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Pattern Analysis of Liver Cancer Based On Fractals

G. Jayalalitha
Associate Professor, Department of Mathematics, Vels University, Pallavaram, Chennai.

Abstract: ***The main aim of this paper is to establish the fact that fractal dimension serves as a tool to identify the stages of cancer. A new scheme of cancer analysis which based on cell structure is also presented. Depending upon the shape of cell, its dimension varies. Distance between the cells decreases with the increase in population of cancer cells. Continuous growth of cells leads to cluster point of malignant cells. In advance stages of cancer the value of Fractal Dimension is higher and it is lesser in the initial stages. Fractal dimension is computed by all the methods show different values. This paper, in all projects, some Fractal Mathematical approaches which are efficient in the analysis of cancer pattern.***

Keywords: ***Cell Growth, Liver cancer, Box-Counting Method, Fractals, HarFA Fractal Analysis.***

I. INTRODUCTION

The liver is the largest gland in the body and is situated slightly below the diaphragm and interior of the stomach. No one can live without liver. The incidence rate of liver cancer in the world is due to the high infective rate of Hepatitis B & Hepatitis C virus and consumption of foods with aflatoxin in liver areas. Hepatocellular Carcinoma (HCC) remains one of the major public health problems throughout the world [1, 2].

A fractal is a shape that appears self-similar on multiple spatial scales, that is any piece of it looks like the whole after a change of scale (magnification). The technical term that describes self-similarity of shapes uner change of observation scale is scale-variance. System that are scale-invariant do not have any characteristic length, that is a typical or mean length. Although the concept and rules of fractal geometry [3] have been used in basic research for several years, recently, the transition between aesthetic contemplation of fractal images and the application of fractal geometry to the analysis of naturally occurring images has been relatively slow. As far as an important characteristic of fractal geometry is the property of self-similarity in a statistical sense, it should have a constant amount of detail as the image is viewed at different levels of magnifications, i.e., at different ranges of scale [4, 5, 6]. These facts have been used for developing methods for the 'complexity measuring' of different natural shapes (cells, particles, geographical objects, etc.) [7, 8, 9, 10].

In other words, shapes can be measured and expressed as comprehensible digits that represent their measure of regularity or irregularity, thereby becoming comparable to other ones. From the literature, we have observed that the research article entitled "Fractal dimension of hepatocytes nuclei in normal liver vs hepatocellular carcinoma (HCC) in human subjects-preliminary result's" said that the nuclear shapes were used for the dimension. Since the nucleus is present in the cell, the shape of the nucleus is not clear in the microscope, so we have used cells. This method shows the results very clearly and accurate to find out the grade of the cancer [12, 14]. The essential and most fascinating property of any fractal is its complexity.

The complexity of the tissue profiles in an experimental cancer model has been investigated using the principle of fractal geometry.

The expected results, concerning cell shape complexity, were that the fractal dimensions of the same cell type differ in their characteristics, depending upon whether they belong to normal or malignant cells, which is to be a numeric evidence of cell's shape and size are complexity and cytoarchitectonic characteristics. The application of fractal geometry to the measurement of the liver cells in the tissue and the availability of the cell's shape and size in the tissue shows the grade of the cancer. Recent work in the analyses of liver cells can be found in [12, 14].

Here, we model the liver cell's formation by Mathematical Model. The shape of the cells can be analyzed by HarFA Fractal Analysis Software.

The shape of the cell can be proved by Contraction Mapping Theorem. The dimensions of the cells size can be calculated by Box Counting Method and HarFA Fractal Analysis.

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II. METHODS

A. *Mathematical Model of cells*

The body is made up of many types of cells. Normally, cells grow and divide into new cells in a controlled and orderly manner. Sometimes, however, new cells continue to be produced when they are not needed. As the result, a mass of extra tissue may develop. The cells grow continuously.

