Volumetric parcellation of the right ventricle for regional geometric and functional assessment.

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\textbf{Abstract}

In clinical practice, assessment of right ventricle (RV) is primarily done through its global volume, given it is a standardised measurement, and has a good reproducibility in 3D modalities such as MRI and 3D echocardiography. However, many illness produce regional changes and therefore a local analysis could provide a better tool for understanding and diagnosis of illnesses. Current regional clinical measurements are 2D linear dimensions, and suffer of low reproducibility due to the difficulty to identify landmarks in the RV, specially in echocardiographic images due to its noise and artefacts. We proposed an automatic method for parcellating the RV cavity and compute regional volumes and ejection fractions in three regions: apex, inlet and outflow. We tested the reproducibility in 3D echocardiographic images. We also present a synthetic mesh-deformation method to generate a groundtruth dataset for validating the ability of the method to capture different types of remodelling. Results showed an acceptable intra-observer reproducibility (< 10%) but a higher inter-observer (> 10%). The synthetic dataset allowed to identify that the method was capable of assessing global dilatations, and local dilatations in the circumferential direction but not longitudinal elongations.

\textbf{1 Introduction}

Cardiac myocytes thicken and/or elongate ([Arts et al., 1994, Grossman et al., 1975, Opie et al., 2006]) as a reaction to altered stimuli (such as pressure or volume loading). These cellular changes are aggregated at organ level, producing size and shape changes in the heart chambers and affecting cardiac function that are referred as remodelling. When this changes help the heart to pump enough blood to satisfy the system oxygen demands while maintaining pressure within physiological range, or maladaptive when changes are not compensated thus provoking a maladjustment that starts damaging the heart or makes it unable to satisfy the systemic oxygen demands and fail.
Even if remodelling is the adaption of individual myocytes as response to very local stimuli, in clinical practice it is often simplified to global changes: a wall thickening with inward motion of the inner wall (thus reducing cavity size and wall stress) as a reaction to pressure loading and a dilatation of the cavity to cope with volume overload so that, without changing the wall deformation during contraction, more stroke volume is ejected with each beat. However, many illnesses have been described as producing regional remodelling: such as for instance the presence of a basal septal bulge induced by hypertension (Baltaeva et al., 2007), a thickening of the septal wall in hypertrophic cardiomyopathies (Olivotto et al., 2012) or a base-to-apex gradient in deformation in deposition diseases such as amyloidosis (Cikes et al., 2010) or thalassemia (HAMDY, 2007). In the clinical community, the quantification of regional patterns is mostly used in segmental motion assessment (particularly in coronary artery disease) rather than local geometry. For the left ventricle (LV), a standardised partition in 17 wall segments has been proposed (Cerqueira et al., 2002), which recently also has been used to quantitatively assess regional strain patterns. However, these wall segments are by definition equal in size and thus of limited utility to assess changes in morphology.

In medical image analysis, the typical method to assess regional morphology is through the creation of an atlas, which is a template shape representative of a population, and registering each patient-specific shape to this atlas (Zhang et al., 2017). This has shown useful to describe inter-individual variations of overall morphology in populations, but is more challenging when following subtle regional remodelling within an individual over time. Additionally, this approach has the drawback that it requires registration (deforming the atlas to match the individual) (Joshi et al., 2004). This is an unstable and computationally expensive process. Especially since there are few and separated landmarks for the ventricles, this registration is based on image intensity/shape patterns, and has no guarantee of the correctness of the point-to-point correspondence. Thus, when using computational meshes to represent the heart through image segmentation, after atlas registration, an important part of the mesh nodes’ positions do not correspond to identifiable anatomic landmarks among different individuals so that point-to-point correspondence cannot be used anymore to assess physiological remodelling.

To avoid explicit registration, some authors have proposed parametrisation methods to create anatomical maps of organs (Nuñez-Garcia et al., 2019; Vera et al., 2013; Paun et al., 2017; Hurdal and Stephenson, 2009) by finding smooth bijective maps from each surface/volume to a common domain, a subset of $\mathbb{R}^2$ or $\mathbb{R}^3$ respectively. The parametrisations of individual anatomies can subsequently be used to obtain a point-to-point correspondence. The mapping is typically obtained through a minimisation of some kind of distortion metric. The most common is trying to force the mapping to be as conformal as possible, ie that locally maintains angles, (Lévy, 2001; Gu et al., 2010). Maintaining angles is not the only possibility: there are other approaches that try to maintain, for instance, local distances (Sorkine and Alexa, 2007) or areas.

Compared to the LV, the right ventricle (RV) has a complex and irregular shape, with more variability (Haddad et al., 2008a) so that regional analysis of the RV is more difficult than of the LV. Its position in the chest produce a bad acoustic window using 3D echo-cardiography and results in low-quality images, limiting the applicability of complex techniques. Instead, in clinical research a segmental approach is more common due to its easier interpretability and the spatial smoothing effect of averaging over the segment. There have been studies referring to a regional analysis of different segments that compose the RV (Addetia et al., 2016, 2018; Moceri et al., 2018). These studies only analyse the epicardium, more specifically its wall curvature. While local curvature is an important component of the wall stress generated by pressure and thus very important in pressure-overload remodelling, an analysis in terms of regional dilatation/volume is needed to correctly assess remodelling from volume-overload. Therefore, there is a need for quantitative approaches that can assess regional shape as well as volume remodelling.
in a clinically relevant and physiological plausible way.

