CHAPTER II LITERATURE REVIEW

II. A. Different measurements of bone mineral density

Diagnosis of osteoporosis and prediction of fracture risk are based on assessment of bone mineral density (BMD) which is principally determined by the mineral content of bone. BMD measurement is very important in clinical management of osteoporosis because its reduction closely correlates to an increased fracture rate (13,28,34,41,58). There are many commonly used methods to evaluate BMD, such as single-photon absorptiometry (SPA), dual-photon absorptiometry (DPA), dual-energy X-ray absorptiometry (DXA) and peripheral quantitative computed tomography (pQCT) (2,24).

Among these measurements, DXA has been accepted almost universally as the methodology of choice in the field of clinical bone fragility. DXA is applied to measure areal BMD (aBMD), which is defined as the bone mineral content (BMC) per projected area. More specifically, DXA is generally considered to be the prime and reliable assessor of the osteopenic/osteoporotic condition. DXA can reveal the correlations of measured BMD with failure load of bones, and the efficacy of remedial bone therapies (5). The DXA machine sends a thin and invisible beam of low-dose x-rays through the bones via two energy streams. It relies on two distinct energy peaks: one peak is

absorbed mainly by soft tissue and the other by bone. The soft tissue amount can be subtracted from the total, and what remains is a patient's BMD. Although DXA is a quick, painless procedure for measuring bone loss, this bone densitometry measures aBMD, adjusted for the projected area of the scanned region but not its depth. Therefore, a higher aBMD in an exercise group compared to a control group maybe due to growth size rather than an increase in the amount of bone (82).

In contrast to DXA, pQCT, which is capable of three-dimensional measurement of bone mass, measures the volumetric BMD (vBMD; in grams per cubic centimeter) and cross-section areas, and allows for separate assessment of trabecular and cortical bone of the appendicular skeleton, such as the radius and tibia (4,24,76,78). Peripheral QCT scanners are in general smaller, less expensive and more mobile. And they do not need additional radiation shielding as compared with multipurpose computed tomography (CT) machines. After selection of the scan location on a projectional scout view a single slice or multiple slice CT scans are performed with slice thicknesses ranging from less than 1 mm up to 2.5 mm. Multiple slice techniques are advantageous with respect to measurement precision by evaluating a larger scan volume and employing algorithms for location matching. The development of higher resolution scanning modes and reductions in slice thickness led to higher geometric resolution. Measurement of true

vBMD is advantageous particularly because BMD measurements are independent of skeletal size. In adults, aBMD is believed to be a good substitute for vBMD, as there is little change in bone size, and the major change occurring is related to the decline in BMC. However, in children and adolescents, growth will inevitably lead to a much greater change in bone size. This may lead to an inappropriate substitution of aBMD for vBMD and has raised questions about the validity of the use of aBMD in pediatrics (39). Further, pQCT can determine bone geometric properties, such as periosteal area, endocortical area and cortical thickness, which are closely related to bone strength, in addition to BMD (16,48,70,71,84).

Due to the differences in imaging principles and dissimilar scan locations between DXA and pQCT, it comes to important to compare the two techniques in order to evaluate the applicability of them for the studies. DXA measurements showed moderate correlations ($r = 0.75$) at the forearm when directly compared with pQCT measurements, however the correlations of DXA and pQCT at the lumbar spine were not higher than $r = 0.44$ (26). Although the moderate correlations between DXA and pQCT measurements were reported, pQCT is more prospective since it allows for separate assessment of trabecular and cortical bone, and it has the ability to measure geometric properties of bone.

Ⅱ. B. Disparity of areal and volumetric bone mineral density

Measurement of aBMD by DXA is a planar measurement dependent on bone size. Areal BMD measurements incorporate information about bone width and height but not depth. Therefore, a bigger bone will be reported as having a higher aBMD compared to a smaller bone when both bones could have the same density of bone within the periosteal envelope (vBMD) (Figure 1). Areal BMD increases during the pre- and peripubertal years because long bones increase in size. The densitometer sees a bigger bone and prints out that the bigger bone has a higher aBMD, giving the impression that as children grow their bones have somehow become denser. However, as the bone grows in length and diameter during the pre- and peripubertal years, the mass of bone inside the periosteum increases in proportion to the enlarging volume of the whole bone including the marrow space (39). It was reported that vBMD of long bones (for example: femur) was independent of age and no different in boys and girls (52) (Figure 2). Therefore, in young adulthood, men and women have the same vBMD, but men have a greater aBMD than women since men have a bigger bone than women. Thus, if the strength of the long bones is greater in older than younger children, or greater in males than females, it is due to differences in bone size, not volumetric bone density,

not the amount of bone within the periosteal envelope of that bone (52). Volumetric BMD also remains independent of age for the vertebral body at least until puberty (25).

Further, vBMD is an overall indicator of bone mineral status since bone size is taken into account. For example, in terms of the attainment of peak aBMD, during young adulthood bone volume continues to increase, and aBMD would continue to increase due to the effect of bone size but vBMD would remain constant (39). And a study had assessed that bone area exerted a greater influence upon aBMD at the lateral spine, while variation in bone area from anteroposterior or lateral scan did not affect vBMD (49) (Figure 3).

