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Review article

High resolution peripheral quantitative computed tomography for the assessment of morphological and mechanical bone parameters

Henrique Fuller[a], *Ricardo Fuller*[b], *Rosa Maria R. Pereira*[a,*]

[a] *Bone Laboratory Metabolism, Rheumatology Division, Medicine School, Universidade de São Paulo, São Paulo, SP, Brazil*
[b] *Rheumatology Division, Hospital das Clínicas, Medicine School, Universidade de São Paulo, São Paulo, SP, Brazil*

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ABSTRACT

High resolution peripheral quantitative computed tomography is a new technology commercially available for <10 years that allows performing *in vivo* assessment of bone parameters. High resolution peripheral quantitative computed tomography assesses the trabecular thickness, trabecular separation, trabecular number and connectivity density and, in addition, cortical bone density and thickness and total bone volume and density in high-definition mode, which additionally allows obtaining digital constructs of bone microarchitecture. The application of mathematics to captured data, a method called finite element analysis, allows the estimation of the physical properties of the tissue, simulating supported loads in a non-invasive way. Thus, high resolution peripheral quantitative computed tomography simultaneously acquires data previously provided separately by dual energy X-ray absorptiometry, magnetic resonance imaging and histomorphometry, aggregating biomechanical estimates previously only possible in extracted tissues. This method has a satisfactory reproducibility, with coefficients of variation rarely exceeding 3%. Regarding accuracy, the method shows a fair to good agreement ($r^2 = 0.37–0.97$).

The main clinical application of this method is in the quantification and monitoring of metabolic bone disorders, more fully evaluating bone strength and fracture risk. In rheumatoid arthritis patients, this allows gauging the number and size of erosions and cysts, in addition to joint space. In osteoarthritis, it is possible to characterize the bone marrow edema-like areas that show a correlation with cartilage breakdown.

Given its high cost, high resolution peripheral quantitative computed tomography is still a research tool, but the high resolution and efficiency of this method reveal advantages over the methods currently used for bone assessment, with a potential to become an important tool in clinical practice.

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* *Corresponding author.*
E-mail: rosamariarp@yahoo.com (R.M.R. Pereira).
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Tomografia computadorizada quantitativa periférica de alta resolução para avaliação de parâmetros morfológicos e funcionais ósseos

Palavras-chave:
Tomografia computadorizada quantitativa periférica de alta resolução (HR-pQCT)
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Rádio
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RESUMO

A tomografia computadorizada quantitativa periférica de alta resolução (HR-pQCT) é uma nova tecnologia disponível comercialmente há menos de 10 anos que permite a feitura de exames *in vivo* para a avaliação de parâmetros ósseos. A HR-pQCT avalia a forma, o número, o volume, a densidade, a conectividade e a separação das trabéculas; a densidade e a espessura do osso cortical e o volume e a densidade total, em alta definição, o que permite a construção digital da microarquitetura óssea adicionalmente. A aplicação de cálculos matemáticos aos dados capturados, método denominado elemento finito (FE), permite a estimativa das propriedades físicas do tecido e simula cargas suportadas de forma não invasiva. Desse modo, a HR-pQCT adquire simultaneamente dados antes fornecidos separadamente pela densitometria óssea, pela ressonância magnética e pela histomorfometria e agrega estimativas biomecânicas antes só possíveis em tecidos extraídos. A reprodutibilidade do método é satisfatória, com coeficientes de variação que raramente ultrapassam os 3%. Quanto à acurácia, os parâmetros apresentam de regular a boa concordância (r^2 = 0,37–0,97).

A principal aplicação clínica é na quantificação e no monitoramento das doenças osteometabólicas, porque avalia de modo mais completo a resistência óssea e o risco de fratura. Na artrite reumatoide permite-se a aferição do número e do tamanho das erosões e dos cistos, além do espaço articular. Na osteoartrite é possível caracterizar as áreas edemasímile que guardam correlação com a degradação da cartilagem.

Restritas ainda a um instrumento de pesquisa, dado o seu elevado custo, a alta resolução e a eficiência mostram-se como vantagens em relação aos métodos atualmente usados para a avaliação óssea, com um potencial para tornar-se uma importante ferramenta na prática clínica.