In this paper we develop the segmental approach further for a clinical application, using images of suboptimal quality, to propose an automatic method for mesh-independent volumetric parcellation of the RV based on the geodesic distance to three easily identifiable landmarks: tricuspid valve, pulmonary valve and apex. To assess the method, to identify clinically relevant and physiologically plausible regional remodelling, we validate it using a synthetic dataset created through regional induction of circumferential and longitudinal elongation and analyse the sensitivity of the parcellation to both global and regional remodelling. To assess the performance, and robustness to noise, in a real setting, we also do an inter- and intra-observer reproducibility analysis, as well as a test/retest comparison of two sequential acquisitions, on the same patient. This technique enables both a regional analysis of anatomy, using the end diastolic (ED) volumes, as well as function, via regional ejection fraction (EF).

2 Methodology

2.1 Parcellation of the right ventricle

The RV has a complex and asymmetric shape and is positioned surrounding the LV. Its anatomy is most commonly described as biaxial: one axis goes from tricuspid valve to the apex, and the other from the apex to the pulmonary valve. The RV can be grossly separated in 3 main anatomically and functionally different parts: the outflow infundibulum, the smooth inlet and the trabeculated apex ([Haddad et al., 2008a,b]). However, there is no consensus on the exact border between these parts, and different experts can draw different region boundaries over the same images. Given that the partition definition is needed to describe volume and shape changes over time when doing follow-up in individuals, we propose an automatic method for volumetric parcellation of the RV, based only on geometric properties. This partition has the advantage of being fully automatic and therefore completely reproducible under the same image and segmentation, however it still depends on image and segmentation quality. To avoid errors due to a bad point-to-point correspondence, our parcellation only uses the geodesic distances from anatomic landmarks that can be clearly identified in 3D echocardiography: the apex, tricuspid and pulmonary valve. The method is independent of the exact triangulation of the ventricular surface.

We applied our method to the analysis of 3D models of the RV generated from 3D echocardiography images using Tomtec software (4D RV-FUNCTION), but it can easily be adapted to other processing platforms and imaging modalities. Figure 1 shows the full process used to parcellate the RV, which is described below.

The first step of our parcellation is the identification of the valves and apex using the provided point-to-point correspondence in the surface mesh (given that these correspond to stable anatomical landmarks in the mesh that can be identified in the image). Next, for each node of the mesh, we compute the geodesic distances to the apex, pulmonary valve and tricuspid valve. The geodesic distances between two points are computed on the surface with an exact algorithm ([Surazhsky et al., 2005]) that computes the length of the minimal on-surface path between two points. The distance between a point and an anatomical substructure is defined as the minimum distance from the point to any point that belongs that anatomical substructure:

\[
\begin{align*}
  d_t(x) &= \min \{d_{geo}(x,y) | y \in \text{tricuspid valve} \} \\
  d_p(x) &= \min \{d_{geo}(x,y) | y \in \text{pulmonary valve} \} \\
  d_a(x) &= \min \{d_{geo}(x,y) | y \in \text{apex} \}
\end{align*}
\]

(1)

Figure 1.a shows the geodesic path from an arbitrary point to the different landmarks, and
Figure 1: Steps to generate the volumetric partition. a) For each point, the geodesic distances to the apex/tricuspid and pulmonary valves are computed. b) The geodesic distances to each of the landmarks define a scalar map over the surface mesh. c) This distance map is extended from the surface to the cavity by tetrahedralising the mesh, and the Laplace equation is used to interpolate values to the interior. d) The ventricle is split in the regions by assigning each point of the cavity to the closest landmark. e-f) Visualisation of the RV parcellation over slices of the original 3D images.
Figure 1b shows distance from every point of the surface to the apex represented as a heatmap: the points furthest to the apex are coloured in red and the closest in blue. After this distance is computed for every point of the surface, the interior of the triangular surface mesh is tetrahedralised using a publicly available software (TetGen version 1.5.1, Shi (2015)) (Figure 1c). The distance defined on the surface of the mesh is propagated to the interior of the ventricle using Laplace’s equation. This equation is discretised using finite elements with a publicly available software (Sfepy Cimrman et al. (2019)). The equation uses the tetrahedralised mesh as domain and Dirichlet boundary conditions specified by the surface-defined distance maps. Formally, this interpolation step is defined as follows, where \( M \in \{ \text{apical, inlet, outlet} \} \), \( \Omega \) refers to the volumetric domain and \( \partial \Omega \) and \( \mathring{\Omega} \) to its boundary (the surface mesh) and interior respectively:

\[
\begin{align*}
\Delta u_M &= 0 & \text{for } x \in \mathring{\Omega} \\
\left. u_M(x) = d_M(x) \right|_{x \in \partial \Omega}
\end{align*}
\]