Let $N(t) =$ cell density observed at time t. Suppose we are able to observe that over a period of one unit time, a single cell divides, its daughters divide, and so forth, leading to a total of K new cells. We define the reproductive rate of a cell by the constant K, $(K > 0)$ that is, K = rate of reproduction per unit time. Now suppose densities are observed at two closely spaced times t and $t + \Delta t$. Ignoring the dead cells, we then expect to find the following relationship

$$N(t + \Delta t) = N(t) + KN(t)\Delta t \quad (2.1)$$

$$\frac{N(t+\Delta t)-N(t)}{\Delta t} = KN(t) \quad (2.2)$$

We now approximate N (strictly speaking a large integer, e.g., $N = 10^6$ cells/ml) by a continuous dependent variable $N(t)$. Then in the limit $\Delta t \to 0$ the equation (2.2) can be approximated by the following ordinary differential equation:

$$\frac{dN}{dt} = KN \quad (2.3)$$

This simple equation is sometimes known as Malthus law.

$$\frac{dN}{N(t)} = Kdt \quad (2.4)$$

$$\ln N(t) = Kt + a \quad (2.5)$$

where $a = \ln N(0)$. This explains the assertion that a log plot of $N(t)$ is linear in time, atleast for that phase of growth for which K may be assumed to be a constant. We also conclude from equation (2.5) that

$$N(t) = N_0 e^{Kt} \quad (2.6)$$

where $N_0 = N(0) =$ the initial population. For this reason, populations that obey equations such as (2.6) are said to be undergoing exponential growth. This constitutes the simplest Mathematical model of cells growth, or indeed, growth of any reproducing population. It is possible to mathematically model the progress of growth of cancer to discover the likely outcome of an epidemic. The majority of liver cancers arise from the liver cells themselves. The cell's growth is a continuous process. The shape and size of the cell's pattern are the main parameters for the growth of cancer. The cell's radius is also very important factor for the growth. This will be helpful to find out the dimension of the cell.

B. *Contraction*

In general, contraction can reduce distance between points by different value depending on the position of the points. The contraction is defined as: A map $f : X \to X$ from the metric space (X, d) into itself is called a transformation. In general, in most applications, a transformation is expected to be bijective, that is, for any point x of X there is some unique point z of X to map into, $f(x) = z$ and there is some unique point u of X to be mapped from, $f(u) = x$. A point $a \in X$ is called a fixed point of the transformation f if $f(a) = a$.

A contraction mapping or contraction, on a metric space X is a function f from X to itself, with the property that there is some real number $k < 1$ such that, for all x and y in X,

$$d(f(x), f(x)) \leq kd(x, y) \quad (2.7)$$

By using the contraction mapping theorem,

Let $f : X \to X$ be a contractive transformation on a complete metric space (X, d). Then the transformation f possesses exactly one fixed point $a \in X$. Moreover, for any $x \in X$, the sequence x, $f(x)$ $f^2(x) = (f(x))$, ·…., $f^k(x)) = f(f^{k-1}(x))$, · · · converges to the fixed point a, i.e.,

$$\lim_{k\to\infty} f^k(x) = a \quad (2.8)$$

A contraction is a transformation T that reduces the distances between every pair of points. That is, there is a number $r < 1$, the contraction factor of T is the smallest r satisfying

$$d(T(x, y), T(x', y')) \leq d(x, y), (x', y') \quad (2.9)$$

for all points of (x, y) and (x', y')

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By using proposition,

Let (x_n) be a sequence a metric space X and let x belongs to X, we say that x is the cluster point of the sequence (x_n) if and only if for every $\varepsilon > 0$ and every $N \in N$, there exist $n \geq N$ with $d(x_n, x) < \varepsilon$.

A sequence (x_n) in a metric space X converges to a point $x \in X$ if and only if for every > 0, there is $N \in N$. So that $d(x_n, x) < \varepsilon$ for all $n \geq N$. This can be written as $\lim_{n\to\infty} x_n = x$. Also x is called limit of sequence (x_n). The point x is a cluster point of the sequence (x_n) if and only if x is the limit of some subsequence of (x_n).

