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Image Data Analysis for Quantifying Scar Transmurality in MRI phantoms for Cardiac Resynchronisation Therapy

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Abstract—The use of implantable cardiac devices has increased in the last 30 years. Cardiac resynchronisation therapy (CRT) is a procedure which involves implanting a coin sized pacemaker for reversing heart failure. The pacemaker electrode leads are implanted into cardiac myocardial tissue. The optimal site for implantation is highly patient-specific. Most implanters use empirical placement of the lead. One region identified to have a poor response rate are myocardial tissue with transmural scar. Studies that precisely measure transmural scar in the left ventricle (LV) are few. Most studies lack proper validation of their transmural measurement technique. This study presents an image analysis technique for computing scar transmural from late-gadolinium enhancement MRI. The technique is validated using phantoms under a CRT image guidance system. The study concludes that scar transmural can be accurately measured in certain situations and validation with phantoms is important.

I. INTRODUCTION

Patients with symptomatic heart failure are commonly treated with procedures such as Cardiac resynchronization therapy (CRT) by implanting a pacemaker for the heart. In this procedure, the electrode leads of the pacemaker are implanted in myocardial tissue to artificially pace the heart. Pacing sites are now being assessed for tissue scarring in order to determine sites that will be responsive to lead placement. The extent of tissue damage or scarring at potential pacing sites is a novel way of performing this assessment [1]. The ultimate goal is to provide a CRT that is patient-specific and hence more effective.

The extent of scarring in cardiac myocardium is also often termed as *transmurality* of scar. A fully transmural scar runs along the myocardium. It is challenging to measure transmural as it must be measured in all three spatial directions from a pixelated three dimensional (3D) reconstructed image of scar. magnetic resonance imaging (MRI) remains the gold-standard for cardiac tissue characterisation. An MRI imaging technique known as late Gadolinium enhancement (LGE) provides 3D visualisation of cardiac tissue with a relative high intensity within scarred areas. Scar assessment with LGE imaging prior to CRT lead placement has shown to improve patient outcomes [1] in these procedures and

transmurality is increasingly being seen as an important scar metric.

A. Previous works

There is little literature on the topic of scar transmural computation and validation is almost always performed using visual assessment. In [2], authors employed a hysteresis thresholding method to assess scar transmural. Transmurality was scored using a five-point scale (0: no infarction; 1: transmural < 25%; 2: transmural from 26% to 50%; 3: transmural from 51% to 75%; 4: transmural from 76% to 100%) and the study found that transmural was generally scored lower when compared to visual assessment.

In a separate study [3], transmural was calculated by dividing the ventricular wall with several equidistant chords ($n = 100$). Signal intensity was analysed at ten equidistant points along each chord and increased signal intensity was expressed as a percentage of left ventricular wall thickness. The average was then taken per segment of the 16-segment LV model. The quantitative values of transmural was compared to visual assessments by two experienced observers scoring transmural using the 5-point scale.

The authors in [4] calculated scar transmural from LGE by integrating along radial spikes of myocardium. These spikes are understood to be lines at regular intervals perpendicular to myocardium. The automated approach was compared to transmural using visual assessment obtained from consensus delineation of scar ($n = 3$ observers). The algorithm found a lower scar transmural score, on average, compared to visual assessment.

The authors in [5] compared four different methods of scar transmural. In their study, transmural was divided into quartiles (1-24%, 25-49%, 50-74% and 75-100%) and scar above 75% was considered as transmural. Images were assessed by an experienced cardiologist and the study found that these methods tended to under-estimate transmural. The study concluded that transmural calculations could vary significantly depending on the chosen method and further studies were necessary to obtain a validated and consensual study method.

B. Motivation

The literature survey indicates the need for a well validated approach for computing transmural. There are no phantom studies in transmural. Furthermore, the development of a state-of-the-art CRT planning and navigation platform within our lab [6] enabled this proposed image analysis technique

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for scar transmuralty to be validated inside a phantom imaged within an actual CRT image guidance environment.

II. MATERIALS AND METHODS

A. Image Analysis

An important pre-requisite for measuring transmuralty is to obtain a visualisation of the myocardium including scar. To visualise myocardium, the LV was imaged along its short-axis (SA) and long-axis (LA) with cine MRI imaging. The contours of myocardium representing its outer and inner layers were extracted using probabilistic analysis of image intensity gray levels [6]. To visualise scar, the LV was imaged with LGE MRI. The cine SA and LA was registered to the LGE MRI using normalised mutual information (NMI) to reveal myocardium in the LGE. This was necessary as it cannot be accurately delineated alone with LGE. Image pixels within scarred areas were obtained by thresholding image intensity to three standard deviations from mean healthy tissue.

