feet through the axial skeleton as a function of tilt-table angle (15, 30, and 45 degrees). SCI subjects and controls demonstrated equivalent transmission of LIV, with greater signal transmission observed at steeper angles of tilt which supports the possibility of the utility of LIV as a means to deliver mechanical signals in a form of therapeutic intervention to prevent/reverse skeletal fragility in the SCI population (Asselin et al., 2011).



Fig. 4. The Galileo Delta A TiltTable offers a wide variety of applications from relaxation to muscle training for a diverse range of patients who are unable to stand without support. The motor driven adjustable tilt angle of the Galileo Delta TiltTable (90°) allows vibration training with reduced body weight from 0 to 100%. This is ideal for deconditioned and disabled patients for gradually increasing training weights up to full body weight. System for application in adults (max. body height: 1.90 m) and children (max. body height: 1.50 m). The Galileo Delta A TiltTable is exclusively available from the manufacturer Novotec Medical GmbH., (with permission).

5.1.3 Drugs

Calcitonin in varying doses and methods of administration has given variable results in paraplegia (preferred dosage regimen, treatment duration, and administration route for adequate efficacy in SCI patients' remains unclear) (Chantraine et al., 1979a; Minaire, 1987). Likewise, the outcome using bisphosphonates has been variable. Etidronate produced long-term benefit in lower limb bone mineral density (BMD) in selected walking SCI patients (Roux et al., 1998); whereas tiludronate appeared effective in reducing bone resorption and preserving bone mass in a histomorphometric study in 20 paraplegic patients (Chappard et al., 1995). Intravenous pamidronate has been shown to attenuate bone loss in SCI and normalize serum calcium in immobilization hypercalcemia (Bauman et al., 2005). Alendronate (1000 times more potent than etidronate), in an open observational study, reversed BMD loss in men with established SCI increased both axial and trabecular bone density and has proven efficacy and safety in men treated for osteoporosis, prevents hypercalciuria and bone loss after bed rest and lower leg fracture (Moran de Brito et al., 2005; Zehnder et al., 2004). Six months after using zoledronic acid in the treatment group BMD showed differences in the response to treatment between the mixed trabecular/

cortical regions (narrow neck and intertrochanteric) and the purely cortical shaft. With respect to cross-sectional geometry, bone cross-sectional area and sectional modulus (indices of resistance to axial and bending loads, where higher values would indicate a positive effect of treatment) increased at the hip and buckling ratio (an index of the instability of thin-walled cross sections, where lower values would suggest that the treatment is improving stability) decreased consistent with improved bone outcomes; at 12 months, narrow-neck femur values declined and intertrochanteric and femoral shaft BMD was maintained vs. placebo group which showed a decrease in bone outcomes and an increase in buckling ratio at the hip at 6 and 12 months, while with respect to bone prevention 4 mg i.v. were effective and well-tolerated to prevent BMD loss at the total hip and trochanter for up to 12 months following SCI (Bubbear et al; Shapiro et al., 2007).

Clinical examination and management of bone loss in SCI	
<ul style="list-style-type: none">• history of the patient (co morbidities, neurologic complications, use of drugs which impair bone metabolism, alcohol, smoking and information about the level of injury, duration of paralysis, immobilization period, onset of rehabilitation, use of assistive devices and orthoses).	<ul style="list-style-type: none">• pharmacological treatment with bisphosphonates p.os and i.v. that have been studied in patients with spinal cord injuries and had positive effects on bone parameters.• Use of calcium supplements (monitoring renal function) and vitamin D.
<ul style="list-style-type: none">• anthropometric parameters (age, weight, body mass index, BMI)• clinical examination (level of injury according to American Spinal Injury Association Impairment Scale, AIS) and assessment of spasticity)	<ul style="list-style-type: none">• Education on falls prevention• Counseling regarding osteoporosis and related factors and identification of fractures in regions of impaired sensation.
<ul style="list-style-type: none">• imaging (bone densitometry by DXA at the hip and spine, and if possible, p QCT at the the tibia or femur)	<ul style="list-style-type: none">• physical therapy including: a) range of motion exercises, b) loading of the skeleton to reduce bone loss, d) therapeutic standing-walking with orthoses, e) passive-active cycling
<ul style="list-style-type: none">• measurement of bone turnover indices in the serum (parathyroid hormone, alkaline phosphatase, calcium, vitamin D, PINP molecule, osteocalcin) and urinary excretion of 24 hour (calcium, hydroxyproline, aminoterminal (NTx) and carboxylterminal (CTx) intermolecular cross-linking domain of bone type-1 collagen), which provide a good indicator of bone resorption.	<ul style="list-style-type: none">• dietary interventions to improve dietary intake of calcium and nutrition indices.

Table 1. An algorithm for the screening and management of osteoporosis in subjects with spinal cord injury (should be read top to bottom starting with the left column); adapted from: Dionyssiotis Y. (2009). Bone loss in paraplegia: A diagnostic and therapeutic protocol. Osteoporos Int Vol. 20 (Suppl 1):S23-S176 (with permission).

