Case report

MICRO-COMPUTER TOMOGRAPHY AND BILATERAL ULTRASOUND OSTEOMETRY OF PATIENTS SUBJECT TO TOTAL HIP ARTHROPLASTY

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Summary

Quantitative ultrasound (QUS) is a device method for assessment of bone density, used in osteoporosis screening. Quantitative ultrasound devices are used to conduct measurements in calcaneus, phalanges, tibia and radius, of which the most common is peripheral sonometry of calcaneus. Micro-computer tomography is a way of quantitative presentation of cancellous bone. It provides a 3D image using dual-energy X-ray images. QUS and CT provide information about bone architecture and bone stiffness. Both methods were used in our study to investigate patients with hip arthroplasty. The bilateral QUS calcaneus measurement was conducted *in vivo*. An *ex-vivo* micro-computer tomography was used for investigation of biopsy material from the femoral neck. The following parameters were estimated: bone mineral density (eBMD), stiffness, bone volume/total volume (BV/TV), trabecular thickness, trabecular number, trabecular separation.

Key words: quantitative ultrasound, micro-computer tomography, osteoporosis

Introduction

According to the 1993 WHO definition of osteoporosis, it is "a systemic skeletal disease characterized by low bone density and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk "[1].

In 2000, The National Health Institute of the USA defined osteoporosis as "a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture"in the "Osteoporosis Consensus – diagnosis and therapy" [2]. This new definition reveals that bone strength measurement provide a basis for fracture prediction [3].

In vivo measured bone mineral density (BMD) is necessary for prediction of future fracture risk [4, 5] but BMD cannot not substitute bone strength (stiffness), and represents only part of it.

In their survey of race horses Kumasaka et al. report that BMD found in the studied group with fractures (536.8mg/cm^3) was significantly higher than the one in the group without fractures

(217.9mg/cm^3, P = 0.002). This suggests that fractures can occur in cases of relatively high BMD [6]. Localizations with higher fracture risk are the hip, vertebra and distal radius. Lifetime fracture risk for each of these sites is 40% for women and 13% for men over fifty years of age [7, 8]. Femoral neck fracture risk increases 10 times for every 20 years of life [9].

Femoral neck fractures caused by osteoporosis occur more often in elderly people, causing pain and loss of independent living. They reduce life expectancy and imply high cost healthcare [10-14].

Indirect mechanism for femoral neck fracture occurrence could be:

side fall on greater trochanter;

jerk external rotation of the leg;

fatigue fracture.

Femoral neck fracture most often occurs after falling in domestic settings, and is felicitously named "fracture among four walls" [15]. It has been established that only 1-2% of these falls lead to femoral neck fractures, while side falls on the hip increase the fracture risk 20 times [16]. Distribution of load in the proximal femur during a side fall depends on the bone architecture of this region. Loading of the cancellous bone at the femoral neck base varies from as low 4% to 70% in the subcapital region [17]. This makes us assume that the cortical bone and cancellous bone both contribute to femoral neck fracture occurrence.

Quantitative ultrasound is a non-invasive method for assessment of bone characteristics such as elasticity, structure and geometry. It can be applied as a method for osteoporosis screening of postmenopausal women [18].

The most widely used technique for diagnosing osteoporosis is the dual-energy X-ray absorbtiometry (DXA). WHO recommends investigation of the femoral neck. This X-ray method is used to assess bone mass and bone loss. QUS and DXA use 2D sections of bone. The bone density assessed using these methods is measured in g/cm^2

Since its introduction back in the 1970s, computer tomography (CT) has radically changed clinical diagnostic practice [19]. Digital geometry processing generates 3D images of the inner side of the objects, using 2D X-ray images.

Micro-computer tomography provides a quantitative 3D presentation of cancellous bone. Feldkamp [20] was the first to use micro-computer tomography, based on X-rays. He obtained 3D objects with a resolution of 50 м [21]. Other researchers use synchronous radiation for obtaining volume resolution of 2 м [22].

