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Fractal Analysis of MRI Data for the Improved Characterization of Brain Tumors

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Abstract

Human brain is the most dynamic and varied system of the body. The brain is composed of neuron and glia. But how do they interact to generate emergent properties like memory, learning, emotion and sleep is little understood. Many such complex systems that exist in non-linear dynamics are characterised by the fractal nature. The fractal dimension (FD) of the human brain quantifies the inherent complexity. Evidences strongly suggest that fractal properties of a biologic system might be related to entropy and metabolism. In several pathologies of the brain such as Alzheimer's, Epilepsy and Stroke, fractal dimension (FD) is altered. FD in combination with other features is emerging as a powerful diagnostic approach at the hands of a clinician. In this study we are focused to understand the changes in fractal properties (FD) of human brain as a whole in glioma. Cancer being a hyper-metabolic disease, should impact the FD of the brain. Tumor increases the Intracranial pressure (ICP) in the brain and destroys the regular shape and equilibrium condition of the human brain. In this paper we made an analysis of fractal dimension of the tumored and non tumored MR brain images. The experimental results shows that the fractal dimension of the tumored images has a significant change as compared to the fractal dimension of the non tumored images.

Keywords: Brain Tumor, Fractal Dimension, Tumor Characterization.

INTRODUCTION

Human brain is the most complex and sophisticated organ in the human body. Brain regulates vital body functions such as emotion, memory, cognition, motor activities, heart rate, respiration, and digestion. The human brain is a complex network of millions of neurons packed in a matrix of glial cells. Brain and spinal cord makes the central nervous system (CNS). The homeostasis and normal functioning of the brain is affected by many complex neurological disorders such as Parkinsons (PD), Alzheimer's, Multiple Sclerosis, Epilepsy, Brain Tumor, Stroke etc. [1].

Brain tumor or intracranial neoplasm is an abnormal growth of cells in the brain or the membranes surrounding the brain. Brain tumor is classified as benign (that do not spread to other parts) or malignant (metastatic, that can spread to other parts). On the basis of origin where the tumor is generated, there are two types of tumors- primary and secondary tumors. Primary tumor of the brain originates from the brain, whereas secondary tumor originates from other parts of the body such as lung, breast, kidney etc. Gliomas, meningomas and medullablastomas are the most common type of primary tumors [2].

Gliomas are populations of glial cells - astrocytes, oligodendrocytes, ependymal cells and microglia - that grow and divide abnormally. Glial cells have a supportive role as a connective tissue in the central nervous system (CNS). World Health Organization classified tumor into four grades on the basis of its histologic features and malignancies. Grade 1 and grade 2 tumors are called low grade tumors. These are benign tumors. Grade 3 and grade 4 are commonly called as high grade tumors. These are malignant tumors that could spread to other parts of the body [3].

Medical imaging is the technique to visualize the internal structure of human body without actually having to open it. Advanced version of many medical imaging modalities are available since the discovery of X-rays by Wilhelm Conrad Roentgen in 1895. Medical imaging modalities can be divided into two types - anatomical modality and functional modality. Anatomical modality is used to represent the structural properties of the human body and functional modality is used to represent the functionalities of the human body. X-ray, Computed Tomography (CT), MRI (Magnetic Resonance Imaging) are the examples of anatomical modality and fMRI (functional MRI), PET (Positron Emission Tomography), SPECT (Single-photon emission computed tomography) are the examples of structural modality [4].

MRI is a non-invasive 3D imaging modality, which is used to represent the soft tissues in the human body. The main advantage of MRI over the other imaging modalities is that it does not emit any ionizing radiations to the patient's body. MRI involves the idea of Nuclear Magnetic Resonance (NMR) wherein the magnetic properties of hydrogen ions is exploited to obtain a signal that is converted to an image. Combing this to the fact that the human body is composed of 70% water makes MRI an effective imaging tool [5]. MRI is commonly used for the diagnosis of various clinical conditions, for instance brain tumor. In modern scanners, MRI is available in many sequences such as T1, T2, DWI, FLAIR, SWI etc. In this work we have used magnetic resonance images for the fractal dimension based characterization of brain tumors.

