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Mandibular Alveolar Bone Mass, Structure and Thickness in Relation to Skeletal Bone Density in Dentate Women

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Grethe Jonasson
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I. Jonasson G, Kiliaridis S, Gunnarsson R. Cervical thickness of the mandibular alveolar process and skeletal bone mineral density. Acta Odontol Scand 1999; 57: 155-61.

II. Jonasson G, Bankvall G, Kiliaridis S. Estimation of skeletal bone mineral density by means of the trabecular pattern of the alveolar bone, its interdental thickness, and the bone mass of the mandible. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2001; 92: 346-352.

III. Jonasson G, Kiliaridis S. The association between the masseter muscle, the mandibular alveolar bone mass and thickness in dentate women. Arch Oral Biol 2004; 49: 1001-6.

IV. Jonasson G, Kiliaridis S. Changes in the bucco-lingual thickness of the mandibular alveolar process and skeletal bone mineral density in dentate women: A five-year prospective study. Eur J Oral Sci 2005; 113: 114-20.

V. Jonasson G, Jonasson L, Kiliaridis S. Changes in the radiographic characteristics of the mandibular alveolar process in dentate women with varying bone mineral density: A five-year prospective study (submitted).

ABSTRACT

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Grethe Jonasson, Department of Orthodontics, Faculty of Odontology, Göteborg University, P.O. Box 450, SE-405 30 Göteborg, Sweden.

The aim of this series of studies was to investigate the relationship between skeletal bone mineral density (BMD) and mandibular alveolar bone mass (MABM), structure, and thickness, as well as to evaluate the possible effect of local functional factors on MABM and alveolar thickness. A further aim was to elucidate whether longitudinal changes in mandibular radiographic characteristics and the bucco-lingual dimension of the alveolar process were related to alterations of BMD. BMD was measured in 160 dentate women using dual X-ray absorptiometry of the forearm. On periapical radiographs MABM was estimated using densitometry and the grey-level value. The alveolar bone structure was evaluated with a visual index and by examining the bone texture on periapical radiographs. The thickness of the masseter was assessed with ultrasound imaging to estimate the masticatory functional factor, and the bucco-lingual alveolar thickness was measured on casts.

MABM and alveolar structure were significantly correlated to BMD. The best correlation was found between BMD and trabecular pattern evaluated with the visual index ($r=0.62$, $p<0.001$). The alveolar thickness was correlated to BMD, and to masseter thickness. MABM was influenced of age, the alveolar thickness, the number of occluding teeth, and the masseter muscle thickness but these factors had no effect on the trabecular structure. After five years, all measurements except the ultrasound imaging of the masseter muscle were repeated in 136 women. The mean BMD, MABM, and alveolar thickness decreased significantly during this period, whereas no significant change was found in the bone structure. In posterior region, the alterations in alveolar bone thickness, radiographic grey-level value, and bone texture were significantly correlated to the changes in BMD. In the anterior region, the alterations in alveolar thickness were not correlated with the changes in BMD. Furthermore, no correlation was found between alterations in MABM, estimated by densitometry, and changes in BMD.

In conclusion, a significant relationship exists between BMD and mandibular alveolar bone mass, structure, and thickness. The local functional factors mainly influence MABM and the alveolar thickness in the molar region, whereas BMD influences the trabecular structure. Dense trabeculation is a strong indicator of high BMD, whereas sparse trabeculation predicts low bone mass. In peri- and postmenopausal women the alveolar shape in the premolar region can be used to predict BMD level. In the lower premolar region, the longitudinal alterations in BMD are related to longitudinal changes in grey-level value, bone texture and alveolar thickness. The decrease in bucco-lingual alveolar thickness may be due to periosteal resorption related to skeletal bone loss.

Key Words: Bone loss, mandible, human, alveolar process, masseter muscle, bone structure.
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After five years, all measurements except the ultrasound imaging of the masseter muscle were repeated in 136 women. The mean BMD, MABM, and alveolar thickness decreased significantly during this period, whereas no significant change was found in the bone structure. In posterior region, the alterations in alveolar bone thickness, radiographic grey-level value, and bone texture were significantly correlated to the changes in BMD. In the anterior region, the alterations in alveolar thickness were not correlated with the changes in BMD. Furthermore, no correlation was found between alterations in MABM, estimated by densitometry, and changes in BMD.

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CONTENTS

PREFACE

This thesis is based on the following papers, which will be referred to by their Roman numerals:

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1. INTRODUCTION

Osteoporosis is a major public health problem that affects around 75 million people in Europe, Japan and the USA. It causes more than 2.3 million fractures a year in Europe and the USA alone (*WHO 2003*). Only Norway has a higher incidence of osteoporotic fractures than Sweden (*SBU Report 2003*). Osteoporotic fractures of the hip and vertebrae are associated with very high morbidity and mortality, and bone mineral density (BMD) is a predictor of survival especially for subjects over 70 *(Johansson et al. 1998).* Though analyses have shown cost-effectiveness in treating high-risk patients with antiresorptive drugs, especially those who have already sustained a fracture, relatively few individuals have had an assessment of their bone density, except for those living in the areas where research on osteoporosis is being conducted (*Johnell & Kanis 2005*).

Studies in rats have indicated that 50-75% of the strength of the bone is determined by its BMD, the trabecular bone structure, and its external geometry *(Ammann & Rizzoli 2003).* Reliable methods have been developed to measure BMD (*Warming et al. 2002, Damilakis et al. 2003*), and new techniques are currently being tried to estimate bone structure (*Geraets et al. 1990*). Bone thickness and bone volume can be assessed by computed tomography (*Garg & Vicari 1995, Lindh et al. 1996a, 1997, Ulm et al. 1997, Herrman et al. 2005*). However, because of cost constraints, the radiation dose (computed tomography), and the limited availability of equipment, there is a need for low-cost screening methods to select high-risk individuals who are likely to benefit from medical treatment.

A large proportion of the population visit their dentist annually, and dental radiographs are often taken on that occasion. These provide information about the alveolar bone at a low cost to the patient and without undue exposure to radiation. Therefore, many research teams have tried to develop methods for using the jawbones to predict skeletal BMD (*Von Wowern 1986, Kribbs et al. 1989, Southard et al. 2000).* Oral radiographic findings associated with osteoporosis have been reported, though the association is rather weak. However, the effect of the local functional factors and their influence on the bone mass and structure of the human jaws, as well as the importance of the bucco-lingual thickness of the alveolar process and its effect on the radiographic image have never been studied. A better insight into these factors might facilitate development of methods based on oral radiographs to identify individuals with low bone mass and increased risk of future fractures. Furthermore, there is a need for longitudinal studies in adult humans to evaluate changes in mandibular bone mass and structure.

2. BACKGROUND

2.1. Bone Tissue

Bone is a connective tissue that consists of cells and a mineralized extracellular matrix. It is classified as either compact (dense) or trabecular (spongy or cancellous). The bones consist of an outer dense compact bone layer (cortex) lined with a periosteum with an outer fibrous layer and an inner more cellular layer of connective tissue. The interior of the bones comprises the trabecular bone and the bone marrow. This sandwich construction gives the bones a high degree of rigidity in combination with low weight. The trabecular bone consists of a network of trabeculae, plates and rods. The trabeculae are oriented predominantly according to stress. The intertrabecular spaces are connected with each other and, like the marrow cavity in the long bones, occupied by marrow and blood vessels. The lining tissue of both the inner surface of the compact bone and the trabeculae is called endosteum. It is often only one cell thick, and the cells have the capacity to differentiate according to stimuli. There are three sorts of bone cells: the osteocytes included in the mineralized bone, plus osteoblasts and osteoclasts on the bone surfaces, where the metabolic activity with formation and resorption takes place. Due to its construction, the trabecular bone has a total surface that is ten times larger than that of the compact bone (*Kanis 1994*).

The skeleton consists of around 80% cortical and 20% trabecular bone. In the spine, the heel, and the maxilla, the trabecular bone dominates (therefore they are called "trabecular bones"), whereas the long bones in the peripheral skeleton and the mandible are "cortical bones". The proportion of trabecular to cortical bone varies at different sites of the same bone. For example, the proportion of trabecular bone in the mid-radius is about 5%, in the distal radius 20% and in the ultradistal radius 40% (*Kanis 1994*). Approximately 20% of the mandible consists of trabecular bone in the premolar region (*Wowern 1977b*), which is the same as the trabecular proportion in the distal radius, where the bone density is measured (*Nilas et al. 1987*).

Bone strength depends on the product of several variables: the shape and size of the bone, the mineral content, crystal size, collagen fibres, the microstructural organization (e.g. lamellae, osteons), material properties (modulus of elasticity, failure stress), and the modelling and remodelling processes (*Martin 1993, Van der Meulen et al. 2001*). Thus it is extremely difficult to assess bone strength, but the bone mineral content (BMC) and bone mineral density (BMD) can be reliably measured, and new techniques can estimate bone structure.

2.2. Bone remodelling

Bone is a living tissue and it is constantly resorbed and formed by the processes known as modelling and remodelling. Bone modelling begins during fetal life and continues until the end of the second decade, when the longitudinal growth of the skeleton is completed. In the modelling process, bone apposition leads to a change in the size and shape of the skeleton. Bone modelling may continue, but to a lesser extent, during adult life with a periosteal bone apposition, which is more pronounced in men than in women. This periosteal bone apposition late in life may be secondary to increased bone resorption at the endosteal surface with enlargement of the internal diameter (*Ulm et al. 1994).*

The role of the bone-remodelling process is to maintain the mechanical integrity of the skeleton by replacing old bone with new bone, thereby adapting to functional loading and repairing small stress fractures. Remodelling occurs simultaneously with modelling during growth and becomes the predominant process during adult life. Bone resorption and bone formation occur at the same location. Both modelling and remodelling respond to hormonal influence and to biomechanical factors. It is stated that, with a few exceptions such as excess of corticosteroid medication, the actions of oestrogen and biomechanical strain are the major physiological mechanisms for bone mass conservation, and major decreases in bone mass do not occur unless one of these two mechanisms is affected (*Riggs et al. 2002).*

Each remodelling cycle starts when the bone-resorbing osteoclasts have identified a bone site in "need" of exchange. They adhere to the bone surface and release acid by a "proton pump" at the site. Thereafter, proteolytic enzymes will resorb the decalcified bone tissue. The whole bone tissue at the site disappears and a lacuna is built. The osteoclasts leave the lacuna and the bone-forming osteoblasts enter to form new bone (*Lerner 2000, Lindh & Lerner 2003).* The osteocytes form a large network in the bone, and one of their functions is to act as mechanosensors in the early stages of bone remodelling, where loaded mechanical stress is converted to a series of biochemical reactions that finally activates the osteoclasts and the osteoblasts (*Nomura et al. 2000*).