6. References

- Apkon, S.D., Fenton, L., & Coll, J.R. (2009). Bone mineral density in children with myelomeningocele. *Dev Med Child Neurol*, Vol. 51, No. 1, pp. 63-67.
- Asselin, P., Spungen, A.M., Muir, J.W., Rubin, C.T., & Bauman, W.A. (2011). Transmission of low-intensity vibration through the axial skeleton of persons with spinal cord injury as a potential intervention for preservation of bone quantity and quality. *J Spinal Cord Med*, Vol.34, No. 1, pp. 52-59.
- Ausili, E., Focarelli, B., Tabacco, F., Fortunelli, G., Caradonna, P., Massimi, L., Sigismondi, M., Salvaggio, E., & Rendeli, C. (2008). Bone mineral density and body composition in a myelomeningocele children population: effects of walking ability and sport activity. *Eur Rev Med Pharmacol Sci*, Vol. 12, No.6, pp. 349-354.
- Bauman, W.A., & Schwartz E. (1997). Calcium metabolism and osteoporosis in individuals with spinal cord injury. *Top Spinal Cord Inj Rehabil*, Vol. 2, pp. 84-96.
- Bauman, W.A., Spungen, A.M., Morrison, N., Zhang, R.L., & Schwartz, E. (2005). Effect of a vitamin D analog on leg bone mineral density in patients with chronic spinal cord injury. *J Rehabil Res Dev*, Vol. 42, No. 5, pp. 625-634.
- Bauman, W.A., Wecht, J.M., Kirshblum, S., Spungen, A.M., Morrison, N., Cirnigliaro, C, & Schwartz, E. (2005). Effect of pamidronate administration on bone in patients with acute spinal cord injury. *J Rehabil Res Dev*, Vol. 42, No. 3, pp. 305-313.
- Bauman, W.A., Schwartz, E., Song, I.S., Kirshblum, S., Cirnigliaro, C., Morrison, N. & Spungen, A.M. (2009). Dual-energy X-ray absorptiometry overestimates bone mineral density of the lumbar spine in persons with spinal cord injury. *Spinal Cord*, Vol. 47, No 8, pp. 628-633.
- Biering-Sorensen, F., Hansen, B., & Lee, B.S. (2009). Non-pharmacological treatment and prevention of bone loss after spinal cord injury: a systematic review. *Spinal Cord*, Vol. 47, No. 7, pp. 508-518.
- Biering-Sorensen, F., Bohr, H.H., & Schaadt, O.P. (1991). Longitudinal study of bone mineral content in the lumbar spine, the forearm and the lower extremities after spinal cord injury. *Europ J Clin Invest*, Vol.20, pp. 330-335.
- Biering-Sorensen, F., Bohr, H.H., & Schaadt, O.P. (1988). Bone mineral content of the lumbar spine and lower extremities years after spinal cord lesions. *Paraplegia*, Vol. 26, pp. 293- 301.
- Bikle, D.D., Halloran, B.P., & Morey-Holton, E. (1997). Spaceflight and the skeleton: lessons for the earthbound. *Gravi Space Biol Bull*, Vol. 10, No. 2, pp. 119-135.
- Bubbear, J.S., Gall, A., Middleton, F.R., Ferguson-Pell, M., Swaminathan, R., & Keen, R.W. (2011). Early treatment with zoledronic acid prevents bone loss at the hip following acute spinal cord injury. *Osteoporos Int*, Vol. 22, No. 1. pp. 271-279.
- Cavanagh, P.R., Licata, A.A., & Rice, A.J. (2005). Exercise and pharmacological countermeasures for bone loss during long-duration space flight. *Gravit Space Biol Bull*, Vol. 18, No. 2, pp. 39-58.
- Chad, K.E., McKay, H.A., Zello, G.A, Bailey, D.A., Faulkner, R.A., Snyder, R.E. (2000). Body composition in nutritionally adequate ambulatory and non-ambulatory children with cerebral palsy and a healthy reference group. *Dev Med Child Neurol*, Vol. 42, No. 5, pp. 334-339.
- Chantraine, A. (1978). Actual concept of osteoporosis in paraplegia. *Paraplegia*, Vol. 16, No 1, pp. 51-58.

