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SIM CARDIO TEST

Technical Report
D3.4 - Report on the database of fluid simulations in virtual population

Work Package 3 (WP 3)
USE CASE 2: LEFT ATRIAL APPENDAGE OCCLUDER

Task Lead: UPF, Spain
WP Lead: UPF, Spain

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Lead authors	Oscar Camara
Contributors	Kristian Valen-Sendstad, Henrik Kjeldsberg, Ehsan Khalili, Travis Schauer, Carlos Albors, Marta Saiz, Jordi Mill, Andy L. Olivares, Hermenegild Arevalo.
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EXECUTIVE SUMMARY

This report defines the virtual population database structure and the workflow for modelling left atrial appendage occluder (LAAO) devices of Use Case 2, detailing the computational algorithms to browse the database, and the model definition in the simulations. The SimCardioTest's cloud-based platform will use these components to conduct in-silico device efficacy and safety studies. The database can be accessed through https://www.simcardiotest.eu/wordpress/activities-resources/software/.

1- Introduction

The focus of Use Case 2 (UC2) in SimCardioTest is on left atrial appendage occluder (LAAO) devices, aiming at identifying the risk of thrombus formation after their implantation in patients with atrial fibrillation, improving patient selection and admission processes, as well as optimising and personalising device settings (e.g., size, positioning).

One of the key factors in the process of thrombus formation is blood stasis [1]. Nowadays, blood velocity is measured at end-diastole at the LAA ostium (i.e., the interface between the LA and LAA), with LAA emptying velocities < 20 cm/s being associated with thrombus formation [2]. Colour Doppler acquisitions are also used to identify peridevice leaks (< 3 mm) after LAAO [3]. However, echocardiographic images cannot fully characterise the complexity of 4D blood flow patterns in the LA. New imaging techniques such as 4D flow magnetic resonance imaging (MRI) or blood speckle tracking are promising but whether they can reach the sufficient resolution to capture the low blood velocities related to thrombus formation is still unclear. Thus, in-silico fluid modelling is a very interesting option to thoroughly assess the haemodynamics inside the LA. Several researchers [4-31] have investigated blood flow patterns in the left atria using computational fluid dynamics (CFD) simulations, in particular in AF conditions. Most of these studies focused on analysing in-silico haemodynamics parameters in the LAA in relation to thrombogenic risk, including explicit models of thrombus formation [19, 22]. Only a few have studied the effect of LAA closure [17, 24, 26], the most advanced investigations having incorporated LAAO devices [12, 32] and the relation thereof to DRT [24, 26, 32]. Table 1 shows a complete review of the corresponding modelling strategies reported in the literature. Arguably, the published investigations are usually based on only a few (< 10) sets of patient-specific LA geometries.

Because of the population variability in LA/LAA morphology (see Figure 1), studies with less than 10 cases limit the credibility of the results. The fluid modelling pipelines developed by SimCardioTest members have made it possible to create much larger cohorts of simulations than those published so far, surpassing 50 cases [24-25]. Therefore, these large studies have allowed us to jointly study blood flow patterns and LA/LAA morphology. For instance, Mill et al. investigated the role of the pulmonary veins in the risk of thrombus formation in 52 cases [24], which has been already extended to 131 different patient-specific LA anatomies.

Overall, the members of SimCardioTest have already performed a total of 230 simulations on patient-specific LA geometries, not only taking into account the variation of LAA morphologies, but also the orientation and number of pulmonary veins. We expect to have a total of 1000 fluid simulations by the end of the project, with different configurations of implanted devices, representing the largest database of LA-based fluid simulations in the field, which will be released as Open Access. Yet, there are still challenges in generating large cohorts of patient-specific LA fluid simulations. The difficulty to access necessary data that is not acquired routinely in hospitals in AF patients but that are necessary to extract the 3D model or set up realistic boundary conditions is still a challenge to overcome.

Table 1. *Review of boundary conditions and different modelling choices for left atrial fluid simulations reported in the literature. PV: pulmonary veins; MV: mitral valve; geoms: number of geometries; lit: literature; vels: velocities; press: pressures; dCT/MRI: dynamic computed tomography/magnetic resonance imaging; diff. DM: dynamic mesh; Diff: diffusion; SB: spring-based;FSI: fluid–structure interaction; IB: immersed boundary method; * synthetic LA and realistic LAA geometries; ** estimated value from element size reported in the paper; *** 256 synthetic and 114 real LAA;*4 onereal case but it is modified to create a cohort N=10.*

Study	PV inlet	MV Outlet	Wall Behaviour	Cardiac Cycles	Mesh Elements (x10^5)	Geoms
Zhang [4]	Lit. vels.	Wall/ 0 mmHg	FSI	3	2	1
Dhal [5]	Patient flow	Added mass flux	Rigid	1	21	1
Koizumi [6]	10 mmHg	Wall/ 8 mmHg	dMRI	5	1.5	1
Otani [7]	dCT vels.	Wall/dCT flow	dCT DM	5	3.6 - 5.5	2
Bosi [8]	0 mmHg	Lit. vels.	Rigid	4	22 - 30	4
Garcia-Isla [9]	Lit. vels.	Wall/ 8 mmHg	Rigid	1	3.5 - 5.0	36*
Dillon-Murhpy [10]	0 mmHg	dMRI flow	dMRI	10	12 **	2
Masci-a [11]	Flow balance	Lit. flow	Sinusoidal	5	17 - 19	5
Aguado [12]	Lit. vels.	Wall/ 8 mmHg	Rigid	1	2 - 9.6	2
Jia [13]	Synthetic vels.	Wall/ 0 mmHg	Rigid	10	0.4	1
Feng [14]	Lit. press.	Lit. press.	FSI	2	1	1
Masci-b [15]	Flow balance	Lit. flow	Sinusoidal	7	8 - 10	2
Wang [16]	10 mmHg	Lit. flow	Rigid	20	24	1
Mill -a [17]	Lit. vels.	Wall/ 8 mmHg	Diff. DM	2	5	2
D'Alessandro [18]	Flow balance	Lit. vels.	Sinusoidal	5	17-19	2
Quereshi [19]	Synthetic vels.	Unknown	dMRI	15	4	2
Garcia-Villalba [20]	Flow balance	Wall/Open	Rigid/dCT	20	5 - 9 **	6
Fang [21]	AF vels.	Wall/ 0 mmHg	FSI	4	Unknown	1*
Sanatkhani [22]	Lit. vels.	Open/ 0 mmHg	Rigid	25	3.5 - 9	16
Fanni [23]	Pressure	Lit. vels.	Rigid	25	23 - 42	4
Mill-b [24]	AF press.	AF vels.	SB. DM	3	8 - 9	52
Morales [25]	Lit. vels.	Wall/ 8 mmHg	Diff. DM	3	3.5 - 9	370***
Mill -c [26]	AF press.	presonalized vels.	Rigid/ Diff. DM	1 - 2	1 - 5	6
Corti [27]	Pressure and vel.	Pressure	harmonic DM	6	1 - 2	4
Dueñas-Pamplona [28]	Velocity	0 mmHg	Rigid	4	8	10****
Gonzalo [29]	personalized vels.	0 mmHg	dCT	15	Unknown	6
Rigatelli [30]	personalized vels.	Wall/Open	IB	16	Unknown	60
Pons [31]	AF press.	Lit. vels.	SB. DM	3	8 - 9	30