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Introduction

In the 1990s, the incorporation of dual energy X-ray absorptiometry (DXA) in clinical practice considerably boosted the knowledge of metabolic bone diseases and the establishment of fracture risk. However, bone strength also depends on tissue microarchitecture. Thus, the histomorphometric analysis has become necessary to supplement the bone evaluation, inferring its spatial properties. But this is an invasive and expensive method that can only be performed from bone samples.

In this scenario, a new *in vivo* method for assessing bone microarchitecture and volumetric bone mineral density (BMD) in high-quality 3D emerges: high resolution peripheral quantitative computed tomography (HR-pQCT). This technology was originally designed for the analysis of materials such as snow, concrete, gems, and so on. Subsequently, the technology came to be used for the study of biological materials such as teeth, implants, bone and, more recently, cartilage. In addition, the method also allowed the analysis of biomechanical properties of the analyzed material, with the use of a complex mathematical process.

Its use for medical purposes has grown rapidly in recent years, because the method reveals in detail the internal structure of *in vivo* and *ex vivo* biological materials. The use of HR-pQCT is still largely confined to the field of scientific research, given that there is less than half a hundred devices worldwide in operation to perform the examination[1] and only two in Brazil. Due to its great potential, we present here a review of methodological aspects of HR-pQCT and its potential clinical application.

What is HR-pQCT?

HR-pQCT is an imaging technique that uses computerized processing of X-ray attenuation (measured in Hounsfield Units, HU) for the acquisition of sectional images, in the same way that a conventional CT scan does. From the slices, it is possible to produce a three-dimensional (3D) high-quality model.

Although HR-pQCT is also often confused with Computed Microtomography (MicroCT or μCT), these terms are not synonymous. While μCT has a very high resolution of up to fractions of μm (micron) and evaluates in great detail the morphology of the samples, its use is restricted to *ex vivo* analysis.[2] On the other hand, HR-pQCT, specifically, is an equipment whose resolution reaches only tens of micrometers; this size is slightly larger than that represented by the trabecular structure, but also allows a detailed analysis of tissue morphology. In addition, this method differentiates itself from μCT as to the possibility to perform rapid tests *in vivo*.[3,4] The study of bone structures with μCT was introduced in 1989,[5] and soon became the gold standard for the evaluation of three-dimensional bone structure.

Currently, there is only one commercial HR-pQCT machine that is able to perform scans at a resolution sufficient to