The LV was divided into the 3D 16-segment American Heart Association (AHA) model (see Fig 1), which is a standard for CRT procedures to determine segments that can be selected for placing pacemaker leads. Within every segment, transmuralty was computed for determining the scar extent. Each segment covered a portion of the LGE image. The segments were further sub-divided into smaller *sectors* such that transmuralty could be calculated for each sector and averaged over all sectors to give a more accurate representation of scar extent. Fig. 2 provides an illustration of a sector within a segment.

Sectors were defined at θ intervals within each segment, where $\theta = 10^\circ$ as illustrated in Fig. 2. Within each sector, transmuralty could be calculated by computing the ratio between the width of scar and width of myocardium in that sector. The width of scar was defined as the distance between the nearest (S_{min}) and the farthest (S_{max}) scar pixels from LV centre: $S_{max} - S_{min}$. The width of myocardium could be obtained directly from the extracted contours. Transmuralty T is given by:

$$T_k = \frac{1}{n} \sum \frac{S_{max} - S_{min}}{M_{max} - M_{min}} \quad (1)$$

where $M_{max} - M_{min}$ is width of myocardium calculated from its contours and averaging the distance ratios over all n sectors to obtain transmuralty for the k^{th} segment (Eq. 1). Fig. 2 illustrates how transmuralty could be calculated in an individual sector within a single segment of the LV's 16-segment model using Eq. 1.

B. Phantom Validation

It is impossible to validate the extent of scar being measured using image analysis in patients undergoing CRT. The absolute truth on the scar's extent even with post-mortem histology has been known to pose challenging conditions as a result of the tissue fixing process, an essential preservation step that alters structural properties of tissue. However, it may be possible to validate image analysis using phantoms

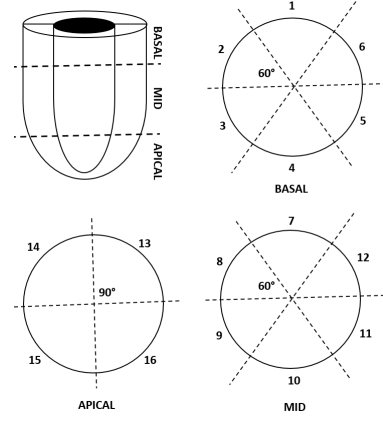


Fig. 1: The sub-division of the left ventricle into 16 segments (outer boundary labels). Segments are subdivided into 60° segments in the basal and mid layers, and 90° segments in the apical or apex layer.

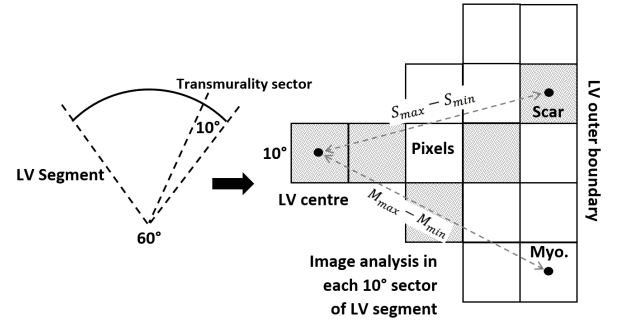


Fig. 2: A schematic diagram for transmuralty calculations within each $\theta = 10^\circ$ sector of a single segment of the LV (left). The instance in this example has 100% transmuralty, due to scar's extent from centre to outer boundary, with distances indicated between LV centre and outermost scar and myocardium (Myo.) pixels.

and this is a common approach. Heart phantoms can be constructed from realistic 3D models and printed with rapid 3D prototyping using only MRI-safe material. The phantom could be imaged with MRI making it possible to calculate and compare scar transmuralty with ground truth.

In this work, an LV phantom was designed with open-source Blender 3D software (Blender Foundation). The dimensions were 55 x 65 mm to allow it to be imaged sufficiently in low-resolution MRI, where a slice thickness of 8 mm allowed between 9-11 slices. The phantoms contained compartments for housing poly-vinyl alcohol (PVA) gel to represent scar. There were three concentric compartments for housing the gel at 33%, 66% and 100% transmuralty. The phantom could only be imaged once the PVA gel reached a state to give it a scar-like intensity in MRI imaging. To attain this state, the PVA gel underwent a freeze/thaw cycle at $-35^\circ\text{C}/+20^\circ\text{C}$ as described in [7]. It was possible to generate five different configurations of transmuralty by using different combinations of compartments in the phantom. These

configurations allowed transmuralty to be validated at: 1) 33%, 2) 66%, 3) 66% using mid and outer compartment, 4) 100%, 5) 100% by leaving an empty mid compartment. Fig. 3 gives a display of all the instances.