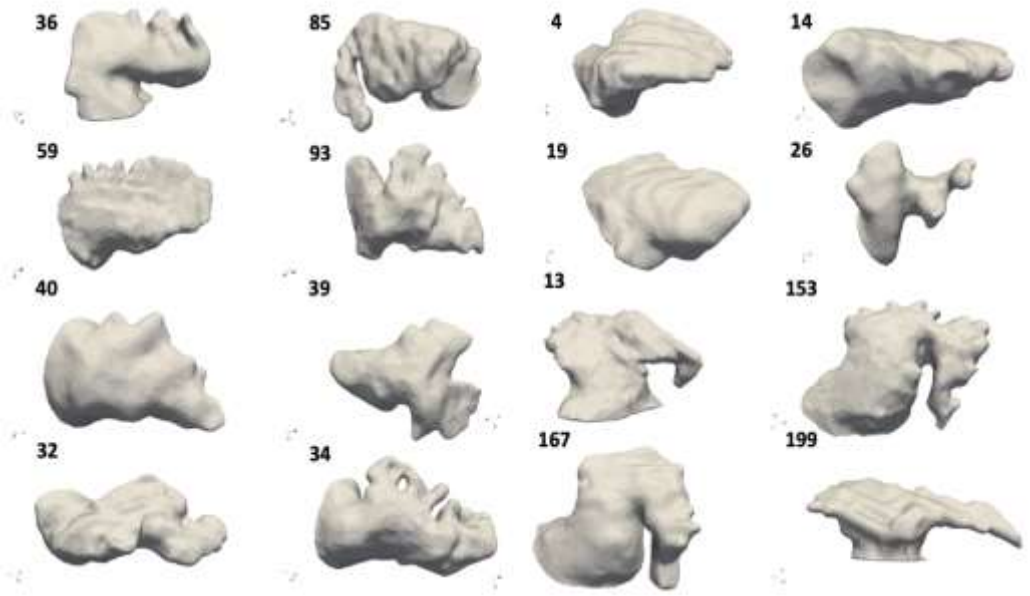


Figure 1. Different left atrial appendage (LAA) morphologies analysed with the developed computational techniques. Among them, LAA shapes corresponding to the different categories in the classical classification of Di Biase et al. [32] can be found, including chicken wing (i.e., n.199), windsock (i.e., 85), cactus (i.e., 40) and cauliflower (i.e., 93) cases. Also, a seahorse shape can be found (199). Depending on the 2D point of view, the perception of the 3D shape can significantly change

To select the best methodological choices for fluid simulations, extensive sensitivity analysis, model calibration, and thorough verification and validation (V&V) assessments are also required, as described in Deliverable D3.2. However, modelling parameters need to be adapted in order to realistically generate hundreds of fluid simulations, involving a trade-off between result accuracy and computational costs. In-silico haemodynamic indices extracted from simulation data are then used to anticipate the benefit of LAAO implantation, and optimise device settings to reduce the risk of device-related thrombus (DRT), in combination with appropriate medication therapy. As part of the project, the computational modelling pipeline will be integrated onto the SimCardioTest InSilicoTrials platform, developed in the project for device manufacturers to run in-silico trials in various contexts of use, such as determining the risk of DRT of different device settings on different populations.

The fluid simulation database described in the present deliverable implies the definition of the modelling pipeline to predict DRT risk in a given patient. The Computational Fluid Dynamic (CFD) method, based on the Navier Stokes equations and finite volume method resolution, is the selected methodology to analyse and solve the fluid flow problem, where discrete representations of the object of interest (i.e., left atria geometry) and imposed conditions on specific regions are the inputs of the model. Simulation outputs comprise 3D vector fields representing blood flow behaviour and velocities, pressures, wall shear stresses, and vorticity indices, among others, to better characterise and interpret the simulated flows. Several components including medical data processing, finite-volume mesh building, in-silico simulations with an input/output standardised format, and visualisation interfaces, involving data from multiple sources and different software tools, have been developed by the different partners of the SimCardioTest consortium for the development of the Use Case 2 (UC2) modelling pipeline. Standards were defined at the beginning of the project (Deliverable D3.1) to ensure seamless connection between the different components of the modelling pipeline.

One of the main goals of WP3 in SimCardioTest is the generation and release as Open Access of a large virtual population of fluid simulations, covering the morphological LAA variability required to perform in-silico tests with devices from different manufacturers. Additionally, the large virtual population of fluid simulations is the basis for the first designed scenario of UC2 in the SimCardioTest's InSilicoTrials platform, where a closest matching algorithm has been developed that, based on input patient characteristics, LA morphology and device settings, outputs the most similar patient in the virtual database of pre-computed fluid simulations along with the corresponding fluid simulation results. The present deliverable (D3.4) describes the process of generating the large virtual database of fluid simulations and its integration with the other components of the SimCardioTest's InSilicoTrials platform.

2- Modelling pipeline for left atrial appendage occluder devices

2.1- Generation of left atrial geometrical domain

The in-silico virtual population modelling pipeline is illustrated in Figure 2.