Fractals is a never ending pattern. Fractals are patterns that are self-similar and scale invariant. Though fractal is a purely mathematical concept, many attributes of nature also display fractal behavior to a limited extent. Menger sponge, snowflakes, shells, coastlines are some examples. Fractal dimension is an index of complexity that measures how a detail in a pattern change with the scale in which it is measured. The word fractal is derived from a Latin adjective fractus, meaning 'fragmented'. The concept of fractal is introduced by Benoit Mandelbrot [6]. Fractal Dimension can be computed using many methods such as Self-Similarity Dimension and Box-Counting Dimension. Among them, box-counting is the most prevalent method. In box-counting method, the image is covered using a grid and count the number of boxes in the grid that are covering part of the image. Repeat the same operation with the smaller boxes. After representing these values in a graph, slope will gives the required fractal dimension of the image.

The concept of mammalian brain as a fractal structure was proposed by Hoffman in 1991 [7]. The emergent properties such as memory, learning, sleep of the human brain are a result of the intrinsic complexity of the brain via neural wiring. Fractal dimension is used for deep-going description of irregular and random phenomenon in nature. Hence the fractal properties of the brain could be perturbed in association with clinical conditions. Over the last years, fractal and multi fractal analysis have been applied extensively in medical signal analysis. The applications of fractal dimension in medical images is broadly divided into two categories-segmentation and characterization [8]. In the context of brain tumor analysis it is used to differentiate the benign and malignant lesions, to differentiate neoplastic and healthy tissues, for analyzing the progress of treatment and for the grade detection of tumors [9].

In a review, Seely et al. has studied the crucial connection between fractal structure and entropy production in the CNS [10]. They conclude that heat production of a biological system is proportional to its entropy production and that Oxygen and Glucose metabolism could serve as proxies for entropy production. Human brain has the most abundant energy requirement. A fractal structure is quite desirable for the brain since such structures are most efficient in energy dissipation. Therefore, in pathologies that alter the metabolism of the brain a change in fractal properties of the brain is observed. In brain tumor, metabolism is severely affected. The hyper metabolism caused by the tumor could cause and increase in fractal dimension if the above hypothesis are to be believed

Another approach is to think of the human brain as a closed system. The pressure within the skull is termed intracranial pressure. The tumor of the brain impact a change in the intracranial pressure (ICP) [11]. In such conditions, the equilibrium pressure which is initially managed by the auto-regulatory processes creates a compensatory change in the cerebral blood volume and cerebrospinal fluid volume outside the brain. The skull is a rigid part and it does not handle this high pressure situation. Therefore the intracranial pressure within the brain will be increased and it changes the regular shape of the brain. This irregularity can be assessed using fractal dimension [7]. In this paper we made a comparative study between the fractal dimension of tumored and non tumored images.

The rest of the paper is organized as follows. Next section describes the related works. Materials and methods includes in the section 3. Section 4 explains experimental results. Conclusion and future direction is described in the last section.

RELATED WORKS

Fractal dimension quantifies the irregularity or complexity of a structure. The fractal dimension reveals deep structural features and facilitates the overall performance of the traditional image processing methods [12]. Fractal dimension is also used in many medical image processing applications. S. L. Free et al. estimated the fractal dimension of the white matter surface of normal brain images and epilepsy patient's images. Their studies offer an additional information about the structure of the cortex in normal brain images and about abnormalities of structure in subjects with suspected but undetected structural abnormalities [13]. Jing Z. Liu et al. proved that the human cerebellum follows a fractal structure. Fractal dimension of the Cerebellum skeleton was determined using the box-counting method [14].