C. Phantom Imaging

The phantoms were immersed in water to better distinguish and visualise the PVA gel from the phantom's plastic wall. Due to the solid nature of plastic there were no free Hydrogens to produce an MRI signal. The signal void from the plastic walls against the high signal provided by pure water was utilised to visualise the phantom more clearly. The imaging technique used was LGE, the same technique used to image myocardium scar in CRT patients. The LGE imaging resolution was 1.7×1.7 mm in-plane with slice thickness of 8 mm. The phantoms were imaged inside a catheter lab within an actual CRT guidance platform environment equipped with X-Ray and MRI imaging capabilities (Siemens Healthineers, Erlangen, Germany). The platform was used to align the phantom to typical patient orientation, allowing Cine MRI to LGE image registration followed by scar reconstruction within the CRT procedure workflow. A description of such a workflow can be found in [6].

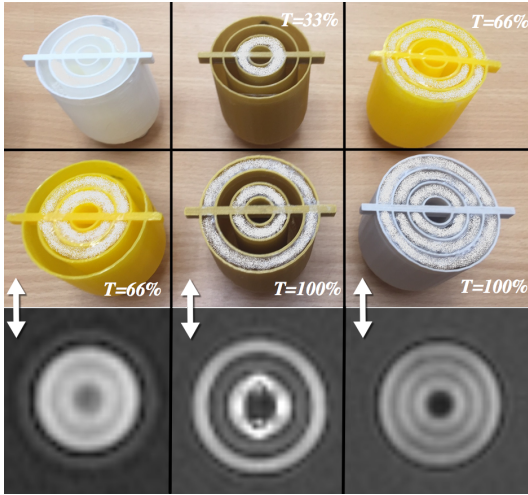


Fig. 3: Phantoms used in validation, with PVA gel filling to simulate five separate configurations of scar transmuralty (T) with their corresponding LGE images (short-axis slice) for three phantoms. Top-left: phantom before PVA freeze/thaw cycle

III. RESULTS

Transmuralty was computed using image analysis within each segment of the LV in the 16-segment AHA model. These values were compared to actual transmuralty that was prepared in the phantoms using PVA gels. For performing this comparison, two metrics were used. Firstly, the mean and median transmuralty as computed using image analysis within each layer (basal, mid and apex) of LV was determined (see Table I). Secondly, the percentage error between computed and actual transmuralty was calculated for each

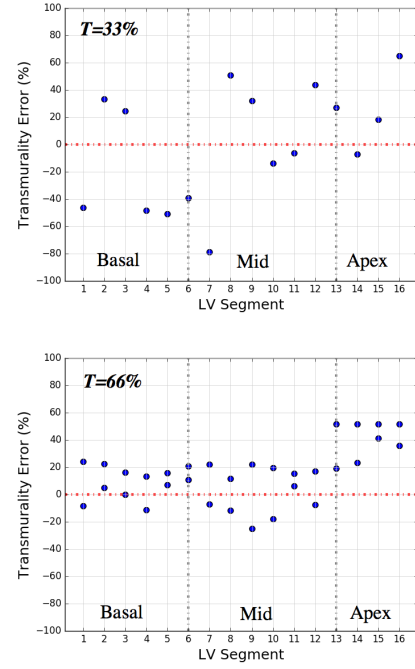


Fig. 4: Error in transmuralty measurements using image analysis in phantoms. Each subplot represents a transmuralty configuration ($T = 33, 66\%$) used in validation. Note the plot for $T = 100\%$ is omitted as image analysis had a near perfect accuracy

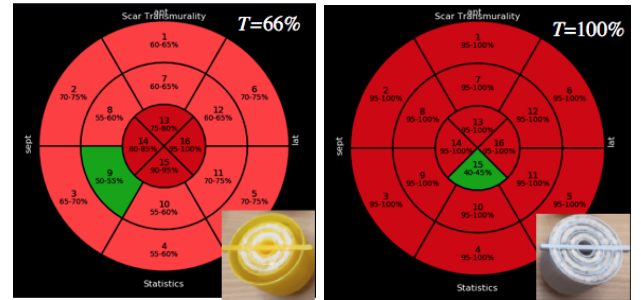


Fig. 5: Bull's eye visualisation of the 16-segment LV model in the validation phantoms (inset) used in this study. The percentage transmuralty using image analysis is noted within each segment

segment. This is shown in each of the sub-plots of Fig. 4, where each sub-plot represents the level of transmuralty being assessed ($T = 33\%$ and $T = 66\%$). Each data point in the plot represents the percentage error in transmuralty measurement within a single Bull's eye segment (Fig. 5).

