Computed Tomography-Derived Myocardial Wall Thickness and Extracellular Volume Quantification and Correlation for Identifying Ischaemic Scar

Iulia Nazarov[1], Luca Azzolin, Aurel Neic, Ursula Rohrer, Ronak Rajani, Gernot Plank, John Whitaker*, Martin Bishop*

[1]King's College London, London, UK

*Joint senior authors

Abstract

Localisation of myocardial fibrosis is an important factor in treatment planning as scar-related ventricular arrhythmias are the main precursor to sudden cardiac death (SCD). Fibrosis may be identified by anatomic properties including a decreased wall thickness (WT), increased extracellular volume (ECV), and late-enhancement cardiac imaging.

Cardiac CT data from a cohort of 7 ischaemic ventricular tachycardia (VT) catheter ablation patients were used to construct personalized 3D models. The left-ventricular WT (LVWT) was computed between the simply connected boundaries of the LV model's endocardial and epicardial surfaces. The ECV was quantified at the CT image level using a late-enhancement protocol and interpolated to the LV model. The paired measurements of the finite elements allow a thorough delineation of myocardial tissue.

Linear regression analysis of LVWT and ECV showed a negative fit for fibrotic ($R^2 = 0.57,\ p < 0.001$) and healthy myocardial regions ($R^2 = 0.98, p < 0.001$).

This preliminary study motivates the investigation of LVWT and ECV as indicators of arrhythmic substrate.

1. Introduction

Sudden cardiac death (SCD) is the greatest risk in the presence of ventricle-originating arrhythmias [1]. Structural cardiac abnormalities and myocardial scar sustain malignant re-entrant circuits and ventricular tachycardia (VT) can degenerate into ventricular fibrillation (VF) and SCD [2].

Cardiac imaging is used clinically to identify the geometry, transmurality, and heterogeneity of fibrosis and potential arrhythmic substrate to better understand VT inducibility and inform treatment planning, including implantable cardiac defibrillator (ICD) implantation and VT ablation [3].

Late-enhancement CMR is the current imaging gold standard for localisation of dense myocardial scar. However, CMR comes with several obstacles and for ICD carriers, the susceptibility of device-related artefacts.

The spatial resolution of CMR scans represents a limitation in differentiating between diffuse interstitial fibrosis and healthy myocardium. Extracellular volume (ECV) calculated from CMR T1 mapping has been established as a global assessment of tissue remodelling [4].

CT offers a sub-millimetric scan resolution, while reducing limitations of CMR. On CT, scar has been shown to correlate with regions of myocardial wall thinning [5].

The shared properties of contrast media used in late-enhancement imaging allow a faster and more affordable method for ECV quantification based on CT attenuation, with proven correlation to CMR-derived ECV [4].

The aim of this study is to investigate the relationship between left ventricular wall thickness (LVWT) and CT-derived myocardial ECV as indicators of fibrosis.

2. Methods

2.1. Study population

The study cohort is comprised of 7 CT examinations of ischaemic patients, conducted prior to VT catheter ablation procedures at St Thomas' Hospital, London.

2.2. Image acquisition

Comprehensive cardiac CT protocols were conducted using a dual-source multi-detector scanner (SOMATOM Force, Siemens Healthineers, Forchheim, Germany). This included a high-energy diastolic phase scan (*Fig.1.A*), unenhanced and late-enhancement CT scans (*Fig.1.E*), and a coronary CT angiogram. The post-contrast CT was obtained at 7 minutes after the pre-contrast CT.

