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Image-based Reconstruction of 3D Myocardial Infarct Geometry for Patient Specific Applications

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Abstract

Accurate reconstruction of the three-dimensional (3D) geometry of a myocardial infarct from two-dimensional (2D) multi-slice image sequences has important applications in the clinical evaluation and treatment of patients with ischemic cardiomyopathy. However, this reconstruction is challenging because the resolution of common clinical scans used to acquire infarct structure, such as short-axis, late-gadolinium enhanced cardiac magnetic resonance (LGE-CMR) images, is low, especially in the out-of-plane direction. In this study, we propose a novel technique to reconstruct the 3D infarct geometry from low resolution clinical images. Our methodology is based on a function called logarithm of odds (LogOdds), which allows the broader class of linear combinations in the LogOdds vector space as opposed to being limited to only a convex combination in the binary label space. To assess the efficacy of the method, we used high-resolution LGE-CMR images of 36 human hearts *in vivo*, and 3 canine hearts *ex vivo*. The infarct was manually segmented in each slice of the acquired images, and the manually segmented data were downsampled to clinical resolution. The developed method was then applied to the downsampled image slices, and the resulting reconstructions were compared with the manually segmented data. Several existing reconstruction techniques were also implemented, and compared with the proposed method. The results show that the LogOdds method significantly outperforms all the other tested methods in terms of region overlap.

Keywords

Interpolation; Logarithm of Odds; Image-based Reconstruction; Myocardial Infarct

1. INTRODUCTION

Myocardial infarction, a condition in which regions of the heart lose viability due to insufficient blood supply, is a prominent cause of lethal cardiac arrhythmia in patients, often leading to sudden cardiac death.¹ Infarct tissue is typically heterogeneous, comprising of

scar tissue (also known as infarct core) and semi-viable myocardium (or border zone). The volume,^{2,3} and surface area⁴ of the infarct region are known to be predictive of clinical outcomes including ventricular arrhythmia and sudden cardiac death. Therefore, accurate reconstruction of the three-dimensional (3D) structure of the infarct regions has significance to the clinical evaluation and treatment of patients with ischemic cardiomyopathy. Importantly, emerging applications in the field of personalized computational modeling of cardiac electrophysiology,^{5–8} which are designed to guide clinicians in therapeutic decisions, require high-resolution 3D finite element models of patient hearts with an edge length smaller than 0.4 mm, to resolve the activation wavefront.⁹

Advances in imaging technologies, particularly in late-gadolinium enhanced (LGE) cardiac magnetic resonance (CMR) imaging, have facilitated the acquisition of the structure of the infarct region. However, while *in vivo* LGE-CMR using experimental protocols can achieve an isotropic voxel size of 1.3 mm,^{10–13} standard clinical LGE-CMR protocols consist of acquiring a sequence of short-axis two-dimensional (2D) multi-slice image sequences,² with a coarse resolution, especially in the out-of-plane direction, where the slice thickness is 8–10 mm. Thus, there is a need for an accurate method to obtain 3D reconstructions of infarct regions with sub-millimeter voxel size from low-resolution clinical images. The objective of this study was to develop such a method. This is a challenging task, as the shape and topology of the infarct region vary widely between patients.

The main contribution of this paper is twofold. Firstly, we propose a novel methodology that uses logarithm of odds (LogOdds) function¹⁴ to obtain an interpolated 3D reconstruction of myocardial infarct geometry from a multi-slice image sequence. Secondly, using high-resolution LGE-CMR images of both animals and humans, we evaluated the efficacy of the proposed interpolation scheme, in comparison with several alternative methods, using overlap-, volume-, boundary distance-, and topology-based metrics.

2. METHODS

We propose a two-step methodology for the infarct reconstruction, the first of which involves delineation of the infarct regions from the image slices of the LGE-CMR image via segmentation. The second step consists of interpolation of the segmented slices to build a 3D reconstruction with desired voxel size. Since the segmentation of the infarct regions from 2D multi-slice LGE-CMR images has been extensively studied,^{15–17} our focus in this study was on the interpolation step.

