Quantification of Myocardial Edema and Necrosis during Acute Myocardial Infarction

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Abstract

Quantification of myocardial edema and necrosis during acute myocardial infarct (MI) is crucial for patient's prognosis. The aim of this study was to evaluate these two parameters from MRI Late Gadolinium Enhancement (LGE) and T2 weighted Short Tau Inversion Recovery (STIR) Black-Blood sequences acquired in 22 patients with MI. To estimate the necrosis and edema volumes, a clustering method based on a fuzzy c-means algorithm was used. Results were compared against a manual delimitation and a semi-automatic thresholding currently reported in the literature. The proposed estimation of the necrosis volume was strongly correlated with both the semi automatic method and the manual delineation (r>0.9). For the quantification of the edema, the approach was valid, except for small size infarcts. Thus the automated quantification of necrosis is reliable compared to conventional approaches, and the method is encouraging for the quantification of edema.

1. Introduction

After an ischemic event, the hypoperfused myocardium is defined as the area at risk. Several factors such as the duration of the occlusion and the coronary anatomy in term of presence of collateral vessels predetermine the reversible fraction of the injured myocardium. Prognostic value of the accurate estimation of infarct size is well established but it is also important to know the size of the area at risk. Indeed, the combined knowledge of these two measurements is important for the optimization of therapeutic procedures as well as drug prescriptions. Several studies show the relevance of magnetic resonance imaging in the assessment myocardial injuries after MI, indeed MRI Late Enhanced Gadolinium (LEG) sequence enables the visualization of necroses [1] while the T2 weighted Short Tau Inversion Recovery (STIR)-Black-Blood sequence enables the visualization of the edema [2].

Since myocardial functional recovery after an acute coronary event is inversely correlated with the extent of injured myocardium, it is crucial to measure it accurately. In this context, several quantitative or semi quantitative approaches have been proposed to overcome the subjective nature of the visual analysis which is commonly used in the clinical routine. The most known methods use thresholds which are based on statistical criteria such as the mean gray level (m) and its standard deviation (SD) in the normal myocardium. The threshold value is defined as [mean intensity value (m)]+k.[standard deviation (SD)], and the factor k varies from 1 to 6 according to the study. However, k=2 or 3 are the most commonly used factors; they have been validated in several studies against histology [3]. A second class of methods was based on full-width at half maximum (FWHM) criteria: the user clicks in the hyperenhanced region, and a multi pass growing algorithm is used to delineate the infarcted area [3]. For all these methods, in addition to the delineation of myocardial borders, the operator has to delineate a region within a remote and/or infarcted tissue which increases variability.

In this paper, a semi-automatic method based on the unsupervised algorithm of the fuzzy c-means clustering which was previously presented in combination with a specific circumferential and radial segmentation of the myocardium to assess the transmural extent of myocardial infarction [4] was used to quantify myocardial necrosis volume and adapted to the T2 weighted STIR images to quantify the edema volume.

2. Methods

2.1. Data Acquisition

MR imaging was achieved according to a standard clinical protocol using a 1.5 Tesla system (Gyroscan Intera, Philips, Best, The Netherland), using a thoracic five-element phased array thoracic coil and the SENSE

technique.

For each patient, 8 to 12 T2 weighted (STIR) short axis slices were acquired (TR= 3.RR ms, RR being the duration of one cardiac cycle, TE= 80 ms, flip angle=90°, matrix size=512x512, slice thickness= 8 mm).

Then 10 to 20 minutes after an intravenous Gd-DTPA injection (0.2 ml/kg), 12 to 16 late enhanced (LGE) short-axis slices were acquired (TR=4 ms, TE=2 ms, flip angle=20°, matrix size=256x256, slice thickness= 6 mm), the inversion time (TI) being chosen in order to minimize the signal in the remote myocardium.

2.2. Manual Analysis

The same procedure was applied to both STIR and LGE data. Extreme basal slices containing bright areas corresponding to the aortic flow tract were excluded from the analysis. The manual contouring was performed using the Philips Viewforum software platform. A first area was defined on the remote myocardium, as large as possible. Mean value and standard deviation of intensity inside that region were computed. A threshold equal to the mean value plus two times the standard deviation was first applied and the infarcted area was then manually contoured. Using this threshold allowed us to define a standardized approach. On STIR data, epicardial enhancement due to inflammatory pericardium was removed. On LGE data, no reflow zones were included in the infarct zone. Results obtained with this procedure are further referenced with "MANU".