The errors within each layer were also determined. For basal, mid and apex these were $13\% \pm 16\%$, $16\% \pm 19\%$, and $25\% \pm 23\%$ respectively. It may be worthwhile to note this could only be obtained from a small number data points in the basal ($n = 32$), mid ($n = 32$), and apex ($n = 16$) layers.

IV. DISCUSSION

A. Contribution

The main contribution of this work is an image analysis approach for measuring the transmural scar from MRI imaging. To our knowledge, although there are image analysis approaches for measuring scar transmural scar, they were not validated with phantoms. The MRI images of our phantoms created in this study are now open-source and can be obtained from: <https://github.com/drkarim>

B. Accuracy

It was noted that the accuracy decreased in the apex layers of the LV. This is evident in the plots of Fig. 4 and Table I. As LV diminishes in the apex layer, there are fewer slices that are required to image an even smaller area. This increases the margin of error. The accuracy was significantly better in $T = 100$ and the validation with these phantoms showed far greater accuracy than $T = 33$ and $T = 66$. As such, this image analysis technique had excellent accuracy for detecting fully transmural scar and could potentially be useful for binarising transmural scar.

TABLE I: Actual transmural scar (T) prepared in the phantom and estimated (\hat{T}) using image analysis in each layer of the left ventricle

| | Actual | $T = 33$ | $T = 66$ | $T = 100$ |
|----------------|--------|------------------|------------------|-----------------|
| Overall | Mean | $\hat{T} = 33$, | $\hat{T} = 76$ | $\hat{T} = 98$ |
| | Median | $\hat{T} = 35$ | $\hat{T} = 77$ | $\hat{T} = 100$ |
| Basal | Mean | $\hat{T} = 27$, | $\hat{T} = 71$, | $\hat{T} = 99$ |
| | Median | $\hat{T} = 18$ | $\hat{T} = 72$ | $\hat{T} = 100$ |
| Mid | Mean | $\hat{T} = 34$, | $\hat{T} = 68$, | $\hat{T} = 100$ |
| | Median | $\hat{T} = 37$ | $\hat{T} = 72$ | $\hat{T} = 100$ |
| Apex | Mean | $\hat{T} = 41$, | $\hat{T} = 92$, | $\hat{T} = 92$ |
| | Median | $\hat{T} = 40$ | $\hat{T} = 97$ | $\hat{T} = 100$ |

C. Transmurality and choice of phantom material

There is no consensus agreement on how transmural scar should be reported. Reporting it as a percentage of myocardium is common, but whether it portrays the correct information of the underlying tissue state is debatable. It is particularly relevant if scar covers inner and outer myocardium (Fig. 3, 2nd column, $T = 100\%$). In this case, although it could be said that $T = 66\%$, but the inner tissue is unresponsive to CRT due to blockage from scar. A categorical measure for transmural scar could be more relevant.

PVA cryogel gel (10% by weight in water) was the material of choice for the scar phantom as it had high water content similar to that of human tissue. It also had a highly elastic medium similar to tissue, which was achieved by repeated freezing (-35°C) and thawing of a uniform PVA solution [7].

D. Limitations

Partial volume effect was a limitation of this study. This introduced errors in the scar reconstruction step, a prerequisite step for transmural scar. Partial voluming can be a limiting factor in MRI where the resolution is relatively low compared to other modalities such as CT. However, MRI is the gold-standard for cardiac tissue characterisation and thus the preferred modality for scar assessment. In our study, a resolution of $1.7 \times 1.7 \times 8$ mm was used to image a phantom 55 by 65 mm and this resulted in some blurred boundaries. There are implications of partial voluming in our work of phantom validation. In some segments, where scar could not be accurately delineated due to unclear boundaries, extra pixels of scar or myocardium introduced errors. A perfect accurate representative image of the prepared phantoms could not be obtained. Future work could involve measuring transmural scar from high spatial resolution. 3T MRI images of scar in animal models exists and is also open-source [8].

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