

Computed Tomography-Based Left Ventricular Tissue Heterogeneity in Ischaemic Cardiomyopathy: Investigation of Adipose Tissue and Fibrosis

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Abstract

Disease-induced cardiac remodeling and the complex healing process post myocardial infarction (MI) are key drivers of arrhythmogenic substrates that predispose patients to ventricular tachycardia (VT).

Ten post-MI patients were imaged using computed tomography (CT). Cardiac magnetic resonance (CMR) imaging was additionally performed on three patients. A fully automated segmentation supplemented by manual correction was used to create high-resolution 3D biventricular models. Adipose tissue was identified and introduced into the model, defining different boundaries for computing the wall thickness (WT). Thresholds were personalized by modeling WT distributions with three Gaussian Mixture Models (GMMs).

Excluding fat in the WT computation showed better agreement with substrate defined by CMR. Our study reports GMM-personalized mean thresholds for fibrosis as 2.88 ± 0.8 mm and borderzone as 4.53 ± 0.7 mm which fall within experimental and clinical values.

The presented reproducible approach for myocardial characterization in post-MI patients, incorporating adipose deposits and personalized WT threshold-defined fibrosis, shows agreement with previous CT studies. This improves identification of arrhythmogenic substrates with highly personalized, patient-specific cardiac models.

1. Introduction

Cardiac remodeling post myocardial infarction (MI) is a complex process and can be associated with a significant risk of potentially lethal late ventricular arrhythmias [1]. The accepted paradigm is that ventricular tachycardia (VT) occurs late after MI as a result of the pro-arrhythmic properties of myocardial fibrosis which results in electrical insulation of viable tissue, creating the substrate for reentry [2], [3]. Post-MI remodeling may also include fat

deposition within and around fibrosis [4]. Recent developments suggest that larger amounts of fat deposition are associated with an elevated risk of VT due to even greater pro-arrhythmic properties than fibrosis [5], [6].

Patient-specific, image-based heart models are widely used in simulated electrophysiology, permit realistic simulations of normal or pathological patterns of electrical activity, and may be used to study the impact of abnormal ventricular geometry and conduction properties on arrhythmia vulnerability and dynamics. Particularly, in-silico simulations can non-invasively predict VT risk [7] and estimate critical sites for termination of the circuit. A key challenge is accurately defining pathological structural cardiac remodeling from clinical imaging studies. The accurate identification of scar and fat represents an important pre-procedural stage which may be helpful for catheter ablation planning and implantable cardioverter defibrillator (ICD) therapy [8], [9].

In this report, we propose a novel and reproducible methodology of personalizing cardiac models by including the computed tomography (CT) biomarkers of adipose tissue and left ventricular (LV) wall thickness (WT)-defined fibrosis.

2. Methods

Study Cohort The study population consisted of 10 ICD recipients with underlying ischaemic cardiomyopathy and no CT contraindications. Cardiac CT imaging was acquired on a dual-source multi-detector scanner (Siemens Force Dual Energy; Siemens Healthineers, Erlangen, Germany). A full retrospective ECG-gated scan was acquired using a FLASH Angiogram sequence at 100kV with a slice thickness of 1mm. Three of the ten patients had additionally undergone cardiac magnetic resonance (CMR) imaging.