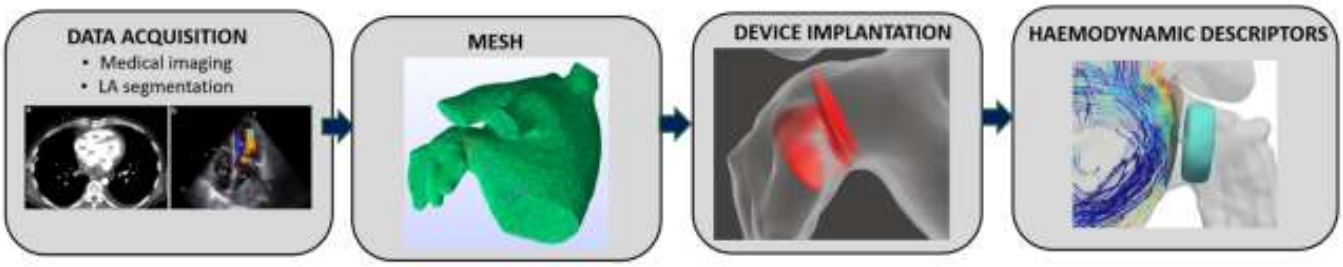


Figure 2: Modelling pipeline to perform fluid simulations on left atrial appendage occluder (LAAO) devices, deriving haemodynamic descriptor to guide in-silico clinical tria

As reported in Deliverable D3.1, binary left atria segmentations are reconstructed from a large database of computed tomography (CT) images composed of pre-occlusion and, if available, post-occlusion scans processed with deep-learning (DL)-based algorithms by SimCardioTest partners (Inria Sofia-Antipolis) in-site (i.e, no sensitive information is leaving the hospital). 3D surface left atria meshes were created from binary masks out of the segmentation algorithm with the flying edges technique available in Slicer 4.11 (https://www.slicer.org/), followed by a smoothing process. The Taubin smooth filter ($\lambda = 0.5$ and $\mu = -0.53$), and removal of self-intersecting/non-manifold edges in Meshlab v2021-07 (http://www.meshlab.net) are applied to correct irregularities generated by the segmentation process. To consistently create the database, a common criterion has been established based on: i) a remeshing process to approximate the number of elements of each surface mesh; and ii) a perpendicular cut through the pulmonary veins and mitral valve for defining the inlets/outlets of the computational models. The PV length is determined by defining the cutoff at the first major branch coming out from the LA and the location of the leaflets for the mitral valve. Around 100 patient-specific LA geometries composed the dataset (see Fig.3) developed in Meshmixer 3.5 (https://meshmixer.com/).

Figure 3: Three patient-specific LA geometries in the virtual population representing morphological and anatomical LAA variability

To model the occlusion procedure, computer-aided designs of the most successful commercial occluder devices were built and virtually implanted with different configurations (i.e, sizes, positions) in tens of LA patient-specific geometries, some with optimised device settings and others with unsatisfactory parameters. The position and final shape of the device, once deployed in the left atrial

appendage, have an important role on the distribution of blood velocities, thus on the risk of DRT. Creating a large database of fluid simulations with optimal and sub-optimal device settings contributes to better understanding which are the best parameters for a given patient-specific LA geometry. In order to improve the realism of the generated fluid simulations, we have developed a phenomenological model of LAAO device deployment, adapting the implanted device (in the landing zone of the LAA) to the surrounding LA wall. The device deployment simulation is fast (< 1 minute), which allows user interaction in tailored interfaces (e.g., changing device parameters to explore a new device deployment), unlike more mechanistic approaches that are associated with long computational times. More details about the LAAO device implantation pipeline can be found in Deliverable D3.5. Currently, the process of selecting device settings can be configured using the web-based platform VIDAA, which UPF have developed during the last years, allowing the user to visualise the left atrial anatomy of a given patient, and virtually place different devices with several configurations.

Finally, 3D volumetric LA geometries with the deployed device were generated to represent the fluid domain inside the cavity using a Delaunay algorithm followed by Netgen optimization of the quality of the tetrahedron elements available in the Gmsh 4.8.4 software (http://gmsh.info). Figure 4 shows an example of the volumetric mesh process. The average number of tetrahedral elements that was selected for the LA meshes to build the virtual population was ~1.1 M. This number is lower than the ideal mesh resolution parameters resulting from the detailed sensitivity analysis we performed (see Deliverable D3.2), where meshes of ~10 M of elements were recommended for full convergence of several simulation metrics. However, such high resolution is associated with prohibitive computational costs that will prevent the construction of the large virtual cohort of fluid simulations, even having unlimited access to supercomputing infrastructures. Therefore, we chose a trade-off based on literature (see Table 1) and our own modelling experience during the last few years, with meshes around 1 M elements being accurate enough to estimate risk of thrombus formation [35].

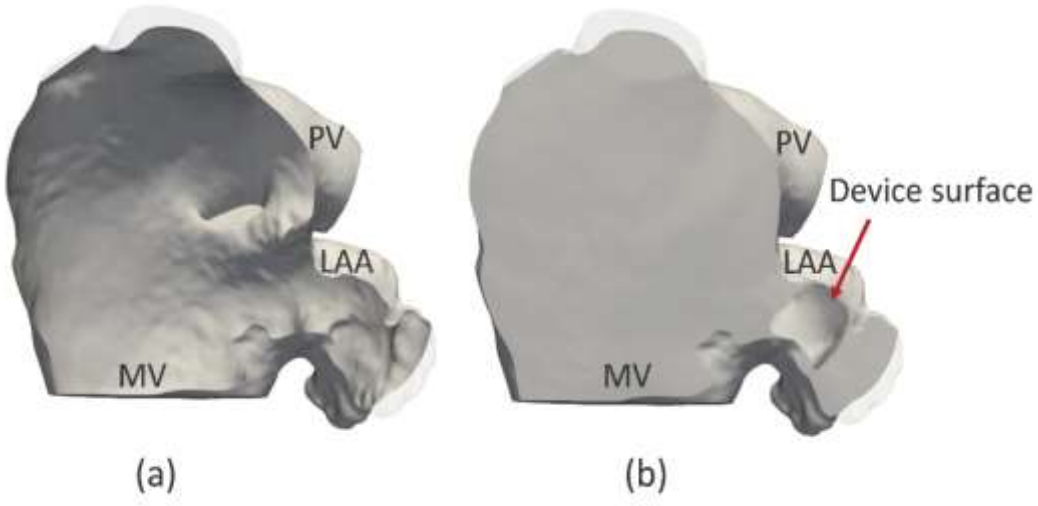


Figure 4. Volumetric mesh generation process. (a) Left atrial surface geometry. (b) Volumetric result including the deployed device. PV: pulmonary veins. MV: mitral valve. LAA: left atrial appendage.

