Original article

Pattern self-repetition allied to complexity and adaptation of different anatomic structures of human body

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Abstract

The first appliances about Chaos Theory in the biological sciences, made by Robert May, turned visible the growth and appliance of this sciences in morphology or even in fisiology, when is stipulated the behavior of very sensitive systems to different conditions, showing complex behavior. Behind this parameters, it was stipulated a morphological study in microscopic and macroscopic scales for pathologic appliances and obtaining new parameters in the anatomy and histology field. We observed that the skin shows the greatest self-repetition pattern, being the largest organ in the human body. The circulatory system has its great blood diffusion in function of a complex branched web of vases in a non-linear shape. It was observed a great fractal patterns in the structure of the heart, and it's frequency must be chaotic in function of the need of the human body and specific activities to avoid muscular hyperplasia. Bones and articulations denote dynamic interaction, what permit temporal adaptations such as the formation of the cranial bone sutures. The encephalic anatomy, specially the sulcus, got a self-repetition pattern. The following step was to stipulate these concepts in dynamical process such as the cell differentiation.

Keywords: fractals, morphology, estructural complexity, chaos theory.

1 Introduction

The western study, in all fields, follows a line of thinking obsessively orderly, mainly due to the influence of Greek mathematic and physic. In the mid sixties of last century, researchers have introduced non-linear science concepts, breaking some concrete classical physic. These studies were inducers of numerous theories, especially in areas with little mathematical prediction, like weather and economy. With the recognition of these theories, especially with studies of dynamical systems and fractal, studies in biology were also carried out effectively. The fractal distribution of intestinal villi, the dynamic organization of the immune system, the projection of the dendrites of multipolar neurons, are some examples of non-linear geometry in human body.

Dynamical systems are based on mathematical theories whose concepts and techniques are applied to a wide range of events. These events are non-linear, being a counterpoint to the world of linear equations governing the simple systems. In human biology, anatomical study, both macroscopic and microscopic, has been evaluated in order to consider it as a simple system with space limitations and complexity apparently known. In this context, studies show, for example, the formation of the continuum of blood vessels, the nature of this branch, which covers an enormous area in a limited space, causes the greatest distance from one cell to a blood vessel of 4 cells. This extensive network of vessels is only about 5% of the total space of the human body. Applying the dynamic study, this branch would be a representative of a Koch curve, characterized by a line of infinite extent in a small area (GLEICK, 1990).

The evaluation of human anatomy, as both the macroscopic to microscopic according to a complex vision provided by chaos theory and fractal geometry were the main goals of this work, aiming not only to provide a new way to explain processes and human physiological adaptations, but bring a comparative for future pathological situations such as a carcinoma, annoikis and inflammation.

2 Methodology

2.1 Macroscopy and microscopy

Macroscopic analysis was performed in the lab of Anatomy, addressing characteristics conducive to articles previously selected for review.

The microscopic analysis of the tissue was performed at the Multidisciplinary Laboratory, Department of Biological and Health Sciences, Universidade Estadual de Ponta Grossa, and the fractality and complexity assessments were performed using the Octave software, available free at <<http://www.gnu.org/software/octave/>>.

2.2 Cell culture

2.2.1 Fibroblasts 3T3 murine parenchyma lung

The strain of murine 3T3 fibroblast cell line is originated from a primary culture of fetal mice, immortalized with viral vectors, established by the NIH (National Institutes of Health) commercially distributed by ATCC (American Type Culture Collection) and transferred to our laboratory studies

by the Experimental Oncology, Faculdade de Medicina, USP. These cells shows elongated with irregular cytoplasmic processes, with clear and oval nuclei with evident vacuoles. It is a lineage that has doubling time less than 24 hours, cultured in DMEM (Dulbecco modified Eagle medium) supplemented with 10% fetal calf serum (FCS). This strain is widely used in various experiments in the laboratory mentioned above.

2.2.2 Analysis of cell morphology

The visualization of the fibers of the cytoskeleton were assessed by incubating cells with phalloidin, which is a fluorescent molecule that binds to F-actin filaments, not binding to G-actin monomer (ZAHM, BACONNAIS, MONIER et al., 2003). The visualization of the nucleus was made with the dye DAPI, which binds to DNA.