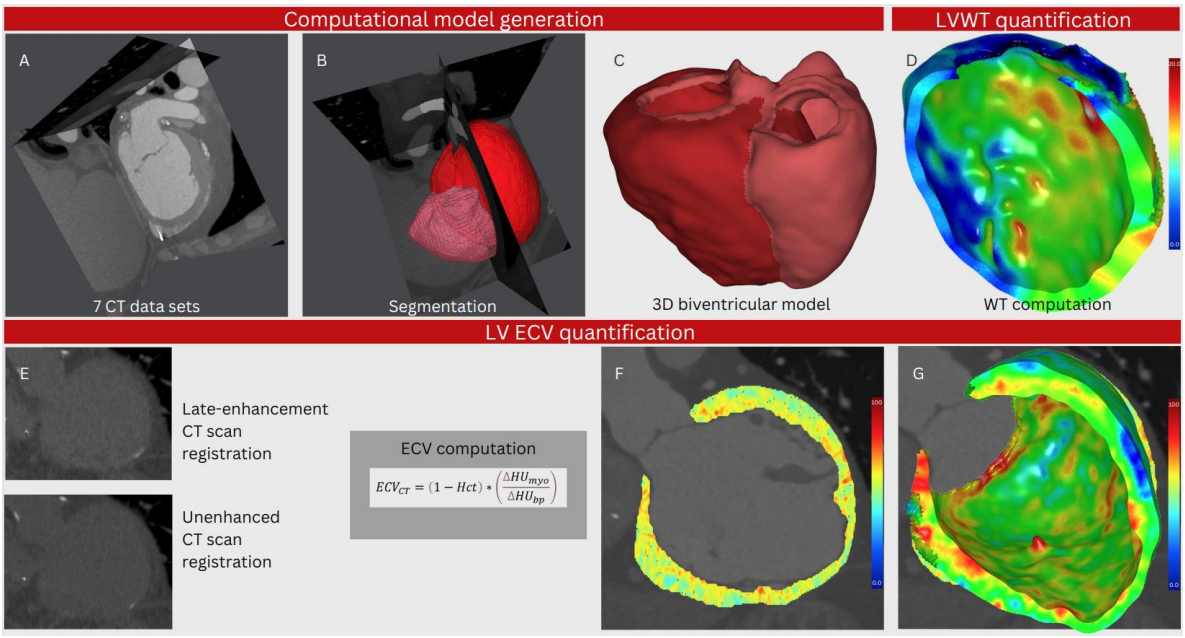

Figure 1, top row: Process of LVWT quantification from segmenting the CT scan *(A&B)*, to the constructed biventricular model *(C)*, and the wall thickness map of the LV model *(D)*.
bottom row: Process of ECV quantification from the pre- and post-enhancement scans *(E)*, to the ECV map computed at the CT image level *(F)*, and interpolation to the LV model *(G)*.

2.3. Segmentation & CT-based 3D models

The heart anatomy was automatically segmented from the CT scan using the CemrgApp open software [7]. The segmentations (*Fig.1.B*) were then manually corrected to close gaps occurring in the LV wall near the ICD leads and their respective artefacts. Highly detailed personalised 3D biventricular models were generated with a fully automated pipeline implemented by NumeriCor (*Fig.1.C*). The models were comprised of an average of 800,000 finite elements with an average mesh resolution of 1 mm. The LV submesh was extracted for detailed thickness computation and ECV interpolation.

2.4. LVWT quantification

The thickness of the LV was computed between the endocardial and epicardial surfaces defined on the model based on a methodology described previously [7]. The tissue is paced with an Eikonal equation with the endocardium as the start, and epicardium as the end surface, and each finite element is assigned a value which represents its distance from the endocardium. Similarly, the tissue is paced starting from the epicardium to the endocardium, to obtain a second set of values representing the distance of each finite element from the epicardium. Once the two measurements are computed, their summation represents the WT quantification of the LV model (*Fig.1.D*). This method has the potential of a comprehensive assessment of myocardial tissue (focal or diffuse fibrosis, healthy myocardium) with the application of personalized thresholds and metrics such as relative thinning. Our study used an end-diastole threshold of 5.0 mm, generally accepted as the cut-off between scarred and healthy tissue [8].

2.5. CT-derived ECV quantification

The properties of late-iodine enhancement CT are used to quantify the differences in the contrast medium as it diffuses through the vascular and extracellular space before being eliminated from the body. In myocardial tissue, an increased ECV is often due to an excess of collagen deposition.

