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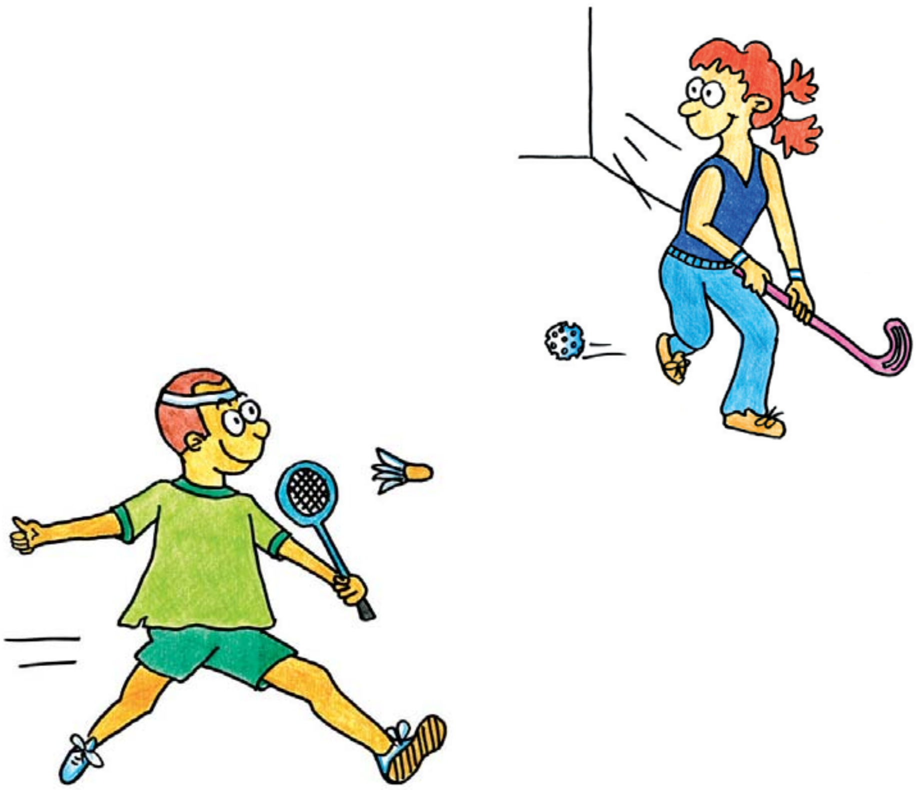
Riku Nikander

Exercise Loading and Bone Structure



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UNIVERSITY OF JYVÄSKYLÄ

JYVÄSKYLÄ 2009

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Cover picture; An example of odd-impact type of exercise loading

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ABSTRACT

Nikander Riku
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Finnish Summary
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The objective of this dissertation was to determine the types of exercise loading that are associated with the strength of bones. Four cross-sectional studies were conducted between 2004 and 2008 including 378 athletes and their 62 referents. Sixteen different sports were classified into five specific categories for the lower extremities and three categories for the upper extremities according to the type of exercise loading.

Besides planar DXA-derived hip structural analysis, pQCT, and MRI methods allowing the assessment of true bone cross-sections were used for the bone structure analyses of the tibia, proximal femur, radius, and humerus.

At the lower extremity, the high-impact exercise loading group (volleyball, hurdling, moguls skiing, triple jump, and high jump) and the odd-impact exercise loading group (soccer, racket games, speed skating, slalom skiing, step aerobics) had 13 to 60% stronger tibia and femoral neck than the reference group. Athletes in high-magnitude exercise loading (weightlifting, powerlifting) did not have more rigid tibia and femoral neck than those in the reference group, while athletes in the repetitive, low-impact loading group (endurance running, orienteering, and cross-country skiing) had some 20 to 30% stronger tibia and their femoral neck also seemed to be 10% stronger than those in the reference group. A novel finding of this study was that, compared to the reference group, the athletes in the high- and odd-impact exercise loading groups had about 20% thicker cortex at the anterior and supero-lateral regions of the femoral neck, the regions that are especially vulnerable in terms of hip fragility.

In the dominant forearm, athletes in both the impact (volleyball and racket games) and high-magnitude (functional weightlifting in soccer and hurdling) exercise loading groups had approximately 15 to 30% stronger radius and humerus than those in the reference group. In the non-dominant forearm, no such difference was found between athletes in impact exercise loading group (racket games) and the reference group, suggesting that there were no substantial inborn differences between these groups.

In conclusion, the type of exercise loading seems to be an important external determinant of the structure of bone. At the lower extremity, the rigid bone structure is especially clear among those engaged with high-impact or odd-impact exercise loading, and, at the upper extremity, among those with impact loading in general. However, the findings of these cross-sectional studies should be tested in randomized controlled trials.

KEY WORDS: Bone structure, exercise, bone density, bone strength, osteoporosis

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In 2002 Professor Esko Mälkiä PhD, University of Jyväskylä, recruited me to do my Master's Thesis on the dose analysis of a famous neck article written by Adjunct Professor Jari Ylinen MD PhD. When finishing up my Master's thesis, Ari Heinonen, at that time new professor of physical therapy and originally from the UKK Institute, had started work at the University of Jyväskylä. From Ari I got advice for the Master's thesis and at the same time he somehow managed to recruit me as a member of the Bone Research Group at the UKK Institute, Tampere for a doctoral dissertation. The dissertation was to focus on exercise loading and bone structure.

Before starting to do my doctoral dissertation, I thought that it would be impossible to find out anything new about the human skeleton and present it to senior bone researchers. The simple question thus was why to write a thesis merely for the sake of an academic title? What would more could I offer compared to those more experienced researchers in the field?

I could probably offer a better understanding of bone issues than many laypersons. But, on the other hand, I was a novice and I did not yet understand much about bones. Maybe, I could find something new which was not obvious to others and demonstrate this new finding to them in an understandable way. Then, at the end of a five-year period of hard work, this small secret turned out to be odd-impact exercise loading, not its high-impact counterpart.

Another thing that worried me at start was the fact that researchers in the field of exercise and bone were arguing, as indeed they still argue, which one of the two main risk factors for bone fractures of older adults is more important for preventing fractures, bone fragility or falling. However, I soon realized that one of the great benefits of exercise is that it can simultaneously prevent bone fragility and falls. Thus, it would be superfluous to argue which one of the risk factors is more important: odd-impact exercise might be the way to bring these issues and researchers together. In fact, the aforementioned idea about the benefits of odd-impact type of exercise pervaded the entire dissertation.

During my five-year journey towards the dissertation, I have met so many great people. I would like to thank you, Esko and Ari, for giving me the first impetus to work in the field of research. It has moreover been my privilege, Ari, to enjoy your company at many conferences abroad. Now I know that 6.30 a.m. is the perfect time for a run. I will never forget your unending support, no matter what has happened.

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If the recruitment was far from easy, so also was organizing the measurements. From the personnel of UKK Institute, Ms. Taru Helenius, Ms. Ulla Hakala, Ms. Ulla Honkanen, Ms. Virpi Koskue, Ms. Kirsi Mansikkamäki MSc, Ms. Salla Peltonen and Ms. Katriina Ojala, and similarly from Tampere University Hospital, Ms. Marjut Keskivinkka, Ms. Anu Kuhanen and Ms. Arja Hilander generously sacrificed many of their weekends for this dissertation.

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FIGURES

TABLES

ORIGINAL ARTICLES

I Nikander R, Sievänen H, Heinonen A, Kannus P 2005. Femoral neck structure in adult female athletes subjected to different loading modalities. J Bone Miner Res 20(3): 520-8.

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ABBREVIATIONS

A	Anterior
aBMD	Areal bone mineral density, g/cm^2
AHA	Advanced hip analysis
ANCOVA	Analysis of covariance
ANOVA	Analysis of variance
BMC	Bone mineral content, g, mg
bmi	Body Mass Index, kg/m^2
BMU	Bone Multicellular Unit
BSI	Bone Strength Index
BUA	Broadband Ultrasound Attenuation
CI	Confidence interval
CoA	Cross sectional area of the cortical bone, mm^2
CoD	Volumetric density of the cortical bone, mg/cm^3
CSA	Cross-sectional area, mm^2
CSMI	Cross-sectional moment of inertia, mm^4
CV	Coefficient of variation, %
CWT	Cortical wall thickness, mm
DR	Distal radius
DT	Distal tibia
DXA	Dual energy x-ray absorptiometry
FN	Femoral neck
H-I	High-impact
H-M	High-magnitude
HS	Humeral shaft
HSA	Hip structural analysis
I	Inferior
L-I	Low-impact
MES	Minimum effective strain
MESS	Minimum effective strain related stimulus
MRI	Magnetic resonance imaging
N-I	Non-impact
O-I	Odd-impact
P	Posterior
pQCT	Peripheral quantitative computed tomography
RCT	Randomized controlled trial
RS	Radial shaft
S	Superior
SD	Standard deviation
SGP	Stress-generated potentials
SOS	Sound of Speed
ToA	Total cross-sectional area of bone, mm^2
TrD	Volumetric density of the trabecular bone, mg/cm^3
TS	Tibial shaft
W	Subperiosteal width of bone, mm
Z	Section modulus, an index of bending resistance, mm^3

CONTENTS

1 INTRODUCTION

From an evolutionary perspective, bipedal walking and long lower extremities, in addition to leaving the hands free, enable greater speed of movement with lower energy expenditure than in quadrupedal walking (Biewener 1989, Galik et al. 2004, Lovejoy 1988, Preuschoft 2004). But what has been the benefit of greater speed for the human? During millions of years of evolution, the form of the human body seems to be developed rather for running than for walking (Bramble & Lieberman 2004). As speculated by Bramble and Lieberman (2004), the capability of human to run long distances "cost-effectively" might have helped to modify the development of brain, *e.g.* by getting to a nutrient-rich carcass. Exercise has had a fundamental role in the development of the human being. Upright posture with functional musculature may have helped to obtain a lot of protein and fat to enlarge the brain capacity in addition to modifying the skeleton (Bramble & Lieberman 2004, Galik et al. 2004). Thus, the history of exercise to remodel bones is millions of years old. More than 100 years ago, it was suggested in Wolff's law that bones adapt to their habitual loading (Frost 2003a,b). The human body is not built to stand still but to move (Ruff 2003a).

Locomotion is the major function of the human musculoskeleton, and from that perspective, the human skeleton does not have a speed limit, well-known in motoring, but a weight limit. The locomotive apparatus is also a mineral reservoir for calcium metabolism, but for other metabolic reasons it needs a weight limit. The body needs to be carried while consuming a minimum amount of energy. Hence, the skeleton has to be light, but rigid and strong (Ruff 2006). The total bone mineral content of an adult, weighing around 2 to 3 kg, is only around 5% of one's bodyweight. From such a limited amount of material, the structure to carry a weight of over 100 kg, reaching a height of 2 meters, or coping with forces that can exceed 20 times bodyweight without fractures needs to be built. This kind of structure also needs to be a framework for all other organs and also a protective shell for some internal organs (Morgan et al. 2008).

Although metals such as steel would not fracture easily (Taylor 2008), it would cost a lot of energy to carry such a heavy structure inside the body. But there are lighter metals, which are also strong. However, light and rigid metal, as known from implants, cannot reshape itself after an orthopedic operation if the loading environment is later changed. Bone, instead, as a vital tissue will constantly adapt to the current mechanical loading environment in principle to provide light and rigid skeleton for locomotive and other purposes (Currey 2002, Morgan et al. 2008, Ruff 2006, van der Meulen 1995).

In his classic Mechanostat theory, Frost (1987) proposed that loading-induced strain magnitudes result in bone modelling and strengthening of bone (Frost 1987, 1990). While the strain magnitude counts, the rate at which the loading induced strains occur is also crucial (Liskova & Hert 1971, McLeod & Rubin 1992, Rubin & McLeod 1994, Turner et al. 1994a,b, 1995). With regard to the complexity of the phenomenon of loading and bone adaptation, not only the strain magnitude and rate (Mosley & Lanyon 1998, Rubin & Lanyon 1985, Turner et al. 1995), but also the strain frequency, direction, and distribution affect bone adaptation to mechanical loading (Lanyon 1987, 1996). Also, bone adaptation is driven by dynamic rather than static loading (Liskova & Hert 1971). In terms of the importance of the loading distribution, the unusual loading direction is more osteogenic than common predictable loading, as proposed by Lanyon (1987).

Exercise is a form of mechanical loading of bone. Impacts observed in running, jumping and falls (Földhazy et al. 2005, Lanyon et al. 1975, Milgrom et al. 2000a,b) can cause high strains and strain rates to the lower and upper extremities. High vertical impacts can be effective in strengthening bones (Burr et al. 1996, Heinonen et al. 1996, Kato et al. 2006, Rubin & Lanyon 1985) but they may also be too demanding for ordinary people. Thus the most effective exercise type is not necessarily the most feasible one. In general, exercise-loading can help to achieve higher mineral content, and the structure *per se* could also become stronger. But could there be a less demanding and equally beneficial exercise loading type to strengthen bones? If such a feasible and demonstrably effective exercise-loading type existed, the prevention of bone fragility might become easier.

Fracture of the proximal femur is one of the most devastating types of fracture. Fragile bone structures (*i.e.*, thin and porous cortices) are especially observed at the anterior and superior segments of the femoral neck (Bell et al. 1999a,b, Crabtree et al. 2001, Mayhew et al. 2005). Thus, a goal for osteoporosis prevention with exercise loading would be to find a feasible but also targeted exercise types for as many ordinary people as possible to strengthen bone structure in these vulnerable regions. In theory, exercise loading including impacts of moderate magnitude, high strain rate, and unusual direction might be feasible in terms of maximizing benefits (Burr et al. 1996, Lanyon et al. 1975, Milgrom et al. 2000a,b). Enjoyable, possible, and regular exercise loading varies between individuals, thus safe, approachable, and demonstrably effective exercise type options are needed to guide and help as many ordinary people as possible to achieve appropriate bone strength. Furthermore, this kind of focused prevention of bone fragility based on natural exercise loading might, at least partly, prevent people from sustaining fractures, thereby saving them and society from extra costs.

The purpose of this dissertation was thus to identify exercise-loading types that are associated with strong bones.

2 REVIEW OF THE LITERATURE

2.1 The Skeleton and Bones

Bone is a vital tissue with three functions: 1) to provide maximal mechanical competence with minimum weight for locomotion, 2) to protect the internal organs, and 3) to participate in mineral and blood cell homeostasis. Thus bone is a complicated but well-designed organ system responding to mechanical and physiological stimuli. (Currey 2002, Morgan et al. 2008)

2.1.1 Bone Tissue Composition and Turnover

Composition

Bone, being a living tissue, consists of inorganic (60% by weight), organic (30%), and water (10%) components and also includes blood vessels and living cells inside the structure itself. The inorganic part of bone is made of calcium hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$) crystals, which are mostly responsible for the stiffness of bone material. These plate-shaped apatite crystals include some impurities, mostly of carbonate, which increase the solubility of bone. Solubility is important for mineral homeostasis, and thus for bone adaptation to exercise loading among other things. (Currey 2002, Morgan et al. 2008)

The organic part of bone consists of type I collagen, some non-collagenous proteins, and bone cells. The organic part also has an essential influence on the mechanical and biochemical properties of the tissue as well as on the structure of the tissue. The organic part, especially collagen, determines the structural organization of both trabecular and cortical bone and is mostly responsible for its flexibility, and thus its capability to absorb energy (Lian & Stein 2008). Type I collagen has low solubility, and its cross-linking influences strength with its triple helix form. The cross-links keep the helixes anchored but fewer cross-links increase the risk of helixes separating, and so bone cracking. On the other hand, more cross-links compromise the flexibility, hence the capability to absorb energy (Morgan et al. 2008, Seeman & Delmas 2006). Collagen fibrils, in turn, are grouped in bundles to form the collagen fibre. In these fibrils, small gaps exist to offer space for noncollagenous proteins (osteocalcin, osteopontin, osteonectin among others). These specialized proteins also have a role in the control of mineralization and reconstruction of bone (Currey 2002) because together with collagen and synthesized by osteoblast bone cells, they accumulate in bone function as nucleators of hydroxyapatite (Lian & Stein 2008).

In addition to the inorganic and organic components, the amount of water in bone is an important factor for its mechanical behaviour. Poorly mineralized bones include a high proportion of water, while bones with a large amount of mineral include more organic material such as collagen. At very high level of mineralization, both water and organic material decline, which leads to stiff but dry, and hence, brittle bone (Boskey & Marks 1985, Boskey 1990, Currey 2002, Morgan et al. 2008, Sedlin and Hirsch 1966).

Turnover

There are cell types such as *osteoblasts*, *osteocytes*, and *osteoclasts* in bone tissue. *Osteoblasts* produce bone matrix and later become either flat lining cells or osteocytes. Osteoblasts are responsible for embryonic and postnatal bone formation and construction called modelling (Frost 2003). *Osteocytes* have a role in calcium homeostasis, and are partly guard the mechanical integrity of bone (Seeman & Delmas 2006). The network of osteocytes transmits mechanical signals based on mechanical forces. With regard to osteoblasts and osteocytes, *osteoclasts* are responsible for resorption, thus the remodelling of bone (Currey 2002, Seeman & Delmas 2006). Calcium homeostasis of bone is normally maintained by the formation and resorption of osteoblasts and osteoclasts respectively, and this interaction called "coupling" is under the control of mechanical forces and metabolic requirements.

Bone *modelling* includes the construction of skeleton by bone formation without prior bone resorption (Seeman 2006). While bone modelling is primarily observed during growth, remodelling occurs throughout life. Bone modelling typically provides more bone mineral than earlier. The amount of new bone will be refined, for instance, lay the mechanical demands that changes all the time as an infant or a child grows (longitudinal growth). While bone micromodelling occurs at cell level organizing cells and collagen, bone macromodelling controls the shape, size, and strength of bone, and all these can strengthen bone. This kind of phenomenon can be observed when bone expands from its outer, periosteal surface, and/or endosteal, inner surface, if a person changes his or her level of exercise. (Frost 1987, 1990, 1991, Kimmel 1993)

Bone *remodelling* also includes bone formation, but only after resorption at different locations of the endosteum and to a lesser extent at the periosteum (Orwoll 2003, Seeman 2006). The Bone Multicellular Unit (BMU) is responsible for the whole remodelling process from the initial bone resorption to final formation. The net change in bone mineral can vary according to anatomic location and the influence of mechanical loading. Typically BMU resorbs and replaces bone to keep the net change in balance. However, vigorous mechanical loading can even change the balance to positive if a level of exercise has increased from that of earlier habitual exercise loading (Frost 1987, 1990). The purpose of modelling and remodelling is to achieve optimal bone strength during growth and early adulthood and if possible to maintain it during later adulthood (Burr 2002, Currey 2002, Seeman 2006).

2.1.2 Micro- and Macrostructure of Bone

Microstructure

Bone is organized in four different ways: woven, lamellar, fibrolamellar, and Haversian bone. *Woven* bone is quite quickly created, randomly oriented, and is mostly seen in the foetus and in the callus immediately after fracture. It can extend to all directions. *Lamellar* bone is more slowly created and more precisely oriented in sheets, which vary in thickness. Different forms of lamellae such as the inner and outer circumferential lamellae of cortical bone, the interstitial lamellae of cortical bone, and lamellae of osteons can be observed. Lamellar bone may occupy large areas, typically circumferentially. *Fibrolamellar* bone is a combination of alternating sheets of woven and lamellar bone. *The Haversian* system is a cylinder of lamellar bone, a secondary osteon. Primary osteon, the functional unit of bone, is not surrounded by a cement sheet, while Haversian system is. Functionally, primary osteon can produce new bone, while Haversian system, *i.e.* secondary osteon can only replace old bone (Buckwalter et al. 1996).

Mechanically, primary bone is stronger than secondary bone (Currey 2002). In fact, it has been suggested that osteon morphology as a microstructure affects the fracture resistance of the *cortical* bone, thereby those with larger Haversian canals and osteons, in addition to fewer osteons seem to have more fractures at the femoral neck (Currey 2002). Thus, smaller osteons may be more effective in energy absorption because more osteons can be packed into the region (Yeni et al. 1997) to obstruct microcrack from travelling through the bone (Nalla et al. 2004, Seeman 2006, Taylor 2007).

Macrostructure

Bone can be classified as *cortical* or *trabecular* bone, although the material *per se* is basically the same. Some 80 weight percent of mature skeleton consists of cortical bone, which mostly occurs at the periosteal surfaces and in the middle of long bones, while trabecular bone is generally observed at the endosteal surfaces and ends of long bones. *Trabecular* bone can be considered to be highly specialized tissue, which has very different mechanical properties from that of cortical bone (Currey 2002). Trabecular bone includes large spaces, which reduce the weight of the bone, while cortical bone is more solid, thus it has greater density and less porosity. The porosity of trabecular bone is mostly over 50%, porosity between 50 and 15% is rarely observed, and porosity less than 15% is typical for cortical bone.

Trabecular bone has approximately 20 times more surface area per unit volume than cortical bone has, and its cells are situated between lamellae or on the surface of the trabeculae, thus they are directly influenced by marrow cells (Buckwalter et al. 1996). Trabecular bone is also more active, because its remodelling rate can be 5 to 10 times higher than the same in cortical bone (Buckwalter et al. 1996, Currey 2002). The organization of trabecular bone seems to be weaker than in cortical bone in terms of strength (Currey 2002). However, cell-covered surface area and blood vessels nearby enable aforementioned high rate of metabolic activity (Buckwalter et al. 1996). While trabeculae do not seem to be well organized in terms of lamellae, a microlevel organization can be close to perfect, since the grain of individual lamellae lies along the length of the struts or sheets, which increase stiffness and strength in that particular direction (Currey 2002). Since trabecular bone is less stiff than cortical bone, it has a useful capability to deform, and hence to absorb energy (Currey 2002, Buckwalter et al. 1996). Several characteristics such as bone volume fraction, trabecular number, thickness, and separation, form of plate or rod in architecture, connectivity density, and degree of anisotropy affect the strength of trabecular bone (Eckstein et al. 2007).

