Semi-automatic tool to identify heterogeneity zones in LGE-CMR and incorporate the result into a 3D model of the left ventricle

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Abstract. Fatal scar-related arrhythmias are caused by an abnormal electrical wave propagation around non conductive scarred tissue and through viable channels of reduced conductivity. Late gadolinium enhancement (LGE) cardiovascular magnetic resonance (CMR) is the gold-standard procedure used to differentiate the scarred tissue from the healthy, highlighting the dead cells. The border regions responsible for creating the feeble channels are visible as gray zones. Identifying and monitoring (as they may evolve) these areas may predict the risk of arrhythmias that may lead to cardiac arrest. The main goal of this project is the development of a system able to aid the user in the extraction of geometrical and physiological information from LGE images and the replication of myocardial heterogeneities onto a three-dimensional (3D) structure, built by the methods described by our team in another publication, able to undergo electro-physiologic simulations. The system components were developed in MATLAB R2019b the first is a semi-automatic tool, to identify and segment the myocardial scars and gray zones in every two-dimensional (2D) slice of a LGE CMR dataset. The second component takes these results and assembles different sections while setting different conductivity values for each. At this point, the resulting parts are incorporated into the functional 3D model of the left ventricle, and therefore the chosen values and regions can be validated and redefined until a satisfactory result is obtained. As preliminary results we present the first steps of building one functional Left ventricle (LV) model with scarred zones.

Keywords: Gray zone · ischaemia · arrhythmia · heart computational model

1 Introduction

Coronary artery disease, characterized by blockages in the coronary arteries, frequently results in infarcted (dead) myocardial tissue, therefore incapable of conducting electrical signal.

Ischemic injuries create not only non excitable portions of myocardial tissue, constituting the scar core, but also damaged portions where the electrical conductivity is low but not zero, these areas are termed gray zones. Although they can also stand alone, often these gray zones constitute the peri-infarct tissue - the scar borders. If they happen to cross the dead scarred zones and reach conductive or semi conductive tissue on the other side, conductive channel (CC) are formed, critical in the ventricular fibrillation as explained in [4].

In clinical decision-making, LGE is the gold-standard to identify and locate scars, allowing to evaluate the scar and gray zone extensions as well as identify the presence of CC. Monitoring the gray zone evolution is critical to help identify the optimal timing and candidates for placement of implantable cardioverter-defibrillator [3]. The conditions may deteriorate or improve due to the fact that damaged myocardium can recover function following coronary revascularization.

In the following chapters, we report the development of a system, using MATLAB R2019b, capable of assembling 3D models of left ventricular myocardium heterogeneities based on patient CMR data. The output of this system allows subsequent virtual eletrophysiological studies to be conducted. Semi-automatic histogram and segmentation methods based on signal intensity (SI) thresholds are used to identify the heterogeneity zones and corresponding conductivity assignment are based on values described in the literature. All the development is made on top of a structure, built by the methods detailed in a previous publication from our team [7], able to be used in electro-physiologic simulations. An overview of the whole system can be seen in figure 1.

2 Methods

2.1 Setup

In order to build and test our application, anonymized 3D CMR datasets in DICOM format from a LGE exam were used as input. The images passed trough the transformations described in detail in a previous publication to obtain the important data in regard of this paper. Therefore the input data of our system is a set of 2D slices representing the cardiac short-axis view (SAX), alongside with a mask identifying the left ventricle myocardium, healthy and damaged tissue alike, the pixels within are used in steps described in the following sections.

2.2 Segmentation

Our approach to the segmentation of the tissue heterogeneities is two-fold: in the first category the user slides a pointer through the masked myocardium histogram, selecting a pixel intensity level above which, all the pixels are labelled as dead tissue, the same process is repeated to select a value bellow which all the pixels are labelled as healthy. All the pixels with intensities between the two selected thresholds are labelled as gray zone (GZ). Henceforward the myocardium is divided in three parts : GZ, healthy tissue (H) and scarred dead tissue (S).

