A Practical Algorithm for Improving Localization and Quantification of Left Ventricular Scar

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Abstract

Current approaches to classification of left ventricular scar rely on manual segmentation of myocardial borders and manual classification of scar tissue. In this paper, we propose an novel, semi-automatic approach to segment the left ventricular wall and classify scar tissue using a combination of modern image processing techniques.

We obtained high-resolution magnetic resonance angiograms (MRA) and late-gadolinium enhanced magnetic resonance imaging (LGE-MRI) in 14 patients who had ventricular scar from a prior myocardial infarction. We applied (1) a level set-based segmentation approach using a combination of the MRA and LGE-MRI to segment the myocardium and then (2) an automated signal intensity algorithm (Otsu thresholding) to identify ventricular scar tissue. We compared results from both steps to those of expert observers. The LV geometry using the semi-automated segmentation method had a mean overlap of 94% with the manual segmentations. The scar volumes obtained with the Otsu method correlated with the expert observer scar volumes (Dice comparison coefficient of 0.85$\pm$ 0.11). This proof of concept segmentation pipeline provides a more objective method for identifying scar in the left ventricle than manual approaches.

1. Introduction

A long-term consequence of ventricular scar formation due to myocardial infarction (MI) is the increased risk of malignant ventricular arrhythmias and sudden cardiac death (SCD).[1] As early revascularization treatment for myocardial infarction has improved, ventricular scar formation has become more heterogeneous than in the past, with an overall increased area of surviving myocardial tissue interspersed with dense scar and transition (border) zones of intermediate scar density [1, 2]. These areas of ventricular scar create the substrate for reentry circuits, leading to ventricular tachyarrhythmia. Such reentry circuits are thought to result from slowed conduction through channels of myocardial scar tissue.[2] Clinical electrophysiologists have learned to target these regions of comprised tissue and especially the border between healthy and scarred myocardium during ablation procedures to eliminate these ventricular tacychardias.[2]

The current standard of care for such cases includes obtaining late gadolinium enhancement magnetic resonance images (LGE-MRIs) before the ablation procedure to visualize scar for procedure planning.[3] Currently physicians simply view the raw LGE-MRIs or use time-consuming and subjective manual image processing techniques to identify the scar tissue. Another approach is to use manual measurements of approximate scar volume percentages, which provide only global metrics and so lack the high-resolution, three-dimensional models of the LV myocardium that provide patient specific, spatial descriptions of scar heterogeneity and architecture. Such spatial models hold promise for identifying potential reentrant channels involved in ventricular arrhythmias as well as assessing individual risk of SCD.

We designed and tested an image processing pipeline that could quickly, accurately, and objectively segment the epicardial and endocardial borders of the LV as well as objectively classify regions of scarred myocardium within the ventricular wall. This pipeline begins with Magnetic Resonance Angiogram (MRA) and a threshold-based level set segmentation algorithm to define the endocardium.[4] We then applied the Otsu threshold method to classify regions of scar tissue within the myocardial wall segmentation.[5]

For validation, we compared all the results from our approaches to manual assessments by expert observers.

2. Methods

LGE-MRI images of the heart were obtained approximately 15 min after the injection of 0.1 mmol/kg gadolinium contrast (Multihance, Bracco Diagnostics, Inc., Princeton, New Jersey) using a 3D respiratory navigated, inversion recovery, prepared gradient echo pulse sequence (repetition time 3.0; echo time 1.4 ms; flip angle 14; bandwidth 740 Hz/pixel; field of view 400 400 110 mm; matrix size 320 320 44; 9% oversampling in the slice encoding direction; voxel size $1.25 \times 1.25 \times 2.5$ mm; phase-encoding direction: left to right; fractional readout 87.5%; partial Fourier acquisition: 90% in phase-encoding direction and 92.5% in slice-encoding direction; generalized autocalibrating partially parallel acquisitions with R = 2 in phase-encoding direction). An inversion pulse was applied every heartbeat, and fat saturation was applied immediately before data acquisition. Data acquisition was limited to 15% of the RR cycle and was performed during LA diastole. To preserve magnetization preparation in the image volume, the navigator was acquired immediately after the data acquisition block.

Typical scan time for the LGE study was 4 to 8 min, depending on heart rate and respiratory pattern. Of the 60 patients identified with a history of myocardial infarction (MI) who also had post MI LGE-MRI performed, 14 had ventricular scar. Three patients were female and eleven patients were male. The mean age of the patients was 71 ± 10.47 years old and the mean LV ejection diffraction was $54.1 \pm 10.4\%$. Twelve of the 14 patients underwent coronary revascularization with either percutaneous coronary intervention or coronary artery bypass grafting.

