Tissue Characterization from Myocardial Perfusion and Autonomic Innervation using MRI and SPECT images in Chagas Disease

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Abstract

Chagas disease is of major clinical relevance, with high incidence.The relation between the myocardial tissue damage, myocardial perfusion and defects in the autonomic innervations is poorly understood. This work proposes the development and application of image analysis methods capable of providing an integrated visualization and analysis of tissue injuries through magnetic resonance imaging (MRI), autonomic innervations and myocardial perfusion, available through photon emission tomography (SPECT). This paper describes and evaluates a method for tissue characterization and quantication. The proposed method is based on segmentation of MRI and registration between MRI images and SPECT images using metaiodobenzylguanidine (MIBG) and 99Tc (m)-methoxy-isobutyl-isonitrile (MIBI). To perform the segmentation of myocardium, we used Geodesic Active Contour. Fibrosis segmentation in MRI images was performed based on the algorithm of maximum Tsallis entropy. Nonrigid registrations was performed based on B-Spline method. Initially, the registration was made between SPECT images using 99Tc (m)-MIBI and MIBG. Then MRI volumes were registered with SPECT images. It is possible to observe regions of brosis and with absence or low synaptic activity comparatively to myocardial perfusion. The relationship of regions of fibrosis and regions with absence of synaptic activity was obtained by Kendall correlation, which provided a correlation coefficient of 0.8788. Thus, the developed tool provides an integrated analysis of information contributing to a better understanding of the relationship between myocardial tissue damage and autonomic innervations injuries caused by Chagas disease.

1. Introduction

Chronic Chagas cardiomyopathy (CCC) is the most serious form of Chagas disease in Latin American countries [1]. It consists on a consequent inflammation and progressive destruction of heart tissue, followed by alterations in the pattern of conduction of electrical impulses and arrhythmias. At the same time, there is a progressive dilatation of the heart, resulting in an inability to pumping, which is called congestive heart failure. In parallel, Chagas disease can also involve the afferent autonomic nervous system (ANS), specifically myocardial sympathetic synapses. Chagas disease, in its form cardiac is characterized by changes in autonomic innervation and fibrosis of the myocardial cells [2]. Diffuse injuries to the myocardium by an inflammatory process due to Chagas disease are visible by late enhancement in magnetic resonance imaging (MRI) with the use of gadolinium (Gd). It is seen that the images acquired with the technique of late enhancement on MRI, the intact myocardium appears with very low signal intensity (dark). Fibrosis occurs in regions of membrane rupture of necrotic myocytes, and therefore, gadolinium may be freely distributed (largest volume of distribution). The myocyte necrosis also causes a change in the kinetics of contrast distribution so that the output of gadolinium areas of fibrosis occurs slower (delayed washout). These two factors mean that the concentration of the contrast, about 10 to 15 minutes after injection, is much higher in the necrotic regions than in normal myocardial tissue, making the white areas of fibrosis (high signal intensity) in the delayed-enhanced images.

Single photon emission computed tomography (SPECT) is a nuclear medicine modality. SPECT can provide information about blood flow and distribution of radioactive substances in the body. After injection of a radioactive tracer, the isotope is extracted from the blood and retained by viable myocytes within the myocyte for a certain period of time [3]. The photons are emitted from the myocardium in proportion to the magnitude of radioisotope uptake. The 2-methoxy-isobutyl-isonitrile (MIBI) is used for perfusion analysis and the metaiodobenzylguanidine (MIBG) is used to view sympathetic innervation.

In the study by Simões [4], disturbances of ventricular sympathetic innervation and abnormalities of myocardial perfusion was detected in various stages of Chagas heart disease. The population of the study consisted of 37 subjects from endemic regions who had positive standard serologic tests for Chagas's disease. They were divided into 3 groups according to the severity of myocardial dysfunction. The subjects were submitted to MIBG scintigraphy for evaluation of cardiac sympathetic innervation. The SPECT images were acquired two hours after injection of MIBG. For perfusion analysis was performed targeting the walls of the left ventricle divided into 17 regions.