This process is repeated to compute and extend to the interior of the cavity of the 3 distances. Once the distances are defined in the volumetric mesh, we partition the ventricle, assigning each point of the mesh to the “closest” landmark, using the interpolated distances. \( M_{\text{inlet}} \), \( M_{\text{apical}} \), and \( M_{\text{outlet}} \) respectively are the partition corresponding to the inlet, apex and outflow. Each point is assigned to the region whose representing landmark is “closer”, using the interpolated \( d_z \), as shown in Figure 1d. The partition does not follow the mesh vertices and edges, but new elements are generated during the partition. We used linear interpolation to define the distance values inside each tetrahedron. A formal definition of the segments is:

\[
\begin{align*}
M_{\text{inlet}} &= \{ x | \text{d}_{\text{tricuspid}}(x) \leq \text{d}_{\text{pulmonary}}(x), \text{d}_{\text{tricuspid}}(x) \leq \text{d}_{\text{apex}}(x) \} \\
M_{\text{outlet}} &= \{ x | \text{d}_{\text{pulmonary}}(x) \leq \text{d}_{\text{tricuspid}}(x), \text{d}_{\text{pulmonary}}(x) \leq \text{d}_{\text{apex}}(x) \} \\
M_{\text{apical}} &= \{ x | \text{d}_{\text{apex}}(x) \leq \text{d}_{\text{tricuspid}}(x), \text{d}_{\text{apex}}(x) \leq \text{d}_{\text{pulmonary}}(x) \}
\end{align*}
\]

This partition can be propagated from the ED-surface to end systolic (ES)-surface using the point-to-point correspondence between surfaces belonging to the same individual, that are obtained via tracking the initial surface, and then extended to the interior cavity via the same Laplacian interpolation. With this procedure, we can compute regional ES volumes and ejection fractions, allowing for regional functional assessment of the RV.

### 2.2 Local and global anatomic frame of reference

To clinically interpret local geometric changes, it is more convenient to work in an anatomical frame of reference, with longitudinal and circumferential directions, instead of the Cartesian system of coordinates. At each point of the mesh, circumferential and longitudinal directions are defined locally using the method proposed by Doste et al. (2019). We defined the longitudinal direction using the stationary heat flow in surfaces, with a cold source in the apex, and two hot sources at the same temperature in the two valves. The heat flow is computed by solving the Laplace-Beltrami linear differential equation on a surface. The Laplace-Beltrami operator (\( \Delta \)) is discretised using the cotangent formulation (Pinkall and Polthier 1993):

\[
\begin{align*}
\Delta u &= 0 \\
\left. u(x) = 0 \right|_{x \in \partial \Omega} \\
\left. u(x) = 0 \right|_{x \in \text{values}}
\end{align*}
\]
The longitudinal direction \( l \) at each point is the result of normalising the resulting temperature gradient. The circumferential \( c \) is chosen to be orthogonal to both the longitudinal and the surface normal at that point \( n \), so that \((l, c)\) form a base of the tangent space at the given point:

\[
\begin{align*}
  l &= \frac{\nabla u}{\|n\|} \\
  c &= l \times n
\end{align*}
\]

Figure 2 shows the local circumferential and longitudinal directions. A global longitudinal direction is computed by averaging all the local ones, and the circumferential directions are defined as orthogonal to the longitudinal.

### 2.3 Remodelling deformation strain

For two meshes, a reference and a remodelled mesh, in point-to-point correspondence, we can compute the strain associated to the remodelling. This strain fully characterises the deformation, modulo rigid body transformations. To interpret this strain, it is more natural to work in the previously defined local anatomical reference frame. For each triangle, we can express each of its edges as a combination of the local anatomical directions \((l, c)\). We note \( E^m_t \) the concatenated vectors corresponding to the edges of triangle \( t \) and mesh \( m \). With this, we can compute the local linear transformation \( F_t \) at triangle \( t \). In a continuous setting, this \( F_t \) corresponds to the Jacobian matrix of the deformation:

\[
F_t = E^{m_{def}}_t \left( E^{m_{ref}}_t \right)^{-1}
\]

From this transformation, we can compute the Cauchy strain tensor for small displacements \( \epsilon = (F^t + F)/2 \), and extract the strain in the longitudinal \( \epsilon_{ll} \) and circumferential \( \epsilon_{cc} \) directions. Note that longitudinal and circumferential directions are not necessarily aligned to the principal strain directions, which are the eigenvectors of the strain tensor.

### 2.4 Generation of synthetic remodeling patterns

For generating a plausible surface of the RV, we used a modification of a linear surface construction method ([Wang et al., 2012]) that generates 3D meshes from a local description. The
Figure 3: Two adjacent triangles $T_i$ and $T_j$, with their respective local systems of reference. $d_{ij}$ is the dihedral angle, which is the angle formed between the two normals. It is represented in the midpoint of the common edge. $f_i$ and $f_j$ are the orthogonal frame of reference associated to each triangle.

remodelled mesh connectivity is an input of the method and it cannot contain a non-manifold edge. The local description consists of the edge lengths and the dihedral angle associated to every edge (the angle formed by the normals of the adjacent triangles). Obviously, not all combinations of lengths and angles define a valid surface, but we can formulate the reconstruction in a minimisation setting so we obtain the surface satisfying as much as possible the local description. We will use this method to simulate remodelling, by locally deforming a template mesh.