Cortical bone plays an important role in fracture prevention (Crabtree et al. 2001). Cortical bone seems to be responsible for most of the strength of whole bones (Crabtree et al. 2001, Haidekker et al. 1999, Pistoia et al. 2003). Cortical bone is needed for long bones, which are levers for loading in locomotion (Seeman 2006). While trabecular bone is better at absorbing energy, cortical bone is a stiff structure, which provides resistance against bending or torsion (Buckwalter et al. 1996, Orwoll 2003). There is high proportion of cell population completely surrounded by bone matrix in cortical bone (Buckwalter et al. 1996). Osteogenic cells at the outer *periosteal* surface affect the size and shape of bone, while cells at the inner *endocortical* surface mainly affect the thickness and position of the cortex in space (Allen et al. 2004). Only modest periosteal apposition can dramatically increase the resistance of bone to bending or torsion by tens of percents (Orwoll et al. 2003), and this periosteal apposition has been suggested to be primarily defined by mechanical loading environment (Judex et al. 1997, van der Meulen et al. 1996). While some 80 to 90% of increased cortical thickness seems to be characterized by periosteal apposition during growth, the remaining 10 to 20% comes from changes in the endocortex (Duan et al. 2001). Because periosteal apposition is greater than net endocortical resorption in youth, cortex is actually thickened even if endocortical apposition is negative. Females especially in adolescence may have positive endocortical apposition, however, most likely because of the estrogen effect as shown in Figure 1 (Järvinen et al. 2003, Lanyon & Skerry 2001).

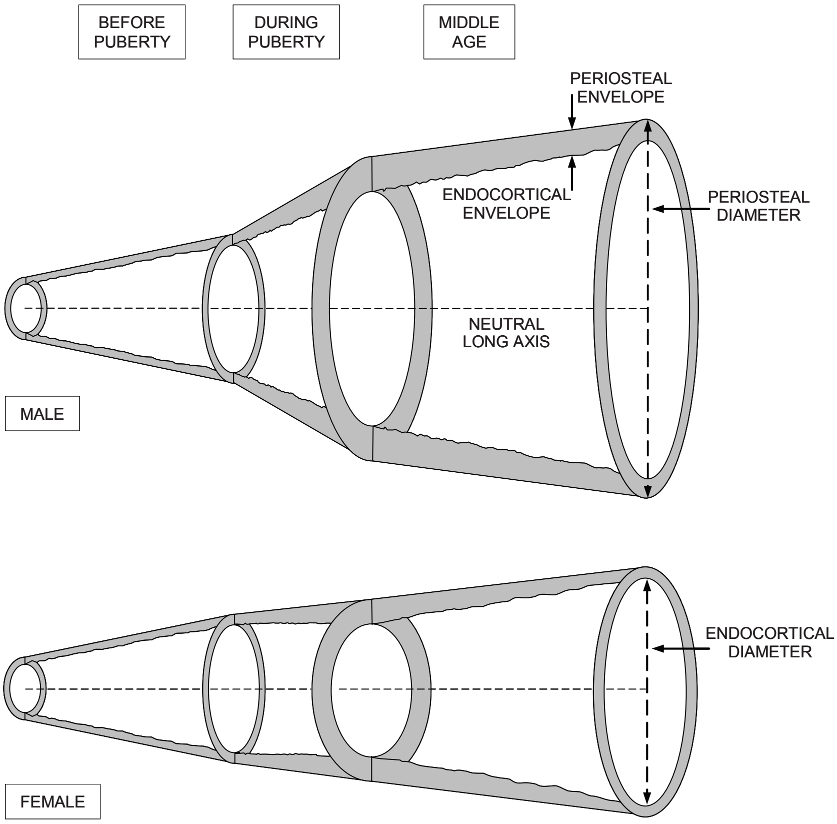


FIGURE 1 Schematic illustration of the behaviour of the periosteal and endocortical surfaces in males and females before puberty, during puberty, and in middle age. The inset shows the greater displacement of a cortex of similar thickness in young adult males than young females. This displacement is greater in middle age. The cortices are the same thickness in males and females in middle age but reduced relative to young age. Adapted from Duan et al. 2003.

2.2 Biomechanics of Bone

Again, it seems that locomotive and loading issues in addition to phylogeny define the specific functional organization and features of the skeleton and musculature. The skeleton is made of rigid bones, shaped for the specific functional purpose and interconnected by joints, attached to tendons, moved by skeletal muscles, supported by ligaments, and controlled by neural system (Currey 2002, Järvinen et al. 2005, Kannus et al. 2008, Sievänen 2005, Uusi-Rasi et al. 2008). Bodyweight induced reaction forces during movement are magnified by the moment arms of the musculoskeleton, which together cause the net muscle forces to be relatively high – multiples of bodyweight (Biewener 1991). From the locomotion perspective, bone must be stiff to resist bending and torsion, somewhat flexible to absorb energy, and light but competent for economical movement (Currey 2002, Seeman & Delmas 2006, van der Meulen 2001). The bone structure is considered the most relevant factor behind the bone fragility (Currey 2003, Järvinen et al. 2005, Kannus et al. 2008, Sievänen et al. 2007a).

2.2.1 Basic Concepts

The structural properties of bone consist of the size, shape, and architecture of bones in addition to the mechanical properties of bone tissue (Bouxsein 2008, Einhorn 1992, Järvinen et al. 2005). Forces such as the gravity and tension of muscles affect bones in habitual locomotion, while sudden impact forces may occur in jumps or falls. Bones are different in shape and size, thus the same force can cause higher compressive stress on smaller than bigger bones, because the same stress is exerted on a smaller area (Bouxsein 2008, Currey 2002). Similarly, the bone tissue should be distributed far from the neutral axis to better cope with bending, or the inadequate horizontal trabeculae can reduce ultimate strength with increasing risk of bone buckling (Duan et al. 2003, Einhorn 1992).

Compression, Tension, and Shear Forces

When a sample of material is compressed in one direction, it expands in the other two directions and this phenomenon is called Poisson's ratio (Currey 2002). In loading, pure longitudinal axial force such as *compression* slightly shortens and widens the bone, while *tension* lengthens and narrows the bone. Bending mainly compress the other side of the long bone and elongates the other. Bone is at its weakest for coping with *shear* forces, better at coping with tension, and at its best for coping with compression (Einhorn 1992, Turner & Burr 1993). Forces in habitual loading are most likely a combination of more than one, however (Einhorn 1992, Turner & Burr 1993). The anisotropic nature of bone reflects its function since bone structure is strongest in the primary loading direction (Bouxsein 2008).

Stress and Strain

When longitudinal axial force is targeted at a long bone, an equal internal resistance but opposite in direction will counter this load. The internal reaction, *stress*, is distributed over the cross-sectional area of the bone and the bone will be deformed, i.e. *strained*, when shortened in the longitudinal direction compared to the original direction (Figure 2, Currey 2002, Einhorn 1992, Turner & Burr 1993). Typical strain (ε) in properly mineralized bone tissue (ash mass 45 to 85% by mass) is small, only some tenths of a percent (Currey 1984, Einhorn 1992, Frost 1987, 2003a,b).

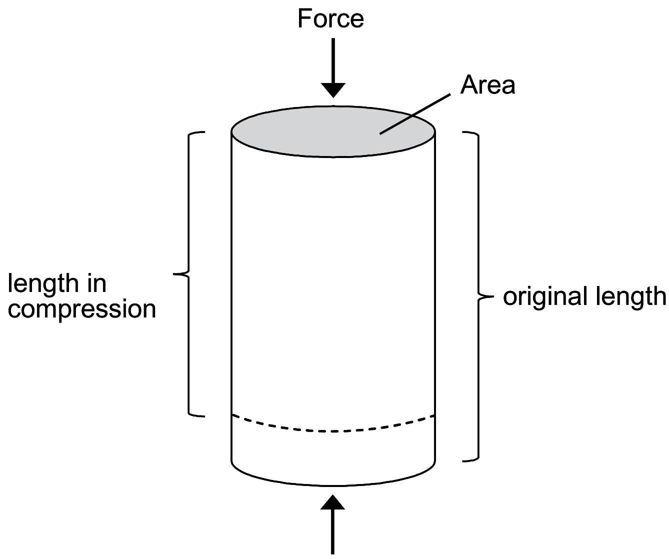


FIGURE 2 Schematic illustrations of stress and strain in bone. Stress is force per area and strain is original length minus length in compression divided by the original length. Adapted from Turner & Burr 1993.

Elasticity and Plasticity

When the stress and strain relationship is known, mechanical properties such as stiffness, strength, energy-absorptive capacity *i.e. toughness*, and deformation can be derived. This relationship is linear before the yield point. The slope of the stress-strain curve represents the modulus of elasticity, *i.e.* Young's modulus, which measures *the stiffness* or rigidity of bone. The trabecular bone structure is less stiff than the compact bone structure, which increases its capability to deform and hence to absorb energy (Buckwalter et al. 1996, Currey 2002). In the elastic region, bone returns to its original shape when unloaded. At a higher level of stress and strain, the elastic limit is exceeded and permanent deformation occurs, this is called *the plastic* region of the curve (Einhorn 1992, Turner & Burr 1993).

Point of Failure

The ultimate strength is achieved and bone fails when maximally stressed (Figure 3). As mentioned, the strength can be tensile, bending, compressive, and torsional depending on the loading conditions. The ultimate compressive strength of cortical bone can be some ten times greater than in cancellous bone (Buckwalter et al. 1996). The area under the elastic and plastic region is the resilience and toughness of bone respectively. When the elastic limit, the yield point is exceeded, the bone does not regain its original form. In other words, permanent damage has occurred, when the deformation occurs in the plastic region. However, bone does have some plastic properties (Einhorn 1992). The material which will fail immediately after its yield point is brittle, like bone in very old age or among osteopetrotic patients (Currey et al. 2007, Einhorn 1992).

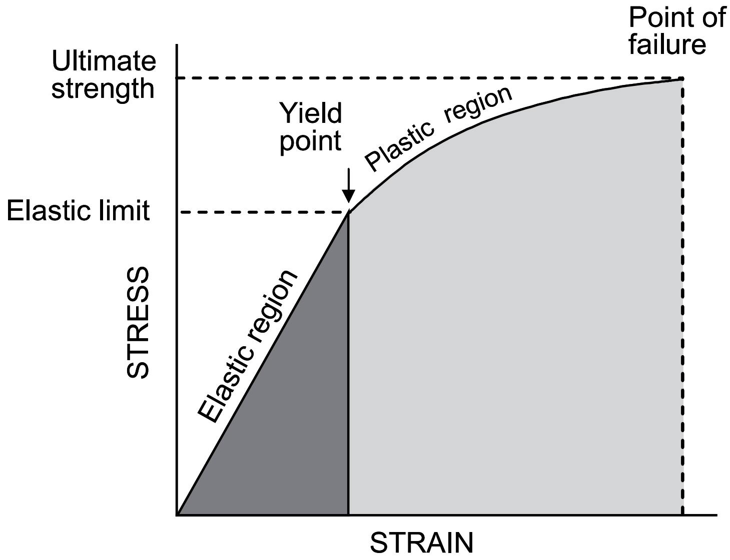


FIGURE 3 Schematic stress-strain curve. At the elastic region, before yield point, loading will result nonpermanent deformation. At the plastic region, however, bone would be permanently deformed by load. The point of failure is known as the ultimate strength of the bone. Adapted from Einhorn 1992.

2.2.2 Whole Bones and Their Mechanical Competence

Whole Bones

Bones as organs can be classified into *short*, *flat*, and *tubular* (long) bones. *Short* bone is irregular in shape, includes thin cortices and is filled with trabecular bone, thus typically formed to carry compressive load (Buckwalter et al. 1996, Currey 2002). *Flat* and *tubular* bones have one direction much shorter or longer than others. *Tubular* bones also have expanded ends, *i.e.* metaphysis and epiphysis at the end of thick-walled tubular diaphysis, which is the middle part of a long bone. Inside mature bone has a central part consisting of fatty or hematopoietic marrow surrounded by bone tissue (Buckwalter et al. 1996, Currey 2002). *Flat* bone typically consists of two thin sheets of cortical bone separated by some trabecular bone and formed either to protect the internal organs or to provide origin of muscles (Currey 2002).

Tubular (long) bones are typically hollow. Although hollow, they also need to be thick walled enough to avoid local crushing called buckling (Currey 2002). With increased bone width it is possible to avoid breaking, but thick walls are for coping with local buckling. A thin-walled hollow bone with large radius would probably rather buckle than break, while the opposite would presumably happen if a thick-walled bone with a small radius is ultimately bent (Rittweger et al. 2000). With unlimited amount of mass, of course, both risks would decrease but metabolic costs in terms energy consumption would increase (Currey 2002). Also, a small curvature typically seen in *tubular* (long) bones is speculated to help

in predicting strain direction (Lanyon 1987, 1996). This curvature is greater in adults than in children (Backman 1957).
Mechanical Competence

Taken together the bone from its mechanical properties at tissue level to whole bone competence as an organ, the primary function of the skeleton is locomotion, which needs rigid and strong bones (Figure 4, Järvinen et al. 2005). The strength of bone can be defined as the force required to produce mechanical failure under a specific loading condition (Beck 2003). The amount of bone mineral represents the bulk of which the whole bone as an organ is made, thus the bulk is not a direct indication of the actual bone strength (Currey 2002, Frost 1990, Sievänen et al. 2000). The strength and rigidity of the whole bone are substantiated by the interaction of material properties, amount of material, organizational, and morphological issues of bone tissue and organ (Järvinen et al. 2005). Although the bone materials *per se* could be better, its structural properties are one of a kind, but a whole bone is a masterpiece (Taylor 2007, 2008). It is the whole bone structure, neither its mass, mineral content nor density alone, which determines the bone's mechanical competence (Järvinen et al. 2005).

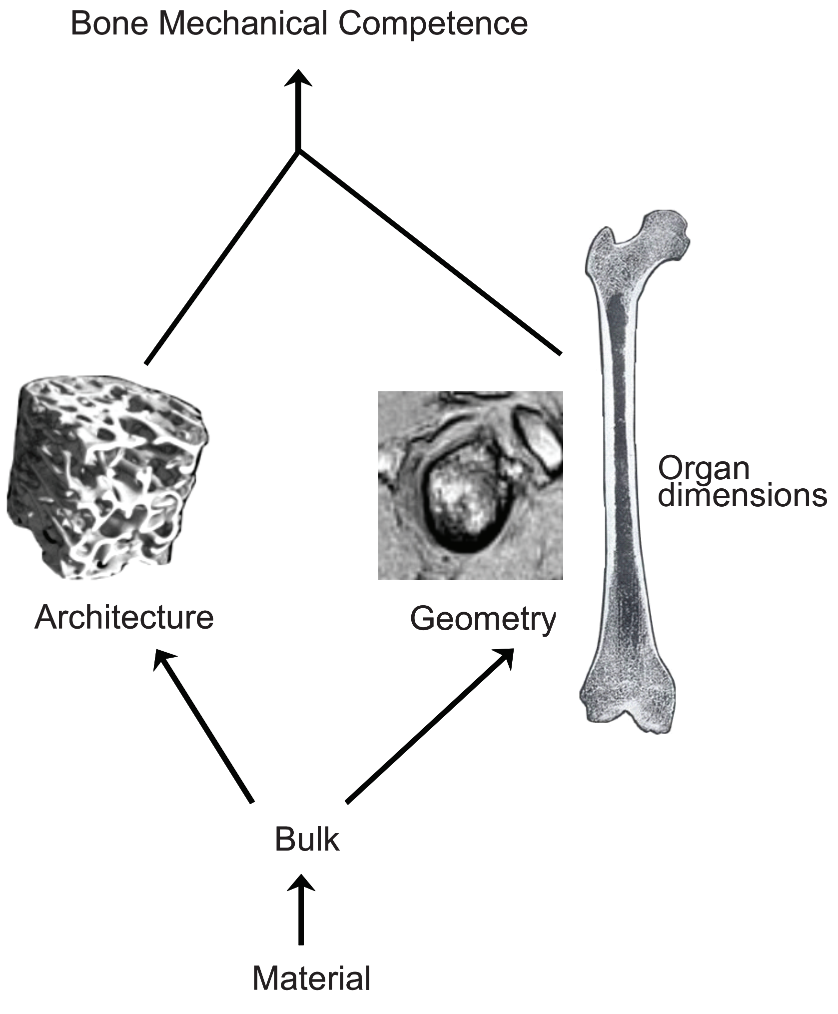


FIGURE 4 Bone mechanical competence and its determinants. Adapted from Järvinen et al. 2005.

2.2.3 Measuring Human Bone Structure *in vivo*

Osteoporosis is defined as a systemic skeletal disease characterised by low bone mass and microarchitectural of bone tissue with a consequent increase in bone fragility and susceptibility to fracture (Consensus development conference 1993). According The World Health Organization (WHO), a person is classified as osteoporotic if she or he has a DXA (dual energy x-ray absorptiometry)-measured areal total bone mineral density (aBMD) under –2.5 T-score, *i.e.* ~30% under the average for a 20-year-old of the same gender (WHO 1994). The challences of measuring bone structural traits *in vivo* are described in the next paragraph.

Dual Energy X-ray Absorptiometry (DXA)

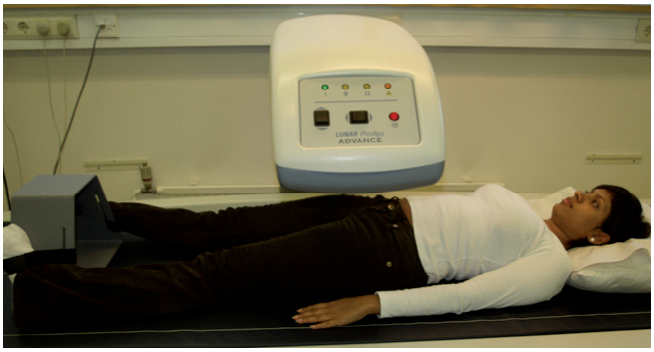
With traditional *DXA*, bone mineral content (BMC), *i.e.* the amount of bone material, can be measured in addition to the BMD (Figure 5, Sievänen et al. 1996). The BMC is the bulk parameter, which cannot describe structural features of bone (Järvinen et al. 2005, Melton III et al. 2005, Sievänen et al. 2000), while BMD offers rough information on bone dimension based on planar scan (Sievänen et al. 1996). At the population level, each standard deviation (SD) of areal bone density (aBMD) decreased at the femoral neck indicates an increased risk of 2.5-fold for hip fracture (Kanis et al. 2008). At the individual level, however, the major part of fractures in elderly people occur in those with normal or somewhat declined but not osteoporotic aBMD (Kanis 2002, Schuit et al. 2004, Stone et al. 2003). DXA is a precise method (<2%) with low radiation dose, but in terms of predicting fractures it could be better (Sievänen et al. 1996, Stone et al. 2003). Areal BMD by DXA explains about 60% of bone rigidity (Järvinen et al. 2008, Wehrli et al. 2002, 2007). One factor causing uncertainty in DXA-measurement stems from the planar nature of scanning, *e.g.*, the rotation of the femur in the measurement situation can affect bone width because the femur is not a completely circular in shape. The inherent inaccuracy of the DXA-measurement arises from soft tissue and bone marrow composition in addition to body size (Sievänen 2000, Bolotin et al. 2001a,b, Bolotin 2003). All these factors can either mask or exaggerate the result (Sievänen 2000).

DXA-based Hip Structural Analysis

Computer programs have been developed to derive femoral neck geometry using stress analysis of single plane (Beck 2007). Hip Structural (HSA) and Advanced Hip Analysis programs (AHA) offer an estimate of structural rigidity from the proximal femur based on the planar DXA-scans (Crabtree et al. 2002). The purpose of this is to improve the predictive value of hip bone mineral data for osteoporosis risk assessment (Beck et al. 1990). Several structural variables can be derived based on DXA-measurement with the limitation of planar scan (Beck 2007, Sievänen et al. 1996). One of those structural variables is the cross-sectional area (CSA, proportional in principle to BMC) of bone, which describes its axial strength, and thus how resistant the bone is to deformation under compression and tension. Bone width (W) affects the resistance of bone to break, a slender bone would likely break but a wider bone would not. Cross-sectional moment of inertia (CSMI) and section modulus (Z) are surrogates for the bone's resistance to bending and torsion on a given plane. CSMI and Z depend on the amount of material in the cross-section where material is distributed. Z varies as a product of the third power of the distance from the central axis, and CSMI varies as a product of the fourth power. As mentioned, the planar DXA-scan can disregard cross-sectional shape of bone, which is other than circularity, however (Ruff 2006).

Peripheral Quantitative Computed Tomography (pQCT)

Peripheral quantitative tomography (pQCT) is a versatile method for measuring human long bone cross-section *in vivo* (Figure 5, Bousson et al. 2006, Rauch et al. 2001, Sievänen et al. 1998). The capability of pQCT to predict the failure load of radius may be better than the same of DXA (Muller et al. 2003). Several structural characteristics such as trabecular and cortical density (TrD, CoD), total and cortical cross-sectional areas (ToA, CoA), bone strength index (BSI), and bone mineral content (BMC) can be measured with some variation in precision (<1% to 8%, Sievänen et al. 1998). A whole body quantitative computed tomography (QCT) would allow the measurement of more central body parts such as the femoral neck but pQCT offers some benefits such as lower cost and radiation exposure than QCT (Sievänen et al. 1998). A limitation of the pQCT is that it cannot be used for the measurement of the proximal femur, the clinically important site in terms of fractures (Sievänen et al. 1998).



