

Measurement of Bone Density and Bone Strength with pQCT

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1. Abstract

Bone densitometry is widely distributed to diagnose osteoporosis and other bone diseases in humans. In preclinical research it is used in the development of anti-osteoporosis drugs in different kinds of animal models. The term density is often used erroneously since it is used for 2-dimensional methods (results in g/cm^2) like DXA. With CT methods it is possible to determine the physically correct density values (g/cm^3). Furthermore it is possible to distinguish between cortical and trabecular bone. It has been shown that trabecular density is the most significant parameter to determine changes in bone metabolism non-invasively.

But bone density does not represent bone strength and therefore fracture risk very well. Bone strength can be described as a combination of bone's material properties and bone geometry. Aside some diseases like osteomalacia and osteogenesis imperfecta the material properties are quite constant even among species. With CT methods bone geometry can be analysed. The calculation of the section modulus is so far the best method to predict bone bending strength.

Harold Frost's mechanostat has taught us that bone strength is regulated by the maximum muscle forces. Therefore it is obvious to relate bone strength to muscle force. Muscle cross sectional area measured by pQCT can be used as a surrogate for muscle force. There is a very close correlation between muscle and bone cross sectional area. This close correlation is currently used to establish muscle parameters as an individual reference for bone strength. It allows the discrimination between a primary bone disease and an osteopenia due to reduced muscle force, but also to see if a drug has a direct influence on bone or on muscle.

2. Density

Bone densitometry is widely distributed to diagnose osteoporosis and other bone diseases in humans. In preclinical research it is used in the development of anti-osteoporosis drugs in different kinds of animal models. Since Archimedes density is defined as mass/volume [g/cm^3]. Since the introduction of x-ray absorptiometry

(DXA) about 20 years ago bone mineral density (BMD) is defined as the bone mass divided by the projected area [g/cm^2] which is in contrast to the definition by Archimedes (Figure 1). This has some important consequences. BMD measured by these methods depends on the size of the object which is especially important for studies in children or growing animals but also in studies where the body size may change as a consequence of the treatment or a disease. If two-dimensional data are compared to statistical normal values, smaller subjects will be diagnosed as osteopenic or even osteoporotic. To overcome these problems CT technology was modified to measure real (volumetric) bone density. This not only solved the size problem but also gave the opportunity to differentiate between trabecular and cortical bone and to determine the bone geometry.

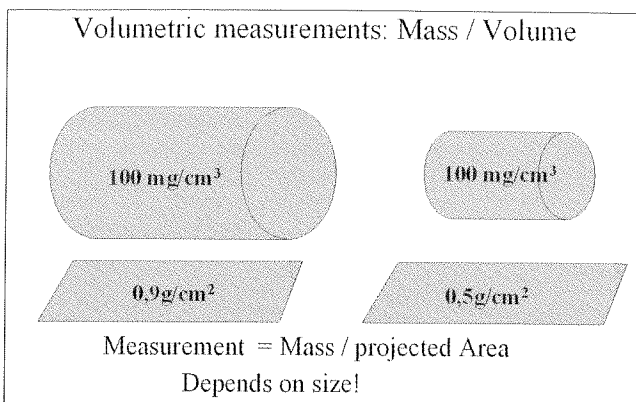


Figure 1

3. Bone

Bone can be regarded at different levels of its biological organization:

1. Material
2. Tissue
3. Organ

Depending on this criteria the term bone density can have different meanings [1]. Bone material is mainly composed of ca. 60 vol% collagen and ca. 40 vol % (Figure 2) hydroxyapatite. The density of collagen is about $1 \text{ g}/\text{cm}^3$, the density of hydroxyapatite $3.2 \text{ g}/\text{cm}^3$. Therefore the contribution of collagen to the bone density is $0.6 \text{ g}/\text{cm}^3$ and of hydroxyapatite is $1.28 \text{ g}/\text{cm}^3$ resulting in a bone material density of ca. $1.9 \text{ g}/\text{cm}^3$. The Stratec pQCT is calibrated in a way that only the contribution of the mineral is taken into account giving a mineral density of $1.3 \text{ g}/\text{cm}^3$. Bone material density is identical for cortical and trabecular bone. It can be affected by

the amount of unmineralized osteoid (reduced in osteomalacia) or changes in the collagen structure (increased in osteogenesis imperfecta). It can only be measured with backscatter electron microscopy.