2.4.1 Local descriptors of the surface

We describe a local frame of reference for each triangle of the mesh from the input data. This frame is arbitrary but uniquely defined, assuming a unique ordering of the nodes inside each triangle. It uses the first node of the triangle as origin, the direction of the first edge as x-axis, the normal as the z-axis and then completes the base to be orthonormal. We will call $a_{ti}$ the coordinates of the i-th point of the triangle expressed in local frame. By convention, $a_{t0} = (0, 0, 0)$, the third coordinate is always 0 for all points (since they are coplanar), and $a_{t1} = (x, 0, 0)$ . Note that by basic trigonometry we can compute the local coordinates in that of the triangle nodes given the 3 lengths, using the constraints that the first node is in 0, and the second one lies in the x-axis.

The unknown variables are the 3D coordinates $x_i$ for each mesh point $i$, and a reference frame $f_t$ associated to each triangle $t$, that corresponds to the mapping from the triangle coordinates $a_t$ to the 3D space. Figure 3 shows two adjacent triangles, with their dihedral angle and the associated frames of reference.

For two adjacent triangles $i$ and $j$, we can obtain the rotation $R_{ij}$ from frame $f_j$ to $f_i$:

$$R_{ij} = f_j^T f_i$$

(10)

We can express $R_{ij}$ using only of the local descriptor: the triangle coordinates and the dihedral angles $d_{ij}$. We call $\phi^v_{\theta}$ to the rotation of angle $\theta$ around the axis of rotation $v$. Let $e$ be the common edge between triangles $T_i$ and $T_j$, we can compute the angle $\theta$ between edge $e$ and the first edge of $T_i$, and $\theta'$ is the respective angle for $T_j$. Then, we can express $R_{ij}$ as the composition of 3 rotations:

$$R_{ij} = \phi^x_{\theta} \phi^z_{d_{ij}} \phi^z_{\theta'}$$

(11)
2.4.2 Linear reconstruction

The reconstruction method is an inverse problem of the computation of the local triangle coordinates as and transition matrices Rs. We operate the previous equations to obtain an equivalent form linear on xs and Rs, and use their quadratic residual as energy, thus formulating an optimisation problem with the world position of the nodes x and the frames f as variables. To easily solve this problem, we do not enforce that matrices fs are rotations, but arbitrary matrices.

By multiplying by fj equation 10 and rearranging terms, we obtain the following equivalent equation:

\[ f_i - f_j R_{ij} = 0 \]  
(12)

For every edge eij in every triangle t, where the nodes have in-triangle indices i and j respectively, we can use that ft to transform from triangle coordinates to world coordinate:

\[ x_i - x_j = f_t (a_{ti} - a_{tj}) \]  
(13)

After moving all terms to the LHS, we obtain:

\[ x_i - x_j - f_t (a_{ti} - a_{tj}) = 0 \]  
(14)

Thus, we have obtained equations for computing x and f from the Rs and as. We create an energy by minimising the squared \(L_2\) error of the sum over all edges of equations 12 and 14. For the matrices we use the Frobenius norm, which is simply the sum of squares of all the elements. We can add weights to each term of the equation (the one that solves for the frames, and the one that solves for the node position) to control their relative contribution to the global solution. This energy is quadratic and sparse, so it can be efficiently solved with linear methods via its normal equations. Its final form reads:

\[
E_I(x, f) = \sum \sum \|x_i - x_j - f_t (a_{ti} - a_{tj})\|^2
\]  
(15)

\[
E_{II}(f) = \sum \sum \|f_t - R_{ij} f_j\|^2
\]  
(16)

\[ E = \lambda_1 E_I + \lambda_2 E_{II} \]  
(17)

2.4.3 Log-domain reconstruction

In the previous formulation, it is not imposed that the frames fs are really orthonormal matrices. This can lead to artefacts where the fs have a determinant < 1 and shrinking of the mesh. To avoid this situation, a solution to that is to enforce that matrices fs are rotations by parametrising them on another domain.

