

# Texture Analysis to Assess Risk of Serious Arrhythmias after Myocardial Infarction

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## Abstract

*Implantable cardioverter-defibrillator (ICD) prevents sudden cardiac death in patients with healed myocardial infarction (MI) at high risk of serious arrhythmias. This study was designed to identify if texture analysis of cardiac magnetic resonance (CMR) images can be used to identify high-risk patients likely to benefit from ICD implantation.*

*Two groups of patients with MI were compared: 24 patients with indication for ICD and 37 patients with healed MI and no ICD indication corresponding to high and low risk of arrhythmia respectively. Statistical and texture descriptors were calculated in segmented late gadolinium enhancement images. ICD- and non-ICD patients were compared using pattern classification methods. The specificity to discriminate ICD- and non-ICD-patients was calculated at a sensitivity of  $\geq 90\%$  by combining one, two or three features.*

*LVEF alone was able to discriminate the two groups with a specificity of 70% (CI:57-81%). Combining LVEF with one texture descriptor of the non-scarred myocardium increased specificity to 81% (CI:69-89%) and with two texture descriptors of non-scarred myocardium and infarct further increased specificity to 84% (CI: 72-91%).*

## 1. Introduction

A large proportion of sudden cardiac death in patients with coronary heart disease is due either to ventricular tachycardia (VT) or ventricular fibrillation. Survival in these patients can be improved by implantable cardioverter defibrillator (ICD)[1]. The failure to identify the most susceptible patients at high risk has led to a strategy of implanting an ICD based upon reduced left ventricular ejection fraction (LVEF)[1]. The use and acceptance of guidelines are controversial, and cost-effectiveness is a great concern. Therefore, a better risk stratification, beyond simple LVEF cut-offs, is required to identify those who benefit

most from ICD implantation.

Cardiac magnetic resonance (CMR) provides a reference method for the assessment of cardiac function and morphology. The use of late gadolinium enhancement (LGE) techniques during CMR examinations allows precise description of scar characteristics and cardiac morphology. LGE studies suggest that the risk of inducible VT is greater in patients with large myocardial infarctions[2]. Expanding on these findings, several recent studies have suggested that the peri-infarct gray-zone may be involved in the generation of fatal arrhythmia[3–5].

These previous studies have quantified both the infarct size and peri-infarct gray-zone by delineating areas of LGE, using different signal intensities to separate the tissues. However, this technique provides limited information: first, only information on the size of scarred and partially scarred myocardium is provided; and second, the technique does not provide information on tissue characteristics from non-scarred myocardium that may also be important for the generation of fatal arrhythmias.

Analysis of image texture can be used to quantify the spatial distribution pattern of gray levels in both scarred and non-scarred areas of the myocardium within the LGE image. The basic principle for the method used in this study is based on estimates of the probability of occurrence of two gray level values for two adjacent pixels (co-occurrence)[6]. The image texture features characterize the underlying structure of the tissue involved.

The purpose of this study is to explore if texture analyses of LGE-CMR images are able to identify patients with low and high risk of arrhythmias.

## 2. Material and methods

The high arrhythmic risk group (ICD-patients) consisted of 36 patients, consecutively examined between 2006 and 2007, with ischemic heart disease, myocardial scars and an indication of the need for ICD implantation. The image quality was insufficient for texture analyses in 12 patients, leaving 24 patients in whom ICD was implanted for sec-

ondary prevention in 18 patients (9 survivors of sudden-cardiac-death and 9 symptomatic VT), and primary prevention in 6 patients with LVEF < 30% and non-sustained-VT (NSVT). The non-ICD-patients consisted of 37 patients with STEMI who had been successfully revascularized with primary PCI one year prior to LGE-CMR examination. The study was approved by the Regional Ethics Committee, and informed consent was obtained from all patients.

CMR was performed with a 1.5 T Philips Intera R 8.3. Functional assessment of LVEF, volumes, and mass were performed according to current recommended standards with the use of steady-state, free precession sequence covering the whole LV with 8-mm thick short axis slices, and an inter-slice gap of 2 mm. After functional assessment, a gadolinium based contrast agent was administered intravenously at a dosage of 0.25 mmol/kg. LGE images were acquired 10-15 minutes later, using an inversion recovery-prepared T1 weighted gradient-echo sequence with a pixel size of 0.82x0.82 mm<sup>2</sup>, covering the whole ventricle with short-axis slices of 10 mm thickness, without inter-slice gaps.

All conventional post-processing (volumes, mass, infarct size) was performed using the View Forum<sup>TM</sup> Software (Philips Medical Systems, Best, The Netherlands). Assessment of LV volumes and mass, as well as scar characteristics, were performed on both full short-axis datasets in a random, blinded fashion. Indexes for LV mass and volumes were obtained by division of body surface area. Scar size was assessed manually with planimetry on each short-axis slice, delineating the hyperenhanced area, and adding all slices to generate scar volume.