To segment the LV wall, we developed a semi-automated algorithm that used the following approach, known as "MRA fusion" implemented in Corview (Marrek, Inc.), a segmentation and analysis tool specifically designed for cardiac MRI processing. Figure 1 contains images of results from a single patient at various stages of this pipeline.

The MRA fusion tool pipeline consists of the following steps:

1. First, an expert user sets an intensity threshold marking the maximum possible extent of the segmentation.
2. The expert selects a seed point inside the ventricle to serve as a starting point for the level-set segmentation algorithm.
3. The level-set based segmentation algorithm performs a region growing process from the seed point to identify the endocardial border.[4, 6]
4. The MRA and LGE are registered using a rigid image-to-image registration technique and a transform is generated.[7, 8] The images from the MRA and LGE sequences generally align very closely in space due to the acquisition parameters and limited time between acquisitions, so a minimal rigid registration is all that is typically necessary.
5. The level-set segmentation result is adjusted via the registration transform to move it into the LGE coordinate system.
6. The resulting transformed segmentation is smoothed with a median image filter and has small islands removed and holes filled. The level set segmentation filter generally provides a smooth edge, however when it is constrained by a threshold, it can produce jagged edges that require smoothing. After the smoothing step, there may be some small islands or holes of a few pixels in area in the segmentation that are corrected using standard erosion/dilation filters.[7]

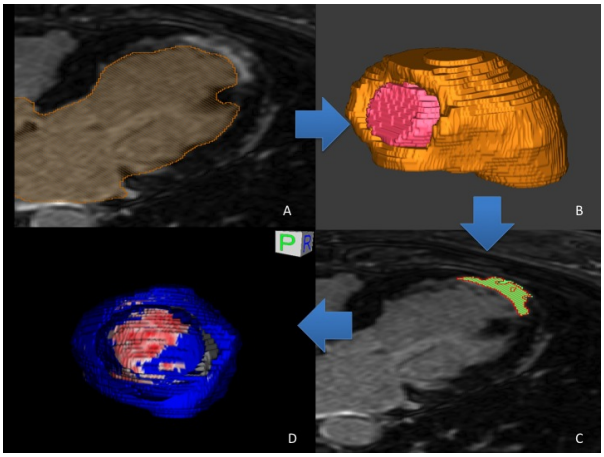

Figure 1. Overview of segmentation and quantification pipeline. [A] Orange mask layer: raw output of semi-automated segmentation tool, [B] Three dimensional reconstruction of the blood pool (pink) and myocardium (orange) following cleanup of small image processing errors, [C] Scar selection of expert user (red) and Otsu method (green), and [D] Three dimensional reconstruction of myocardium (blue) with scar location and architecture (red hue).

After the endocardial segmentation is complete, the epicardial border is defined using a dilation of seven pixels from the endocardium followed by minor manual modifications to fit against the epicardial border visible in the images.

The Otsu thresholding algorithm performs a classification of image pixels into foreground and background by finding an optimal bimodal clustering of the intensity distribution in the image.[5] In our case, the goal was separation of the relatively bright, enhanced pixels that are associated with scar in the LGE-MRI from the relatively dark

pixels associated with normal myocardium. Some manual adjustments were then necessary to eliminate extraneous bright pixels in the normal myocardium that represent image noise.

To validate our LV wall segmentation method, we compared against a ground truth dataset from five subjects created using fully manual segmentation by an expert observer. The expert identified and traced the endocardium in each slice of the LGE-MRI and we compared the results to those from the MRA fusion method. Statistical comparison of segmentations of the semi-automated and manual methods was by means of the Dice coefficient.[9] To compare efficiency of both methods, we measured and compared the real time required for the both approaches.

We tested separately the accuracy of the Otsu thresholding technique by comparing the scar volumes manually defined by two expert observers to those of the Otsu method using the correlation coefficient and the Dice coefficient. We also carried out qualitative comparisons based on visualization of both sets of results.

3. Results

The endocardial segmentations using the MRA fusion method were slightly faster than the manual approach (46±8.9 m versus 50.6±7.53 m). Although not statistically improved, the time required for the MRA fusion segmentation approach demonstrates over 5 subjects a trend towards increased efficiency. More important, the accuracy of the semi-automatic segmentations compare very favorably with the ground truth manual segmentations (mean Dice coefficient = 0.94±0.01) (See Table 1 for a summary of results).