Was plaqued 6×10^4 cells (3T3) in 24-well plate containing coverslips with 500 mL of RPMI 1640 supplemented with 10% Fetal Bovine Serum (FBS). After 48 hours, the RPMI was taken and the treatment began in pre-determined time. The cells were fixed with 1% paraformaldehyde in PBS pH 7.4 for 15 minutes. Washed three times with PBS/BSA 2%. Phalloidine was added (1:400, v/v) for 30 minutes at room temperature in a moist chamber. Washed with PBS/BSA 0.2% for 3 times. DAPI was added (1:1000, v/v) for 5 minutes in a dark room, to mark the nucleus. Washed with PBS/BSA 0.2%, 3 times. The lamine was made with glycerol and common enamel.

2.3 Cell biology

The microscopic anatomy and more recently the molecular anatomy shows increasing the knowledge of man in need of new tools for identifying the proximity of the real. In this non-linear vision we note that each cell has a high degree of complexity that makes it special in its morph functional. Figure 1 show the complex fractality of actin fibers that comprise the cellular cytoskeleton, this complexity is critical for migration and proper functioning of any cell. (HAVLIN, BULDYREV and SIMONS, 1995; ZAHM, BACONNAIS, MONIER et al., 2003). Figure 2 shows that one of the earliest events that occurs in a programmed cell death, apoptosis, is the simplification of the cytoskeleton. This figure is an example of melanoma cells, the control group treated with an agent and inducer of cell death.

2.4 Fractal dimension

The presence of fractal dimension is one of two characteristics necessary for an object or an image to be considered a fractal. In the literature are found several methods for estimating this dimension according to the nature of your sample and precision of results you wish to obtain (OTT, 1993). One of the easier methods to generate results with high accuracy is the Box-counting method (BACKES and BRUNO, 2005). The technique consists of using a grid, determined experimentally by the investigator through the dimensions in the image. It is then computed a count of how many parts of the grid were occupied. Applying the neperian logarithm of the number of squares filled of side (l), and (l) tends to 0 (zero), divided on the neperian logarithm of the inverse of the side (l) of their squares, being the equation of Hausdorff described:

$$df = \lim_{l \to 0} \frac{\ln N(l)}{\ln(1/l)} \quad (1)$$

The computer analysis was performed using the Octave software, freeware available in the electronic network that requires the presence of an interface of Linux® operating system. Models were then created to determine the complexity and extention of the British coast and the results showed that the larger the scale approximation made for the endorsement of the perimeter of the coast, the greater the extent length, and concluded that frequent assessments would result in smaller scales to a result which would tend to infinity, because microscopic variations would be taken into account. The same is proposed in the histological section of epithelial tissue, where it has an edge with self-repeating patterns and fractal dimension, emphasizing the complexity present in the dynamics of peeling of the epidermis (Figure 3).

3 Results

3.1 Chaotic patterns of the cardiovascular system

The cardiovascular system is presented as a complex pathway for fluid communication and exchange of substances through cells, tissues, organs and systems. Pathways to control of this system, as electrophysiologic factors, hemodynamic factors and control via the sympathetic and parasympathetic, lead to a nonlinear dynamics in the phenomena involved with the heart and consequent different behavior of other

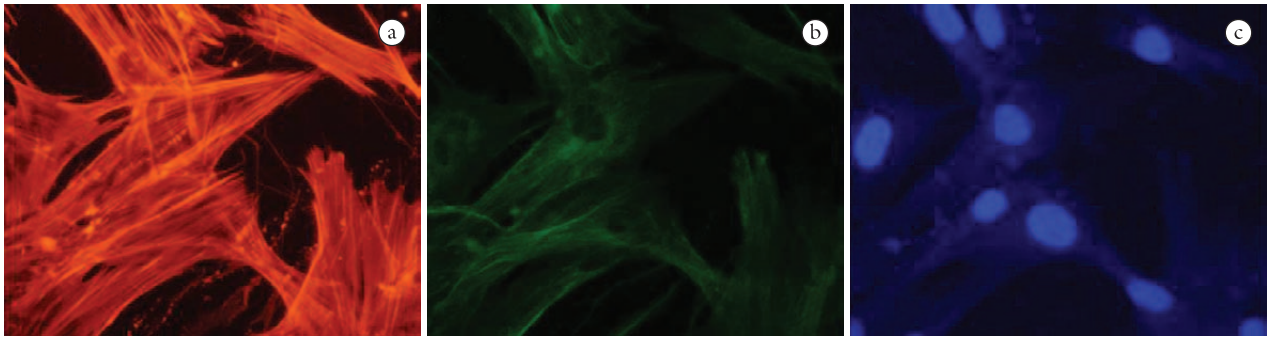

Figure 1. Visualization of actin fibers (a), tubulin (b) and core (c) 3T3 fibroblasts. Note the fractal distribution of the fibers that comprise the cytoskeleton, it is clear the independence of scale, self-similarity, infinite extent and depth of these fibers.

