Deep Learning for Ventricular Arrhythmia Prediction Using Fibrosis Segmentations on Cardiac MRI Data

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Abstract

Many patients at high risk of life-threatening ventricular arrhythmias (VA) and sudden cardiac death (SCD) who received an implantable cardioverter defibrillator (ICD), never receive appropriate device therapy. The presence of fibrosis on LGE CMR imaging is shown to be associated with increased risk of VA. Therefore, there is a strong need for both automatic segmentation and quantification of cardiac fibrosis as well as better risk stratification for SCD.

This study first presents a novel two-stage deep learning network for the segmentation of left ventricle myocardium and fibrosis on LGE CMR images. Secondly it aims to effectively predict device therapy in ICD patients by using a graph neural network approach which incorporates both myocardium and fibrosis features as well as the left ventricle geometry.

Our segmentation network outperforms previous state-of-the-art methods on 2D CMR data, reaching a Dice score of 0.82 and 0.77 on myocardium and fibrosis segmentation, respectively. The ICD therapy prediction network reaches an AUC of 0.60 while using only CMR data and outperforms baseline methods based on current guideline markers for ICD implantation. This work lays a strong basis for future research on improved risk stratification for VA and SCD.

1. Introduction

Sudden cardiac death (SCD) is a leading cause of mortality worldwide. SCD is usually caused by ventricular arrhythmia (VA) [1]. Effective prevention for VA is the implantation of an implantable cardioverter defibrillator (ICD). However, current guidelines for receiving an ICD lead to under- and overtreatment: many people suffer from VA and SCD, without meeting the criteria of receiving an ICD [1]. Conversely, 78-83% of the primary prevention ICD patients do not receive appropriate device therapy in the first four years after implantation [1].

Prior studies demonstrated the presence of myocardial fibrosis on late gadolinium enhanced (LGE) cardiac magnetic resonance (CMR) imaging to be associated with high risk of VA [2]. Fibrosis segmentation in the left ventricle (LV) on LGE images is often done manually but that task is time-consuming and needs expert knowledge [3]. Therefore, there exists a strong need for automatic methods to segment fibrosis in the LV. Even though much previous work has been done on the automatic segmentation of fibrosis in CMR images, current state-of-the-art results by Moccia and Zhang (MICCAI 2020 EMIDEC challenge winner) only reach Dice scores of 0.713 and 0.712 respectively [4], [5].

Over the last decade, many deep learning models have been proposed to solve a variety of medical tasks. However, the application of deep learning for the risk stratification of patients for developing VA has barely been investigated. Graph neural networks (GNNs) have shown promising results in several domains, including the medical domain, where the data can be naturally presented in the form of graphs, such as 3D mesh classification [6]. As the shape and structure of the LV scar tissue is considered to be of importance for the development of VA events [7], GNNs show potential for the prediction of VA and SCD.

The contribution of this work is therefore two-fold; 1) it presents a novel two-stage deep learning model, based on U-net, which can accurately segment fibrosis regions in the LV and 2) it introduces a GNN architecture which uses the myocardium and fibrosis segmentation for the prediction

