Acta of Bioengineering and Biomechanics
Vol. 9, No. 2, 2007

The application of the cell method in a clinical assessment of bone fracture risk

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The aim of this paper is to introduce a new technique for in vivo quantification of bone structure fracture risk. The elastic properties of the architecture obtained from bone digital radiographic images are determined using the cell method. Compression tests are simulated and the results of the numerical analysis are indexed. Such an index is considered to be indicative of the bone structure capabilities. The first clinical validation was carried on at CSMMO, Centro Studi Malattie Metaboliche dell'Osso (Gorizia, Italy), showing that this technique can improve the diagnosis and help a physician in the identification of an actual fracture risk. The examination is not expensive, uses instrumentation that is widely available and therefore could be easily introduced in clinical use as a complement to the current osteoporosis diagnosis methodologies.

Key words: trabecular bone, fracture risk, cell method, osteoporosis, structural analysis

1. Introduction

This paper describes a new technique for in vivo analysis of bone structure architecture, implemented in a software developed at the University of Trieste. The analysis starts with a conventional radiographic image and gives a result that can indicate possible pathological modifications of the bone and helps a physician in the early diagnosis of fracture risk. One of the goals of our research was to diagnose the fracture risk before the fracture occurs.

Osteoporosis is bone disease, disease where the bones become thin, porous and brittle that predisposes a patient to a higher risk of fracture. Osteoporosis affects an estimated 75 million people in Europe, USA and Japan [1], being responsible for more than 1.5 million fractures annually; one out of two women and one out of four men over 50 will have an osteoporosis-related fracture in her/his remaining lifetime. The estimated US national direct care expenditures for osteoporotic fractures reached $18 billion in 2002, and these costs are rising [2].

Osteoporosis is often called a "silent disease" because bone loss occurs without symptoms and people may not know that they suffer from osteoporosis until their bones become so weak that a sudden strain, bump or fall causes a fracture or a vertebra collapse. This disease is characterized by two factors: bone mass loss and micro-architectural deterioration of bone tissue [3].

At present there are no ways to measure accurately bone strength in clinical practice and osteoporosis is currently diagnosed by two methods:

1. Occurrence of an unexplained, non-traumatic fracture.

2. Measurement of bone density.

DEXA (Dual Energy X-ray Absorptiometry) considered to be the gold standard for measuring bone density is currently used both for the diagnosis and for

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Received: March 21, 2007,
Accepted for publication: June 12, 2007

the evaluation of treatment effectiveness. Nevertheless, the medical community is aware that based on mineral density measures we are able to consider only the first aspect of this disease, related to bone mineralization, and we forget the importance of the trabecular architecture to determining the fracture risk (figure 1).

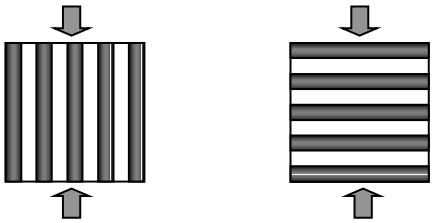

Fig. 1. Structures of the same density may have different load bearing capabilities. The different orientations of the bars with respect to the load applied clearly result in their different resistances

Obviously, the resistance of bone structure depends not only on bone density, but also on the load bearing capabilities of the trabecular spatial arrangement. The procedure proposed focuses on this aspect.

In recent years, research has been carried out in order to relate bone strength to its morphological parameters and elastic properties as obtained from micro-numerical analysis with the finite element method or the cell method [4], [5], [6]. These techniques necessitate an accurate representation of the trabecular bone architecture, achievable only with 3D imaging. The drawbacks of this approach come from the limited diffusion of μCT and μMRI units and from the examination cost, therefore a clinical use of the methods based on the 3D definition of the trabecular structure seems unlikely to be recommended in the near future.

Given the aforementioned limitations, the authors are interested in investigating whether the information contained in a 2D image is sufficient to give a clinical indication of the bone structure load bearing capabilities, even at the cost of a loss in accuracy. The determination of the properties of the bone structure obtained from digital radiographic images has been possible by applying a new numerical method, the cell method [8]. The results of the elastic numerical analysis have been further indexed which allows the load bearing capability to be summarized.