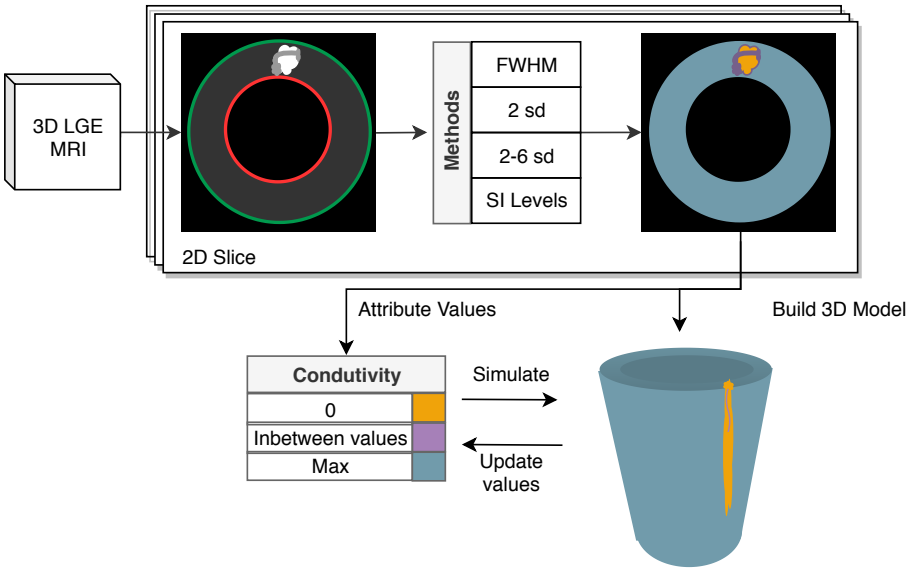


Fig. 1: Overview of the system being developed, starting from the 3D CMR segmentation, passing through the heterogeneities analysis and conductivity values assignment until the 3D structure generation.

The user may decide that the thresholds have the same value and the GZ will be disregarded.

The second category of our approach is to let the user chose between previously validated SI threshold algorithms: full width half max (FWHM), 2-6 standard deviation (sd) and 6 sd, to identify the S and GZ. [1] [2] [5]

Considering the histogram for the pixels inside the masked myocardium, using the FWHM, the infarct area is made by all the pixels which intensities are above 50% of the maximum intensity. Using this method, the S zones are distinguished from the H, but if GZ are present they will be considered part of S as well. They may be distinguished on a later step.

To apply the 2-6 sd and sd methods, the mean intensity of the healthy tissue is calculated from the largest contiguous area of myocardium with no visually apparent enhanced areas or artefacts, selected during a previous step that leads to the masked myocardium.

The 2-6 sd method recognize all the pixels, of the masked myocardium, with intensities bellow the mean plus 2sd to be healthy, pixels with intensity values between the mean plus 2sd to the mean plus 6 sd as gray zones and pixels with intensities above the mean value plus 6 sd to be scars.

The 6 sd method works similarly but the pixels that are recognised as part of gray zone have intensities between the mean and the mean value plus 6 sd .

For both types of segmentation, the next (optional) step is to take the GZ, or in FWHM case the S, and split it into a number of levels the user decides,

limited by the quantity of unique values in the region. Defining more sub-regions within the GZ.

This strategy is applied to every 2D slice, both parts of the approach and all the methods can be applied to evaluate the results, however to conclude the segmentation the same procedure must be applied to the whole set. The results are stored in a 3D matrix where every zone is identified by a distinct integer number.

2.3 Conductivity assignment

Considering an electrical propagation bidomain model, the myocardium cells have extracellular medium between them, thus the intra and extra cellular conductivities must be defined for the H zones. The assigned values will be based on the ones listed in [8]. After any chosen division, the myocardium has at least two different portions, H and S. S zones conductivity is set to zero in every direction. H zones intra conductivities are set to 3.75 S/m in the longitudinal direction (along the tissue fibres) and 2.14 S/m transversal and normal and the extra cellular conductivities 4.69 S/m and 0.47 S/m respectively.