Table 1. Segmentation Comparison by means of Dice Coefficients. The Dice coefficient for each of the five cases tested showed excellent overlap between semi-automated and manual approaches

Scan	Dice Coefficient
1	0.95
2	0.94
3	0.93
4	0.96
5	0.94
Mean	0.94 ± 0.01

We compared the results among expert observers to determine the inter-observer variability in manual classification of scar and found a mean Dice coefficient of 0.83±0.18 across the 2 observers and 14 scans. The Otsu threshold method had even better overall agreement to the results of the two observers, Dice coefficient 0.89±0.08 vs. Observer 1, and 0.82±0.13 vs. Observer 2 (overall mean Dice coefficient = 0.85±0.11). The Otsu scar classifications was within the variability of expert observers. It should be emphasized that the Otsu method, a deterministic, fully automatic method, provides repeatable, consistent classifications with no variability for a given input. Clinically, these results suggest that this automated method can accurately describe the ventricular scar patterns in patients post MI with greater consistency than expert observers.

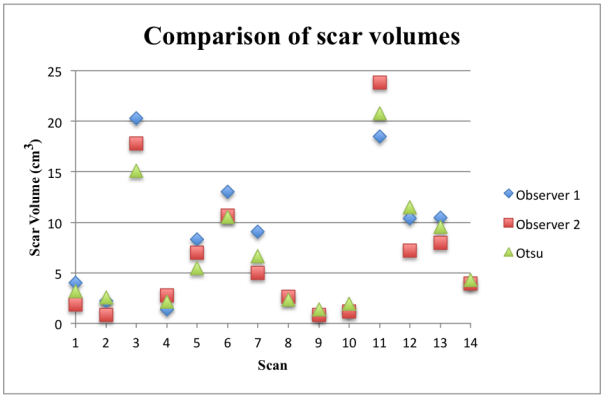

Figure 2. Plot of scar volumes from two expert observers and the output of the Otsu method.

4. Discussion

In this study, we proposed and evaluated a semi-automated approach for detection of LV scar from LGE-MRI images for procedure planning. Our results suggest that an automated approach may provide a more robust and repeatable way to identify LV scar than a manual thresholding approach. While not achieving statistical significance, the trend toward more rapid completion of the evaluation is promising.

The clinical importance of this segmentation pipeline lies in the requirement for physicians to accurately visualize scarred myocardial tissue following a MI in order to evaluate risk and plan subsequent therapy. Only by first identifying and characterizing the scar that forms, is it possible to begin to evaluate the risk that such scar poses for subsequent arrhythmic events and even sudden cardiac death. Providing the results of such an evaluation to the physician prior to ablation procedures (the only current treatment with truly curative potential) would support accurate integration of myocardial scar into ventricular substrate mapping and thus increase the efficiency and potentially the success of the outcome of the ablation procedure. This pipeline could also be used to track the rate, the extent, and the pattern of scar development over time in patients suffering from non-ischemic cardiomyopathies.

The method we describe is also more robust than the current manual segmentation and classification methods. Our results show that the semi-automated segmentation approach can produce segmentations with high agreement to ground truth data and suggests a trend toward decreased segmentation time. Another advantage of automated and semi-automated approaches is the increased consistency and repeatability. Although we are not able to demonstrate decreased inter-observer variability with our limited dataset, we plan to show this in the future with an expanded dataset.

Currently, scar is typically classified by pixel intensity alone based on a threshold set a fixed number of standard deviations above the mean intensity of the healthy myocardium. Our experts have noted that this type of subjective analysis can lead to both under- and over-estimation of scar volume. The Otsu threshold method provides a valid, consistent, and objective differentiation of scar tissue from normal myocardial tissue, without setting a fixed threshold across the patient population.

In conclusion, this proof of concept pipeline development with the incorporation of MRA images and Otsu thresholding improves the accuracy and may decrease the time required for segmentation and quantification of myocardium in the LV. The resulting three-dimensional images can then be used for targeted ablation therapy and are easily incorporated into the interventional workflow of the clinical electrophysiologist for ventricular tachyarrhythmia mapping and ablation. Future approaches to decrease the segmentation time might include different types of growth-based segmentation algorithms or atlas based approaches. Additional methods to improve scar detection include tuning K-means clustering to isolate several distributions of tissue as well as texture based analysis for more accurate selections of scar without user input. The scar detection could also incorporate a location bias to eliminate known regions of noise, including, for example, healthy fibrotic tissue surrounding each valve, from the scar selection.

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