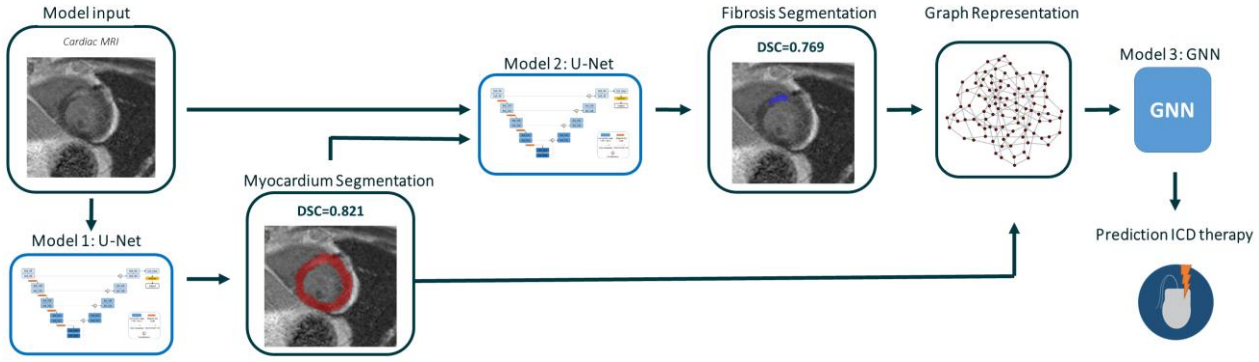

Figure 1: Complete architectural pipeline

of device therapy in ICD patients. To the best of our knowledge, this is the first study that directly uses fibrosis segmentation for the prediction of VA or ICD therapy in a deep learning setting.

2. Methods

2.1. Dataset

This study made use of the DEEP RISK dataset. This dataset contains CMR images, ECG data as well as clinical variables of a cohort of 1,261 ICD patients which received an ICD between 2007 and 2017 [8]. For this research, short axis (SAX) LGE CMR images were used. All patients were included with a minimum of 7 SAX LGE CMR slices and CMR acquisition within 365 days before ICD implantation, which resulted in 515 patients which are used for the ICD therapy prediction. The patients were monitored during a mean follow-up time of 48.6±34.3 months and outcome measures, including mortality and ICD device therapy, were reported. From the set of these 515 patients, a random subset of 117 patients was sampled to use for fibrosis segmentation and their SAX LGE CMR 2D slices were manually annotated.

2.2. Segmentation models

For the segmentation process, a two stage U-net is proposed as previous work has shown that an initial segmentation of anatomical structure (myocardium in our case) seems essential for an accurate segmentation of fibrosis regions as it opposes a reliable initialization for the scar segmentation [9]. Therefore, our first U-net, named *M-Unet*, segments the myocardium from the raw 2D SAX LGE slices. It consists of a regular U-net structure with four down sampling (i.e., max pooling) operations in the encoder and four up sampling (i.e., deconvolutions) in the decoder part. The pixel-wise myocardium probability maps are then stacked with the SAX LGE images and used as input for the second U-net. In this way, the myocardium probability maps act as a location prior in which the fibrosis regions should be detected without introducing any manual annotations. The second U-net, named *F-Unet*, is designed and trained to segment the fibrosis regions.

The stack of 2D SAX LGE images can be considered as pseudo 3D data as the voxel spacing is inconsistent between the in-plane and between planes. To both address this fact and utilize the 3D structure, we test three different types of models for the F-Unet:

1. 2D F-Unet; This model consists of a regular 2D U-net, with almost the same architecture as the M-Unet. It takes as input the 2D SAX LGE slices and treats the independently.
2. 2.5D F-Unet; This model takes the 2D F-Unet architecture and replaces the four 2D convolution operations in the 'bottom' of the U-net structure with 3D convolutions.
3. 3D F-Unet; This model replaces all 2D convolution operations with 3D convolutions.

Both the 2.5D and the 3D F-Unet take as input the complete stack of SAX LGE slices.

2.3. ICD therapy classification models

As studies have shown that LGE of myocardial fibrosis is a strong predictor of both VA risk and SCD, we propose a GNN model which incorporates both the myocardium and fibrosis segmentation features as well as the 3D structure of the LV for the prediction of ICD therapy.

For every patient, a graph $G = (V, E)$ consisting of nodes $v_i \in V$ and edges $e_i \in E$, is constructed by randomly sampling 100 fibrosis voxels based on the probability outputs of the F-Unet and 500 myocardium voxels based on the probability outputs of the M-Unet. Every node is connected to its 25 closest neighbouring nodes.

Our GNN consists of five graph convolutional layers, based on equations 3, 5 and 6 from the E(n) equivariant graph neural network implementation [10], followed by a dense classification layer with 64 hidden units.. For the hidden representation of the nodes, two options are experimented with: 1) the voxel's output of the M-Unet model, named *myo-GNN* and 2) the voxel's output of the F-Unet model, named *fib-GNN*. The complete pipeline (from raw image, to segmentation, to prediction) can be viewed in Figure 1.