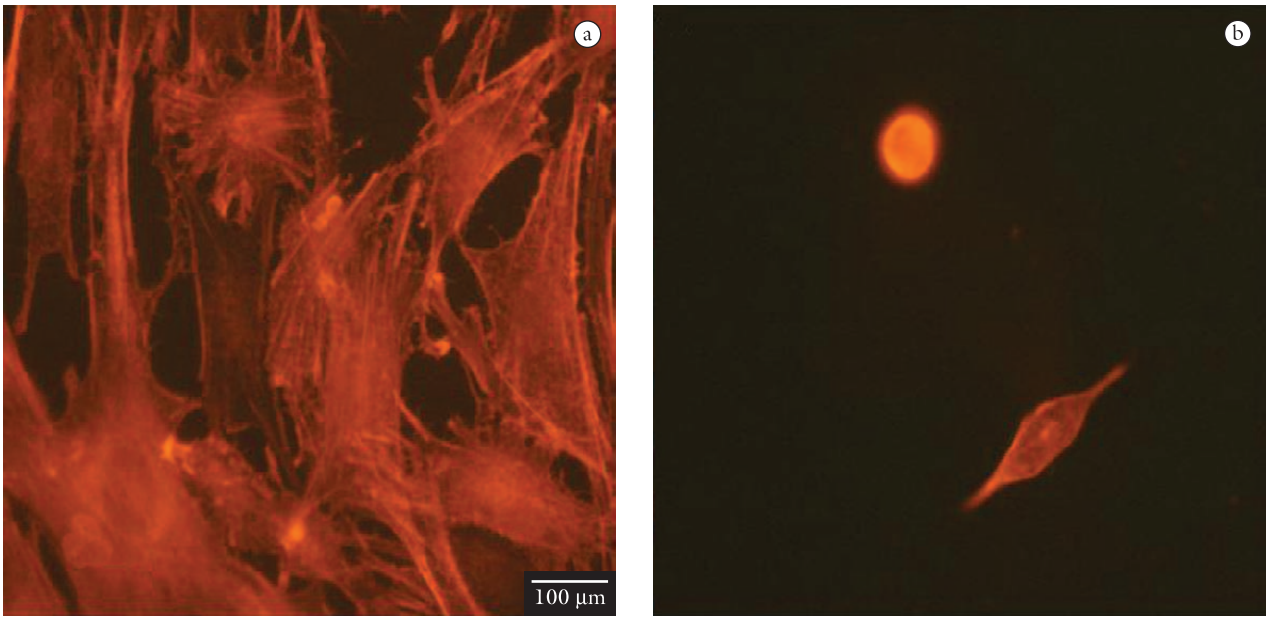

Figure 2. Observation of morphological changes associated with loss of complexity of the cytoskeleton, this event is one of the early to apoptotic cell death, or loss of complexity leads to simplicity, which leads to an incompatibility with life.

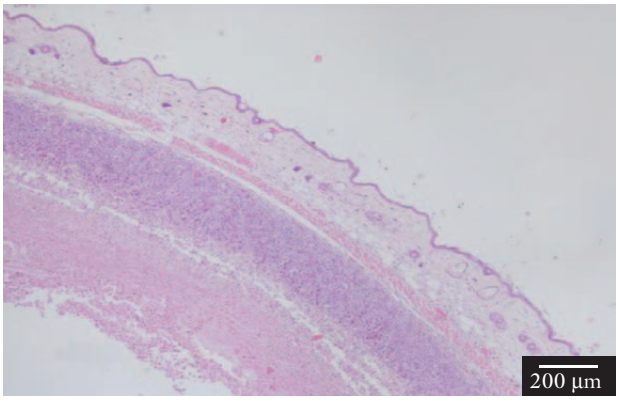

Figure 3. Presence of fractal dimension and self-similarity at the edge near the epithelial tissue, demonstrating complexity in the processes of scaling (fractal dimension: 1.107).