For the first approximation, the conductivity values will be chosen in the following way: the number of intervals is selected (it may be only one) and the conductivities for each will be set by a simple linear regression function, trained by one vector with all the intensities of the other zones (H and S) and one with the corresponding conductivities. The function will then attribute a conductivity value to each pixel intensity of the GZ. The chosen value for the whole sub-interval (when working with more than one are) is the median value of all the conductivities set to this sub-interval.

The outset values may be changed later on, analysing the results from electrophysiological simulations run on the generated model will give an understanding of the accuracy level of the modelled tissue.

The in-between values assignment function should also be improved based on the results until a satisfactory approximation is obtained.

2.4 Output data assembling

From now on, the term *region* will be use to refer to the groups of adjacent voxels that are labelled as the same zone. Distinct parts of the muscle can have the same level of heterogeneity, therefore the zone is the same but the region is different. The regions are generated by reading the 3D matrix, where the zones are stored and assorting the adjacent voxels that have the same value to a region.

The resulting regions representing the heterogeneities volumes have to be translated into a format suited for simulation software. Our team chose to work with the open source software CHASTE (Cancer, Heart and Soft Tissue Environment) [6] to solve and visualize the propagation of excitation waves. In this program the simulation settings are read from a extensible markup language (xml) file where several physiologic parameters, including conductivities, can be

defined. The heterogeneities regions can be defined in the parameters file, as parallelepipedal volumes, specifying a pair of a upper and lower 3D coordinates.

Since the regions are not rectangular shapes, each one has to be divided into into smaller rectangular shapes. As the parallelepipedal structures are grouped and can form larger ones, these last are the ones validated to be part of the final structure, this is important to minimize the number of nodes read by the simulation software, if each voxel was simply assigned to one region, the parametrization file would become unreadable. In figure 2, a region of a single slice divided into cubes - as the slice has thickness - is exemplified.

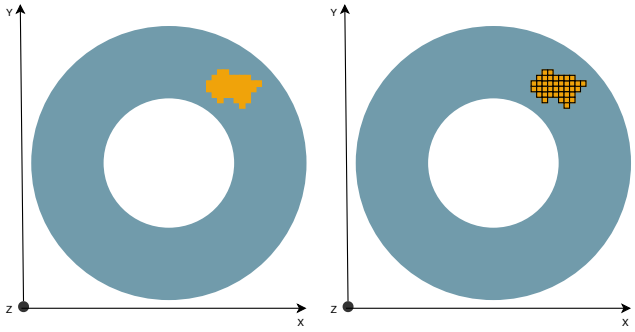


Fig. 2: Splitting a region of one slice into small cubes with the original voxels dimensions.

Figure 3 exemplifies how a region that spans through two consecutive slices [left] is split into three cubes [right], which corners coordinates will be registered into the parametrization file.

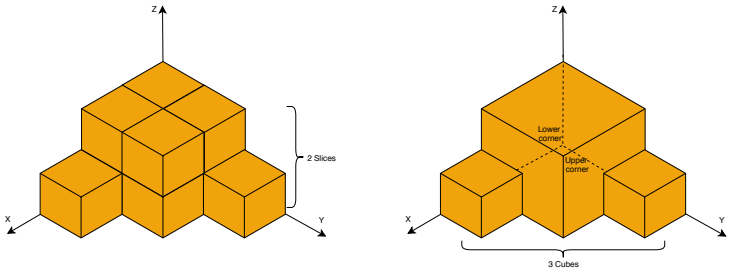
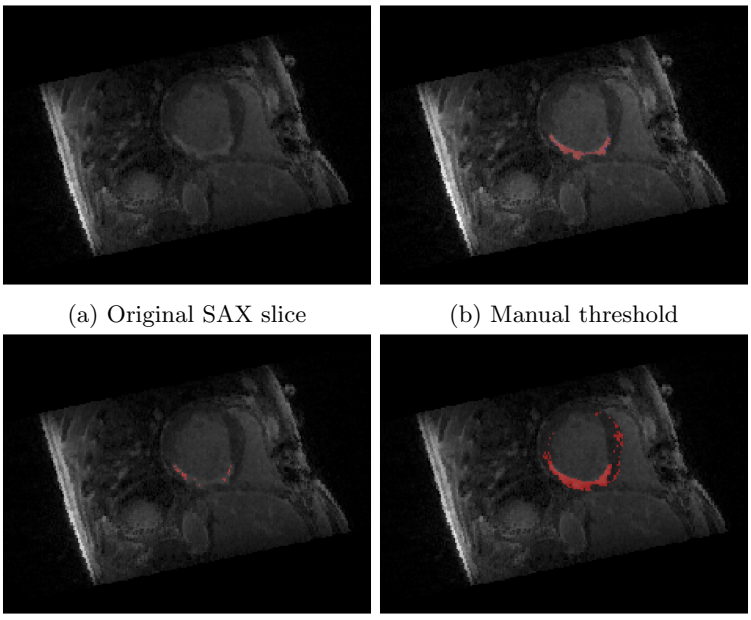