Therefore, to study the relationships between myocardial tissue injury and autonomic synaptic defects in the context of Chagas disease, it is necessary to observe simultaneously the images of MRI and SPECT.

In this study, was developed methods of research of chronic Chagas cardiomyopathy from methods of image processing to enable the study of topographic correlation between images of MRI and SPECT. Was used techniques of image processing to perform the segmentation of myocardium and to perform segmentation of fibrosis. Moreover, was performed the registration between SPECT images of perfusion SPECT imaging of the sympathetic innervation and MRI images. In this case, was assessed the correlation between the denervated regions and fibrosis regions. Furthermore, was verified the presence of myocardial perfusion defects.

2. Materials and Methods

This study was conducted from the adaptation and improvement of a system that has been successful in using some techniques of image processing to segment myocardial regions in images of MRI [5]. This system was developed to implement the methods of segmentation of epicardial and endocardial borders as well as segmentation and quantification of fibrous tissue in myocardial, for assess patients with infarction. Segmentation of edges (epicardial and endocardial) was based on geodesic active contour [6]. The segmentation of the area of fibrosis was made from the maximum entropy method based on the analysis of texture images and using morphological operators. The user has the option to limit and correct a region of interest to be done processing. The segmentation of the myocardial tissue was taken from the implementation of the method Tsallis entropy. Inspired by multifractal concepts, Tsallis has proposed a generalization of Boltzmann-Gibbs statistics-Shannon (BGS), which is based on generalized entropic form [7]. The q-entropy has been implemented in the system from the following expressions:

$$S_q = \frac{1 - \sum_{i=1}^{k} (pi)^q}{1-q} \quad (1)$$

$$S_q(H_b+H_w) = S_q(H_b)+S_q(H_w)+(1-q)S_q(H_b)S_q(H_w) \quad (2)$$

Where k is the total number of possibilities of the system and the actual number, q is an entropic index that characterizes the degree of non-additivity. H_b represents the entropy of black pixels and H_w represents the entropy of the white pixels.

The quantification of fibrosis on MRI images was performed based on the percentage of fibrosis in relation to the segmented infarction area. The segmentation of the region with low uptake in SPECT images using 99Tc (m) - (MIBI) was performed using the thresholding with threshold equivalent to 50% of the maximum intensity pixel in the segmented myocardium. The segmentation of the region with low uptake in SPECT images with use of MIBG was performed using the thresholding with threshold regarding 30% of the maximum pixel intensity in the segmented myocardium.

To realize the implementation of registration between MRI and SPECT images were used two registration steps. The first step was performed by using the method of Affine registration, for an initial alignment between the MRI and SPECT images. An affine transformation is defined mathematically as a linear transformation plus a constant offset. Then, was used the non-rigid registration method B-Spline, which is implemented in ITK. The B-Spline is a non-rigid registration method which belong to the set of methods that perform free form deformations, of which processing is described by a B-Spline third-order.

The development of the system was continued in the programming language C + + with Qt interface, and was used tools ITK and VTK to perform the segmentation, quantification and visualization of images. The ITK (Insight Toolkit) is a multi platform that provides developers with a comprehensive set of software tools for analysis, segmentation and image registration. The VTK consists of a library that provides a set of tools for visualization and processing images.

The images of the exams are in DICOM format, which is a set of standards for treatment, storage and transmission of medical information in an electronic format, structuring a protocol. Images used in the system must be MRI and SPECT. The MRI images are delayed enhancement using gadolinium. SPECT images were employed using 99Tc (m)-MIBI and SPECT images using MIBG.

3. Results and Discussion

From the application of Geodesic Active Contour and maximizing the Tsallis entropy, it was possible to perform the segmentation of myocardium and the region of fibrosis. After application of the non-rigid B-Spline co-registration between images, were segmented regions of low uptake in SPECT imaging with use of 99Tc (m)-(MIBI) at rest and stress images and SPECT using the MIBG.