Florian Michallek and Marc Dewey proved that Fractal dimensional analysis is a suitable way for measuring heterogeneity from radiological and nuclear medicine perfusion images under a variety of circumstances and in different organs [8]. R. Lopes et al. proposed an efficient method for the automatic classification of voxels as tumored and non tumored voxels. They used this method for the detection of tumor in the peripheral zone of the prostate. They combined multi-fractal and fractal features in order to have both global and local descriptions of the heterogeneities of the image texture. The fractal dimension was computed using the variance method; the multi-fractal spectrum was estimated by an adaptation of a multi-fractional Brownian motion model [15]. Rangaraj, M. Rangayyan and Thanh M. Nguyen analyzed the fractal dimension of the breast masses. They found that there is a substantial change in fractal dimension between malignant tumors and benign masses. When FD was combined with other shape features, the classification accuracy was enhanced [16].

From the literature we can see that there are lots of fractal dimensional analysis applications is performed in brain imaging also. Letizia Squarcina et al. computed the fractal dimension of schizophrenia (SCZ) or bipolar disorder (BD). They implemented this work for the classification of healthy and pathological brains tissues. They found that low FD values of gray matter both in BD and in SCZ patients with respect to healthy patients [17]. S. Farahibozorg et al. found that age and sex of a human being makes the significant change in the fractal dimension of white matter in the brain. They also reported gender differences, with men showing larger fractal dimensions than women, and age-related effects were more observable in the left hemisphere of men, but in the right hemisphere of women [18].

Francisco J. et al. proved that fractal dimension in the gray matter- white matter regions of the multiple sclerosis disease affected persons has a significant change with the controls. They concluded that fractal dimension can be used to detect multiple sclerosis in the early stages [19, 20]. Anca-Larisa Sandu et al. computed the fractal dimension in the gray–white matter border of the patients with dyslexia disease. Changes were found in the measured volumes of both gray and white matter and were best reflected in the ratio of gray-white matter and in fractal dimension values, particularly in the left hemisphere. They also found that although dyslexia disease is rare in female, the structural differences in the brain are more pronounced in their cases [21]. Richard D. King et al. analyzed the fractal dimension of three cortical models (pial surface, gray-white surface and entire cortical ribbon) of Alzheimer's disease affected persons were computed using a custom cube-counting triangle-intersection algorithm. The fractal dimension of the cortical ribbon indicated highly significant changes between control and Alzheimer's disease subjects [22].

Luduan Zhang et al. made a fractal dimension assessment of brain white matter for finding the effect of stroke in the upper-extremity motor functions. They applied fractal dimensional metric onto skeletonized brain white matter images to evaluate the internal structural complexity. They concluded that the white matter complexity was lower in the stroke-affected hemisphere [23]. Using fractal dimension, Anca-Larisa Sandu proved that the adults have a lower cortical complexity than the adolescents, which was substantial for complete brain, left and right hemisphere, frontal and parietal lobes for both genders, and only for males in left temporal lobe [24]. Elina Kalmanti and Thomas G. Maris found that cerebral cortex undergoes significant change during the aging process. They computed fractal dimensions of slices taken from left and right hemispheres. Their results showed a significant degree of lateralization in the left hemisphere [25].

It is to be noted that the change in fractal dimension in pathologies of the brain correlates ell to the metabolic state of the brain. In conditions of hyper metabolism an increase in fractal dimension is observed and in cases of hypo-metabolism a decrease in fractal dimension has been observed. This observation has been seen to be consistent with ageing, epilepsy, multiple sclerosis, Alzheimer's, Stroke, Brain tumor indicating a close relation as reviewed by Seely et al. [10]. Though the underlying reason is yet to be clearly establish this correlation could be exploited to identify pathological states.