Myocardial CT-derived ECV quantification is based on the distribution of the contrast media between the unenhanced and late-enhancement CT scans, by calculating the differences in Hounsfield units (HU):

$$ECV_{CT} = (1 - Hct) * \left(\frac{\Delta HU_{myo}}{\Delta HU_{bloodpool}}\right) \quad (1)$$

where Hct represents the haematocrit of the patient, ΔHU_{myo} the change in myocardial attenuation, and $\Delta HU_{bloodpool}$ the change in blood pool attenuation.

Subtracting the pre- from the post-contrast image produces a "difference" CT scan that quantifies the ΔHU_{myo} and $\Delta HU_{bloodpool}$ terms. This operation required the late-enhancement scans to be registered with a non-rigid transformation. To account for the unavailable

patient Hct data, a synthetic Hct was calculated based on its linear relationship with the attenuation value of the blood pool, as found in a previous study [9]. The ECV computed at the CT image level is then interpolated to the LV model (*Fig.1.G*).

2.6. Analysis

A negative correlation is expected between LVWT and ECV for an assessment of the LV substrate.

The patient measurements are averaged for each of the 17 American Heart Association (AHA) segments. The segments are further grouped into basal, mid-cavity, and apical regions to be compared against LVWT reference values, and septal and non-septal regions to observe the effects of ICD leads artefacts on the quantification of ECV.

To capture regions of fibrosis indicated by the LVWT, a cut-off value of 5.0 mm was chosen to differentiate fibrotic regions and healthy myocardium. Additional thresholds were defined with a 0.5 mm stepwise increase for LVWT measurements $<= 5.0\,mm$, and a $1.0mm$ increase for LVWT $> 5.0\,mm$. The finite elements which adhered to the thresholding criteria were grouped, as seen in *Fig.2*, and their LVWT and ECV values subjected to linear regression analysis. Clinically nonviable results such as above 100% or negative values of the ECV were neglected.

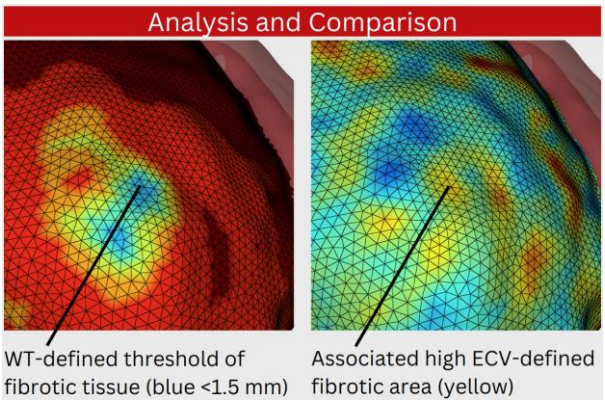

Figure 2, left: Low LVWT region (blue, $< 1.5\,mm$) right: Associated ECV of the same region (orange, 36%)

3. Results

This study measured the mean LVWT in the basal region at $9.06\,mm \pm 1.02$, mid-cavity at $9.88\,mm \pm 1.46$, and apical at $8.95\,mm \pm 1.45$, values in accordance with clinical assessments [8]. The mean ECV was calculated in the basal region at $38.08\% \pm 10.84$, mid-cavity at $33.75\% \pm 11.04$, and the apical region at $31.92\% \pm 9.77$.

The ECV in septal regions was found to be at a mean of $40.45\% \pm 10.75$, and in all other regions at a mean of $32.36\% \pm 9.83$. Though a substantial difference occurs in ECV, the LVWT maintains a similar mean of $9.34\,mm \pm 1.39$ in the septal regions and $9.31\,mm \pm 1.27$ in all other segments. This trend is evidenced in *Fig.3.*