systems. The applications of quantitative methods for the analysis of variations in heart rate and electrical analysis of cardiac activity became exhaustive and with few results, since a long series of experiments should be collected and then adjusted the linear systems that have inconclusive results. However, the use of tools of nonlinear dynamics has brought results which yielded an effective step forward for the area cardiopatology in assessing patients with recent myocardial infarction and Chagas disease (SOARES, CESAR JUNIOR, LEANDRO et al., 2003; OLIVEIRA, GOMES, GUIMARÃES et al., 2006). A non-linear methods that yielded effective results was the use of Lyapunov exponent, given by:

$$\lambda = \lim_{n\to\infty} \frac{1}{n} \sum_{i=0}^{n-1} \log_e \left| f'(x_i) \right| \qquad (2)$$

Where is evaluated the system sensitivity to initial conditions or not by the divergence points of attractor after a sufficiently necessary integrations over time for the method. If the Lyapunov exponent assume a negative value near the orbits converge and the evolution of the system is not chaotic. If the Lyapunov exponent taking a value 0 (zero), the flow of the system tends to a stationary non-dissipative behavior and when the value of the Lyapunov exponent is positive, nearby points move away, the nearby trajectories diverge and the evolution of the system is chaotic (GUMIERE, FURLAN, SCHWARTZ et al., 2002; OLIVEIRA, GOMES, GUIMARÃES et al., 2006). Synthesis studies for signs of heart rate variability demonstrated the presence of positive Lyapunov exponent of the variation in heart rate for a certain time (24 hours). This fact indicates non-linearity in the behavior of the frequency of heart beats, which assume the chaos as physiological to the system system.

Cardiomyopathy in patients with Chagas disease has as one of its acquired characteristics linearization of heart rate, then leaving a chaotic condition for a constant frequency. Interestingly, the main phenomenon Anatomopathologycal observed in these carriers of the parasite is myocardial hypertrophy, demonstrating the intrinsic complexity of the system to normal operating condition. Also caused damage to the ganglia of the parasympathetic nervous system leading to a partial reduction or total reduction in the release of hemodynamic factors or regulation by paths of control of the autonomic nervous system, which also leads to a loss of complexity of cardiac activity, as to the behavior of variation in heart rate. The internal anatomy of the heart consists of highly complex architectural structures that are the trabeculae carnea, structures that form the inner walls of the ventricles (Figure 4).

Being part of the cardiovascular system, blood vessels play a major role in transporting blood and nutrients to all cells of the body, being a vehicle for the maintenance of homeostasis and processes in the body's defense. However, the passage of nutrients is not directly to the cell, it must occur through diffuse processes to the main branch vessel so that it can reach the other cells, a minimum distance must

exist for the communication be made. Another important factor for efficient communication is the blood flow velocity in the smaller branches, such as meta-arteries and capillaries. For these factors be kept constantly, requires an intelligent and complex organization of this network of vessels with significant changes for each system, organ and tissue. This organization follows with statistical self-similarity in scales, and the Hausdorff dimension, more commonly known as fractal dimension. This dimension allows us to experience a huge change in cross-sectional area in regions where there are processes of filtration and absorption. With the increase of sectional area, the velocity of blood flow decreases, is also another important factor for the efficiency of the process. The fractal architecture of the blood vessels also appears as a characteristic physiological, pathological finding arises when a variation in this dimension. The loss of fractal dimension and consequent linearization of the vessels present in patients with diabetic retinopathy are clear demonstrations that architectural changes of the vessels leading to subsequent failures in the nutrition of a range of cells and subsequent death of them (SOARES, CESAR JUNIOR, LEANDRO et al., 2003; OLIVEIRA, GOMES, GUIMARÃES et al., 2006). In the development of malignancies, angiogenic factors form a dense amount of vessels that have a fractal dimension higher than that normally present in the area affected. It is considerer thus the tumor as an entity more dynamic, complex and adaptive to its own "host", due to varying complexity of a network of vessels to another.