2.3. Quantification of scared tissue and edema

Endocardial and epicardial borders were first manually delineated by a cardiologist on each slice of the T2 weighted and LGE sequences.

Conventional thresholding methods were implemented in order to compare them with the proposed method. Thus, the cardiologist defined a remote region, the mean value (m) and standard deviation (SD) of intensity in that region were computed and pixels with values higher than m+k.SD, k being an integer between 1 and 6 were counted as "enhanced pixels". Results obtained with this procedure are referenced with "m+kSD".

Our approach was based on the fuzzy c-means algorithm, which classifies image pixels by computing their measure of membership for a specified class [4]. For both necrosis and edema two classes were considered: (1) for LGE data the algorithm was applied slice by slice on a region of interest which includes myocardium and cavity. The first class contains enhanced pixels, i.e. cavity and scare while the second class characterizes non enhanced pixels, i.e. remote myocardium. Of note, the cavity was considered in the classification process to be able to define both the enhanced and the non enhanced classes even in normal slices. (2) On the T2 weighed images, the cavity is dark while the myocardium can be whether dark gray, in normal regions, or bright in abnormal regions. Accordingly, on these datasets the fuzzy c-means algorithm was applied on the myocardial volume and two classes were defined: bright pixels corresponding to the edema and dark gray pixels corresponding to the remote myocardium. Results obtained with this procedure are referenced with "FUZZ".

2.4. Comparison of approaches

Surface areas and volumes were computed for the different methods and expressed as a percentage of the total myocardial area and volume which was estimated from the manual contouring of endocardial and epicardial borders. Linear regression (LIN REG) was applied to the different automated methods versus the manual approach. A second linear regression with zero intercept was carried out (LIN0 REG). Equations and coefficient of correlation (CC) were also reported. Moreover to take into account that the manual contouring was not a "perfect" gold standard, Bland-Altman plot was used to compare each pair of methods. Mean differences (MD) and standard deviation of differences (SDD) were then reported.

3. Results

Concerning the "m+kSD" approach, only results obtained with k=2 and k=3 were presented, since larger biases were obtained with k=1 or k>3.

3.1. Necrosis estimation from LGE studies

Table 1 indicates the comparison of the "m+2SD", "m+3SD", and "FUZZ" approaches with the "MANU" estimation of the area surfaces. Table 2 indicates the comparison of the previous methods for the global volumes. Figures 1 and 2 are the plots of surface areas for "FUZZ" and "m+2SD" approaches versus the manual contouring. On both figures, the linear regression with zero intercept was indicated by straight lines.

Table 1. Comparison of the surfaces of the infarcted areas that were estimated by the different approaches versus the manual contouring (n=222 slices).

	"FUZZ"	"m+2SD"	"m+3SD"
LIN REG	0.77x +0.01	0.76x+ 0.06	0.69x+0.02
CC	0.90	0.90	0.87
LIN0 REG	0.80x	0.98x	0.77x
CC	0.90	0.81	0.85
MD	-1.9%	2.8%	-1.5%
SDD	5.5%	5.6%	6.4%

Table 2. Comparison of the volumes of the infarcted areas estimated by the different approaches versus the manual contouring (n=22 patients).

	"FUZZ"	"m+2SD"	"m+3SD"
LIN REG	0.80x +0.01	0.80x+ 0.05	0.73x+0.02
CC	0.93	0.94	0.93
LIN0 REG	0.81x	1.09x	0.82x
CC	0.93	0.86	0.91
MD	-2.3%	2.6%	-1.7%
SDD	3.0%	2.7%	3.3%

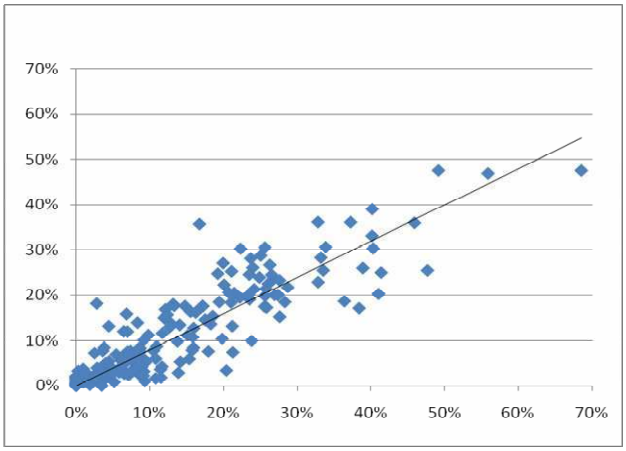

Figure 1. Comparison of the surfaces of myocardial infarcts estimated by the "FUZZ" approach versus the "MANU" approach.