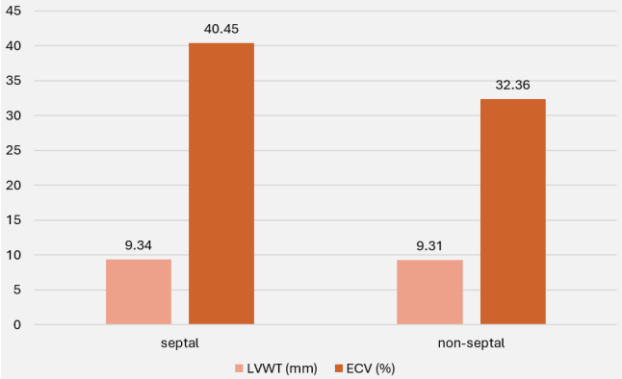

Figure 3: Bar chart comparing mean LVWT and mean ECV of the septal segments compared to all other segments

After thresholding the LVWT, the fibrotic regions of measured LVWT and ECV returned a negative linear relation ($R^2 = 0.57,\ p < 0.001$). This negative relation was found to be a stronger fit in regions of healthy myocardium ($R^2 = 0.98,\ p < 0.001$). Highest averaged ECV (50.5%) was observed in the LVWT region measuring $> 2.5\ \&\ < 3.0\,mm$, and lowest ECV (39.9%) was observed in regions of $> 10.0\ \&\ < 15.0\,mm$. The LVWT and ECV measurements and their plotted trendline for the fibrotic and healthy myocardium regions can be observed in *Fig.4.*

4. Discussion

Regions of fibrosis of the LV may be interpreted from anatomic properties such as thinning WT and high ECV; this study observed their negative correlation.

A major concern in CT-derived ECV lies in ICD carriers. Beam hardening effects and streak artefacts that are evident in the CT scan (*Fig.1.A*) can result in negative or high ECV values that are clinically nonviable.

As evidenced by the ECV between the septal segments (closest to the right ventricle ICD lead) being higher than the ECV of all other segments, even as the LVWT values do not increase (*Fig.3*). Another aspect to consider is the effect streak artifacts have on raising the HU values of the LV blood pool in relation to calculating the synthetic Hct. In addition to this, the lack of a real patient Hct can result in differences as high as 8% [9].

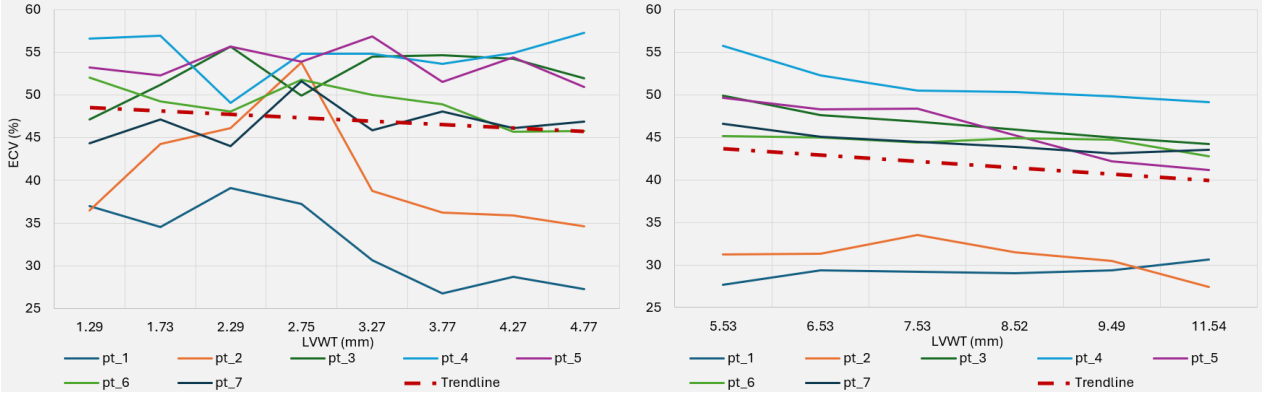

Figure 4, left: ECV is higher ($45\% - 50\%$) in regions of low LVWT ($<= 5\ mm$) indicative of fibrosis. right: ECV decreases ($40\% - 45\%$) in areas of LVWT ($> 5\ mm$) that describe healthy myocardium.