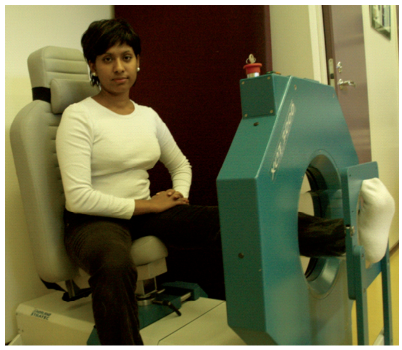


FIGURE 5 Example of a DXA-measurement (on left) and a pQCT-measurement (on right).

Magnetic Resonance Imaging (MRI)

Recently, MRI has been used for bone measurements in addition to its more common usage in evaluating soft tissues (Figure 6, Duncan et al. 2002, Forriol & Shapiro 2005, McKay et al. 2004, Murdoch et al. 2002, Sievänen et al. 2007b, Wehrli 2007, Woodhead et al. 2001). One of benefits of MRI is the absence of radiation dose, which allows measurements for women of fertile age, for instance (Sievänen et al. 2007b). Also, MRI seems to be reasonably accurate method (~1% in evaluating the outer surface, Sievänen et al. 2007b) but it also includes challenges. One of these, especially at the femoral neck, is related to the detection of the endosteal boundary of the cortex, where the red marrow can increase the inaccuracy (Wehrli 2007). At the periosteum, tendons and ligaments can be mistakenly assigned to cortical bone. Also, a chemical shift artefact between fat and water may affect the accurate detection of the periosteal boundary (Wehrli 2007). MRI is also still quite an expensive method, although already widely available in hospitals. On the other hand, MRI allows evaluation of muscles and other soft tissues in addition to bone.

FIGURE 6 Example of a Magnetic Resonance Imaging device.

Other Methods

There are also methods for estimating bone rigidity. The traditional clinical variables of ultrasound to measure are sound of speed (SOS) and broadband ultrasound attenuation (BUA) (Kanis 2002, López- Rodríguez et al. 2003, Sievänen et al. 2001, Weeks et al. 2008). However, new ultrasound methods to better project the structure of bone are under development (Barkmann et al. 2008, Glüer 2007, Karjalainen et al. 2008, Moilanen 2008). Also, radiography has been used to investigate structural properties of the proximal femur (Pulkkinen et al. 2008).

2.2.4 The Interaction of Muscles and Bones

It is essential to know and measure the structure of bones. However, the body movements and forces that bones must be able to resist are produced by coordinated contractions of skeletal muscles (Biewener 1989, Ducher et al. 2005, Runge et al. 2004, Sasimontonkul et al. 2007). The concentric or eccentric muscle work comprises the fundamental source of mechanical loading on the skeleton – the resultant loading pattern within the affected bones can vary substantially in many ways. In order to survive, the musculoskeleton must be able to adapt to the changes of the loading environment (Biewener 1989, Kannus et al. 2008, Kazakov 1997, Lovejoy 1988, Turner 1998, Uusi-Rasi et al. 2008). Muscles transmit forces through tendons and forces can be transmitted directly from ground reaction forces. Muscles are often attached close to the joints, which increases disadvantage in terms of muscle force production and advantage in terms of speed production from joints (Currey 2002). Thus, muscle forces must overcome the resistance of bodyweight using these weak *lever arms*, the reason why muscle forces against bones at muscle insertions seem to be two to ten times higher compared to ground reaction forces alone (Currey 2002, Frost 1987). An example of interaction of muscles and bones in force production is shown in Figure 7.

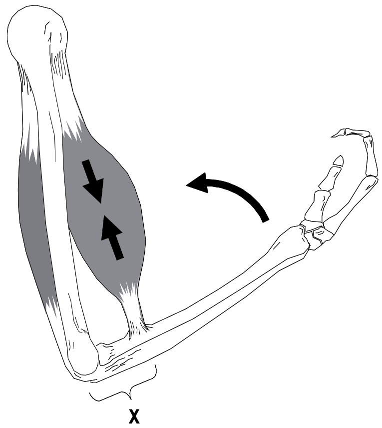


FIGURE 7 Illustration of a muscle-bone interaction in force production to provide movement. The close insertion of the tendon of musculus biceps brachii from the elbow joint increases the need for muscle force to provide movement. Adapted with permission from Józsa & Kannus 1997.

Muscles as Stabilizers and Movers of the Body

The human, professional athletes excluded, no longer needs to run for his or her nutrition, which was the case for our ancestors (Bramble and Lieberman 2004). Our upright posture (bipedality) places the centre of mass almost directly over the lower extremities (Lovejoy 1988). The upper body needs to be stabilized over the centre of mass, which has an effect on our musculature: the gluteus maximus (buttock muscle), which previously served as a mover of the hip joint, has mainly become a stabilizer of upper body position during walking (Biewener 1989, Lovejoy 1988, Ohman et al. 1997). Today, glutei muscles are the largest muscle group in the human body. By adopting an upright posture, humans align their limbs more closely with the ground reaction force, reducing the forces that muscles must exert and bones must resist at the same time. The joint moments and energy expenditure are reduced relative to the magnitude of the ground reaction force (Biewener 1989).

Bones as Levers of Movement

The mechanical loading of an exercise performance is caused by a combination of bodyweight and muscle tension (Biewener 1991, Bitsakos et al. 2005, Lanyon et al. 1975). Tubular (long) bones typically work as levers of movement. In movement, the role of joint moment behind bone rigidity is still contradictory (Anderson et al. 1996, Bareither et al. 2006, Grabiner 2006, Moisio et al. 2004, 2006). While static factors such as body mass and height have been suggested to explain bone rigidity in the weight-bearing lower extremities, few have analysed these variables as part of the dynamic loading situation (Petit et al. 2005). In a dynamic loading situation, body mass (as a surrogate of force) and height (as a surrogate of leverage) have been suggested as determinants of the joint moment (Moisio et al. 2004). This means that movement, which increases leverage, and thus the distance between the ground reaction force and the centre of gravity, also increase bending forces against the bone. Similarly, a movement with higher ground reaction force would increase the stress and strain of the loaded bone via increased axial forces in addition to bending forces. Walking would cause ground reaction forces of three times bodyweight, while jogging and hopping would cause more (Anderson et al. 1996, Moisio et al. 2004, Vainionpää et al. 2006). Also, a similar jump from the same height causes a greater load for a heavier but equally tall person's hip, or conversely, a taller, but lighter person can experience high loads at the hip, because of the greater lever arm of the femoral neck on landing.

2.3 Adaptation of Bone to Mechanical Loading

Bone form follows its function (Huiskes 2000a, Ruff 2005, Ruff et al. 2006). Wilhelm Roux was the first to state (in 1881) that bone adaptation was a result of a self-regulating system at the cell level (Huiskes 2000a,b). Julius Wolff (in 1892) refined and several other researchers processed and also criticized the idea of bones as mechanically optimal structures, which can adapt to current loading conditions (Frost 1987, 1990, 2003a,b; Huiskes 2000a, Ruff et al. 2006, Verhulp et al. 2008). Briefly, the idea of the theory is the following: increased strain compared to typical level would cause an error signal, which would lead to the deposition of more bone tissue through the feedback system, while decreased strain would lead to resorption of bone (Frost 1990, Lanyon 1990, Ruff et al. 2006). The typical strain level could vary between skeletal sites, and several other factors such as hormones and nutrition in addition to loading affect the process (Lanyon 1987, Lanyon & Skerry 2001, Marenzana & Chenu 2008, Sievänen 2005).

2.3.1 Mechanotransduction

At microlevel, a current theory of mechanical signals and how they are transmitted and translated to adaptation of bone is known as *mechanotransduction*. There are different theories of loading signals and how they are turned into effect on bone, however: In *stress-generated potentials-theories* (SGP), the effect is suggested to be transmitted through electricity. In *piezoelectricity theory*, mechanically unstrained crystals are polarized with respect to each other when bone is loaded. In *streaming potentials theory*, extracellular fluid will be charged when in contact with the solid surface (Currey 2002). Currently, *the theory of slight shear strain caused by fluid flow* is suggested as the most promising theory of stimulus for adaptive response of bone (Bababac et al. 2005, Currey 2002, Frost 1987, Martin 2000, Mi et al. 2005, Scott et al. 2008, Taylor et al. 2006). Originally these stress induced strains arise from the muscle work of locomotion and convert part of this mechanical energy into chemical energy, which eventually results in the synthesis of new bone tissue (Currey 2002, Frost 1987, Martin 2000).

The theory of *mechanotransduction* requires phases from *mechanocoupling* to the final *effector response*. Mechanocoupling describes the process of load signalled to cells. With regard to mechanotransduction, mechanical signals can directly affect bone cells or be turned into chemical signals and affect via secondary messengers. Finally, the effector cells such as osteoblasts and osteoclasts respond to the original stimulus via a complicated cascade of events (Currey 2002, Forwood 2001, Frost 1987,1990, Turner & Pavalko 1998, Scott et al. 2008, Zernicke et al. 2006). The details of this microscopic mechanosensory system and associated pathways from mechanical stimulus to the formation or resorption of bone tissue are complex and not yet fully established (Karsenty 2003). The goal of the mechanosensory control system, however, is to maintain the mechanical competence of the loaded bone to be reasonable in terms of the predominant loading environment while keeping the loading-induced deformations well within a specified safety range (Currey 2002).

2.3.2 Mechanostat Theory

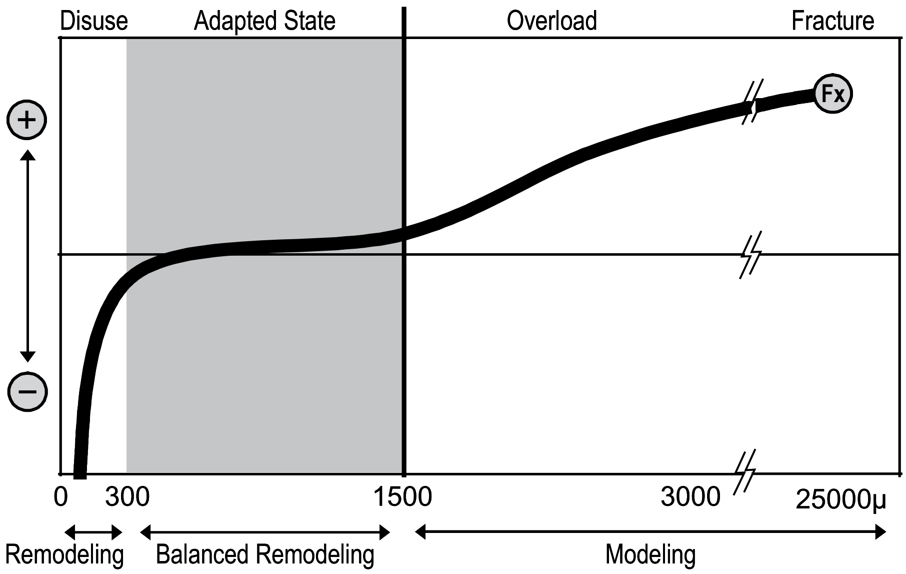


FIGURE 8 Schematic illustration of Mechanostat theory. The modelling dominates at the overload region, while the remodelling dominates at the disuse region. In the adapted state, bone resorption and formation are in balance and bone rigidity is maintained. Adapted from Frost 2003b.

The theory behind bone adaptation is known as *the Mechanostat theory* (Figure 8, Frost 1987,1990) on analogy to a thermostat regulating room temperature. In his classic Mechanostat theory, Frost (Frost 1987) proposed that loading-induced *strain magnitudes* within the range from 1500 to 3000με result in bone modelling and strengthening of bone, while strains below 100 to 300 με lead to remodelling (Frost 1987, 1990). He defined the lower threshold as minimum effective strain (MES). Lanyon (1987) refined this notion and suggested that rather than only magnitude based MES, a more comprehensive concept called MESS, minimum effective strain related stimulus, would better describe the bone adaptation to mechanical loading. As the acronym implies, MESS is a complex phenomenon influenced by many major modulating factors (Lanyon 1987). While the strain magnitude counts, *the strain rate, i.e. the speed of load at which the loading induced strains occur during one cycle*, is essential (McLeod & Rubin 1992, Rubin et al. 2002, Rubin & McLeod 1994, Turner et al. 1994, 1995). In line with this notion, in the 1970s, Liskova and Hert (1971) already observed that bone adaptation is driven by dynamic rather than static loading, which was corroborated in further studies (Lanyon & Rubin 1984, Turner 1998). Besides the strain magnitude and rate, the strain distribution is also important, meaning that the unusual loading direction is more osteogenic than common predictable loading as proposed by Lanyon (1987).

2.3.3 Experimental Loading and Skeletal Response

Skeletal adaptation to increased mechanical loading is a very slow process and can take several months to years to observe changes, which can be detected by measurement. Deterioration of bone structure is much faster than its strengthening (Sievänen et al. 1994). Skeletal adaptation to loading is affected by the magnitude of the strains within the bones, the strain rate, the strain distribution, in addition to the number and frequency of repetitions (Borer 2005, Gross et al. 2004, Duncan & Turner 1995, Lanyon 1984, 1987, 1996, Umemura et al. 2002).

Strain Magnitude

Strain magnitude clearly is one of the major factors behind bone adaptation (Carter 1984, Rubin & Lanyon 1985). Rubin & Lanyon (1985) characterized the wing-flapping of turkey ulna and divided the applied load into compressive and tensile loads. It was shown that 1000 to 4000 $\mu\varepsilon$ increased percentual change in bone area quite linearly. Microradiograph demonstration indicated evidence of bone formation on outer periosteal surface but no evidence of intra-cortical remodeling or endosteal, inner surface, resorption (Rubin & Lanyon 1985).

Strain Rate

Although peak applied strain seemed to be a major factor influencing bone adaptation, it was stated that large strain alone might not to be enough for activating bone cells. In the early 1980's, in fact, it was suggested that strain magnitude would only increase 10% of the surface new bone deposited after accounting for strain rate in applied loads (O'Connor & Lanyon 1982). Thus it would not be the only factor directly proportional to bone strength as proposed by Frost in his earlier publications (Frost 1983, Turner et al. 1995, Weinbaum et al. 1994). Indeed, high strain rate was also required to stimulate bone formation (McLeod & Rubin 1992, O'Connor & Lanyon 1982, Rubin & McLeod 1994, Turner et al. 1994, 1995). In animal experiments, Rubin and McLeod (1992, 1994) used rather low magnitude of load, but higher strain rate still seemed to strengthen bone compared to lower strain rate. Also, the high strain rate has been suggested to demonstrate 50% greater osteogenic effect than moderate strain rate, which, in turn, has been suggested to demonstrate over 10% greater effect than that of low strain rate (Mosley & Lanyon 1998).

Frequency of Repetitions

The major finding of the pivotal studies of Rubin and McLeod (1992, 1994) was that the magnitude and *frequency, i.e. number of repetitions per time*, were quite linearly related to bone adaptation, except possibly at high loading frequencies (Turner 1998). In detail, a strain magnitude of 2000με with a load cycle per second produced exactly the same bone effect as 100με with 20 load cycles per second (Rubin and McLeod 1992, 1994, Turner 1998). It has also been shown that a frequency of 20 Hz can more than double the effect compared to one Hz (Rubin et al. 1990, Rubin & Lanyon 1985, Rubin & McLeod 1994). Also, a great number of very low magnitude strains at low rate may stimulate the osteogenic effect of high magnitude strain stimulus (Mosley 2000).

Strain Distribution

With regard to the strain distribution and its role in bone adaptation, Lanyon (1992) suggested that osteogenic response would be increased if the distribution of strain were unusual (Frost 2003a,b, Lanyon 1982, 1992, Turner et al. 1995). For example, loading in torsion might be more osteogenic than loading in normal longitudinal compression (Lanyon 1992). On the other hand, torsion is a minor component of the normal loading experienced by most long bones (Biewener 1991). Now, finite element modelling offers an opportunity to explore strain distribution, although not much has so far been examined. Based on the few models, unusual loading such as a fall seems to cause unusual strain distribution for the femoral neck, thus the superior region of the neck can be most vulnerable in initiating fracture in such cases (Carpenter et al. 2005, Verhulp et al. 2008).

Dynamic Loading

In the 1970s, the first study was accomplished to test if static or dynamic loading would better affect bone (Liskova & Hert 1971). In their animal experiments, Lanyon and Rubin (1984) used mixture of bending load, compression and torsion with similar magnitude in static and dynamic cases and showed that dynamic load is actually much more efficient for strengthening bones. Particularly, the change in geometry of bone seemed to be directly proportional to peak applied strain in dynamic loading situation (Lanyon & Rubin 1984).

Duration and Cycles

To be effective, the duration of a single training session does not need to be long (Lanyon 1984, 1992, Umemura et al. 1997, 2002). Rubin and Lanyon (1984) suggested that only some 40 loading stimuli, repeated more than once a day, would be enough to improve bone strength (Rubin & Lanyon 1984). Dividing loading into two sessions including four hours rest between, can even double this positive effect. Also, a 30-second interval rather than a 3-second interval would intensify the process (Umemura et al. 2002). Bone adaptation is indeed load and time-dependent and the rest period between the loading sessions can modulate the osteogenic response (Rubin & Lanyon 1984, Turner & Robling 2003, 2005, Umemura et al. 1997, 2002). Moreover, the initial mechanosensitivity to loading returns after a day and night of nonloading period (Turner & Robling 2003, 2005).

2.4 Exercise Loading and Human Bone

Exercise as a functional stimulus produces a combination of compressive, tensile, and shear forces in bone (Einhorn 1992, Rubin & Lanyon 1985). The way this combination of mechanical load in exercise loading is produced seems to explain bone rigidity (Haapasalo et al. 2000, Heinonen et al. 2001a, 2002, Kaptoge et al. 2003a, Liu et al. 2003). Exercise can, indeed, cause very different mechanical loading in terms of measured or estimated loading magnitude, the strain rate, the strain distribution, and the number and frequency of repetitions.

2.4.1 Measuring Actual Strain in Human Bone Loading

Knowledge of actual strains occurring in human bones during different exercise activities is still scarce. Few human studies have been accomplished with rather small numbers of participants and wide individual variance has occurred in all activities. Also, the background of the participants has varied greatly and only a couple of exercise-loading activities have been tested (Burr et al. 1996, Földhazy et al. 2005, Lanyon et al. 1975, Milgrom et al. 2000a, b) such as walking, bicycling, stepping, leg pressing, and running for lower extremities (Burr et al. 1996, Lanyon et al. 1975, Milgrom et al. 2000a, b) and push-ups and arm-curl for upper extremities (Földhazy et al. 2005). Because strain gauge attachment among other related factors may differ between studies, caution may be needed when interpreting the forthcoming results.

Strain and Strain Rate for the Tibia

In Table 1, actual strains and strain rates in different activities are characterized for human tibia (Burr et al. 1996, Lanyon et al. 1975, Milgrom et al. 2000a,b). When the peak of a single strain was tested alone, compressive strain magnitudes in the same exercise activities were higher compared to tensile strain magnitudes in all activities. In terms of minimal effective strain (MES), around 1500με was achieved in leg press and drop jumps (Milgrom et al. 2000a, b). When strain magnitude of uphill zig-zag running (classified as moderate magnitude impact loading) caused somewhat under 1500με, drop jumps (classified as high magnitude impact loading) from different heights caused clearly higher compressive strain, around 2000με (Milgrom et al. 2000b). Furthermore, drop jumps from lower heights caused equal but not higher strains compared to greater heights because of increased range motion during landing (Milgrom et al. 2000b).

While the differences between the activities in strain magnitudes were high, the strain rate differences were even higher. The strain rate in walking, bicycling, stepping, and leg pressing were under 10000με/s, and exceeded 10000με/s in drop jumps (Burr et al. 1996, Lanyon et al. 1975, Milgrom et al. 2000a,b). However, the strain rate was ~20000με/s in uphill zig-zag running and ~30000με/s in the sprinting. Thus sprinting straight forward and jogging caused highest strain rates but uphill zig-zag running was not far behind (Burr et al. 1996).

TABLE 1 Actual strains of the human tibia in different activities.

Activity	Compressive Strain (με)	Tensile Strain (με)	Compressive Strain Rate ($\mu\varepsilon * s^{-1}$)	Tensile Strain Rate ($\mu\varepsilon * s^{-1}$)	Study
Walking (~5 km/h)	430 to 540	400 to 840	3300 to 7200	4000 to 11000	Burr et a. 1996, Lanyon et al. 1975, Milgrom et al. 2000a
Bicycling (60 cycles/s, 100W)	290	270	1500	1300	Milgrom et al. 2000a
Stepmaster	1010	740	3100	3000	Milgrom et al. 2000a
Leg press	1680	1380	9800	8200	Milgrom et al. 2000a
Jogging (8 to 10 km/h)	580 to 880	630 to 850	27400	12000 to 13900	Burr et a. 1996, Lanyon et al. 1975
Uphill zig-zag running	1230	740	20900	13600	Burr et a. 1996
Sprinting (14 to 17 km/h)	970 to 2100	650 to 1420	14500 to 34500	7800 to 20200	Burr et a. 1996 Milgrom et al. 2000b
Drop jump (26 cm height)	1910	900	13200	7600	Milgrom et al. 2000b
Drop jump (39 cm height)	1990	920	11300	5000	Milgrom et al. 2000b
Drop jump (52 cm height)	2100	1010	8700	4800	Milgrom et al. 2000b

Strain and Strain Rate for the Radius

Actual strains and strain rates for radius have been tested only in few exercise-loading activities (Table 2, Földhazy et al. 2005). In compression, arm curl movement caused ~800με, while ~3000με were achieved during push ups and fall. Tensile strains during the same movements were mostly under 500με, chin-up hanging causing ~1000με, however. Moreover, the dorsal radius was under constant compression in the push-up exercise loading (Földhazy et al. 2005).

The strain rates were respectively 45000με/s and 20000με/s after falling from standing and kneeling. These strain rates were far beyond the strain rates in other activities such as arm curl, chin-up hanging, push-ups, and wrist curl, all of which caused less than 5000 με/s (Földhazy et al. 2005).