Any scalar function that can be expressed by a Taylor series can be converted to a matricial function, by using the matrix product instead of the scalar to compute the powers of the variable. The matrix exponential is defined as:

\[
\exp(X) = \sum_n \frac{X^n}{n!}
\]  
(18)

A well known result is that the matrix exponential of a matrix A is a rotation if and only if A is antisymmetric, so, we can make \(f_i = \exp(w_i)\), where \(w_i\) is an antisymmetric matrix. An antisymmetric matrix can be parametrised by its 3 lower triangular components. We define \([v]_x\) as the mapping from the parameters v to the associated antisymmetric matrix, where \(v \in \mathbb{R}^3\):
\[
[v]_\times = \begin{pmatrix}
0 & -v_3 & v_2 \\
v_3 & 0 & -v_1 \\
-v_2 & v_1 & 0
\end{pmatrix}
\] (19)

This parametrization disrupts the linearity of the previous energy (Eq 15), but we are still able of computing the derivatives. Usually matrix functions are very cumbersome to differentiate, but for the particular case of the matrix exponential of a 3D antisymmetric matrix, there exists a closed formula ((Gallego and Yezzi, 2015)). Specifically, when applied to a fixed vector, and using the notation \( f = \exp([v]) \), where \( v \) is the reduced parameters of an antisymmetric matrix:

\[
\frac{\partial f(v)}{\partial u} = -f[u] \times vv^t + (f' - Id)[v]_\times \|v\|^2
\] (20)

Using the derivative formula of the matrix exponential, and typical matrix calculus we find the derivatives of the previous expressions. We use the trick that, for any orthonormal base \((e_0, e_1, e_2)\) and any matrices \( A, B \in \mathbb{R}^{3\times3} \):

\[
(A, B)_F = \sum_k \langle Ae_k, Be_k \rangle
\] (21)

The first dot product is the Frobenius product between matrices, and the second is the usual dot product between vectors. With this trick, we can compute the derivatives for each rotation defined over a face \( f_i \), and each node position \( x_i \). We note as \( D(v)[u] \) the derivative \( \frac{\partial f(v)}{\partial v} \) to avoid a cumbersome notation. After some trivial computations and reordering, we obtain:

\[
f_i = \exp(v_i)
\] (22)

\[
\nabla_{f_i} E_I(v, x) = 2 \sum_k \sum_{t_i \sim t_j} D(f)[e_k](f_i e_k - R_{i,j} f_j e_k) \] (23)

\[
\nabla_{f_i} E_{II}(v, x) = 2 \sum_{c=(u,v) \in t_i} D(f)[a'_u - a'_v] (x_u - x_v - f(a'_u - a'_v)) \] (24)

\[
\nabla_{x_i} E_I(v, x) = 2 \sum_{c=(i,j) \in t_i} (x_i - x_j - f(a'_i - a'_j)) \] (25)

\[
\nabla_{x_i} E_{II}(v, x) = 0 \] (26)

Since we can analytically compute the gradient, we can use a first order optimisation method. We use the L-BFGS quasi-Newton algorithm ((Dennis and Moré, 1977; Nocedal, 1980)).

### 2.5 Global remodelling

Global remodelling involves large changes that correspond to overall size rather than the local shape remodelling. It corresponds to the variability due to for instance the individual’s height and weight. The global longitudinal direction \( l_{glob} \) is determined similar to the mean local longitudinal direction. The longitudinal and circumferential remodelling transformations are modelled as linear function for each \( t \in \mathbb{R} \), which is the factor of stretching in the desired direction. The longitudinal transformation is defined as \( (Id + t * l_{glob} \otimes l_{glob}) \), and the circumferential as \( (Id + \sqrt{t} * (Id - l_{glob} \otimes l_{glob})) \), where \( Id \) is the 3x3 identity matrix and \( t \) the scaling parameter.
2.6 Data acquisition

3D echocardiographic images of 5 university-league American style football players were acquired in a modified apical 4 chambers view using an EPIQ7 ultrasound system (Philips Medical Systems, Andover, MA) equipped with a 1 to 5 MHz transthoracic matrix array transducer (X5-1). For each patient, 4-6 different ECG-gated subvolumes were acquired in a single breath-hold to be compounded into the full 3D+t images of 2 complete cardiac cycles. A written informed consent form was obtained from all study participants.

A control was imaged in two consecutive acquisitions by different operators to obtain an estimate on the variability due to the imaging process.

The image loops were processed using a clinically validated software (4D RV-FUNCTION Tomtec-Arena TTA2, Tomtec Imaging Systems GmbH, Unterschleissheim, Germany ([Niemann et al., 2007])) to segment the RV and obtain a 3D-model for each patient. These models were exportable in ued, a standard file format. All 3D models had the same topology: a triangular watertight mesh with 938 nodes and 1872 faces. The points were in approximate point-to-point correspondence. The segmentation pipeline consisted of the following steps: first the clinician segments the RV endocardium contour of the frame corresponding to the R peak using the semiautomatic tool, and the result is tracked during a full cycle. Afterwards, the clinician can adjust the ES and ED (defined as the peak of the R wave in the ECG) segmentation iteratively until visually satisfied with the resulting contours. This processing was repeated 3 times for each acquisition by two different operators, to assess the inter- and intra-observer repeatability.