The first results obtained in a first clinical validation carried out at CSMMO, Centro Studi Malattie Metaboliche dell'Osso (the University of Trieste and Azienda Sanitaria n.2 Isontina, Gorizia, Italy), have shown that the above index can give an indication of the pathological modifications of bone structure.

2. Method

Since the experimental work of BREAR et al. [7], who found a linear relationship between the compressive strength of cancellous bone and its Young modulus, it has been suggested that inferences can be drawn from the failure properties of trabecular bone and the elastic modulus measures.

In the present work, the apparent Young modulus of the structure examined was computed by simulating a compression test and by assuming elastic, homogeneous and isotropic properties of the base material. The numerical method used is the cell method, which can be regarded as an alternative to more widely used methods such as FEM. Without going into details, it can be pointed out that a peculiarity of the cell method is that models where heterogeneities are the same size of the cell and the constitutive matrix varies freely from one cell to the neighbour can be solved. Details about the formulation can be found in [9]. This method has already given good results in estimating the elastic properties of porous materials in 2D simulations [10], [11], [12].

The anatomical region selected for the analysis in the present study is the proximal side of the first phalanx of the non-dominant hand. In fact in this site, despite the irregular bone shape, it is possible to discern the trabecular pattern in a plane radiographic image.

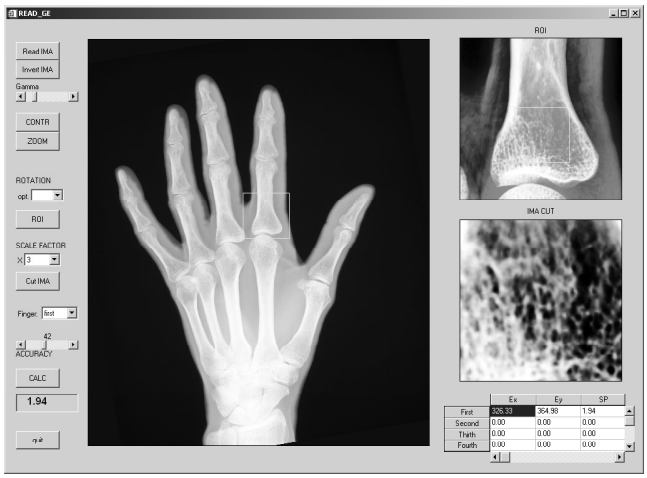

Fig. 2. Operator's interface snapshot: radiographic hand image (left), zoom of the region of interest (upper right) and trabecular zone selected for the structural analysis (bottom right)

Figure 2 is a snapshot of the operator's interface, showing the selection of the region for structural analysis inside the hand examined. The structure used

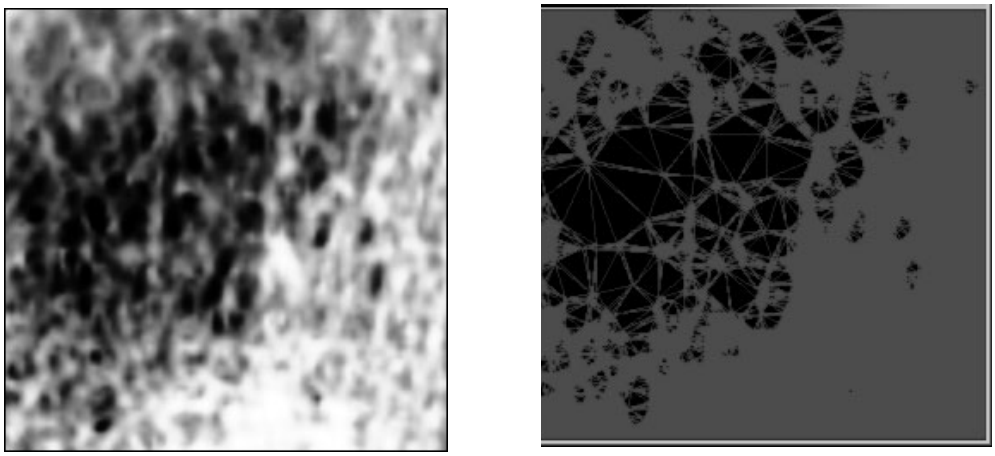

Fig. 3. Radiographic image of the region under analysis (a), automatic mesh generation (triangular cells) (b)

for the numerical analysis is obtained from the digital radiographic image in the following steps:

1. The trabecular pattern examined is enhanced by a sub-threshold erosion non-linear filter. Each pixel of the image in the zone selected has a shade value between 0 and 255.

