FRACTAL DIMENSION IN MORPHOLOGY AND MEDICINE: THEORETICAL BASES AND PRACTICAL APPLICATION (REVIEW)

Maryenko N., Stepanenko O.

Kharkiv National Medical University, Ukraine

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Abstract
Morphometry is an integral part of most modern morphological studies and the classic morphological morphometric methods and techniques are often borrowed for research in other fields of medicine. The majority of morphometric techniques are derived from Euclidean geometry. In the past decades, the principles, parameters and methods of fractal geometry are increasingly used in morphological studies. The basic parameter of fractal geometry is fractal dimension. Fractal dimension allows you to quantify the degree of filling of space with a certain geometric object and to characterize the complexity of its spatial configuration. There are many anatomical structures with complex irregular shapes that cannot be unambiguously and comprehensively characterized by methods and techniques of traditional geometry and traditional morphometry: irregular linear structures, irregular surfaces of various structures and pathological foci, structures with complex branched, tree-like, reticulated, cellular or porous structure, etc. Fractal dimension is a useful and informative morphometric parameter that can complement existing quantitative parameters to quantify objective characteristics of various anatomical structures and pathological foci. Fractal analysis can qualitatively complement existing morphometric methods and techniques and allow a comprehensive assessment of the spatial configuration complexity degree of irregular anatomical structures. The review describes the basic principles of Euclidean and fractal geometry and their application in morphology and medicine, importance and application of sizes and their derivatives, topological, metric and fractal dimensions, regular and irregular figures in morphology, and practical application of fractal dimension and fractal analysis in the morphological studies and clinical practice.
Keywords: *morphometry, size, dimension, fractal dimension, fractal analysis, lacunarity.*

Morphometry (from the Greek μορφή – form, shape and μέτρον – measure, size) is the basis of numerous modern morphological methods and is an integral part of most modern morphological studies. Despite the fact that traditional morphology is based on classical fundamental descriptive studies of the structure of various organs and structures, modern morphology is gradually moving from qualitative-descriptive to quantitative-morphometric studies, and morphometry and statistics have become its evidence base. In most modern studies, the quantitative parameters of the studied structures are determined. There are many methods and algorithms of morphometry, which are used in classical morphology, but also are often borrowed for research in other fields of medicine and clinical practice. The diagnosis of diseases of various organs and systems often involves morphometry: determining the size of cells, organs, structures, etc. The choice of methods and algorithms of morphometry primarily depends on the features of the spatial configuration of the studied structures and the aim of the study [1-3]. The majority of morphometric techniques are derived from Euclidean geometry and allow the quantification of anatomical structures by determining simple geometric parameters: linear measurements, area and volume. Thus, morphometry usually involves measuring of the size of anatomical structures or pathological foci. In addition, the derivatives of the certain sizes are calculated: relative or specific sizes, ratios, indices, etc. [1-3]. These quantitative characteristics provide a lot of useful information and in most cases allow to achieve the aim of the study. Such morphometry tech niquesare the

Corresponding Author:
Nataliia Maryenko, MD, PhD, Senior lecturer of Department of Histology, Cytology and Embryology, Kharkiv National Medical University, Ukraine. E-mail: maryenko.n@gmail.com

most informative in the studies of regular structures with a geometrically simple shape (for example, spherical or prismatic), determining the size of which is simple and unambiguous. However, irregularity is much more common among anatomical structures. Irregular anatomical structures are difficult to assess using traditional morphometric techniques, and simple quantitative characteristics (sizes and their derivatives) do not allow to comprehensively characterize the spatial configuration of these structures.

Thus, traditional quantitative characteristics are not enough to give a comprehensive morphological characteristics of irregular anatomical structures, as it is necessary to assess the qualitative characteristics – shape and spatial configuration. Can these qualitative characteristics be quantified? The answer to this question depends on features of studied object. Different indices and indicators are quite useful and informative in the studies of objects with a simple shape. For example, the cranial index (the ratio of width to length of the skull) allows us to determine the craniotype – an indicator that describes the shape of the neurocranium [4] and is quite informative (if we know that a skull is brachy, meso- or dolichocranial, we clearly and unambiguously understand the features of skull shape).