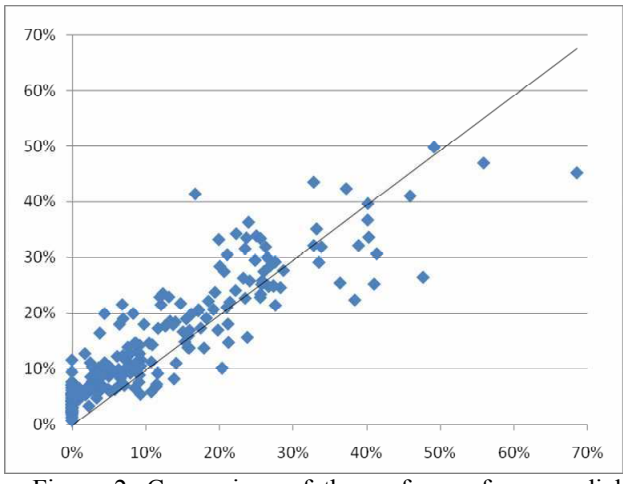

Figure 2. Comparison of the surfaces of myocardial infarcts estimated by the "m+2SD" approach versus the "MANU" approach.

3.2. Edema estimation from STIR studies

The comparison of the different methods was applied to a preliminary subgroup of 10 patients on a total of 64 slices. The table 3 indicates the comparison of the three methods "FUZZ", "m+2SD", and "m+3SD" with the manual contouring of hyperenhanced areas on STIR images. Linear regression with zero intercept was not reported since it was not appropriate in that case.

Table 3. Comparison of surfaces of the edematous areas detected by the different approaches versus the manual contouring (n=64 slices).

	"FUZZ"	"m+2SD"	"m+3SD"
LIN REG	0.55x +0.19	0.61x+ 0.17	0.61x+0.06
CC	0.59	0.67	0.77
MD	4.7%	5.4%	-6.2%
SDD	17%	15%	12%

4. Discussion and conclusions

The validation of infarct size on human studies is not possible, since there is no way to have an access to experimental measures. Thus, in this situation, there is no gold standard. In these conditions, the validation of any computer software is difficult. However, several studies on animal studies have shown a good correlation of volumes estimated by manual contouring on MR data with volumes estimated on histological sections. Moreover, a recent study has shown excellent intra- and inter-operator [5] reproducibility in the manual estimation of infarct size. Similarly, it was shown that the "m+2SD" or "m+3SD" approaches provided also correct estimations. However, several studies (e.g. [3]) have pointed out a slight overestimation of the infarcted volumes, when using the "m+2SD" approach in a canine model.

In this study, results obtained on the volumetric estimation showed a reduced bias and a reduced standard deviation when comparing each automated method with the manual one (Table 2). Moreover, results of linear regression with zero intercept tend to show that the "m+2SD" overestimates the volume, while the "FUZZ" method and the "m+3SD" tend to underestimate this volume (Table 2). This latter result remains true when considering the surface areas for each individual slice (Table 1). Using the "m+2SD" approach, Figure 2 indicates that the surface area of the myocardial infarct tend to be overestimated in small infarcts (especially when it is less than 10% of the myocardial area) and underestimated in larger infarcts. The underestimation can be explained by the fact that none of these approaches include no reflow areas in the infarct volume, while the manual approach include these areas in the infarct. As this 'no reflow' pattern occurs more frequently for large infarct size, the underestimation effect is more pronounced in those cases. To take the 'no

reflow' pattern into account, some supplementary rules should to be added to the segmentation process in order to add in the infarct region the pixels with low gray level values but included inside an enhanced region. Finally the thorough comparison of Figures 1 and 2 show that for small infarct size, the "FUZZ" approach is more adapted than the "m+2SD" approach, since it does not provide a systematic overestimation of the volume. Indeed, this capacity of the "FUZZ" method to process slices, even if there is no necrosis, was already demonstrated in [4] and is successful thanks to the inclusion of the cavity for the segmentation in two classes.