The proposition is applied in the growth of the cells. Here we consider (x_n) as a cell's sequence. A cell's sequence has a cluster point ' x ' [13]. This cluster point' x ' shows that the cell is normal or abnormal. The cell sequence can be provided by contraction. This contraction satisfies the metric space property. So every cell in the sequence has an analytic function that can be modeled by Mathematical Model. From this we conclude that the shape and size of the cell are the main parameter for the growth of cells in the tissue. This can be proved by the methods of shape such as Gradient, Laplace and Sobel and this was done by HarFA Fractal Analysis Software (Fig. 2).

C. Computational Procedure To Determine Cell Fractal Dimension

Cells of the liver tissue were examined to determine their peculiar shape as a result of certain construction of Fractal Mathematics. Morphometric measurements of the cell perimeter were made at several levels of cell height by measuring the intracellular boundaries that appear on electron micrographs true cross sections. The fractal dimension is used to measure the quantity of the cells growth in the tissue. For that we need perimeter and area of the cell which can be calculated by Box-Counting Method. Power law describes the empirical scaling relationships that are emergent quantitative features of biodiversity. The starting point to determine the fractal dimension of a cell is to acquire the cell image by an electronic microscope, converting it to a computer based format such as bitmap, tiff or jpeg. The computational procedure is developed by Box Counting Method Algorithm. This method consists of covering a geometric figure with non- overlapping boxes with different size r and to determine the minimum number of boxes required $N(r)$ to completely cover the figure. Clearly this number is expected to be a function of r, $N(r)$. For more complex images, the general relationship between $N(r)$ and r is expected to be

$$N(r) = K r^{D} \qquad (2.10)$$

where K being a constant and D a real number, so called fractal dimension. Solving for D the result is

$$D = \log K - \log[N(r)] / \log r \qquad (2.11)$$

which is a characteristic of the figure maintained even in infinitesimal scale.Since D is the angular coefficient of the straight line representing $\log(N(r))$ versus $\log(1/r)$, one can plot a set of points $(r, N(r))$ in a logarithmic scale to obtain D. This programme was given by the following algorithm and it was performed by MATLAB software, which is depicted in the (Fig.1and Fig. 2). The table 1 and table 2 show the fractal dimension values for the Normal and Abnormal liver cancer cells.

1) Algorithm

a) Step 1: The image is divided into regular meshes with a mesh size of r.

b) Step 2: Count the number of square boxes that intersect the image $N(r)$.

c) Step 3: The number is dependent on the choice of r.

d) Step 4: We repeat for several size r values and count the corresponding number $N(r)$.

e) Step 5: We plot the slope D formed by plotting $\log(N(r))$ against $\log(1/r)$.

Step 5 indicates the degree of complexity or dimensions of the fractal. Finally a straight line is fitted to the plotted points in the diagram using the least squares method. The linear regression equation used to estimate the fractal dimension. When the measurements were made over a range of scale lengths, the fractal dimension, D of the cell perimeter was found to increase from 1.2 to 1.9.

D. HarFA Fractal Analysis

Boundaries are linked edges that characterized shape of an object. They are useful in computation of geometry features such as size or orientation. A problem of fundamental importance in image analysis is edge detection. Edges characterize object boundaries and are therefore useful for segmentation, registration, and identification of objects in scenes. Edge points can be thought of as pixel location of abrupt black and white change. Here we can find the cell shape by using three methods such as Laplace, Gradient and Sobel. Edge detect filters search for shape between different colours and also can detect

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contour of objects. HarFA Fractal Analysis Software can be used to find out the shape of the cells in the tissue. The shape is very important factor for the growth of the cancer (Fig.1 and Fig. 2). From the above said methods, we can find out the fractal dimensions. This gives the stage of the cancer (Fig. 3) (Table. 3, 4 and 5). This will help to find the stage of the cancer.