2.2 -Definition of boundary conditions

To give realism and credibility to the in-silico models, a generic clinical information gathered from an atrial fibrillation patient is used to define the boundary conditions (BC) of the model. After the sensitivity analysis on the ideal BC set for LA-based fluid modelling, a velocity profile from Doppler echocardiographic images at the mitral valve and catheter pressure data at the pulmonary veins are defined. Furthermore, despite the modelling community's debate about LA wall movement, with some researchers assuming rigid LA walls and arguing for very limited LA movement in AF patients [2,8], a dynamic spring-based technique depicting a longitudinal movement of the mitral valve annulus ring has been implemented. Even in those patients, passive movement of the LA induced by the left ventricle (LV) still occurs. Figure 5 shows the generic boundary conditions applied to the LAAO model.

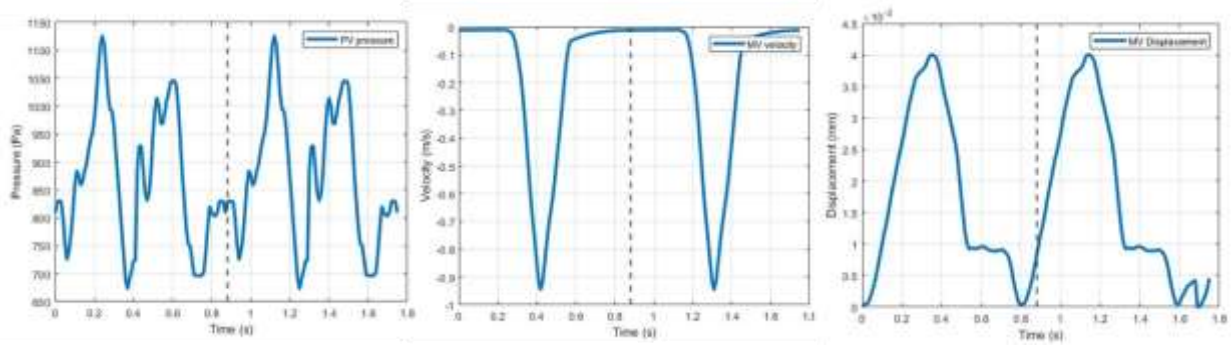


Figure 5. Generic boundary conditions applied in a given patient of the virtual population. From left to right, pulmonary veins pressure-inlet profile, mitral valve velocity-outlet and spring-based dynamic mesh approach with the longitudinal mitral valve annulus ring displacement.

2.3 - Settings of the fluid solver

In-silico fluid flow simulations are performed in the computational fluid dynamics solver Ansys Fluent 2020 (ANSYS INC., United States) where the Navier-Stokes equations are solved with the finite volume numerical discretization technique in the LA volumetric meshes. A second-order, node-based spatial discretization with a coupled pressure-velocity scheme, enhances the accuracy in resolving the fluid domain. Two cardiac cycles were simulated, under laminar and Newtonian flow with a time step of 0.01 s and 88 steps per beat, according to the heart rate (HR) of the patient with atrial fibrillation condition Post-processing and visualisation of simulation results were conducted in ParaView (https://www.paraview.org/), with special emphasis on detecting the device-related thrombus (i,e. high thrombogenic risk areas after the LAAO procedure). The simulated blood flow patterns were qualitatively assessed through streamline representation together with average flow velocities in key LAA regions near the device surface. Moreover, the endothelial cell activation potential (ECAP) was estimated since it has been demonstrated to identify regions with high risk of thrombus formation. The mentioned indices were calculated on the second simulated cardiac beat to avoid convergence and pre-conditioning problems.

3- Integration of the virtual population dataset onto the InSilicoTrials platform

The integration of the modelling pipeline in the SimCardioTest platform consists of two scenarios. Scenario 1 is based on having a virtual database of pre-computed in-silico fluid simulations on a large cohort of patients with specific LA geometries and device settings. A scheme of this scenario can be observed in Figure 6.

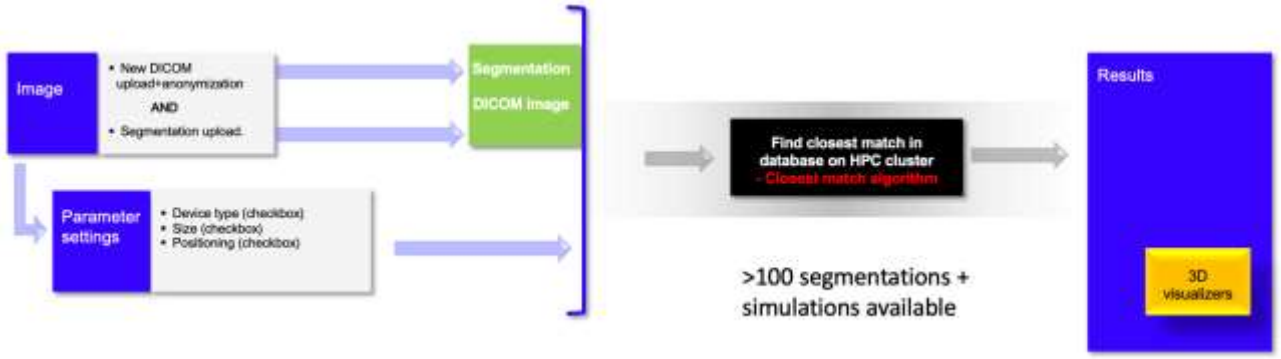
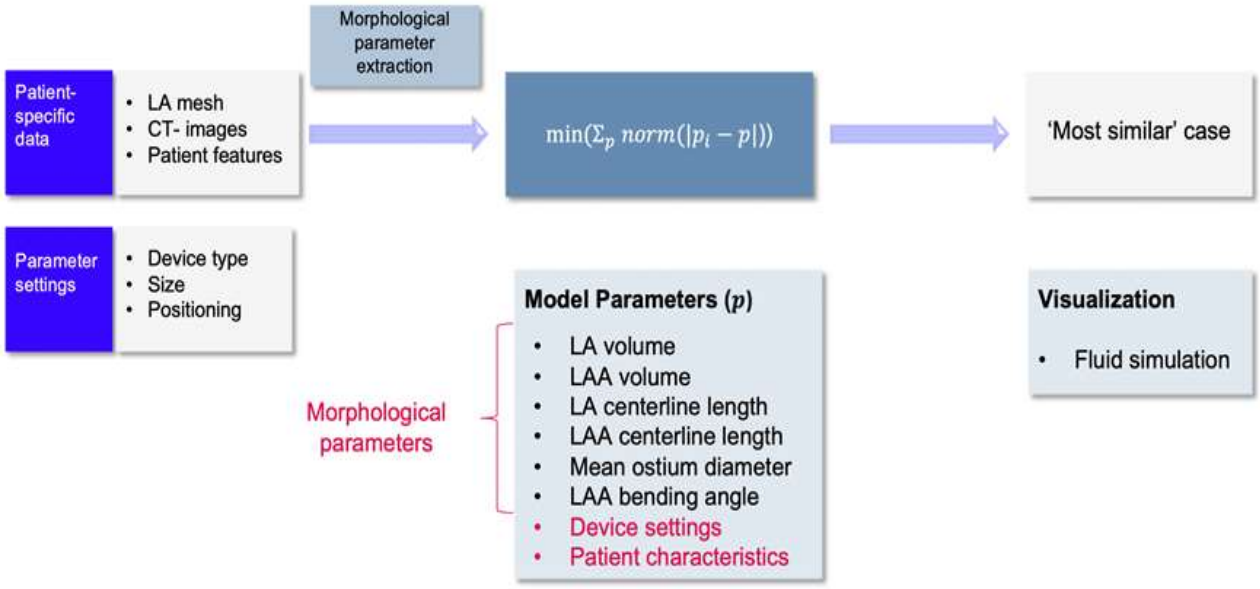


