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Research Paper

Evaluation of the structural quality of bone in a case of progressive osteoporosis complicating a Complex Regional Pain Syndrome (CRPS) of the upper limb

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ABSTRACT

Densitometry is considered to be the gold standard in bone quality assessment. However, since its introduction, the medical community has been aware that mineral density is only one of the factors that influence the bone risk of fracture, which also depends on the bone's trabecular arrangement and, in particular, on the trabecular architecture's load bearing capabilities. At the University of Trieste, in recent years, a test has been developed that simulates the application of compressive loads on trabecular architecture's reconstructions extracted from digital radiographs. In this work, the test is described, and the results obtained by applying the appraisal in a particular case of severe osteoporosis of the hand, complicating a Complex Regional Pain Syndrome (CRPS) type II, are presented. The test was able to quantify the pathological alterations of bone micro-architecture by means of a Structural Index (*SI*), which was absolutely significant and relevant to the clinical situation. Important research and clinical opportunities of application of the test include accurate evaluation of osteoporotic bone diseases, careful clinical follow-up and monitoring of responses to therapeutic approaches, and, prospectively, reliable quantification of biological damage (forensic field).

1. Introduction

According to the National Institutes of Health (NIH) definition, osteoporosis is a disease in which the bones become weak and are more likely to break (National Institutes of Health, 2011). The Dual Energy X-ray Absorptiometry (DEXA) is currently the golden standard for measuring bone density (BMD) and the diagnosis is made based on the number (*T*-score) of standard deviations below the young Caucasian female adult mean BMD (World Health Organization Scientific Group, 2008). However, even though a low value of bone mineral density is considered to increase the fracture risk, the majority of fractures take place in post-menopausal women and elderly men at moderate risk (Pasco et al., 2006; Siris et al., 2004; Sornay-Rendu et al., 2005; Szulc et al., 2005).

Abbreviations: CRPS, Complex Regional Pain Syndrome; BMD, bone mineral density; *CF*, content factor; CM, Cell Method; *E**, apparent elastic modulus; ROI, region of interest; *SI*, Structural Index

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The medical community has long been aware that there are two factors that increase bone weakness: bone mineralization loss and micro-architectural deterioration (Consensus Development Conference, 1993). In effect, without prejudice to the importance of the contribution to bone resistance provided by mineralization, it is well known that the ability of bone to resist the applied loads also depends on the structural architecture of the trabeculae, an aspect which the techniques currently available are not able to take into account (Liu et al., 2009; Yeni et al., 2009; Haiat et al., 2009).

Estimating the bone density alone is not, therefore, a parameter sufficient for a complete evaluation of the load bearing capability of the bone, and, for a better quantitative understanding of bone quality, also the spatial arrangement of the trabecular tissue should be taken into consideration.

An example is given to emphasize this point. Fig. 1 shows two portions of micro-CT slices from a pig humerus, in which the trabecular phase has been meshed with triangular cells. Assumed the elastic modulus ($E=1000$ MPa) for the trabecular phase in the two images, the stress distributions obtained by simulating a compression test along the long side of the slices are very dissimilar, as depicted by the Von Mises stress in Fig. 1. The bone fraction BF in both images is the same (BF=39.9%), but the effective elastic modulus (computed by simulation) of the top slice is only 25.9% of the bottom one. The images were obtained by phase-contrast micro-CT at the Elettra synchrotron radiation facility in Trieste, with a resolution of 14 μm. It must be noted that they represent two particular portions from two different slices (not projected images) and cannot be used alone to assess the bone tissue fraction in the bone.

