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# Fractal dimension: A complementary diagnostic indicator of osteoporosis to bone mineral density

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ABSTRACT

Morbidity of osteoporosis is increasing as the world population grows and ages, but bone mineral density (BMD) as a common-used diagnostic indicator is not omnipotent in predicting the bone fragility. According to the definition of osteoporosis by World Health Organization (WHO), the present hypothesis proposes an additional fractal-dimension indicator less than 3 to measure the structural change of bones, and further to diagnose osteoporotic patients with complications, to which BMD is insensitive. Literature reports support that the fractal dimension is more sensitive than BMD in specific cases. The hypothesis shows a promise not only in improving the accuracy of screening osteoporotic patients as a complementary indicator to BMD, but also in evaluating mechanical properties of osteoporotic bone and bone-repair effect of bone tissue engineering.

## Introduction

Osteoporosis is a disease occurring in older people, and its morbidity and mortality increase with the increasing aged population. In accordance with the WHO definition [1], osteoporosis is characterized by two factors: low bone mass and deteriorated micro-architecture (Fig. 1, [2]), which enhance subsequent fracture risk due to bone fragility. The present diagnosis on the osteoporosis mainly relies on the BMD measurement of bone mass, but the measurement on the deteriorated micro-architecture is absent.

### *Diagnostic limitation of the BMD in clinics*

Clinically, BMD value indicating the bone mineralization is often employed to judge the occurrence of osteoporosis (i.e., T scores $< -2.5$) and predict the risk of osteoporotic fracture (ROF). However, BMD was not sensitive to the vertebral compression fracture (VCF) resulting from osteoporosis in type 2 diabetic women [3], and it failed to predict the ROF between the younger and elder postmenopausal women [4]. Since BMD cannot effectively predict the ROF for the specific cases, new measurement is needed for the diagnosis of osteoporosis.

### *Diagnostic necessity of structural change of osteoporotic bone*

The micro-architecture of human bone is porous and interconnecting. Despite of the correlation between the BMD and the micro-architecture, bone densitometry or related medical devices examining the patients' BMD tell a little about the structural change of abnormal bone. Moreover, bone fragility is a result of the failed structural adaptation, not just low bone mass, and the failed structural adaptation results from a broken balance of bone remodeling [5]. It is the broken balance that causes the osteoporosis, which features trabecular thinning and re-patterning (the ratio of rod- and plate-like trabecula, [6]). Thus, in terms of the structural change of abnormal bone, diagnosing osteoporosis from the standpoint of bone structure is necessary.

### *Fractal dimension describing structure of abnormal bone*

Fractal geometry is often used to describe irregular porous media, which are characterized by a non-Euclidean fractal dimension, and the fractal dimension is a non-integer. In the fields of medicine, it has been employed to treat the structure of abnormal bone, such as osteoarthritis [7] and osteoporosis [8]. Then, addressing the diagnostic limitation of the BMD, is the fractal dimension able to measure the structural change of osteoporotic bones and overcome the limitation? If so, clinicians can diagnose the osteoporosis and further predict bone fracture risk by

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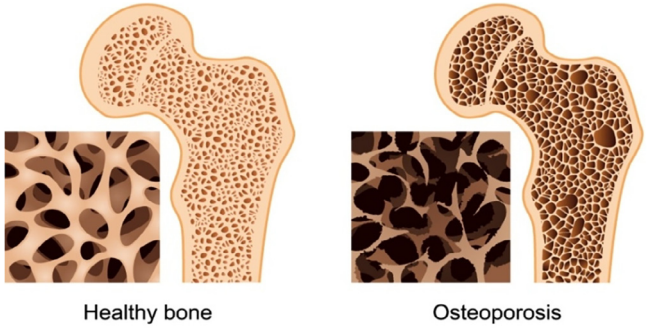


**Fig. 1.** Morphologies of health and osteoporotic bone [2].

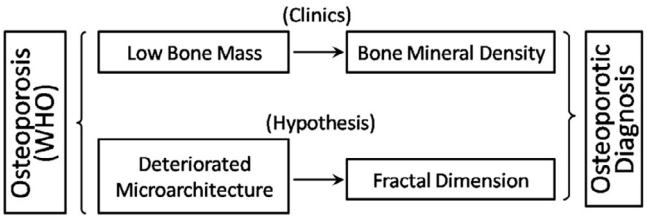


**Fig. 2.** Complementary diagnosis of fractal dimension and BMD.

combining the proposed fractal indicator with the conventional BMD index, see Fig. 2.