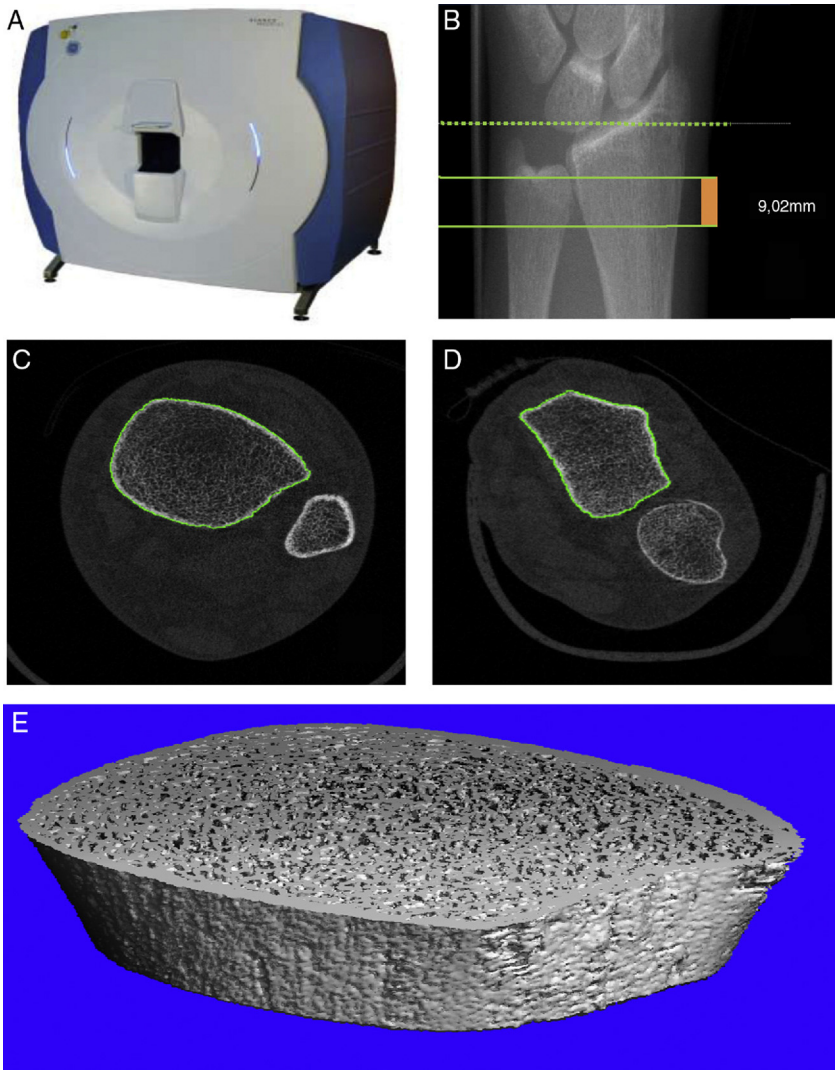


Fig. 1 – (A) Scanco XtremeCT HR-pQCT device. (B) Reference standardized planes for HR-pQCT. The dotted line indicates the reference plane, while the solid lines indicate initial and final planes of the test, comprising a thickness of 9.02 mm. (C) The sectional image of the leg, highlighting the tibial periosteum contour (in green). (D) The sectional image of the forearm, highlighting the radial periosteum contour (in green). (E) Construction of a 3D model of tibia, after initial analysis.

measure three-dimensional human bone microarchitecture *in vivo*, the XtremeCT (SCANCO Medical AG, Brüttisellen, Switzerland). (Fig. 1A). Nevertheless, the ability to measure the average trabecular thickness is still limited by the maximum resolution of the machine.[6–8]

Despite the ability to carry on morphological scanning of the tissue microstructure, there was still no proper way to estimate the mechanical properties of the material under analysis *in vivo*. The improved resolution of 3D images provided by this new device coupled with computer-based finite element analysis (FEA) modeling[9] provides estimates of functional properties of the material.

Image acquisition and results

The standard test with XtremeCT evaluates distal radius and tibia *in vivo*.[10] The limb being scanned is immobilized in a carbon fiber shell to avoid artifacts resulting from motion, which could lead to the need for rescanning.[11–13] Initially, a scout view, essentially a two-dimensional X-ray scan, is obtained to determine a precise region for the three-dimensional measurement (Fig. 1B). Each site includes 110 computerized tomography slices, totaling an extension of 9.02 mm along the axial axis of the bone. The acquisition of these images takes about 3 min. The standard protocol is typically conducted with the following settings: X-ray tube current = 95 mA, X-ray tube potential = 60 kVp, voxel size = 82 μm, and a 1536 × 1536 matrix.

The HR-pQCT single-scan effective radiation dose is less than 5 μSv.[14] Some studies estimate that it is around 3 μSv per measure.[15] The international recommendation is that the average annual dose for planned radiation exposure must not exceed 20 μSv/year, measured over a defined period of five years.[16,17] For comparison, a chest X-ray exposes to a radiation dose of 20 μSv.

Table 1 – HR-pQCT main bone parameters.

Abbreviation	Parameter	Description	Unit
Structural parameters			
BV/TV	Bone volume ratio	Ratio between bone volume and total volume of tissue	–
Tb.N	Trabecular number	Mean number of trabeculae	per mm
Tb.Th	Trabecular thickness	Mean thickness of trabeculae	mm
Tb.Sp	Trabecular separation	Mean space between trabeculae	mm
Tb.1/N.SD	In homogeneity of network	Standard deviation of the inverse of number of trabeculae	mm
Ct. Th	Cortical thickness	Average cortical thickness	mm
Co.Po	Cortical porosity	Ratio between pore volume and total cortical volume	–
Tt.Ar	Total bone area	Cross-sectional area	mm^2
Ct.Ar	Cortical bone area	Mean of the area occupied by cortical bone	mm^2
Tt.Ar	Trabecular bone area	Mean of the area occupied by trabecular bone	mm^2
Density parameters			
BMD (D100)	Bone mineral density	Total volumetric density	mg HA/cm^3
Tb.BMD (Dtrab)	Trabecular bone mineral density	Trabecular volumetric density	mg HA/cm^3
Dmeta	Meta trabecular bone mineral density (40%)	External trabecular volumetric density (40% of trabecular volume)	mg HA/cm^3
Dinn	Inner trabecular bone mineral density (60%)	Inner trabecular volumetric density (60% of trabecular volume)	mg HA/cm^3
Meta/Inn	Ratio meta to inner bone mineral density	Ratio between outer and inner trabecular bone density	–
Ct.BMD (Dcomp)	Cortical bone mineral density	Cortical volumetric density	mg HA/cm^3