- Chantraine, A., Heynen, G., & Franchimont, P. (1979). Bone metabolism, parathyroid hormone, and calcitonin in paraplegia. *Calcif Tissue Int*, Vol. 27, No. 3, pp. 199-204.
- Chantraine, A., van Ouwenaller, C., Hachen, H.J., Schinas, P. (1979). Intra-medullary pressure and intra-osseous phlebography in paraplegia. *Paraplegia*, Vol. 17, No. 4, pp. 391-399.
- Chantraine, A., Nusgens, B., & Lapiere, C.M. (1986). Bone remodeling during the development of osteoporosis in paraplegia. *Calcif Tissue Int*, Vol. 38, No. 6, pp. 323-327.
- Chen, S.C., Lai, C.H., Chan, W.P., Huang, M.H., Tsai, H.W., & Chen, J.J. (2005). Increases in bone mineral density after functional electrical stimulation cycling exercises in spinal cord injured patients. *Disabil Rehabil*, Vol. 27, No. 22, pp. 1337-1341.
- Cosman, F., Nieves, J., Komar, L., Ferrer, G., Herbert, J., Formica, C., Shen, V., & Lindsay, R. (1998). Fracture history and bone loss in patients with MS. *Neurology*, Vol. 51, No. 4, pp. 1161-1165.
- Coupaud, S., McLean, A.N., & Allan, D.B. (2009). Role of peripheral quantitative computed tomography in identifying disuse osteoporosis in paraplegia. *Skeletal Radiol*, Vol. 38, No. 10, pp. 989-995.
- Clasey, J.L., Janowiak, A.L., & Gater, D.R. (2004). Relationship between regional bone density measurements and the time since injury in adults with spinal cord injuries. *Arch Phys Med Rehabil*, Vol. 85, pp. 59-64.
- Dauty, M., Perrouin-Verbe, B., Maugars, Y., Dubois, C., & Mathe, J.F. (2000). Supralesional and sublesional bone mineral density in spinal cord-injured patients. *Bone*, Vol. 27, No. 2, pp. 305-309.
- de Bruin, E.D., Frey-Rindova, P., Herzog, R.E., Dietz, V., Dambacher, M.A., & Stussi, E. (1999). Changes of tibia bone properties after spinal cord injury: effects of early intervention. *Arch Phys Med Rehabil*, Vol. 80, No. 2, pp. 214-220.
- Demirel, G., Yilmaz, H., Paker, N., & Onel S. (1998). Osteoporosis after spinal cord injury. *Spinal Cord*, Vol. 36, No. 12, pp. 822-825.
- Dionyssiatis, Y., Trovas, G., Galanos, A., Raptou, P., Papaioannou, N., Papagelopoulos, P., Petropoulou, K., & Lyritis, G.P. (2007). Bone loss and mechanical properties of tibia in spinal cord injured men. *J Musculoskelet Neuronal Interact* Vol.7, No. 1, pp. 62-68.
- Dionyssiatis, Y., Petropoulou, K., Raptou, C.A., Papagelopoulos, P., Papaioannou, N., Galanos, A., Papadaki, P., & Lyritis, G.P. (2008). Body composition in paraplegic men. *J Clin Densitom*, Vol.11, No.3, pp. 437-443.
- Dionyssiatis, Y., Lyritis, G.P., Papaioannou, N., Papagelopoulos, P., & Thomaidis, T. (2009). Influence of neurological level of injury in bones, muscles, and fat in paraplegia. *J Rehabil Res Dev*, Vol. 46, No 8, pp. 1037-1044.
- Dionyssiatis, Y. (2009). Bone loss in paraplegia: A diagnostic and therapeutic protocol. *Osteoporos Int*, Vol. 20, (Suppl 1):S23-S176.
- Dionyssiatis, Y., Lyritis, G.P., Mavrogenis, A.F., & Papagelopoulos, P.J. (2011a). Factors influencing bone loss in paraplegia. *Hippokratia*, Vol.15, No. 1, pp. 54-59.
- Dionyssiatis, Y. (2011b). Bone loss and fractures in multiple sclerosis: focus on epidemiologic and physiopathological features. *Int J Gen Med*, Vol. 4, pp. 505-509.
- Dionyssiatis, Y. (2011c). Spinal cord injury-related bone impairment and fractures: An update on epidemiology and physiopathological mechanisms. *J Musculoskelet Neuronal Interact*, Vol.11, No. 3, pp. 257-265

- Dionyssiotis Y. (2011d). Bone Loss in Spinal Cord Injury and Multiple Sclerosis. In: JH Stone, M Blouin, editors. *International Encyclopedia of Rehabilitation*. Available online: <http://cirrie.buffalo.edu/encyclopedia/en/article/340/>
- Doty, S.B., & DiCarlo, E.F. (1995). Pathophysiology of immobilization osteoporosis. *Curr Opin Orthop*, Vol.6, No. 5, pp. 45-49.
- Dovio, A., Perazzolo, L., Osella, G., Ventura, M., Termine, A., Milano, E., Bertolotto, A., & Angeli, A. (2004). Immediate fall of bone formation and transient increase of bone resorption in the course of high-dose, short-term glucocorticoid therapy in young patients with multiple sclerosis. *J Clin Endocrinol Metab*, Vol. 89, No. 10, pp. 4923-4928.
- Dudley-Javoroski, S., & Shields, R.K. (2008). Dose estimation and surveillance of mechanical loading interventions for bone loss after spinal cord injury. *Phys Ther*, Vol. 88, No 3, pp. 387-396.
- Dudley-Javoroski, S., & Shields, R.K. (2008). Muscle and bone plasticity after spinal cord injury: review of adaptations to disuse and to electrical muscle stimulation. *J Rehabil Res Dev*, Vol. 45, No. 2, pp. 283-296.
- Dudley-Javoroski, S., & Shields, R.K. (2010). Longitudinal changes in femur bone mineral density after spinal cord injury: effects of slice placement and peel method. *Osteoporos Int*, Vol. 21, No. 6, pp. 985-995.
- Eisman, J.A. (2001). Good, good, good... good vibrations: the best option for better bones? *Lancet*, Vol. 358, No. 9297, pp. 1924-1925.
- Eser, P., de Bruin, E.D., Telley, I., Lechner, H.E., Knecht, H., & Stussi, E. (2003). Effect of electrical stimulation-induced cycling on bone mineral density in spinal cord-injured patients. *Eur J Clin Invest*, Vol. 33, No 5, pp. 412-419.
- Eser, P., Frotzler, A., Zehnder, Y., Wick, L., Knecht, H., Denoth, J., & Schiessl H. (2004). Relationship between the duration of paralysis and bone structure: a pQCT study of spinal cord injured individuals. *Bone*, Vol. 34, No. 5, pp. 869-880.
- Eser, P., Frotzler, A., Zehnder, Y., & Denoth, J. (2005). Fracture threshold in the femur and tibia of people with spinal cord injury as determined by peripheral quantitative computed tomography. *Arch Phys Med Rehabil*, Vol. 86, No. 3, pp. 498-504.
- Eser, P., Frotzler, A., Zehnder, Y., Schiessl, H., & Denoth, J. (2005). Assessment of anthropometric, systemic, and lifestyle factors influencing bone status in the legs of spinal cord injured individuals. *Osteoporos Int*, Vol. 16, No. 1, pp. 26-34.
- Fattal, C., Mariano-Goulart, D., Thomas, E., Rouays-Mabit, H., Verollet, C., & Maimoun, L. (2011). Osteoporosis in persons with spinal cord injury: the need for a targeted therapeutic education. *Arch Phys Med Rehabil*, Vol. 92, No. 1, pp. 59-67.
- Faulkner, M.A., Ryan-Haddad, A.M., Lenz, TL, & Degner, K. (2005). Osteoporosis in long-term care residents with multiple sclerosis. *Consult Pharm*, Vol. 20, No. 2, pp. 128-136.
- Frotzler, A., Coupaud, S., Perret, C., Kakebeeke, T.H., Hunt, K.J., Donaldson, Nde. N., & Eser, P. (2008). High-volume FES-cycling partially reverses bone loss in people with chronic spinal cord injury. *Bone*, Vol. 43, No. 1, pp. 169-176.
- Frotzler, A., Coupaud, S., Perret, C., Kakebeeke, T.H., Hunt, K.J., & Eser, P. (2009). Effect of detraining on bone and muscle tissue in subjects with chronic spinal cord injury after a period of electrically-stimulated cycling: a small cohort study. *J Rehabil Med*, Vol. 41, No. 4, pp. 282-285.