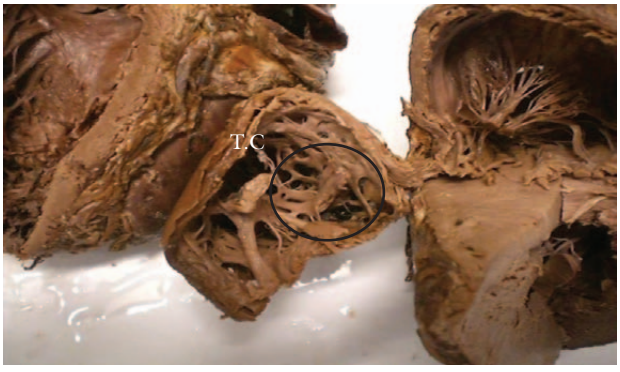

Figure 4. Analysis of fractal dimension (Df = 2.73541) and self-similarity across scales in trabecula carnea (CT).

3.2 Fractality and complexity of bones and articulations

The architecture in areas of bone joints or unions shows a remarkable interest for the evaluation of dynamic multifunctional process due to these highly complex structures. These structures include the presence of a cancellous bone (trabecular bone) present in a region surrounded by a cortical layer. The spongy structure corresponds to a cubic lattice complex denoted high fractal dimension and that by the process of bone demineralization through the passage of time, fractures are generated compromising the ability of strength and support (WALDROP, 1992). The stipulation of chaotic architecture of joints in this study comes from the complexity of stereotypes created by body movements and adaptive capacity that such structures have before stimulus as exercise associated with gymnastics (BURLANDO, 1993). One case alleged that relates the variation or complexity as the fractal dimension and temporal evolution, are the structure of joints in the skull of the newborn. In these locations, the sutures appear as large areas of fibrous tissue, forming the fonticulus.

The mesh formed by fibrous connective tissue and the conection with the bone following fractal architecture, makes the skull of children more complex than of adults and proportionately more resistant to impact. Thus, the skull bones of an elderly already present a great loss of fractal dimension of the joints, especially sutures (Figure 5). This reduction of complexity makes bones less resistant to shocks, because fractal structures behave to dissipate energy through scales applied to the system (MANDELBROT, 1977). In this way, clarifies the relationship of the complexity present in bone architecture and their interactions on the performance on nutrient uptake and impact resistance (LIEBOVITCH, 1998; WALDROP, 1992).

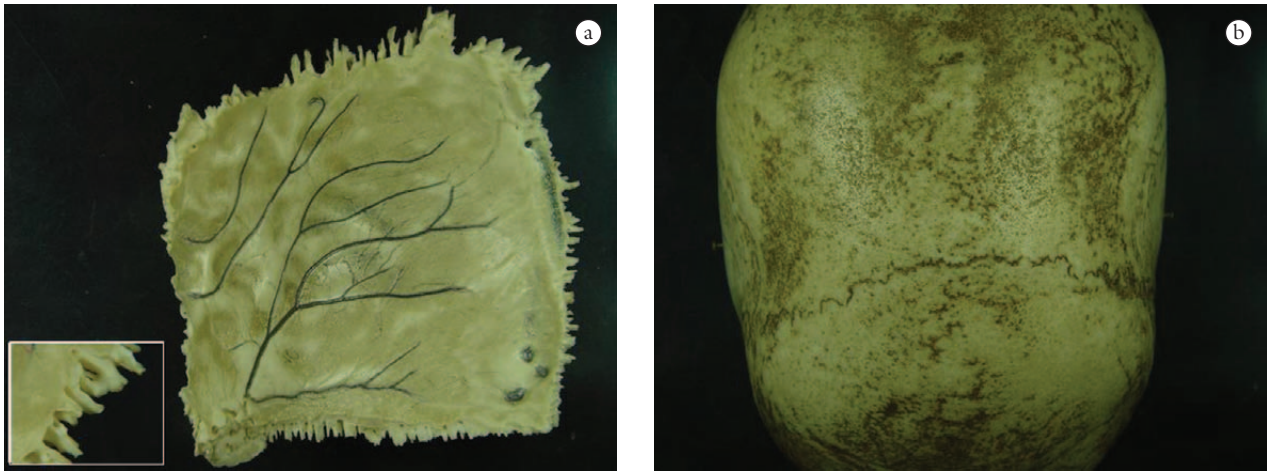

Figure 5. a) Pattern of self-similarity and fractal dimension (2.159 - sagittal edge) in the parietal bone and venous grooves along the bone itself. Left box shows approaching the edge of the sagittal parietal bone to demonstrate the pattern of self-similarity along the projections. b) Elderly skull with the absence of the sagittal suture, making it less complex and more fragile to trauma.

