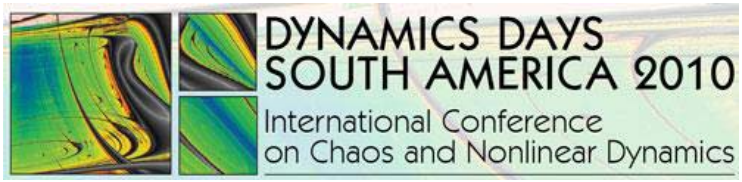


INPE – National Institute for Space Research
São José dos Campos – SP – Brazil – July 26-30, 2010

Fractal Dimension as a Marker of Cellular Rejection in Myocardial Biopsies from Patients Submitted to Heart Transplantation

Leandro Alves Neves [1], Roberto Douglas Moreira [2], Antonio Roberto Moriel [3], Moacir Fernandes de Godoy [2]

1Universidade Estadual Paulista, IGCE, DEMAC, Rio Claro, SP, Brazil, laneves@rc.unesp.br
2Faculdade de Medicina de São José do Rio Preto, São José do Rio Preto, SP, Brazil, mfgodoy@famerp.br
3Instituto de Anatomia Patológica e Citopatologia, São José do Rio Preto, SP, Brazil

Abstract: The preset work describes an algorithm for quantifying patterns of cardiac cellular rejection in myocardial biopsies from patients submitted to heart transplantation. The model is based on multiscale fractal dimension (FD). The algorithm also uses automatic multilevel thresholding with maximum entropy for image segmentation and confidence intervals in order to quantify cellular rejection groups. The results obtained provide more information on cellular rejection and reveal the groups of patients that merit greater attention.

keywords: Fractal Dimension; Cellular Rejection; Myocardial Biopsies; Heart Transplantation.

1. INTRODUCTION

Many studies attempt to produce artificial visual systems with the same efficiency as biological systems. This task is highly complex, especially when implementing one of the most obvious problems: the quantification and qualification of informations represented in different fields, such as intensity of gray level, edges, contours and texture. Another difficulty is that phenomena and shapes found in nature have behaviors that are not easily quantified and qualified with techniques available in conventional mathematics, as observed in images of human body organs.

These difficulties are present in the evaluation of cardiac cellular rejection (CR), which has been standardized in four groups (R0 to R3) by International Society for Heart and Lung Transplantation (ISHLT) [1]. For pathologists, there are features in each group, especially in R2, of tiny clusters of inflammation with one or two damaged cells or the presence of considerable infiltration with muscle cell lesions. As a result, a number of centers do not treat some patients and recommend monitoring with biopsies at intervals of one to two weeks.

One possible solution to minimize difficulties presented is a computer program that can assist physicians in developing a diagnosis. The specificity and sensitivity required for a Computer Aided Diagnosis (CAD) applied in CR can be obtained if produced with techniques fractals, especially Fractal dimension (FD). The efficiency of FD is enhanced when combined with one of the most interesting properties of objects in nature, which is exhibition of different characteristics when observed on different spatial scales. This association is known as multiscale fractal signature [2].

In this context, this paper presents an algorithm based on multiscale fractal dimension to assess images of myocardial biopsies after heart transplantation in human patients and describe patterns of CR This method can provide more information and assist in supporting the diagnosis.

2. METHODS

The algorithm was developed with automatic multilevel thresholding and involves the methods of group histogram quantization, analysis of the percentage of histogram slope and the calculation of maximum entropy to define the threshold [3]. Thresholding based on maximum entropy is achieved from probabilistic calculations.

We consider an image as a result of a random process, where probability pi corresponds to the probability of a pixel in the image taking a value of intensity i (i = 1, .., n), as shown in (1); H is the entropy of the image; n is the total number of outputs; pi is the probability of gray level i being found in the image; n_i represents the number of pixels with intensity i; and N is the total number of pixels in the image. The gray level of the group indicated with the highest entropy is identified as a threshold.

$$H = -\sum_{i=1}^{n} p_i * \log p_i, \qquad p_i = \frac{n_i}{N} \qquad (1)$$

Fractal dimension was calculated with the Box-counting method [4], one of the most known. A multiscale approach was obtained with a grid of cubes placed on the image analyzed. The luminance of the pixel is defined as the height. The number of cubes (N) that contains part of an image varies with the size of the cube (with side r). The association used to calculate the fractal dimension (D_f) is (2). The cubes count N is performed for different values of r, using the regression of log-log graph of N by r. The fractal dimension is defined as D_f=-α (angular coefficient).