Current guidelines for ICD implantation rely heavily on

the left ventricle ejection fraction (LVEF)[11]. In addition, studies have showed that the sole presence of LGE is a strong predictor of VA and SCD as well. Therefore, we would like to compare the effectiveness of our models to the ICD therapy predictions based on LVEF and LGE. Our GNN models are compared against two logistic regression baseline models which use only 'LGE presence' or 'LVEF' as variables.

2.4. Training details

For the segmentation task, the dataset is split in training, validation and test sets (70/10/20%) and trained on the training set. The validation set is used for hyperparameter tuning, learning rate adaption and model selection. The test set is used to report final performance.

The M-Unet is trained using a novel loss function:

$$L_{AW} = 1 - ((1-\alpha)\cdot sDice_{myo} + \alpha \cdot sDice_{fib})$$

$$sDice_{myo} = \frac{2\sum_i^N p_i t_i^{(m)} + 1.0}{\sum_i^N p_i^2 + \sum_i^N t_i^{(m)} t_i^{(m)} + 1.0}$$

$$sDice_{fib} = \frac{2\sum_i^M p_i t_i^{(f)} + 1.0}{\sum_i^M p_i^2 + \sum_i^M t_i^{(f)} t_i^{(f)} + 1.0}$$

where N is the total number of pixels, M is the number of fibrosis pixels, p_i is the predicted myocardium probability for pixel i ($p_i \in [0,1]$), $t_i^{(m)}$ is the ground truth myocardium mask value for pixel i ($t_i^{(m)} \in \{0,1\}$) and $t_i^{(f)}$ is the ground truth fibrosis mask value for pixel i ($t_i^{(f)} \in \{0,1\}$). As alpha is increased during training, the model first focuses on getting the myocardium segmentation right and gradually starts paying more attention to the fibrotic regions which improves results for fibrosis segmentation.

The F-Unets are trained using the regular smoothed Dice loss.

For the classification task five-fold cross validation is used and the model is trained using the binary cross entropy loss function.

3. Results

3.1. Segmentation results

Table 1: Results for the segmentation models. All results are averaged over 5 different seeds and the standard deviation is displayed in brackets. For the F-Unets, the highest score per metric is indicated in bold.

Model	Segmentation task	DSC (sd)	AHD (sd)
2D M-Unet	Myocardium	0.821 (0.005)	11.17 (0.73)
2D F-Unet	Fibrosis	0.752 (0.019)	23.15 (2.88)
2.5D F-Unet	Fibrosis	**0.769** (0.009)	**21.39** (1.20)
3D F-Unet	Fibrosis	0.723 (0.021)	27.94 (2.57)

Table 1 shows the results for the segmentation tasks using the Dice similarity coefficient (DSC) and the average Hausdorff distance (AHD). The table shows that both the 2D and the 2.5D F-Unet reach good scores with the 2.5D F-Unet slightly outperforming the 2D F-Unet.

Figure 2 shows the segmentations in one slice for three different patients. Row A shows the patient with largest difference in predicted fibrosis volumes and ground truth fibrosis volumes. This example illustrates the overall trend that the 2D F-Unet is very dependent on the myocardium segmentations and has difficulties overcoming missed fibrosis spots by the M-Unet. The 2.5D and 3D U-net suffer less from this problem and can still detect fibrosis spots in areas that were not segmented by the M-Unet.

The slices from patient B and C show good performance for all four models. They also show that the 2.5D and 3D F-Unets have the tendency to oversegment while the 2D F-Unet often undersegments fibrosis.