3.3 Self-repeating pattern of lung histology

Among one of the most important substances transported by blood through the systemic circulation is the presence of two gases, mainly. First, O_2 is the final acceptor of electrons from the final process of breathing achieved in the mitochondrial membrane. As a product of the respiratory process, the CO_2 must be transported of the all cells to the external environment, being the carbon dioxide a factor leading to metabolic acidosis and also has neurotoxic effects. This dynamic process of gas exchange through a fluid is a role performed by the lungs, through its complex fractal architecture (Figure 6). It is known that the passage of these gases via filtration or absorption (carbon dioxide, oxygen) occurs by passive diffusion through a concentration gradient and that among the factors that influence the diffusion process is the distance from one system to another. One factor, even more important is the need that every cell of our body to produce ATP, which for the completion of the process requires the presence of the final acceptor (oxygen). For this supply of gas, the lung has a fractal structure of infinite complexity, giving a branch which estimated a similar area about fifty times the area of our skin. Studies also confirm the complex kinetic and chaotic mixture formed in the airways, especially at smaller scales, in the level of the bronchioles alveoli, where the fluid was related to a set of attractors, directing each to regions of different sizes (TSUDA, 2002; ZAMIR, 2001).

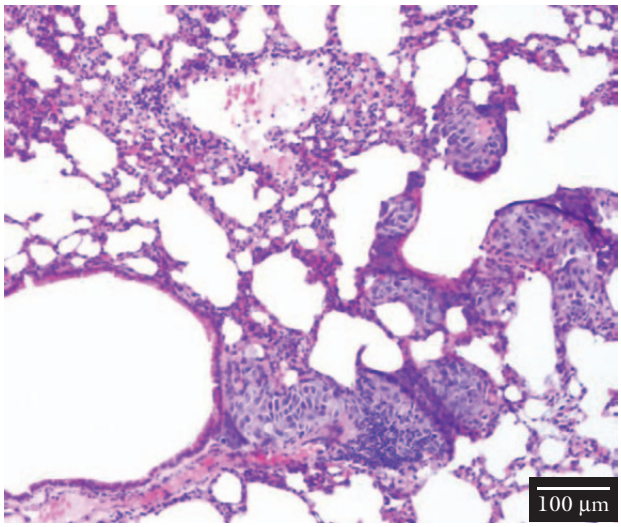

Figure 6. Fractal Alveolar architecture (fractal dimension: 2.126). BT - terminal bronchioles.

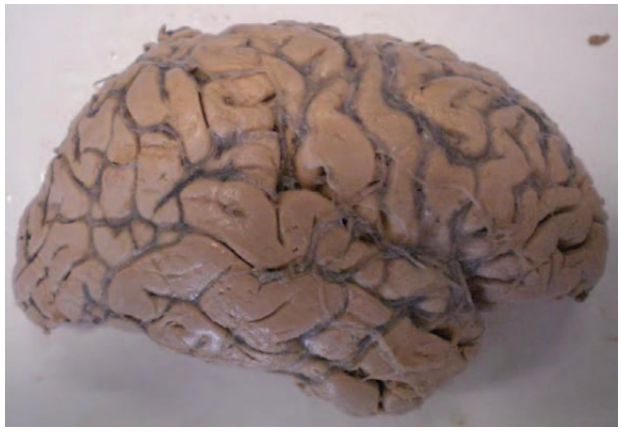

Figure 7. Adult human brain, showing the presence of fractal dimension (furrow cortex: 1.3822) and high-similarity.