3 Experimental setting

3.1 Reproducibility of the 3D models

We use the re-quantified individuals to assess the stability of the segmentation, the generated 3D models and the point-to-point correspondence. For each pair of re-analysed surfaces derived from the same images, we computed the difference of global volumes and the Dice coefficient of the different segmentations, a standard measure for comparing two different segmentations (noted as $S_1$ and $S_2$) and defined as:

$$\text{Dice}(S_1, S_2) = \frac{2|S_1 \cap S_2|}{|S_1| + |S_2|}$$

(27)

As a measure of the mesh node stability, we computed for each node the registration error as the euclidean difference between nodes with the same indices from different analyses as well as the point-to-surface distance (distance from a point to the closest point on the mesh, that might lie inside a face) for every node. For visualisation, we show the mean point-to-point (resp point-to-surface) error map, averaged over the different individuals. This map was plotted over a template mesh, which was the population mean shape computed via Generalised Partial Procrustes Analysis ([Dean 2000]).

Since the test/retest segmentations come from different images, we cannot use the previous metrics that depends on image coordinates. Therefore, we assessed the resulting 3D models only qualitatively.

3.2 Reproducibility of the parcellation method

The RV parcellation provided by our method is dependent on the RV segmentation. Therefore, even if the method is automatic and 100% reproducible under the same image and segmentation,
we need to evaluate the robustness of the method to the segmentation variability that is present in a normal clinical setting.

We used the re-analysed dataset to test the reproducibility of the regional volumes and EF in the inter- and intra-observer tests. We report the mean and percent absolute difference in volumes and EF. For the data obtained in the test-retest setting, we report the regional volumes for both acquisitions, as well as the absolute and percent differences.

3.3 Validation of the parcellation method

To validate our method, given the lack of a clinical ground truth, we remodelled a template shapes synthetically, both locally and globally. Since we imposed the remodelling, we know the specific areas as well as the exact amount. We also compute the global difference in volume between the template and the remodeled meshes.

For each RV segment (apical, inlet, outflow), we generate two localised remodelling patterns: one elongating in the longitudinal direction, and the other in the circumferential. The localisation of the remodelling is achieved by imposing a decay on the desired strain magnitude: the strain at each triangle decays proportional to a Gaussian function of the distance from the center of the triangle to the anatomical landmark defining the segment (apex, tricuspid, pulmonary valve). The circumferential and longitudinal strains are defined as follows:

\[ \epsilon_v(x) = v_{\text{max}} \exp \frac{d_M(x)^2}{\omega^2} \]  

Where \( v \in \{\text{longitudinal, circumferential}\} \), and \( M \in \{\text{tricuspid, pulmonary, apical}\} \). The maximal strain \( V_{\text{max}} \) is chosen to satisfy a predefined total volume increment of 5 ml. The valves’ annuli are composed of fibrous tissue and do not show much remodelling in most cases, but they can passively stretch in severe volume overload. Since this localised model is primarily aimed to assess short-term remodelling only, the strain is set at 0 in the triangles corresponding to a valve. Shear strain is currently not included in our work.

The global remodelling was generated by applying the linear transformation corresponding to a scaling range that increases from 0% to 10% the global volume.

We applied our parcellation method to the template mesh and the remodelled meshes. Afterwards, we compute the differences in regional volumes from the template, and assess our method’s accuracy. The global remodelling homogeneously affects all regions: the volume percentages of each region have to be preserved. The local remodelling only affects one region, and therefore only the deformed region must increase its volume.

4 Results

4.1 Regional and global volumes of our population

Table 4 shows the regional and global volumes, as well as the EF and the heart rate (HR) of all individuals composing our test populations. All generated 3D models and associated parcellations can be seen in Figure 8. There is a lot of variability in both the global shape and the volumes, specially in the basal part of the inlet and outflow tract. Visually, the apical segment presents less variability, but the separation line between the inlet and outflow presents more heterogeneity. In the following sections we will assess how much of it corresponds to noise and our method’s unstability, and how much is due to the natural variability of the RV.
Table 1: Intra and inter-observer variability (in ml and percent) of the segmentations and node positions.

| Metric                        | Interobserver | Intraobserver |
|-------------------------------|---------------|---------------|
| Volume difference             | 13ml (9%)     | 6ml (4%)      |
| Dice coefficient              | 0.64          | 0.89          |
| Mean node error               | 7.6mm ± 2.3mm | 6.2 ± 1.5mm   |
| Mean point-to-surface error   | 1.8mm ± 1.0mm | 1.3mm ± 0.5mm |

4.2 Reproducibility of the 3D models

Here we present the analysis of the inter- and intra-observer reproducibility of the ED shapes, as acquired from 3D echocardiography. Table I shows the mean error of the different metrics to assess shape differences: total volume difference, Dice coefficient and mean point-to-point and point-to-surface distances. As expected, interobserver reproducibility was lower than intraobserver. The total volume error was below 10% for both inter- and intra-observer, but the other metrics, that evaluated local differences, indicated lower stability. In particular, the interobserver Dice coefficient (0.64) was considerably lower than the intraobserver one (0.89).

Figure 4 shows the regional mean inter- and intra-observer point-to-point distance. We can see that the anterior insertion points, specially near the right ventricular outflow tract (RVOT), presents a higher level of instability with mean distances above 1cm. Instability is not only present in the anterior wall, but also affects the septum. Figure 5 shows the mean error using the point-to-surface distance instead of the point-to-point, thus assessing the stability of the contours independently of the node placement. The mean error is lower compared to the point-to-point case and contained to the outflow.