During childhood and adolescence the formation of bone dominates over the resorption of bone. In the mature adults there is a balance between bone formation and bone resorption. After the menopause in women and with aging in men, bone resorption exceeds bone formation, leading to a net bone loss. This lack of balance in formation and resorption might lead to osteoporosis, whether it is a result of deficiency of either sex hormone, hyperparathyroidism, hyper-thyroidism, chronic renal failure, post-transplantation or medication with gluco-corticosteroids (*WHO 2003).*

2.3. Methods for measuring bone density and bone structure

2.3.1. Radiography

Osteopenia is difficult to detect with routine radiographs, since a minimum bone mass loss of 30 %, and possibly as much as 50% or 60 %, is needed before significant osteopenia/ osteoporosis can be detected. Radiographs can be used to measure the cortical thickness of the metacarpal bones and to evaluate the Singh index, which is an estimate of the appearance of the trajectories in the proximal femur *(Masud et al. 1995)*.

2.3.2. Single and dual photon absorptiometry

The techniques of single and dual photon absorptiometry (SPA and DPA) use 125-iodine as the energy source coupled with a scintillation detector, which together scan across the area of interest. They are very precise and accurate techniques, but the isotopes must be changed at least once a year. SPA is used in the forearm (*Christiansen et al 1981, Riis & Christiansen 1988, Hassager et al. 1991, Hansen et al. 1991, Melton et al. 1993)* and DPA in lumbar spine *(Riis & Christiansen 1988, Hassager et al. 1991, Feyerabend & Lear 1993, Melton et al. 1993, Jacobs et al. 1996),* in hip (*Feyerabend & Lear 1993, Melton et al. 1993),* and in total body *(Gotfredsen 1990, Feyerabend & Lear 1993*).

2.3.3. Single and dual X-ray absorptiometry

In this technique the photons have been replaced with an X-ray source: single and dual X-ray absorptiometry (SXA and DXA). The advantages of SXA and DXA are no use of isotopes, higher beam intensity, and therefore a faster scan and improved spatial resolution. SXA is used in the forearm (*Hansen et al. 1991, Borg et al. 1995)* and in the heel (*Johansson et al. 1998),* but it cannot be used in the axial skeleton. DXA is used in the forearm *(Ryan et al. 1992, Arlot et al. 1997, Löfman et al. 1997, Proctor et al. 2000, Southard et al. 2000, Magnusson et al. 2001a, b*), in the vertebrae (*Gluer et al. 1990, Löfman et al. 1997, Southard et al. 2000, Rubin et al. 2002,*) and the hip (*Gluer et al. 1990, Karlsson et al. 1993, Arlot et al. 1997, Löfman et al. 1997, Proctor et al. 2000, Pluskiewicz et al. 2000, Southard et al. 2000, Rubin et al. 2002*), and the upper half of the skull (*Magnusson et al. 2001a, b).*

Currently, DXA is the best evaluated technique for assessing BMD, and it is regarded as the "golden standard", with which the performance characteristics of less well-established techniques can be compared (*WHO 2003*). Assessment of BMD with DXA gives a value of mineral content per area, but as the third dimension of bones is not taken into consideration, osteoporosis is overdiagnosed in small persons with thin bones and underdiagnosed in tall persons with bigger bones *(Pors Nielsen et al. 1998*). Similarly, men have

greater area BMD than women, but adjusting for height reduces or eliminates these differences (*Melton et al. 2000*).

2.3.4. Quantitative computed tomography

In quantitative computed tomography (QCT), a thin transverse slice of the bone is imaged. The image can be quantitated to give a measure of volumetric BMD, and trabecular bone can be measured independently of surrounding cortical bone (*Lang et al. 1998, Link et al. 1999).* The disadvantage of QCT is the very high cost and the radiation dose *(Cann 1988).* QCT has been applied to the spine (*Cann et al. 1980, Guglielmi et al. 1994)*, but not yet to the hip (*WHO 2003*). Magnetic resonance measurements may be employed in the future for assessment of the trabecular structure, but they are still expensive and time-consuming (*Lang et al. 1998).*

2.3.5. Ultrasound

Two methods of using ultrasound have been evaluated: broadband ultrasound attenuation (BUA) and speed of sound (SOS) at the heel. The advantage of this technique is that there is no ionized radiation. It may provide information on the structural organization of bone in addition to bone mass, but no diagnostic criteria for osteoporosis have been developed yet (*Graafmans et al. 1996, Gluer 1997, Pluskiewicz et al. 2000, Cortet et al. 2004).*

2.3.6. Assessment of bone structure

New techniques have been developed to assess the architecture of the bones (*Link et al. 1999).* Mathematical operators (like erosion, dilation, and skeletonization) are changing the images to facilitate the analysis of trabecular width, spacing, geometry and orientation (*Geraets et al. 1990, 1993, Korstjens et al. 1996).*

Direct measurements of trabecular width and separation/intertrabecular space have been made in autopsy specimens *(Weinstein & Hutson 1987).* The results showed that the increase in distance between adjacent trabeculae accounted for more than twice the age-related bone loss compared to the decrease in trabecular width *(Weinstein & Hutson 1987).* However, to date, these new techniques have not been fully developed for use in clinical practice.

2.4. The influence of loading

The architecture of the bones is the result of genetically controlled growth and an adaptive response to functional loading (*Lanyon 1987*). The bones remodel to reach the shape that best withstands mechanical stresses. For example, prolonged bending of a long bone deforms it and causes one side to become more concave and the other side more convex. This would stimulate bone

apposition on the surface becoming more concave and bone resorption on the surface becoming more convex. Thus, the bone would change shape, straighten up and adopt a configuration that minimizes its deformation during physiological function (*Frost 1994*). In adult weightbearing bones, loading may lead to periosteal apposition, thereby increasing the cross-sectional area in the vertebrae (*Mosekilde 2000*), and in long bones (*Ruff & Hayes 1988, Ahlborg et al. 2003*).

Loads on bone and muscle function can also affect bone quality and quantity. Weightbearing and contractions of the regional muscles are the chief biomechanical factors influencing the skeleton. Which of these that contributes most significantly to the determination of bone mass and structure is a matter of controversy, but it seems that muscles exert a larger influence than fat mass, body weight and age on the bone mineral content (BMC) in the whole body and lower limbs, regardless of the gender and reproductive status of the individual (*Capozza et al. 2004*). The effect of sport-induced loads on the forearm is demonstrated by the finding that young professional tennis players show bone hypertrophy and an increased bone density in the stroke arm compared to the controlateral arm (*Krahl et al. 1994*). Furthermore, rowers and swimmers have low leg bone mineral density (BMD) and high arm BMD, whereas participants in team sports like soccer and rugby had high leg BMD and high arm BMD (*Magnusson et al. 2001b).* After a hip fracture the activity level is reduced, and BMD decreases in the legs, which under normal conditions are weight-loaded regions. BMD remains the same in a partly loaded region like the arms, and increases in the skull of the head (*Magnusson et al. 2001a*). Women in all age groups have a higher percentage of bone mass in the head and a lower percentage in arms and legs compared to men (*Fujita et al. 1999).*

Several cross-sectional studies have demonstrated a positive correlation between muscular strength and BMD in the hip, spine or forearm bones *(Snow-Harter et al. 1990, Madsen et al. 1993, Di Monaco et al. 2000*). Muscle strength is found to be an independent predictor of BMD, accounting for 15-20% of the total variance in bone density in young women (*Snow-Harter et al. 1990*).

2.5. Peak bone mass and bone loss

The "peak bone mass" is the maximal amount of bone tissue present in the young adult. The bone mass of an individual at a given time is a function of the attainment of peak bone mass in early adulthood and the amount of experienced bone loss. Racial and genetic factors are important determinants of peak bone mass, with a lower risk in black people. Nutritional factors such as calcium, vitamin D, and malnutrition are especially important in growing individuals for obtaining peak bone mass and in the elderly to limit bone loss. Load-bearing

training and daily physical activity are positive factors at all ages for attaining peak bone mass and counteract bone loss, whereas a sedentary life and space flight are negative factors leading to rapid bone loss. Fat mass and leptin, which is secreted mainly by white adipose tissue, are positively associated with BMD in women but only weakly or inconsistently predictive of BMD in men (*Thomas et al. 2001*). Thus, in heavy women both the increased loading of the skeleton and the building of oestrogen in fat tissue probably limit bone loss (*Kanis 1994, Riggs et al. 2002).* Oestrogen and testosterone are key regulators of skeletal growth and maturation, and oestrogen together with growth hormone and insulin-like growth factor initiate the pubertal growth spurt that doubles bone mass (*Riggs et al. 2002*).

2.6. Osteoporosis

Osteoporosis is defined as a systemic skeletal disease characterized by low bone density and microarchitectural deterioration of bone tissue with a consequent increase in susceptibility to fracture (*WHO 1994*).

The new techniques for measuring BMD are used at different sites: forearm, spine, hip, and heel, and the absolute values obtained cannot be compared directly since the equipment used also differs. Therefore, the standard deviation (SD) of BMD is used as a working definition for handling osteoporosis and osteopenia, since it is a relative value that can be compared, Thus, normal bone mass is the same as peak bone mass in a reference group, plus or minus 1 SD (also denoted T-score). Osteopenia means peak bone mass minus 1-2.5 SD; osteoporosis is more than 2.5 SD below peak bone mass (*WHO 1994).* However, the same SD/ T-score derived from different sites and techniques yields different information on fracture risk, so that the reference standard for diagnostic purposes is currently the proximal femur, using dual energy X-ray absorptiometry (DXA) (*Kanis et al. 2001*).

The aetiology of osteoporosis is multifactorial and includes a number of risk factors such as increasing age, female gender, heredity, low body mass index, early menopause, smoking, certain medical disorders and medication (*Kanis 1994).*

2.7. Pathophysiology of osteoporosis

In a model for the pathophysiology of osteoporosis, oestrogen deficiency is identified as the major cause of age-related bone loss in both women and men. Oestrogen suppresses bone turnover, and it is the key hormone for maintaining balanced rates of bone formation and resorption. Furthermore, oestrogen affects

the generation, life span, and functional activity of both osteoclasts and osteoblasts (*Eriksen et al. 1999, Riggs et al. 2002).*

The oestrogen deficiency leads to an increased bone turnover with a prolonged resorption phase and a shortening of the formation phase in the remodelling cycle. Normally up to 1-2 millions of remodelling sites can be found in the skeleton. The number of remodelling sites is increased in patients with oestrogen deficiency, as in postmenopausal osteoporosis, due to the increased number of bone-resorbing osteoclasts. The number of bone-forming osteoblasts is also increased, but the function of the cells is impaired due to the oestrogen deficiency, and therefore the result is a net bone loss. As a consequence of these changes, the volume of the resorption cavity, created by the osteoclasts in the remodelling cycle, is increased beyond the capacity of the osteoblasts to refill it (*Riggs et al. 2002).* Thus, oestrogen deficiency might lead to rapid bone loss in the first years after the menopause due to a loss of restraining effects of oestrogen on bone turnover and a reduced sensing of biomechanical strain by bone cells (*Riggs et al. 2002*). Bone loss also occurs as a result of changes in parathyroid hormone and vitamin D deficiency (*Kanis 1994*).