TABLE 2 Actual strains of the upper extremities in different activities. *

Activity	Compressive Strain (με)	Tensile Strain (με)	Compressive Strain Rate ($\mu\varepsilon{*}s^{-1}$)	Study
Arm curl with 7 kg weight	800	400	<5000	Földhazy et al. 2005
Chin-up hanging	200	1000	<5000	Földhazy et al. 2005
Push-ups on knees	3200	-	<5000	Földhazy et al. 2005
Wrist curl in flexion with 2 kg weight	800	500	<5000	Földhazy et al. 2005
Wrist curl in extension with 2 kg weight	200	500	<5000	Földhazy et al. 2005
Fall forward from kneeling **	1500	100	20000	Földhazy et al. 2005
Fall forward from standing **	2700	300	45000	Földhazy et al. 2005

** Only rough estimates are given because the exact numbers were not reported (Földhazy et al. 2005)*
*** landing on extended hands*

2.4.2 Estimating Strain in Human Bone Loading

While direct strain measurements are difficult to accomplish and thus rarely carried out (Burr et al. 1996, Földhazy et al. 2005, Lanyon et al. 1975, Milgrom et al. 2000a,b), indirect strain and strain rate estimation are more often used for the lower extremities (Table 3). In all exercise loading types, ground reaction forces or forces estimated by acceleration in relation to bodyweight may vary greatly depending on the measurement device utilized, or site of measurement in addition to the group studied. Stepping, vigorous running, slalom skiing or jumping can cause ground reaction forces from two to ten times bodyweight, triple jump even up to twenty times bodyweight (Bassey et al. 1995, 1998, Daly et al. 1999, Heikkinen et al. 2007, Heinonen et al. 1996, 2001a, Vainionpää et al. 2006, van der Bogert et al. 1999, Weeks & Beck 2008a,b). Ground reaction forces for the upper extremities have only been measured in gymnastics, mean forces being between 1.5 and 3.6 times bodyweight and rate of movement being 25 to 70 ms (Daly et al. 1999).

TABLE 3 Load magnitude and load rate measurements in human bone loading in different exercises.

Activity	Peak GRF (BW)	Rate of Force (BWs^{-1})	Effective load rating ($BW * BW s^{-1}$)	Study
Walk (3 km/h)	1.2 to 1.8	N.A.	N.A.	Vainionpää et al. 2006
Walk (5 km/h)	1.2 to 2.5	8	10 to 20	Heinonen et al. 2001a, Vainionpää et al. 2006, van der Bogert et al. 1999, Weeks & Beck 2008
Dance step	2.7	50	130	Weeks & Beck 2008
Multidirectional stepping	2.1 to 5.6	N.A.	N.A.	Heinonen et al. 1996, Vainionpää et al. 2006
Side step in tennis or soccer	2.9	120	340	Weeks & Beck 2008
Hop	3.4	50	160	Weeks & Beck 2008
Heel drop	3.6	40	130	Weeks & Beck 2008
Cross-country skiing	4.0 to 4.6	N.A. *	N.A.	van der Bogert et al. 1999
Slalom skiing (steep/short turn)	7.8	N.A.	N.A.	van der Bogert et al. 1999
Moguls skiing	8.3 to 12.4	N.A.	N.A.	van der Bogert et al. 1999
Run (13 km/h)	2.6 to 5.2	50 to 125	120 to 240	Heikkinen et al. 2007, van der Bogert et al. 1999, Weeks & Beck 2008
Stop and turn from running	1.8	40	80	Weeks & Beck 2008
Jump	4.5 to 4.7	70	300 to 320	Vainionpää et al. 2006, Weeks & Beck 2008
Lateral or vertical jumping (8 to 20 cm height)	3.0 to 4.0	N.A.	N.A.	Bassey et al. 1998, Heinonen et al. 2001a, Vainionpää et al. 2006
High jump take-off	3.5	120	430	Weeks & Beck 2008
Long or triple jump take-off	3.5	140	480	Weeks & Beck 2008
Drop jump (from 0.3 m height)	5.3-6.5	140 to 170	760 to 910	Heikkinen et al. 2007, Vainionpää et al. 2006, Weeks& Beck 2008
Drop jump (from 0.5 m height)	4.4	N.A.	N.A.	Heinonen et al. 2001b
Gymnastics, jump	3.7 to 10.4	110 to 610	410 to 6350	Daly et al. 1999
Triple jump, second contact	14.0 to 22.0	N.A.	N.A.	Heinonen et al. 2001a
Foot stomp	4.6	470	2180	Weeks & Beck 2008

* *N.A., not available*

2.4.3 Exercise Loading Effect on Bone Structure

When measuring the bone structure of athletes, it has been suggested that athletes especially in sports involving impacts or high forces can have a greater amount of bone mass in addition to better geometry, and thus apparently more rigid bones compared with habitual exercisers (Daly et al. 1999, 2004, Ducher et al. 2005, Duncan et al. 2002b, Faulkner et al. 2003, Greene et al. 2005, 2006, Haapasalo et al. 2000, Heinonen et al. 1993, 1995, 2000, 2001a,b, 2002, Helge & Kanstrup 2002, Kaptoge et al. 2003, Kemmler et al. 2006, Kontulainen et al. 2002, Liu et al. 2003, MacDonald et al. 2007, MacKelvie et al. 2004, Proctor et al. 2002, Sardinha et al. 2008). However, exercise loading differs greatly between anatomic locations, some of the sports could be better to lower and some for the upper extremities (Faulkner et al. 2003, Haapasalo et al. 2000, Heinonen et al. 2001, Kontulainen et al. 2003, Liu et al. 2003).

Evidence from meta-analyses

Knowledge of the exercise-loading effects on bone structure by *in vivo* measurements is still scarce. The results based on meta-analysis show some inconsistency and most of these have indicated BMD effects (not effects on structure) of less than 1% to 2% and ~2.5% among premenopausal women and men (>30 years of age) respectively (Kelley et al. 2000, 2001, Kelley & Kelley 2004, Wallace & Cumming 2000, Wolff et al. 1999). Among children and adolescents, the most positive effect of ~1 to 6% on BMC have been observed in pre- and early pubertal children, while an effect of 0.5 to 2% was observed in pubertal children and adolescents. In all these studies, exercise-loading mostly consisted of impact exercises and resistance training and the effects were observed at various sites such as the lumbar spine and femoral neck. However, none of the meta-analyses and very few of randomized controlled trials (RCTs) concentrated on bone structural rigidity between puberty and premenopause (Hind & Burrows 2007, Kelley et al. 2000, 2001, Kelley & Kelley 2004, Wallace & Cumming 2000, Wolff et al. 1999).

Evidence from RCTs

A systematic literature review of recent RCTs (last five years) from exercise-loading and bone structural rigidity of prepubertal boys and girls (aged ten years or older) to middle-aged men (50 years or more) and menopausal women was accomplished. Total of 62 studies were found when exercise terms such as exercise, exercise therapy, exercise training, physical activity, physical training, sports, physical fitness were used with bone structure, strength, rigidity, geometry or bone in general. However, some of these studies concerned rather neck and back problems than effects on bone structure. Therefore, some essential earlier studies were also included (Heinonen et al. 2000, Petit et al. 2002). Again, the results of these RCTs are somewhat inconsistent. Anyhow, effects between 0.2 to 8% were observed in four studies, while three studies did not show effects (Table 4, Heinonen et al. 2000, MacDonald et al. 2007, MacKelvie et al. 2004, Petit et al. 2002, Vainionpää et al. 2007, Ward et al. 2007, Weeks et al. 2008). In general, observed effects have been larger in puberty than in adulthood.

TABLE 4 Randomized controlled trials of exercise-loading to increase or maintain bone rigidity between puberty (10 y) and middle age (50 y) in women and middle age in men.

Authors	Site	Effect of ex vs. controls, %	Group	Age, y
Heinonen et al. 2000	tibia	NS. *	girls	10 to 13
MacDonald et al. 2007	tibia	~2% on BSI (boys only) **	boys and girls	10 to 11
MacKelvie et al. 2004	FN	~8% on Z ***	boys	9 to 12
Petit et al. 2002	FN	~4% on Z (early pub only)	girls	10 to 11
Vainionpää et al. 2007	tibia, femur	0.2% on ToA ****	women	35 to 40
Ward et al. 2007	tibia, radius	NS.	female gymnasts	10 to 11
Weeks et al. 2008	FN	NS.	boys and girls	13 to 14

** NS., non-significant*
*** BSI, Bone Strength Index*
**** Z, Section Modulus, an index against bending and torsion*
***** ToA, Total Area, measured by QCT*

Observational Studies

Also, a systematic literature review with the same searchwords and same age-range was accomplished for observational studies. With regard to the few RCTs, a few observational studies (altogether 56) investigating exercise loading and bone structural rigidity from prepuberty (ten years of age) to middle age (fifty years of age) or menopause were found (Table 5, Ashizawa et al. 1999, Daly et al. 1999, 2004, Dowthwaite et al. 2007, Ducher et al. 2005, Duncan et al. 2002b, Faulkner et al. 2003, Greene et al. 2005, 2006, Haapasalo et al. 2000, Heinonen et al. 2001b, 2002, Kemmler et al. 2006, Kontulainen et al. 2002, Liu et al. 2003, Sardinha et al. 2008). Again, some of these observational studies addressed slightly different issues than effects on bone structure and most but not all of these studies suggested differences in structure of bone between active and sedentary people.

TABLE 5 Association of exercise-loading and bone rigidity between puberty (10 y) and middle age (50 y) in females and males according to the prospective and cross-sectional studies.

Authors	Site	difference vs. controls, %	Group	Age, y
Lower Extremities				
Duncan et al. 2002b	mid-femur	~20% on BSI * (triathletes) ~85% on BSI (runners)	female cyclists, runners, swimmers, and triathletes	15 to 18
Faulkner et al. 2003	FN	~9% on Z **	female gymnasts	10 to 14
Greene et al. 2005	tibia	~40% on BSI	female runners	13 to 18
Greene et al. 2006	tibia and FN	NS.*** (males) and NS. (both)	male and female runners	14 to 18
Heinonen et al. 2001b	tibia, femur	~20 to 30% on BSI and Z	male, female triple jumpers	19 to 25
Heinonen et al. 2002	tibia	NS. ~12% on BSI	male weightlifters	24 to 37
Kemmler et al. 2006	FN	NS. ~7% on CWT****	male rock climbers	21 to 35
Liu et al. 2003	tibia	~50 to 80% (females only)	male and female jumpers and swimmers	18 to 23
Sardinha et al. 2008	FN	~10% on BSI	vigorous physical activity	10
Upper Extremities		loaded vs. unloaded, %		
Ashizawa et al. 1999	radius	~20% on SSI *****	male, female tennis-players	18 to 24
Daly et al. 2004	humerus	~5 to 15% on ToA, Ipol ******	female tennis-players	8 to 17
Dowthwaite et al. 2007	radius	~25 to 40% on IBS *******	female gymnasts	~10
Ducher et al. 2005	radius	~6 to 14% on ToA	female and male tennis-players	19 to 31
Haapasalo et al. 2000	radius, humerus	~25 to 35% on BSI	male tennis-players	25 to 35
Heinonen et al. 2002 **	radius	~40% on BSI	male weightlifters	24 to 37
Kontulainen et al. 2002	radius, humerus	~15 to 25% on BSI	female racket-players	18 to 34

** BSI, Bone Strength Index*
*** Z, Section Modulus, an index against bending and torsion*
**** NS., non-significant*
***** CWT, cortical wall thickness*
****** SSI, Stress-Strain Index*
******* ToA, Total Area; Ipol, Polar Moment of Inertia*
******** IBS, Index of Structural strength*

According to the literature review of exercise loading and human bone structure, there is reasonable evidence that vigorous exercise that includes jumps and leaps can be effective for building rigid bones at the lower extremities as suggested in some of the meta-analyses, RCTs, and several prospective and cross-sectional studies (Daly et al. 1999, Duncan et al. 2002b, Faulkner et al. 2003, Greene et al. 2005, 2006, Heinonen et al. 2000, 2001b, 2002, Hind & Burrows 2007, Kelley et al. 2000, 2001, Kelley & Kelley 2004, Kemmler et al. 2006, Liu et al. 2003, MacDonald et al. 2007, MacKelvie et al. 2004, Petit et al. 2002, Sardinha et al. 2008, Vainionpää et al. 2007, Ward et al. 2007, Weeks et al. 2008, Wallace & Cumming 2000, Wolff et al. 1999). However, athletes in non-weightbearing sports such as swimming have shown equally dense bones compared with common exercisers mostly using weightbearing exercises (Duncan et al. 2002).

At the upper extremities, the positive association between exercise-loading and rigid bone structure has been best demonstrated in racket-sport studies (Ashizawa et al. 1999, Daly et al. 2004, Dowthwaite et al. 2007, Ducher et al. 2005, Haapasalo et al. 2000, Kontulainen et al. 2002). As the constant weight-bearing component is absent from the upper extremities, the muscle activity, in conjunction with the exercise loading type, becomes an important determinant of rigid bone structure (Daly et al. 2004, Trappe & Pearson 1994). For example, swimmers and tennis-players load their bones in very different ways during their sports activity. When hitting the ball, the upper extremity of a tennis-player must be able to cope with the very high momentary load (eccentric muscle work) because of the extended lever arm (the extremity and the racket together) and the heavy impact of the high-velocity ball. A swimmer, in turn, should only resist the drag of the water through coordinated and repeated, mostly concentric, muscle activity (Trappe & Pearson 1994).

2.4.4 Exercise Loading, Unloading, and Injuries

Bone will adapt to increased loading with increased rigidity while unloading would lead to some deterioration and injury to severe deterioration of bone (Eser et al. 2004, Houston & Zaleski 1967, Kontulainen et al. 1999, 2001, 2004, Lang et al. 2006, Rittweger et al. 2005, Sievänen et al. 1994, Ward et al. 2006). On the other hand, deteriorated bone could be strengthened again if muscle function, physical ability, and bone loading could be returned to normal (Kannus 1994). These findings pinpoint the need for continuous loading of the skeleton to avoid overloading, unnecessary risks, and, immediate rehabilitation after a possible injury (Haapasalo et al. 2007, Muir et al. 2007, Qiu et al. 2005, Rome et al. 2005). The risk of injury can be relatively high in some sports and thus the benefits and risks of sports and exercise need consideration and attention (Haapasalo et al. 2007, Natri et al. 1999, Parkkari et al. 2004).

Injuries in Recreational Activities and Competitive Sports

According to meta-analyses, the adverse effects of bone interventions in premenopausal women have been rare (Kelley 2001, 2004, Wallace 2000, Wolff 1999). In general, regular recreational exercise activities do not seem to cause joint osteoarthrosis, however, competitive exercise loading for more than four hours a day can increase the risk of knee and hip arthrosis (Anonymous 2007, Garrick & Requa 2003). The information of possible adverse effects of exercise on articular cartilage is scarce (Torvinen et al. 2003).

According to a large Finnish injury risk study, 5% of all injuries in active living occurred in commuting activities, 22% in lifestyle activities, and 73% in recreational and competitive sports (Parkkari et al. 2004). In recreational sports, the overall injury risk was higher in men than women, except in endurance sports. In recreational and competitive sports, injury incidence rate was highest at the age of 15 to 24 years (men and women 4.2 and 3.1 per 1000 hours of participation), while it was much lower at older ages (~1 per 1000 hours). Most of the injuries in absolute numbers occurred in leisure-time activities such as walking and swimming, but this was because of their frequent participation in the Finnish population (Parkkari et al. 2004).

The individual injury risk per exposure time is low in repetitive, nonimpact exercise loading such as swimming, while it is moderate in low-impact exercise loading such as cross-country skiing, cycling, and running and in high-magnitude exercise loading such as gym training. However, the injury risk per exposure time is higher in high-impact and odd-impact type of exercise-loading such as track and field sports, volleyball, squash, tennis and soccer (Table 6).

Another perspective for the injury issue is the injury severity between the sports in exercise-loading groups. In swimming, cross-country skiing, dancing, downhill skiing, orienteering, and squash, most of the injuries were mild causing no breaks from the sport or/and work. However, injuries in commuting activities, track and field sports, and volleyball also caused a day or more time loss from the sport or/and work (Table 6).

TABLE 6 Number of injuries and proportion of injuries according the injury level in different exercise-loading groups. Adapted from Parkkari et al. 2004.

Exercise-loading/ Sport	Number of injuries / 1000 hours of participation (95% CI)	Proportion of injuries according to the injury level (%) *		
High-impact		Mild	Moderate	Severe
Volleyball	7.0 (5.4 to 9.1)	31	46	22
Track and field sports	3.8 (1.8 to 8.0)	50	25	25
Odd-impact				
Squash	18.3 (11.4 to 29.4)	71	24	6
Tennis	4.7 (2.9 to 7.7)	50	43	7
Soccer	7.8 (6.3 to 9.7)	42	49	9
Aerobics	3.1 (2.5 to 3.9)	50	45	5
Dancing	0.7 (0.6 to 1.0)	60	33	8
High-magnitude				
Gym training	3.1 (2.5 to 3.8)	41	49	11
Repetitive, low-impact				
Running	3.6 (2.9 to 4.4)	35	59	6
Cross-country skiing	1.7 (1.3 to 2.2)	55	38	8
Walking	1.2 (1.0 to 1.3)	38	49	13
Repetitive, nonimpact				
Swimming	1.0 (0.7 to 1.4)	59	33	7

** Mild: Injury or pain not affecting sports or other leisure time physical activity, or, only modified duration or intensity of the activity without missing any activity session; Moderate: Injury or pain resulting in missing of a sports or other leisure-time physical activity session at least once; Severe: Injury or pain resulting missing of work or corresponding activity at least for one day*

2.5 Age, Gender, Nutrition, Heredity and Bone Structure

In addition to mechanical loading, factors such as age, gender, nutrition, and heredity affect bone structure. Also, abuse of alcohol and smoking affect bones adversely. On the other hand, athletes' eating disorders and strict training may cause weight loss, amenorrhoea, and even osteoporosis. Contraceptives can also have a minor negative effect on bone rigidity, and hormones in general can have either a deteriorating or strengthening effect on bone (Heaney et al. 2000a). Fortunately, most athletes have healthy lifestyles.

Age and Peak Bone Mass

In principle, the capacity of the human skeleton to adapt to mechanical loading, *i.e.* physical training, is substantially different between the childhood (the period of axial growth) and adulthood. Training started before or at puberty, seems to be most effective for high accrual of bone mass and consequent strengthening of bone (Hind & Burrows 2007, Kannus et al. 1995). Particularly the growth spurt at puberty seems to be the right time for enhancing bone strength and laying the foundation for mechanically competent bones in later life. In general, the period of young adulthood until 30 to 40 years of age is good for further strengthening of bones and muscles.

The peak bone mass, the greatest amount of bone mass achieved during life, is most often achieved during young adulthood at the age of 20 years (Figure 9). However, the variation is considerable between different skeletal sites and individuals at that age. High peak bone mass is important for protection against fragility fractures later in life (Heaney et al. 2000a).

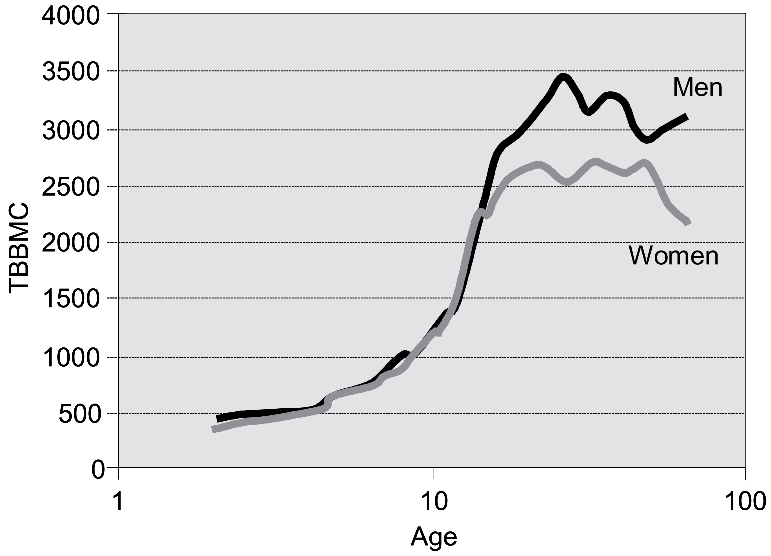


FIGURE 9 Total body BMC plotted against age (logarithmic scale). The peak bone mass is achieved at the age of 20 years. Men have higher peak bone values compared to women. Data adapted from Zanchetta et al. 1995 and Rico et al. 1994, and the figure adapted from Kannus et al. 2008.

Gender and Hormones

Men are taller than women, thus they have bigger bones with greater amount of mineral mass and wider cross-section. Hormone balance also differs between genders, which has an effect on the adaptation of bone to loading (Frost 2003a,b). Many hormones such as estrogens, glukocorticoids, thyroid hormones, insulin-like-growth factors (IGF), and androgens regulate skeletal growth and calcium homeostasis (Turner 1991). The set-point of the mechanosensory system, MESS (minimal effective strain related stimulus) has been suggested to change through the reproduction of estrogen but the issue is controversial (Järvinen et al. 2003, Sievänen 2005, Turner 1991). The onset of puberty increases the bone mass of young women via the effect of estrogen (Gilsanz et al. 1988) and studies of muscle-bone relationships between boys and girls before and after puberty have suggested that girls have more bone in relation to muscle mass during adolescence (Figure 10, Forwood et al. 2004, 2006, Riggs et al. 2004, Schönau et al. 2000, 2001, 2002, Sievänen 2005, Zanchetta et al. 1995). It has been suggested that the extra bone reserve of women in youth, and especially the lack of it in men, may explain why men seem to have a greater response of bone to mechanical loading in adolescence and early adulthood (Järvinen et al. 2003, Kontulainen et al. 2005, Rico et al. 1994, Seeman 2001, Sievänen 2005).