After the acquisition of images, the system automatically performs an initial evaluation that consists of two processes: (1) processing of digital data in sectional images (Fig. 1C and D) and (2) construction of a 3D model (Fig. 1E). Subsequently, it is necessary to determine the compartments. The first contour is characterized by the outer envelope of the radius, which is then used to define the full compartment. The software is provided with a semiautomatic contouring algorithm (Fig. 1C and D).

After obtaining this contour, the next necessary step is to determine the inner contour delineating cortical from trabecular bone, with the goal of obtaining isolated data relating to each of the compartments. This is a complex process, because their boundary is not always well defined. Where the cortex is rather thick or highly porous, the boundary between the compartments may be inaccurate.[18] This procedure automatically creates the different compartments based on image processing.[19,20]

Another aspect that must be established with respect to trabecular bone is to describe and quantify the plate and rod-like structure of bone. While rod-like trabeculae have two connections (called disjunctive) attached to the adjacent bone and only one contact surface with the bone marrow, plate-like trabeculae have only one contact surface with the adjoining bone (in all its perimeter) and two with the bone marrow (one on each side of the disc).[20] This process of rod-like and plate-like trabeculae separation is performed automatically by the software, having an influence on the results of some of the parameters.

A series of tests to determine the main bone parameters used in the literature follows.[1] Thus, mathematical algorithms are required that allow such calculations. The manufacturer's software already includes computer scripts containing the equations.

These scripts include the definition of bone volume, bone volume density, structure model index, trabecular thickness, trabecular separation, trabecular number and connectivity density, and cortical thickness. The degree of cortical porosity is the most relevant cortical data obtained. Table 1 discriminates the main parameters and their terminology, as used in the medical literature.

Finite element analysis modeling

FEA is a numerical technique of engineering, which, when applied to medicine, allows a quantitative and qualitative estimation of biomechanical properties resulting from bone microarchitecture, by means of complex differential equations.[21–23]

After standard-data acquisition from microarchitecture, the addition of the specific finite element analysis script becomes possible, thus allowing the estimation of bone functional properties from data collected in a static manner. The