- Garland, D.E., Stewart, C.A., Adkins, R.H., Hu, S.S., Rosen, C., Liotta, F.J., & Weinstein, D.A. (1992). Osteoporosis after spinal cord injury. *J Orthop Res*, Vol. 10, No. 3, pp. 371-378.
- Garland, D.E., Foulkes, G.D., Adkins, R.H., Stewart, C.A., & Yakura, J.S. (1994). Regional osteoporosis following incomplete spinal cord injury. *Contemporary Orthopaedics*, Vol. 28, pp. 134-139.
- Garland, D.E., Adkins, R.H., Matsuno, N.N., & Stewart, C.A. (1999). The effect of pulsed electromagnetic fields on osteoporosis at the knee in individuals with spinal cord injury. *J Spinal Cord Med*, Vol. 22, No 4, pp. 239-245.
- Garland, D.E., Adkins, R.H., Stewart, C.A., Ashford, R., & Vigil, D. (2001). Regional osteoporosis in women who have a complete spinal cord injury. *J Bone Joint Surg Am*, Vol. 83-A, No. 8, pp. 1195-200.
- Garland, D.E., Adkins, R.H., Kushwaha, V., & Stewart, C. (2004a). Risk factors for osteoporosis at the knee in the spinal cord injury population. *J Spinal Cord Med*, Vol. 27, No. 3, pp. 202-206.
- Garland, D.E., Adkins, R.H., Scott, M., Singh, H., Massih, M., & Stewart, C. (2004b). Bone loss at the os calcis compared with bone loss at the knee in individuals with spinal cord injury. *J Spinal Cord Med*, Vol. 27, No. 3, pp. 207-211.
- Giangregorio, L.M., & Blimkie, C.J. (2002). Skeletal adaptations to alterations in weight-bearing activity: a comparison of models of disuse osteoporosis. *Sports Med*, Vol. 32, No 7, pp. 459-476.
- Giangregorio, L.M., & Webber, C.E. (2004). Speed of sound in bone at the tibia: is it related to lower limb bone mineral density in spinal-cord-injured individuals? *Spinal Cord*, Vol. 42, No 3, pp. 141-145.
- Giangregorio, LM, Craven, B.C., & Webber, C.E. (2005). Musculoskeletal changes in women with spinal cord injury: a twin study. *J Clin Densitom*, Vol. 8, No. 3, pp. 347-351.
- Giangregorio, L.M., Thabane, L., Debeer, J., Farrauto, L., McCartney, N., Adachi, J.D., & Papaioannou, A. (2009). Body weight-supported treadmill training for patients with hip fracture: a feasibility study. *Arch Phys Med Rehabil*, Vol. 90, No. 12, pp. 2125-2130.
- Griffiths, H.J., Bushueff, B., & Zimmerman, R.E. (1976). Investigation of the loss of bone mineral in patients with spinal cord injury. *Paraplegia*, Vol.14, No. 3, pp. 207-212.
- Gutin, B., & Kasper, M.J. (1992). Can vigorous exercise play a role in osteoporosis prevention? A review. *Osteoporos Int*, Vol. 2, No. 2, pp. 55-69.
- Hamdy, R.C., Krishnaswamy, G., Cancellaro, V., Whalen, K., & Harvill, L. (1993). Changes in bone mineral content and density after stroke. *Am J Phys Med Rehabil*, Vol. 72, pp. 188-191.
- Henderson, R.C., Lin, P.P., & Greene, W.B. (1995). Bone-mineral density in children and adolescents who have spastic cerebral palsy. *Journal of Bone and Joint Surgery*, Vol. 77A, pp. 1671-1681.
- Henderson, R.C., Lark, R.K., Gurka, M.J, Worley, G., Fung, E.B., Conaway, M., Stallings, V.A., & Stevenson, R.D. (2002). Bone density and metabolism in children and adolescents with moderate to severe cerebral palsy. *Pediatrics* Vol. 110, No.1, p.5.