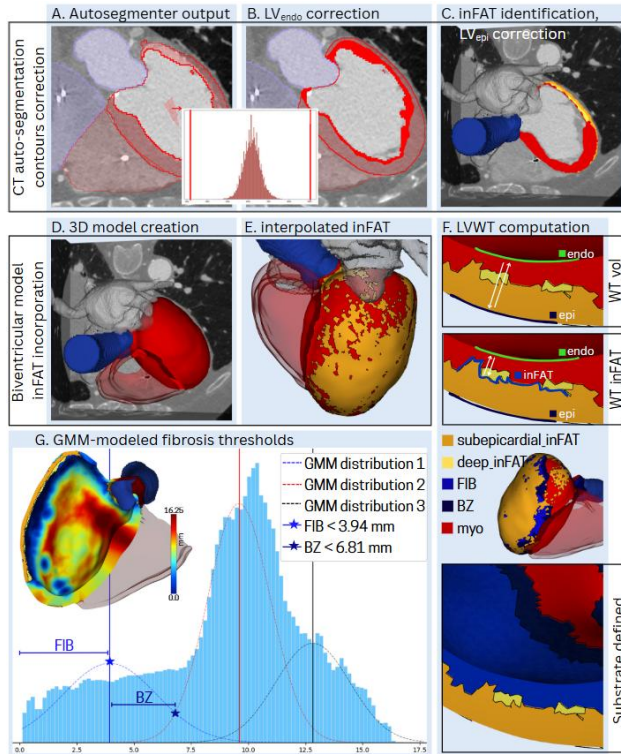


Figure 1. Integration of patient-specific CT biomarkers.

Segmentation Ventricular blood pools and LV wall were segmented using the autosegmenter provided by Studio (<https://numericor.at/rlb/wordpress/products/>). Minor manual corrections were required to smooth discontinuity near the ICD-induced artefacts (Fig.1.A).

Blood Pool Mask To clearly define the LV endocardium and account for the complex trabeculation topography, the distribution of an LV blood pool sample was assessed. The lower and upper segmentations thresholds were defined as standard deviations away from the lowest and highest value, respectively, and the LV blood pool mask was amended and smoothed (Fig.1.B).

Adipose Tissue Identification To overcome misclassification of the LV epicardial contour from the automatic segmentation and to account for fat deposition co-localizing with infarcted areas, which might be visually difficult to differentiate, fat was included in the cardiac model. Thus, the adipose tissue is identified on the CT scan as hypoattenuation ranging from -180 HU to -5 HU. This identification was further separated into deep intramyocardial infiltrated fat (inFAT), and thinner layers of subepicardial inFAT (Fig.1.C), based on the transmural extent of adipose deposition [10].

CT-Based Models Personalized 3D biventricular models were generated from the CT segmentation using CardioTwin, an automated model generation pipeline (<https://numericor.at/rlb/wordpress/products/>). The model

resolution was 0.85 mm on average and comprised of approximately 4.5 million finite elements. From these models, the LV submesh (Fig.1.D) was extracted to facilitate the detailed spatial mapping of adipose tissue (Fig.1.E) and the computation of thickness maps.

LVWT Tissue thickness was quantitatively assessed by computing the distance between the boundaries that define the LV. In a first case, the boundaries were defined as the surface of the endocardium (LV_{endo}) and the boundary of the epicardial surface excluding the subepicardial inFAT region (LV_{inFAT}). A visual representation of the boundaries is presented in Figure 1.F. To calculate transmural thickness, an Eikonal-based approach was employed using a methodology previously proposed [11]. Here, the equation was solved first by assigning the distance of every mesh element away from LV_{endo} , and then inversely by solving from LV_{inFAT} toward LV_{endo} . The cumulative result of these two orthogonal distance maps provides a symmetric transmural WT map as a finite element-wise representation of the LV thickness (WT_{inFAT}), as seen in the clipping of the LV model in Fig.1.G.

Additionally, WT_{vol} was computed for the whole LV volume as is described above between the endocardial, LV_{endo} , and epicardial, LV_{epi} , surfaces (Fig.1.F) i.e. not accounting for epicardial fat.

GMM Thresholds To enhance interpretability and identify regions of relative thinning, a personalized thresholding approach was implemented. The distribution of WT values was modeled using a GMM with three components, which probabilistically decompose the data into distinct tissue thickness profiles (Fig.1.G.). GMM 1 captures the distribution of abnormally thin WT values, likely reflecting fibrotic tissue. GMM 2 represents tissue with normal WT, corresponding to healthy myocardium. GMM 3 models regions with abnormally thickened myocardium, which may arise from pathological remodeling or inclusions of trabeculae and papillary muscles near the endocardial surface. This classification can be observed in the last panel of Fig.1.

CMR Data Acquisition & Processing The late enhancement CMR protocol was performed on a 1.5 Tesla scanner (MAGNETOM Sola or MAGNETOM Aera, Siemens Healthineers, Erlangen, Germany), acquired using a short axis late-gadolinium enhancement (LGE) under free breathing conditions.