3.4 Brief analysis of complex nonlinear nervous system

Statistical studies have shown that knowledge in the nervous system has doubled every period of approximately nine months, in which advances in techniques for determining molecular mechanisms of electrophysiological, physiological and physiopathological. The increase in research and discoveries appeared to reflect the emerging state of transition and post-epidemiological transition, where it is found that in the future will be the predominance chronic degenerative diseases, including a large portion of diseases affecting the nervous system. Many of the tools used by researchers are those that discuss an overview of nonlinear dynamics in the nervous system. Already in the basic principles, the nervous system presents as a complex anatomical structure with fractal dimension in the cortical region, where many centers are integrated for a response via afferent or efferent that occur as the reflex of chronic pain. The existence of large compressed areas became necessary, being the fractal dimension present in the grooves formed in evolutionary processes (Figure 7). At the cellular level, dendritic endings of neurons are structured through a fractal architecture, which enables electrical synapses occur with high speed and the electric charge is forwarded to a large contact area. Involved also in electro physiology, the myelin sheath acts as a booster for the transmission of electrical signal by the axon through a linearization of the momentum, while this trend to be dissipative. The genesis of myelin sheath occurs through processes of stretching and folding, (featuring a complex fractal structure). Small changes in the formation of this sheath lead to subsequent failure or delay in communication synaptic chemical communication, leading to subsequent frames of generalized deficits at the level of intellectual activities and metabolic processes. This demonstrates the very low coefficient of sensitivity that the system has and is easily altered by minimal variations in the first conditions.

The presence of pumps sodium/potassium/ATPase indicates that the actual phenomena of potential graduate and action potential in a cell are extremely complex and hypersensitivity, needing to be regulated through a dynamic point of view, for oscillators harmonics, for the maintenance of physiological events. Other chaotic event that occurs in the human body is the sensitivity that the system has of a wide range of chemicals for activation and modulation of sympathetic and parasympathetic nervous system, characterized by strange attractors in afferent and efferent. Was demonstrated that by controlling and understanding chaotic events, was possible to build an associative memory through the instigation of strange attractors consisting of the neural network and further development of the memory system, where the very system maintains its orbit without another stimulus after the first signal, information was stored (FRANOVIC´ and MILJKOVIC´, 2007; WAGNER and STUCKI, 2002).

3.5 Practice anatomopathological applications

The nonlinear studies can help in a complementary way to diagnose the situations already encountered. The magnitude of processes such as inflammatory process and necrotic tumor may be described in a fractal way, approaching the intensity of the pattern of complexity vs. simplicity (Figure 8). It is quite true that the conditions that present a more complex way are representative of most deadly diseases, considering, for example, the presence of edge and visual separation of benign tumors in contrast to the disorganization observed in malignant neoplasms.

4 Discussion

Evolutionary processes in the study of science were in great frequency, associated with a break and change of paradigm and, consequently, a possible change in a viewpoint for the same object of study. A large part of the school introduced a Western philosophical thinking of linearity, where nature would behave in an orderly and stable way. Even lines of nonlinear reasoning such as Heraclitus of Ephesus, saying: "No one bathes in the same river twice." Have been distorted and disowned before other philosophers, by breaking the concept of perfection and order in nature behavior. On the other hand, Eastern philosophy, has accepted more clearly the uncertainty, unpredictability and freedom for the phenomena that occur in nature, how to fold parts of Taoism. Even in modern times, the view of nature was seen with total linearity and order, as in Einstein's assertions that God does not play dice and that the concepts of probability were just a human incapacity due to the presence of hidden variables. However, with advances in the study of quantum, it was seen the fragility and sensitivity that existed in 'nano-world', where the probability and uncertainty prevailed.

Already in the sixties of last century, Edward Lorenz, a researcher in meteorology from MIT, discovered what today is known and called as chaos theory. Victim of a 'rounding', Lorenz observed the exponential growth in your chart of oscillation of the wind, when the initial condition of a variable was changed in micrometric scale. From this result, other concepts have been inserted as a strange attractor, where the flow lines of an invariant set of orbits depended significantly on the initial conditions, which may evolve through a process of stretching and bending. The behavior of systems such as the strange attractor shown how the system was sensitive to initial conditions, terminology called the butterfly effect.

This work aimed to take a different view of anatomy, histology and physiology of the human body based on chaos theory and its concepts from, which is not so explored in the biological sciences. Many behaviors and structures of the human body behave unknown or not so well understood and, in our view, chaos theory could explain a wide range of events and justify the presence and morphology of certain structures in accordance with the need to survival of the human showing complexity, dynamism and adaptive capacity that is necessary to maintain a homeostatic condition by demonstrating that linearity is almost always associated with some condition that induced disease in humans.