- Houlihan, C.M., & Stevenson RD. (2009). Bone density in cerebral palsy. *Phys Med Rehabil Clin N Am*, Vol. 20, No. 3, pp. 493-508.
- Jiang, S.D., Jiang, L.S., & Dai, L.Y. (2007). Changes in bone mass, bone structure, bone biomechanical properties, and bone metabolism after spinal cord injury: a 6-month longitudinal study in growing rats. *Calcif Tissue Int*, Vol. 80, No.3, pp. 167-175.
- Jiang, S.D., Jiang, L.S., & Dai, L.Y. (2007). Effects of spinal cord injury on osteoblastogenesis, osteoclastogenesis and gene expression profiling in osteoblasts in young rats. *Osteoporos Int*, Vol. 18, No 3, pp. 339-349.
- Jones, L.M., Legge, M., & Goulding, A. (2002). Intensive exercise may preserve bone mass of the upper limbs in spinal cord injured males but does not retard demineralisation of the lower body. *Spinal Cord*, Vol. 40, No. 5, pp. 230-235.
- Kannisto, M., Alaranta, H., Merikanto, J., Kroger, H., & Karkkainen, J. (1998). Bone mineral status after pediatric spinal cord injury. *Spinal Cord*, Vol. 36, No 9, pp. 641-646.
- Karlsson, A.K., Friberg, P., Lonnroth, P., Sullivan, L., & Elam, M. (1998). Regional sympathetic function in high spinal cord injury during mental stress and autonomic dysreflexia. *Brain*, Vol. 121, pp. 1711-1719.
- Kiratli, B.J., Smith, A.E., Nauenberg, T., Kallfelz, C.F., & Perkash, I. (2000). Bone mineral and geometric changes through the femur with immobilization due to spinal cord injury. *J Rehabil Res Dev*, Vol. 37, No. 2, pp. 225-233.
- Kondo, H., Nifuji, A., Takeda, S., Ezura, Y., Rittling, S.R., Denhardt, D.T., Nakashima, K., Karsenty, G., & Noda, M. (2005). Unloading induces osteoblastic cell suppression and osteoclastic cell activation to lead to bone loss via sympathetic nervous system. *J Biol Chem.*, Vol. 280, pp. 30192-30200.
- Kurban, S., Akpınar, Z., & Mehmetoglu, I. (2008). Receptor activator of nuclear factor kappa B ligand (RANKL) and osteoprotegerin levels in multiple sclerosis. *Mult Scler*, Vol.14, pp. 431-432.
- Lakatos, P., Nagy, Z., Kiss, L., Horvath, C., Takacs, I., Foldes, J., Speer, G., & Bossanyi, A. (2000). Prevention of corticosteroid-induced osteoporosis by alfacalcidol. *Z Rheumatol*, Vol. 59, Suppl 1, pp. 48-52.
- Lanyon, L.E., Rubin, C.T., & Baust, G. Modulation of bone loss during calcium insufficiency by controlled dynamic loading. (1986). *Calcif Tissue Int*, Vol. 38, pp. 209-216.
- Lazo, M.G., Shirazi, P., Sam, M., Giobbie-Hurder, A., Blacconiere, M.J., & Muppidi, M. (2001). Osteoporosis and risk of fracture in men with spinal cord injury. *Spinal Cord*, Vol. 39, No 4, pp. 208-214.
- LeBlanc, A.D., Evans, H.J., Engelbretson, D.A., & Krebs, J.M. (1990). Bone mineral loss and recovery after 17 weeks of bed rest. *J Bone Miner Res*, Vol. 5, pp. 843-850.
- LeBlanc, A.D., & Schneider, V. (1992). Countermeasures against space flight related bone loss. *Acta Astronaut*, Vol. 27, pp. 89-92.
- LeBlanc, A.D., Spector, E.R., Evans, H.J., & Sibonga, J.D. (2007). Skeletal responses to space flight and the bed rest analog: a review. *J Musculoskelet Neuronal Interact*, Vol. 7, No. 1, pp. 33-47.
- Leslie, W.D., & Nance, P.W. Dissociated hip and spine demineralization: a specific finding in spinal cord injury. *Arch Phys Med Rehabil*, Vol.74, pp. 960-964.
- Leeds, E.M., Klose, K.J., Ganz, W., Serafini, A., & Green, B.A. (1990). Bone mineral density after bicycle ergometry training. *Arch Phys Med Rehabil* Vol. 71, No. 3, pp. 207-209.

- Levasseur, R., Sabatier, J.P., Potrel-Burgot, C., Lecoq, B., Creveuil, C., & Marcelli, C. (2003). Sympathetic nervous system as transmitter of mechanical loading in bone. *Joint Bone Spine*, Vol. 70, pp. 515-519.
- Lofvenmark, I., Werhagen, L., & Norrbrink, C. (2009). Spasticity and bone density after a spinal cord injury. *J Rehabil Med*, Vol. 41, No 13, pp. 1080-1084.
- Maimoun, L., Couret, I., Micallef, J.P., Peruchon, E., Mariano-Goulart, D., Rossi, M., Leroux, J.L., & Ohanna, F. (2002). Use of bone biochemical markers with dual-energy x-ray absorptiometry for early determination of bone loss in persons with spinal cord injury. *Metabolism*, Vol. 51, No.8, pp. 958-963.
- Maimoun, L., Couret, I., Mariano-Goulart, D., Dupuy, A.M., Micallef, J.P., Peruchon, E., Ohanna, F., Cristol, J.P., Rossi, M., & Leroux, J.L. (2005). Changes in osteoprotegerin/RANKL system, bone mineral density, and bone biochemical markers in patients with recent spinal cord injury. *Calcif Tissue Int*, Vol. 76, No. 6, pp. 404-411.
- Maimoun, L., Fattal, C., Micallef, J.P., Peruchon, E., & Rabischong, P. (2006). Bone loss in spinal cord-injured patients: from physiopathology to therapy. *Spinal Cord* Vol. 44, No. 4, pp. 203-210.
- Marrie, R.A., Cutter, G., Tyry, T., & Vollmer, T. (2009). A cross-sectional study of bone health in multiple sclerosis. *Neurology*, Vol. 73, No 17, pp. 1394-1398.
- Modlesky, C.M., Bickel, C.S., Slade, J.M., Meyer, R.A., Cureton, K.J., & Dudley, G.A. (2004). Assessment of skeletal muscle mass in men with spinal cord injury using dual-energy X-ray absorptiometry and magnetic resonance imaging. *J Appl Physiol* Vol. 96, pp. 561-565.
- Moran de Brito, C.M., Battistella, L.R., Saito, E.T., & Sakamoto, H. (2005). Effect of alendronate on bone mineral density in spinal cord injury patients: a pilot study. *Spinal Cord*, Vol. 43, No. 6, pp. 341-348.
- Nieves, J., Cosman, F., Herbert, J., Shen, V., & Lindsay R. (1994). High prevalence of vitamin D deficiency and reduced bone mass in multiple sclerosis. *Neurology*, Vol. 44, No. 9, pp. 1687-1692.
- NIH. (2001). NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. *JAMA*. pp. 785-795.
- Okurowska-Zawada, B., Konstantynowicz, J., Kulak, W., Kaczmariski, M., Piotrowska-Jastrzebska, J., Sienkiewicz, D., & Paszko-Patej, G. (2009). Assessment of risk factors for osteoporosis and fractures in children with meningomyelocele. *Adv Med Sci*, Vol. 54, No 2, pp. 247-252.
- Ozgocmen, S., Bulut, S., Ilhan, N., Gulkesen, A., Ardicoglu, O., & Ozkan, Y. (2005). Vitamin D deficiency and reduced bone mineral density in multiple sclerosis: effect of ambulatory status and functional capacity. *J Bone Miner Metab*, Vol. 23, No 4, 309-313.
- Parfitt, A.M. (1981). Bone effects of space flight: analysis by quantum concept of bone remodelling. *Acta Astronaut*, Vol. 8, No. (9-10), pp. 1083-1090.
- Perez Castrillon, J.L., Cano-del Pozo, M., Sanz-Izquierdo, S., Velayos-Jimenez, J., & Dib-Wobakin, W. (2003). Bone mineral density in patients with multiple sclerosis: the effects of interferon. *Rev Neurol* Vol. 36, No. 10, pp. 901-903.
- Phaner, V., Charmetant, C., Condemine, A., Fayolle-Minon, I., Lafage-Proust, M.H., & Calmels, P. Osteoporosis in spinal cord injury. Screening and treatment. Results of