$$D_f = \frac{log(\mathrm{N})}{log(\frac{1}{\mathrm{r}})} \qquad (2)$$

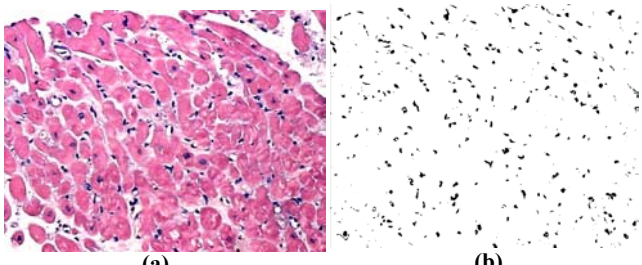
The algorithm was applied to 120 myocardial images from cardiac biopsies, separated into four groups: R0 (22 images); R1 (24 images); R2 (29 images) and R3 (43 images). The confidence interval (5) was used to ascertain the limits of each group. This approach can be an important descriptor of the behavior of each rejection class, from the perspective of the main parameters of the fractal geometry.

$$\bar{X} \pm Z\frac{s}{\sqrt{n}} \qquad (3)$$

in which $\bar{X}$ is the sample mean; Z is the value obtained from the table of standard normal distribution (95%), S is the standard deviation; and n is the sample size.

3. RESULTS

The technique was applied to myocardial biopsies from patients submitted to heart transplantation (Figure 1a). The cell core or tissue with rejection was segmented (Figure 1b) and analyzed with FD. Table 1 displays the data for each degree ranges on the behavior of each group, along with the mean average and standard deviation (SD). Figure 2 shown the behavior identified with the overlap found in each rejection group.



(a) **(b)**

Figure 1 - Example of R0 cardiac cellular rejection in myocardial biopsies from a patient submitted to heart transplantation (a); result of image processing (b), with cell core separated.

Table 1 – Average fractal dimension for each CR group and respective 95% confidence intervals.

Parameters	R0	R1	R2	R3
Average	1.021	1.135	1.262	1.323
SD	0.140	0.088	0.143	0.170
95% Confidence Intervals				
Lower Value	0.944	1.089	1.194	1.257
Upper Valuer	1.097	1.181	1.330	1.389

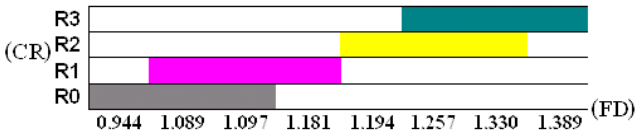


Figure 2 - Behavior of each CR group based on FD, calculated on the basis of confidence intervals and their overlaps.

3. DISCUSSION AND CONCLUSIONS

It was possible to verify that an image of myocardial biopsy from a transplanted heart can be categorized correctly if the value of FD is close to the average of the group, Table 1. This task is not trivial when FD is closer to the lowest or highest values of the sets. This finding is grounded in the group overlaps (Figure 2), demonstrating patients with CR in development or regression. This quantification provides data that underscore the importance of greater attention at diagnostic centers that treat patients in the R2 group, as they may actually be in the R3 group or may progress to this group.

This paper presents a study on CR degrees from the perspective of FD, which allowed identifying the groups that merit greater attention. FD can provide informations for more effective treatments, ensuring a greater survival rate among patients with heart transplants. The results allowed to identify successfully the behavior of each cardiac rejection group.

References

[1] Stewart et al. "Revision of the 1990 Working Formulation for the Standardization of Nomenclature in the Diagnosis of Heart Rejection", The Journal of Heart and Lung Transplantation, Vol.24,pp.1710–1720, 2005.

[2] L. F. Costa, A. G. C. Bianchi, "A outra da Dimensão Fractal", Ciência Hoje, Vol. 31, No.183, 2002.

[3] F. A. Peres, F. R. Oliveira, L. A. Neves, M. F. Godoy, "Automatic Segmentation of Digital Images Applied in Cardiac Medical Images", to appear in Proceedings of the Pan American Health Care Exchanges – Conference and Workshops IEEE, Lima (Peru), March 2010.

[4] A. G. Manousaki, A. Manios, E. I. Tsompanaki, A. D. Tosca, "Use of color texture in determining the nature of melanocytic skin lesions – a qualitative and quantitative approach", Computer in Biology and Medicine, Vol.36, pp. 419-427, 2006.