Figure 6. Scheme of scenario 1 for the Use Case 2 on left atrial appendage occluder devices in the SimCardioTest platform.

The user would upload patient data to the platform and a closest match algorithm would output the most similar patient in the virtual database based on LA and LAA morphological properties. Additionally, patient characteristics and device settings can also be introduced to refine the search. The algorithm pipeline is as follows. First, the user would upload a 3D surface mesh reconstruction of a left atria, obtained from the binary segmentation performed on-site where the original computed tomography scans are available. From the LA surface mesh reconstruction, the algorithm automatically extracts morphological parameters to characterise the geometry of LA/LAA such as: LA/LAA volume, LA/LAA centerline length, mean ostium diameter, LAA bending angle. Given the extracted morphological features and other input characteristics such as device settings and patient features, the algorithm uses an explainable similarity metric based on the Euclidean distance (i.e., the sum of absolute differences) to find the most similar patient. Figure 7 shows the algorithm pipeline, which can be described by the following components:

- Input of algorithm: LA mesh geometry, device settings and clinical data
- Output of algorithm: 2 or 3 most similar cases in the virtual database based on a set of automatically extracted LA/LAA morphological characteristics, device settings and patient characteristics.
- Visualisation of results: From the algorithm output, the platform will send the most similar cases together with the simulation results for visualisation. The simulation results of the most interesting samples will be individually shown in 3D with different LAAO configurations. Additionally, the aligned LA geometries of input and most similar cases may also be visualised in a superimposed manner to assess the degree of geometrical similarity.

Scenario 2 is based on running the fluid simulations on the introduced LA geometries. The main advantage of Scenario 1 is that computationally costly fluid simulations (up to 24 h per patient, depending on simulation settings) are not required since they have been pre-computed in many



cases. Figure 8 shows an example (without device) of the closest match algorithm output, visualised through input/output LA mesh superposition and input/output simulation results (i.e., ECAP).

Figure 7. Pipeline of closest match algorithm for Scenario 1 in the SimCardioTest InSilicoTrials platform for Use Case 2

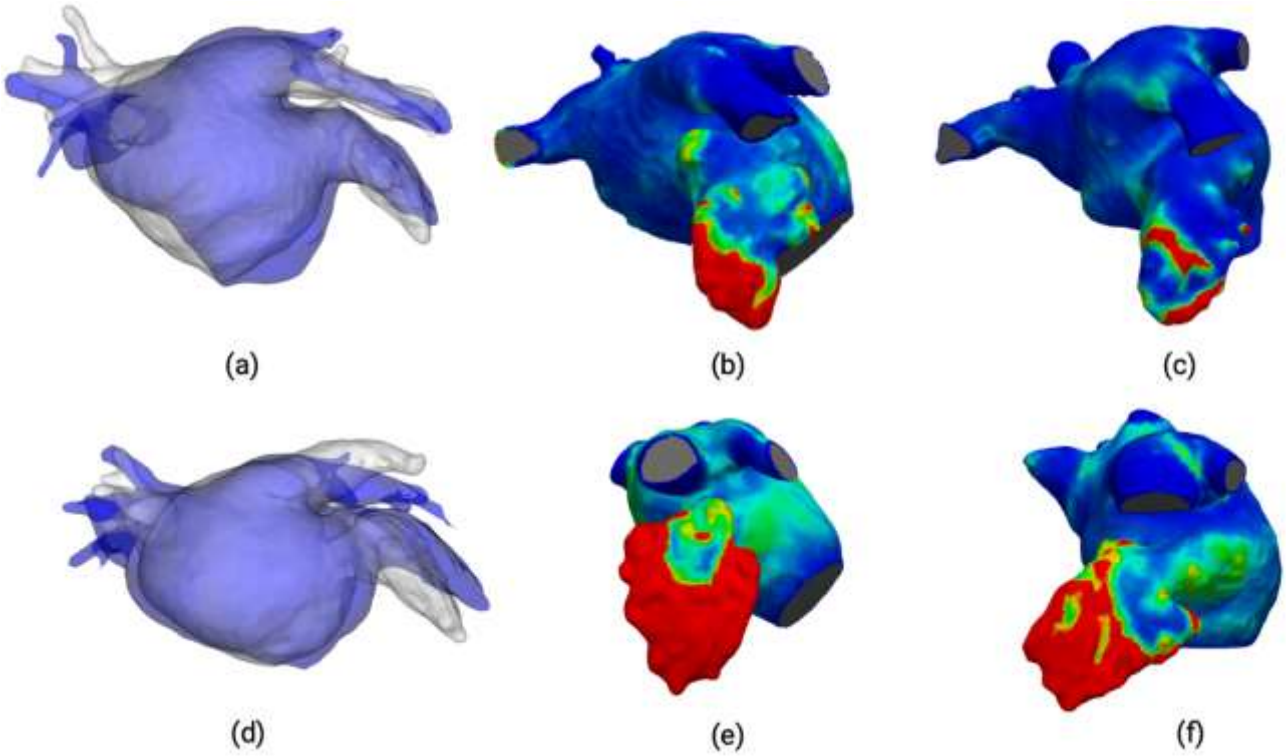


Figure 8. Two examples of input patient and closest match algorithm output with endothelial cell activation potential (ECAP) visualisation, determining the risk of thrombus formation (e.g., red and blue indicate a higher and lower risk, respectively. (a, d) Two examples of superposition of LA meshes from input patient (grey) and most similar patient (blue). (b,e): input patient ECAP visualisation. (c,f) output most similar patient ECAP visualisation.