However, it is quite difficult to describe the shape of irregular anatomical structures using derivative indices calculated on the basis of size values. For example, the shape factor (SF) may have the same values for structures whose spatial configuration differs significantly (Fig. 1).

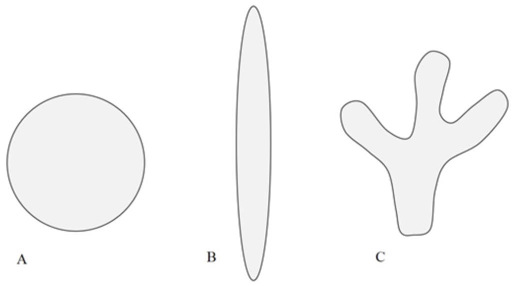

Figure 1. Figures of different shapes. The values of the shape factor (SF): A – circle, SF = 1; B – oval, SF = 0.25; C is an irregular branched structure, SF ≈ 0.25.

Therefore, in some cases it is not enough to determine *the sizes and their derivatives* for morphometry alone. In these cases, another characteristic of geometric shapes and space – *space dimension or dimensionality* – comes in handy.

Spatial dimension (D) is a parameter that characterizes the spatial configuration of a geometric figure (object, structure) and the degree of filling of space with this figure. There are topological and metric dimensions [5, 6]. Most often, when we mention the spatial dimension, we mean the topological dimension, which belongs to the traditional (Euclidean) geometry [6].

The topological dimension (Euclidean dimension, Lebesgue dimension) of various geometric objects has only integer values – 1, 2 or 3. The topological dimension is equal to the minimum number of parameters (coordinates) required to unambiguously characterize the point of the object in space. For example, in order to characterize a point of a straight line, it is enough to specify one coordinate, a point of a plane – two coordinates, a point of a cube – three coordinates. In Euclidean geometry, the topological dimension usually coincides with the minimum number of linear parameters (n) that are needed to characterize an n-dimensional object (for example, length, width, and height for three-dimensional objects). Thus, the topological dimension of lines that can be characterized by only one linear dimension – length (one-dimensional linear objects), is equal to 1; the dimension of surfaces (planes), which in addition to the two linear dimensions (length and width) also have their derivative value – area (two-dimensional flat objects or planes), is equal to 2; and the dimension of three-dimensional objects, which in addition to the three linear dimensions (length, width and height) and area also have a volume, is equal to 3 [5-11].

The terms "one-dimensional" (1D), "two-dimensional" (2D) and "three-dimensional" (3D) come from the topological dimension. Two-dimensional or three-dimensional images can be used for morphometry [1-3], and when we say that the image is two- or three-dimensional, it means the topology of the images: two-dimensional or three-dimensional (Fig. 2, Fig. 3). Any anatomical structure can be represented in a two-dimensional or three-dimensional topology (the topological dimension of the space in which a certain structure is represented is 2 or 3, respectively) [12].

There is also a *metric dimension*. The values of metric and topologic dimensions may be the same or different. The metric dimension of ideal geometric figures coincides with the topological dimension. The metric dimension (D) of an ideal line is equal to one, D of the ideal plane (surface) is equal to 2, D of the filled cube is 3. Such structures fill all available space in the corresponding coordinate system: one-dimensional, two-dimensional or three-dimensional [5-12].

