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# Fractal dimension analysis a supplementary mathematical method for bone defect regeneration measurement☆

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ABSTRACT

*Aim or purpose:* The geometry of a bone defect is very complex. Its shape is too complicated to measure or compare with other bone defects using only traditional measuring methods Traditional measuring techniques based on the histomorphometric analysis of a bone specimen require supplementary measuring. For the fractal dimension analysis (FDA) mathematic formulas are used to describe complicated and chaotic shapes. The FDA offers a possibility of a comparison between complicated and complex shapes such as a histological image of a bone defect.

The aim of this study was to evaluate the FDA of bone defects as a supplementary method for a defect regeneration assessment.

*Materials and methods:* For the purpose of this study, microscopic photographs of bone specimens stained with hematoxylin and eosin obtained during a block biopsy were used. The bone blocks used in this study were obtained during a rat animal model study. Specimens were collected from 36 Wistar rats where a cranial defect was created and augmented with five different novel biomaterials and compared to the unfilled defect in the control group. New bone formation in every specimen was histomorphometrically measured by two independent operators and compared to FDA measurements.

*Results:* Both traditional and FDA techniques have shown statistically significant differences between bone formation in test groups compared to the control one; on the other hand, no statistically significant difference was found between other groups. The Pearson's r-test was conducted to measure the linear dependence (correlation) between standard measurements and the FDA, and a positive linear correlation was found $-r = 0.94$.

*Conclusions:* The FDA can be used as a supplementary method for bone regeneration measurements.



## 1. Introduction

The fractal dimension analysis (FDA) is a very promising mathematical method widely used to describe complicated and chaotic shapes when classic methods fail. A fractal is a shape described by potentially simple mathematic formulas. If these formulas are iterated into infinity, they may create shapes that can be continuously magnified endlessly and every time the infinity of the shape's details can be seen — a self-similarity feature. In classical Euclidean geometry, the dimension is an integer — it is the number of coordinates needed to describe a point inside a shape, for example if a point has no dimension, it is equal to 0. Only one dimension (length) is needed to describe a straight line. The rectangle features length and width, whereas a three-dimensional shape needs to have width, length and height. Classic examples of fractals are: the Cantor set, Koch snowflake, and Sierpinski triangle (Fig. 1).

The fractal dimension (FD) of the Cantor's set equals approximately to 0.631. It means that this shape is something intermediate between a point and line. With Koch snowflake with $FD \approx 1.262$ the shape is closer to a line than to a flat figure; in contrast, the Sierpinski triangle with $FD \approx 1.585$ is nearly a half way in between a line and a flat figure.

Some natural shapes may be treated as fractals, for example: coastlines, trees, clouds, and mountains. In a living organism nerves and blood vessels branches, a structure of brain neurons and a bone

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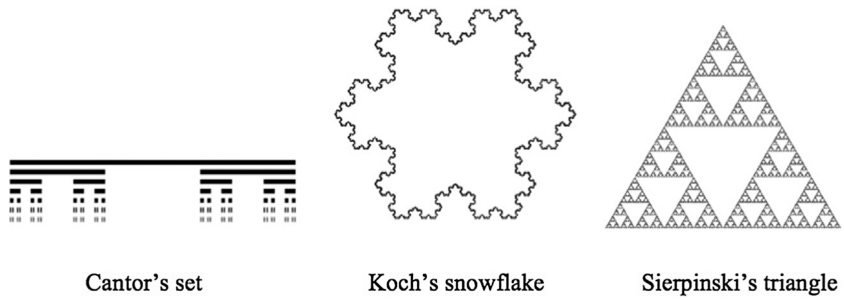


**Fig. 1.** Examples of fractals. The Cantor set on the left is the prototype of a fractal; Koch snowflake in the middle is one of the earliest fractals to have been described; Sierpinski triangle on the right is a fractal and one of the basic examples of self-similar sets.

structure are examples of fractals. These shapes are too complicated to measure or compare between each other using traditional methods based on Euclidean geometry. In such cases the fractal dimension analysis is very useful.

It is important to mention that the fractal dimension analysis offers a possibility of a comparison between complicated shapes. The value of FD describes only a way of point distribution (on a surface or in space), which creates these shapes in opposite traditional ways of physically describing the dimension of a shape.