4- Open release of in-silico models to the community

In order to fulfil Impact 9 of the SimCardioTest project (contribution to the European Cloud initiative by providing open, reusable data and in-silico models for clinical trials), the developed in-silico models for this task will be openly released, as well as the closest match algorithm. The in-silico simulations virtual database will also be publicly available and efforts will be made to curate and prepare the data to ensure its usability.

The aforementioned actions will be performed within the Oracle Research program, which will contribute by providing hardware infrastructure to run the required fluid simulations and to host the large database of virtual simulations developed, in such a way that can be made freely accessible for researchers worldwide to become a reference repository for this field of research. It will permit setting up benchmarks where researchers could test their computational techniques on the same data, collectively moving forward investigation in this area. As part of SimCardioTest dissemination activities, we recently organised a workshop with contributions from the most active research groups in the field of LA fluid simulations (https://youtu.be/p7sg55CBeI8). One of the main conclusions was the need for common databases such as the one presented in this deliverable, to facilitate joint work and build a community to foster collaborations on this topic.

5- Examples of fluid simulations in large datasets

5.1- Study on the role of pulmonary vein configuration for thrombogenic risk

To study the influence of the PV configuration, we run fluid simulations in a population of 131 atrial fibrillation patients using the modelling pipeline presented in this deliverable. Additionally, a set of angles describing the topological relationships between the PV, the LAA, the mitral valve (MV) and the main cavity of the LA, were computed in close collaboration with researchers at Inria Sophia-Antipolis (France), following the approach presented in Harrisson et al. [34]. By being able to simulate such a large cohort of patients we were able to see the great variability of LA between individuals as their haemodynamics changed according to the configuration of their pulmonary veins, as can be seen in Figure 9. It has an obvious impact on LA haemodynamics, especially on the location of flow collisions in the LA and how flow is reaching the LAA, thus potentially influencing blood stasis in that area. Figure 10 depicts blood flow patterns with different PV orientations. It can be seen in the figure how with the same number of PV but different positions and orientations, blood flow patterns substantially change (Scenario 3 and 4 in Figure 10).

Another important finding is that when blood flow from the left PV collides at the superior part of the LA, due to their orientation, it is subsequently directed to the LAA ostium, which is usually located just under the left superior pulmonary vein (LSPV). In consequence, the α and β angles, which characterise the angular difference between the PV in the same LA side (left and right, respectively), had a considerable effect on the resulting blood flow patterns. In our cohort, the angle between the left PV (β) varied less than the right PV one (α).

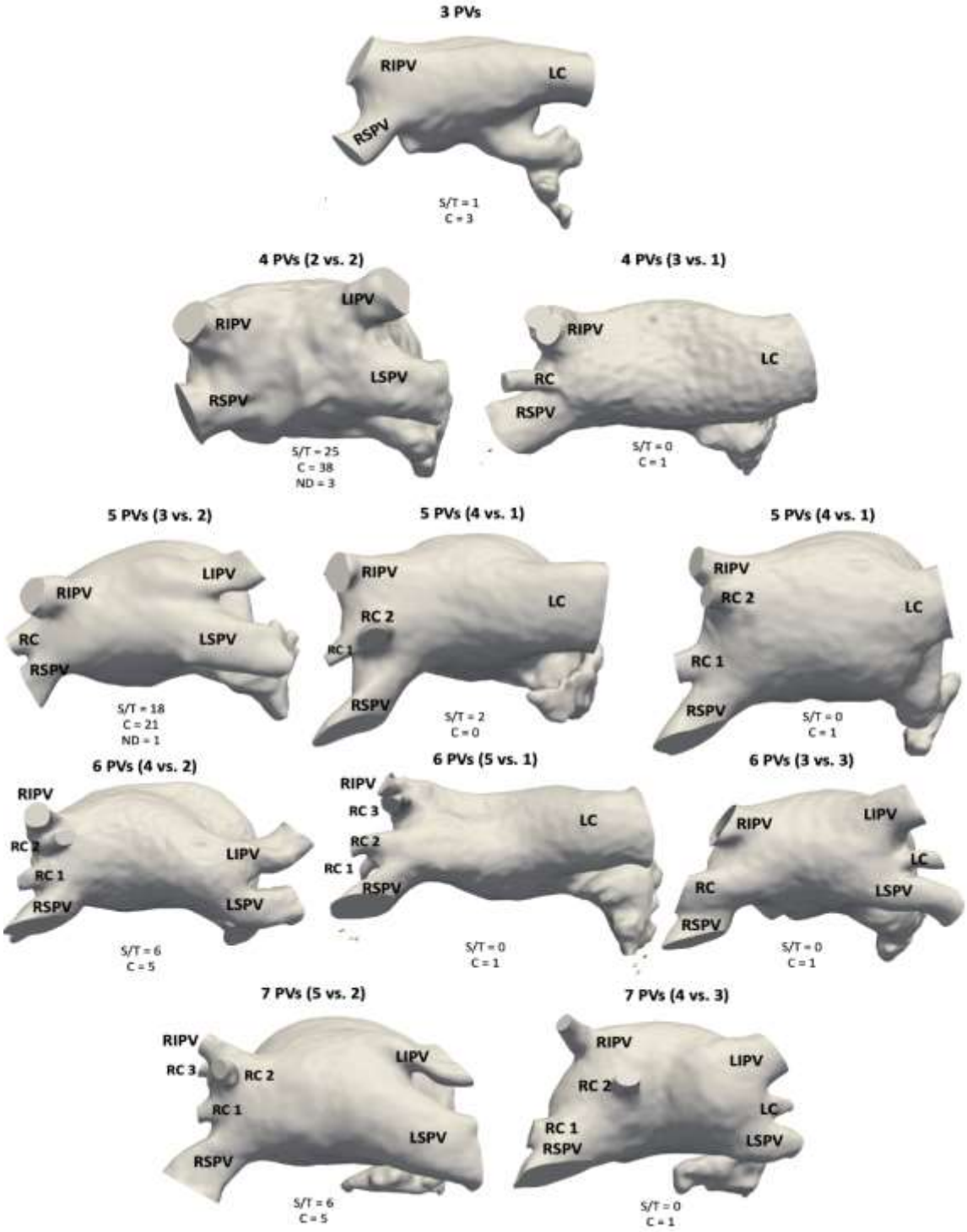


Figure 9. Different types of pulmonary vein (PV) topological configurations in the left atria (LA) found in the studied cohort. Between brackets the distribution of PV according to the right vs. left side of the LA. RIPV/RSPV: right inferior/superior PV. LC/RC: left/right central pulmonary vein. LIPV/LSPV: left inferior/superior PV. RC1: right central PV that is closest to the RSPV; RC2: right central PV that is closest to the RIPV if there is no RC3; with an existing RC3, RC2 is in between RC1 and RC3; RC3: right central PV that is closest to the RIPV. T/S: thrombus or stroke group. C: control group.