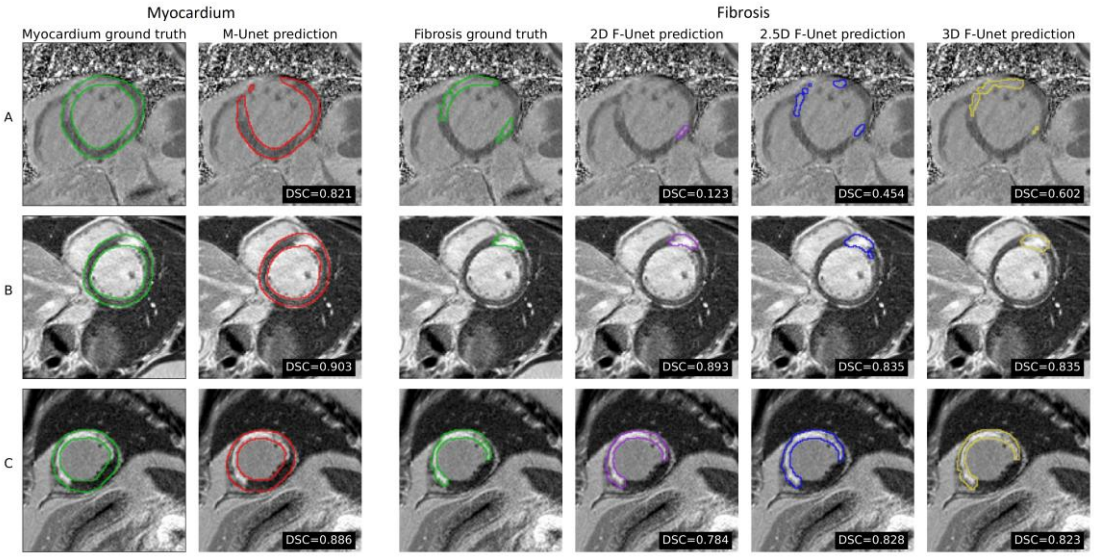

Figure 2: Segmentation examples for three different patients

3.2. ICD therapy prediction results

Table 2: Results for the ICD therapy prediction in the complete follow-up period. The results are averaged using 5-fold cross validation and the standard deviation is shown in brackets.

Model	AUC	Accuracy
Logistic regression (LGE)	0.549 (0.061)	0.410 (0.055)
Logistic regression (LVEF)	0.501 (0.032)	0.464 (0.037)
Myo-GNN	**0.600** (0.055)	**0.577** (0.035)
Fib-GNN	0.567 (0.021)	0.478 (0.107)

Table 2 shows the results for the ICD therapy prediction for both (baseline) logistic regression models as well as the two GNN models. The table shows the area under the receiver operating curve (AUC) and the accuracy. We can see that both GNN models outperform both logistic regression models. The logistic regression model based on LVEF performs very poorly. This is surprising as the LVEF is an important indicator for ICD implantation in current guidelines. We can see that the myo-GNN model performs best, reaching an AUC score of 0.600.

4. Conclusions and discussion

We conclude that our proposed LV fibrosis segmentation pipeline is fully automatic and has excellent performance. The DSC of 0.769 for the segmentation of fibrosis improve upon state-of-the-art 2D LV fibrosis segmentation scores by Moccia and Zhang [4], [5].

Secondly, this work introduced a novel technique that incorporates both myocardium and fibrosis segmentation features and the geometry of the LV using a GNN approach for the prediction of ICD therapy. Both proposed GNN methods outperform the two baseline methods of which one is based on LVEF which is an important indicator for ICD implantation in current guidelines. Besides, our myo-GNN model slightly improves upon first results from the PROFID study (Dagres et al. Data presented at the European Heart Rhythm Association annual meeting 2022, Kopenhagen, Denmark) with an AUC of 0.598 for predicting SCD in ICD patients using clinical and biomarker characteristics as well as CMR data while our method solely relies on CMR data.

However, the ICD therapy results are not yet suitable for clinical use and need to be improved. A promising step for improvement would be to combine the myocardium and fibrosis features with other clinical data, such as ECG and clinical variables, in a larger multimodal DL setting.

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