Antonio Di Ieva et al. proved that Ultra high field magnetic resonance imaging is very useful for finding the brain tumor in the early stages [26]. They used susceptibility weighted imaging (SWI) for the tumor detection. At the initial stage they computed the fractal dimension of four patients. They analyzed the fractal dimension of patient's image on before and after the treatment. They made a conclusion that the fractal dimension in susceptibility weighted images of 7T MRI is useful for the treatment of brain tumors. Later, on another study, they proved that fractal dimension in 7T SWI can be used for the tumor grade analysis [27]. Justin M. Zook and Khan M. Iftekharuddin used fractal dimension as tool for identifying whether an image contains tumor or not and for identifying the location of the tumor [28]. They made two conclusions: tumor location is recognized by sub-images with lower fractal dimension than the average fractal dimension of the non-tumor tissue and tumor location can be detected by a negative fractal dimension difference between a sub-image in one half and its corresponding sub-image in the other half of an image.

MATERIALS AND METHODS

Characterization of brain tumors from MR images is a challenging task in the area of medical image processing. Since tumors changes the regular shape of the brain, fractal dimension can be used as a measure to assess the complexity of the tumors.

MR Image Dataset

We have examined a total of 26 patient's images of age between 30 and 65 (13 healthy and 13 tumored), collected from a Medical College Hospital. From each patient's data we have selected 10 slices. Thus a total of 260 images are processed. All the images are of T2 axial slices with dimension of 512x512.

Pre-Processing

Image pre-processing plays an important role in the medical image processing applications. An efficient pre-processing method will improve the accuracy of the results. In this paper we are trying to compute the fractal dimension of tumored and non tumored brain images. Repeated experiments shows that the presence of skull in the images will be negatively affects the fractal dimensional value. So as a pre-processing stage we have to eliminate the skull region from the brain images. We have applied the skull stripping algorithm proposed by Benson. C. C and Lajish. V. L [29]. This algorithm used mathematical morphology based method for the skull removal.

Fractal Dimension

Fractal dimension is a measure which is used to compute the complexity of an object. The fractal dimensional theory is developed by Benoit Mandelbrot [30, 31]. He wants to identify the fractal dimension of some irregular real world objects. Mandelbrot found that the Euclidean dimension may not be properly express the morphology of real world objects. His work is based on the theories proposed by two mathematicians Hausdorff and Besicovitch [32]. Computing the fractal dimension of self-similar objects like Cantor set, Koch curve, Sierpinski triangle, Sierpinski carpet, Menger sponge etc. are comparatively easy than the other objects in the real world.

Many methods are proposed for the computation of fractal dimension of irregular objects. Among them, box-counting is the simple and widely used method. In box-counting method, compute the number of boxes, N(S), which will cover the entire outline of the object, Where S is the width of the box. Then box-counting fractal dimension, D can be computed using the following equation.

$$D = \lim_{S \to 0} \left(\frac{\log N(S)}{\log(1/S)} \right) \tag{1}$$

If we reduce the value of S, then the number of boxes, N(S) will be increased. In some cases, the value of the S taken as the power of 2. That is, 2, 4, 8, 16… Since zero cannot be applied for the real world objects, we computed the fractal dimension with the following equation.

$$D = m \tag{2}$$

Where m is the slope of the graph in which X-axis contains log (N(S)) and Y-axis contains log (1/S). Resize the value of S continuously and plot all the value on the graph. Find the best line that fits for all the points. Slope of the line gives the fractal dimension value.

Fractal dimension analysis is effectively used in many medical image processing applications. Tumor in the brain cells changes the regular structure that cells. This will affects the morphology of the entire brain. If we can identify these structural changes with the fractal dimensional analysis, we can classify the tumored and non tumored images easily. The experimental results are given in the next section.