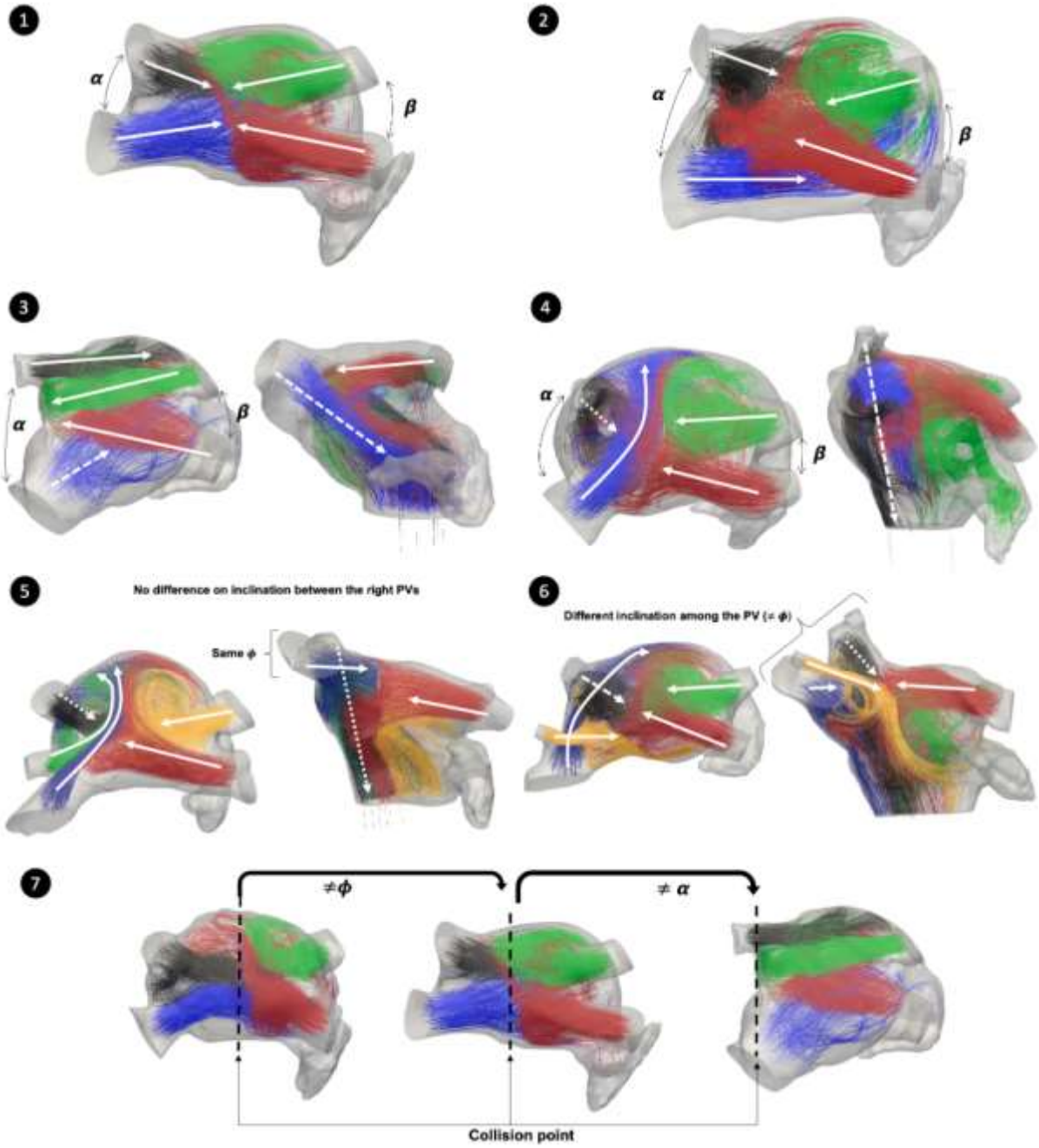


Figure 10. Different scenarios of pulmonary vein (PV) configurations and angles. Each colour represents flow coming from the same PV. Scenarios 1-4,7 (4 PV): green/red represents the left inferior/superior PV (LIPV/LSPV); black/blue represents the right inferior/ superior PV (RIPV/RSPV). Scenario 5 (5 PV): orange/red represents LIPV/LSPV; black/blue/green represents right inferior/central/superior PV (RIPV/RSPV/RCPV). Scenario 6 (6 PV): green/red/black/blue/orange represents LIPV/LSPV/RIPV/RSPV/RCPV. The black dashed line depicts flow collision points. The solid white line is the direction of the flow coming from the PV, the white dashed line having a higher inclination (higher ϕ). The snapshots were taken at the end of the diastole when the maximum velocity of the A wave is usually reached, just before mitral valve closing

5.2- Study of different left atrial appendage occluder device settings on the risk of device-related thrombosis

Figure 11 represents a qualitative assessment of the DRT risk using the streamlines resulting from a fluid simulation on a specific patient of the virtual population. Blood flow complex patterns defining recirculations at low velocities are seen in a susceptible area of high thrombogenic risk, the triangle area (Figure 11 (a) LAAO configuration Red arrow). With an optimised device configuration covering the pulmonary ridge, proposed as a possible independent DRT risk factor, high velocities with a laminar behaviour are observed (Figure 11 (a) Optimized configuration), suggesting a better device implantation. Similar simulations have already been performed in around 30 different LA geometries, resulting in more than 80 fluid simulations with different device designs and settings, which are currently being used as a proof of concept of the virtual population to set up the whole pipeline with the SimCardioTest InSilicoTrials platform.