The LV endo- and epicardial contours were segmented and manually adjusted in ADAS3D (Galgo Medical, Barcelona, Spain) by processing the 2D LGE-CMR images to generate 3D LV models. Intensities of the LGE imaging were normalized between 0, indicating healthy tissue, and 1, which indicates dense fibrosis. The exported ADAS data were used to generate an LV finite element model of ~ 1 mm resolution with each tetrahedra containing its corresponding mapped normalized LGE intensity [12].

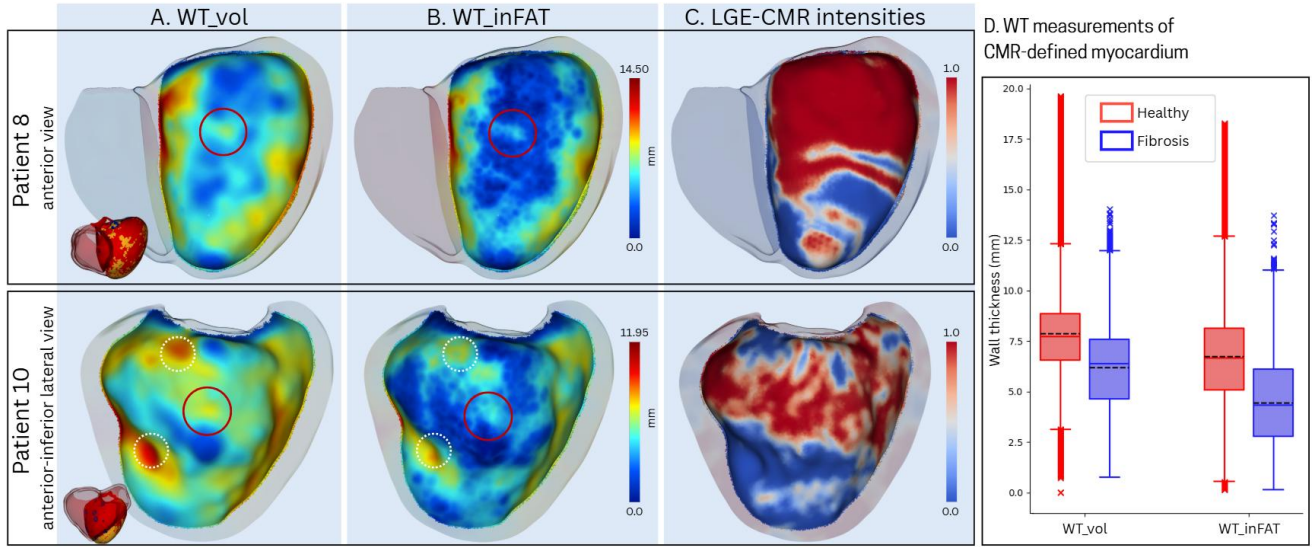


Figure 2. WT_{vol} (panel A) and WT_{inFAT} (panel B) maps show distinct differences in the comparison between low WT and high LGE-CMR intensities (panel C) that define fibrosis. WT_{inFAT} distinguishes regions of thinning (red circle) while maintaining regions of healthy myocardium (white circles). Panel D shows quantitative differences in the WT distributions.

3. Results

For the three matched CT-LGE data sets, Figure 2 illustrates regional differences in LVWT as visualized through the two distinct approaches, WT_{vol} (panel A) and WT_{inFAT} (panel B). Panel C shows the comparison with LGE-CMR intensities, where red regions indicate fibrosis and border zone tissue (panel C). Notably, the spatial distribution of WT differs substantially between these two methods. The WT map accounting for inFAT (Panel B) demonstrates a sharper delineation and higher propensity of regions with pronounced wall thinning (dark blue) compared to Panel A, which corresponds to areas of elevated LGE-CMR intensities (red). In particular, WT_{inFAT} overrides tissue regions previously defined as healthy myocardium by WT_{vol} and re-defines them as thinned myocardium (red circles), while simultaneously preserving healthy myocardial or thickened regions of tissue (white circles). These differences in wall thinning and thickness shown by WT_{inFAT} in Panel B agree with the LGE-CMR intensities of the same regions, presented in Panel C.