Estrogen clearly plays a role in achieving high peak bone mass, but the mechanisms behind the relationship of estrogen and mechanical loading are under debate (Järvinen et al. 2003, Lanyon & Skerry 2001, Pajamäki et al. 2008). Among young women, amenorrhoea is likely to result in bone loss, sometimes because of exhaustive exercise training, while the bone mass is regained if the normal menstruation cycle is restored (Drinkwater et al. 1984, 1986).

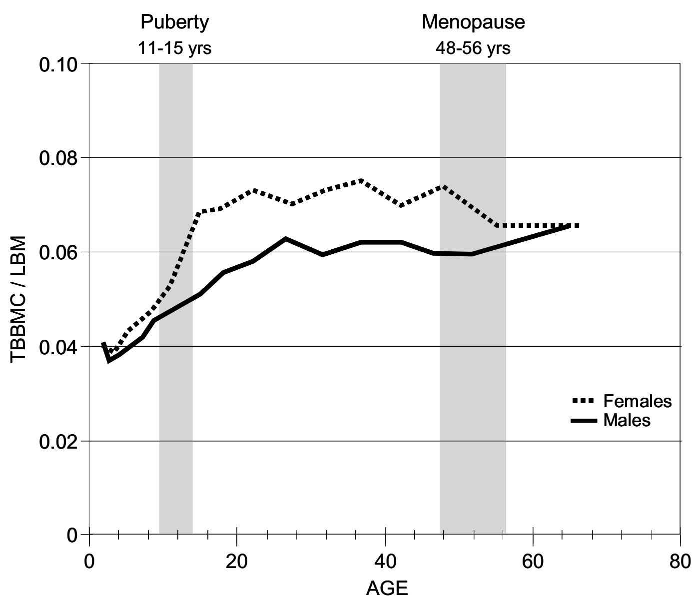


FIGURE 10 Ratio of total body BMC to lean body mass plotted against age. Data adapted from Zanchetta et al. 1995 and Rico et al. 1994, and the figure adapted from Järvinen et al. 2003.

Nutrition

Bone cells are dependent on nutrition. Calcium, vitamin D, and phosphorus are the most important determinants of bone nutrition, but there are many others. *Calcium* is the most common mineral in the human body. Milk and milk products are rich in calcium, and green vegetables have a variable content of calcium which is not mostly well absorbed (Heaney et al. 2000b, Heaney & Weaver 2003). Calcium intake is associated positively with bone mass gains in children and adolescents (French et al. 2000). Calcium is considered a threshold nutrient, *i.e.* calcium intake that exceeds a certain level (about 1200 mg/day) does not contribute further to bone mass (Matkovic & Heaney 1992). During young adulthood bones do not grow in length and this period is characterized by a decline in calcium absorption and retention, while calcium output increases (Matkovic & Heaney 1992). The current recommendation for calcium intake for young adults is 900 mg/day, but during the development of peak bone mass, intake up to 1500 mg/day can be recommended (Heaney et al. 2000b, Lanou 2005, Weaver 2000).

Vitamin D influences on calcium absorption being its main function. It stimulates intestinal absorption of calcium by inducing the synthesis of calcium-binding protein in cells (Heaney et al. 2000b). Vitamin D insufficiency can result from inadequate exposure to sunlight and/or low intake of sources *per se*. Traditionally, fish and fortified food products are the main sources of vitamin D, and these fortified products have decreased the vitamin D deficiency (Heaney et al. 2000b, Heaney & Weaver 2003). Vitamin D is considered a threshold nutrient for bone health. Although the daily requirement for vitamin D is uncertain, traditional oral intake recommendations are 400 IU or 10 μg/day (Heaney & Weaver 2003). Vitamin D is essential for normal mineralization of the skeleton throughout life. In general, there is reasonable evidence to support the positive effect of vitamin D on bone density for children and adolescents (Brannon et al. 2008). Also, vitamin D is suggested to positively affect muscle function (Ward et al. 2009).

Phosphate constitutes more than half the mass of bone mineral, thus phosphorus is needed in the diet to mineralize and to maintain the skeleton. However, phosphorus is widely distributed in many foods, and adequately present in most diets and is thus not a limiting nutrient (Heaney et al. 2000b).

Heritability of Bone Rigidity

Heredity has been suggested to explain more of the variation in bone rigidity between individuals than the environmental factors (Eisman 1999, Harris et al. 1998, Howard et al. 1998, Hui et al. 2006, Lenchik et al. 2004, Mikkola et al. 2008, Nguyen et al. 1998, Pocock et al. 1987, Sun et al. 2006, Xu et al. 2006, Yang et al. 2006). However, the effect of heredity seems to vary greatly between various bone sites (Havill et al. 2007, Hui et al. 2006, Mikkola et al. 2008). In most recent publications, genes have explained ~80% of interindividual variation in radial rigidity and ~60% in tibial rigidity (Mikkola et al. 2008).

The genes involved are largely unknown, but those related to body size via growth hormone, bone mass via vitamin D receptor, and estrogen receptor are of importance (Heaney et al. 2000b, Lanyon & Skerry 2001). These are likely to interact since body size is associated with bone size (Heaney et al. 2000b). In twin studies, the genes behind the bone size explained ~20 to 75% of the size variation at the radius, while the same numbers were ~90% at the tibia (Havill et al. 2007, Mikkola et al. 2008).

2.6 Summary of the Literature

Bone is a vital tissue and one of main functions of bone is to provide maximal mechanical competence with minimum weight for locomotion. Locomotion needs rigid and strong bones (Järvinen et al. 2005).

Exercise as a functional stimulus is a combination of different types of mechanical forces (Einhorn 1992, Rubin & Lanyon 1985). Different forms of exercise can cause very different mechanical loadings. It is known that athletes in sports entailing impacts or high forces can have greater areal BMD compared with those in more usual loading (Heinonen et al. 1993, 1995, Helge & Kanstrup 2002, Proctor et al. 2002). Less is known about the association between exercise loading and bone structure (Haapasalo 2000, Heinonen et al. 2001a,b, 2002).

Weak bone structure predisposes to low-energy fractures. A goal for osteoporosis prevention with exercise-loading would be to strengthen bone structure at all vulnerable skeletal regions and identify feasible targeted exercise protocols for as many people as possible. In this respect, childhood and adolescence are times of great importance.

If such a feasible and effective-proven exercise loading type existed, the prevention of bone fragility and thus fractures might become easier. Enjoyable, reasonable, and habitual exercise loading vary between individuals, and thus, safe, approachable, and effective-proven exercise options are needed to guide and help as many people as possible to achieve strong bones. Further, this kind of focused prevention of bone fragility might at least partly prevent people from sustaining fractures and the society from financial costs.

3 PURPOSE OF THE STUDY

The purpose of this study was to investigate the associations between exercise loading types and the strength of bones in young adulthood. More specifically, the aims of this dissertation, based on four different cross-sectional studies, were:

1) To assess the relationship between the exercise loading types and bone structural traits at the lower and upper extremities.

2) To examine in detail the relationship between the exercise loading types and the femoral neck cortex in anatomic regions considered vulnerable in terms of hip fragility.

4 MATERIAL AND METHODS

This doctoral dissertation consists of four different cross-sectional studies. These studies were designed and conducted between 2004 and 2008 at UKK Institute for Health Promotion Research in collaboration with Tammer-Magneetti (Study III), Tampere University of Technology (Study IV), and Tampere University Hospital (Study IV). The approval of the local ethics committee and written informed consent from all subjects were duly obtained before the studies.

4.1 Subjects

Personal characteristics of the subjects in the four original studies are shown in Table 7. Study I consisted of 255 female athletes and their reference group, the latter including 30 women performing noncompetitive leisure time physical activity exercises only. Most of the data of Study I was a reanalysis of our athlete databasis completed with a few more athletes using the Hip Structural Analysis program (Heinonen et al. 1993, 1995). In Study II, 113 athletes and 30 reference subjects were included. Most of them also participated in Study I. In Study III, 11 male athletes and their 12 matched reference subjects participated. For Study IV, 91 female athletes and their 20 referents were recruited. Altogether, 378 athletes and their 62 referents participated in the studies forming the dissertation. All but one study included female participants only; men were studied in Study III on moguls- and slalom skiing, because there were not enough top-level competitive female athletes in these sports in Finland.

The athletes representing the sports in Studies I, II, and IV were players of volleyball, soccer, squash, tennis and badminton, and competitors in high jumping, triple jumping, hurdling, speed skating, weightlifting, power-lifting, swimming, cycling, orienteering, long-distance running, and cross-country skiing. We also had step aerobics instructors in Study I. The competitive athletes were contacted via National Athletics Federations and Organizations. The reference group consisted of volunteer students of medicine and nursing who were recruited from a local medical school and university of applied sciences.

TABLE 7 Characteristics of the subjects representing different types of exercise-loading in the four original studies.

Type of Exercise *Lower/Upper Extremity*	Sports	N	Age, years	Height, cm	Weight, kg	Study
High impact/Impact	Volleyball	21	21.2 (3.0)	179 (5)	74.4 (8.3)	I,II
High impact/High Magnitude	Hurdlers	24	20.2 (2.1)	170 (6)	62.1 (4.0)	I,II
High impact	Moguls skiing	5	22.6 (4.5)	182 (7)	77.2 (8.4)	III
High impact	Triple jump	9	23.2 (4.4)	170 (4)	60.0 (6.5)	IV
High impact	High jump	10	21.5 (3.8)	178 (4)	60.5 (4.6)	IV
Odd impact	Squash	20	24.8 (3.9)	166 (5)	61.9 (6.0)	I
Odd impact/High Magnitude	Soccer	19	21.4 (3.0)	168 (6)	63.4 (6.2)	I,II
Odd impact	Speed Skating	15	21.9 (8.1)	167 (6)	62.7 (6.4)	I
Odd impact	Step aerobic-instructing	27	28.3 (3.7)	166 (5)	57.3 (4.2)	I
Odd impact/Impact	Racket games *	23	23.6 (4.5)	167 (7)	64.0 (10.0)	II
Odd impact/Impact	Racket games *	23	23.6 (4.5)	167 (7)	64.0 (10.0)	II
Odd impact	Slalom skiing	6	24.5 (2.9)	174 (4)	76.6 (4.3)	III
Odd impact	Squash	10	28.8 (7.2)	168 (9)	63.6 (9.1)	IV
Odd impact	Soccer	9	21.5 (3.0)	162 (5)	57.8 (6.6)	IV
High magnitude	Weightlifting	19	23.8 (5.0)	166 (7)	65.8 (9.6)	I
High magnitude	Power lifting	17	27.5 (6.3)	158 (3)	63.3 (13.2)	IV
Repetitive, low impact	Orienteering	29	23.5 (3.1)	169 (5)	59.2 (4.7)	I
Repetitive, low impact	Cross-country skiing	25	21.2 (3.1)	169 (6)	61.1 (8.8)	I
Repetitive, low impact	Long-distance running	18	28.9 (5.6)	168 (5)	53.7 (3.4)	IV
Repetitive, non-impact	Cycling	29	24.1 (5.4)	166 (5)	61.6 (7.8)	I
Repetitive, non-impact	Swimming	27	20.6 (2.8)	169 (6)	62.1 (7.0)	I,II
Repetitive, non-impact	Swimming	18	19.7 (2.4)	173 (5)	65.1 (5.6)	IV
Referents		30	24.3 (3.1)	165 (5)	60.7 (7.9)	I,II
Referents		12	24.3 (3.6)	181 (4)	76.2 (7.9)	III
Referents		20	23.7 (3.8)	164 (5)	60.0 (7.4)	IV
		442				

** In Study II, the 23 players in racket games included 2 squash players, 13 tennis players, and 8 badminton players. Please note that some athletes participated in more than one study, thus, altogether 378 athletes and 62 referents participated in this dissertation.*

4.2 Exercise Loading Types and Their Classification

In this study, the athletes representing different sports were classified into the sport-specific exercise loading types separately for the lower and upper extremities (Table 7). This classification was theoretic, qualitative in nature, and was accomplished before analysing the data. The basis of the classification rests on a scientific consensus of earlier publications such as Vuori & Heinonen (2000). However, the earlier classification was partly refined in this dissertation. Sports that were earlier classified in the high-impact exercise-loading group for the lower extremities, were now divided into high-impact and odd-impact exercise-loading groups. Similarly, a partly new classification was proposed for the upper extremities. All in all, the theoretic basis of the classifications rested on the experimental studies of the mechanical adaptation, which were presented in Section 2.3. For the lower extremities, the difference between the high-impact and odd-impact exercise loading was refined in this study based on the idea of unusual loading direction (Lanyon 1987). When the loading direction was similar to normal movement, the sport was classified as high-impact exercise loading. However, if the loading direction was unusual to normal movement, the sport was classified to odd-impact type of exercise-loading. The definitions of all the exercise-loading types do not take only typical sports performance into account, but also the typical training form, which together establish the exercise-loading type of the given sports.

4.2.1 Lower Extremity

Volleyball, hurdling (Studies I and II), moguls-skiing (Study III), triple jump and high jump (Study IV) include either maximal vertical jumps and leaps or high impacts from certain previously known direction during a typical sports performance and training. These sports were considered to represent *the high-impact exercise loading type.*

Squash and soccer (Study I, II, IV), speed skating, step aerobics instructing (Study I), and slalom skiing (Study III) are vigorous sports and include rapidly accelerating and decelerating movements, often in directions the body and the hip region are not normally accustomed to. In addition, kicking and receiving the ball in soccer can result in impacts to the feet and shins. These sports also include moderate to high impacts or moderate to high bending forces. These sports were considered to represent *the odd-impact exercise loading type.*

Weightlifting (Study I) and powerlifting (Study IV) involves well-coordinated movements with simultaneous, very high muscle force production, and these sports were considered to represent *the high-magnitude exercise loading type*.

Orienteering, cross-country skiing (Study I), and long-distance running (Study IV) are typical endurance sports including a great number of similar, small weightbearing impacts or bending forces against ground, and these sports were considered to represent *the repetitive, low-impact exercise loading type.*

Swimming (Studies I, II, and IV) and cycling (Study I) are likewise endurance sports with a great number of movements but the training lacks virtually all ground impacts, and these sports were considered to represent *the repetitive, nonimpact exercise loading type.*

4.2.2 Upper Extremity

Both volleyball and racket games (Study II and IV) include a great number of high-velocity ball impacts on hands and forearms, or onto the racket, from different directions. In racket games, the racket also increases the lever arm magnifying the incident joint moments within the upper extremities. These sports were considered to represent *the impact exercise-loading type*.

Swimming entails a great number of high joint moments, which are due to the substantial drag of the water against the movements of the upper extremities. These movements are almost all generated by repeated concentric muscle activity. Although swimmers also use functional weightlifting in their training, it is mainly performed with pulleys and small weights without high eccentric muscle work (Trappe & Pearson 1994). Accordingly, swimming was considered to represent *the repetitive, nonimpact exercise-loading type.*

Soccer, hurdling (Study II), triple jump and high jump (Study IV) are sports in which the upper extremities are not particularly loaded during typical sports performances, but functional weightlifting forms an essential part of the training programme in both of these sports. Weightlifting exercises require high muscle strength and power production by upper extremities during training. Accordingly, these sports were considered to represent *the high-magnitude exercise loading type*. More specific information concerning exercise-loading types is available in the original articles.

4.3 Measurements

Measurements of anthropometry, muscle performance, in addition to the health and training history, and calcium intake questionnaires in the original studies are shown in Table 8.

4.3.1 Questionnaires

The training history questionnaire included sports-specific training hours during the previous year, sports-specific training years, and total weekly training sessions including all sporting activities during a week. This information was documented via a training recall questionnaire, which covered at least a five-year-training history. In addition, information on medication, diseases, alcohol and coffee consumption, and sports and other injuries and previous fractures suffered during the adult years were elicited.

Calcium intake was estimated from a seven-day calcium intake diary and analysed by Micro-Nutrica software (Social Insurance Institution, Helsinki, Finland). Also, the use of calcium supplements was elicited and screened in all subjects. Menstrual status was also elicited and if a woman had menses less than once in six months she was classified as being amenorrhoeic. In addition, the use of contraceptives during the previous year was elicited.

TABLE 8 Measurements of anthropometry, muscle performance, in addition to the health and training history, and calcium intake questionnaires in original studies.

Measurement	Studies	Methods
Anthropometry		
Height	I,II,III,IV	tape measure
Weight	I,II,III,IV	scales
Fat-%	IV	DXA
Muscle performance		
Isometric leg strength	I, II, III, IV	dynamometer
Static jump	II, III, IV	force plate
Counter movement jump	II, III, IV	force plate
Single leg jump	IV	force plate
Dynamic balance		
Figure-8 running	II,IV	track
Questionnaires		
Health	I,II,III,IV	questionnaire
Training history	I,II,III,IV	questionnaire
Calcium intake	I,II,IV	diary

4.3.2 Muscle Performance Measurements

In Studies I, II, III, and IV, the maximal isometric extension strength of lower extremities was measured with an isometric leg press dynamometer (Tamtron, Tampere, Finland; Table 8, Figure 11). *In vivo* precision of repeated measurements (CV,%) of these muscle force measurements is ~5% (Heinonen et al. 1994). Dynamic maximal take-off force and power were measured with a force platform (Kistler Ergojump 1.04, Kistler Instrumente AG, Winterthur, Switzerland) during a static, counter movement, and one leg jump (Figure 11). Functional agility was assessed via a figure-8 test by measuring the time for running two laps around two poles placed 10 m apart.

FIGURE 11 An example of maximal isometric leg press test of the lower extremities (on left) and maximal jump test (on right). Published with permission.

4.3.3 Bone Measurements

The methods, variables, and sites of bone measurements reported in the original studies are listed in Table 9. In Studies I, II, and III, the right lower and upper extremity was measured. In Study IV, however, the dominant lower extremity and the non-dominant upper extremity were measured. More specific information about the methods is reported in the original articles.

TABLE 9 Methods, variables, and sites of bone measurements reported in original studies.

Variables	Studies	Method	Sites *
Bone mineral mass (BMC, g)	II,III	pQCT	DT, TS, DR, RS, HS
Bone mineral density (aBMD, g/cm^2)	I,III,IV	DXA	FN, LS
Cross Sectional Area, (mm^2)	I,II,III,IV	HSA, pQCT, MRI	FN, DT, TS, DR, RS, HS
Bone width, (mm)	I,III,IV	HSA	FN
Section modulus, (mm^3)	I,II,III,IV	HSA, pQCT, MRI	FN, DT, TS, DR, RS, HS
Cortical wall thickness (CWT, mm)	II, III, IV	pQCT, MRI	FN, DT, TS, DR, RS, HS
Trabecular density (TrD, mg/cm^3)	II, III	pQCT	DT, DR
Cortical density (CoD, mg/cm^3)	II, III	pQCT	TS, RS, HS
Cortical cross-sectional area (CoA, mm^2)	IV	MRI	FN
Cortical/Total area (CoA/ToA)	IV	MRI	FN
Antero-posterior diameter, mm	IV	MRI	FN
Infero-Superior diameter, mm	IV	MRI	FN
Anterior cortical wall thickness, mm	III,IV	MRI	FN
Posterior cortical wall thickness, mm	III,IV	MRI	FN
Superior cortical wall thickness, mm	III,IV	MRI	FN
inferior cortical wall thickness, mm	III,IV	MRI	FN

** DT= distal tibia, TS= tibial shaft, DR= distal radius, RS= radial shaft, HS= humeral shaft, FN= femoral neck, LS= lumbar spine*

DXA-based Hip Structural (HSA) and Advanced Structural Analysis (AHA)

In Studies I and IV, the HSA and AHA were used in addition to the conventional aBMD analysis of the femoral neck (Beck et al. 2000). First, the proximal femur measurements were done with dual energy X-ray absorptiometry (Study I: Norland device, XR-26, Norland, Fort Atkinson, WI, USA; Study IV: Lunar Prodigy Advance, EnCORE 9.x, GE Medical Systems Lunar, Madison, WI, USA) and then the HSA and AHA software was used to assess the structural characteristics of the femoral neck. For the Norland and Lunar devices, the *in vivo* precision of the total body BMC, lumbar spine BMC, and femoral neck BMC is ~1-3% in our laboratory (Sievänen et al. 1996, Sievänen et al. 2005, unpublished). For the HSA and AHA, the structure of the narrowest section of the femoral neck was carried out and then cross-sectional area occupied by bone mineral (CSA), subperiosteal width (W) in a given scan projection, and the section modulus (Z, an index of bone strength against bending) were determined. In our laboratory, the coefficients of variation (CV) for HSA and AHA, based on repeated measurements of 30 subjects, are 2.7% and 2.3% for CSA, 2.5% and 1.2% for W, and 4.8% and 3.8% for Z respectively.

Although the correlation between the analysed bone traits was from 0.93 to 0.97 between the HSA and AHA software, the values of the same bone traits of the same subjects varied between the software. Furthermore, the group-level between-software differences were mostly explained by body height. Thus the calibration seems to vary between the software.

pQCT measurements

In Studies II, III, and IV peripheral computer tomography (pQCT, XCT 3000, Stratec Medizintechnic GmbH, Pforzheim, Germany) was used to measure several sites of lower and upper extremities. In Study II, the shaft of the tibia (50% from the distal end), radius (30%), humerus (50%), and the distal tibia (5% from the distal end), and radius (4%) were measured. In Study III, only tibial shaft and distal tibia were measured. In Study IV, both distal site and shaft of the tibia and radius were measured. Standardized scanning and analysis procedures were used (Sievänen et al. 1998). For the shaft regions, bone mineral content (BMC, mg), total cross-sectional area (ToA, mm^2), proportion of cortical to total area (CoA/ToA), mean cortical cross-sectional wall thickness (CWT, mm), cortical density (CoD, mg/cm^3), and density-weighted polar section modulus (BSI, an index of bone strength against torsion and bending, mm^3) were determined. In addition to the above-mentioned variables (CoD excluded), trabecular density (TrD, mg/mm^3) was determined for the distal sites of tibia and radius. In our laboratory, the CV of these pQCT measurements ranged from 0.9% (TrD) to 4.2% (BSI) for the distal tibia, from 0.7% (CoD) to 2.5% (BSI) for the tibial shaft, from 2.2% (TrD) to 7.7% (BSI) for the distal radius, from 0.8% (CoD) to 4.3% (BSI) for the radial shaft, and 0.5% (CoD) to 5.6% (BSI) for the humeral midshaft (Sievänen et al. 1998).