III. RESULTS AND DISCUSSIONS

Based on Mathematical Model the cells are growing continuously in the tissue. The cancer grows and the cell's shape increases day after day. The shape of the cell is complex. By applying the Proposition [2.2.2] and Contraction Mapping Theorem in the cell's growth, we identify the cluster point or fixed point in the liver cancer. The distance between the cells can be calculated by Pixel Profile Software (Fig. 4). When the distance between the cell size changes, the shape also changes. From this we can find the cluster point or fixed point. The graph of the Pixel Profile Software shows the intensity of the colours Red, Green and Blue. If the DNA (Deoxyribonucleic Acid) of each cell is damaged the cell's shape will change. This is due to cell's contraction. This contraction is analysed by distance between the cells. This can be measured using Histo Stretch software (Fig.4 and Fig.5). The figure 4 exhibits that the distance between the abnormal cells. When distance between the cells increase due to the contraction. It shows by the graphical representation. Similarly, the figure 5 shows that the distance between the normal cells. It shows by the graphical representation. The length of scale found in the range of 20 m (micron), and to represent the approximate dimensions of actual cell processes.

By using Box Counting Method we have found the dimension of Normal and Abnormal cell images (Fig. 1). If the dimension of the cell shows like 0.59, 0.89, 0.91, 0.92, etc., then we say that the cells are like normal tissue and it has lower grade and it is called Grade-I. Here cells are well differentiated. If the dimension of the cell shows like 1.1, 1.2, 1.3 then we say that the cancer is Grade-II. Here cells are moderately differentiated. If the dimensions of the cells shows like DB=2 then we say that the cancer is Grade-III. Here cells are poorly differentiated and it is higher-grade. It attains the metastatic cancer. When the measurements were made over a range of scale lengths, the fractal dimension, DB of the cell perimeter was found to increase from 0.59 to 2. From this we understand that the dimension is the main characteristic for the cell growth Table 1 and Table 2. By using HarFA Fractal Analysis Software also we can find the dimension of normal and abnormal cell images. In this Software we have used two forms, namely, Discrete and Continuous Spectrum. In discrete and continuous spectrum the dimension varies in normal & abnormal liver cell. The B + BW show the dimension of the cells shape (Table 3, 4 and 5) by using three methods such as Gradient, Laplace and Sobel. In the discrete form the cells are spread randomly in the tissue and in the continuous form the cells are very closely in the tissue. Thus dimension varies due to cell's shape. This shows the variations of the distance between the cells. So we conclude that the distance between the cells is also important parameter for the cell growth. This is due to form of cell's shape. This will be helpful to find the grade and the stage of the cancer.

IV. CONCLUSION

Fractal geometry is a rapidly growing area of mathematics with immense potential Here we conclude that the fractal dimension is a main tool to find out the growth of cells in the tissue. The fractal analysis applied on digitized cell shapes and size are a reliable method for all complexity measurement that can be used alone or as an additional parameter along with morphometrical measurements both in routine work and research. Our measurement clearly shows that there is a significant difference between the normal cell and abnormal cell. Due to the cell's shape and the size the dimension varies. This dimension is an objective measure of the complexity of the cell's shape, which undoubtedly indicates the fractal nature of the cell type. From this we can confirm the stage of the cancer. This will be helpfulto the pathologist to diagnose whether the growth is benign or malignant.