Oestrogen is supposed to interact also with the biomechanical forces (muscle contraction and gravitational forces) on the bone. This hypothesis is supported by the findings of oestrogen receptors on all bone cells, even on the osteocytes, which are the cells sensing biomechanical strain. Probably the osteocytes are acting in the bone "mechanostat", in determining the level of bone mass according to the biomechanical forces. The theory of a bone mechanostat is proposed and described by Frost (*2004*). It is a feed-back-system, which regulates bone mass. It suggests that in normal adult activity, bone remodelling is "set" on conservation of bone mass. With growth and extreme physical activity, the higher strain level will induce a modelling mode that increases bone mass by periosteal bone apposition. In contrast, chronically low strain levels, disuse, or space flight will lead to remodelling and to bone loss on the endosteal surfaces. Possibly there are different cytokines in the bone marrow that induce the endosteal resorption (*Ferretti et al. 2003, Riggs et al. 2002*).

2.8. The mandibular alveolar process: bone composition and bone mass changes

The alveolar process is defined as the part of the mandible and maxilla that surrounds and supports the teeth on all sides. The occlusal border of the alveolar process, which is located near the cervix of the tooth, is referred to as the alveolar crest. The alveolar process is composed of the lamina dura, which is the bone of the wall of the tooth socket, the buccal and lingual cortices, and the trabecular bone with bone marrow filling the spaces between the trabeculae. In

some areas, the alveolar process is thin and contains little or no trabecular bone, and the lamina dura and the cortices are fused (*Lindhe et al. 1998*). The alveolar process develops as a result of tooth root elongation and tooth eruption. Alveolar bone matures as the teeth gain functional occlusion; later, if the teeth are lost, the alveolar process is reduced. The teeth are important in the development and maintenance of the alveolar process. The alveolar crest is located about 1 to 1.5 mm below the cemento-enamel junction of the teeth, and is rounded in the anterior region and more flat in the molar area. The functional demands on the mandible are different in the three regions, incisor, premolar, and molar. Furthermore, the role of the alveolar process differs from that of the mandibular body, where the attachment of the muscles differs from region to region. Therefore, there is a great variation in shape, course of trajectories, and thickness of the cortices within the mandible (*Von Wowern 1977a, b).*

In growing rats on a soft diet, the bone mass in regions subjected to direct loads or bending forces become less dense than in rats on a hard diet *(Kiliaridis et al. 1996).* The cross-sectional area and the width of the molar alveolar process become smaller in rats on a soft diet than in rats on a hard diet *(Bresin et al. 1994).* This reduction in function induced by the diet causes a local loss of bone mass. Similarly, after tooth extraction there is also bone loss due to the reduced function (*Elovic et al. 1995, Von Wowern et al. 1979*) and a great inter-individual variation in the remodelling pattern of the edentulous areas, with some individuals losing little bone and others undergoing extensive resorption *(Carlsson & Persson 1967, Tallgren 1972, Von Wowern 1986).* The reduction in bone height after tooth extraction is more pronounced in the mandible than in the maxilla (*Tallgren 1972*). Several studies have concerned the association between skeletal bone mass and residual ridge resorption after tooth extraction (*Kribbs et al. 1989, 1990a, b, Von Wowern 1992, Klemetti et al. 1993a, 1996*), but no association, or only a weak one, has been found. Decrease in bone size seems to be specific to the alveolar process, since it has not been recorded in any other bone. This has been shown in edentulous regions but not in dentate areas. It has also been demonstrated that the alveolar ridge region has a lower bone density both in dentate and toothless areas in older individuals than in younger ones *(Boyde & Kingsmill 1998*). The mandible undergoes the same ageing processes as other bones (*Von Wowern 1985a, b).* The porosity of the mandibular bone increases with age. In elderly women the bone structure of the jaws is characterized by thin porous cortices and a decreased amount of trabecular bone (*Von Wowern 1977a, b, Atkinson & Woodhead 1968*). The density of the buccal cortex varies throughout the mandible, and it is dependent on age and gender, but the lingual cortex is not (*Von Wowern 1977a, Klemetti et al. 1993b).* The BMD of both cortices is influenced by functional stresses exerted by the masseter muscle (*Klemetti et al. 1994b).* The trabecular bone shows an extreme variation in trabecular bone volume and connectedness within and between jaws

independent of age *(Von Wowern 1977b, Klemetti et al. 1993b, Lindh et al. 1996a, Ulm et al. 1997)*. Increased trabecular bone density is more frequently seen in anterior than in posterior regions *(Von Wowern 1977b, Lindh et al. 1996a)*. The trabecular bone just inferior to the root apex is affected by sex and age, whereas the trabecular bone, located more basally but still superior to the mandibular canal, is mostly sensitive to dental status *(Chöel et al. 2003)*. The age changes are more pronounced in alveolar bone than in mandibular basal bone *(Atkinson & Woodhead 1968)*.

In contrast to the alveolar bone, the bone mass in the mandibular basal bone may increase, due to an increased thickness of the cortical bone. This has been demonstrated in atrophic edentulous mandibles, where the amount of inner cortical bone of the male mandibles may increase as a functional adaptation in order to preserve the stability of the jaw. In the mandibles of women, postmenopausal osteoporosis seems to prevent an analogous compensation mechanism *(Ulm et al. 1994)*. Increased density in the mandibular body with age has also been reported in other studies *(Kingsmill & Boyde 1998a, b)*, with the highest densities matching the sites thought to experience the highest functional strains *(Kingsmill & Boyde 1998a)*. The same authors conclude that the mandible differs sufficiently from postcranial skeletal sites that it would be unwise to extrapolate from findings in the jaw to the circumstances elsewhere *(Boyde & Kingsmill 1998)*. There are numerous studies of the bone mass and density of the mandible, but they are difficult to compare since they have involved different sites, different age groups and groups with different dentition. However, the alveolar bone mass seems to decrease with aging, and bone mass in the mandibular body may increase slightly with age.

2.9. The maxillary alveolar process

Similarly to the mandibular alveolar process, the maxillary alveolar process is dependent on age, sex and dentition, but only a few studies exist concerning bone mass in the maxilla *(Devlin et al. 1998, Ulm et al. 1999, Southard et al. 2000, 2001, Lindh et al. 2004)*.

In the maxilla, the cortices are much thinner than in the mandibular alveolar process. The maxilla is a predominantly trabecular bone, and therefore it is hypothesized that bone loss should be seen earlier in the maxilla than in the mandible. The sinuses occupy a large part of the maxilla, so it is easier to measure bone mass in the frontal segment than in the lateral segment. In the maxilla, tori are rear and they are situated in the palate, not on the alveolar process. The same methods for assessing bone mass and structure in the mandible can be applied to the maxilla, except the ones that evaluate the thickness and erosion of the basal cortex of the mandible.

Significant correlations are found between the maxillary alveolar process bone density and the spine (*Southard et al. 2000, Lindh et al. 2004*), the density of the mandibular alveolar process, the hip and the radius (*Southard et al. 2000*). There is an extreme variation in trabecular bone volume between individuals (*Lindh et al. 2004*), between regions (with the lowest in the molar region due to sinus), and between genders (*Ulm et al. 1999*).

2.10. Methods of measuring mandibular alveolar bone mass

Oral radiographs have been used for measurements of the optical density (the degree of darkening of the exposed film) of the bone to estimate bone mass in the mandibles *(Kribbs et al. 1983, 1989, 1990a, b, Mohajery & Brooks 1992, Jacobs et al. 1996).* Digital image analysis techniques for quantitating bone mass have been applied to oral radiographs too (*Shrout et al. 1996, 1998, 1999, Hildebolt 1993, Hildebolt et al. 1994, Southard et al. 1996, 2001).*

Dual photon absorptiometry (DPA) has been used in the edentulous mandible (*Von Wowern 1985a, b),* and DXA (*Corten et al. 1993, Denissen et al. 1996, Horner et al. 1996, Horner & Devlin 1998, Pluskiewicz et al. 2000, Horner et al. 2002, Chöel et al. 2003*) and quantitative computed tomography (QCT) too (*Klemetti et al. 1993a, b, 1994, Taguchi et al. 1996, Lindh et al. 1996a, 1997).* Ultrasound has been used to estimate mandibular bone mass (*Pluskiewicz et al. 2000*).

The architecture of the bones has been assessed using mathematical operators (like erosion, dilation, and skeletonization). With this technique the image of the trabecular pattern is changed to "skeleton of lines" to facilitate the analysis of trabecular width, spacing, geometry and orientation (*Shrout et al. 1998, White & Rudolph 1999, Couture 2003*). Morphological features of the trabeculae and marrow regions have been examined in patients with osteoporosis and normal controls, and it was found that patients with osteoporosis had a reduction in trabecular length and periphery plus reduction in complexity of the trabecular pattern in comparison with controls (*White & Rudolph 1999*).

Furthermore, in vitro studies have used digital subtraction of oral radiographs (*Southard et al. 1994, Christgau et al. 1998*) and fractal dimension (*Southard et al. 1996*) to detect density changes in simulated osteoporosis. Fractal dimension is a measure of "the roughness of the surface" calculated by complex algorithms. However, to date, these new techniques have not been fully developed for use in clinical practice.

In order to evaluate the quality of the bone prior to implant treatment, visual classifications have been proposed *(Lekholm & Zarb 1985, Lindh et al. 1996b, Taguchi et al. 1997*). The two latter classifications are based on the coarseness of the trabecular pattern, whereas the first classification includes both an assessment of the thickness of the cortices and the trabecular pattern plus an evaluation of the bone shape. On dental panoramic film it is possible to see a reduction in the density and thickness of the inferior mandibular cortex in comparison with the jawbone in a young adult. The basal cortex has been classified by using its degree of resorption "Mandibular Cortical Index" (*Klemetti et al. 1994a, Taguchi et al. 1996*). The cortical width at the gonion *(Bras et al. 1982, Kribbs et al. 1983, 1989, 1990),* the width of the lamina dura (*Mohajery & Brooks 1992*) and the width of the mandibular cortex have been evaluated (*Klemetti 1993c, Horner & Devlin 1998, Horner et al. 2002, Devlin & Horner 2002)*. It seems that a width of the inferior mandibular cortex of less than three mm is associated with low skeletal bone mass (*Horner et al. 2002).* An analysis of clinical and panoramic predictors has identified the thickness of the inferior cortical border of the mandible and age to be the most useful factors for identifying subjects with low bone density (*White et al. 2005).* Other indices are the panoramic mandibular index, which was calculated as a ratio of the cortical thickness to the distance from the inferior margin of mental foramen to the inferior border of the mandible (*Benson et al. 1991*), and the alveolar process/ mandibular height ratio (*Goldberg et al. 1988).*

2.11. Osteoporosis and mandibular bone mass and structure

Conflicting results have been reported in the literature concerning the association between osteoporosis and oral bone loss, with some studies finding no association and others only a weak one *(Hildebolt 1997).* Mandibular bone mineral content is reduced in subjects with osteoporotic fractures (*Von Wowern et al. 1994*). BMD of the buccal cortex, but not the lingual cortex and the trabecular portion, correlates with osteoporosis (*Klemetti et al. 1993b*). Mandibular bone density measured with DXA correlates with skeletal BMD (*Horner et al. 1996*). Using film densitometry most researchers (*Horner & Devlin 1992, Jacobs et al. 1996)* but not all (*Mohajery & Brooks 1992, Southard et al. 2000*) have found that the optical density (the degree of darkening) is increased in subjects with low bone density. The optical density of the mandibular radiographs correlates with vertebral BMD in osteoporotic women (*Kribbs et al. 1989),* in normal women *(Kribbs et al. 1990a*), and in women with a history of vertebral fracture (*Kribbs 1990b, Law et al. 1996*). Reduction in crestal alveolar bone density has been reported in longitudinal studies to correlate with osteoporosis (*Payne et al. 1997, 1999),* and postcranial and oral bone mass increase in postmenopausal women receiving hormone replacement therapy (*Civitelli et al. 2002*).