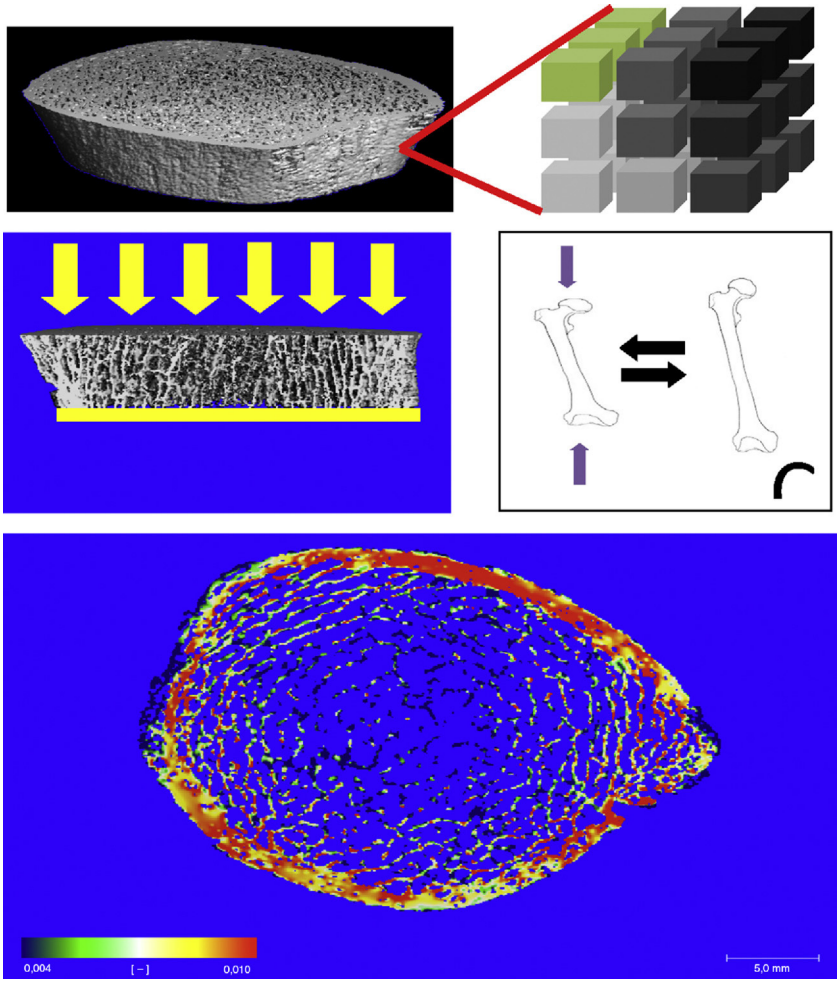


Fig. 2 – (A) Voxel conversion technique. In the scheme, each of the cubes to the right is a voxel with a specific elasticity, here represented by different shades of gray. (B) Virtual compression test, performed by the finite element software. Application of compressive forces (in yellow). (C) Illustration of Young's modulus. The removal of the compression forces (in yellow) causes the material to return to its original shape. (D) Example of the result of an analysis with the finite element method; axial bone section. In red, areas subjected to greater stress; in green, areas under less stress.

software employs the so-called "voxel conversion technique" (Fig. 2A) to create finite element models (Finite Element Software, V.1.13, Scanco Medical AG, Switzerland, January 2009 Manufacturer Handbook). In this technique, the vector information obtained in the model is converted into blocks called voxels, which have identical shape and size. The voxels are shaped like cubes, being the smallest unit that makes up the image of the analyzed material. Each voxel is registered with one among 255 gradations of elasticity recognized by the system to perform the mathematical calculations. The standard analysis of FEA comprises a virtual resistance test, namely, the computer estimates and analyzes the behavior of the bone tissue when it is submitted to a compressive force along its major axis (Fig. 2B).

For analysis of FE, two mechanical properties of the bone under study must be estimated, considering that no histofunctional study of bone tissue is being carried out:

- The first of them is the Young's modulus, a measure of the ability of a material to return to its original shape after removal of a stress force, thus indicating the tissue's elasticity. This measure is valid only in the range of forces in which the elastic deformation occurs, namely, when there is neither microrupture nor change in bone structure, enabling it to return to its original form.
- The second mechanical property is a measure of the Poisson effect, which is the tendency of a material to become thinner when it is stretched at a given axis. In other words, when a material is pulled, it increases its size in the axis of traction, and decreases its size in the other two axes. In response to the tensile force applied, the elasticity of the material will tend to bring it to its original shape. This trend can be understood as a force that will shrink the material in the direction of its stretching and will increase it in the other directions. The Poisson ratio is a ratio between the first and second forces.[24]

Table 2 – Mechanical parameters obtained by Finite Element.

Abbreviature	Parameter	Description	Unit
S	Stiffness	Tissue stiffness	N/mm
F.ult	Estimated ultimate failure load	Estimate of maximum supported load	N
(Tb.F/TF)dist	–	The ratio between the load supported by trabecular bone and the load supported by the whole bone, at its distal end	–
(Tb.F/TF)prox	–	The ratio between the load supported by trabecular bone and the load supported by the whole bone, at its proximal end	–
E.app	Apparent modulus	Apparent modulus (gauges stress)	N/mm^2
Tb.VM	Trabecular Van Mises stress	Trabecular stress (gauges pressure on trabeculae)	N/mm^2
C.VM	Cortical Van Mises stress	Cortical stress (gauges pressure on the cortex)	N/mm^2
Tb.ES	Average equivalent strain trabecular bone	Measures average trabecular deformation	–
Ct.ES	Average equivalent strain cortical bone	Measures average cortical deformation	–

The values of these variables are not yet fully established, and hence their use varies according to the literature used. The normal range of Young's modulus used is between 10 GPa and 22.5 GPa (Giga Pascal is a multiple of the standard unit of pressure in the international system, defined as Newton/m^2). The Young's modulus can be set separately for both trabecular and cortical bone. On the other hand, the Poisson ratio is 0.3 for most studies.[25–30]

The application of this technique has produced, in a simple and fast way, a huge amount of data, previously only obtained from invasive, costly and time-consuming procedures. These are data that estimate the supported load and the deformations of the bone as a whole, and in each of its regions. Table 2 lists the main parameters obtained from this method.