Ⅱ. C. Peak bone mass and starting age of exercise

Osteoporosis was defined as "a disease characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and increased risk of fracture" (97). Maximization of bone mass during adolescence and early adulthood is important in reducing the risk of osteoporosis and the associated fractures that occur later in life. Since skeletal mass in adulthood is the result of both the amount of bone gained during growth and its subsequent rate of loss, it is clear that the factors affecting bone density during growth are important determinants of future

skeletal resistance to fracture (73).

Peak bone mass which corresponds to the amount of bony tissue present at the end of skeletal maturation, is an important determinant of osteoporotic fracture risk, such as those observed at the radial, vertebral, or femoral sites in osteoporotic patients. Therefore, strategies of primary prevention of osteoporosis and associated fractures consist in increasing bone mass acquisition during skeletal growth (56,95). Achieving a good peak bone mass is important in reducing the risk of osteoporosis in later life because it means that bones are strong before loss begins.

The majority of bone mass is achieved during the first two decades of life. And it reaches a peak in the third decade - the peak bone mass or peak bone density. Several studies have given strong evidence that 95-99% of the peak bone mass is gained during the first two decades of life (6,31,56,95). Peak bone mass is influenced by a variety of genetic and environmental factors: gender, race, hormonal factors, nutritional status and physical exercise. It can be increased by ensuring that the diet contains adequate amounts of calcium and vitamin D during childhood, adolescence and early adulthood, and further increased by regular physical exercise especially weight-bearing exercise (62,74,85).

It has long been known that physical exercise has been proposed as one strategy

for improving or maintaining the structural competence of bone. Regular exercise develops the high peak bone mass and produces high levels of mechanical force on bone. Many DXA-based studies have shown that the greatest BMC or aBMD increase can be obtained if bones are loaded during the growing years (7,37,53,90). One of these studies stated that the growing bone is sensitive to exercise. The moderate and readily accessible weight-bearing exercise undertaken before puberty may increase femoral volumetric BMD by increasing cortical thickness (7). And another study reported that increased bone mass can be achieved in a population-based cohort of boys by moderate increased physical exercise within the school curriculum from 12 to 16, and the same results could be seen in girls if the intervention starts at an earlier age (89).

Moreover, a pQCT study assessed the effect of long-term impact-loading on humerus and radius by comparing female tennis young starters with old starters (46). It was found that the side-to-side difference in the cortical area of the humeral shaft was more than twice as large in the young starters as in old starters. The ability of bone to adapt to mechanical loading is much greater in the growing than in the matured bone and exercise after maturity has a much smaller effect (67). Furthermore, the manner in which the recruitment and function of bone cells are coordinated differs between the growing and the matured bone. In the former, modeling is the dominant mode, and in

the latter it is remodeling (1).

Ⅱ. D. Effects of different types of exercise on bone

It has been well known that physical exercise had the positive effect on human bone mass. The classic examples of the positive effects of exercise on bone were DXA studies of the side-to-side difference on unilateral tennis player's arms (22,29,30), in which the effects of exercise were not confounded with the other factors such as genetic, hormonal and nutritional factors. The greater mineral deposition in the dominant playing arm of tennis players was found, compared with the non-dominant arm across different age groups. The positive effects of exercise on human bone mass have also been well documented in many cross-sectional DXA studies (7,14,23,32,43,47,64,92) comparing athletes with sedentary controls. Comparison of aBMD among athletes revealed the importance of weight bearing activity to increase aBMD. Weight bearing activities (in the presence of gravitational forces), which generate external loads on the human body of 3-5 times to 7-10 times body weight at impact, might be expected to stimulate the modeling process. However, non-weight bearing activities, which actively load the skeleton through muscular contraction, have not had an established influence on BMD (27). It has been demonstrated that young female athletes who engaged in

weight bearing activities, such as volleyball and gymnastics, had a greater aBMD at a majority of skeletal sites when comparing to athletes in a non-weight bearing activity (swimming) and controls (Table 1). And even for postmenopausal women, exercises are effective and feasible means to preserve aBMD when comparing with sedentary controls (63).

Compared with DXA, pQCT does not only assess BMD, but also is available for assessing bone geometry measurement. The studies applying the pQCT on vBMD began to appear in late 1990', and the first study of tennis players' radii revealed that tennis playing led to a slight decrease in cortical vBMD but increase in bone area at dominant arm than non-dominant (or tennis arm than control arm). Furthermore, measurements of bone areas at mid-radius using pQCT showed that average cortical thickness of the playing arm increased, accompanied by periosteal mineral apposition and endosteal bone resorption, leading the center of the cortex to be further away from the neutral axis (cortical drift). Together with an increase in cortical thickness, cortical drift toward periosteal direction resulted in a significant improvement of the mechanical characteristics of the players' dominant radius (1). The preceding observations have been confirmed in the later studies of professional tennis players, triple jumpers and volleyball players (33,38,75) (Table 1).