Figure 6 shows the 3D models generated from the test/retest experiment and their parcellations. Differences in the parcellations will be described in next subsection. Both meshes have the same total volume, but differ in shape: acquisition #2 has a higher tricuspid valve and in acquisition #1 the pulmonary valve is further. Also, acquisition #1 presents a displaced anterior insertion "line". Acquisition #2 segmentation has a wider septum, that extends further in the anterior segment. Acquisition #2 has a more spherical apex and a flatter posterior wall.

4.3 Reproducibility of the parcellation method

In this section we report the stability of the measurements obtained with the proposed parcellation method. Reproducibility was estimated using the meshes obtained from the data used for the inter- and intra-observer reproducibility test. Table 2 shows the mean intra- and interobserver errors and the mean value of the variables for the regional and global ED volumes and EF. We can observe large errors in the interobserver case (¿12%), but lower for the intraobserver case (6 – 8%). The outflow segmented had the biggest error for volume(11%), and regarding function, the apical EF has the biggest error.

We used the test/retest acquisition to verify whether the level of noise is higher in that situation. The 2 generated 3D models can be found in Figure 6, and we can see clear differences in shape. Table 3 shows the quantitative analysis of the regional volume differences. The errors found in the test/retest experiment corresponded to the ones observed in the intraobserver reproducibility test.
Figure 4: Mean point-to-point registration error for each node on the interobserver and intraobserver reproducibility test. We can see that the biggest errors are concentrated near the outflow tract, and in the anterior wall. The posterior wall and apical regions are more stable.

Table 2: Intra- and inter-observer variability of the segmental and total end-diastolic volumes and EF, expressed as the mean error and mean percent error (in parenthesis).

|       | Interobserver error | Intraobserver error | Mean value |
|-------|---------------------|---------------------|------------|
| RV EDV | 12.7ml (9%)         | 6.2ml (4%)          | 144ml      |
| Outflow EDV | 5.1ml (14%)   | 3.9ml (11%)        | 36ml       |
| Inlet EDV  | 9.3ml (13%)      | 4.2ml (6%)         | 68ml       |
| Apex EDV  | 4.7ml (14%)       | 3.0ml (8%)         | 39         |
| RV EF     | 6% (12%)           | 3% (6%)            | 50%        |
| Outflow EF | 6% (14%)          | 4% (8%)            | 42 %       |
| Inlet EF  | 8% (16%)           | 3% (8%)            | 50%        |
| Apex EF   | 9% (15%)           | 6% (10%)           | 61%        |
Figure 5: Mean point-to-surface distance for each node on the interobserver and intraobserver reproducibility test. The errors are much lower than the point-to-point case, and concentrated in the boundaries, specially the outflow tract, and a fragment of the posterior wall near the apex that is usually cut in the images.

Table 3: Regional volumes resulting from two consecutive acquisitions of the same patient.

|                  | Outflow (ml) | Inlet (ml) | Apex (ml) |
|------------------|--------------|------------|-----------|
| Acquisition #1   | 20.81        | 50.82      | 18.64     |
| Acquisition #2   | 22.45        | 47.51      | 20.0      |
| Absolute error   | 1.64         | 3.25       | 1.40      |
| Relative error   | 7.5%         | 6.8%       | 7.3%      |
Figure 6: The two generated 3D models and their parcellations. Even if they have the same approximate size, they have significant differences especially in the anterior wall. These regional differences in the 3D models affects the parcellations: the biggest parcellation differences are in the center of the septum and free wall.
Figure 7: Regional volume differences between the synthetically remodelled meshes and the reference RV, for both regional and global. The regional remodelling consists of an increment of up to 5ml in a certain region only. We can see that the method is able to capture between 90% and 80% of the circumferential remodelling, but is not able to identify the procedence of longitudinal remodelling.

4.4 Validation of the parcellation method

We used the synthetic remodelling method to generate different types of localised and global remodelling in the longitudinal and circumferential directions. As template we used the mean shape of our control population, obtained using the Partial Generalised Procrustes Analysis. The local remodelling scaling parameters are set to obtain a total volume increase of 5ml, with all combinations of affected part (apical, inlet or outflow) and direction (longitudinal or circumferential). Figure 9 shows the locally deformed meshes. Several meshes were generated for the global remodelling, its volume increase ranging from 0% to 10%. An example of the generated meshes using this method can be seen in Figure 10.

The first column of Figure 7 shows the regional dilatation (%) response to a global circumferential and longitudinal scaling. The expected output is that all regions increase their volume in the same proportion, which is corresponds to the identity line. We can see that global remodelling distributes quite homogeneously for both longitudinal and circumferential remodelling (with a 90% accuracy), with circumferential scaling presenting a much lower noise than longitudinal scaling. Note that, by construction, the result of a pure scaling maintains exactly the volume proportions. Among the different regions, the outflow presents bigger variability. The other columns of Figure 7 show the changes of regional volumes after applying the local synthetic remodelling. The desired result is that all of the volume increment is located in the segment that suffers the remodelling (identity line), and the other segments do not change their volume. We see that circumferential remodelling is mostly associated to the correct segment (80–90%) in the apex and inlet, while the method is not suited to capture local longitudinal elongations.
5 Discussion

In this paper we proposed a mesh-independent method to volumetrically parcellate the RV in 3 clinically relevant regions: inlet, outlet and apex, with the aim to quantify inter- or intra-individual remodelling in regional morphology.