Accuracy

The analyses of HR-pQCT accuracy are based on the gold standard for measurement of bone microarchitecture, the μCT. Comparisons are performed on cadaver data, mostly due to the inability to perform *in vivo* tests with μCT devices.

Overall, the parameters exhibit good to moderate agreement ($r^2 = 0.37–0.97$). It is noted, however, that some parameters such as BV/TV ($r^2 = 0.91–0.97$)[3,31] and Tb.Sp ($r^2 = 0.91$)[3] exhibited an excellent correlation, while parameters such as Tb.1/N.SD ($r^2 = 0.62–0.71$)[4] and Tb.Th ($r^2 = 0.42–0.64$)[3,31] had a lower correlation.

Tjong et al.[3] also investigated the impact of different voxel sizes on HR-pQCT and its correlation with gold standard parameters. Alternating between standardized values by XTremeCT (41 μm; 82 μm; and 123 μm), it is possible to significantly change the accuracy. With a voxel of 123 μm, Tb.Th presents $r^2 = 0.37$; increasing the resolution to 41 μm one reaches $r^2 = 0.82$. Similarly, Tb.Sp can vary from $r^2 = 0.78$ to $r^2 = 0.95$. But some parameters, especially BMD, are little influenced by the increased resolution. Tb.BMD remains at $r^2 = 0.84–0.85$ in the various resolutions compared. While improving the accuracy, decreasing the voxel size implies in a greater examination time and, therefore, the chances of occurrence of artifacts resulting from patient motion are multiplied.

Total bone mineral density (D100), in addition to the other BMD parameters obtained with HR-pQCT, may also be compared with those obtained by Dual energy X-ray densitometry (DXA). It is important to note, however, that while HR-pQCT and μCT calculate volumetric densities (vBMD), DXA calculates density per area (aBMD). The correlation shown in the comparison between HR-pQCT and DXA, depending on the parameter analyzed, can vary from $r^2 = 0.37$ to $r^2 = 0.73$, being maximum when the comparison is made between total vBMD and aBMD.[32] It can be noted, however, that there are still few studies focused on showing the correlation between these parameters.

Reproducibility

To date, few studies reporting the reproducibility of results obtained by HR-pQCT were published. Most of these studies show that the equipment, when used in accordance with standardized and well-defined protocols, reaches low coefficients of variation. Several aspects influence the reproducibility of results, among which stand out the parameter being analyzed, the protocols used, the bone being evaluated and the correct accomplishment of calibration protocols.

The parameters derived from HR-pQCT can be divided into those concerning structural measures and those related to BMD (Table 1). Comparing the reproducibility, it can be noticed that this factor is greater in the second *versus* first group. While the structural measures can achieve coefficients of variation of up to 3.2–4.4%, those relative to bone mineral density hardly exceed 1%.[33,34] The explanation for this fact is that, in the evaluation of BMD, an average value of bone tissue concentration by total volume is used, and this parameter is little influenced by the small shape features. On the other hand, structural measures vary significantly with any change in the acquisition angle, or with movement.

As for the protocols employed, these must be very well defined, to improve reproducibility. They include: patient positioning, fixing the limb into the support shell, and the choice of the reference plane, among others. Basically, all these factors can give rise to three types of errors: artifacts of movement, reducing the overlap in different measurements, and changes in angulation. The lack of a comfortable position and the non-fixation into the support shell can lead to patient motion, which increases the variation between tests. The choice of the reference plane (boundaries of bone area analyzed) can cause significant discrepancies in the results obtained[33]; in this measurement, the change of only 1 mm can lead to a variety of 11% in the tissue sample analyzed. As to the bone evaluated, according to Boutroy et al.[34] in most cases the results for the tibia have higher coefficients of variation, when compared to similar parameters for the radius. But MacNeil et al.[33] observed that radius measurements are more prone to movement artifacts.