RESULTS AND EVALUATION

Result of pre-processing is given in the figure 1. We have measured the fractal dimension of each slice and computed the average fractal dimension of every patient. Experiment results shows that human brain have a constant fractal structure and brain tumor changes this normal fractal structure. Table 1 represents the mean and standard deviation of fractal dimension of non tumored patients and table 2 represents fractal dimension of tumored patients. We got the fractal dimension of normal brain as 1.92 ± 0.005 and fractal dimension of tumored brain is found as 1.93 ± 0.008. This indicates that tumor changes the normal fractal structure of human brain. In both cases SD is considerably small. Statistical t-test with alpha level at .05 indicates that there is a significant difference exists between the fractal dimension of tumored and non tumored images.

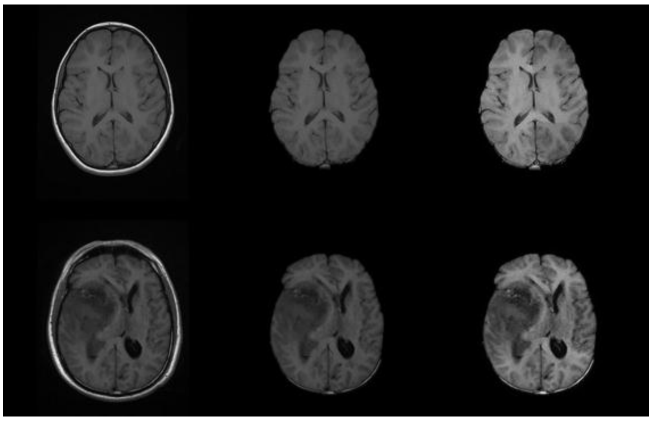

Figure 1. Result of Pre-Processing

Table 1. Fractal dimensional analysis of non tumored patients

Non tumored Patients		
Patient	**Mean**	**SD**
Patient 1	1.92291	0.006125
Patient 2	1.92338	0.007328
Patient 3	1.92115	0.006415
Patient 4	1.92414	0.006245
Patient 5	1.93011	0.005148
Patient 6	1.92671	0.006500
Patient 7	1.92719	0.004321
Patient 8	1.92115	0.006254
Patient 9	1.93008	0.005617
Patient 10	1.92058	0.006156
Patient 11	1.92569	0.006333
Patient 12	1.92276	0.004811
Patient 13	1.92504	0.006100

Table 2. Fractal dimensional analysis tumored patients

Tumored Patients		
Patient	**Mean**	**SD**
Patient 14	1.93223	0.005946
Patient 15	1.93555	0.006152
Patient 16	1.94189	0.005856
Patient 17	1.93956	0.006179
Patient 18	1.93614	0.004814
Patient 19	1.93757	0.005699
Patient 20	1.93615	0.006184
Patient 21	1.94011	0.005918
Patient 22	1.92994	0.004587
Patient 23	1.93466	0.005596
Patient 24	1.93579	0.007015
Patient 25	1.92689	0.006439
Patient 26	1.93234	0.005933

CONCLUSIONS AND FUTURE WORKS

In this work we analyzed the fractal dimension of tumored and non tumored images. We found that human brain has a constant fractal structure and brain tumor changes this fractal structure. We got the fractal structure of normal brain as 1.92 ± 0.005 and abnormal brain as 1.93 ± 0.008. Statistical t-test value confirmed that tumored images have high fractal dimensional value than non tumored image. This result can be utilized to classify the tumored and non tumored images efficiently. Further it agrees to our hypothesis that the metabolic changes of the brain reflects on its fractal properties.

In this paper we have computed the fractal dimension of entire brain for normal people and people with tumor from a stack of 2D MR images. It would be interesting to reconstruct the brain in 3D and then analyse the change in fractal properties. Furthermore different grades of gliomas could indicate a different metabolic state and consequently unique fractal dimensions. The effect of gliomas on gray and white matter should be studied by the segmentation and computing fractal dimension to observe how the fractal properties change in white matter and gray matter relative to controls. In patients who get treated for brain tumor it would be interesting to see whether medicines alter the fractal property whether medicines alter the fractal property of the brain. This could indicate a role of fractal dimension and patient prognosis.

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