However, among anatomical structures and pathological foci, such figures are extremely rare. Most anatomical structures and different foci are irregular, and their metric and topological dimensions differ [6]. For example, some anatomical structures and their parts are linear objects – the outer linear contours of various structures and foci, vessels, nerves, fibers, etc. But these structures are almost never ideal lines with a metric dimension of 1. Much more often, linear structures are represented by curves that can be wavy, coiled, zigzag, etc. These objects are not ideal straight lines, so they have a metric dimension greater than one. At the same time, they are not planes, so they have a dimension less than 2. Thus, they fill more space than a straight line, but less than a plane (Fig. 2). Taking into account this feature, we can conclude that the value of the metric dimension of irregular lines can be in the range from 1 to 2 [8, 10].

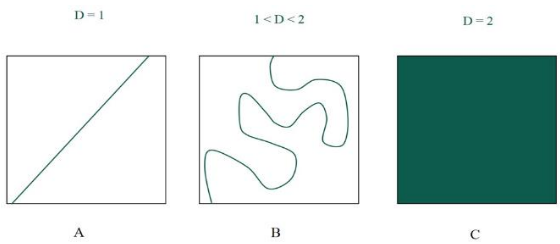

Figure 2. Geometric figures with different degrees of space filling, two-dimensional topology of images. A is an ideal line that practically does not fill the space, B is an irregular curve, C is an ideal plane that fills all available two-dimensional space.

Ideal planes (perfectly flat surfaces), the metric dimension of which is 2, are also usually non-existent in organisms of humans and animals. Much more often the surfaces are not smooth (they are wavy, rough, etc.) and fill more space than the ideal plane, but less than the filled cube (Fig. 3). By analogy with irregular curves, we can conclude that the value of the metric dimension of irregular surfaces will be in the range from 2 to 3 [8].

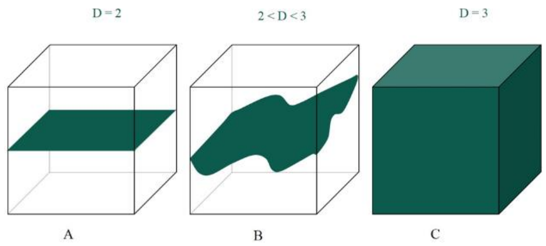

Figure 3. Geometric figures with different degrees of space filling, three-dimensional topology of images. A is an ideal plane (regular surface), B is an irregular surface, C is an ideal filled cube that fills all available three-dimensional space.

Thus, the metric spatial dimension can be not only an integer but also a fractional number. This dimension is called fractal or fractional (from the Latin fractus – fractional) [5-15]. Fractal dimension allows you to quantify the degree of filling of space with a certain geometric object and to characterize the complexity of its spatial configuration. Among natural objects, including anatomical structures, in addition to irregular curves and surfaces, there are also many objects with complex shapes that cannot be unambiguously and comprehensively characterized by methods and techniques of traditional geometry and traditional morphometry [6]. These are structures with complex branched, tree-like, reticulated, cellular or porous structure, etc. [3, 16, 17].

Fractal analysis is used to determine the fractal dimension of geometrically irregular objects, including anatomical structures and pathological foci [16, 17].

In the study of linear structures, the fractal dimension characterizes the degree of spatial complexity of their shape (how twisted, tortuous or wavy these linear structures are), so it is an informative indicator for quantitative assessment of spatial complexity degree of various fibers and other linear structures.

In addition to irregular linear structures, fractal analysis and fractal dimension are relevant for the quantitative characterization of irregular surfaces. These include surfaces formed by various membranes, the surfaces of the brain cortex and white matter, the outer and inner surfaces of various organs and pathological foci (tumors, foci of necrosis, fibrosis, gliosis, etc.). In this case, such surfaces can be represented both in three-dimensional topology (on three-dimensional reconstructions) and in two-dimensional topology (on two-dimensional images) as an anatomical, histological, or tomographic sections, projections, etc. Irregular surfaces in two-dimensional images often look like linear objects, such as linear contours of structures and foci and cross-sections of various membranes. Therefore, it is informative to estimate the spatial configuration of linear contours of three-dimensional structures on two-dimensional images. Determining the complexity (tortuosity and irregularity) of the contour of tumors can provide information about the degree of tumor invasion into the surrounding tissues. Thus, fractal analysis was used for quantitative research and interpretation of mammography results [18]. Determining the complexity of the spatial configuration of the cerebral cortex (entire surface on 3D images and its linear contour on 2D images) can quantify the degree of atrophic changes in the brain [19]. In ophthalmology, fractal analysis was used to analyze the configuration of the Bowman's membrane of cornea [20].