- a survey of physical medicine and rehabilitation physician practices in France. Proposals for action to be taken towards the screening and the treatment. *Ann Phys Rehabil Med*, Vol. 53, No. 10, pp. 615-620.
- Pouilles, J.M., Ribot, C., Tremollieres, F., & Guell, A. (1992). Vertebral, femoral and radial bone density in simulation of prolonged weightlessness. Experience with healthy volunteers. *Presse Med*, Vol. 21, No 4, pp. 160-164.
- Quan, A., Adams, R., Ekmark, E., & Baum, M. (1998). Bone mineral density in children with myelomeningocele. *Pediatrics*, Vol. 102, No. 3, E34.
- Quan, A., Adams, R., Ekmark, E., & Baum, M. (2003). Bone mineral density in children with myelomeningocele: effect of hydrochlorothiazide. *Pediatr Nephrol* Vol. 18, No 9, pp. 929-933.
- Ramnemark, A., Nyberg, L., Lorentzon, R., Englund, U., & Gustafson, Y. (1999). Progressive hemiosteoporosis on the paretic side and increased bone mineral density in the nonparetic arm the first year after severe stroke. *Osteoporos Int*, Vol. 9, No. 3, pp. 269-275.
- Ramnemark, A., Nyberg, L., Lorentzon, R., Olsson, T., & Gustafson, Y. (1999). Hemiosteoporosis after severe stroke, independent of changes in body composition and weight. *Stroke*, Vol. 30, No. 4, pp. 755-760.
- Reiter, A.L., Volk, A., Vollmar, J., Fromm, B., & Gerner, H.J. (2007). Changes of basic bone turnover parameters in short-term and long-term patients with spinal cord injury. *Eur Spine J*, Vol.16, No. 6, pp. 771-776.
- Roberts, D., Lee, W., Cuneo, R.C., Wittmann, J., Ward, G., Flatman, R., McWhinney, B., & Hickman, P.E. (1998). Longitudinal study of bone turnover after acute spinal cord injury. *J Clin Endocrinol Metab*, Vol. 83, No. 2, pp. 415-422.
- Runge, M., Rehfeld, G., & Schiessl, H. Skeletal adaptations in hemiplegic patients. (2004). *J Musculoskelet Neuronal Interact*, Vol. 4, No 2, pp. 191-196.
- Rubin, C., Xu, G., & Judex, S. (2001). The anabolic activity of bone tissue, suppressed by disuse, is normalized by brief exposure to extremely low-magnitude mechanical stimuli. *Faseb J*, Vol. 15, No 12, pp. 2225-2229.
- Ruck, J., Chabot, G., & Rauch, F. Vibration treatment in cerebral palsy: A randomized controlled pilot study. *J Musculoskelet Neuronal Interact*. Vol.10, No 1, pp. 77-83.
- Sabo, D., Blaich, S., Wenz, W., Hohmann, M., Loew, M., & Gerner, H.J. (2001). Osteoporosis in patients with paralysis after spinal cord injury. A cross sectional study in 46 male patients with dual-energy X-ray absorptiometry. *Arch Orthop Trauma Surg*, Vol.121, No. (1-2), pp. 75-78.
- Sato, Y., Maruoka, H., Oizumi, K., & Kikuyama, M. (1996). Vitamin D deficiency and osteopenia in the hemiplegic limbs of stroke patients. *Stroke*, Vol. 27, pp. 2183-2187.
- Sato, Y., Maruoka, H., Honda, Y., Asoh, T., Fujimatsu, Y., & Oizumi, K. Development osteopenia in the hemiplegic finger in patients with stroke. *Eur Neurol*, Vol. 36, pp. 278-283.
- Sato, Y., Maruoka, H., & Oizumi, K. Amelioration of hemiplegia associated osteopenia more than 4 years after stroke by 1 alphahydroxyvitamin D3 and calcium supplementation. *Stroke*, Vol. 28, pp. 736-739.