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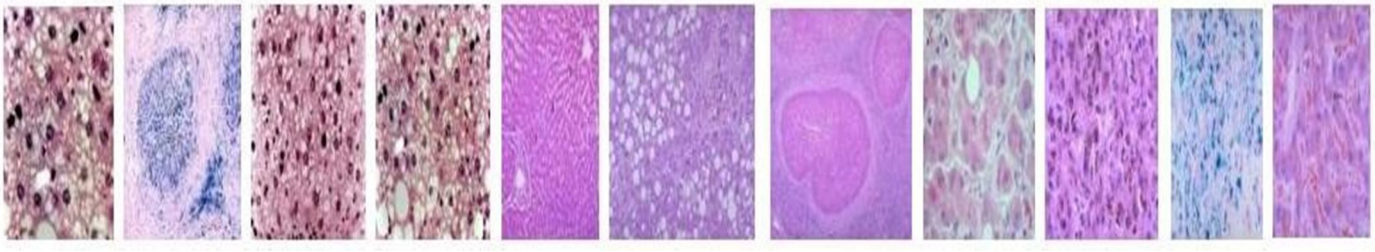


Figure 1: Normal and Abnormal Cells in Liver

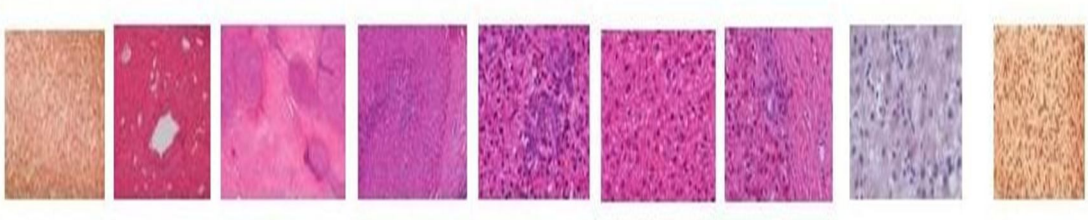


Figure 2: Different shapes of cells in the tissue

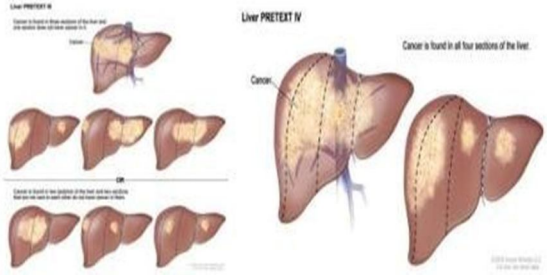
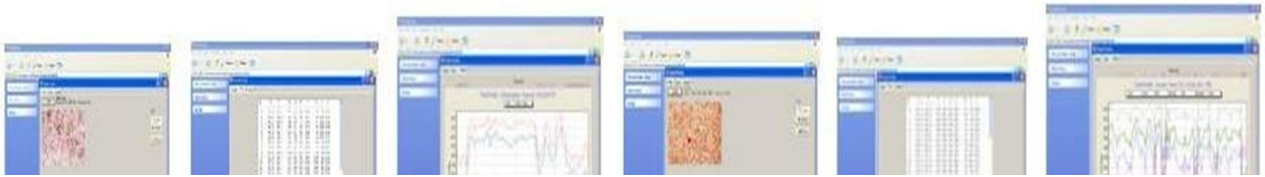


Figure 3: Growth of Liver Cancer in the tissue



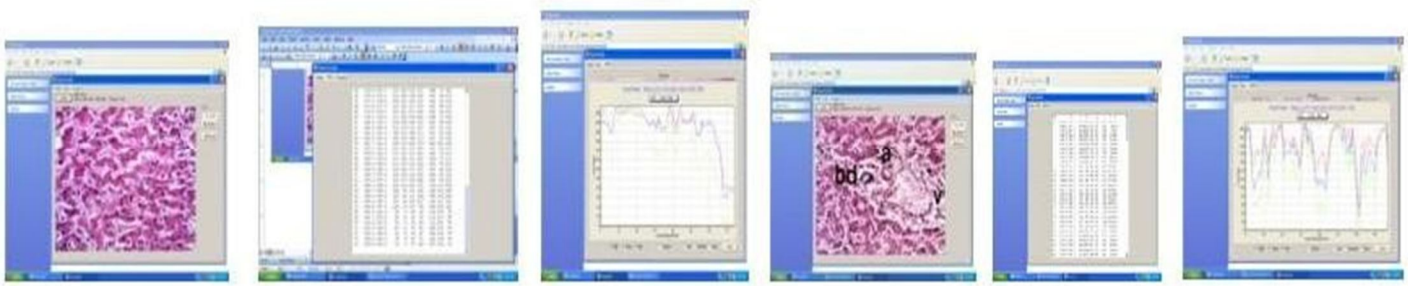
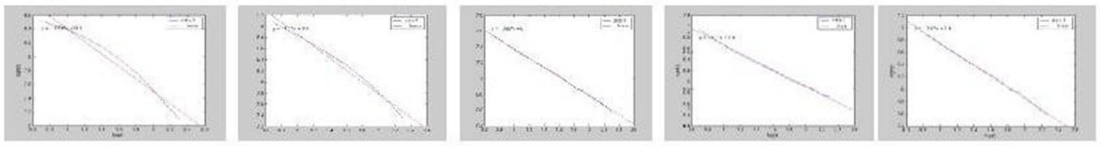