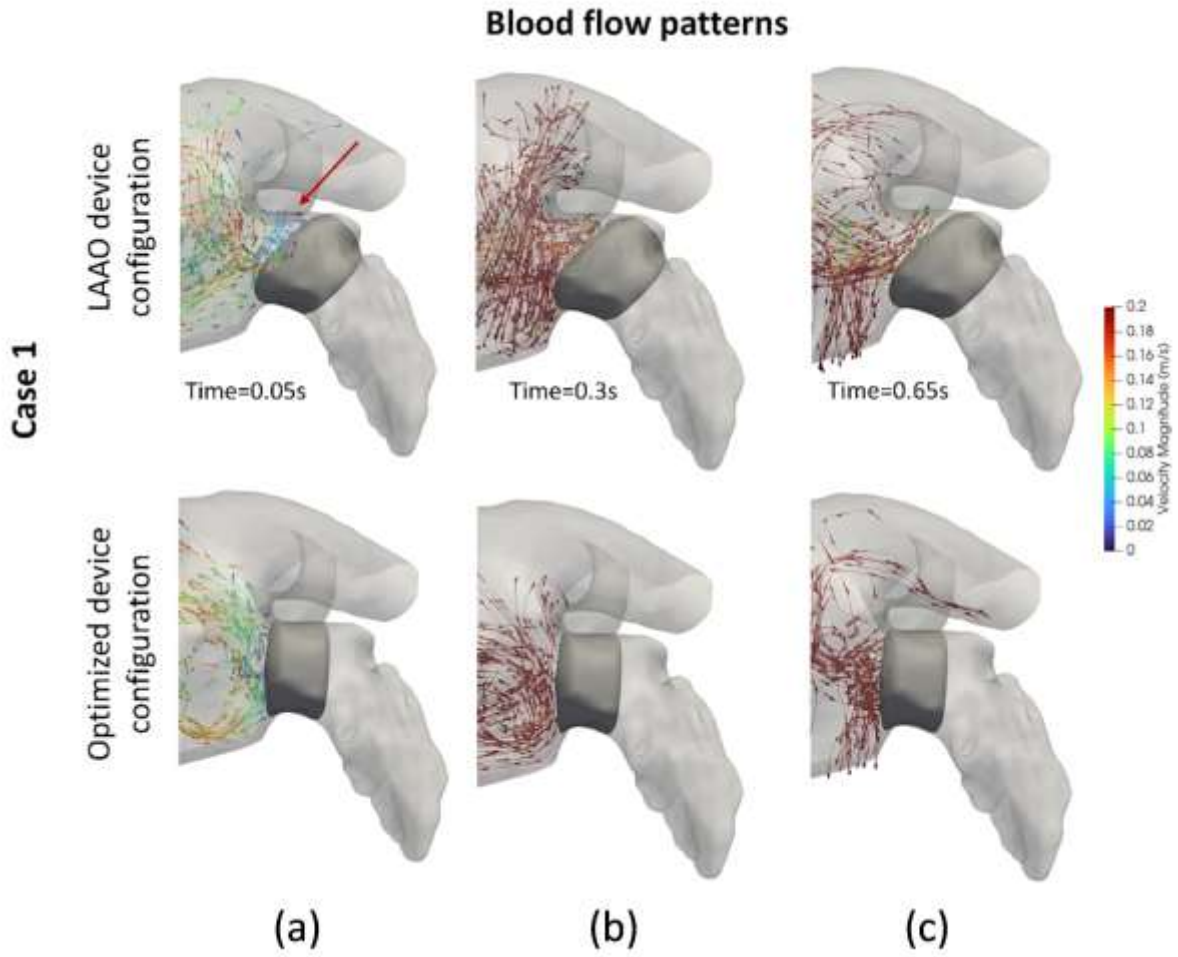


Figure 11. Blood flow streamlines in early-, late-diastole and late-systole cardiac cycle times (a, b, and c, respectively) from fluid simulations in a patient with an implanted Watchman FLX (Boston Scientific, United States) occluder device. LAAO: left atrial appendage occluder. (a-c) represents different frames of the cardiac cycle. The top row shows a sub-optimal LAAO device implantation, which could lead to device-related thrombus due to the creation of regions near the device with complex flow and low velocities (red arrow). With a better LAAO implantation, virtually performed with the tools developed in SimCardioTest, the risk of thrombus formation is reduced (bottom row)

6- Discussion

During the first part of the SimCardioTest project, all partners involved in WP3 and Use Case 2 on left atrial occluder devices have jointly developed the computational tools required to create the largest database of patient-specific LA fluid simulations performed so far. We have already run > 300 fluid simulations with different LA anatomies of atrial fibrillation patients provided by CHU Bordeaux. Part of these simulations have demonstrated the role of the PV configuration in the blood flow patterns in the left atria, thus in the risk of thrombus formation, which was neglected until now. Moreover, we have generated tens of different device configurations, varying the device design, sizing and positioning, on multiple LA geometries, to build the virtual population of fluid simulations that will be the basis of some scenarios for the SimCardioTest InSilicoTrials platform. During the next few months, now that the modelling pipeline has been established, these numbers will easily escalate to increase the size of the virtual population. For doing so, we are collaborating with Oracle, within their Research program, so that they will provide the computational infrastructure to run the required simulations and host the resulting database of simulations, which will be released as Open Access, to foster collaborations with researchers working in this field. Moreover, device manufactures will largely benefit from having access to a database of LA anatomical models to test their own device designs, since it is quite often difficult for them to get medical data with enough anatomical variability. In the next months, we will explore in SimCardioTest the best ways to release this database, with the required protection and exploitation mechanisms.

One of the main challenges for generating such a large database of fluid simulations is the potential high computational costs of the models to run, depending on the chosen parameters. For a relatively regular model, using a commercial software such as Ansys, every simulation can last 24 hours. Moreover, following guidelines from the sensitivity analyses reported in Deliverable D3.2, where several parameters such as time-steps, mesh resolution and cardiac beats, among others, were analysed to find their values to ensure convergence (e.g., meshes of 10 M elements, 10 K time-steps), would result in prohibitive times to obtain simulations in hundreds of cases. Therefore, a trade-off between convergence, accuracy and computational cost was made, to get accurate enough results at reasonable times. For instance, based on literature review and our previous experience, we selected meshes with a resolution of 1 M elements. The resulting simulations, already in the order of hundreds, have demonstrated that they can have a meaningful impact to find new important indices to better determine the risk of thrombus formation (e.g., the role of the PV configuration) and to find the most critical device settings to avoid abnormal events after implantation (e.g., device-related thrombus).

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