The fractal dimension analysis is useful in medicine. Examples of using the FDA in medicine are the analysis of mammographic images, estimation of tumor neoangiogenesis or the pattern of coronary vessels (Zyout & Togneri, 2016; Saidov et al., 2016; Yipintsoi et al., 2016). The fractal dimension analysis of jawbone CBCT images is very useful in the diagnosis of osteoporosis (Güngör et al., 2016).

The border between an augmented bone and a bone defect is an irregular line. Fractal dimension analysis of that line may be a useful method to estimate the regeneration state of an augmented bone defect. The aim of this study was to evaluate FD measurements as a supplementary method of bone defect regeneration assessment in implant dentistry.

## 2. Materials and methods

For the fractal analysis purposes, microscopic photographs of the bone specimens stained with hematoxylin and eosin obtained during a block biopsy for other independent author's research were used (with a previously approved research protocol by the ethical committee of the Polish Academy of Sciences and the Animal Welfare Committee) (Hadzik et al., 2016). The data acquisition of the bone specimens was performed using the light microscope BX61 with the integrated camera Color View II (Soft Imaging System, Olympus Optical GmbH, Hamburg, Germany).

The evaluated microscopic photographs of bone specimens were obtained during the Wistar rat study where 36 Wistar rats (2-month old, body weight between 250 g and 350 g and of both sexes) were used for a novel biomaterial examination. Each rat had a midline skin and periosteum incision performed on the skull and a bone defect with a diameter of 5 mm (using a pre-designed template) created in each parietal region of the cranium with a trephine under constant cooling as described in the authors' previous rat study [5]. Five different biomaterials were evaluated during the study (Group 2–5) and compared to the control group (Group 1); xenogenic bone substitute materials and alloplastic materials were evaluated and compared to the unfilled defect (the control group). The bone specimen samples were divided into six separate groups with the same number of samples according to the bone graft materials used, as shown below:

Group 1: No biomaterial, unfilled defect, control — 6 rats.

Group 2: Xenogenic, bovine derived bone substitute — 6 rats.

Group 3: Xenogenic, bovine derived bone substitute + marine delivered collagen — 6 rats.

Group 4: Experimental nano-hydroxyapatite — 6 rats.

Group 5: Experimental nano-hydroxyapatite material, additionally covered by the collagen membrane — 6 rats.

Group 6: Experimental nano-hydroxyapatite material with the combination of β-TCP — 6 rats.

### *2.1. Histomophrometric measurements analysis*

For the purpose of this study, all samples were evaluated to assess the degree of bone regeneration. New bone formation and the line between an old and a new bone was marked. The diameter and depth of the bone defect was measured, while the total area of the bone defect and the total area of the newly created bone were calculated. The degree of regeneration was given in percentages as mean ± standard deviation. The evaluation of bone formation was carried out by two independent observers and performed on pictures showing the complete cavity with a magnification of 100×. The percentage of bone tissue regeneration was determined. The data for the field measurement analysis was given as means ± standard deviation.

### *2.2. Image preparation for fractal analysis*

Microscopic photographs of stained bone specimens (6044 × 2990 resolution) were evaluated. All graphical operations were performed using GIMP version 2.8.0. The white balance point was set on each photo in empty space of slides to normalize contrast of all images. In the center of the bone defect, a square with 500 μm side length was selected. A border between a natural bone and an augmented bone was passing through opposite corners of the square. Such a prepared fragment of the image was cut off from the original photo. Then this fragment was converted into gray scale and after that converted into a bitmap (with a threshold of 50%). The file was saved into TIFF format without any compression algorithms. All graphical operations are shown in Fig. 2. The prepared files were the basis for calculating the FD.

### *2.3. Fractal dimension analysis*

For the fractal dimension analysis Fractalyse ver. 2.4 (Fractalyse by Gilles Vuidel) software was used. The Fractalyse software makes it possible to measure the fractal dimension using a box-counting method. The fractal dimension ($D_s$) was calculated with the formula presented in Fig. 2 (Grizzi et al., 2005). That formula shows a theoretical base of the counting box method. It is the limit of the quotient decimal logarithm of the minimal number of boxes needed to cover the examined shape in function of the length of the box side to the inverse of the box side length when the box length is going to zero. For geometrical interpretation there are marking points in