2.1 Logarithm of Odds (LogOdds)-based Reconstruction

LogOdds is an example of a class of functions that map the space of discrete label maps to Euclidean space. The application of LogOdds functions in image analysis was demonstrated by Pohl *et al.*¹⁴ in the generation of probabilistic atlas maps for segmentation and temporal interpolation of 3D brain structures. Let $p \in \mathbb{P}$ be the probability that a voxel is assigned to a particular anatomical structure. The LogOdds of p denoted by $\text{logit}(p)$, is the logarithm of the odds between the probability p and its complement. i.e.,

$$\text{logit}(p) = \log \frac{p}{(1-p)}. \quad (1)$$

The LogOdds space is defined as $\mathbb{L} = \{\text{logit}(p) | p \in \mathbb{P}\}$. The inverse of the LogOdds function $\text{logit}(\cdot)$ is the generalized logistic function

$$P(t) = \frac{1}{1+e^{-t}}, \quad (2)$$

where $P(\cdot)$ maps each element $t \in \mathbb{L}$ to a unique probability $p \in \mathbb{P}$, thus, the function $\text{logit}(\cdot)$ and its inverse comprise a homomorphism between $\mathbb{P}$ and $\mathbb{L}$.¹⁴ LogOdds maps define boundary of a shape as the zero-level set of a function of type $\Omega \rightarrow \mathbb{L}$, where $\Omega \subset \mathbb{R}^2$. We used smoothing by spatial Gaussians to map values of voxels in a binary image to probabilities, where the standard deviation σ of the Gaussian function was determined empirically. Although it was possible to use alternatives, such as signed distance map, to convert binary image values to probabilities, our experimental results yielded higher accuracy using Gaussian smoothing. The Gaussian smoothing was applied to binary image slices obtained from segmentation, and the resulting probability maps were transformed to LogOdds space using the logit function. The cubic spline method was then used to interpolate the 2D LogOdds maps into a 3D image. The interpolation result was finally mapped back to the binary space by using the logistic function followed by a thresholding step.

2.2 Validation Pipeline

2.2.1 Overview—Our validation pipeline of the LogOdds method is shown in Fig. 1. Initially, an expert manually segmented left-ventricular (LV) infarct regions in 3D. Subdivision of manually segmented infarct regions into core and border zones was achieved using an image thresholding approach described elsewhere.² The out-of-plane slice thickness of the infarct regions was then increased to 8 mm by downsampling, to mimic the resolution of the clinical LGE-CMR data. The LogOdds method was then used to interpolate the downsampled total infarct and core regions back to the original voxel size. The border zone was obtained by subtracting the reconstructed core region from the reconstructed total infarct region. Using a variety of metrics, the reconstructed infarct regions were then compared to those obtained from manual segmentation.

2.2.2 Study Subjects and Imaging—We used three canine heart datasets for optimizing the standard deviation σ of the Gaussian smoothing step in the LogOdds methods, and 36 clinical datasets for evaluation of the proposed approach. To acquire these canine heart datasets, myocardial infarctions were induced in three adult mongrel dogs. Gd-DTPA (Magnevist) was then injected (0.2mmol/kg), and the animals were sacrificed 20 minutes after injection. T1-weighted gradient recalled echo MRI was then performed on the explanted hearts, at a resolution of $0.25 \times 0.25 \times 0.50 \text{ mm}^3$, to obtain the LGE-CMR images.

For the acquisition of clinical datasets, 36 study subjects presenting with myocardial infarction were recruited at Robarts Research Institute of Western University (London, ON)

during which they received LGE-CMR examination using a whole-heart, respiratory navigated, 3D inversion recovery gradient echo pulse sequence (Siemens 3T Trio, Erlangen, GER) during and 30 minutes following infusion of 0.2 mmol/kg Gadovist (Bayer, Toronto, ON). The study protocol was approved by the Research Ethics Board of Western University, after receiving written consent from 160 the subjects. The images were acquired at isotropic voxel size of 1.3 mm and reconstructed to a resolution of $0.625 \times 0.625 \times 1.3 \text{ mm}^3$.