The thickness of the inferior border tends to be reduced in subjects with osteoporosis (*Kribbs et al. 1989, Klemetti et al. 1993c, Bollen et al. 2000*), although some studies have found no relationship (*Mohajery & Brooks 1992, Law et al. 1996*). In the mandibular cortical index, subjects with osteoporosis are more likely to show erosions of the inferior border of the mandible than controls (*Klemetti et al. 1994a, Taguchi et al. 1996b, Bollen et al. 2000*). In some cross-sectional studies (*Kribbs et al. 1989, Von Wowern & Kollerup 1992*) and in longitudinal studies correlations have been found between loss of alveolar height and osteoporosis (*Payne et al. 1999, Civitelli et al. 2002*). However, these findings are not consistent since other studies did not find any correlations between changes in marginal bone level and osteoporosis (*Elders et al. 1992, Mohammad et al. 1996*).

The structure of trabecular bone has been analysed in relation to osteoporosis with fractal analysis (*Law et al. 1996, Southard et al. 2000, 2001*) but results are conflicting. In healthy women, the radiographic fractal dimension of the alveolar process is significantly related to the alveolar process density but not to the skeletal density (*Southard et al. 2001).*

Morphometric analyses have been used to quantify structural elements in radiographic images of bone trabeculae (*Geraets et al. 1990*), and a weak correlation has been found between features of the trabecular pattern and BMD of the spine. The thickness of the trabeculae, spacing between the trabeculae, and the trabecular connectivity are altered in patients with osteoporosis compared to normal subjects (*White & Rudolph 1999*).

3. AIMS

The purpose of the present work was to investigate if mandibular alveolar bone mass, structure and alveolar thickness are different among individuals with varying skeletal bone density and if alterations in the skeletal bone density lead to changes in the mandibular alveolar bone characteristics. To achieve that goal, the specific aims were to:

- study the differences in alveolar thickness and shape among individuals with varying BMD (*Paper I*).
- investigate the differences in MABM and structure among individuals with varying BMD (*Paper II*).
- study the importance of the masticatory loading on individuals with varying BMD, and estimate this effect on the alveolar bone (*Paper III*).
- investigate possible changes during a 5- year period in the bucco-lingual dimension of the alveolar process in dentate women, and if these are related to alterations in BMD (*Paper IV*).
- analyse the changes in mandibular bone mass and structure during a 5-year period and if these changes are related to alterations in BMD (*Paper V*).

4. MATERIALS AND METHODS

4.1. Subjects

Out of 175 women who were approached consecutively, a total of 160 were recruited to the five projects during three periods in the years 1995-1997. A further five women were not asked to participate due to negligent oral hygiene and active gingivitis. The age range in the first group recruited was 47-55 years, but it was later extended to 38-67 years, and after that to 20-78 years (*Table 1*). The criterion for participation was that the subjects should be dentate with one (*Papers II, III, IV, V*) or two mandibular premolars on one side (*Paper I*). Exclusion criteria were advanced periodontal disease (*Papers I-V*), torus mandibularis (*Paper I*), extreme gingival recession (*Paper I, IV*), and extreme mandibular crowding (*Paper I*). The subjects had no deepened pockets in the examined premolar region and a healthy gingiva. Age distribution and medical history are reported (*Table 2*).

In the longitudinal studies, 24 women (out of 160) were not examined: 3 had died, 4 were seriously ill and unable to participate, 12 had moved out of the area (mostly young people) and could not be reached, and 5 declined for other reasons. In paper IV, a total of 19 subjects were excluded: three individuals because of fracture of the non-dominant arm, 12 women because of either periodontal disease or/and major changes in their dental status due to extensive prosthetic constructions. Furthermore, four subjects were excluded due to differences in the crown dimensions on the dental casts. In paper V only 5 women were excluded from the follow-up study: three because of fracture of the non-dominant arm and two because of tooth extractions and extensive prosthetic constructions. The interdental alveolar thickness is less sensitive to prosthetic changes than the dimensions measured at the middle of the roots.

Table 1. Number and age range of the participants in the 5 studies.

	Participants n	Age range
Paper I	72	38-67 yr
Paper II	80	20-78 yr
Paper III	62	40-75 yr
Paper IV	117	22-75 yr
Paper V	131	22-75 yr

Table 2. Age distribution and medical history affecting BMD in 131 women followed for five years. HRT = hormone replacement therapy, n = number of subjects, % = percentage of the subjects participating in the study.

Recording	Initial recording	Five years after
Subjects	N	N
<45 yr	35 (26.7%)	19 (14.5%)
45-55 yr	67 (51.2%)	45 (34.4%)
>55 yr	29 (22.1%)	67 (51.1%)
Premenopausal	74 (56.5%)	40 (30.5%)
Postmenopausal	57 (43.5%)	91 (69.5%)
HRT	22 (16.8%)	31 (23.7%)
Hysterectomy	14 (10.7%)	19 (14.5%)
Oophorectomy (unilateral)	5 (3.8%)	5 (3.8%)
Oophorectomy (bilateral)	4 (3.1%)	7 (5.3%)
Malabsorption syndromes	9 (6.9%)	16 (12.2%)
Treated for cancer	6 (4.6%)	10 (7.6%)
Hyperthyroidism	5 (3.8%)	10 (7.6%)
Active smokers	29 (22.1%)	20 (15.3%)

4.2. Methods

4.2.1. Clinical examination and questionnaire

An intraoral examination was performed including registration of pocket depth, and recording of the number of occluding teeth. Together with the examiner the participants answered a questionnaire concerning life style factors, weight, length, hormone replacement therapy, number of years after menopause, calcium intake, coffee-drinking, physical activity, previous fractures and medical history (*Appendix I*). Information was given about osteoporosis, risk factors, the importance of physical activity and a proper diet. All participants received written information and their consent was obtained. The studies were approved by the Scientific Ethical Board of Göteborg University, Sweden.

4.2.2. Dual X-ray absorptiometry of the forearm

The area bone mineral density (BMD) was determined in the distal forearm of the non-dominant arm by SXA (group C in *Paper I*) and by dual energy X-ray absorptiometry (in all other subjects) (Osteometer DTX-100 and DTX-200, Osteometer, Rödovre, Denmark). The patients were subjected to a low radiation dose, below 2 mrem, during the X-ray scan. The operator dose is also low and no shielding is required.

4.2.3. Systematic morphological mapping of the alveolar process

Three bucco-lingual dimensions of the alveolar process were assessed on dental casts at 35 predetermined sites with a dial calliper (Kori-HSL 6871-0201, range 0-15mm or Kori-HSL 250-00, range 0-10mm, *Figure I*). Furthermore, the bucco-lingual thickness of the teeth at the cemento-enamel junction was measured (*Paper I)*.

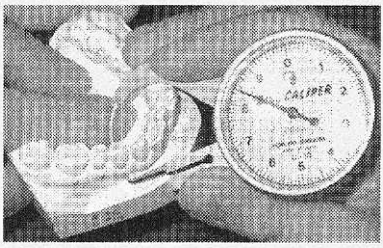
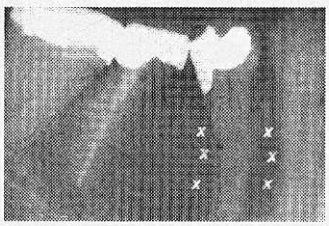


Figure 1. Measuring with the dial calliper.

4.2.4. Radiography

A periapical radiograph (Kodak Ultra-Speed DF-58, Eastman Kodak, Rochester, NY, USA) of the premolar region was obtained by using standardised paralleling technique with an Eggen film holder. The mandibular bone mass was estimated by means of "classical" densitometry (*Figure 2),* (and presented in aluminium equivalents, mm) and density histograms of the grey-level values of the bone combined with a simple calibration method using a separate reference radiograph of aluminium step wedges (*Figure 2).* The bone structure was evaluated with a visual index (*Lindh et al. 1996b, Paper II*), and with the help of a new method for calculating the bone texture (*Paper V*).



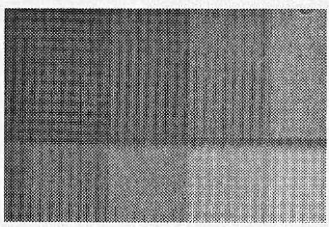


Figure 2. The six sites, three along each side of the root of the first premolar, for estimating MABM with densitometry, and the step-wedges for calibration.

4.2.5. Ultrasound imaging of the masseter muscle

The thickness of the masseter was measured with an ultrasound scanner and a 7-MHz transducer (Acuson 128, Acuson Corporation, Mountain View, CA, USA) by one examiner (SK). The transducer was orientated perpendicularly to the ramus, close to the level of the occlusal plane, where the masseter was thickest. The measurements were performed when the masseter was contracted during centric occlusion (*Figure 3)*. The mean thickness of two measurements of the right masseter muscle during contraction was used in the regression analyses (*Kiliaridis & Kälebo 1991, Paper III).*

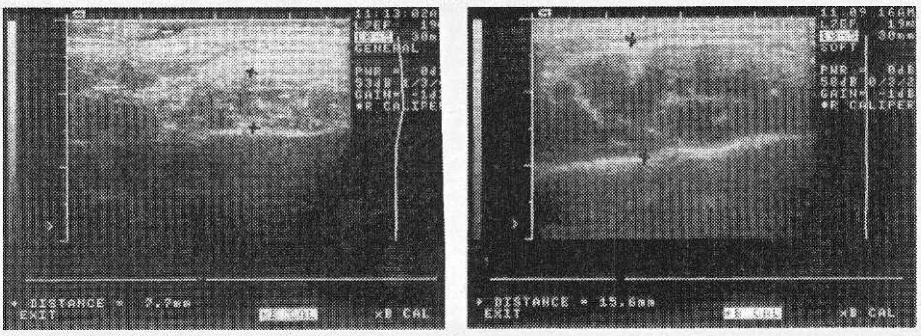


Figure 3. Transverse ultrasound scans of the masseter muscle. The wide white shadow on the top depicts the skin echo. The image of the masseter muscle mass is the darker area under the skin. The tendinous structures are the white stripes in the darker area. Under the muscle, the echo from the bone of ramus is observed as a white stripe. The two crosses point to the location of the electronic callipers used for measuring the thickness of the masseter. To the left is a scan of a thin muscle (7.7mm thick) with small black areas representing muscle mass and blurred tendinous structures. The dark areas are smaller and less distinct than the muscle mass to the right because of an accumulation of adipose cells, which results in a greater intramuscular echo intensity. To the right is a scan of a thick muscle (15.6mmm thick) with large dark areas representing the muscle mass and distinct fan-like tendinous structures. The line at the right side depicts the position of the buttons on the control panel of the equipment.