Figure 4: Distance between the Abnormal Cells Figure 5: Distance between the Normal Cells

Table 1: Data Analysis of Normal Cells of Liver Cancer using Box Counting Method

Image	Scaling									DB
	2	3	4	5	6	7	8	9	10	
1	4113.5	3163.33	2548.75	2116.79	1819.99	1588.29	1406.75	1270.22	1111	0.89
2	1492	1225	1048	905.2	818.33	713.72	638	571.78	492.4	0.67
3	5004	4194.67	3490.7	2568.60	2386.70	1962.86	1643	1396.55	1204.80	0.91
4	3113.5	2298.33	1802	1442.60	1221.67	1040.14	926	792.33	729.09	0.92
5	1121	763	599.7	502.4	41.5	376.57	327.3	282.33	254.2	0.9
6	1904	1481.33	1274	1124	990.67	916.43	847.75	784.26	713	0.59
7	1419	907.66	645	499.600	392.6666	334.2858	293	255.444	230.5601	1.1

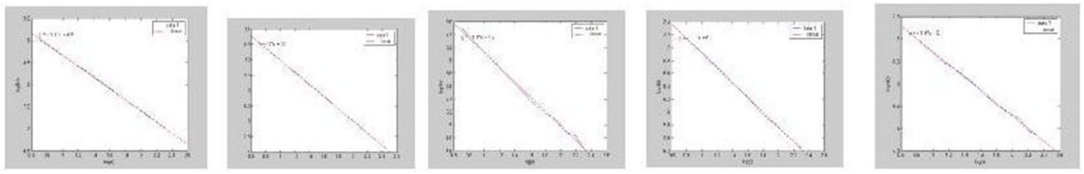


Graphical Representation of Normal Liver Cancer Cells

Table 2: Data Analysis of Abnormal Cells of Liver Cancer using Box Counting Method

Image	**Scaling**									DB
	2	3	4	5	6	7	8	9	10	
1	369	2194.4	1499	1169.0	932.1	765.7	629	573.0	482.9	1.3
2	478	2778	1946	1459.7	1136.1	925.3	775	654.7	563.9	1.3
3	392	17861.9	10122.	6495.35	4512.1	3317.8	2546.2	2015.8	1625.9	2
4	837	5117.6	366.5	2728.	2134.1	1758.4	1491.8	1269.2	1088.9	1.3
5	4569	2857.3	2139	1682.6	1382.8	1200.7	1044	900.5	824.2	1.1
6	244	1234.3	7944.	5468.7	4011.1	3049.7	2397.8	1933.5	1605.23	1.1
7	730	5857.6	4773	4004	3296.3	2756.4	2311.7	1946.9	1696	1.2
8	129	687.66	489	344.6	252	210.714	188	141.333	127	1.4