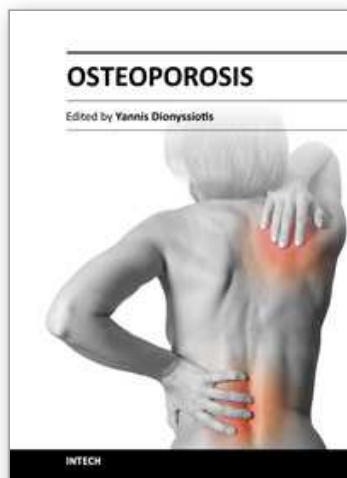
- Sato, Y., Fuiimatsu, Y., Kikuvama, M., Kaii, M., & Oizumi, K. (1998). Influence of immobilization on bone mass and bone metabolism in hemiplegic elderly patients with a long-standing stroke. *J Neural Sci*, Vol. 156, pp. 205-210.
- Sato, Y., Kaji, M., & Oizumi, K. (1999). An alternative to vitamin D supplementation to prevent fractures in patients with MS. *Neurology*, Vol. 53, No. 2, pp. 437.
- Sato, Y. (2000). Abnormal bone and calcium metabolism in patients after stroke. *Arch Phys Med Rehabil*, Vol. 81, pp. 117-121.
- Schwarzman, R.J. (2000). New treatments for reflex sympathetic dystrophy. *N Engl J Med*, Vol. 343, pp. 654-656.
- Shaw, N.J., White, C.P., Fraser, W.D., & Rosenbloom L. (1994) Osteopenia in cerebral palsy. *Archives of Disease in Childhood*, Vol. 71, pp. 235-238.
- Schwid, S.R., Goodman, A.D., Puzas, J.E., McDermott, M.P., & Mattson, D.H. (1996). Sporadic corticosteroid pulses and osteoporosis in multiple sclerosis. *Arch Neurol* Vol. 53, No. 8, pp. 753-757.
- Shields, R.K. (2002). Muscular, skeletal, and neural adaptations following spinal cord injury. *J Orthop Sports Phys Ther*, Vol. 32, No 2, pp. 65-74.
- Shojaei, H., Soroush, M.R., & Modirian, E. (2006). Spinal cord injury-induced osteoporosis in veterans. *J Spinal Disord Tech*, Vol. 19, No.2, pp. 114-117.
- Shuhaibar, M., McKenna, M.J., Au-Yeong, M., & Redmond, J.M. (2009). Favorable effect of immunomodulator therapy on bone mineral density in multiple sclerosis. *Ir J Med Sci* Vol. 178, No. 1, pp. 43-45.
- Sioka, C., Kyritsis, A.P., & Fotopoulos, A. (2009). Multiple sclerosis, osteoporosis, and vitamin D. *J Neurol Sci*, Vol. 287, No (1-2), pp. 1-6.
- Smeltzer, S.C., Zimmerman, V., & Capriotti, T. (2005). Osteoporosis risk and low bone mineral density in women with physical disabilities. *Arch Phys Med Rehabil*, Vol. 86, pp. 582-586.
- Smith, E.M., Comiskey, C.M., & Carroll, A.M. (2009). A study of bone mineral density in adults with disability. *Arch Phys Med Rehabil*, Vol. 90, No 7, pp. 1127-1135.
- Smith, S.M., Zwart, S.R., Heer, M.A., Baecker, N., Evans, H.J., Feiveson, A.H., Shackelford, L.C., & Leblanc, A.D. (2009). Effects of artificial gravity during bed rest on bone metabolism in humans. *J Appl Physiol*, Vol.107, No 1, pp. 47-53.
- Sniger, W., & Garshick, E. (2002). Alendronate increases bone density in chronic spinal cord injury: a case report. *Arch Phys Med Rehabil*, Vol. 83, No.1, pp. 139-140.
- Spector, E.R., Smith, S.M., & Sibonga, J.D. (2009). Skeletal effects of long-duration head-down bed rest. *Aviat Space Environ Med* Vol. 80, No. (5 Suppl):A23-8.
- Stenager, E., Jensen, K. (1991). Fractures in multiple sclerosis. *Acta Neurol Belg* Vol. 91, No 5, pp. 296-302.
- Szollar, S.M., Martin, E.M., Sartoris, D.J., Parthemore, J.G., & Deftos, L.J. (1998). Bone mineral density and indexes of bone metabolism in spinal cord injury. *Am J Phys Med Rehabil*, Vol. 77, No. 1, pp. 28-35.
- Takamoto, S., Masuyama, T., Nakajima, M., Seikiya, K., Kosaka, H., Morimoto, S., Ogihara, T., & Onishi T. (1995). Alterations of bone mineral density of the femurs in hemiplegia. *Calcif Tissue Int*. Vol. 56, pp. 259 -262.
- Takata, S., & Yasui, N. (2001). Disuse osteoporosis. *J Med Invest*, Vol. 48, No. (3-4), pp. 147-156.