The obvious initial advantage of micro-CT was the opportunity to study changes in bone architecture in 3D. This was thought to yield more valuable information than traditional methods, which used 2D sections of bone. New methods and computer algorithms were developed to characterize the 3D architecture. One important goal of introducing 3D morphometry measures of cancellous bone was to identify the morphometric parameters, which correlated with other more clinically related parameters of bone, such as mechanical strength, stiffness or the fracture risk of a patient. In part, the new micro-CT-based parameters were 3D versions of architectural parameters, which were already in use in 2D bone histomorphometry [23].

Materials and methods

For the purpose of our study, biopsy material (cancellous bone) from the femoral neck region and bone samples sized up to 1 cm^3 were necessary. Our research showed it was not possible to purchase an appropriate tool for obtaining the samples. This imposed the invention of an extraction tool with the characteristics needed. (Fig.1)

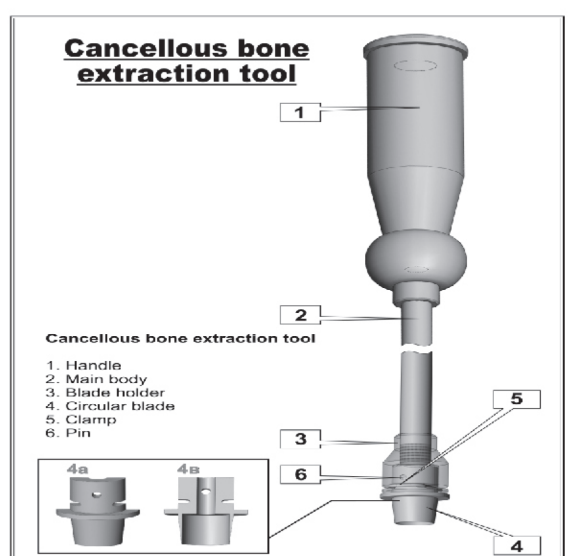

Figure 1. Cancellous bone extraction tool

The tool was tested with Cosmos Xpress 2008 Service Pack 5 by Advanced EET Incorporated, and a prototype was constructed (Registration form of utility model №1691/16.10.2009).

The project was presented to the Ethics Commission for Scientific Research at the Medical University of Pleven. After inspection according to the legal procedure, a permission № 109 of 28.05.08 of the Ethics Commission for Scientific Research at the Medical University of Pleven was obtained to conduct the experiment.

One of the patients (case history 6066) was operated on for hip arthrosis, and the other (case history 6067) - for femoral neck fracture. Bone samples were collected intraoperatively, using the cancellous bone extraction tool we invented.

After obtaining the biopsy material, the samples were placed in containers with 10% of formaldehyde solution and sent for micro-computer tomography investigation at the University of Antwerp, Belgium.

An *ex vivo* micro-computer tomography was made with Skyscan 1072 (Skyscan, Belgium). The following parameters were used:

energy source: 80 kV/100 µA;

filter: aluminium 1mm;

180° rotation, 0.675° step of rotation;

6.9 s exposition time;

pixel size: 13.82 µm;

Virtual cross sections were reconstructed by a Feldcamp cone beam algorithm. For analysis, images were inverted, pixel size was reduced to 27.64 µm and CT-Analyzer software was used (software obtained from Skyscan). A 'volume of interest' was chosen so that it was situated in the middle of the sample and contained as much bone as possible. Threshold was set at 90-250 grey values. Subsequently, the 'volume of interest' was analyzed threedimensionally.

Bilateral quantitative ultrasound calcaneus measurement [24] was carried out on both patients with quantitative ultrasound device Sahara, Hologic Inc., USA. Three consecutive measurements of each calcaneus were made. Quantitative ultrasound index (QUI) and body mass index (BMD) were also estimated.