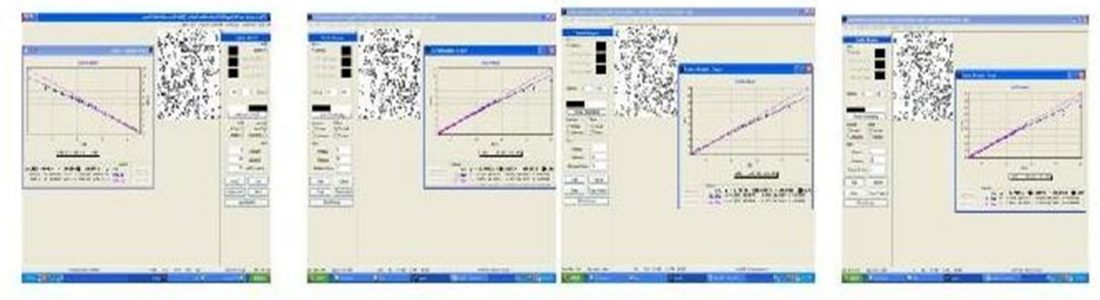
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Graphical Representation of Abnormal Liver Cancer Cells

Table 3: Data Analysis of different shapes of the Liver cells using Gradient method

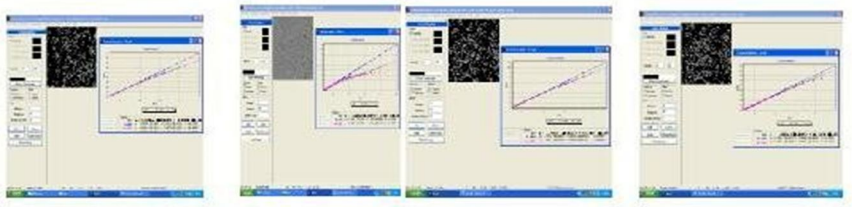
Image	Gradient					
	Discrete			Continuous		
	BW	B+B	W+B	BW	B+B	W+B
1	0.651	1.660	1.041	0.937	1.819	1.108
2	1.001	0.927	1.999	1.281	1.807	1.895
3	1.109	1.009	1.999	1.219	1.814	1.343
4	1.704	1.666	1.914	1.794	1.759	1.988
5	1.783	1.738	1.976	1.857	1.821	1.985



Graphical Representation of different shape of the Liver cells (Gradient)

Table 4: Data Analysis of different shapes of the Liver cells using Laplace method

Image	Laplace					
	Discrete			Continuous		
	BW	B+B	W+B	BW	B+B	W+B
1	0.903	1.660	1.210	1.214	1.819	1.338
2	0.383	1.637	0.885	0.568	1.807	0.811
3	0.528	1.651	0.961	0.786	1.814	0.983
4	1.678	1.988	1.605	1.166	1.99	1.223
5	1.753	1.987	1.675	1.833	1.992	1.775

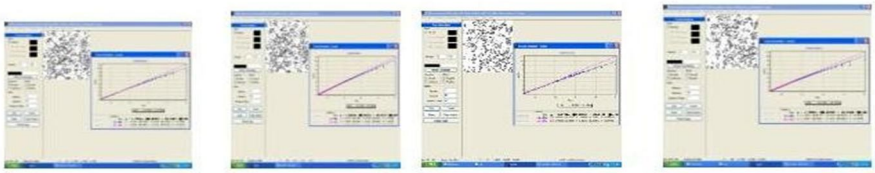


Graphical Representation of different shape of the Liver cells (Laplace)