Fig. 3: Example of how eight cubes, four at each consecutive slice, are reduced to one in the final structure.

For every region block, the pairs of upper and lower coordinates and the designated conductivity are written to a xml file formatted to be compatible with CHASTE. Once again following the methods from our previous publication, a volumetric model of the LV is generated. Our system gives the possibility to define a series of physiologic parameters that are also included in the xml.

3 Preliminary results

Using as input a LGE CMR we first tested the identification of enhanced zones, meaning scarred tissue that may include gray zones. In figure 4 three segmentation methods on a the SAX slice. The manual segmentation was accomplished by dragging two lines, one for each threshold, on top of the histogram, visualizing the segmentation result on real-time and stopping when the highlighted are was clearly an enhanced area.

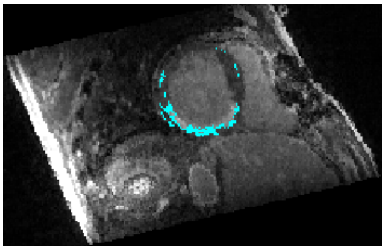


(a) Original SAX slice (b) Manual threshold

(c) 6sd (d) FWHM

Fig. 4: Scarred myocardium zone (in red) segmented by different methods b) User input thresholds, c)6 sd and d) FWHM

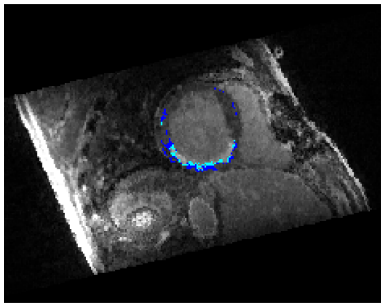
Selecting only one gray zone we obtain the area highlighted in blue in figure 5[left] and three levels of longitudinal conductivity as seen in 5[right].



	Zone	Condutivity S/m
1	Healthy	4.69
2	G Zone 1	2.3449
3	Scar	0

Fig. 5: Gray zone for the given slice highlighted in light blue. The corresponding conductivity values to this area and the other two are presented on the table on the right.

Taking the same gray zone, and telling our system we want to split it into two sub-zones, the image on the left of figure 6 is returned.



	Zone	Condutivity S/m
1	Healthy	4.69
2	G Zone 1	3.0516
3	G Zone 2	2.7089
4	Scar	0

Fig. 6: Two gray zones for the given slice highlighted in light blue and blue. The corresponding conductivity values to these areas and the other two are presented on the table on the right.

The conductivity values for the 'G Zone 1' and 'G Zone 2' are calculated by the linear regression function described in the previous chapter, the other two values are pre-setted but as stated previously can be updated if the simulation results indicate that they should.

To simplify the rest of our initial testing, the area that resulted of the manual segmentation on figure 4b was exported to the CHASTE parametrization file, with a conductivity of zero mS/cm in every direction.