MRI measurements

In Study III, MRI (Gyroscan 1.5T Intera Power, Philips Medical Systems, Best, The Netherlands) was used at the narrowest femoral neck cross-section according to the scanning principles found appropriate for analysis of cortical bone (Sievänen et al. 2007). This measurement was carried out at the Tammer-Magneetti company. Based on assessments of the periosteal and endosteal circumference of the cortical wall, the ToA was determined, and the torsional rigidity (BSI) of the thin-walled cross-section of the femoral neck was estimated using the Bredt's formula (Sievänen et al. 2007b). In addition, direction-specific mean cortical wall thickness (CWT) at anterior, posterior, superior, and inferior quadrants of the cortical bone was separately assessed. In our laboratory, the *in vivo* precision of periosteal and endocortical delineations of the femoral neck cortex is ~1% (Sievänen et al. 2007b).

In Study IV, the MRI scans (Siemens 1.5T, Avanto Syngo MR B15, Erlangen Germany*)* were taken following the aforementioned scanning principles (Sievänen et al. 2007b). These measurements were carried out at Tampere University Hospital. The whole proximal femur from the femoral caput to the subtrochanteric level of the femoral diaphysis was scanned. For Study IV, one anatomically distinct femoral neck cross-section at the insertion of articulation capsule was chosen to represent the region of the proximal femur that is apparently subjected to exercise-specific loading without direct involvement of muscle attachments (Figure 12). Two adjacent MRI slices from this site were transferred to a separate workstation, where they were manually segmented by delineating the periosteal and endocortical boundaries of the cortical bone with the help of ITK-SNAP-program (http://www.itksnap.org/).

All the segmentations of the MRI images described above were done as in Study III, except now blind to the exercise loading classification, and the measurements and calculations were done in Matlab environment (Math Works Inc., Natick, MA). The mean data from the two adjacent MRI slices were used in the statistical analysis.

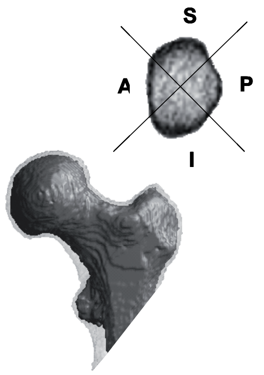


FIGURE 12 MRI-based three-dimensional reconstruction of the proximal femur (below) and a cross-sectional scan of the femoral neck (above). I = inferior, A = anterior, S = superior and P = posterior direction.

4.4 Statistical Methods

Statistical analyses were done with SPSS (Version 11.0 and 15.0.1; Inc., Chicago, IL.). Means and standard deviations (SD) are given as descriptive statistics. One-way analysis of variance (ANOVA) was used for evaluating subject characteristics and differences between the groups in muscle performance, training history and calcium intake in addition to proportion of cortical to total area (Studies I-IV). Otherwise group differences in bone characteristics were estimated by analysis of covariance (ANCOVA) using age, weight and height (Studies I, II, and IV) or height (Study III) as covariates. Sidak correction was used in post-hoc tests of the ANOVA and ANCOVA (Studies I, II, and IV). Due to the skewed distributions in some of the outcome variables to obtain the between-groups differences, log-transformed variables of all outcomes were used in the analysis of covariance. Proportional (%) differences and their 95% confidence intervals (CI) were achieved by the antilog of mean differences between the groups. Forced regression model was used to determine whether the classified type of exercise loading could be an important determinant of the estimated strength of the lower and upper extremities. In all studies, a p-value less than 0.05 was considered statistically significant.

5 RESULTS

The results are presented anatomically site by site. First, as an example, the training history and muscle performance results of the female participants in Studies II and IV, and male participants in Study III are presented. Second, the pQCT results based on the pooled data of the female athletes from the original Studies II and IV (altogether 204 female athletes and their 50 referents) are shown for the tibia. Third, the main pQCT results of male athletes of the Study III are shown for the tibia. Fourth, the DXA-based HSA and AHA results from Studies I and IV and the MRI results from Study IV among the females are given for the femoral neck. Because different DXA devices and software were used in these studies, the HSA and AHA results are shown separately. Fifth, the pQCT data of the dominant and non-dominant radius and humerus of the female athletes from Study II and IV are presented. Finally, important comparisons of bone characteristics between the athlete groups are shown (Studies I, II, III, and IV).

5.1 Training History and Muscle Performance

The training history of athletes in Studies II and IV (Table 10) and in Study III (Table 11) was long and intense in all of the exercise-loading groups. Also, athletes were lean and their muscle forces were in general high. In Study I, the calcium intake of athlete groups ranged from ~900 to 1400 mg, and the intake in the reference group was 911 mg/day. No medications to affect bone were reported.

TABLE 10 Training history and muscle performance of the female athletes in studies II and IV.

	N	Body mass index (kg/m^2) *	Sport-Specific training hours/ week	Competing career (years)	Isometric leg extension force (kg)	Power of counter movement jump (W/kg)
Exercise-loading						
High-impact	64	21.5 (2.2)	11.8 (2.8)	9.8 (3.3)	191 (38)	47.8 (7.0)
Odd-impact	60	22.5 (2.1)	7.8 (3.1)	9.9 (4.0)	180 (36)	41.0 (5.5)
High-magnitude	17	25.2 (4.2)	9.1 (2.7)	8.0 (4.7)	226 (39)	47.8 (7.1)
Repetitive, low-impact	18	19.0 (1.1)	10.9 (3.4)	12.4 (6.7)	170 (46)	38.9 (5.1)
Repetitive, nonimpact	45	21.7 (2.1)	17.2 (5.6)	10.0 (3.8)	163 (40)	40.1 (5.2)
Reference group	50	22.1 (2.4)	2.9 (1.5)*	-	141 (23)	35.5 (4.6)

** Age, weight, and height are reported in the methods section.*

TABLE 11 The training history and muscle performance of the male athletes in study III.

	N	Age (y)	Height (cm)	Weight (kg)	Isometric leg extensor force (kg)	Power of counter movement jump (W/kg)
Exercise-loading						
High-impact	5	22.6 (4.5)	181.9 (7.2)	77.2 (8.4)	320 (40)	60.8 (3.5)
Odd-impact	6	24.5 (2.9)	173.5 (3.7)	76.6 (4.3)	351 (34)	59.9 (5.7)
Referents	12	24.3 (3.6)	180.6 (3.7)	76.2 (7.9)	267 (45)	N.A. *

** N.A., not available.*

5.2 Structure of the Tibia

5.2.1 Females

Bone Mineral Content (BMC) and Bone Strength Index (BSI)

Body height, weight and age adjusted comparison of the BMC and BSI between the exercise-loading groups and the reference group at the distal tibia and tibial shaft are illustrated in Figure 13. Significant between-group differences were observed.

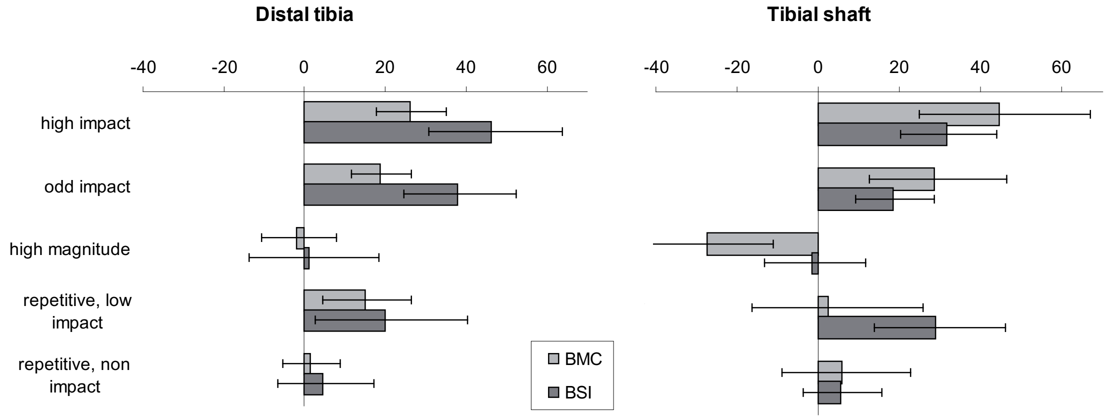


FIGURE 13 The data is pooled from Studies II and IV. The age, weight, and height adjusted mean percentage differences (95% CI) between the female athletes and the nonathletic referents (the 0% line indicates the mean of the reference group) in the bone mineral content (BMC) and bone strength index (BSI) of the distal tibia (left panel) and tibial shaft (right panel). The bars indicate the mean difference and the whiskers 95% confidence intervals. If zero is not included in the confidence interval, the difference is statistically significant. The exercise-loading type is indicated on the left.

First, the athletes in the high-impact (volleyball, hurdling, and triple and high jump) and odd-impact (soccer, squash, tennis, and badminton) exercise loading groups had much greater values compared with the reference group, the mean differences being some 20 to 45% for BMC and BSI. Second, the mean BMC was ~30% lower in the high-magnitude (powerlifting) exercise loading group than in the reference group at the tibial shaft, while BSI was similar; at the distal tibia the values were similar. Third, the athletes in the repetitive, low-impact exercise loading group (endurance running) showed 15% greater BMC at the distal tibia with no mean difference at the tibial shaft. However, the repetitive, low-impact exercise loading group had from 20 to 30% higher BSI both at the distal tibia and tibial shaft. Fourth, the BMC and BSI at both the distal and shaft regions of the tibia in the repetitive, nonimpact (nonweight-bearing swimming) exercise loading group were not different than the referents.

Total area (ToA) and ratio of cortical to total area (CoA/ToA)

With regard to the ToA and CoA/ToA of the female athletes, significant between-group differences were also observed (Figure 14).

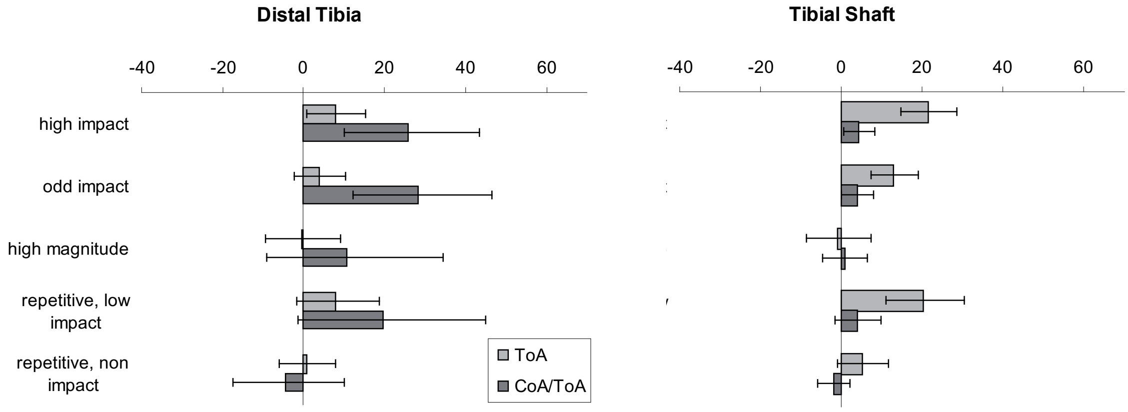


FIGURE 14 The data is pooled from Studies II and IV. The age, weight, and height adjusted mean % differences (95% CI) between the female athletes and the nonathletic referents (the 0% line indicates the mean of the reference group) in the total area (ToA), and unadjusted mean % differences in the ratio of cortical to total area (CoA/ToA) of the distal tibia (left panel) and tibial shaft (right panel). For further details, see the caption of Fig. 13.

First, compared to referents the ToA at the distal tibia was significantly higher in the high-impact (volleyball, hurdling, and triple and high jump) exercise loading group only, and even in this group the mean difference was less than 10%. Second, athletes in the high-impact (volleyball, hurdling, and triple and high jump) and odd-impact (soccer, squash, tennis, and badminton) exercise loading groups showed over 25% greater CoA/ToA at the distal tibia. At the tibial shaft, the athletes in the high-impact and odd-impact exercise loading groups showed ~15 to 20% greater values in ToA and ~5% in CoA/ToA. Third, the high-magnitude (powerlifting) exercise loading group had comparable ToA and CoA/ToA with the referents. Fourth, athletes in the repetitive, low-impact (endurance running) exercise loading group had, in turn, ~20% greater ToA at the tibial shaft.

Trabecular density (TrD) and cortical density (CoD)

Some significant differences were also found in the TrD at the distal tibia and CoD at the tibial midshaft, and these differences are shown in Figure 15.

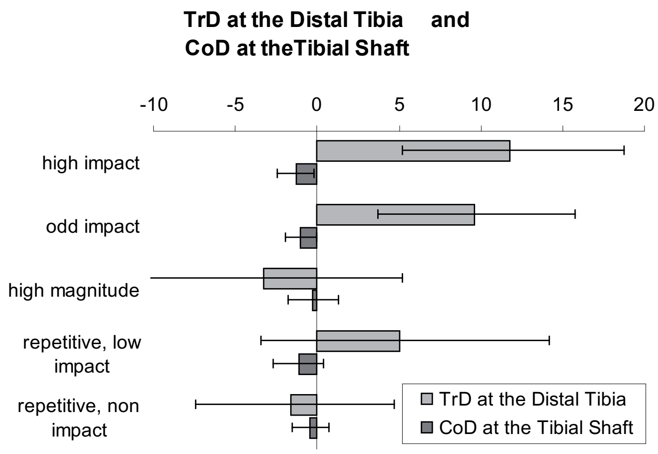


FIGURE 15 The data is pooled from Studies II and IV. The age, weight, and height adjusted mean % differences between the female athletes and the nonathletic referents (the 0% line indicates the mean of the reference group) in the trabecular density (TrD) of the distal tibia and cortical density (CoD) of the tibial shaft. For further details, see the caption of Fig. 13.

The TrD was ~10% greater while CoD was 1% lower in the high-impact (volleyball, hurdling, and triple and high jump) and odd-impact (soccer, squash, tennis, and badminton) exercise loading groups than in the reference group. Also, the athletes in the repetitive, low-impact (endurance running) exercise loading group had a similar trend in TrD and CoD, while the athletes in the high-magnitude (powerlifting), and repetitive, non-impact (nonweight-bearing swimming) exercise loading groups showed similar values to the referents.

5.2.2 Males

Like the females, compared with the reference group the male athletes in the high-impact exercise-loading (moguls skiing) group had approximately 25% and 40% greater BMC and BSI at the distal tibia (Figure 16). At the tibial shaft, these values were 25% and 30%. Also, athletes in the odd-impact exercise-loading (slalom skiing) group had 40% and 60% greater BMC and BSI at the distal tibia, and 20% and 15% (latter non-significant) greater values at the tibial shaft.

Interestingly, the shape of the tibial midshaft seemed to be different in the athletes in high and odd-impact exercise loading type (Figure 16). The antero-posterior diameter was elongated and the relative thickness of the anterior cortical wall was higher among the odd-impact exercise loading type represented by the moguls-skiers ($p<0.05$).

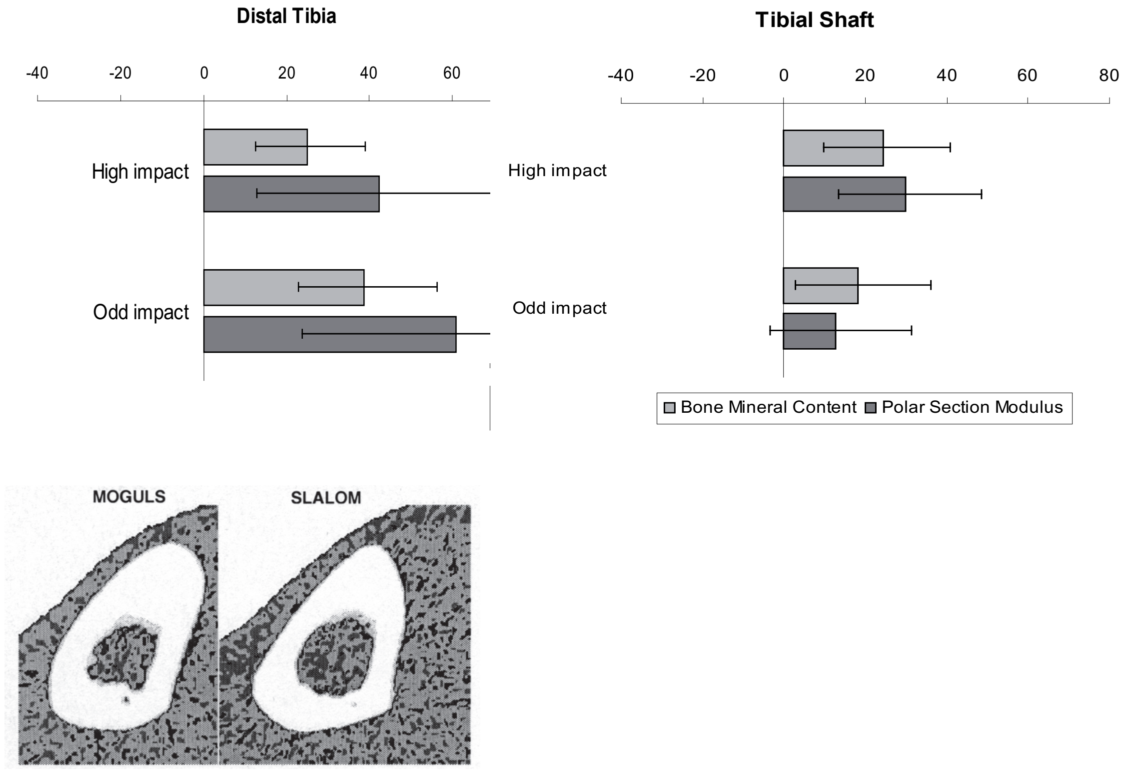


FIGURE 16 The age, weight, and height adjusted mean % differences (95% CI) between the male athletes (Study III) and the nonathletic referents (the 0% line indicates the mean of the reference group) in the bone mineral content (BMC) and bone strength index (BSI) of the distal tibia (left upper panel) and tibial shaft (right upper panel). The exercise-loading type is indicated on the left. PQCT images of the tibial midshaft scanned from a moguls-skier (lower left panel) and a slalom skier (lower right panel). Please note the distinct difference in the shape of the bone cross-section. The antero-posterior diameter was elongated and the relative thickness of the anterior cortical wall was greater among the moguls-skiers ($p<0.05$).

5.3 Structure of the Femoral Neck

First, the results from HSA and AHA analyses are shown separately for Studies I and IV. Then, the MRI results obtained from the Study IV are shown.

DXA-derived axial strength (CSA) and bending strength indices (Z)

Based on the HSA and AHA of Studies I and IV, the association between high-impact and odd-impact exercise-loading type and strong femoral neck (FN) compared with the reference group was obvious (Figure 17).

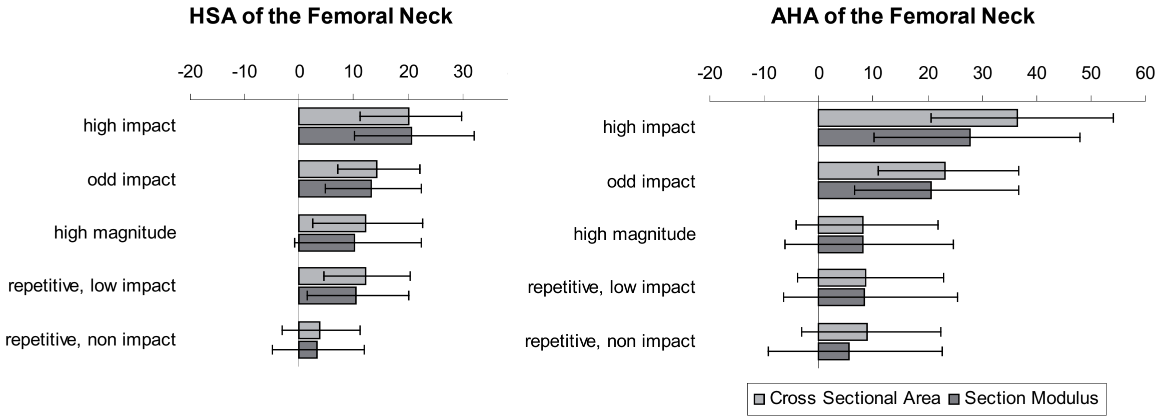


FIGURE 17 The age, weight, and height adjusted % differences (95% CI) between the female athletes and the non-athletic referents (the 0% line indicates the mean of the reference group) in the cross-sectional area (CSA) and section modulus (Z) of the femoral neck (FN). The bars represent 95% CI. The exercise-loading type is indicated on the left. Athletes in Study I (left panel) were measured by Norland device (XR-26; Norland, Fort Atkinson, WI, USA) and analysed by Hip Structural Analysis software. Athletes in Study IV (right panel) were measured by Lunar Prodigy Advance (EnCORE 9.x; GE Medical systems Lunar, Belgium, Europe) and analysed by Advanced Hip Analysis software.