Regarding XtremeCT, it is important to note that the proper conduct of daily and weekly calibration protocols was extremely important for maintaining high standards of reproducibility and low variability in the short and long term, besides multicenter reproducibility.[35]

Applications

The use of HR-pQCT in biological tissues generated an enormous range of possibilities for scientific research, and this can be observed by the exponential increase in the number of publications that make use of this technology in recent years. The functional analysis with the finite element method has further expanded the number of applications of the technique.

Since its first use for bone assessment, this has been the main application of HR-pQCT. Studies indicate that it is possible to evaluate the profile of bone microarchitecture throughout life, the risk of fractures, mineralization and the development of bone diseases (*e.g.*, osteoporosis). The effect of drugs and diets in bone formation, resorption and morphology also can be verified. Currently, the use of HR-pQCT has been extended to the diagnosis and monitoring of inflammatory arthropathies, such as rheumatoid arthritis and osteoarthritis. However, the practical use of the method still seems much more promising for, and responds to gaps in, osteoporosis; in osteoarthritis and rheumatoid arthritis, its usefulness is still more related to research.

The use of HR-pQCT in osteoporosis and fracture risk assessment

Osteoporosis (OP) is characterized by a compromised bone strength, predisposing the individual to the risk of fractures.[36] Dual emission X-ray densitometry (DXA) is still the gold standard for diagnosis, monitoring and clinical investigation of the patient with osteoporosis.[37] However, bone mineral density (BMD) only corresponds to a part of bone strength.[38] Thus, for the assessment of fracture risk, BMD measurements should be associated with other factors that influence bone strength: cortical thickness and porosity, trabecular microstructure and bone geometry.[39] These combined factors contribute to define the biomechanical properties of bone tissue, such as stiffness and supported load.[31]

The ability of HR-pQCT to define these parameters of bone architecture, in conjunction with the ability of the FEA for estimating biomechanical properties, makes this technique an excellent tool for osteoporosis evaluation. It has been shown by several studies that this data set is closely linked to the risk of fractures in OP,[10,22,40] and also that individuals with similar results obtained by DXA may have large differences in fracture risk, due to the above factors.[41,42]

The use of HR-pQCT in monitoring therapy

Some,[43–46] but not all,[47] studies suggest that changes in BMD during the therapy of osteoporosis correlate to the reduction in fracture risk. A meta-analysis of 12 clinical trials concluded that a BMD improvement in the spine comprises only a small part of the reduction in fracture risk.[48] Thus, to evaluate the therapeutic aspects, the use of parameters that measure not only the BMD is in order, but also the bone microarchitecture.

Several studies already published have demonstrated that therapeutic treatments for osteoporosis can bring improvement in many bone parameters. Thus, HR-pQCT is a tool that allows a much more detailed assessment of treatment compared with DXA.

Cheung et al.[1] reported several studies on the use of HR-pQCT in monitoring osteoporosis treatment. Research conducted with alendronate,[49–52] zoledronic acid,[53] ibandronate,[54,55] denosumab,[51] strontium ranelate,[49,50] odanacatib[56,57] and teriparatide[53,58] can demonstrate changes mainly in the parameters of vBMD for the various bone compartments, cortical thickness, maximum supported load and trabecular number.

The use of HR-pQCT in rheumatoid arthritis

Bone erosions are closely linked to the progression of rheumatoid arthritis (RA). Therefore, monitoring of these lesions is an early prognostic parameter and an important input to monitor the effectiveness of treatment.[59,60] Currently, among the imaging methods, conventional radiography is the most used tool in clinical practice to aid in the diagnosis and monitoring of RA for evaluating erosions and bone loss,[61] but besides being a semiquantitative procedure, the identification of lesions in this type of test takes 6–12 months to become apparent.[62]

Stach et al.[63] showed that it is possible to adapt the HR-pQCT device for evaluating the volume of bone erosions. This information is obtained by measuring distances in various directions in the slices made.[64,65] The current analysis method is still not automated nor standardized, but preliminary results of some studies show that the high-resolution of HR-pQCT allows a precise characterization of bone erosions on a much greater degree of detail than traditional methods.[61] The technique also allows the evaluation of the joint space of metacarpophalangeal and proximal interphalangeal joints,[66] an important parameter in the evaluation of RA.