Bone tissue can be either cortical or trabecular. Cortical bone tissue density is about 90–95% of the material density and is influenced by the number and size of osteons and by the volume of the remodelling space. Trabecular bone tissue density depends mainly on the number and size of the trabeculae within the marrow and is typically 15–20% of the material density. In clinical and preclinical studies trabecular bone density is the most sensitive non-invasive parameter to show changes in bone metabolism [2,3]. Cortical density is very sensitive to changes in mineralisation and allows the discrimination of osteoporosis and osteomalacia.

The bone organ density varies among different bones. It is influenced by the relative amount of cortical and trabecular structures within the bone. It can be measured by pQCT (total density) but its diagnostic value is limited.

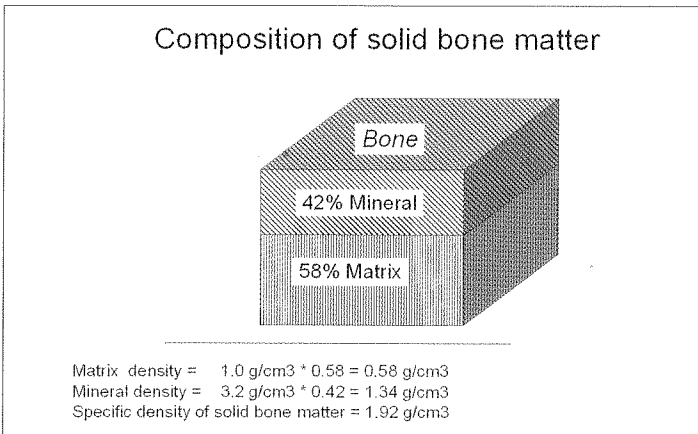


Figure 2

4. Bone strength

The ultimate goal of bone density measurements is to supply information about bone strength and fracture risk. This goal fails because of two reasons: 1. Bone density does not reflect bone strength and fracture risk is mainly dependent on fall risk in humans rather than low-bone density [4]. Of course fall risk cannot be determined by pQCT, but how about bone strength? As in all other structures bone strength is defined as a combination of material properties and geometry. Since the invention of bone by evolution several hundred million years ago bone material

properties were optimized and there is very little variation even between different species. Since CT gives information about the cross sectional information of bone it can be used to calculate the section modulus (Figure 3) that determines bending and torsional strength and cross sectional area that determines compressive strength. Studies from Ferretti [5] in rat femurs and Wilhelm [6] in human radius specimens were able to show a high correlation between geometry and bending strength. In textbooks for engineers a formula can be found that allows the direct prediction of fracture load from the pQCT-derived section modulus (Figure 4). The application of this formula to the 3-point- bending tests is shown in Figure 5.