In Study I, the CSA and Z were ~15 to 20% greater than those of the reference group in the high-impact (volleyball and hurdling) and odd-impact exercise-loading groups (soccer and squash). Similarly in Study IV, CSA was ~25 to 35% and Z was ~20 to 30% greater in high-impact (triple and high jump) and odd-impact exercise-loading groups (soccer, squash, speed skating, and step aerobics). Athletes in the high-magnitude (weightlifting and powerlifting) and in the repetitive, low-impact exercise-loading group (endurance running, cross-country skiing, and orienteering) seemed to have around 10% greater CSA and Z compared with the same of the reference group in Studies I and IV (only a trend in Study IV).

Width (W), Total area (ToA), and ratio of cortical to total area (CoA/ToA)

Note that the FN width (W) was similar between the exercise loading groups and the reference group among female athletes (Studies I and IV). Also, based on MRI measurements (Study IV), the ToA was similar among the exercise loading groups and the reference group – being in line with the above-mentioned observations on FN width. However, athletes in high-impact and odd-impact exercise loading groups had ~20% greater CoA/ToA than that of the reference group (data not shown).

Direction-specific cortical thickness (CWT)

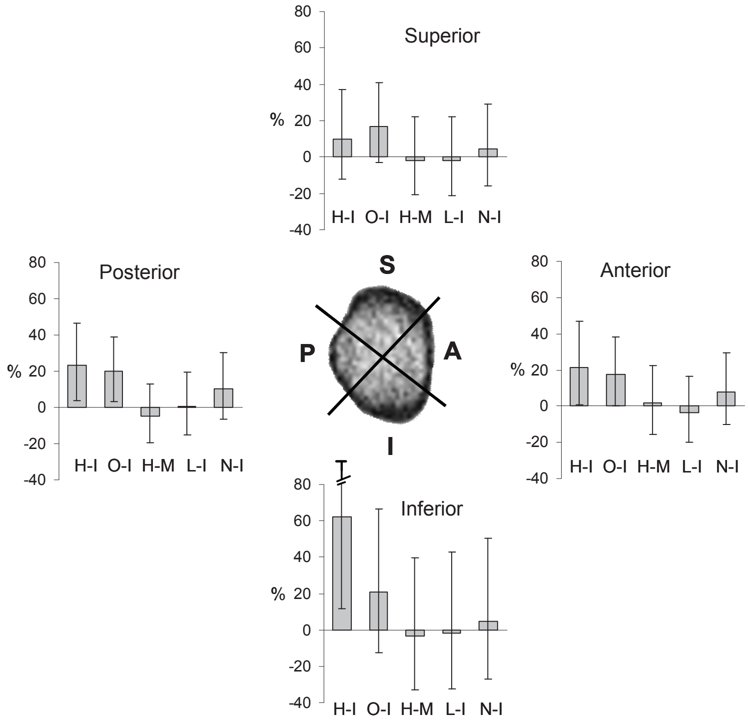
The clear difference in CWT between the athletes in the high-impact and odd-impact exercise loading types compared with the reference group were observed in the regional analysis (Table 12, Figure 18).

TABLE 12 Absolute cortical thickness (CWT) of the athletes and referents in different regions of the femoral neck (FN) and in different exercise loading types. Mean (SD).

		FN, CWT (mm)			
Exercise-loading type	N	Inferior	Anterior	Superior	Posterior
High-impact	19	3.0 (0.9)	1.8 (0.3)	1.9 (0.5)	1.8 (0.2)
Odd-impact	19	2.3 (1.0)	1.8 (0.4)	2.2 (0.6)	1.8 (0.4)
High-magnitude	17	1.7 (0.4)	1.6 (0.3)	2.0 (0.4)	1.5 (0.2)
Repetitive, low-impact	18	1.9 (0.5)	1.4 (0.2)	1.7 (0.3)	1.5 (0.2)
Repetitive, non-impact	18	1.9 (0.8)	1.6 (0.3)	1.8 (0.3)	1.6 (0.3)
Nonathletic referents	20	1.9 (1.0)	1.5 (0.3)	1.9 (0.3)	1.5 (0.3)

The age, weight, and height-adjusted difference between the CWT of the high-impact exercise loading group compared with the reference group was ~60% at the inferior, ~20% at the anterior, ~25% at the posterior, and ~10% (only a trend) at the superior quadrant of the FN (Figure 18.). The difference between the CWT of the odd-impact exercise loading group compared with the reference group was ~20 % (only a trend) at the inferior, anterior, posterior, and superior quadrant (only a trend) of the FN. The direction specific CWT of the other exercise-loading groups did not differ significantly from that of the reference group.

A



B

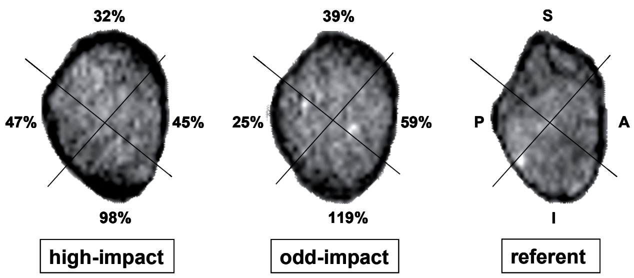


FIGURE 18 The age, weight, and height-adjusted mean % differences (95% CI) in the inferior, anterior, superior and posterior cortical thickness (CWT) of the femoral neck (FN) between the exercise-loading groups (Study IV) and the reference group (the 0% line indicates the mean of the reference group) (A). Examples of FN cross-sections from a high-impact athlete (left), odd-impact athlete (middle), and referent (right) with similar height, weight, and age (B). The values denote the % differences in the given athletes' CWT compared to the referent's respective thickness. H-I = high impact, O-I =odd-impact, H-M =high-magnitude, L-I =low-impact, and N-I =non-impact exercise loading. I = inferior, A = anterior, S = superior, and P = posterior. The sports represented were triple and high jump (H-I); soccer, squash, tennis, and badminton (O-I); powerlifting (H-M), endurance running (L-I), and swimming (N-I).

5.4 Structure of the Radius

Bone Mineral Content (BMC) and bone strength index (BSI)

At the dominant distal radius, athletes in both impact exercise loading and high-magnitude exercise loading groups had less than 20% greater bone traits in BMC and ~20 to 30% in BSI compared with the reference group. Also, athletes in the repetitive, nonimpact exercise loading group had ~15% greater BMC than the reference group. At the dominant radial shaft, differences between impact and high-magnitude exercise-loading compared with the reference group seemed to be 5 to 10% in BMC and they were 15 to 20% in BSI (Figure 19).

At the non-dominant radius, only differences between the athletes in exercise-loading types compared with reference group were observed at the distal radius. Athletes in high-magnitude and repetitive, non-impact exercise loading groups had ~20% greater traits in BSI than the reference group (Figure 19).

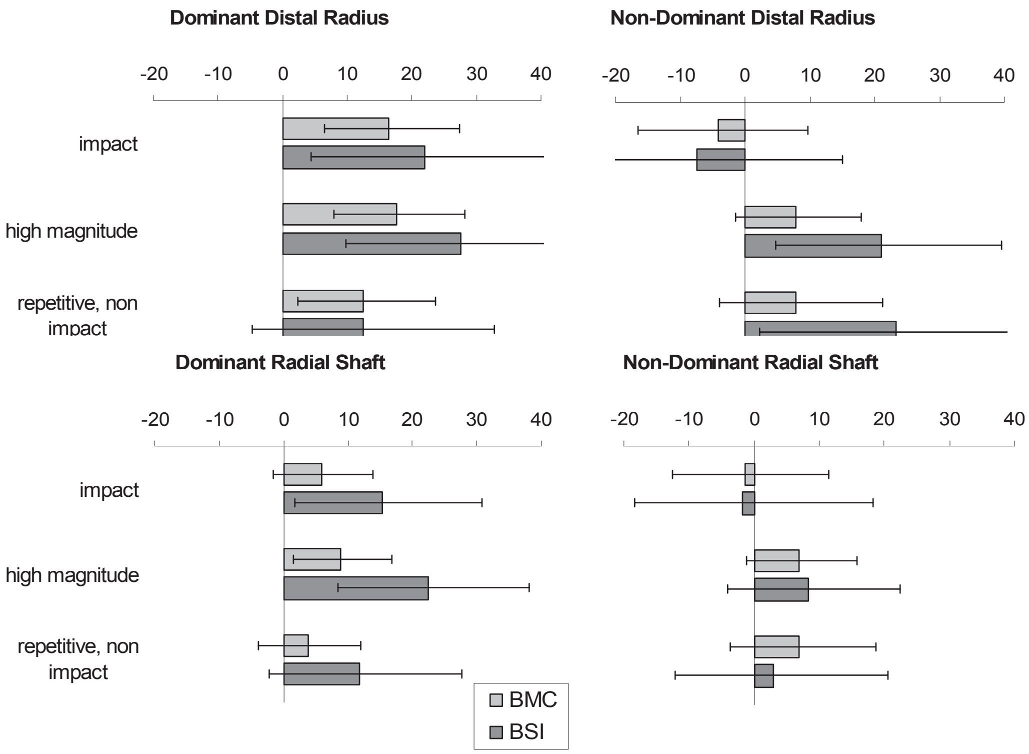


FIGURE 19 Age, weight, and height adjusted mean % differences (95% CI) between the female athletes (Studies II and IV) and the nonathletic referents (the 0% line indicates the mean of the reference group) in bone mineral content (BMC) and bone strength index (BSI) of the dominant (left upper panel) and non-dominant distal radius (right upper panel), and the dominant (left lower panel) and non-dominant radial shaft (right lower panel). The exercise-loading type is indicated on left. Please note that the sports represented in Study II were volleyball, squash, tennis, badminton (impact exercise-loading); hurdling, soccer (high-magnitude exercise-loading); and swimming (repetitive, nonimpact exercise-loading), while the sports represented in Study IV were squash (impact exercise-loading), soccer, triple jump and high jump (high-magnitude exercise-loading), and swimming (repetitive, nonimpact exercise-loading).

Total Area (ToA) and Ratio of Cortical to Total Area (CoA/ToA)

At the dominant radius, ToA, but not the CoA/ToA, seemed to be 10 to 15% greater in all of the exercise-loading groups than in the reference group among the female athletes. At the non-dominant radius, no differences between the athletes in exercise-loading types compared with reference group were observed (Figure 20).

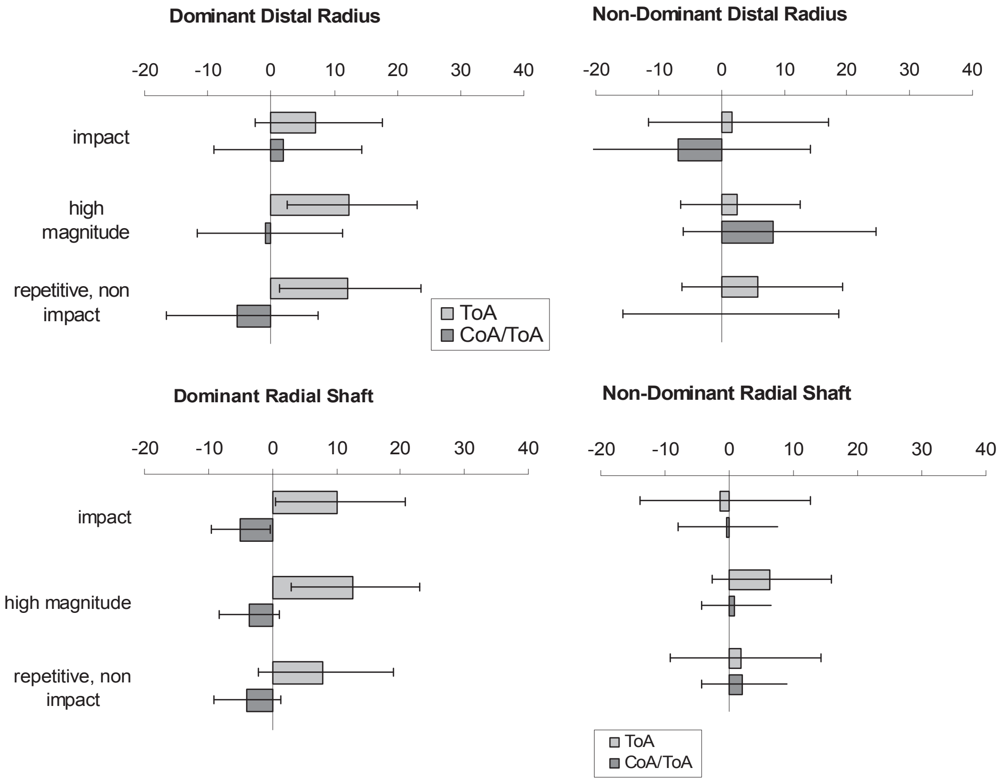


FIGURE 20 Age, weight and height adjusted mean % differences (95% CI) between the female athletes (Studies II and IV) and the nonathletic referents (the 0% line indicates the mean of the reference group) in the total area (ToA) and unadjusted mean % differences in the ratio of cortical to total area (CoA/ToA) of the dominant (left upper panel) and non-dominant distal radius (right upper panel), and dominant (left lower panel) and non-dominant radial shaft (right lower panel). The exercise-loading type is indicated on the left. Please note that the sports represented in Studies II and IV were partly different (see caption of Figure 19).

Trabecular Density (TrD) and Cortical Density (CoD)

TrD was not greater between the exercise-loading groups than the reference group at the distal radius, although a trend of more than 5% at the dominant distal radius indicated greater density in impact exercise-loading group. However, CoD of all of the exercise loading groups compared with the reference group was significantly more than a percent lower at the dominant but not at the non-dominant radial shaft. (Figure 21).

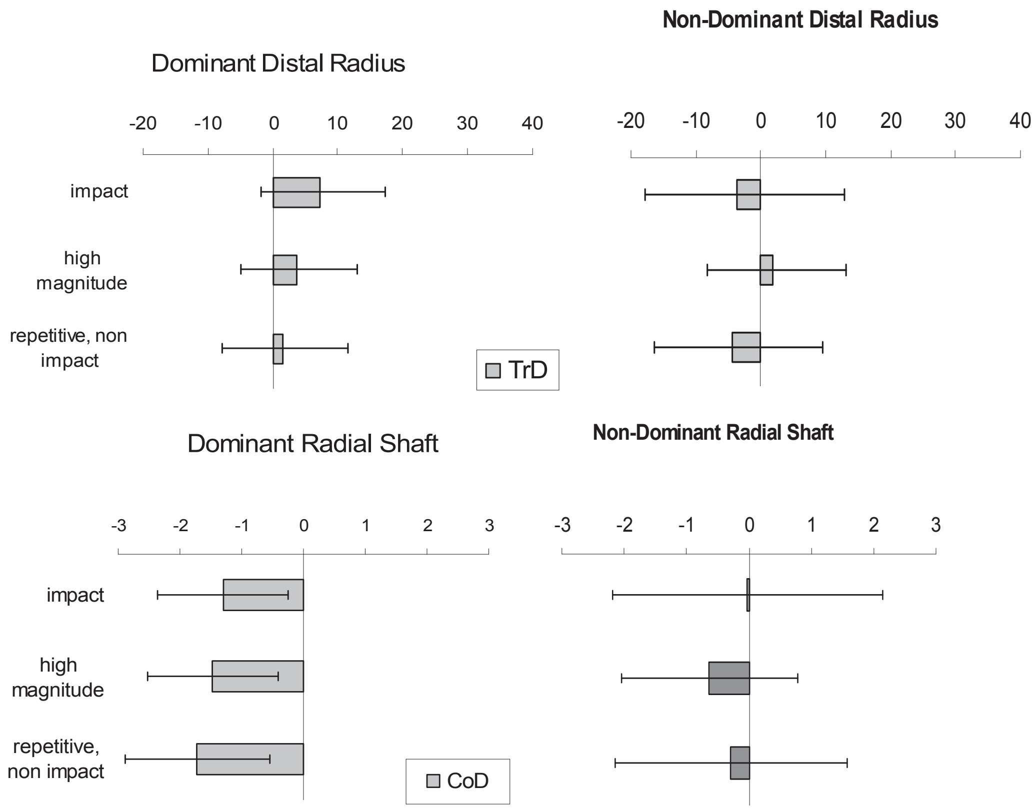


FIGURE 21 Age, weight and height adjusted mean % differences (95% CI) between the female athletes (Studies II and IV) and the nonathletic referents (the 0% line indicates the mean of the reference group) in the trabecular density (TrD) of the dominant (upper left panel) and non-dominant (upper right panel) distal radius and dominant (lower left panel) and non-dominant radial shaft (lower right panel). The exercise-loading type is indicated on the left. Please note that the sports represented in Studies II and IV were partly different (see caption of Figure 20).

5.5 Structure of the Humerus

The humerus was only measured from the dominant side. At the dominant humeral shaft, athletes in impact, high-magnitude, and repetitive, non-impact exercise loading groups showed ~10 to 15% greater traits in BMC and 20 to 25% in BSI compared with the reference group. At the dominant humeral shaft, ToA was 10 to 15% greater in all of the exercise-loading groups than the reference group among the female athletes, while athletes in the impact exercise-loading group had ~5% lower CoA/ToA (Figure 22).

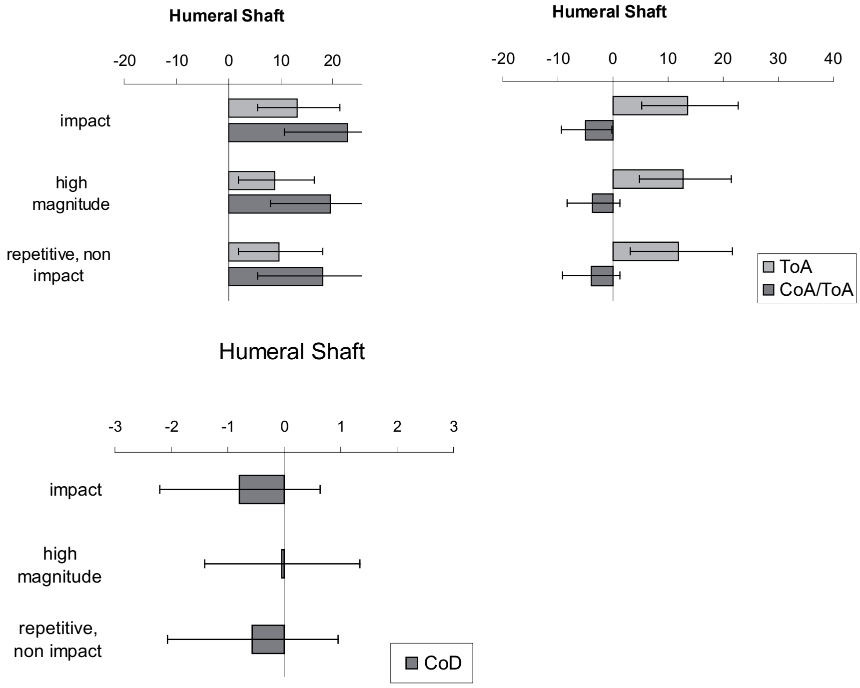


FIGURE 22 Age, weight and height adjusted mean % differences (95% CI) between the female athletes (Study II) and the nonathletic referents (the 0% line indicates the mean of the reference group) in the bone mineral content (BMC) and bone strength index (BSI) (upper left panel), total area (ToA) and unadjusted ratio of cortical to total area (CoA/ToA) (upper right panel), and cortical density (CoD) (lower panel) of the dominant humeral shaft. The exercise-loading type is indicated on the left.

5.6 Differences in Structure of Bone between the Athlete Groups

High-impact and odd-impact exercise-loading at the lower extremities

Both female and male athletes in high-impact and odd-impact exercise loading groups appeared to have stronger bones at the lower extremities than the reference group. Differences between the high-impact and odd-impact exercise loading types were only observed at the tibial shaft and narrowest section of the FN. At the tibial shaft, female athletes in the high-impact exercise loading group had ~10% greater BSI, while male athletes in the high-impact group seemed to have ~40% lower CWT at the anterior segment of narrowest section of the FN (data shown earlier in the results section).

Bone Strength Index (BSI) at the dominant and non-dominant upper extremities

No between-the-athlete-group differences were observed at the dominant radius. At the non-dominant radius, however, athletes in high-magnitude and repetitive, non-impact exercise loading groups had ~30% greater BSI than the same of the impact exercise loading group.

6 DISCUSSION

The objective of this study was to investigate the association between exercise loading types and the strength of bones in young adulthood. More specifically, the aims of this dissertation were, first, to assess the relationship between exercise loading types and the bone structural traits at the lower and upper extremities, and second, to examine in detail the relationship between the exercise-loading types and the femoral neck cortex in anatomic regions considered vulnerable in terms of hip fragility.

6.1 Findings of the Study

6.1.1 Lower Extremity

High-impact and odd-impact exercise loading

It is known that age and body size (height and weight) are associated with bone rigidity, however, mechanical loading has also been suggested to be major determinant of the strength of bones (Borer 2005, Carter 1984, Duncan & Turner 1995, Frost 1987, 1990, 2003, Gross et al. 2004, Huiskes 2000b, Lanyon 1984, 1987, Rubin & Lanyon 1985, Ruff 2006, Umemura et al. 2002). With regard to the association of exercise-loading and bone rigidity, it was shown that specific long-term exercise loading, especially when producing moderate to high magnitude impacts from usual directions (high-impact exercise loading) or moderate to high magnitude impacts from unusual directions (odd-impact exercise loading) was associated with ~15 to 60% stronger tibia and femoral neck. A novel finding was that athletes in these two groups seem to have clearly and equally ~20% thicker cortex at the vulnerable anterior and supero-lateral regions of the femoral neck. In the long term, these initially thicker cortices may provide a vital reservoir of cortical bone to be lost with aging, and thus turn out to be crucial in maintaining femoral neck stability at these vulnerable regions (Bell et al. 1999a,b, Lotz et al. 1995, Mayhew et al. 2005), and subsequently prevent the femoral neck from fractures.