- Takeda, S., Elefteriou, F., Levasseur, R., Liu, X., Zhao, L., Parker, K.L., Armstrong, D., Ducy, P., & Karsenty, G. (2002). Leptin regulates bone formation via the sympathetic nervous system. *Cell*, Vol. 111, pp. 305-317.
- Teasell, R.W., Arnold, J.M., Krassioukov, A., & Delaney, G.A. (2000). Cardiovascular consequences of loss of supraspinal control of the sympathetic nervous system after spinal cord injury. *Arch Phys Med Rehabil*, Vol. 81, pp. 506-516.
- Tsuzuku, S., Ikegami, Y., & Yabe, K. Bone mineral density differences between paraplegic and quadriplegic patients: a cross-sectional study. *Spinal Cord*, Vol. 37, pp. 358-361.
- Uebelhart, D., Demiaux-Domenech, B., Roth, M., & Chantaine, A. (1995). Bone metabolism in spinal cord injured individuals and in others who have prolonged immobilisation. A review. *Paraplegia*, Vol. 33, No 11, pp. 669-673.
- Ward, K.A., Alsop, C.W., Brown, S., Caulton, J., Adams, J.E., & Mughal Z. (2001). A randomized, placebo controlled, pilot trial of low magnitude, high frequency loading treatment of low bone mineral density in children with disabling conditions. *J Bone Miner Res*, Vol.16: S173.
- Wilmschurst, S., Ward, K., Adams, J.E., Langton, C.M., & Mughal, M.Z. (1996) Mobility status and bone density in cerebral palsy. *Archives of Disease in Childhood*, Vol. 75, pp. 164-165.
- Weinstock-Guttman, B., Gallagher, E., Baier, M., Green, L., Feichter, J., Patrick, K., Miller, C., Wrest, K., & Ramanathan, M. (2004). Risk of bone loss in men with multiple sclerosis. *Mult Scler*, Vol. 10, No. 2, pp. 170-175.
- Whalen, R.T. A.S., & Grindeland, R.E. Proceedings of the NASA symposium on the influence of gravity and activity on muscle and bone; 1991. pp. 1-178.
- Whedon, G.D. (1984). Disuse osteoporosis: physiological aspects. *Calcif Tissue Int*, Vol.36, Suppl 1:S146-150.
- WHO. (1994). Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. Geneva, pp. 1-129.
- Wilmet, E., Ismail, A.A., Heilporn, A., Welraeds, D., & Bergmann, P. (1995). Longitudinal study of the bone mineral content and of soft tissue composition after spinal cord section. *Paraplegia*, Vol. 33, No 11, pp. 674-677.
- Wronski, T.J., & Morey, E.R. (1983). Alterations in calcium homeostasis and bone during actual and simulated space flight. *Med Sci Sports Exerc*, Vol.15, No. 5, pp. 410-414.
- Zehnder, Y., Risi, S., Michel, D., Knecht, H., Perrelet, R., Kraenzlin, M., Zach, G.A., & Lippuner, K. (2004). Prevention of bone loss in paraplegics over 2 years with alendronate. *J Bone Miner Res*, Vol. 19, No 7, pp. 1067-1074.
- Zehnder, Y., Lüthi, M., Michel, D., Knecht, H., Perrelet, R., Neto, I., Kraenzlin, M., Zäch, G., & Lippuner, K. (2004). Long-term changes in bone metabolism, bone mineral density, quantitative ultrasound parameters, and fracture incidence after spinal cord injury: a cross-sectional observational study in 100 paraplegic men. *Osteoporos Int*, Vol. 15, pp. 180-189.
- Zhang, H., & Wu, J. (2010). A cross-sectional study of bone health in multiple sclerosis. *Neurology* Vol. 74, No. 19, pp. 1554; author reply 1555.
- Zhang, P., Hamamura, K., & Yokota, H. (2008). A brief review of bone adaptation to unloading. *Genomics Proteomics Bioinformatics*, Vol. 6, No.1, pp. 4-7.

- Zhao, W., Liu, Y., Cahill, C.M., Yang, W., Rogers, J.T. & Huang, X. (2009). The role of T cells in osteoporosis, an update. *Int J Clin Exp Pathol*, Vol.20, No.2, pp.544-552.
- Zorzon, M., Zivadinov, R., Locatelli, L., Giuntini, D., Toncic, M., Bosco, A., Nasuelli, D., Bratina, A., Tommasi, M.A., Rudick, R.A & Cazzato, G. (2005). Long-term effects of intravenous high dose methylprednisolone pulses on bone mineral density in patients with multiple sclerosis. *Eur J Neurol*, Vol. 12, No. 7, pp. 550-556.

IntechOpen

IntechOpen



Osteoporosis

Edited by PhD. Yannis Dionyssiotis

ISBN 978-953-51-0026-3

Hard cover, 864 pages

Publisher InTech

Published online 24, February, 2012

Published in print edition February, 2012

Osteoporosis is a public health issue worldwide. During the last few years, progress has been made concerning the knowledge of the pathophysiological mechanism of the disease. Sophisticated technologies have added important information in bone mineral density measurements and, additionally, geometrical and mechanical properties of bone. New bone indices have been developed from biochemical and hormonal measurements in order to investigate bone metabolism. Although it is clear that drugs are an essential element of the therapy, beyond medication there are other interventions in the management of the disease. Prevention of osteoporosis starts in young ages and continues during aging in order to prevent fractures associated with impaired quality of life, physical decline, mortality, and high cost for the health system. A number of different specialties are holding the scientific knowledge in osteoporosis. For this reason, we have collected papers from scientific departments all over the world for this book. The book includes up-to-date information about basics of bones, epidemiological data, diagnosis and assessment of osteoporosis, secondary osteoporosis, pediatric issues, prevention and treatment strategies, and research papers from osteoporotic fields.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Yannis Dionyssiotis (2012). Neurological Osteoporosis in Disabilities, Osteoporosis, PhD. Yannis Dionyssiotis (Ed.), ISBN: 978-953-51-0026-3, InTech, Available from:

<http://www.intechopen.com/books/osteoporosis/neurological-osteoporosis-in-disabilities>

INTECH
open science | open minds

InTech Europe

University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China

Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

© 2012 The Author(s). Licensee IntechOpen. This is an open access article distributed under the terms of the [Creative Commons Attribution 3.0 License](https://creativecommons.org/licenses/by/3.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

IntechOpen

IntechOpen