2. On the resultant image a grid of nodes is deposited. The nodes are automatically connected together to form the mesh, being constituted of a complex of triangular cells, as shown in figure 3.

3. The elastic modulus of each cell is assigned by a scaling procedure based on the grey level in the vertexes, barycentre and middle points of the sides of the cell, and by normalizing the result to 1000 MPa. The cells with an index of 0 do not possess any mechanical characteristics. The Poisson ratio is assumed to be equal to 0.3. An elastic-linear isotropic constitutive law is assumed. By means of steps 1–3, the original image has been transformed into a structure depicted in figure 4.

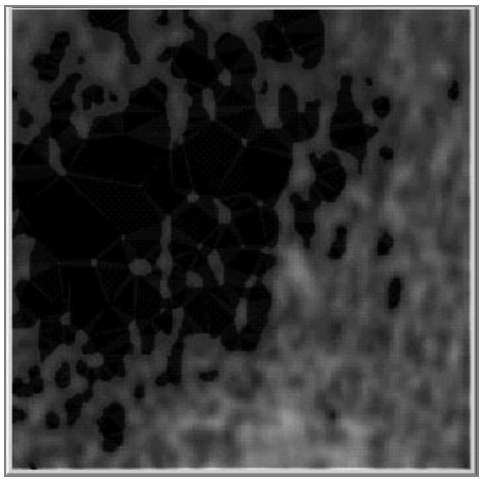

Fig. 4. A final structure

4. The structure obtained is subjected to simulated compression tests along two orthogonal axes, as a results of which the values of Young moduli E_x, E_y are obtained.

5. A content factor *CF*, sum of shade values of all the cells normalized to 100 and indicative of the matter content in the region examined, is used with E_x and E_y to define a structure parameter *SP* (the *SP* formula is omitted because of confidential nature).

The time required for each analysis, comprising both image elaboration and model computation on a common PC, is a few minutes.

3. Clinical trial

A clinical validation of the test is currently being conducted and its results will be the object of further work. Some preliminary findings are presented in this paper. The bone structures of the non-dominant hand of 17 females of age ranging from 32 to 79 have been examined both by DEXA and by the new methodology. As already mentioned, DEXA allows the bone mass to be measured. The result of the test is usually in the form of a T-score, used to estimate the risk of developing a fracture. This is the number of standard deviations from mean BMD in young adults of the same gender. A T-score above –1 is considered normal. A score between –1 and –2.5 is classified as osteopenia, a less severe condition corresponding to the first stage of bone loss. A score below –2.5 is defined as osteoporosis [13].

According to the clinical evaluation performed by Professors Moro and Rizzatto and their staff at CSMMO seven of the subjects suffered from osteopo-

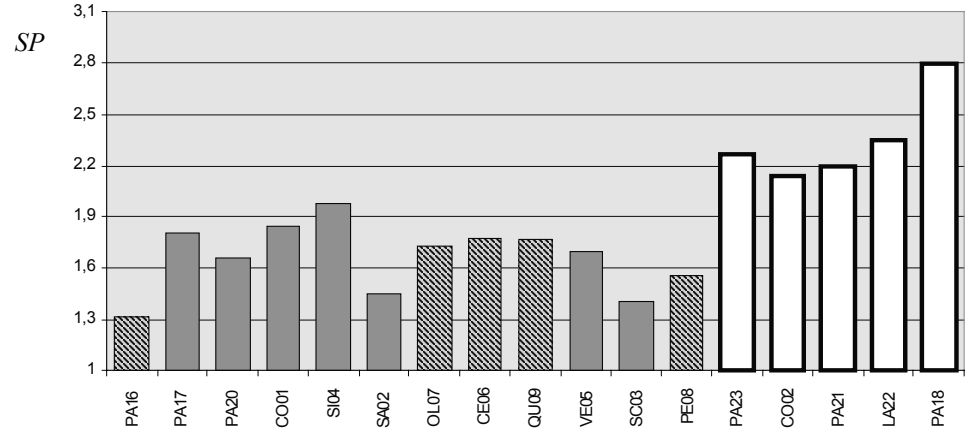

Fig. 5. Structural parameter (*SP*) in osteoporotic patients (grey), patients with osteopenia (striped), and healthy subjects (white); clinical evaluation performed by two specialists on the basis of DEXA