For validation, we additionally presented a method to synthetically remodel meshes in a localised and global manner, thus generating a synthetic dataset resembling closely monitoring clinical remodelling. From these, we found that the parcellation had a good sensitivity to circumferential or global remodelling, able to attribute it to the correct segment (80/90% of the volume was assigned to the correct segment). However, our method is less accurate when analysing local longitudinal localised remodelling. This is not a major problem given that in many clinical scenarios, regional volume and shape remodelling is often in the circumferential direction ([D’Ascenzi et al., 2016]).

The interobserver reproducibility test of meshes resulting from the segmentation of 3D echocardiography, show that, even if the mean volume difference was under 10%, the Dice coefficient was very low (0.64). This implies that RV shapes segmented by different operators cannot be directly compared and pooled together in an analysis. On the other hand, the intraobserver reproducibility was much higher using the same image (Dice coefficient = 0.89). A test/retest experiment presented significant visual differences. Moreover, the point-to-point (6.2mm) error was much higher than the point-to-surface (1.3mm): the interior nodes of the mesh do not correspond to any anatomical landmark but are equally distributed, thus their correct position does not depend only on the correct segmentation of the RV contour in their position, but on the whole segmentation.

Consequently, regional volumes and EF also present a high error (¿10%) in the interobserver reproducibility test. On the other hand, the intraobserver reproducibility presented a more reasonable error: in volumes only the outflow had a variability ¿10%, while inlet and apex were below (6% and 8%) respectively. The outflow is complicated to segment given the images there often have lower quality. A qualitative analysis of the partitions showed big differences in the middle of the RV since this is the furthest from all landmarks and the method has no information to make the exact parcellation. The inclusion of anatomical landmarks in that area could improve the reproducibility of the method. Regarding the EF, the most unstable was the apical part. This is likely caused by the presence of trabeculations introducing variability in the segmentation as well as the nearfield effect playing a role there and making the full visualisation of the apex challenging.

6 Conclusion

We proposed a geometry processing method to parcellate the RV in 3 regions: inlet, inflow and apical for analysing regional morphology of the RV without depending on point-to-point correspondence of image-based segmented meshes. This parcellation also allowed to assess function via regional EF. We analysed the reproducibility of the regional measurements, and found it below 8% in both apex and inlet segments for the intraobserver, but above 12% in the interobserver case and outflow. Given that most of the instability comes from segmentation errors in the outflow portion, the addition of extra landmarks (like for example in the middle of the septum) would allow to improve reproducibility. We also proposed and used a novel method to generate localised remodelling patterns. We used it to generate synthetic remodelling surfaces to validate our parcellation method and showed that it captures global scaling of the ventricles as well as localised remodelling in the circumferential directions, but has difficulties in local longitudinal elongations.
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Table 4: Global and regional RV descriptors of the population.

|                          | Ind. #1 | Ind. #2 | Ind. #3 | Ind. #4 | Ind. #5 | Ind. #6 |
|--------------------------|---------|---------|---------|---------|---------|---------|
| Heart rate [bpm]         | 45      | 63      | 56      | 63      | 51      | 66      |
| RV EDV [ml]              | 131     | 143     | 167     | 126     | 134     | 161     |
| RV ESV [ml]              | 62      | 81      | 75      | 71      | 70      | 97      |
| RV EF [%]                | 52      | 43      | 55      | 44      | 47      | 39      |
| Outflow EDV [ml]         | 38      | 31      | 44      | 28      | 25      | 39      |
| Inlet EDV [ml]           | 62      | 80      | 84      | 65      | 78      | 79      |
| Apex EDV [ml]            | 30      | 30      | 38      | 32      | 29      | 41      |
| Outflow EF [%]           | 42      | 35      | 48      | 42      | 34      | 28      |
| Inlet EF [%]             | 54      | 41      | 52      | 48      | 47      | 37      |
| Apex EF [%]              | 64      | 58      | 70      | 39      | 58      | 55      |

A Individual results

In this section we provide the individualised results of the parcellation for the 6 participants of the study.
Figure 8: Parcellation and 3D models of all individuals of the population in apical (red), outflow (blue) and inlet (green). We can observe that there is a big variability in size and shape of the RV, which is reflected in the parcellation differences.

B Synthetically generated meshes
Figure 9: Generated meshes with the local synthetic remodelling method. The colour map shows the longitudinal / circumferential strain with respect to the template, which is showed in the right column.
Figure 10: Generated RV meshes for the global synthetic remodelling, corresponding to a 10% dilation in both the longitudinal and circumferential. The colour map shows the strain of the deformation from the template.