2.2.3 Manual Segmentation of Infarcts—Infarct regions were segmented from 3D LGE-CMR images using a multi-planer software platform. Full-width at half maximum thresholding technique² was used to divide the total infarct region into core and border zones (see Fig. 1). The infarct core was defined as the hyper-intensity region with image intensity >50% of the maximal image intensity of the total infarct region.

2.3 Evaluation of Accuracy in Infarct Reconstruction

2.3.1 Evaluation Metrics—The accuracy of the computed reconstructions was assessed using volume-, overlap-, boundary distance-, and topology-based metrics. The volume-based metrics included percentage absolute volume difference (δV) and percentage surface area difference (δSA), expressed as a percentage ratio with respect to the manual measurement. We used the Dice similarity coefficient (DSC) as a measure of overlap and spatial fidelity. Root mean square error (RMSE), defined as the RMS of the shortest distance from each point on the surface of the computed reconstruction to the surface of the manual reconstruction was used to measure sensitivity to outliers. To compare smoothness, we used a metric based on curvature of the surface. This metric was defined as the Bhattacharyya distance (Bh)¹⁸ between the probability distributions of mean curvatures at each point on the surfaces of the manual and computed reconstructions. To assess the topological fidelity of the reconstructed infarct volumes, we used absolute differences in Euler characteristic between the computed and manual reconstructions ($\delta\chi$).

The parameter (*i.e.*, σ , the Gaussian standard deviation) of the LogOdds method was optimized for DSC by iterative refinement using the canine datasets. The LogOdds method yielded the highest mean DSC of $75.5 \pm 7.4\%$ at $\sigma = 3$ voxels. The algorithm with the optimized parameter was then tested on the clinical datasets. The statistical analyzes were performed using GraphPad Prism 6.2 (GraphPad Software, Inc., La Jolla, CA) and α of 0.05 was considered as the level of significance.

2.3.2 Comparison of Performance of the Developed Method with Alternative Techniques—To our knowledge, the performances of various methods in reconstructing infarct geometries have never been compared. Therefore, to conduct such a comparison, we implemented four reconstruction methods already being used in medical imaging applications, including the signed distance transform-based method (SDM),¹⁹ the modified signed distance based-method (MSDM),²⁰ nearest neighbor (NN) interpolation, and variational implicit (VI) method.²¹ The SDM¹⁹ was an implicit interpolation method, in which the segmented slices were first converted to grayscale images, where the pixel intensity was its shortest distance to the boundary of the segmentation. These grayscale image slices were then linearly interpolated. The MSDM was similar to SDM except that it

used cubic splines for the interpolation. The NN method, the interpolation that underlies the widely employed Simpson's rule²² for calculating volumes in the clinic, directly interpolated the binary label maps. The VI method used thin-plate spline interpolation, in which a function was computed to fit the given data and maximize the smoothness of the reconstruction. All computed reconstructions were built using Matlab (Mathworks Inc., Natick, MA) on an Ubuntu 12.04 workstation with eight Intel Core i7 CPU of 3.4 GHz and 32 GB RAM.

3. RESULTS

The mean computation time for the VI method was about 33 s, while it was less than 3 s for all the other methods. Infarct surfaces reconstructed by each of the methods for two example LGE-CMR images are shown in Fig. 2. Except for the NN and VI methods, all methods generated smooth and anatomically realistic surfaces. Qualitatively, the LogOdds method generated surfaces that matched most closely with the surfaces of manual reconstructions. Summary of quantitative evaluation of the methods for reconstructing the total infarct is given in Table 1. The LogOdds method yielded a mean DSC of $82.10 \pm 6.58\%$. Normality test using Shapiro-Wilk test showed that DSCs do not follow a Gaussian distribution. Therefore, Wilcoxon signed rank sum tests were used to identify statistically significant differences between the mean DSC of the LogOdds method and that of the others. The LogOdds method yielded significantly higher DSC than all the other methods. Paired t-tests were performed on log-transformed volumes of total infarct regions, after testing for normality using Shapiro-Wilk test. Volumes of the infarct reconstructions generated by the LogOdds method were significantly closer to those of manual reconstructions. Similar to the volume measurements, the LogOdds method yielded smaller error for the surface area of the infarct. With respect to topological measures, the LogOdds method provided the smallest $\delta\chi$. The accuracy of the LogOdds method in terms of the smoothness metric Bh was comparable to those of other methods, except the NN method, which reported a substantially lower value.