Among irregular anatomical structures, tree-like branched structures are quite common [21] (vascular network of internal organs, bronchial tree, duct system of exocrine glands, dendritic trees of neurons, cerebellar white matter). Fragments of such structures may have a network-like, or reticulated configuration (for example, the vascular network is essentially a tree-like structure, but its fragment may have a reticulated structure). In addition, some structures may have a reticulate structure without tree-like branching (for example, a network of fibers in fibrous connective or reticular tissue, myeloarchitectonics of the brain white matter, etc.). The fractal dimension makes it possible to quantify the degree of branching of the branched structures and the density of the network of the reticulated structures.

Fractal analysis in morphology and medicine was often used in the studies of the vascular network [22, 23]. The fractal dimension of the vascular network allows to characterize the degree of branching of blood vessels and the degree of filling of the space with blood vessels within the studied organ. This method was used in the studies of the retinal vessels [24], the kidneys arterial tree [25], vessels of lungs [26], heart [27] and pituitary gland [28]. The vascular network of the brain also has fractal properties [29]. A quantitative assessment of the superficial vascular network of the cerebellum was performed using fractal analysis of anatomical preparations [30]. Fractal analysis of brain vessels is used in neuroimaging with diagnostic purpose, for example, for analysis of the shape complexity degree of arteriovenous malformations [31].

Fractal analysis was used in the studies of the bronchial tree, and the pattern of bronchial branching and lung morphogenesis was considered fractal [32].

Fractal analysis was also used to characterize the arborization (branching) of the dendritic trees of neurons. Various types of neurons were studied by fractal analysis, including Purkinje cells [33], pyramidal cells [34], spinal cord neurons [35], and retinal nerve cells [36]. Fractal analysis was used to classify retinal nerve cells according to the degree of branching of their dendritic tree and functional characteristics [6, 36].

Fractal analysis was used in the studies of glia cells. This method was used to analyze astroglia and revealed morphological changes in astrocytes in stroke and dementia [37], revealed significant differences in the fractal dimension of different types of astrocytes – protoplasmic and fibrous [38]. Fractal analysis revealed changes in microglia in inflammation of nerve tissue, and fractal dimension values were used to develop a classification of glia by the degree of its activation [39].

Fractal analysis was informative in the studies of the human cerebellum white matter ("arbor vitae cerebelli"), which has a complex branched tree-like configuration. The cerebellar white matter was studied by fractal analysis in our previous work [40, 41] and the works of other scientists [42-44].

Fractal analysis is also informative and appropriate method for the study of *cellular*, *porous or spongy objects* and allows you to quantify their porosity and density by assessing the degree of filling of the space by the studied structures. For example, fractal analysis was used to study the density of the spongy bones (most often – the spongy bone tissue of the skull, mainly in dentistry and for the diagnosis of osteoporosis) [45], dental images [46].

Porous structures also include the tissue of the respiratory portion of lungs (lung alveoli), so the fractal dimension can be an informative parameter for the quantitative assessment of the lung tissue density.

In some cases, fractal analysis includes two quantitative parameters: in addition to the fractal dimension, the *lacunarity index* may be determined. The classical fractal analysis determines the degree of filling of space with a certain structure and determines fractal dimension (areas of space which are occupied by the studied structure are taken into account). But lacunarity index characterizes the degree of *filling of space with empty areas* (*lacunae*, or areas of space which *are not* occupied by the studied structure are taken into account). In other words, fractal analysis is performed and the fractal dimension is calculated, but for the lacunae – space around and inside studied structure. The lacunarity index usually is determined during fractal analysis (two parameters are determined at the same time – fractal dimension and lacunarity index) and makes it possible to characterize the "hollowness" of the studied structure [47, 48]. Thus, the lacunarity index was used in the studies of cellular, porous or spongy structures or structures, an important characteristic of which is the density: bone tissue [49], tooth tissue [50] and tumors [51, 52].