4.3. Clinical design

The series of investigations started with a cross-sectional observational study, where the alveolar thickness was assessed, and where a group of 24 women was used as a test group to identify the most useful model for predicting BMD from the measurements of the mandibular alveolar process. This model was then cross-validated by applying it to predict BMD in two other independent groups of women (*Paper I*).

Another cross-sectional study was undertaken, where radiographs of 80 women were analysed to evaluate if MABM, estimated by densitometry, or the trabecular pattern were more closely associated with BMD (*Paper II*).

In a third cross-sectional study, the functional factors, expressed by the thickness of the masseter muscle and the number of occluding teeth, in 62 women were analysed and their role in the relationship between BMD and MABM was elucidated (*Paper III*).

In a five-year prospective observational cohort study, the changes in bucco-lingual thickness of the mandibular alveolar process in 117 women were investigated. Furthermore, the thickness changes were related to BMD changes and to age and menopausal status (*Paper IV*).

In the same five-year prospective cohort the changes in MABM, estimated by densitometry and the grey-level value of the alveolar bone, the trabecular pattern and the bone texture were examined in 131 women and the changes were related to changes in BMD and alveolar thickness (*Paper V*).

4.4. Measurements

4.4.1. Dual X-ray absorptiometry of the forearm

The measurements determined area BMD in the non-dominant forearm as a percentage of the mean BMD of age-matched women (*Paper I*) and of young women (*Papers II-V*).

With the Osteometer equipment, 1 SD corresponds to 12% of the mean BMD of young women. SD indicates if the patient has normal values (within 1 SD from the mean, which corresponds to BMD $\geq$ 88%, osteopenia (between 1 and 2.5 SD from the mean, which corresponds to a BMD between 71%-87%), or osteoporosis (more than 2.5 SD below the mean, which corresponds to BMD $\leq$ 70%).

4.4.2. Thickness of the mandibular alveolar process

The bucco-lingual dimensions were measured at the middle of the roots of the teeth (*Figure 4*) from molar to molar at two sites (a total of 24 sites) and between two adjacent teeth (*Figure 5*) from molar to molar (a total of 11 sites).

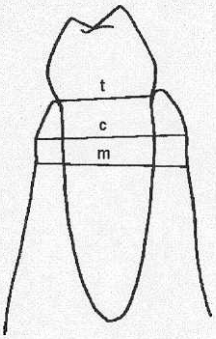


Figure 4: The measurement sites of mandibular alveolar thickness. t is the bucco-lingual dimension of the tooth, c is the cervical crestal thickness of the alveolar process 2.5mm midbuccal and 2mm midlingual apically from the cemento-enamel junction, m is the mid-crestal thickness, midbuccally 6mm from the cemento-enamel border and midlingually 5mm from the cemento-enamel junction.

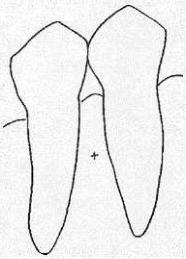


Figure 5: The location between the mandibular premolars, 6mm from the estimated cemento-enamel junction, to measure the interdental thickness, and to place the rectangular tool when assessing the grey-level value of the bone and the bone texture.

The changes in alveolar thickness were estimated: A: for each tooth on the right side of the mandible; B: for the anterior and posterior region; C: for the cervical and mid-crestal level sites separately; D: for the interdental thickness.

Decrease or increase in alveolar thickness was defined as a mean change in a region exceeding 0.1 mm for the six sites in the region. A mean change in alveolar thickness during the five-year period of between –0.1 mm and +0.1 mm was considered to be no measurable change due to possible measurement error.

4.4.3. Apical radiographs

4.4.3.1. Mandibular alveolar bone mass estimated by measuring the optical density

The optical density is the degree of darkening of the exposed film. It is lower in dense bone and higher in bone with sparse trabeculation. The optical density was measured with a densitometer with an aperture of ~2mm (Macbeth TD-500, Macbeth Division of Kolmorgen Co., Newburgh, N.Y.) at six locations on the radiograph (*Figure 2*) and on each step of the step wedges. The values of the ten steps were plotted against the corresponding thickness of aluminium and provided the corresponding aluminium equivalents (al. eq., mm) to the measured

mean optical density of the alveolar bone. In this way an estimate of the mandibular alveolar bone mass was obtained.

4.4.3.2. Mandibular alveolar bone mass estimated by examining the mean grey-level values of the alveolar bone on digitised radiographs

The radiographs were digitised with a resolution of 600 dpi by using Photo-Smart S20 (Hewlett Packard, Palo Alto, CA, USA). Pixel intensity value 255 was representing the lightest area on the film, and zero representing the black areas. The image density histogram in the Photoshop software (Adobe System, Edingburgh, Scotland) provided the mean grey-level value of a bone segment between the two right premolars on the radiographs of the subjects and of the 6mm step of the step-wedge on the reference radiographs, which were used for calibration. The measured bone segment was an area located between the premolars halfway between the crestal and the apical area with the centre 6mm from the estimated cemento-enamel junction (*Figure 5*).

4.4.3.3. Calibration of digitised radiographs

Because of the differences in exposure and processing conditions, all radiographs were calibrated using the reference radiographs. It was chosen to adjust the brightness of the 6mm thick step of the step-wedge to a mean grey-value of 60 (out of 256 grey level values). After the reference radiographs were calibrated, the radiographs of the alveolar bone were adjusted in brightness corresponding to this calibration. Thus, if the 6mm step had an initial grey-level value of 54, the brightness of both the reference radiograph and the radiograph of the individual was adjusted by +6. If the 6mm step was 68 initially, the brightness of both the reference radiograph and the radiograph of the individual was adjusted by –8. In this way, we were able to compare both intra- and interindividual changes over a period of five years.

4.4.3.4. Visual evaluation of the radiographic bone trabeculation

Three periapical radiographs of the right premolar area of the mandible with varying trabeculation were used (*Figure 6*) to assess the trabeculation pattern. With the help of these radiographs, the trabeculation of the alveolar process was classified as either sparse (regarded as an ordered numerical variable: grade 1), alternating dense and sparse (grade 2) or dense (grade 3). The classification was made of both the initial and the final radiographs.

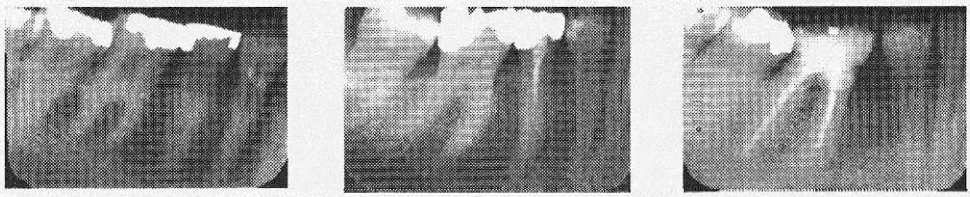


Figure 6. The three reference radiographs used to assess the trabecular pattern with the visual index: sparse trabeculation, alternating dense and sparse trabeculation, and dense trabeculation.

When the trabeculation was evaluated as sparse or dense, the whole radiographed area had the same degree of trabeculation. Furthermore, in the radiographs with alternating dense and sparse trabeculation it was noted if there were small interruptions in the trabecular network (*Figure 7*) similar to the described condition focal osteoporotic bone marrow defect (*Barker et al. 1974, Crawford et al. 1974).*

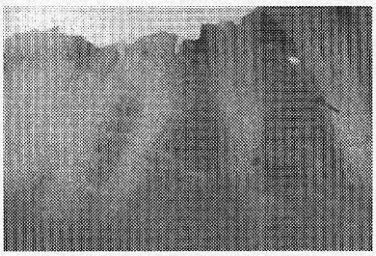


Figure 7. Radiograph of an osteoporotic woman with "focal osteoporotic bone marrow defects" on both sides of the second premolar.

4.4.3.5. Texture analysis of the trabecular bone pattern on digitised radiographs
The digitised, calibrated radiographs were analysed in Matlab (MathWorks, Natick, MA, USA) using traditional statistical description of the bone texture in the image. A radiograph represents a two-dimensional projection of the trabecular bone architecture, and the pattern of these projections is the texture in the image. The features used in the calculations are the transitions from bone trabeculae to the intertrabecular spaces, extracted from 36 radiographs with "typical bone trabeculation" (sparse, alternating dense and sparse with thin trabeculae, alternating dense and sparse with thick trabeculae, and dense trabeculation). These selected radiographs form a training set for the program and are used to set weights in the classification algorithm. With these weights known, any new image can be classified into one of the four subgroups with a simple linear classifier by extracting the same features as in the training set. The analysed bone was selected with a rectangular tool in the standard area, between the premolars, halfway between the crest and the apical area.

4.4.4. Ultrasound imaging of the masseter muscle

Scanning the masseter obliquely would increase the thickness of the muscle and the transducer was therefore oriented perpendicularly to the ramus. The angle was altered until the best echo of the mandibular ramus surface could be achieved. The site of the measurements was in the thickest part of the masseter, close to the level of the occlusal plane, approximately in the middle of the mediolateral distance of the ramus. To avoid tissue compression, a generous amount of gel was used under the probe.

4.4.5. Occluding teeth

The number of occluding teeth from the canine to the wisdom tooth was recorded using a thin cellulose strip (0.05 mm) between opposing teeth.

4.5. Reliability of measurements

Duplicate measurements were made of the alveolar thickness. The random error of the method was calculated according to Dahl berg's formula:

$$S_e = \sqrt{\frac{\sum d^2}{2n}}$$

where d is the difference between two measurements. The reliability was calculated according to a method proposed by *Houston 1983*: $1\text{-}S_e^2 / S_i^2$, (S^2_i is the total variance of the measurement). Furthermore, the random errors of the method and the reliability were calculated for BMD, the radiographic measurements and the masseter thickness (*Table 3*). The trabeculation was assessed twice in 24 subjects by one observer (GJ) with an interval of a week, and the strength of agreement on the bone texture was very good (kappa = 0.89). Paired t-tests between the first and the second evaluations of all methods tested revealed no systematic error between the two occasions.