The results of evaluating the accuracy of infarct reconstruction of the core and border zones are shown in Table 2. The DSCs for the core and border zones were smaller than those for the total infarct. Similarly to the DSC results for total infarct, the LogOdds method yielded significantly higher DSC than the other methods for both core and border zones. Further, the LogOdds method reported significantly smaller errors than the other methods. The variation of DSC with the inter-slice distance (ISD) is shown in Fig. 3, where the error bars represent one standard deviation. For each method, the DSC gradually decreased with the increase of ISD, but the LogOdds method consistently yielded higher DSC than the other techniques at each ISD.

4. CONCLUSIONS

We have developed a novel method for reconstructing 3D infarct geometry from segmented slices of clinical multi-slice LGE-CMR images. The developed method has outperformed alternative approaches in reproducing expert manual reconstructions. This study is the first that has developed and evaluated a method specifically for 3D infarct reconstruction from

multi-slice clinical images. As future work, we will further evaluate the efficacy of the developed method by comparing results of simulations of cardiac (dys)function performed with computed and manual reconstructions.

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Figure 1.

Our processing pipeline for evaluation of the reconstruction accuracy of the proposed method using metrics based on infarct geometry. The pipeline involves manual segmentation of the infarcted regions in 3D LGE-CMR images, downsampling of the segmented images to the desired resolution, computation of infarct reconstructions from downsampled images by the LogOdds method, and comparison between computed and manual reconstructions.

Figure 2.

Comparison of the surfaces of total infarct reconstructions obtained using the various interpolation methods (columns) from two LGE-CMR images (rows). The different methods are the manual segmentation (Manual), LogOdds approach we have developed (LogOdds), signed distance transform-based method (SDM), modified SDM (MSDM), variational implicit technique (VI), and nearest neighbor method (NN).

Figure 3. Variation in DSC of the difference methods as a function of inter-slice distance. The error bars represent one standard deviation.

Table 1

Results for evaluation of accuracy of the various infarct reconstruction methods using the 36 3D LGE-CMR images. Statistical analyses were performed for the DSC and volumes, where an asterisk before a number indicates significant difference between the corresponding technique and the LogOdds method.

Method	DSC (%)	δV (%)	RMSE (mm)	δSA (%)	Bh	Euler $\delta \chi$
LogOdds	82.10±6.58	7.23±6.2	1.08±0.15	7.29±5.58	0.89±0.02	6.25±4.94
SDM	*65.43±12.86	*48.77±14.3	1.34±0.21	28.15±11.3	0.90±0.01	11.6±12.37
MSDM	*75.99±8.57	*25.67±10.15	1.20±0.28	12.22±8.94	0.90±0.02	9.12±11.83
VI	*60.35±17.36	*96.32±60.66	4.31±3.36	18.02±17.5	0.89±0.02	5.36±5.1
NN	*74.13±6.90	*8.1±14.56	1.54±0.19	9.94±4.7	0.68±0.02	12.51±8.10

Table 2

Results for evaluation of accuracy of the reconstruction methods for core and border zones of the infarct using 36 3D LGE-CMR images. Statistical testing was performed for DSC and infarct volumes. An asterisk before a number indicates significant difference between the corresponding technique and the LogOdds method.

Method	DSC (%)		δV (%)		RMSE (mm)	
	Core	Border zone	Core	Border zone	Core	Border zone
LogOdds	70.44±10.26	59.45±15.36	11.93±7.89	7.5±7.73	1.33±0.23	1.56±0.40
SDM	*51.42±13.2	*43.60±18.89	*60.1±11.8	*38.87±16.4	1.33±0.16	2.25±0.57
MSDM	*65.34±11.20	*53.02±15.89	*33.6±12.28	*20.7±12.4	1.46±0.57	2.48±0.90
VI	*45.54±18.96	*32.35±34.35	*93.17±45.05	*120.5±143.3	5.02±2.95	2.36±1.18
NN	*64.8±9.70	*52.94±14.54	*11.2±7.14	*10.4±10.1	1.60±0.20	1.73±0.47