## The hypothesis

Considering the complex structure of bones, we hypothesize that the fractal dimension of bone matrix (less than 3) could be a complementary indicator to BMD to diagnose the osteoporosis. This is because the fractal dimension represents the changes of bone microstructure, and the BMD indicates the changes of bone mineralization, thus, with both indicators, screening osteoporosis could be more accurate, see Fig. 2. For osteoporosis, a greater fractal dimension of bone matrix indicates smaller loss of bone (or smaller porosity), while a smaller fractal dimension of bone matrix shows a greater loss of bone (or larger porosity). This can be understood by an extreme case, namely, when porosity in bone tends to 0, the fractal dimension approaches Euclidian dimension of 3.

## Evaluation of the hypothesis

Fractal growth was considered as a design principle in biological organisms [9]. As a fundamental parameter of fractal geometry, fractal dimension is used to characterize the bone structure, and some studies evidenced that the fractal dimension could be used as a novel strategy to quantify the structural change of bone [10–13].

### *Calculation of the fractal dimension of bone*

The fractal dimension is usually determined by a box-counting approach [13], and the classical expression is $N \sim \delta^{-D}$, where $N$ is the number of boxes with characteristic size $\delta$ used to cover porous media, and $D$ is the fractal dimension. Apparently, $D$ is dependent of the characteristic size $\delta$. However, when calculating bone's $D$ on the basis of medical image, we must bear in mind that an appropriate box size should be selected [7], even though low resolution cannot produce a significantly different fractal dimension of an image (or resolution-independent) to an extent [13]. For example, the appropriate size ranges from 65 μm to 1000 μm for trabecular bone in the proximal femur [11], whereas for subchondral trabecular bone in the severe osteoarthritis of the hip, the size is between 30 μm and 4400 μm. Outside the scale, the fractal dimension may be not correctly calculated [14]. This may be because the box-counted trabecular bone is fractal within the range [7,10]; otherwise, it is non-fractal.

With the box-counting method applied on few selected 2D radiographical images, the values of the fractal dimension were calculated between 1.05 and 1.84 [7,13]. Some literature performed sample analysis in 3D space and reported that the fractal dimension was between 2.08 and 2.75 [15–18]. However, the examination of osteoporotic bones is always regional, and fractal analysis on few selected 2D radiographical images cannot fully describe the structural change of the examined region, thus, 3D sample analysis is more suitable. Moreover, the increased porosity is negatively correlated to the fractal dimension of solid phase [19]. In this sense, the fractal dimension of the cancellous bone influenced by severe osteoarthritis is smaller than that of the normal [7], and this supports the hypothesis, namely, a smaller fractal dimension of bone matrix shows a greater loss of bone.

### *Higher sensitivity of the fractal dimension than BMD for postmenopausal women*

Compared to BMD, fractal dimension has been used to assess the osteoporosis [20–23]. For example, it was reported that the fractal dimension was superior to the BMD by studying the 2D X-ray images of control and osteoporotic groups [21,22]. In detail, a group of postmenopausal women with osteoporotic vertebral fractures and an age-matched control group of women were discriminated by evaluating the fractal ability, and the result showed that the discrimination was stronger than the commonly-used BMD [21]. This solves the problem of the similar BMD between the younger and older groups of postmenopausal women [4]. Also, the trabecular bone in knee osteoarthritis was analyzed, and it was found that the fractal dimension quantifying the structural changes of the trabecular bone is more sensitive to BMD [22]. Moreover, the statistical significance of the fractal dimension for the mandibular and alveolar bone of the postmenopausal women was found [12,23]. In particular, the relationship between the fractal-related Hurst parameter $H$ and BMD of the vertebrae, hip and wrist, were explicitly discussed, and their independent and complementary information was presented, which indicated that the fractal indicator along with BMD opens a new way to diagnose the osteoporosis [20]. In addition, the accuracy of the fractal analysis on screening the osteoporotic patients could reach 95% [24], and this is higher than the BMD result reported in [25], which identified the undiagnosed low BMD in 200,160 postmenopausal women over fifties. Anyhow, all the above-mentioned evidences support the superiority of the fractal dimension to BMD to diagnose the osteoporosis for postmenopausal women.

## Consequences of the hypothesis and discussion

With the evidence by evaluating the applicability of the fractal dimension to distinguish the osteoporotic patients, the hypothesis may be significant to clinicians, due to its non-invasiveness and simplification on the complex bone structure. As a complementary indicator to BMD, we must independently conduct correlation analyses of the fractal dimension and the BMD to osteoporosis. Then, the osteoporosis can be discriminated through combining their correlations. However, under the hypothesis, we cannot identify the cases in which the fractal dimension is more sensitive than the BMD, e.g. osteoporotic patients in type 2 diabetic and postmenopausal women [3,4], and other cases in which the fractal dimension is less sensitive. Moreover, the threshold values of the fractal dimension like T scores of the BMD should be determined. The limitations could be overcome by a large number of cases studies.

Not only for the clinical diagnosis of osteoporosis, the hypothesis could also be used in evaluating the effect of scaffold-guided bone repair or regeneration in tissue engineering. This is achieved by the fractal-dimension compatibility between the after-repaired sites and