Table 3. The random error calculated according to Dahlberg's formula and the reproducibility calculated according to a method proposed by Houston 1983 after duplicate measurements in 20 cases.

	Random error	Reproducibility
BMD (%)	1.17	98,1%
$MABM_{od}$ (al. eq.)	0.15	98.0%
Grey-level value (1 of 256 steps)	1.04	98.7%
Bucco-lingual root dimension (mm)	0.06	99.1%
Alveolar thickness changes (mm)	0.09-0.11	97.3-98.0%
Interdental Thickness (mm)	0.09	97.8%
Masseter thickness (mm)	0.23	98.4%

4.6. Statistical methods

The Pearson correlation coefficient (r) was used to assess the amount of agreement between BMD and the mandibular alveolar measures (alveolar thickness, MABM, grey-level value, gingival recession and alveolar bone height) plus masseter thickness. Spearman's rank correlation coefficient (r_s) was used when the trabeculation and the bone texture were involved. BMD change was correlated to the change in the alveolar measures and weight change. Multiple regression analyses were performed with BMD and the mandibular alveolar measures as dependant variables. Independent variables were variables from the questionnaire (age, height, weight, body mass index, hormone replacement therapy, struma, gastro-intestinal disease etc) plus the mandibular alveolar measures and masseter thickness. The null hypothesis was used to test if there was a difference in BMD, changes in BMD, alveolar bone thickness and changes in alveolar thickness due to menopausal status. The null hypothesis was rejected at the 0.05-level of significance. A paired t-test was applied to detect the 5-year changes in body weight, BMI, BMD, alveolar thickness, MABM, grey-level values, and alveolar height. The Chi squared test was used to detect if there was any significant difference over time regarding the bone texture.

4.7. Comments on subjects and methods

4.7.1. Subjects

The variation among the subjects in age, health, medication and life style was very large. However, it is valuable to examine a consecutively selected cohort, which is representative of women attending a public dental clinic in Sweden. The 15 women who initially declined participation were all old (>70 years old), whereas the women in the longitudinal study, who had moved out of the area, were mostly young. It may have been easier to obtain major associations between BMD and mandibular variables if a homogeneous group of perimenopausal women had been selected as in *Paper I*, where the subjects with tori, malposition and major gingival recession were excluded. Tori were found in 9.3% of the participants and major gingival recession (>3mm) in 3.2% of them (unpublished data).

No direct intervention was performed, but the participants were carefully informed about positive and negative factors affecting their skeletal bone status. Some of the peri- and postmenopausal women started medication to increase their bone mass, whereas several of the pre-menopausal women succeeded in increasing their BMD by changing diet, giving up smoking, and increasing their physical activity. However, the possible factors that may have influenced the

BMD during the five years were not considered, since this was not within the scope of our study.

4.7.2. BMD measurements of the forearm

The golden standard for fracture risk is BMD of the proximal femur measured with dual X-ray absorptiometry (*Kanis et al. 2001)*. The present study is not large enough to assess fracture risk, and its focus was to compare skeletal bone loss with mandibular alveolar bone changes. The distal forearm was used because it has the same bone composition as the premolar area in the mandible: 80-87% compact bone and 13-20% trabecular bone (*Nilas et al. 1987, Von Wowern 1977b)*. Furthermore, the largest age-related skeletal bone loss is found in the forearms (*Warming et al. 2002, Uusi-Rasi et al. 2001)*. SXA cannot compensate for the fat content in the forearm, but DXA can with a "manual" procedure. In all but the thickest forearms, measurements with SXA and DXA were similar within 1-2%. SXA has probably the highest reliability because it has an automatic procedure, whereas DXA "used manually" may be more valid of the two methods.

4.7.3. Measurements of the alveolar thickness on casts

The best method for measuring alveolar bone thickness is application of computed tomography, but this method is expensive, and not ethical defensible in healthy women due to the radiation exposure. The next best method in cross-sectional studies may be ridge mapping intraorally with a bone calliper, which penetrates the mucosa until the bone is reached (*Wilson 1989*). However, besides the ethical problems arising from the method, it induces lesions in the gingiva, and it is difficult to replicate in longitudinal studies in the same safe manner as measurements on casts.

In the fully dentate mandible the cortices are nearly parallel and the bucco-lingual dimension can be reliably measured with the dial calliper on dental casts. The changes measured in the alveolar bucco-lingual dimension reflect changes in alveolar bone provided that the thickness of the gingiva does not change with age during the five-year period. Interindividual variation in gingival thickness has been found previously (*Olsson & Lindhe 1991, Muller et al. 2000),* and in a little cross-sectional study, adolescents had thicker gingiva than adults *(Vandana & Savitha 2005).* However, the changes measured in alveolar thickness in the present work varied considerably both intra- and interindividually, which means that only a minor proportion of the changes can be attributed to possible age-related changes in the gingiva. No longitudinal study concerning age-related changes in gingival thickness has been reported, leading us to conclude that possible changes during a five-year study are probably of minor importance. In

cross-sectional studies, the importance of the gingival thickness is eliminated when the alveolar shape is used as in *Paper I.*

4.7.4. Radiographic procedures

The exposure parameters were never changed. The annual technical inspection showed no fluctuations in tube kilovoltage, and the variation in dose per exposure (reflecting tube current and exposure time) was under 3%. Furthermore, test radiographs showed no heel effect from the X-ray apparatus. Standardised conditions in the scattering of the x-ray beams were obtained by placing the film on a flat acrylic plate, thus preventing other materials from exerting any influence during exposure.

For ethical reasons, only one periapical radiograph was taken though it would have been valuable to have radiographs of the maxilla and of other regions of the mandible too. Most of the subjects were regular attendants at the clinic so it was important to limit inconvenience and avoid unnecessary radiation, since a certain dependence on the examiner could not be avoided.

There are several advantages of using separate step-wedges instead of a step-wedge attached to the film-holder: A): All ten steps of the step-wedges (3-13mm thick) are well imaged without reflections from other structures. B): There is no superposition of the step-wedge on the teeth so it is not necessary to repeat the radiographic exposure of the patient. C): The cheek has a heterogeneous tissue structure and a large variation in thickness both intra- and inter-individually. The varying thickness of the cheek does not influence the radiographic image of the step-wedge when the step-wedge is separated from the film-holder and placed outside the mouth. In contrast, when the step-wedge is attached to the film-holder, the cheek affects the different steps heterogeneously.

In the initial phase of the study, tests were performed in order to estimate the influence of the soft tissue of the cheek on the steps of a step-wedge included in a film holder. Large inter- and intraindividual variations were found in cheek thickness. The thinnest step placed most distally under the cheek was affected at least three times more than the step placed at the mouth angle. In order to standardise at least the radiographic image of the step-wedges, we decided to use the "separate" ones. It must be noted that it was very difficult to get good measurements for the steps in an "included" step-wedge due partly to anatomical structures and partly to artefacts such as shadows on the steps. However, in a longitudinal study where the difference in optical density between two radiographs is calculated, the influence of the soft tissue is less important than in a cross-sectional study.

The two methods for estimating alveolar bone mass, densitometry and the grey-level value, used continuous variables, which demonstrated the large variation in alveolar bone mass. Both methods for assessing bone structure used ordered categorical variables. The visual index may be more practical in the clinic like it is: with three categories, but the bone texture could easily and without any inconvenience consist of more categories. Assessment of bone structure is not sensitive to reasonable variations in exposing and processing radiographs, whereas calibration methods are mandatory when density histograms of the grey-level values of the bone are applied. We used calibrated radiographs when the bone texture was assessed, but only in one case did we find a difference between use of calibrated and non-calibrated radiographs.

4.7.5. Ultrasound imaging of the masseter muscle

The masseter muscle was chosen to represent the masticatory muscles (*Weijs & Hillen 1985).* Ultrasonography is an accurate and reproducible method for measuring the masseter thickness in vivo (*Kiliaridis & Kälebo 1991, Raadsheer et al. 1994).* One observer made all the measurements so that any errors would have influenced the whole material equally. All masticatory muscles contribute to the functional environment of the mandible, but the masseter seems to be a good representative, since the variation in the total cross-sectional area of all masticatory muscles appears to be the result mainly of variation in the masseter cross-sectional area (*Raadsheer et al. 1994).*

5. RESULTS

5.1. Paper I

In a test group consisting of 24 perimenopausal women (38-65 years), a regression analysis of cervical crestal thickness in the lower first premolar region (*c*) on the bucco-lingual dimension of the tooth (*t*) gave a highly significant result ($r = 0.90$, $p < 0.001$). A regression analysis of mid-crestal thickness (*m*) on the bucco-lingual dimension of the root (*t*) gave a significant result ($r = 0.74$, $p < 0.001$) too.

Linear regression analyses gave high coefficients of correlation between BMD and measure *m* in the area of the canine and the first premolar, ($r = 0.45$-0.55, $p < 0.05$) but only in the canine area when BMD and measure *c* was correlated ($r = 0.41$, $p < 0.05$). Also the correlation between the interdental thickness in the canine and first premolar area was significant ($r = 0.61$, $p < 0.01$). Furthermore, linear regression analysis of BMD on *mid-crestal bone mass (m-t)* gave a highly significant result ($r = 0.70$, $p < 0.001$ in the region of the first premolar).

The best correlation was between BMD and *the cervical alveolar shape* (*m-c)* in the region of the first premolar: $r=0.90$, $p< 0.001$ when the mean value of 44-34 was used. The linear regression analysis of BMD on the cervical alveolar shape (*m-c*) gave the following equation: $y = 23.2x_1+97.4$, where y denotes BMD and x_1 denotes (*m-c*). In order to make a cross-validation, this equation was used to predict BMD in two other groups. Linear regression analyses between predicted and observed BMD was highly significant ($r = 0.90$-0.91, $p < 0.001$).

In younger women, the association between alveolar shape and BMD was weaker, and in the whole cohort, when all age groups were included, only subjects with tori excluded, the correlation between BMD and alveolar shape was also significant but not at the high level as in the perimenopausal group ($r = 0.61$, $p < 0.001$, $n = 122$, unpublished data).

5.2. Paper II

5.2.1. Mandibular alveolar bone mass estimated by densitometry

In 80 subjects, significant correlations were found between MABM, estimated by densitometry and interdental thickness ($r = 0.49$, $p<0.001$), skeletal BMD ($r=0.46$, $p<0.001$), and age ($r<-0.31$, $p<0.01$). Skeletal BMD and the interdental thickness of the alveolar process were both highly statistically significant explanatory variables when MABM, estimated by densitometry, was used as a dependent variable in a multiple regression analysis ($R^2=0.44$, $p<0.001$, Table 4).

Table 4. Multiple regression analysis to test the significance of the interdental thickness between the premolars and BMD on mandibular alveolar bone mass, estimated by densitometry in 80 women. $R^2 = 0.44$, $p < 0.001$).