The Figure 1 shows the results of segmentation and reg-

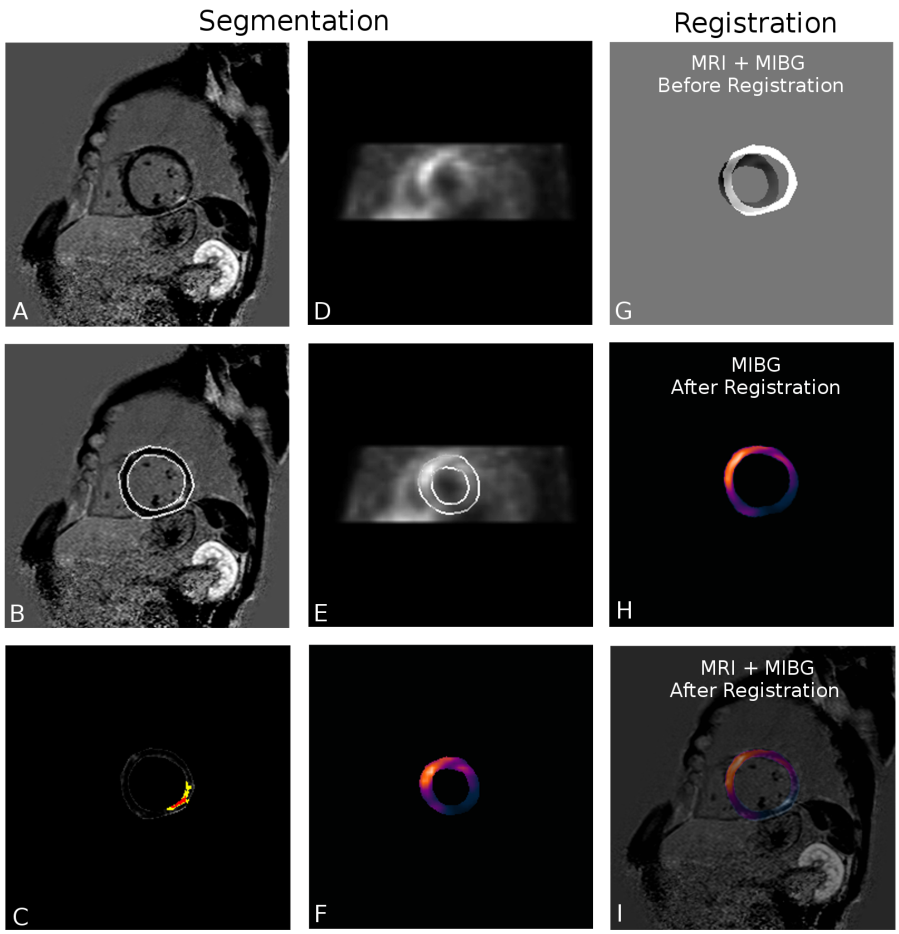

Figure 1. Results of segmentation and registration of MRI and SPECT-MIBG images.

istration of MRI and SPECT images. The image A represents the short axis of the MRI image. The images B and E are observed the endocardial and epicardial borders of myocardium. At image C, it is seen the result of myocardium segmentation, And the segmentation of fibrosis regions. The image D represents the short axis of SPECT-MIBG image. The image F represents the result of myocardium segmentation of the SPECT-MIBG image. The images G and H represents the union of the myocardium in MRI and SPECT-MIBG before and after registration, respectively. At image I, it is observed the result of overlay between MRI and MIBG images after registration, allowing visualization of structural information from MRI and functional information from SPECT in a single image.

From these segmentation and registration, were obtained quantitative data concerning the percentage of fibrosis in the segmented images of MRI and the percentage uptake of MIBG in SPECT images. In Table 1, are found the data obtained from 12 patients with Chagas disease.

With these data, it is possible to show the correlation between damage of myocardial tissue and autonomic innervation. To calculate this correlation, was used the non parametric Kendall correlation test. Was found the Kendall correlation coefficient of 0.8788, indicating a strong correlation between the presence of fibrosis and autonomic denervation. The Figure 2 shows a scatterplot of the vari-

Table 1. Percentage amounts of fibrosis and percentage of uptake of MIBG in patients with Chagas disease.