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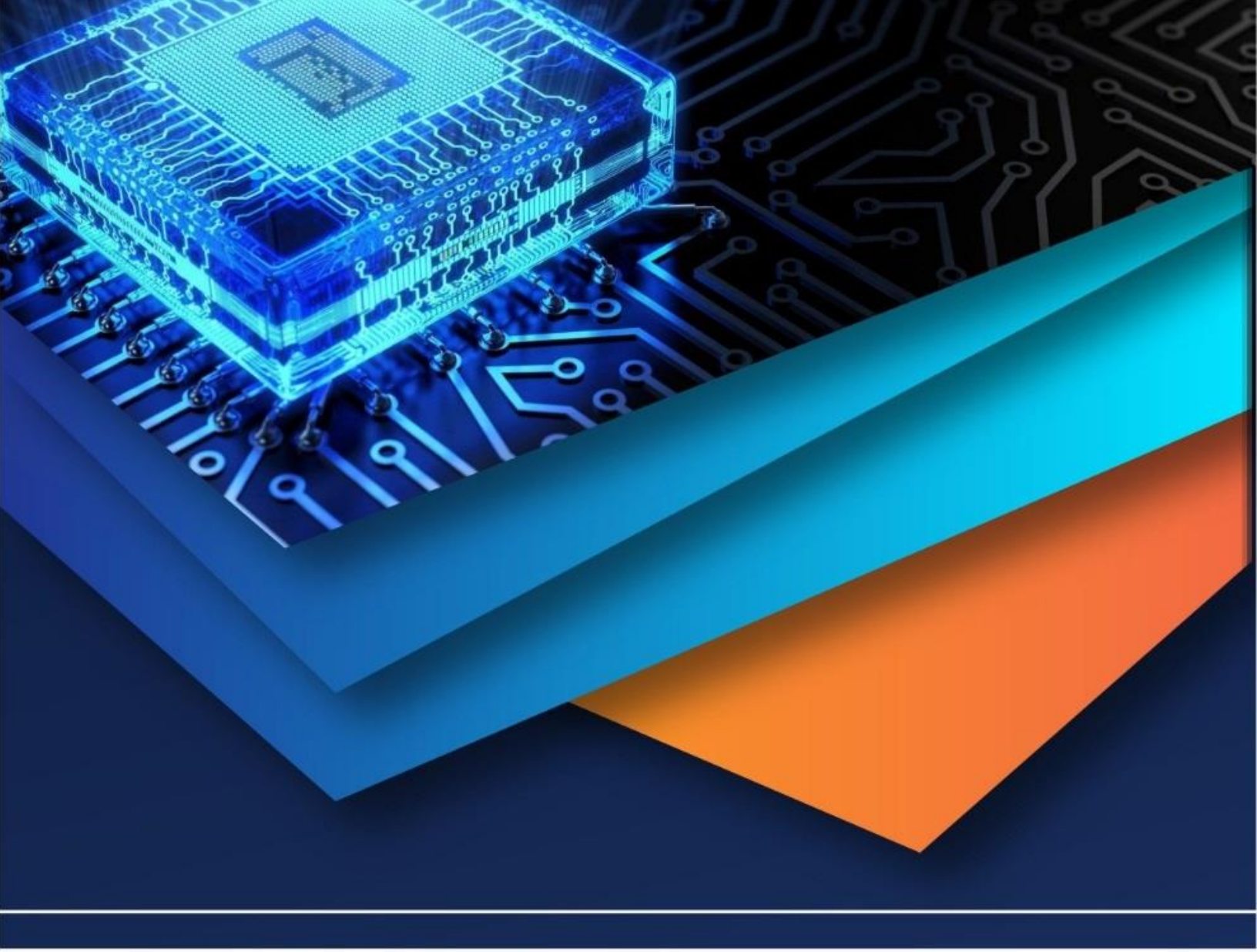
Table 5: Data Analysis of different shapes of the Liver cells using Sobel method

Image	Sobel					
	Discrete			Continuous		
	BW	B+B	W+B	BW	B+B	W+B
1	0.741	1.660	1.102	1.027	1.819	1.183
2	0.637	1.637	1.032	0.918	1.807	1.092
3	0.645	1.651	1.036	0.942	1.814	1.112
4	1.719	1.658	1.985	1.788	1.766	1.984
5	1.796	1.732	1.981	1.865	1.817	1.988



Graphical Representation of different shape of the Liver cells (Sobel)

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