Recent studies show that the data obtained with HR-pQCT in patients with RA have a higher sensitivity, when compared to data obtained by conventional radiographs in correlation with markers of bone catabolism and anabolism ($r = 0.393–0.474$).[67] This shows that HR-pQCT can not only evaluate momentarily RA, but also show disease progression.

The use of HR-pQCT in osteoarthritis

In osteoarthritis (OA), a cartilage lesion is accompanied by alterations in subchondral bone and marrow space. Magnetic resonance imaging can connect cartilage injury to regions where there are the so-called bone marrow edema-like (BMEL) injuries, which are areas of high signal on T2-weighted images.[68] In these places it is possible to observe, in addition to edema, necrosis of adipocytes, increase of fibrous tissue and an accelerated bone metabolism. However, the magnetic resonance is unable to determine which changes in bone microarchitecture are present, and how they relate to disease.

There are still few studies demonstrating the efficacy of assessment with HR-pQCT in the diagnosis and prognosis of OA, but Kazakia et al.[69] demonstrated that, in BMEL injuries, important changes occur in some bone parameters. These authors[69] evaluated fragments of subchondral bone of the tibia in patients treated with knee arthroplasty due to osteoarthritis. They found that there was a significant increase in volumetric bone mineral density (vBMD) and bone volume/total volume (BV/TV), along with trabecular thickening (Tb.Th). Also in this study, when data obtained with HR-pQCT were coupled to the bone spectroscopic analysis, a reduction in the mineral/matrix ratio was noted. In fact, histological evaluations reveal that, in these BMEL areas, an infiltration of marrow spaces by a fibrous collagen network and intense bone remodeling occur. The relationship between these bone changes with cartilage damage is not yet fully known. It is possible that the measurement of these data may have an important clinical role in OA.

Perspectives

Although HR-pQCT has been launched on the market less than 10 years ago, this technology has already a myriad of medical applications. Groups of researchers worldwide have been working to find new ways to exploit its full potential. For now, the device is still a tool restricted to research; but considering the things it has been able to assess, the underlying view is that, in a short time, HR-pQCT will become an important clinical tool. However, the current costs are still an obstacle to its full clinical use.

Its high resolution and non-invasive characteristics, the evaluation *in vivo*, and its speed and efficiency are advantageous points over traditional methods of measuring bone mineral density and histomorphometry for bone studies. Thus, HR-pQCT can be used for an efficient and accurate assessment of the development of diseases such as osteoporosis, osteoarthritis and rheumatoid arthritis. Thus, in the future, the incorporation of the measurements of this technology on classification criteria and in the staging of various clinical conditions may occur. It will be absolutely essential to carry out further studies on safety, accuracy and reproducibility of the analyses promoted by HR-pQCT in various diseases and in the aging process, when compared to what is already established by μCT, DXA and histomorphometry.

It will be important also to determine and consolidate the standards of normality for different populations. Some studies using control groups for comparison have been published, but there is still not one comprehensive study in this direction for the Brazilian population. Presently, the study group at the Laboratory for Bone Metabolism, Medicine School, Universidade de São Paulo (LIM-17) is conducting a study to determine normality curves for HR-pQCT and Finite Element Analysis parameters with a sample of over 400 healthy women aged over 20 years.

At this point, it is worth mentioning some limitations of the assessments performed with HR-pQCT and in the application of finite element analysis modeling. One of them is that the achievement of parameters of strength and stiffness depends on functional estimates and on the application of mathematical models that, in many cases, are not entirely reliable representations of reality. Moreover, it is not yet really clear how the morphofunctional changes observed in peripheral bones (radius and tibia) may correlate with the rest of the skeleton. Another limitation to be emphasized is related to the resolution of the device that, despite being the highest available today for testing *in vivo*, is not still sufficient to individually assess trabeculae.

Finally, it is necessary to consolidate the standardization of methods of acquisition and analysis of images with HR-pQCT technology. To do so, one must keep in mind the patient positioning, system settings, the initial and final planes of imaging for the site measurements and the most important parameters in the various assessments. Regarding finite element analysis modeling (which only recently is being used in bone studies), it is really important to define patterns of bone functional properties (*Young's modulus* and *Poisson's ratio*).

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Conflict of interest

The authors declare no conflict of interests.

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