Figure 7 gives a 3D perception of the scarred area from inside the ventricle. The slices upfront represent the base of the LV. This image was generated only as an visual aid to understand the extension of the area on the final volume.

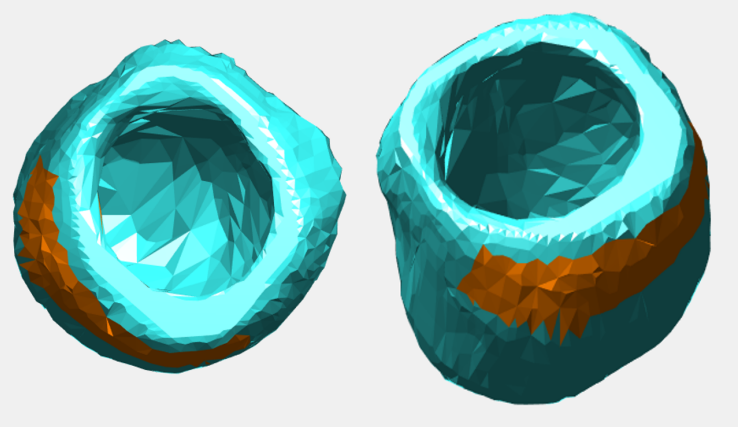


Fig. 7: 3D view of the LV myocardial surface represented in blue and the scarred zone in orange

Both the parametrization file with the scarred zone near the base and the generated LV model were used in CHASTE to visualize the electrical wave propagation. On figure 8 the LV wall around the scar is being depolarized - by a stimuli we defined - while the scarred area maintains its potential at zero.

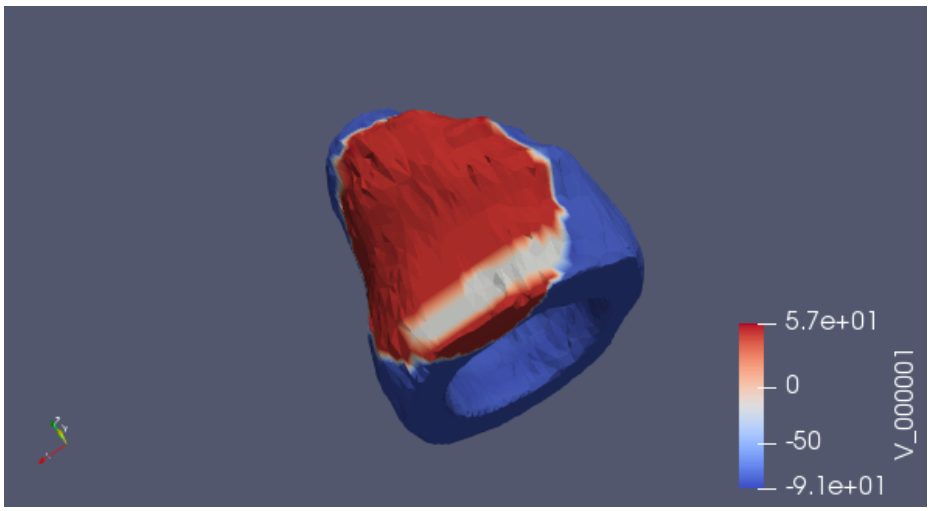


Fig. 8: Signal propagation on the LV wall (in red) with a dead zone

4 Conclusion

The system described in this paper, may be a valuable asset in the assembling of personalized heart computational models. Offering the possibility to include heterogeneities adds a very important component in the study of arrhythmia mechanisms and risk assessment. In the future we aim to extend the reported methods to include the right ventricle, therefore obtaining a more faithful model. Another crucial goal is to compare the simulation results with real electrical maps from the same patient that provided the CMR, the evaluation of the results using this data will then be used to fed the method described in the chapter 2.3 therefore new and more accurate conductivity values could be defined and the assignment function well improved. Overall, although this project is still at an early stage and needs several improvements, our approach proven to be worthwhile as an add-on to the parallel cardiac simulations on our ongoing research.

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