Results

After completing the micro-CT investigation, data were gathered about the interrelation bone volume/total volume, trabecular thickness, trabecular number and trabecular separation (Table 1).

The distribution of trabecular thickness in the samples analyzed yielded information on bone structure of the sample (Fig.2). Sample material collected from the first patient (Fig. 3) possessed thinner trabeculae as compared to that from the second patient (Fig. 4).

Threefold bilateral calcaneus measurement was completed. Average values for left and right calcanei were calculated (Table 2).

The average value of QUI/ Stiffness was 124.3 in the first patient, and 67.8 – in the second patient. The average value of the estimated BMD was 709.5 g/cm^2 in the first patient, and 287.2 g/cm^2 in the second patient.

Table. 1. Bone analysis results. [1]BV/TV - bone volume / total volume, [2]Trab. Thick.- trabecular thickness, [3]Trab. Number - trabecular number, [4]Trab. Sep.- trabecular separation.

	6066	**6067**
BV/TV (%)[1]	8.92	8.42
Mean Trab. Thick. (µm)[2]	145.8	192.4
Mean Trab. Number (1/mm)[3]	1.22	0.44
Mean Trab. Sep. (µm)[4]	1053.2	949.0

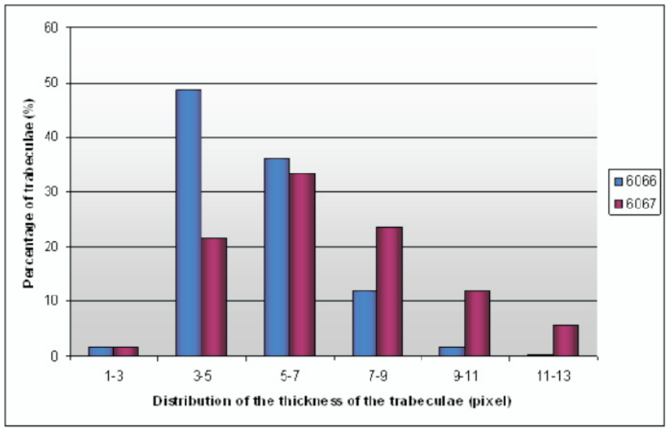

Figure 2. Distribution of the thickness of the trabeculae. Pixel size = 27.64 μm.

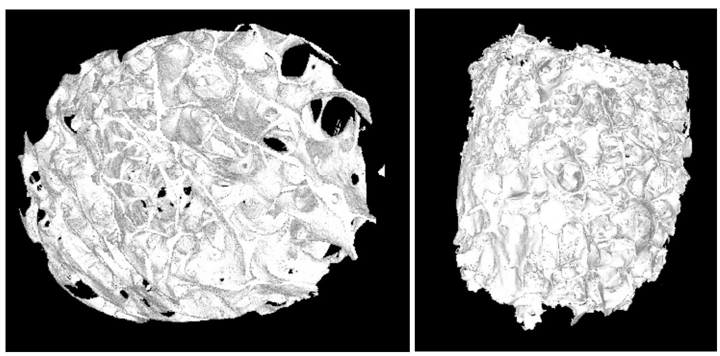

Figure 3. Human biopsies #6066 3D analysed

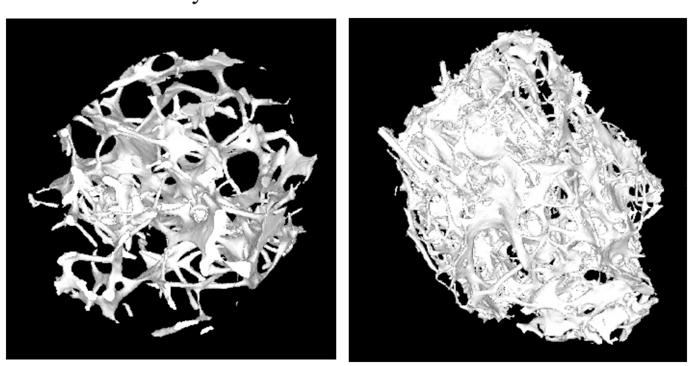

Figure 4. Human biopsies 6067 3D analysed

Table 2. Average values from bilateral ultrasound measurement of left and right calcanei