Different *methods, techniques and algorithms of fractal analysis* are used in morphology. The box counting method or grid method is most often used. Less commonly used methods are caliper method, dilatation method, mass-radius method, cumulative intersection method, grid intercept method and some other methods [6, 13-17]. A detailed description of the methods of fractal analysis is given in the review of the methodology of fractal analysis in morphology [53] and in other reviews related to the use of fractal analysis in various fields of medicine [6, 16, 17, 36].

Thus, techniques and parameters derived from fractal geometry can be used in morphometric studies of various anatomical structures of human and animal organisms alongside with traditional techniques and indicators derived from Euclidean geometry. Fractal dimension is a useful and informative morphometric parameter that can complement existing quantitative parameters to quantify objective characteristics of various anatomical structures and pathological foci. Fractal analysis can qualitatively complement existing morphometric methods and techniques and allow a comprehensive assessment of the spatial configuration complexity degree of irregular anatomical structures.

Declarations

Statement of Ethics

The author has no ethical conflicts to disclosure.

Consent for publication

The author gives her consent to publication

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Data Transparency

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Disclosure Statement

The author has no potential conflicts of interest to disclosure.

References

1. Avtandilov, G.G. (1990). Medicinskaja morfometrija [Medical morphometry]. Moscow: Medicina. [In Russian]

2. Hudoerkov, R.M. (2014). Metody komp'juternoj morfometrii v nejromorfologii: uchebnoe posobie (bazovyj kurs) [Methods of computer morphometry in neuromorphology: a textbook (basic course)]. Moscow: FGBU «NCN» RAMN. [In Russian]

3. Nikonenko, A.G. (2013). Vvedenie v kolichestvennuju gistologiju [Introduction to Quantitative Histology]. Kiev: Kniga-Pljus. [In Russian]

4. Speranskij, V.S., & Zajchenko, A.I. (1980). Forma i konstrukcija cherepa [Skull shape and construction]. Moscow: Medicina. [In Russian]

5. Blei, R. (2003). Analysis in integer and fractional dimensions. New York: Cambridge university press.

6. Jelinek, H. & Fernandez, E. (1998). Neurons and fractals: How reliable and useful are calculations of offractal dimensions?. Journal of Neuroscience Methods. 81. 9-18. 10.1016/S0165-0270(98)00021-1.

7. Aleksandrov, P.S., & Pasynkov, B.A. (1973). Vvedenie v teoriju razmernosti [Introduction to Dimension Theory]. Moscow: Nauka. [In Russian]