Thus, this experimental study shows the robustness of the segmentation approach based on the fuzzy c-means algorithm. Indeed, good results were obtained to define the infarct area in two different studies: the present one and the one published in [4] that were conducted in two different centers, with two different scanners.

The first results that were obtained on STIR data (Table 3) confirm that the "m+3SD" method as proposed by [7] is acceptable to delineate semi automatically the percentage of enhanced area surface. Nevertheless, results obtained by the automated approaches are less convincing on STIR data than on LGE data. However, the thorough examination of these results revealed an outlier patient. When removing the 7 slices associated to this patient a large improvement was observed (Table 4) in the performances of the automated methods, the "FUZZ" method providing a fine estimation. Moreover, this outlier patient was the patient having a small edematous volume. It is possible that the separation into two classes (normal tissues and edematous tissues) failed in that particular case. Further tests need thus to be carried out in order to evaluate the automated approaches on STIR data.

Table 4. Comparison of the surfaces of the edematous areas estimated by the different approaches versus the manual contouring, when removing the outlier patient (n=57 slices).

	"FUZZ"	"m+2SD"	"m+3SD"
LIN REG	0.73x +0.10	0.75x+ 0.10	0.68x+0.02
CC	0.80	0.79	0.84
MD	0.4%	2.0%	-8.6%
SDD	12%	12%	10%

In conclusion, the approach based on the c-means algorithm allows an objective estimation of necrosis and edema volumes and showed to be strongly correlated to the conventional methods, which are either manual or semi automatic. Combined with an automated detection of the endocardial and epicardial borders, this method may prove clinically useful and save time in the measurement of volumes. This task is difficult when considering only LGE studies, due to the inhomogeneities in the myocardial wall and the possible confusion between the infarct and the cavity. But it could be performed more easily on STIR data or cine data and then reported on LGE data. To achieve it, the segmentation method proposed in [8] is currenly under investigation.

References

[1] Gerber BL, Garot J, Bluemke DA, Wu KC, Lima JA. Accuracy of contrast-enhanced magnetic resonance imaging in predicting improvement of regional myocardial function in patients after acute myocardial infarction. Circulation 2002; 106:1083–1089.

[2] Aletras AH, Tilak GS, Natazon A, Hsu LY, Gonzalez FM, Hoyt RF Jr, Arai AE. Retrospective determination of the area at risk for reperfused acute myocardial infarction with T2-weighted cardiac magnetic resonance imaging: histopathological and displacement encoding with stimulated echoes (DENSE) functional validations. Circulation 2006; 113(15):1865-70.

[3] Amado LC, Gerber BL, Gupta SN, Rettmann DW, Szarf G, Schock R, Nasir K, Kraitchman DL, Lima JA. Accurate and objective infarct sizing by contrast-enhanced magnetic resonance imaging in a canine myocardial infarction model. J Am Coll Cardiol 2004; 44:2383–2389.

[4] Kachenoura N, Redheuil A, Mousseaux E, Herment A, Frouin F. Robust assessment of the transmural extent of myocardial infarction in late gadolinium-enhanced MRI studies using appropriate angular and circumferential subdivision of the myocardium. Eur Radiol 2008; (in press).

[5] Thiele H, Kappl MJ, Conradi S, Niebauer J, Hambrecht R, Schuler G. Reproducibility of chronic and acute infarct size measurement by delayed enhancement-magnetic resonance imaging. J Am Coll Cardiol 2006; 47(8):1641-5.

[6] Hsu LY, Natanzon A, Kellman P, Hirsch GA, Aletras AH, Arai AE. Quantitative myocardial infarction on delayed enhancement MRI. Part I: Animal validation of an automated feature analysis and combined thresholding infarct sizing algorithm. J Magn Reson Imaging 2006; 23:298–308.

[7] Ibanez B, Prat-González S, Speidl WS, Vilahur G, Pinero A, Cimmino G, García MJ, Fuster V, Sanz J, Badimon JJ. Early metoprolol administration before coronary reperfusion results in increased myocardial salvage: analysis of ischemic myocardium at risk using cardiac magnetic resonance. Circulation 2007; 12;115:2909-2916.

[8] El Berbari R, Kachenoura N, Redheuil AB, Herment A, Bloch I, Mousseaux E, Frouin F. An Automated Evaluation of Regional Left Ventricular Function on Cine MR Images. Computers in Cardiology, 2008.

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