Additionally, the ECV quantification appears to be highly susceptible to the errors arising from the registration of the late-enhancement CT scans. As can be observed in *Fig.4*, the ECV data in fibrotic regions is noisier than the linear ECV data in healthy myocardium. This is likely due to the non-affine registration of a thin LV wall region which could introduce LV blood pool or pericardium HU values in the ECV quantification, as seen in the dark red regions in *Fig.1.F*. These values are more likely to be significant in thinner regions and the base of the LV, as they do not get sufficiently smoothed by enough LV HU values. However, the ECV data computed in areas of thinning LVWT could be significant due to their noise and could be used as a marker for further investigations.

Due to the limited data set of this study, the relationship between CT-derived LVWT and ECV as a global assessment of the LV substrate remains to be further validated. Although LVWT can be used as an additional metric in defining fibrosis in ischaemic patients, ECV is noisy, susceptible to registration and artefact errors, and not solely informative.

Acknowledgements

This work was supported by the CDT in Digital Twins for Healthcare, and the Wellcome/EPSRC Centre for Medical Engineering (WT203148/Z/16/Z)

References

[1] P. Harris and D. Lysitsas, ‘Ventricular arrhythmias and sudden cardiac death’, *BJA Educ*, vol. 16, no. 7, pp. 221–229, Jul. 2016, doi: 10.1093/bjaed/mkv056.

[2] K. Zeppenfeld *et al.*, ‘2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death’, *Eur Heart J*, vol. 43, no. 40, pp. 3997–4126, Oct. 2022, doi: 10.1093/eurheartj/ehac262.

[3] S. Mahida *et al.*, ‘Cardiac Imaging in Patients With Ventricular Tachycardia’, *Circulation*, vol. 136, no. 25, pp. 2491–2507, Dec. 2017, doi: 10.1161/CIRCULATIONAHA.117.029349.

[4] G. Cundari, N. Galea, V. Mergen, H. Alkadhi, and M. Eberhard, ‘Myocardial extracellular volume quantification with computed tomography—current status and future outlook’, *Insights Imaging*, vol. 14, no. 1, p. 156, Sep. 2023, doi: 10.1186/s13244-023-01506-6.

[5] M. Ghannam *et al.*, ‘Correlation between computer tomography-derived scar topography and critical ablation sites in postinfarction ventricular tachycardia’, *J Cardiovasc Electrophysiol*, vol. 29, no. 3, pp. 438–445, Mar. 2018, doi: 10.1111/jce.13441.

[6] O. Razeghi *et al.*, ‘CemrgApp: An interactive medical imaging application with image processing, computer vision, and machine learning toolkits for cardiovascular research’, *SoftwareX*, vol. 12, p. 100570, Jul. 2020, doi: 10.1016/j.softx.2020.100570.

[7] A. J. Yezzi and J. L. Prince, ‘An eulerian pde approach for computing tissue thickness’, *IEEE Trans Med Imaging*, vol. 22, no. 10, pp. 1332–1339, Oct. 2003, doi: 10.1109/TMI.2003.817775.

[8] P. Stolzmann *et al.*, ‘Reference values for quantitative left ventricular and left atrial measurements in cardiac computed tomography’, *Eur Radiol*, vol. 18, no. 8, pp. 1625–1634, Aug. 2008, doi: 10.1007/s00330-008-0939-4.

[9] T. A. Treibel *et al.*, ‘Automatic quantification of the myocardial extracellular volume by cardiac computed tomography: Synthetic ECV by CCT’, *J Cardiovasc Comput Tomogr*, vol. 11, no. 3, pp. 221–226, May 2017, doi: 10.1016/j.jcct.2017.02.006.

Address for correspondence:

Iulia Nazarov
Dept. of Digital Twins, 4th Floor Lambeth Wing, St Thomas’ Hospital, London SE1 7EH, UK
iulia.nazarov@kcl.ac.uk