Patients	%Fibrosis	%MIBG
1	9.8	12.62
2	44.79	42.59
3	29.26	27.69
4	35.75	42.98
5	32.43	34.40
6	28.27	23.60
7	28.64	25.72
8	16.01	13.57
9	27.75	25.46
10	40.88	40.70
11	29.70	31.34
12	41.32	49.92

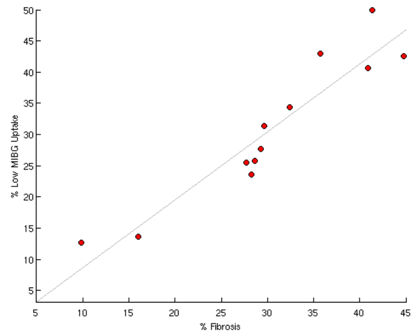

Figure 2. Scatter plot of data related to fibrosis and reduced uptake of MIBG.

able referring to the percentage of fibrosis (X axis) and the variable referring to the percentage of uptake of MIBG (Y axis).

The quantification of MIBI at stress and at rest in SPECT was conducted to perform the analysis of myocardial perfusion. This measurement was performed after co-registration between images acquired at rest and stress. The data obtained are found in Table 2. The average difference obtained between the percentage of uptake of MIBI at stress and at rest was 11.07.

This investigation presented results related to the quantification of fibrosis of MRI images and quantification of MIBG and MIBI in SPECT images. The results obtained in relation to presence of fibrosis and reduced uptake of MIBG showed a great correlation, allowing to relate the presence of injury in myocardial tissues with autonomic denervation in patients with Chagas disease. From the dispersion graphic (Figure 2), is seen a significant relationship between the two variables.

Table 2. Percentage amounts of fibrosis and percentage of uptake of MIBG in patients with Chagas disease.

Patients	%(MIBI-rest)	%(MIBI-str)	%MIBI Str - MIBI Rest
1	18.34	63.18	44.83
2	2.12	3.30	1.17
3	8.57	15.56	6.98
4	31.70	42.38	10.68
5	0.78	6.24	5.45
6	24.07	26.87	2.60
7	6.22	16.62	10.39
8	0.62	4.20	3.57
9	1.83	8.74	6.90
10	2.94	3.21	0.26
11	0	28.66	28.66
12	0.08	11.44	11.36
Mean	8.10	19.20	11.07

From the values found in Table 2, defects of myocardial perfusion are observed in some patients, due to the fact that there is not a homogeneous distribution of the radiotracer throughout the myocardium in stress and rest images.

4. Conclusion

This study showed the advantage of using techniques of segmentation and registration between images, providing combination of tissue characterization and quantification of cardiac innervation.

Thus, the developed tool provides an integrated analysis of information, enabling a better understanding of the relationship between tissue damage and defects in myocardial autonomic innervation, in others words, the relationship between fibrosis and absence or low synaptic activity caused by Chagas disease.

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References

[1] Control of chagas's disease: second report of the who expert committee. World Health Organization 2002 ;905.

[2] Landesmann M, Pedrosa R, Albuquerque J. Cintilografia cardíaca com metaiodobenzilguanidina marcada com iodo-123 em pacientes no estgio inicial da fase crnica da doena de chagas. SOCERJ 2007;20:40–46.

[3] Braunwald E, Libby P, Bonow R, Mann D, Zipes D. Braunwald heart's disease: A textbook of cardiovascular medicine. Saunders 2008;.

[4] Simões M, Pintya A. and BMG, Sarabanda A, Antloga C, Pazin-Filho A, Maciel B, Marin-Neto J. Relation of regional sympathetic denervation and myocardial perfusion disturbance to wall motion impairment in chagas cardiomyopathy. The American Journal Of Cardiology 2000;86:975–981.

[5] Barizon G, Murta-Junior L, Schmidt A. Sistema de segmentação e quantificação de tecidos com insuficiłncia cardíaca por ressonância magnética 2012;.

[6] Ranganath S. Contour extraction from cardiac mri studies using snakes. Medical Imaging IEEE Transactions 1995; 14:328–338.

[7] Tsallis C. Nonextensive statistics: Theoretical, experimental and computational evidences and connections. Brazilian Journal of Physics 1999;29.

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