	6066 - left	6067 - left	6066- right	6067- right
QUI/ Stiffness	125.9	68.96	122.6	66.66
Estimate heel BMD g/cm^2	720	229.3	699	345

Discussion

The bone tissue quality measured quantitatively as bone stiffness is a continuous process of remodeling of the bone cell extracellular matrix. This remodeling occurs at tissue level and leads to bone mass distribution and maintenance of structural and metabolic functions of bone cells[25]. The bone architecture is defined by a combination of porosity (volume fraction), connectivity (degree of connection of trabecular fibers), and anisotropy (orientation dependence of connectivity) [26].

Ultrasound variables are speed of sound (SOS) and broadband ultrasound attenuation (BUA). Indirect and/or *in vitro* experiments have suggested that ultrasound investigations may be useful to measure bone density, as well as bone architecture and elasticity [27, 28].

Speed of sound (SOS) and broadband ultrasound attenuation (BUA) are included in the formula for estimation of the quantitative ultrasound index (QUI): QUI = 0.41(SOS) +0.41(BUA) – 571.

This index, also called *stiffness*, gives information about the stiffness of the bone. Results from the micro-CT investigations show that the number of the beams in sample 6067 is almost three times smaller as compared to the number found in sample 6066. QUI of patient 6067 is twice as low in value, as compared to the QUI of patient 6066. Interestingly, there is a small difference between the two samples as regards the BV/TV ratio, having in mind the difference in the estimated bone density found in the two patients, respectively 709.5 g/cm^2 and 287.2 g/cm^2.

The data we obtained lead us to an assumption that there is a correlation between bone architecture and fracture risk for postmenopausal patients. More extensive research using both QUS *in vivo* and micro-CT *ex vivo* could possibly clarify the correlation between bone architecture and fracture risk. This could provide further information about QUS as a device approach for defining the fracture risk in femoral neck zone.