The feature analyses were performed on stored DICOM (Digital Imaging and Communications in Medicine) images with a pixel resolution of 512x512, using MATLAB (The MathWorks, Inc., Natick, MA, USA). The images were segmented as illustrated in Figure 1. The left ventricular area and the scar area were assessed interactively on each short-axis slice, delineating the left ventricle and the hyper-enhanced area. An optional number of coordinates, marked as gray dots on the figure, is set by an experienced CMR cardiologist (S) using the mouse pointer. The contours are generated as cubic spline interpolations of these coordinates. The yellow contours mark the inner and outer boundary of the myocardium. The red line marks the contour of the the scar area. In this work we define two other areas; the core zone and the border zone. The core zone is defined for each image as follows: the highest intensity value of the pixels in the scar area, max-level, is found, as well as the standard deviation, SD scar, of the pixel values in the scar area. All pixels in the scar area with intensity level greater than (maxlevel - 2\*SDscar) defines the core zone. Thus, the core zone may either be a single connected

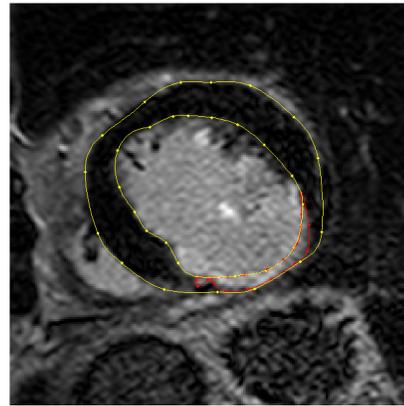


Figure 1. Segmentation of myocardium and scar.

area, or it might consist of a number of islands within the scar area. The border zone is defined by several operations. Firstly, the convex hull of the scar area is found. The convex hull area of the scar divided by the scar area is called the contour around the scar, and if close to 1, the scar area is quite regular. The convex hull area is further enlarged by performing a morphological dilation being limited to the segmented myocardium area. Finally the border zone is defined as the dilated area after subtraction of the core zone.

An important approach in describing the affected region is to quantify and describe its texture, which provide measures of its properties such as smoothness, coarseness and regularity. Textures can be described in three principal approaches: statistical, structural and spectral.

In all features calculated from the non-scarred myocardium, (ie. the normal tissue), the border zone + core zone (i.e. the dilated scar area) is subtracted from the segmented myocardium. This is done to ensure that tissue regarded as normal tissue does not include a border area with a potential different texture. A number of features describing sizes, statistics and textures of the segmented and defined areas of the LGE-CMR images might be indicative of differences between the ICD- and non-ICD-patients. Several hundred features are investigated for each patient according to the principles for exploratory data analysis described in [7], with the exception that for the texture parameters derived from cooccurrence matrix the values derived from the different angles are averaged.

Maximum likelihood estimation based Bayes classifiers are used to determine decision regions to discriminate the ICD- from the non-ICD-patients. A probabilistic approach is used to control the relative size of the decision regions to yield predefined TP values and to calculate the correspond-

ing TN values[8]. From the ROC curve corresponding to the calculated (TP,TN) coordinates, the area under the curve is determined as a measure of discriminatory power. The experiments are conducted, using a “leave one out” re-sampling technique in which a classifier is designed from a training set of data from all patients except one which is left out for testing the model. This procedure is repeated so that eventually all patients will have been tested. The performance is evaluated by calculating the ROC curves from the classification model, from the training set and from the tested data denoted respectively as training, reclassification and testing performance. In the evaluation of different feature combinations, all 1D-combinations are first evaluated. Furthermore, all 2D combinations of features with 1D-AUC performance exceeding a specific level are also evaluated. The same principle is used when higher dimensional combinations are evaluated.

The test results corresponding to the sensitivity set to 95% in the training, are presented if the mean sensitivity is between 90% and 95%. These results are ranked according to descending values of specificity. In the presentation of results from combining two or three features, multiple occurrences of a specific feature are reduced to the one with the best performance. Patent is pending for the method of characterization and prediction.

### 3. Results

During one year follow-up, VT was recorded in 20 out of 24 ICD-patients. There were no recorded ventricular arrhythmia, deaths or resuscitated cardiac arrests in the non-ICD-patients. The groups were equal according to gender, body surface area, and treatment with angiotensin-converting-enzyme inhibitors or angiotensin type 2 receptor blockers. ICD-patients were older, and had a longer history of CHD, lower LVEF, and larger scars, larger volumes and LV mass. ICD patients had higher creatinine, and were more often treated with beta-blockers than the non-ICD-patients.