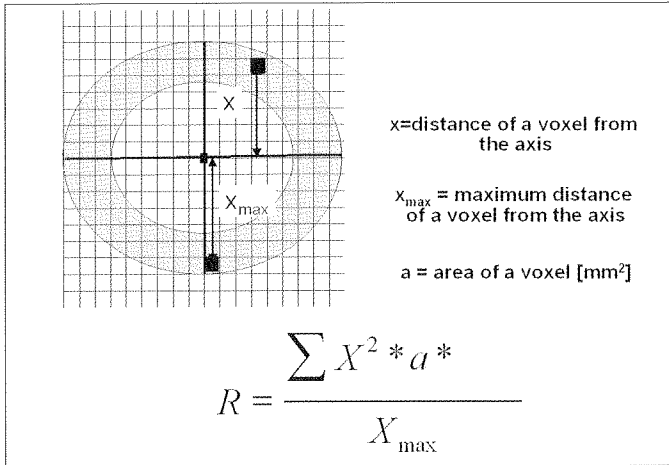


Figure 3

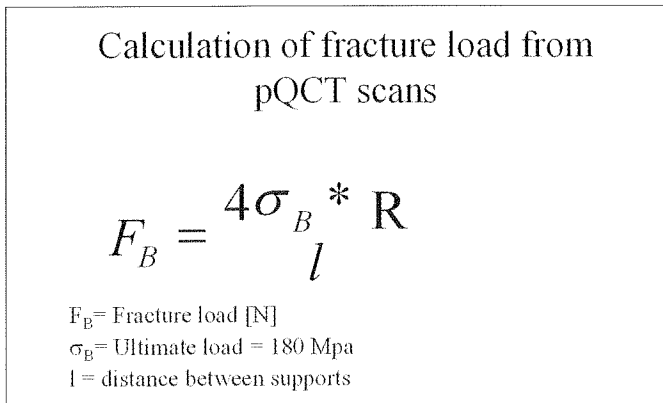


Figure 4

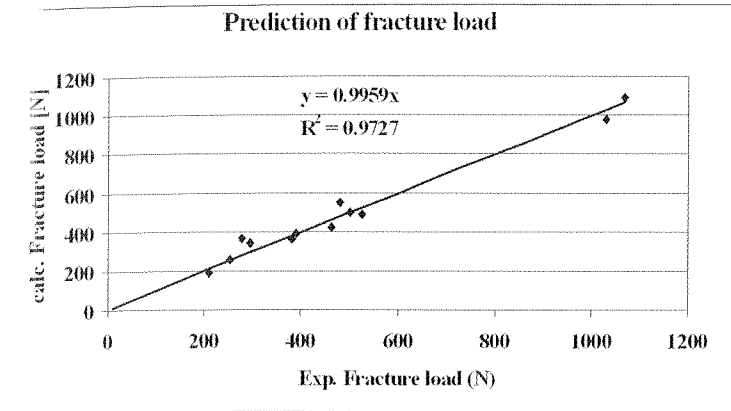


Figure 5

5. Influence of muscles

Harold Frost's mechanostat theory has taught us that bone strength is regulated by maximum muscle forces [7]. Bone's ultimate goal is to withstand the forces that act on it without fractures with a minimum amount of material. Osteocytes act as strain sensors that detect bone deformations caused by muscle contractions. If strains exceed a certain threshold value a signal to add material and therefore strengthen bone is generated. If a certain lower strain threshold is not regularly exceeded, a signal to remove bone is generated. Therefore it is obvious to relate bone strength to muscle forces. Muscle cross sectional area determined by pQCT can be used as a surrogate for muscle force. Meanwhile several studies showed the close correlation between muscle force and bone strength in humans and animals [8–10]. In children and growing animals it turned out that during puberty females acquire more bone with respect to the muscle than males [11]. This strong correlation between muscle and bone parameters can be used to differentiate a true osteoporosis from an osteopenia due to low muscle force. Eckhard Schönau [12] proposed a two-step algorithm in which the muscle force (or area) is used as an individual reference for bone strength thus avoiding the problems of statistic age related normal values (Figure 6). Also for the development of new drugs muscle-related normal values might be an important tool to determine the effect on muscle and bone.

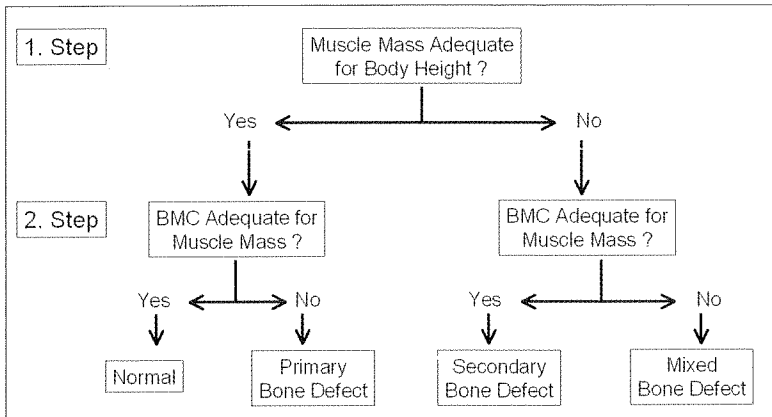


Figure 6

6. Conclusion

pQCT is able to determine changes in bone metabolism very sensitively. Furthermore it allows the accurate prediction of bone strength. Muscle related bone strength indices allow the discrimination of a true osteoporosis from an osteopenia induced by low muscle forces.

7. References

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