8. Feder, J. (1988). Fractals. New York: Plenum Press.
9. Kronover, P.M. (2000). Fraktaly i haos v dinamicheskih sistemah. Osnovy teorii [Fractals and chaos in dynamical systems. Foundations of the theory]. Moscow: Postmarket. [In Russian]
10. Harte, D. (2001). Multifractals. London: Chapman & Hall.
11. Falconer, K. (1990). Fractal geometry: mathematical foundations and applications. Chichester: John Wiley.
12. Fomenko, A.T. (1993). Nagljadnaja geometrija i topologija [Descriptive geometry and topology]. — Moscow: MGU. [In Russian]
13. Mandelbrot, B.B. (1975). Les Objets fractals: forme, hasard et dimension. Paris: Flammarion. 214 p.
14. Mandelbrot, B.B. (1977). Fractals – form, chance and dimension. San Francisco: W. H. Freeman. 365 p.
15. Mandelbrot, B.B. (1982). The fractal geometry of nature. San Francisco: W.H. Freeman and Company. 470 p.
16. Di Ieva, A., Grizzi, F., Jelinek, H., Pellionisz, A. J., & Losa, G. A. (2014). Fractals in the Neurosciences, Part I: General Principles and Basic Neurosciences. The Neuroscientist : a review journal bringing neurobiology, neurology and psychiatry, 20(4), 403–417. https://doi.org/10.1177/1073858413513927
17. Di Ieva, A., Esteban, F. J., Grizzi, F., Klonowski, W., & Martín-Landrove, M. (2015). Fractals in the neurosciences, Part II: clinical applications and future perspectives. The Neuroscientist : a review journal bringing neurobiology, neurology and psychiatry, 21(1), 30–43. https://doi.org/10.1177/1073858413513928
18. Rangayyan, R. M., & Nguyen, T. M. (2007). Fractal analysis of contours of breast masses in mammograms. Journal of digital imaging, 20(3), 223–237. https://doi.org/10.1007/s10278-006-0860-9
19. King, R. D., George, A. T., Jeon, T., Hynan, L. S., Youn, T. S., Kennedy, D. N., Dickerson, B., & the Alzheimer's Disease Neuroimaging Initiative (2009). Characterization of Atrophic Changes in the Cerebral Cortex Using Fractal Dimensional Analysis. Brain imaging and behavior, 3(2), 154–166. https://doi.org/10.1007/s11682-008-9057-9
20. Ţălu, Ş., Stach, S., Sueiras, V., & Ziebarth, N. M. (2015). Fractal analysis of AFM images of the surface of Bowman's membrane of the human cornea. Annals of biomedical engineering, 43(4), 906–916. https://doi.org/10.1007/s10439-014-1140-3
21. Kamiya, A., & Takahashi, T. (2007). Quantitative assessments of morphological and functional properties of biological trees based on their fractal nature. Journal of applied physiology (Bethesda, Md. : 1985), 102(6), 2315–2323. https://doi.org/10.1152/japplphysiol.00856.2006
22. Zamir M. (1999). On fractal properties of arterial trees. Journal of theoretical biology, 197(4), 517–526. https://doi.org/10.1006/jtbi.1998.0892
23. Lorthois, S., & Cassot, F. (2010). Fractal analysis of vascular networks: insights from morphogenesis. Journal of theoretical biology, 262(4), 614–633. https://doi.org/10.1016/j.jtbi.2009.10.037
24. Tălu S. (2011). Fractal analysis of normal retinal vascular network. Oftalmologia (Bucharest, Romania : 1990), 55(4), 11–16.
25. Cross, S. S., Start, R. D., Silcocks, P. B., Bull, A. D., Cotton, D. W., & Underwood, J. C. (1993). Quantitation of the renal arterial tree by fractal analysis. The Journal of pathology, 170(4), 479–484. https://doi.org/10.1002/path.1711700412
26. Helmberger, M., Pienn, M., Urschler, M., Kullnig, P., Stollberger, R., Kovacs, G., Olschewski, A., Olschewski, H., & Bálint, Z. (2014). Quantification of tortuosity and fractal dimension of the lung vessels in pulmonary hypertension patients. PloS one, 9(1), e87515. https://doi.org/10.1371/journal.pone.0087515
27. van Beek J. H. (1997). Is local metabolism the basis of the fractal vascular structure in the heart?. International journal of microcirculation, clinical and experimental, 17(6), 337–345. https://doi.org/10.1159/000179250
28. Di Ieva, A., Grizzi, F., Gaetani, P., Goglia, U., Tschabitscher, M., Mortini, P., & Rodriguez y Baena, R. (2008). Euclidean and fractal geometry of microvascular networks in normal and neoplastic pituitary tissue. Neurosurgical review, 31(3), 271–281. https://doi.org/10.1007/s10143-008-0127-7