In general, the trabecular arrangement influences not only the elastic properties of cancellous bone, but also its mechanical strength (Kleerekoper et al., 1985; Uchiyama et al., 1999). In effect, the mechanical properties of bone are regulated by the composition and by the structural organization at the micro- and nano-scale (Zysset et al., 1999). Also the failure mechanisms in trabecular bone are related to the tissue composition and the microstructure (Morgan, 2008), but, in this case, the non-linearity of the load-deformation curve must be taken into account (Linde, 1994). Both elastic modulus and ultimate strength of cortical and cancellous bone decrease in humans with increasing age (Bouksein et al., 2008) and, even if a direct relation has not been established, inferences can be drawn between the failure and the elastic properties of trabecular bone (Brear et al., 1988) that can be very useful for the purpose of bone quality ranking.

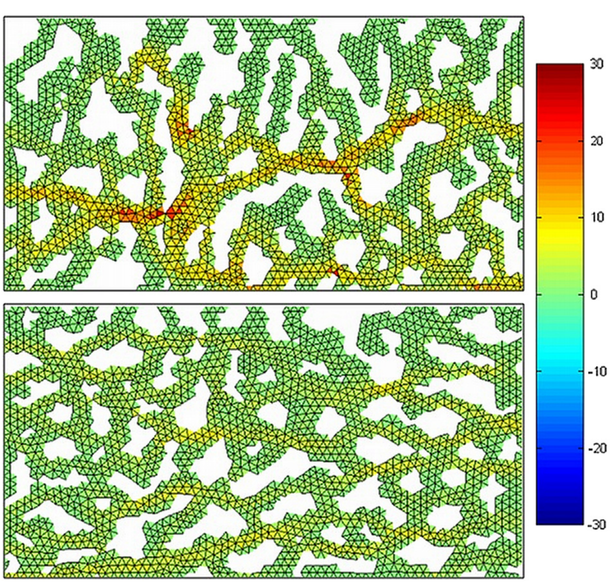

Fig. 1 – Different Von Mises stress distribution (MPa) obtained by simulating a compression test in two micro-CT slices of equal bone fraction from a pig humerus.

Micro-numerical models applied to 3D micro-CT or micro-MRI reconstructions, based on finite elements or alternative methods, have been developed to compute the elastic properties of trabecular structures (Cosmi et al., 2009; Niebur et al., 2000; Viceconti et al., 2004, Zysset, 2003) and to perform strength predictions by incorporating the post-yield behavior of the trabecular bone tissue (Verhulp et al., 2008). Nevertheless, a widespread clinical application of 3D methods seems unlikely in the near future, given the examination costs and computational requirements. These considerations led us to investigate whether the information contained in a 2D digital radiographic image can contribute, along with the methods already in use, to give a clinical indication, namely a ranking, of the bone structure's load bearing capabilities.

The approach followed in this work focuses on the characterization of the bone structure by numerical simulation, obtained from conventional radiographic images of suitable anatomical districts. In a few seconds, the test can quantify the possible pathological alterations of bone micro-architecture by means of a Structural Index (*SI*), which is calculated from the elastic response of the reconstructed structure and the normalized sum of gray tones, indicative of the mineralization in the region under examination (Cosmi, 2008).

For the assessment of bone quality ranking in age-related osteoporosis, after the first tests on a small number of subjects (Cosmi and Dreossi, 2007a), a wider clinical validation has been recently conducted (Cosmi et al., 2011). The very positive results obtained in these studies, the low cost of the examination and the wide availability of the necessary equipment, make the proposed method a highly promising tool, able to equip the physician with a simple, inexpensive and readily available complementary technique, useful for providing information on the patient's bone tissue quality, thus completing the data supplied by the methods currently in use, for a more accurate assessment and also for screening purposes.

In this paper we present the results obtained by applying the test to a particular case of rapidly progressing, limb-confined osteoporosis, which occurred in a case of Complex Regional Pain Syndrome (CRPS) of the arm.

We chose this particular (and rare) case of CRPS-linked, severe osteoporosis, since, among other bone diseases, this unique clinical situation provides all the elements necessary for proving the validity of the proposed computational method for a wide range of research and clinical applications in osteoporotic pathologies (see below).

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