Panel D in Figure 2 highlights the difference in WT distributions in the LV regions that are defined as fibrotic (FIB) and healthy myocardium by the LGE-CMR intensities. As observed, fibrotic WT values are appreciably lower than measurements in healthy regions, with fibrotic WT_{inFAT} returning the lowest mean.

To compare the performance of the GMM-defined substrate thresholds (borderzone and fibrosis), Figure 3 combines all patient-specific thresholds computed using the WT_{vol} and WT_{inFAT} data sets. Mean dense fibrotic and borderzone threshold of 4.71 ± 0.6 mm and 6.11 ± 0.6 mm

was given by WT_{vol} compared to WT_{inFAT}, which yields a mean dense fibrotic threshold of 2.88 ± 0.8 mm and defined a relative borderzone thinning as 4.53 ± 0.7 mm.

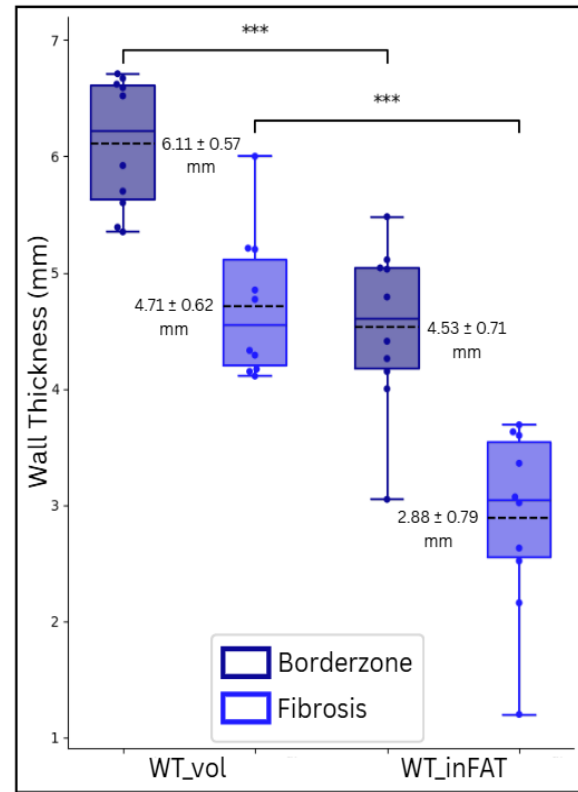


Figure 3. GMM-modeled WT thresholds for borderzone (dark blue) and fibrosis (light blue) across all patients.

4. Discussion

In this study, we propose novel and reproducible methodologies of utilizing CT-based biomarkers of blood pool HU values, adipose tissue, and GMM-modelled WT distribution for fibrosis localization for fast, inexpensive, and accurate identification of substrate for personalization of cardiac models.

Accounting for inFAT in our study yields a mean dense fibrotic threshold of 2.88 ± 0.8 mm and mean borderzone as 4.53 ± 0.7 mm. Compared to WT_{vol}-defined thresholds (Fig.3), these measurements better agree with previously reported data. Specifically, in a study of post-infarct VT patients referred for ablation, Ghannam et al. (2018) showed that abnormal electrograms and critical ablation sites corresponded to CT-defined ridges (WT: 4.2 ± 1.2 mm) bordered by areas of thinning (WT: 2.6 ± 1.1 mm) [13]. Similarly, Takigawa et al. (2019) demonstrated that VT isthmuses in postinfarction patients had a very high sensitivity for co-localizing with relatively preserved wall thickness surrounded by dense scar (median 2.4 mm vs 1.5 mm) [14]. Our thresholds suggest that accounting for inFAT yields a more conservative and more specific delineation of fibrotic regions.

In addition to incorporating inFAT, modelling WT by using a GMM with 3 components allows for patient particularities to be accounted for and introduced into the substrate identification, as can be observed in Figure 2.

CT-defined biomarkers of GMM-modelled WT-fibrosis, inFAT, and an accurate LV blood pool mask provide simple but novel methodologies to personalize cardiac models that improve characterization of arrhythmogenic scar in post-infarct patients and may assist in identifying effective target sites for VT catheter ablation.

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