29. Helthuis, J., van Doormaal, T., Hillen, B., Bleys, R., Harteveld, A. A., Hendrikse, J., van der Toorn, A., Brozici, M., Zwanenburg, J., & van der Zwan, A. (2019). Branching Pattern of the Cerebral Arterial Tree. Anatomical record (Hoboken, N.J. : 2007), 302(8), 1434–1446. https://doi.org/10.1002/ar.23994

30. Stepanenko, A.Yu., & Maryenko, N.I. (2015). Fraktal'nyj analiz kak metod morfometricheskogo issledovanija poverhnostnoj sosudistoj seti mozzhechka cheloveka [Fractal analysis as a method of morphometric study of the superficial vascular network of human cerebellum]. Medytsyna syohodni i zavtra, 4(69), 50–55. [In Russian]

31. Di Ieva, A., Niamah, M., Menezes, R. J., Tsao, M., Krings, T., Cho, Y. B., Schwartz, M. L., & Cusimano, M. D. (2014). Computational fractal-based analysis of brain arteriovenous malformation angioarchitecture. Neurosurgery, 75(1), 72–79. https://doi.org/10.1227/NEU.0000000000000353

32. Glenny, R. W., Krueger, M., Bauer, C., & Beichel, R. R. (2020). The fractal geometry of bronchial trees differs by strain in mice. Journal of applied physiology (Bethesda, Md.: 1985), 128(2), 362–367. https://doi.org/10.1152/japplphysiol.00838.2019

33. Takeda, T., Ishikawa, A., Ohtomo, K., Kobayashi, Y., & Matsuoka, T. (1992). Fractal dimension of dendritic tree of cerebellar Purkinje cell during onto- and phylogenetic development. Neuroscience research, 13(1), 19–31. https://doi.org/10.1016/0168-0102(92)90031-7

34. Puškaš, N., Zaletel, I., Stefanović, B. D., & Ristanović, D. (2015). Fractal dimension of apical dendritic arborization differs in the superficial and the deep pyramidal neurons of the rat cerebral neocortex. Neuroscience letters, 589, 88–91. https://doi.org/10.1016/j.neulet.2015.01.044

35. Milosević, N. T., & Ristanović, D. (2006). Fractality of dendritic arborization of spinal cord neurons. Neuroscience letters, 396(3), 172–176. https://doi.org/10.1016/j.neulet.2005.11.031

36. Fernández, E., & Jelinek, H. F. (2001). Use of fractal theory in neuroscience: methods, advantages, and potential problems. Methods (San Diego, Calif.), 24(4), 309–321. https://doi.org/10.1006/meth.2001.1201

37. Pirici, D., Mogoantă, L., Mărgăritescu, O., Pirici, I., Tudorică, V., & Coconu, M. (2009). Fractal analysis of astrocytes in stroke and dementia. Romanian journal of morphology and embryology = Revue roumaine de morphologie et embryologie, 50(3), 381–390.

38. Reichenbach, A., Siegel, A., Senitz, D., & Smith, T. G., Jr (1992). A comparative fractal analysis of various mammalian astroglial cell types. NeuroImage, 1(1), 69–77. https://doi.org/10.1016/1053-8119(92)90008-b

39. Karperien, A. L., & Jelinek, H. F. (2015). Fractal, multifractal, and lacunarity analysis of microglia in tissue engineering. Frontiers in bioengineering and biotechnology, 3, 51. https://doi.org/10.3389/fbioe.2015.00051

40. Stepanenko, A.Y., & Maryenko, N.I. (2017) Fraktal'nyj analiz belogo veshhestva mozzhechka cheloveka [Fractal analysis of the human cerebellum white matter]. World of Medicine and Biology, 3(61), 145–149. [In Russian]

41. Maryenko, N.I., & Stepanenko, O.Y. (2017) Fraktal'nyj analiz biloi' rechovyny pivkul' mozochka ljudyny [Fractal analysis of white matter of the human cerebellum hemispheres]. Ukr. ž. med. bìol. Sportu, 2 (4), 38-43. [In Ukrainian]