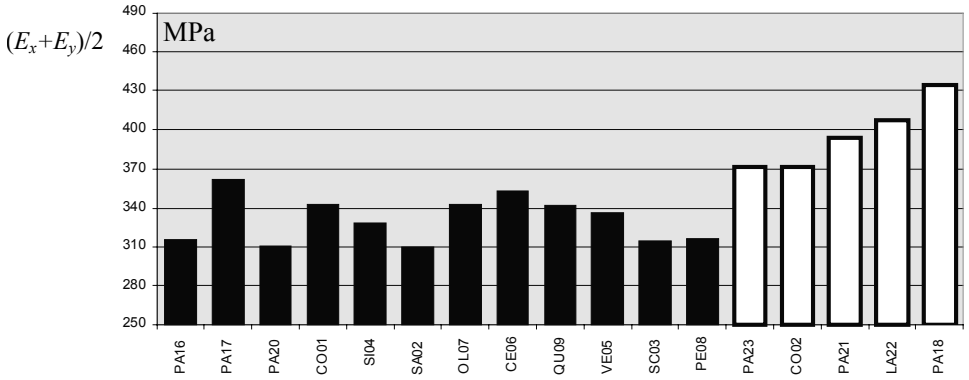

Fig. 6. Average Young modulus in DEXA positive (black) and negative (white) subjects

rosis, five had osteopenia and five were healthy, that is clinically negative.

4. Results and discussion

The results of the analysis carried out are summarized in figure 5, where the *SP* values are given for all the subjects together with the diagnosis based on DEXA T-score, and in figure 6 that shows the contribution of the average Young modulus calculated along the two directions of analysis. It can easily be recognized that the *SP*, and to a lower degree the average value of elastic modulus $(E_x + E_y)/2$, of the clinically positive subjects exhibits the values that are significantly lower than those found in the healthy ones, allowing us to distinguish definitely the two groups. This is due to the differences in the structures examined.

In the hypothesis that the bone portion analyzed is representative of the overall skeletal condition, we can expect that the lower the *SP* value, the higher the fracture risk.

The fracture risk identified by *SP* in clinically positive subjects does not always coincide with the risk identified only on the basis of DEXA. This result is to be expected, because in two analyses different aspects of bone fracture risk are taken into account: in DEXA – the mineral content, in the new methodology – the architectural load bearing capabilities of the trabecular structure.

Particularly interesting is the case of a woman PA16. She has a DEXA hip T-score = –1.72, indicating osteopenia, but she is known to have already suffered from fractures of osteoporotic nature. Her *SP* = 1.32 clearly indicates a high risk of fracture, as confirmed by her anamnesis.

5. Conclusions

A new methodology for fracture risk evaluation has been tested in a clinical trial. The technique, based on the cell method, estimates a parameter related to the elastic properties and the matter content of the

trabecular structure as obtained from planar digital radiographic images. Notwithstanding the information loss due to the use of a 2D acquisition system and the difficulties in clinical evaluation of degenerative pathologies, positive results have been obtained indicating that the method can help the physician in the identification of the actual fracture risk.

Acknowledgements

Area Science Park funded the work presented in this paper. Radiographic acquisitions and clinical evaluations were performed by Professor Moro and Professor Rizzatto and their staff at CSMMO, Centro Studi Malattie Metaboliche dell'Osso (Gorizia, Italy). The authors wish to thank Dr. eng. M. Hoglievina and Dr. eng. L. Loschi for their contribution.

Patent: PCT WO03/082118 2002 deposited by the University of Trieste.

This contribution was partially presented at the 23rd Danubia-Adria Symposium on Experimental Methods in Solid Mechanics, Podbanské, 2006.

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