Recently, with the wide dissemination of the Olympic Games, we were faced with a linear studies where researchers at the Institute of Biomedical Research and Sports Epidemiology (IRMES) in Paris, led by Professor Toussaint, who had stipulated the limit of the human body for each Olympic event and the dates when it will be impossible to break records. This study was performed using the statistical analysis of the 3623 sporting records, recorded between the first Olympics of the modern era in 1896, and 2008. The linear statistical confidence was such that the French group has stipulated the maximum possible performance in each sport. For example, the best time possible proof of 100 m, according to the calculations, would be 9.67 seconds, also have set a date for the human physical stagnation, which would be in 2068. After the Olympics, the group became a little in disbelief as we had a huge amount of records broken, some, like the 100, the duty would be broken only in the next decade.

This study did not take into account the evaluation of the human body in a critical, complex, adaptive and more importantly non-linear view. While there is a more significant knowledge of the human body based on these new concepts, such as those presented in this work, we are far short of the prediction suggested by groups like the teacher Toussaint.

A good representation was written by James Gleick, "The more naive among scientists is the one that thinks that the perfect model explains perfectly the reality." (GLEICK, 1990).

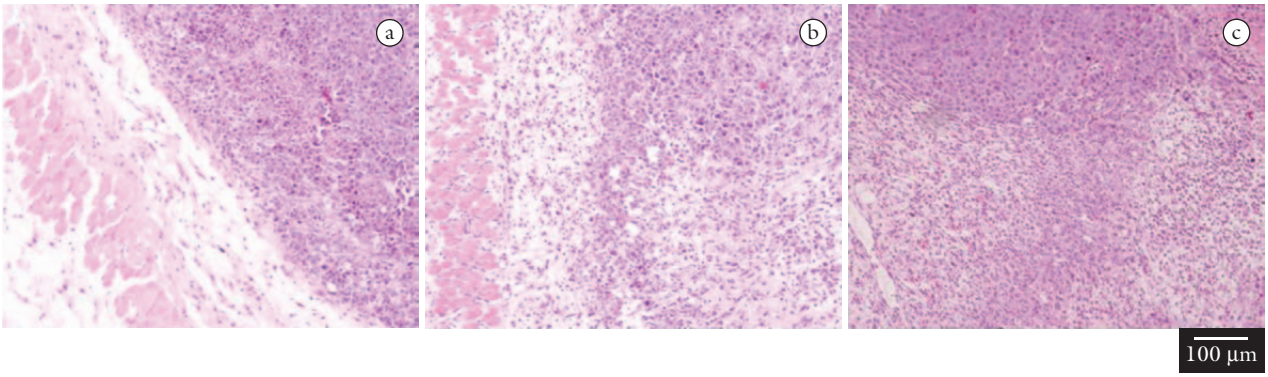

Figure 8. Examples of different stages of inflammation associated with induced dorsal melanoma in mice. a) The tumor appears more limited to a region (fractal dimension: 0.911), stromal reaction presenting with low inflammation. b) Tumor with greater complexity (fractal dimension: 1.2433), presenting as a more aggravated and moderate inflammatory reaction. c) Evolution of the complexity of tumor associated with intense inflammation (fractal dimension: 1.97888).

5 Conclusions

We can conclude that the evaluations showed fractal dimension, occurring variations in dimensions according to the complexity of each structure.

We conclude that the skin had the highest repetition pattern of our body, being the largest organ we have and a small fraction may be representative of a whole. The circulatory system presents its range of blood spread due to the presence of a complex network of branching rather linear way, which allows a remote area of vessels for the chemical changes, osmotic fluid and plasma and the functionality of the inflammatory processes occur. Otherwise, a simplified network would have impossibilities as the diffusion of nutrients to cells located in less accessible tissues. The heart showed various fractal structures and its frequency must necessarily be chaotic so that does not occur hyperplasia and blood flow is regular according to specific human activity. Bones and joints sinartroses (real estate) have dynamic interaction of high complexity that allows adaptive processes in accordance with the evolution, as the formation of the sutures of the cranial bones and the constant ion exchange between phosphate and calcium. The brain anatomy, specifically the grooves, shows a pattern of self-similarity, comprising an extensive area of cerebral cortex in this portion, known especially for being one of many terminals via synaptic processes such as the route of pain. The non-linear evaluation of inflammatory processes may be ancillary to more advanced studies of determined diseases such as cancers where the tumor tissue was more complex as their distribution than the normal tissue.

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Received April 25, 2010
Accepted February 19, 2011