	(β)	se(β)	t-value	p
Interdental thickness 45-44	0.566	0.108	5.22	<0.001
BMD (%)	-0.390	0.080	4.90	<0.001

Constant: -5.73.

5.2.2. Trabeculation

Mean BMD in 25 individuals with sparse trabeculation was 76.6± 11.7%. Out of these, 21 were osteopenic. Mean BMD in 43 women with alternating sparse and dense trabeculation was 88.5 ± 10.6%. Mean BMD in 12 subjects with dense trabeculation, was 99.3% ± 6.4%. One subject with dense trabeculation, an ulcerous colitis and corticosteroid medication more than 25 years had a slight osteopenia. There was a statistically significant difference in mean skeletal BMD between the women with sparse, alternating sparse and dense, and dense trabeculation ($p < 0.001$).

Out of the individuals with alternating sparse and dense trabeculation, 11 women with a mean BMD of 82.9%±10.0% (range 62-92%) had transluscent lesions (*Figure 7)*, whereas the rest of the group with alternating dense and sparse trabeculation had a mean BMD of 90.4%±10.4%. There was a significant difference between those with and without transluscent spots ($p < 0.05$).

The coarseness of trabeculation was correlated to skeletal BMD ($r=0.62$, $p<0.001$). No statistically significant correlation was found to age, MABM, and to interdental thickness. The coarseness of trabeculation and age were both highly statistically significant explanatory variables when skeletal BMD was used as a predictive variable in a multiple regression analysis ($R^2=0.52$, $p<0.001$, Table 5).

Table 4. Multiple regression analysis to test the significance of the trabecular pattern and age on BMD in 80 women. $R^2 = 0.52$, $p < 0.001$.

	(β)	se(β)	t-value	p
Trabecular pattern	11.59	2.09	5.52	<0.001
Age	-0.400	0.09	4.67	<0.001

Constant: 83.52.

5.3. Paper III

Of the variables from the questionnaire, only age, hormone replacement therapy, struma, and gastro-intestinal disease were significantly associated with BMD. Masseter thickness was negatively correlated to age ($r = -0.31$, $p < 0.05$) and positively to MABM ($r = 0.40$, $p < 0.001$). Multiple regression analyses showed that the masseter thickness, the number of occluding teeth, years after the menopause, struma/gastro-intestinal disease were significant independent variables regarding MABM, explaining 42 % of the variance in the model, when the whole group was included. However, when the 14 women with struma and/or gastro-intestinal disease were excluded, masseter thickness, years after the menopause and occluding teeth explained 52 % of the variance in MABM (Table 6).

Table 6. Multiple regression analysis to test the significance of the masseter thickness, the number of years after the menopause, the number of occluding teeth, and BMD in 48 women on MABM.

	(β)	se(β)	t-value	p
Masseter thickness (1/10mm)	0.27	0.08	3.24	<0.01
Years after menopause	-0.56	0.22	2.57	<0.05
Number occl. teeth lat	3.44	1.62	2.12	<0.05
BMD (%)	0.02	0.13	0.17	>0.05

Constant: 20.82

The strongest significant determinant of alveolar thickness in all measured areas was the bucco-lingual root dimension (table 5). This parameter together with occluding mandibular teeth in the right segment and masseter thickness, explained 70 % of the variance in interdental thickness between the molar and the second premolar in the total group. Including the non-significant variable BMD in the multiple regression analysis, increased the explained variance of the model to 71 % (Table 7).

Table 7. Multiple regression analysis to test the significance of tooth dimension, number of occluding teeth, masseter thickness and BMD on the interdental thickness between the first molar and the second premolar in 62 women.

	(β)	se(β)	t-value	p
Tooth dimension (1/10mm)	0.90	0.13	6.91	<0.001
Number Occl. teeth lat	6.12	1.60	3.83	<0.001
Masseter thickness (1/10mm)	0.14	0.06	2.30	<0.05
BMD (%)	0.11	0.10	1.10	>0.05

Constant: -21.82

5.4. Paper IV

5.4.1. Changes in alveolar thickness in the posterior and anterior region

The mean alveolar thickness in both regions decreased during a period of five years especially in perimenopausal women. A decrease in the mean alveolar thickness, exceeding a cut-off value of 0.1 mm, was found in 60% and an increase was found in 3% of the subjects. No measurable change was found in 37% of the women. In the anterior region, a decrease was found in 41%, an increase in 6%, and no change was found in 52% of the individuals. The mean change in alveolar thickness (six sites) in the posterior region (-0.22±0.20 mm) was greater than in the anterior region (-0.16±0.19 mm, $p < 0.01$). The mean changes in alveolar thickness in the posterior and anterior regions were moderately correlated to each other ($r = 0.58$, $p < 0.001$).

5.4.2. Changes in alveolar thickness in relation to age and menopausal status

In the posterior region, the change in alveolar thickness was positively correlated with age ($r = 0.40$, $p < 0.001$). The most pronounced change in the posterior alveolar thickness was seen in older women. In contrast, in the anterior region, the change in alveolar thickness was negatively correlated with age ($r = -0.30$, $p < 0.001$), which means that the changes in anterior alveolar thickness took place mostly in the younger women.

5.4.3. Changes in alveolar thickness associated with changes in bone mineral density

In the posterior region, the BMD change was correlated to the changes in alveolar thickness, both at the mid-crestal level site ($r = 0.56$, $p < 0.001$) and the cervical level site ($r = 0.35$, $p < 0.001$). In the anterior region, the changes in alveolar thickness were not correlated to BMD change. The initial BMD was negatively correlated to the changes in alveolar thickness in the posterior region at the cervical level site ($r = -0.35$, $p < 0.001$), but not at the mid-crestal level site. The initial BMD was negatively correlated to changes in alveolar thickness at both level sites in the anterior region ($r = -0.28$, $p < 0.01$).

In multiple regression analyses, differences between the posterior and the anterior regions were also found. In the posterior region at the cervical level site, 25% of the variance in the mean alveolar thickness decrease was explained by initial BMD and BMD change ($R^2 = 0.25$, $p < 0.001$) (table 8). At the mid-crestal site in the posterior region, only the BMD change was a significant factor explaining 33% of the variance in the mean alveolar thickness decrease ($R^2 = 0.33$, $p < 0.001$). In the anterior region, initial BMD and BMD change could not

explain a significant part of the variance in the mean alveolar thickness decrease (table 9).

Table 8. Multiple regression analysis to test the significance of BMD change and initial BMD on alterations of the alveolar thickness at the cervical sites in the posterior region in 117 women. $R^2 = 0.25, p < 0.001$.

	(β)	se(β)	t-value	p
BMD change	0.736	0.200	3.68	<0.001
Initial BMD	-0.265	0.082	3.24	<0.001
Constant: 31.45.				

Table 9. Multiple regression analysis to test the significance of BMD change and initial BMD on alterations of the alveolar thickness at the mid-crestal sites in the posterior region in 117 women. $R^2 = 0.33, p < 0.001$.

	(β)	se(β)	t-value	p
BMD change	1.533	0.232	6.62	<0.001
Initial BMD	-0.043	0.093	0.46	>0.05
Constant: 8.98.				

5.5. Paper V

5.5.1. MABM estimated by optical density of analogue radiographs

Mean MABM, estimated by densitometry, decreased during the 5-yr period ($p<0.001$). In 22.0% of the subjects it increased and in 44.2% it decreased more than 0.40 al. eq., mm. The changes in MABM were neither associated with the changes in BMD nor with the changes in interdental alveolar thickness.

5.5.2. MABM estimated by the mean grey-level value of the alveolar bone

The mean grey-level value decreased during the 5-year period ($p<0.05$). In 31.9% of the subjects it increased and in 35.1% it decreased more than 4 steps (out of 256 grey level values). The change in grey-level value, measured between the premolars, was correlated to the change in BMD ($r=0.33$, $p<0.001$), to the change in optical density ($r=0.36$, $p<0.001$) but not to the change in interdental alveolar thickness.

5.5.3. Visual evaluation of the radiographic bone trabeculation

In all but three women, the overall trabecular pattern did not change during the 5-year period. Two of them were fast bone losers and lost more than 0.40 al. eq., mm in MABM (0.70 and 0.41 al. eq., mm).

5.5.4. Texture analysis of the trabecular pattern

The change in texture was significantly correlated to the BMD change ($r = 0.39$, $p < 0.001$), to the change in optical density ($r = 0.28$, $p < 0.01$), and change in mean grey-level value ($r = 0.24$, $p<0.05$). The change in bone texture was not correlated to the change in interdental alveolar thickness.

6. DISCUSSION

The present investigation has shown that mandibular alveolar bone mass, structure and alveolar thickness differ between women with normal BMD and osteopenic women, and that age-related changes in BMD have an impact on these characteristics of the mandibular alveolar process.

6.1. Alveolar thickness and shape

Both the cervical and the mid-crestal thickness in the premolar region are closely related to tooth dimension, but the mid-crestal in a lesser degree than the cervical thickness, indicating that other factors, like skeletal BMD, are more important at that site. This is also demonstrated by the findings that the changes in mid-crestal thickness are more closely correlated to BMD changes than those at the cervical sites. These correlations were our reason for choosing the interdental bone at the mid-crestal level when we evaluated the alveolar bone mass with the grey-level value and the alveolar bone texture. Our findings in the cross-sectional study (*Paper I)* indicated that the alveolar shape would change in osteopenic perimenopausal women, and this was confirmed in the longitudinal study (*Paper IV)* where both the decrease in the cervical and the mid-crestal thickness in the posterior region were related to BMD reduction. The alveolar process is subjected to rapid periosteal resorption after tooth extraction (*Botticelli et al. 2004, Araujo & Lindhe 2005),* and the decrease in the thickness of the alveolar process strongly indicates that a slow periosteal resorption may occur even without tooth extraction.

In perimenopausal women without tori, the alveolar shape was significantly correlated to BMD, though the correlation is weaker in younger women. The changes in alveolar thickness vary, not only at the cervical level compared to the mid-crestal level, but also in the anterior compared to the posterior sections, and they are most pronounced in peri-menopausal women (*Paper IV*), which may indicate that oestrogen deficiency, known to influence BMD (*Rizzoli & Bonjour 1997, Riggs et al. 2002, 2003*), plays a role in the remodelling of the alveolar process. This is demonstrated in longitudinal studies of periodontal disease in post-menopausal women (*Jacobs et al. 1996, Payne et al. 1999*), where treatment with hormone replacement therapy ameliorated the periodontal condition and the local bone mass. The largest decrease in alveolar thickness in the elder women is found in the posterior segment, which may be explained by an age-related atrophy of the masseter muscle. The muscle mass and strength decrease with age (*Willmore 1991, Newton et al. 1993*), and dental state (*Newton et al. 1993*) and thus the biomechanical strain on the posterior alveolar process is reduced at the same time as bone remodelling in the oestrogen-deficient women leads to bone loss in the whole skeleton.