References

1. Consensus development conference: diagnosis, prophylaxis, and treatment of osteoporosis. Am J Med. 1993;94(6):646-50.
2. Osteoporosis prevention, diagnosis, and therapy. NIH consensus statement. 2000; 17(1):1-45.
3. Davison KS, Siminoski K, Adachi JD, Hanley DA, Goltzman D, Hodsman AB et al. The Whole Is Greater Than the Sum of Its Parts. Semin Arthritis Rheum. 2006;36:22-31.
4. Chevalley T, Rizzoli R, Nydegger V, Slosman D, Tkatch L, Rapin CH at al. Preferential low bone mineral density of the femoral neck m patients with a recent fracture of the proximal femur. *Osteoporosis Int.* 1991;1(3):147-54.
5. Cummings SR, Black DM, Nevitt MC, Browner W, Genant HK, Cauley J et al. Bone density at various sites for prediction of hip fractures: the study of osteoporonc fiactures. *Lancet.* 1993;341(8837):72-5.
6. Kumasaka S, Asa K, Kawamata R, Okada T, Miya-ke M, Kashima I. Relationship between bone mineral density and bone stiffness in bone fracture, Oral Radiol. 2005;21(1):38-40.
7. Cummings SR, Kelsey JL, Nevitt MC, O'Dowd KJ. Epidemiology of osteoporosis and osteoporotic fractures. Epidemiol Rev.1985;7:178-208.
8. Melton 3rd LJ, Chrischilles EA, Cooper C, Lane AW, Riggs BL. Perspective. How many women have osteoporosis? J Bone Miner Res. 1992;7:1005-10.
9. Melton 3rd LJ. A "Gompertzian" view of osteoporosis. *Calcif Tissue Int*. 1990;46(5):285-86.
10. Lewiecki EM. Management of osteoporosis. *Clin Mol Allergy*. 2004;2:1-11.
11. Jacobsen SJ, Goldberg J, Miles TP, Brody JA, Stiers W, Rimm AA. Race and sex differences in mortality following fracture of the hip. *Am J Public Health*. 1992;82:1147-50.
12. Stavrou ZP, Erginousakis DA, Loizides AA, Tzevelekos SA, Papagiannakos KJ. Mortality and rehabilitation following hip fracture. A study of 202 elderly patients. *Acta Orthop Scand* Suppl. 1997;275:89-91.
13. Ray NF, Chan JK, Thamer M, Melton LJ. Medical expenditures for treatment of osteoporotic fractures in the United States in 1995: Report from the National Osteoporosis Foundation. *J Bone Miner Res*. 1997;12:24-35.
14. Melton LJ. How many women have osteoporosis now? *J Bone Miner Res.* 1995;10:175-77.
15. Takov E, Tivchev P. The fractures. Sofia: Venel; 1996. p. 581-604. (In Bulgarian)
16. Parkkari J, Kannus P, Palvanen M, Natri A, Vainio J, Aho H et al. Majority of hip fractures occur as a result of a fall and impact on the greater trochanter of the femur: a prospective controlled hip fracture study with 206 consecutive patients. Calcif Tissue Int. 1999;65:183-7.
17. Lotz JC, Cheal EJ, Hayes WC. Stress distributions within the proximal femur during gait and falls: Implications for osteoporotic fracture. Osteopor Int. 1995;5:252-61.
18. Heaney RP, John A. The Interpretation and Utility of Ultrasound Measurements of Bone. Bone. 1996;18(6):491-92.
19. Hounsfield GN. Computerized transverse axial scanning (tomography). Part 1. Description of system. *Br J Radiol*. 1973;46, 1016-22.
20. LA Feldkamp, SA Goldstein, AM Parfitt, G Jesion, M Kleerekoper. The direct examination of three-dimensional bone architecture in vitro by computed tomography. J Bone Miner Res. 1989;4(1):3–11.
21. Müller R, van Campenhout H, van Damme B, van der

Perre G, Dequeker J, Hildebrand Tet al. Morphometric Analysis of Human Bone Biopsies: A Quantitative Structural Comparison of Histological Sections and Micro-Computed Tomography, Bone. 1998;23(1):59–66.

22. Bonse U, Busch F, Gunnewig O, Beckmann F, Pahl R, Delling G. Morphometric analysis of bone biopsies: Histology vs. mCTHahn, M., and Graeff, W. 3D computed X-ray tomography of human cancellousbone at 8 mm spatial and 1024 energy resolution. Bone Miner. 1994;25:25-38.
23. Day JS, Ding M, Odgaard A, Sumner DR, Hvid I, Wei-nans H. Parallel plate model for trabecular bone exhibits volume fraction-dependent bias. Bone. 2000;27:715-20.
24. Minkov D., Rossmanov V. Bilateral quantitative ultrasound calcaneus measurements or two is more than one. J Ortop Trauma.2009;46(1):18-24. (In Bulgarian)
25. Menta SS, Antich PP, Daphary MM, Dwight G. Bron-son and Edmond Richer, Bone material ultrasound velocity is predicative of whole bone strength Ultrasound in Med. & Biol. 2001;27(6):861–867.
26. Langton CM. The clinical role of BUA for the assess-ment of osteoporosis: a new hypothesis. Clin Rheum. 1996;14:414-415.
27. Langton C M, Palmer C R, Porter R W. The measure-ment of broadband ultrasonic attenuation in cancellous bone. Eng Med. 1984;13:8-91.
28. Kaufman J J, Einhoru T. A. Perspectives: Ultrasound assessment of bone. J Bone Min Res.1993;8:517-525.