An overview of the ability of the parameters to discriminate between ICD- and non-ICD-patients for the best 1D, 2D and 3D combinations are shown in Figure 2 with 95% confidence intervals. LVEF alone was able to discriminate the two groups with a specificity of 70% (CI:57-81%). Combining LVEF with one texture descriptor of the non-scarred myocardium increased specificity to 81% (CI:69-89%) and adding scar size as a third descriptor further increased specificity to 84% (CI: 72-91%).

### 4. Discussion

This study demonstrates that texture analyses of CMR images provide additional information beyond that of conventional parameters for the assessment of patients with

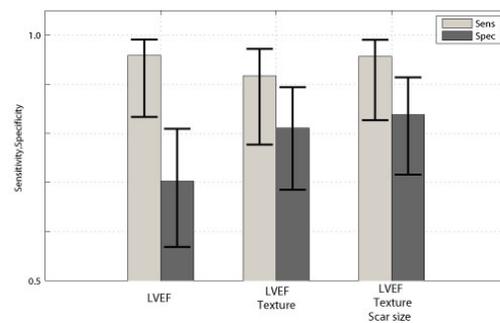


Figure 2. Performance for the best 1D, 2D and 3D feature combinations.

high risk of arrhythmia and ischemic heart disease. The results indicate that when LVEF is combined with texture measurements of myocardium and infarct, the ability to identify patients with high risk of arrhythmia improves. Moreover, it suggests that structural alterations within the non-infarcted myocardium may be important substrates for life-threatening arrhythmia.

This study assesses different approaches for the utilization of texture analysis in a clinical setting, attempting to improve the identification of patients at risk of serious arrhythmias. In this study we did not correlate our findings directly with a histopathological assessment. We therefore cannot be certain of a specific relationship between texture features and histopathological changes. However, several lines of evidence suggest that texture features are related to specific tissue characteristics. The histopathological correlation of fibrosis and hyperenhancement of postinfarct scar is well documented[9, 10]. Texture features characterize the underlying structure of the objects shown in the image. MRI images of tissue do not provide microscopic information, but histological alterations may cause texture changes amenable to texture analysis.

Quantitative features, such as size of non-infarcted myocardium, infarct zone, core- or gray zone have previously been used as indexes of tissue heterogeneity[2–5, 11]. Despite significant differences by univariate analyses, with the exception of core assessment, these features were inferior in comparison with texture features in their ability to distinguish ICD- from non-ICD-patients. This is in line with a previous publication that suggests that important pathophysiological information is lost if only the size of the enhanced myocardium is assessed by CMR in patients with ischemic heart disease[11]. In follow up studies we have further explored methods to express tissues by texture methods for improving our assessment of these patients[12, 13].

This is a small study with a large number of features assessed and it is a possibility our results may have appeared

by chance. To evaluate the degree of chance, we have randomized the categorization of the patients into ICD- and non-ICD-patients (Figure 3). The figure indicates that for

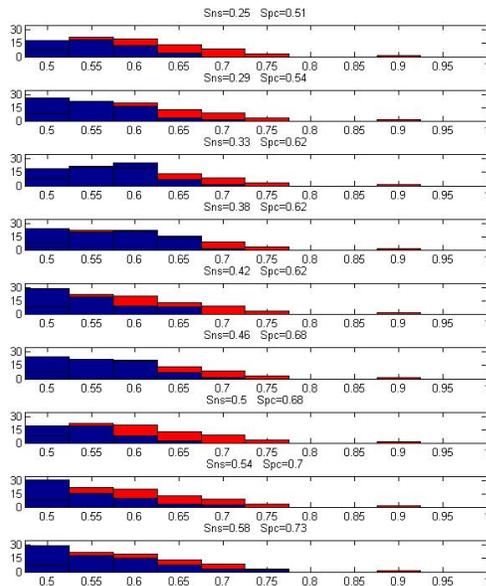


Figure 3. AUC histograms for true (red) and corrupted (blue) class divisions for 1D features. The proportion of the original patient categorization is increased from top to bottom.

the random classes, there are few features achieving high AUC values, but the AUC value increases as a larger proportion of the true categorization is observed. This indicates that the results have not appeared purely by chance. To evaluate the impact of texture analyses on risk of arrhythmias we needed to compare our high-risk group with MI patients clinically found to be at low risk of arrhythmias, although short episodes of VT in the controls cannot be excluded, since these patients were not constantly monitored with ICD. We used an arbitrary signal-intensity (SI) threshold (Max.SI-2SD) to delineate the core infarct. The selected method to study the gray zone is also a limitation since the border of this zone is currently not known.

## 5. Conclusion

The use of texture analysis in LGE-CMR images has been explored using pattern classification methods. The present study demonstrates that texture analyses of LGE-CMR contain information with the potential to increase prediction of serious ventricular arrhythmias.

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