A wide femoral neck has been shown to be associated with increased risk for hip fractures in the elderly (Duan et al. 2003, Gómez- Alonso et al. 2000, Nelson et al. 2000, Theobald et al. 1998). Thus by showing that the femoral neck width and total area were similar between the athletes in exercise-loading types and referents, it can be concluded that exercise does not seem to result in greatly enlarged periosteal dimensions at the femoral neck, at least in early adulthood. Endocortical contraction, however, without extensive external enlargement at the femoral neck seemed to be a specific mechanism of the adaptation. The cortical thickness and geometry are particularly crucial for a mechanically competent bone structure, the cortical bone being most likely its strongest determinant (Augat et al. 1996, Crabtree et al. 2001, Pistoia et al. 2003, Power et al. 2003, Verhulp et al. 2008). A finding that high-impact and odd-impact type of exercise loading were associated with both the periosteal expansion and endosteal apposition of tibial geometry supported the aforementioned interpretation of the relevance of cortical thickness.

High-magnitude exercise loading

With regard to a common belief about the osteogenicity of high-magnitude exercises, the present findings were partly contradictory. Powerlifting, typifying well the pure high-magnitude exercise-loading involving basically only maximal muscle forces was not at all associated with greater BMC or more robust tibia. The findings at the tibia and also at the clinically relevant femoral neck showed no difference between powerlifters and referents in terms of total cross-sectional area, cortical area or estimated rigidity. These results among powerlifters could be explained by the fact that all movements during a typical powerlifting performance (e.g., a squat or dead-lift) require maximal muscle forces that are produced slowly and in well coordinated fashion. Apparently this keeps the muscle contraction induced strain rate low. As regards the axiomatically osteogenic known impact-loading, the rate of load induced strain is much higher (Burr et al. 1996, Milgrom et al. 2000a,b). The rate of load induced strain may also be slightly higher in weightlifting, which is a very different sport from powerlifting, despite the fact that in both sports athletes lift weights (Kraemer et al. 2001). Anyhow, the ~10% greater mineral mass of weightlifters compared to that of the referents at the femoral neck was clearly less than that in high-impact and odd-impact sports. The slight difference of athletes in high-magnitude exercise-loading compared with the referents in this study was a somewhat contradictory finding to earlier studies on weightlifters (Heinonen et al. 2002).

Anderson et al. (1996) suggested that when the loading direction is expected and typical in contrast to odd-impact exercise-loading situations, the concomitant lower strain rate only results in moderate or no bone response, despite the apparent high magnitude stress (Anderson et al. 1996). Hence it seems that the high strain rate (rapid deformations within the bone structure) arising from dynamic and unusual movement directions primarily enhances the osteogenic effect of exercise loading on bone mass, and importantly, on its structure. Impact exercise loading in general has also been suggested to be associated with thickened cortical bone at peripheral bones in earlier studies (Heinonen et al. 2001, Kontulainen et al. 2002).

Repetitive, low-impact exercise loading

Another noteworthy finding in this study was that the athletes representing repetitive, low-impact loading had similar tibial shaft BMC to the referents but simultaneously ~30% greater total bone cross-sectional area. This result can be viewed as a reflection of the major principle of bone adaptation; the amount of bone material (mass) is utilized to construct such a bone structure that is most appropriate for the prevailing mechanical environment and functional purpose. It may well be that the periosteal enlargement particularly regarding this exercise-loading type is the most reasonable adaptive mechanism resulting in a rigid but relatively light bone structure to cope with a great (~ >10 000) number of successive bending and low-impact loads caused by long-distance running. Substantial increase in bone outer diameter in response to exercise-loading has also been observed in other long bone sites such as in tibia in earlier studies (Ashizawa et al. 1999, Haapasalo et al. 2000, Heinonen et al. 2002, Liu et al. 2003). At the femoral neck, the case was different. The total cross-sectional area did not differ between the groups but the BMC and thus the rigidity of the femoral neck seem to be ~10% greater than in the referents. The percentage differences compared with the referents were quite similar between the two studies using computer structural analysis but the lack of power in the second study may have compromised the results of athletes in repetitive, low-impact exercise-loading group.

Running *per se* produces strain rates that are comparable to those produced during jumping (Milgrom et al. 2000b). In this context it is noted that repetitive, non-impact exercise loading (swimming) likewise showed no benefits concerning the structure and rigidity of the tibia nor femoral neck. Apparently the great number of loads caused by leg movements against the water and accompanying muscle contractions do not provide a sufficient stimulus for bone adaptation, at least to the extent that it would override normal habitual locomotion. Further, regarding the bones of the long-distance runners, the human musculoskeleton has evolved for endurance running over millions of years, as proposed recently by Bramble and Lieberman (2004). In this respect, the skeleton should be light but rigid and strong allowing efficient locomotion (Currey 2003, Ruff 2006), being in fully line with our finding among long-distance runners.

Since the bone mineral mass represents the bulk of material of which the bone structure is made, higher BMC values in loaded bones of athletes in high-impact and odd-impact exercise loading groups could have been anticipated, and this is a fairly well-known fact among many athlete groups (Heinonen et al. 1993, 1995; Helge & Kanstrup 2002, Nevill 2004, Proctor et al. 2002). A massive skeleton is probably a strong one, but in evolutionary and locomotive terms, a mechanically adequate structure should not cause excess metabolic cost for locomotion as an unduly heavy organ, which was observed in long-distance runners representing repetitive, low-impact loading. Consequently, mechanically competent bone structures should evolve in relation to the magnitude and type of predominant loading of the skeleton.

6.1.2 Upper Extremity

The dominant side

At the dominant upper extremity, female athletes in the impact exercise loading group and, in contrast to the results of the lower extremities, also athletes in high-magnitude group had between 10 and 30 % greater mineral content and rigidity. While swimmers representing repetitive, non-impact exercise loading group had no other differences except that of 10 % greater BMC at the distal radius than the reference group, the case was different at the humerus. These athletes with vigorous muscle activity without receiving any impacts, had quite equally strong humeral midshaft as also athletes in impact or high-magnitude exercise loading. Large muscles (biceps brachii, triceps brachii, and the lower part of deltoid muscle) are attached to humeral diaphysis and the diaphysis is used as a lever arm against moderate bending forces. This functional relation may explain this finding. Presumambly comparable magnitude of force and rate of strain can be produced by several different exercise-loading types.

Moreover, the athletes in all the exercise loading groups seemed to have greater total cross-sectional area of the bone, while the ratio of cortical to total area was comparable to the reference group at the dominant upper extremity. Accordingly, periosteal enlargement, again, was observed at the dominant upper extremity in analogy to the athletes in repetitive, low impact exercise-loading at the lower extremity. In addition, no statistical difference was observed, however the tendency for increased trabecular density at the distal radius suggested that the bones of athletes in impact exercise loading type could absorb more load energy per unit volume than to referents (Currey 2002). Interestingly, female athletes in all the exercise loading groups had slightly but significantly lower cortical density at the radial but not at the humeral diaphysis. Again, all these observations are quite logical in terms of the minimal weight and rigidity of bones. Lower density and thus lighter distal radius would decrease joint moment and hence improve the cost-effectiveness of energy consumption (Ruff 2006). Relatively thick walls could indeed be appropriate for coping with high or moderate impact exercise-loading such seen at the lower extremities (Currey 2002).

The non-dominant side

With regard to the results of the non-dominant upper arm, a non-significant trend of approximately 10% greater BMC and a significant 20% more robust non-dominant distal radius of the athletes in high-magnitude exercise-loading and repetitive, nonimpact exercise-loading groups indicated that the load of these exercise types is borne with both hands. During a jerk performance in high-magnitude loading, the forearm in particular is subjected to substantial bending moments (Heinonen et al. 2002). The athletes in the impact exercise loading group, in contrast to their dominant radius, however, had comparable rigidity to that in the reference group at the non-dominant radius. This implies that there were no substantial inherent group-differences between the bone traits of especially athletes studied in the impact exercise loading group and the reference group.

6.2 Strengths of the Study

The total number of athletes measured for this study was quite high. Also, measurements of various sites strengthen the information of these cross-sectional studies. The fact that data on almost 400 athletes and their referents were analysed for this dissertation strengthens the capability of this data to reveal differences between exercise loading types and their relation to bone structure. Moreover, the athletes involved represented the top class in Finland. This does not mean that they were all world-class athletes, but they were almost without exception the best representatives of their sports in Finland and, quite a few of them had won a medal in world championships.

A new classification scheme for different exercise-loading types, although qualitative in nature, and especially the term odd-impact exercise-loading, was created and introduced to enhance the information of the earlier exercise studies. The classification cannot be unambiguous; it was not quantitative in nature, and actual differences between the high-impact and odd-impact exercise loading types might be subtle. However, the new classification can help to understand that bone strengthening does not necessarily require high-impact type extreme sports, while common odd-impact type vigorous sports such as racket games and soccer could be sufficient for bone strengthening. Comparison of this classification and more quantitative classifications of exercise-loading (Burr et al. 1996, Földhazy et al. 2005, Heinonen et al. 1996, 2001, Lanyon et al. 1975, Milgrom et al. 2000a,b, Vainionpää et al. 2006, Weeks & Beck 2008) shows fairly consistent results. High-impact and odd-impact exercise-loading, causing either high or moderate strains but clearly very high strain rates, were associated with rigid tibia and femoral neck. Again, classification of exercise-loading at the upper extremities also needs further investigations: the quantification of functional weightlifting could have been more accurate. At any rate, high strains and strain rates of impact type and high-magnitude type of exercise loading have been well quantified at the radius (Földhazy et al. 2005).

6.3 Limitations of the Study

The cross-sectional study design is compromised by the possibility of selection bias and confounding variables and the inability to show direct causal effect. Thus, individuals with genetically strong musculature and skeleton may be physically more active and more likely to start an athletic career in their youth. On the other hand, the large differences observed in this dissertation in general could be difficult to explain by selection bias alone and the results obtained were adjusted for the observed potential confounders (age, height, and weight). This suggests that the between-group differences could indeed have been caused by exercise loading and not heredity.

Bone mineral density cannot describe bone structural traits unambiguously (Sievänen 2008). Nor can it accurately predict fractures later in life (Stone et al. 2003), thus new methods to measure the structural components of bone need to be developed. Osteoporosis can impair trabecular tissue and cortical bone shell.

From the methodology used, the structure of the femoral neck was analysed from the planar DXA images in the two studies, which may be sensitive to alterations in bone alignment (Bolotin et al. 2001a,b, Sievänen 2000). The femoral neck is not a hollow cylinder although assumed to be such in HSA and AHA programs. Despite the limitation of DXA-based HSA and AHA, the results were in line with other measurements. Also, because the cortex is quite thin at the femoral neck in general, the resolution of the used MRI-devices in Studies III and IV could have been better and the automation of the cortical analysis still needs further improvement.

For this dissertation, the data from two different pQCT studies were combined (Studies II and IV). The large number of participants enhanced the information obtained by raising details of bone determinants that can be deemed reflections of different mechanisms in the adaptation process, but the groups were somewhat unbalanced. However, the number of competitive powerlifters and long-distance runners is limited in Finland. Thus, the combined data included only seventeen athletes in the high-magnitude exercise loading and eighteen in the repetitive, low-impact exercise loading group, while in other groups there were tens of athletes.

Also, differences in the starting age, duration, intensity, and frequency of competitive athletic training may have confounded the present findings. On the other hand, all the studied female athletes are nationally top-level, some of them even world-class athletes, and they all had had a particularly long and intense training history in their sports. Thus, their bones had had a plenty of time to receive the maximal loading stimuli from their sports. Additionally, it is recalled that the reference group comprised healthy students who took various recreational sports and exercises about three times a week on average. This being the case, it is possible that actual loading-induced benefits could be even greater if compared with a sedentary reference population.

6.4 Clinical Implications of the Study

Although the studies of this dissertation were cross-sectional, the observed tens of percents of differences in the bone strength of the lower and upper extremities can be considered clinically important. Such large differences represent more than standard deviation benefits at the population level, which suggests a substantial reduction in fracture risk (Cummings et al. 2002). The ultimate question, however, is whether and how these clear benefits in bone mechanical competence obtained in young adulthood could be maintained until the age when the fragility fractures typically occur (Kontulainen et al. 2004, Zanker et al. 2004).

Of all the modifiable risk factors for fragility fractures, regular physical activity is unique because it can strengthen both bones and muscles, improve balance and gait, and subsequently prevent falling (Kannus et al. 2005), the predominant cause of hip fracture (Parkkari et al. 1999). Evidence based on RCTs is lacking, but according to prospective cohort studies, moderate to vigorous exercise loading is associated with hip fracture risk reduction of 45% among men and ~40% among women (Moayyeri 2008). Furthermore, two large epidemiological cohort studies using a statistical estimate called population attributable risk have reported that if the aging population exercised briskly 3 to 4 hours a week, the number of hip fractures could diminish by one third (Feskanich et al. 2002, Michaelsson et al. 2007). Whether any of the exercise loading types would be particularly effective in reducing the incidence of such fractures is not yet known. Only one recent cohort study of elderly former soccer and ice-hockey players representing odd-impact type of exercise-loading who had stopped active playing more than 30 years earlier, suggested that the incidence of fragility fractures among athletes was half that of their age-matched peers without athletic background (Nordström et al. 2005).

Even a fragile proximal femur can cope with normal living (Currey 2003), *e.g.* the mechanical demands caused by slow walking. Falling is common among elderly people, and in a sideways fall the consequent impact on the hip imposes a large stress on the femoral neck from a direction it is not particularly adapted to (anterior and superior directions) and thus the bone is very prone to fail (Hayes et al. 1996, Jang et al. 2008, Lotz et al. 1995). The observations of this study on an equally strong association between the high-impact and odd-impact exercise loading and the segmental cortical thickness of the femoral neck, manifest as ubiquitously distributed ~20% thicker cortex around the femoral neck, is a highly relevant finding concerning the prevention of hip fragility (Bell et al. 1999a,b, Lotz et al. 1995, Mayhew et al. 2005).

Lanyon (1987) proposed that the loading coming from atypical (odd) directions is more osteogenic than common predictable loading (Lanyon 1987). According to the aforementioned and Turner's three rules (Turner 1998), high-impact exercise complies well with bone functional adaptation, and this type of exercise-loading can be considered axiomatically very osteogenic, which was also suggested in the present dissertation. Speculatively, in odd-impact exercise-loading type of racket or ballgames, the players attempt to challenge each other all the time. In tennis, the sluggish player would be run all over by the opponent and the poor backhand stroke of a player would be used against him or her by the opponent. Thus, the players would be challenged by their weaknesses all the time. Hence a weakness of the player would become the strength *per se* in the long run. From this ideal perspective, high-impact but also odd-impact type of versatile exercise loading might offer a solution to combine prevention of bone fragility and fall prevention together. When intensity of such exercise-loading apparently seems to be enough for bone strengthening in young adulthood, it could be too little for bone strengthening in the middle-aged but still enough to improve muscle strength and balance (Kemmler et al. 2004). This hypothesis should be tested in a randomized controlled trial, however.

With regard to randomized controlled trials, the movements of high-impact and odd-impact exercise loading type from tennis can be modified to a common step-aerobics programme. In fact, this type of randomized controlled trial is being accomplished in a multicentre study including our UKK Institute including 560 breast cancer patients recovering from the adverse bone effects related to their cancer treatment. The results of this ongoing RCT are not yet known, however. In such programmes, the duration, frequency and intensity of training could be customized to different age-groups with varying background in physical ability and interests (Bergström et al. 2008, Heinonen et al. 1996, Karinkanta et al. 2007, Korpelainen et al. 2006, Liu-Ambrose et al. 2004, Uusi-Rasi et al. 2003, Vainionpää et al. 2006).

6.5 Future Studies

Finally, the study series of this dissertation suggest that more specific imaging information is needed from the entire femoral neck, not only from one site, because the size, shape, and thus rigidity *per se* vary widely between sites (Zebaze et al. 2005, 2007). The 3-dimensional analysis of the entire femoral neck would facilitate this work, and the use of finite element modelling together with a 3-dimensionally recontructed bone could add important pieces of information.

Measurements such as pQCT and MRI offer useful methods for cortical analysis, the latter also enables the analysis of clinically important proximal femur. MRI is a method without causing any ionizing radiation (Sievänen et al. 2007b). This might be important when measuring women's hip region in fertile age. One of the near-future goals in bone methodology is to develop a protocol and software for analysing proximal femur in three dimensions. Such software would allow the analysis of any region from whatever direction. The process in still ongoing and seems to be promising for comparing the benefits of different exercise-loading types. Based on a variety of measurements in this study, site-specific information of bone traits in different exercise-loading types was observed.

7 CONCLUSIONS

The objective of this study was to investigate the associations between the exercise loading types and the strength of bones in young adulthood.

The study series of this dissertation showed that the qualitatively-classified exercise-loading type was an important external determinant of the loaded bone structure. At the weight-bearing lower extremities, most athletes' bone mass was, as expected, substantially superior to that of the nonathletic referents, but more pertinently for the locomotive perspective, the loading-induced additional bone mass seemed to be used to build mechanically strong and appropriate bone structure. High-impact exercise loading was associated with improved structure of bone, but, in most cases, the association between the odd-impact exercise loading type and structural rigidity of bone was as high as in the high-impact exercise loading. No such clear association was observed in the high-magnitude exercise loading. Repetitive, low-impact loading seemed to be associated with strong tibia and possibly strong femoral neck. A specific finding for the lower extremities was that athletes in the high-impact and odd-impact exercise types had equally thick cortex at the vulnerable regions of the femoral neck in terms of hip fractures.

At the dominant upper extremity, all athlete groups classified in the impact, high-magnitude, or repetitive, non-impact exercise loading group had quite similar rigid bones to the non-athletic reference group. However, athletes representing racket sports and classified in impact type of exercise loading had only similar rigid non-dominant radius to those of nonathletic referents, while athletes representing powerlifting and swimming and classified in the high-magnitude and repetitive, non-impact loading group had more rigid radius than that of the referents.

Overall, the strong bone structure is especially obvious among those engaged with impact type of exercise-loading. The observed tens of percents of differences in the bone strength of the lower and upper extremities can be considered clinically important. Such large differences represent more than standard deviation benefits at the population level, which suggests a substantial reduction in fracture risk. The findings of these cross-sectional studies have to be tested in randomized controlled trials, however.

YHTEENVETO

Väitöskirjatutkimuksen tarkoituksena oli määritellä luun lujuuteen yhteydessä olevat liikuntakuormitusmuodot. Väitöskirjatutkimusta varten toteutettiin vuodesta 2004 vuoteen 2008 neljä erillistä poikkileikkaustutkimusta, joihin osallistui 378 urheilijaa ja verrokkiryhmässä 62 liikunnallisesti aktiivista henkilöä. Tutkimusta varten 16 eri urheilulajia luokiteltiin viiteen alaraajoihin kohdistuvaa liikuntakuormitusta kuvaavaan liikuntakuormitustyyppiin ja kolmeen yläraajoihin kohdistuvaa liikuntakuormitusta kuvaavaan tyyppiin.

Tutkimuksessa mitattiin luun rakennetta luuntiheysmittaukseen perustuvan tietokonepohjaisen lonkan rakenneanalyysin, tietokonetomografian ja magneettikuvauksen avulla, jotka kaikki mahdollistavat luun rakenteen arvioinnin. Mitatut luustokohdat olivat sääriluun, reisiluun yläosan, värttinäluun ja olkaluun alueella.

Voimakasta iskukuormitusta sisältäneiden lajien urheilijoilla (lentopallo, aitajuoksu, kumparelasku, kolmiloikka ja korkeushyppy) ja iskuja vaihtuvista suunnista sisältäneiden lajien urheilijoilla (jalkapallo, mailapelit, pikaluistelu, pujottelu ja step-aerobic) oli 13–60 prosenttia lujempi sääriluu ja reisiluu kuin aktiivista kuntoliikunta harrastaneilla verrokkiryhmän jäsenillä. Voimakuormitusta sisältäneiden lajien urheilijoilla (painonnosto ja voimanosto) sääriluun ja reisiluun lujuus oli vastaava kuin verrokkiryhmän jäsenillä. Toistotyyppistä kevyttä iskukuormitusta sisältäneiden lajien urheilijoiden (kestävyysjuoksu, suunnistus ja maastohiihto) sääriluu oli sen sijaan noin 20–30 prosenttia lujempi kuin verrokkien vastaava, ja myös heidän reisiluunsa vaikutti olevan noin 10 prosenttia lujempi. Väitöskirjassa havaittiin uutena löydöksenä, että voimakasta iskukuormitusta ja iskuja vaihtuvista suunnista sisältävien lajien urheilijoilla oli noin 20 prosenttia paksumpi kuoriluu reisiluun kaulan etu- ja yläseinämässä. Nämä reisiluun kaulan seinämät ovat erityisen alttiita haurastumaan iän myötä. Hallitsevassa yläraajassa sekä iskukuormitusta että voimakuormitusta sisältävien lajien urheilijoilla oli 15–30 prosenttia lujempi värttinäluu ja olkaluu kuin verrokkiryhmän jäsenillä. Heikommassa yläraajassa tällaista eroa ei sen sijaan havaittu iskutyyppistä kuormitusta sisältävien lajien urheilijoiden ja verrokkien välillä, mikä puolestaan viittaa siihen, ettei kyseisten ryhmien välillä ollut perimän mukanaan tuomaa eroa luun lujuudessa.

Osatutkimusten tuloksista voidaan todeta johtopäätöksenä, että liikuntakuormitusmuoto on selvästi yhteydessä luun rakenteeseen. Alaraajoissa lujat luut havaitaan voimakasta iskukuormitusta tai iskuja vaihtuvista suunnista sisältävien urheilulajien edustajilla ja yläraajoissa iskutyyppistä liikuntakuormitusta sisältävien lajien edustajilla. Johtopäätösten varmistamiseksi väitöskirjan poikkileikkaustutkimusten perusteella luodut tutkimusoletukset pitäisi testata satunnaistetussa kontrolloidussa koeasetelmassa.

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