Our findings may have been influenced by the vertical changes of the alveolar bone due to the continuing eruption of the teeth in adults, as seen on lateral cephalograms taken 20-yr apart on subjects who had previously been dental students (*Forsberg et al. 1991*). Indications of increase in the vertical distance between the cemento-enamel junction and the mandibular canal have also been found in ancient skull materials (*Whittaker et al. 1985, Varrela et al. 1995*), but in these studies the level of the alveolar crest did not change in height in adults. However, at that period the oral hygienic standard might have been minimal or non-existing. Another factor that may have contributed to the measured changes in the cervical crestal level is the influence of excessive tooth brushing on the periodontal tissues (*Serino et al. 1994*), explaining some of the decrease of bucco-lingual alveolar thickness on the cervical sites.

6.2. Mandibular alveolar bone mass

The attenuation of the X-ray beam passing through the alveolar process depends on the mineral content and the thickness of the alveolar process, consisting of bone and soft tissue. Therefore, it is not surprising that MABM, estimated by densitometry, was correlated to the alveolar thickness. To our knowledge, only one research team has considered the bucco-lingual dimension of the mandible in order to obtain a measure of the mandibular bone density (*Kribbs et al. 1989*), but it is not estimated at all in research on oral bone loss due to periodontal disease (*Payne et al. 1997, 1999, Civitelli et al. 2002*). MABM, estimated by densitometry, was significantly correlated to BMD and age (*Paper II*) and to struma and gastro-intestinal disease (*Paper III*). Numerous studies have found a lower mandibular bone mass in older subjects than in younger subjects (*Von Wowern 1977a, b, Von Wowern et al. 1988, Kribbs et al 1983, 1989, Klemetti et al. 1993a, b*). Furthermore, we found that the number of years after menopause correlated with MABM, estimated by densitometry, indicating that oestrogen might have an influence locally, which corroborates findings in other investigations (*Jacobs et al. 1996, Payne et al. 1999*).

The changes in MABM and the changes in alveolar thickness were not significantly correlated. This lack of correlation can be due to methodical errors but also to a possible time-delay in response to aging, since probably more time is needed for the alveolar thickness to decrease than to detect change in MABM. Besides the functional factors MABM seemed to be influenced by systemic factors (hormones and gastro-intestinal disease) and may therefore change more rapidly than the bucco-lingual thickness. This result is in accordance with numerous studies of other parts of the skeleton, where a significant relationship is found between muscle mass, strength and local bone mass (*Snow-Harter et al. 1990, Madsen et al. 1993, Di Monaco et al. 2000)*. Bone tissue is continuously remodelling in response to mechanical stress (*Lanyon 1987, Frost 1994,*

Nomura et al. 2000) though this mechanism is impaired in elder persons. According to Frost (*1994*), decreased loading changes the mechanostat to a mode that leads to bone loss. This is demonstrated in the jaws after tooth extraction (*Von Wowern et al. 1979, Elovic et al. 1995, Botticelli et al. 2004, Araujo & Lindhe 2005*). The masseter muscle and the occluding teeth may stimulate the bone and counteract local bone loss, at least as long as the masseter muscle retains its functional strength (*Wilmore 1991, Mavropoulos et al. 2004),* and the maxillary antagonist teeth are preserved (*Von Wowern et al. 1979, Elovic et al. 1995).* In this way, the mandibular bone alterations due to the systemic factors might be counteracted (*Paper III*).

6.3. Alveolar bone structure

The radiographic trabecular pattern was not dependent on age, the alveolar thickness, and reasonable variations in exposing and processing of the radiographs. Together with age it explained half of the variation in skeletal BMD. Previously it was thought that the trabecular pattern apparent in radiographs of the radius was formed in the "conjunction zone" between the cortical and the trabecular bone (*Van der Stelt 1985*). However, in a recent study in cadaver specimens, the trabecular bone in the alveolar process was found to account for most of the visible fine structures in the dental radiographs (*Couture et al. 2003*). When we studied the radiographs with alternating dense and sparse trabeculation from the crest and towards the basal bone, the crestal alveolar bone was denser than that in the middle, whereas under the apices of the molars the trabecular network could be "cystic" in appearance (*Parfitt 1962*). In the basal part of the mandible, the bucco-lingual dimension is much wider than in the crestal part and the cortical bone much thicker, suggesting that reinforcement with trabeculae is probably not as important as in the thin crestal part.

Alveolar bone structure is significantly correlated with BMD *(Papers II and V*), and the visual trabecular pattern may become a useful diagnostic tool for identifying women with high or low BMD (*Paper II*). In the group with alternating dense and sparse trabeculation, there is a large variation in BMD, and possibly it would be better to divide this group into subgroups, since the women with thick trabeculae and thick lamina dura have a normal BMD, and the women with focal osteoporotic bone marrow defects have significantly lower BMD than those without these translucent spots (*Paper II*). This finding is in agreement with other studies where thinner trabeculae, a lower connectedness of the trabeculae and larger inter-trabecular spaces were found in subjects with osteopenia than in subjects with normal BMD (*Geraets et al. 1990, 1993, Korstjens et al. 1996, White & Rudolph 1999, Shrout et al. 2000).* Increase in the distance between adjacent trabeculae accounts for more than double the age-related bone loss compared to that caused by the decrease in trabecular width

(Weinstein & Hutson 1987). Patients with osteoporosis have a reduction in the area and the periphery of the trabeculae and a reduction in the complexity of the trabecular pattern in the posterior alveolar bone in comparison with controls *(White & Rudolph 1999)*. Similarly, in the cross-sectional study we found that there was a significant difference in skeletal BMD in individuals with dense, alternating dense / sparse, and sparse trabeculation *(Paper II)*.

After the menopause, oestrogen deficiency leads to increased number of lacunae and porosities and later on to thinner cortical plates *(Kribbs et al. 1989, Klemetti et al. 1994a, Taguchi et al. 1996b)* and thinner trabeculae *(Weinstein & Hutson 1987)*. When the cortices and trabeculae are thinner, the trabecular pattern is maintained but the mandibular bone mass decreases, which may explain that only three individuals changed in trabecular structure, when evaluated with the visual index. It seems that the inter-trabecular spaces increase in osteopenic women, resulting in fewer transitions from trabeculae to inter-trabecular spaces in the ROIs resulting in the change in radiographic bone texture *(Paper V)*.

6.4. Clinical implications

Osteoporotic fractures of the hip, spine and forearms are a huge problem for the public health service and the individual. In order to identify women in all age groups with low bone mass, an evaluation of the alveolar bone structure with the visual index *(Lindh et al 1996, Paper II)* may be a simple and effective tool together with an appropriate questionnaire. Previous studies proposed the use of the Mandibular Cortical Index, where the basal cortex is classified by using its degree of resorption *(Klemetti et al. 1994a, Taguchi et al. 1996b)*, as a simple method to be used in clinics with pantomography equipment. The diagnostic potential of the latter method could probably be improved if the trabecular pattern was considered in addition to the evaluation of the basal cortex, a possibility that should be tested in future research. It is important to consider the existence of several known risk factors such as previous fractures, weight loss, certain medications, struma, gastro-intestinal disease, smoking and decreased physical activity, together with oral radiographic findings and clinical observations such as the alveolar thickness and shape, to find a more effective scoring system in order to estimate the risk of future osteoporotic fractures *(White 2002, Cadarette et al. 2001)*.

Our findings may be of direct interest to the dental profession too, since a periapical radiograph showing dense trabeculation indicates a need to exercise greater prudence when drilling for implants due to increased heating and consequently an increased risk of local necrosis *(Friberg et al. 1991)*. A periapical radiograph revealing sparse trabeculation may indicate a need of

cortical fixation and long duration of the healing process before the implant can be loaded (*Friberg et al. 2001*).

Many systemic diseases are reflected at the level of the periodontium, and conflicting results have been reported on the correlation between periodontitis and osteoporosis (*Von Wowern & Kollerup 1992, Elders et al. 1992, Hildebolt 1997, Payne et al. 1999*). Our findings indicate that the lack of consistency in the results may be due to differences in the alveolar bone structure and thickness, which were not considered. This could be supported by the findings that individuals with high mineral values in the skeleton seem to retain their teeth with deep periodontal pockets more easily than those with osteoporosis (*Klemetti et al. 1994c*). Furthermore, individuals with broad dense jaws have more bone substances to loose than those with thin jaws and therefore the size of an individual may play an important role for the vertical changes of the alveolar process (*Klemetti et al. 1997*). The possible influence of the alveolar thickness, MABM and alveolar bone structure on the normal periodontium may be an interesting study in the future.

In adult orthodontics, a different tissue reaction could be expected when moving teeth in bone with sparse or dense trabeculation. This could be supported by the findings that rats with lower initial bone density have a faster orthodontic tooth movement than rats with significantly higher initial bone density (*Bridges et al. 1988*). Orthodontic tooth movement was also found to be faster in rats on a calcium-deficient diet than in rats on a normal diet (*Goldie & King 1984*). Furthermore, the age-related decrease in bone width found in our longitudinal studies may imply an increased risk of future bone dehiscence and gingival recession in adult subjects undergoing orthodontic treatment. However, further studies are necessary to elucidate this matter.

6.5. Conclusions

From the results in this thesis the following conclusions were drawn:

- A significant relationship exists between BMD and mandibular alveolar bone mass, structure, and thickness.

- The local functional factors influence mainly MABM and the alveolar thickness in the molar region, whereas BMD influence the trabecular structure.

- Dense trabeculation is a strong indicator of high BMD, whereas sparse trabeculation predicts low bone mass.

- Longitudinal changes in grey-level value, bone texture and alveolar thickness in posterior region are related to alterations of BMD.

- The decrease in bucco-lingual alveolar thickness may be due to a periosteal resorption related to skeletal bone loss.

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APPENDIX

Questionnaire for osteoporosis

Name_____ Age_____ Telephone_____

How tall are you?
What is your weight?
Have you lost much weight? How many kg?
How many glasses of milk or yoghurt do you drink per day?
How many pieces of cheese do you eat per day?
How many cups of coffee do you drink per day?
Do you use hormone replacement therapy? In what form and in what concentration?
How long have you used hormone replacement therapy?
Have you had an operation on your ovaries? One or both? A hysterectomy?
At what age did your menstruation stop? (Write 0 if you still have it.)
Have you had a medication with cortisone/ steroid for more than 3 month?
Any other medication?
Do you have or have you had gastro-intestinal disease, struma, and rheumatism?
Other serious diseases?
Do you smoke? How many cigarettes per day? How many years?
Previous smoking? How much? How many years?
How many children do you have?
How many months did you breast-feed?
What is your profession? Are you physically active in your work?
Do you have a dog? How far do you walk with the dog?
Do you walk more than 5 km a day during working hours and privately?
How often are you physically active more than half an hour during a week?
Have you carried heavy loads for a longer period or trained extremely hard?
Were you very active physically before the age of 25 years?
Did you have a fracture in adult age? How many and where?
Did your mother suffer from osteoporosis?
Do you press or grind your teeth? Do you have an occlusal device?

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