42. Akar, E., Kara, S., Akdemir, H., & Kırış, A. (2015). Fractal dimension analysis of cerebellum in Chiari Malformation type I. Computers in biology and medicine, 64, 179–186. https://doi.org/10.1016/j.compbiomed.2015.06.024

43. Liu, J. Z., Zhang, L. D., & Yue, G. H. (2003). Fractal dimension in human cerebellum measured by magnetic resonance imaging. Biophysical journal, 85(6), 4041–4046. https://doi.org/10.1016/S0006-3495(03)74817-6

44. Wu, Y. T., Shyu, K. K., Jao, C. W., Wang, Z. Y., Soong, B. W., Wu, H. M., & Wang, P. S. (2010). Fractal dimension analysis for quantifying cerebellar morphological change of multiple system atrophy of the cerebellar type (MSA-C). NeuroImage, 49(1), 539–551. https://doi.org/10.1016/j.neuroimage.2009.07.042

45. Gulec, M., Tassoker, M., Ozcan, S., & Orhan, K. (2021). Evaluation of the mandibular trabecular bone in patients with bruxism using fractal analysis. Oral radiology, 37(1), 36–45. https://doi.org/10.1007/s11282-020-00422-5

46. Kato, C. N., Barra, S. G., Tavares, N. P., Amaral, T. M., Brasileiro, C. B., Mesquita, R. A., & Abreu, L. G. (2020). Use of fractal analysis in dental images: a systematic review. Dento maxillo facial radiology, 49(2), 20180457. https://doi.org/10.1259/dmfr.20180457

47. Smith, T. G., Jr, Lange, G. D., & Marks, W. B. (1996). Fractal methods and results in cellular morphology--dimensions, lacunarity and multifractals. Journal of neuroscience methods, 69(2), 123–136. https://doi.org/10.1016/S0165-0270(96)00080-5

48. Ling, E. J., Servio, P., & Kietzig, A. M. (2016). Fractal and Lacunarity Analyses: Quantitative Characterization of Hierarchical Surface Topographies. Microscopy and microanalysis : the official journal of Microscopy Society of America, Microbeam Analysis Society, Microscopical Society of Canada, 22(1), 168–177. https://doi.org/10.1017/S1431927615015561

49. Dougherty, G., & Henebry, G. M. (2001). Fractal signature and lacunarity in the measurement of the texture of trabecular bone in clinical CT images. Medical engineering & physics, 23(6), 369–380. https://doi.org/10.1016/s1350-4533(01)00057-1

50. Yasar, F., & Akgünlü, F. (2005). Fractal dimension and lacunarity analysis of dental radiographs. Dento maxillo facial radiology, 34(5), 261–267. https://doi.org/10.1259/dmfr/85149245

51. Park, Y. W., Kim, S., Ahn, S. S., Han, K., Kang, S. G., Chang, J. H., Kim, S. H., Lee, S. K., & Park, S. H. (2020). Magnetic resonance imaging-based 3-dimensional fractal dimension and lacunarity analyses may predict the meningioma grade. European radiology, 30(8), 4615–4622. https://doi.org/10.1007/s00330-020-06788-8

52. Smitha, K. A., Gupta, A. K., & Jayasree, R. S. (2015). Fractal analysis: fractal dimension and lacunarity from MR images for differentiating the grades of glioma. Physics in medicine and biology, 60(17), 6937–6947. https://doi.org/10.1088/0031-9155/60/17/6937

53. Maryenko, N.I., & Stepanenko, O.Yu. (2021). Fraktal'nyj analiz zobrazhen' u medycyni ta morfologii': bazovi pryncypy ta osnovni metodyky [Fractal analysis of images in medicine and morphology: basic principles and methodologies]. Morphologia, 15(3), 196-206. https://doi.org/10.26641/1997-9665.2021.3.196-206 [In Ukrainian]

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