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Abbreviations

<table>
<thead>
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<th>Description</th>
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<tr>
<td>AV</td>
<td>Aortic Valve</td>
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<tr>
<td>EWVT</td>
<td>Extended Weighted Voronoi Tesselation</td>
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<tr>
<td>FE</td>
<td>Finite Element</td>
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<tr>
<td>LV</td>
<td>Left Ventricle</td>
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<tr>
<td>SPH</td>
<td>Smoothed Particle Hydrodynamics</td>
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<td>VPS</td>
<td>(ESI-Group software)</td>
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**General Description**

The main objective of D5.4 is to describe how the methodology developed in preceding stages of the project, as described in deliverables D4.1, D5.1 and D5.2 [1-3], can be applied to patient specific geometries. For the simulation of the blood flow from the left ventricle (LV) into the aorta, the following assumptions have been made:

- The flow is driven by the deformation (contraction) of the LV wall
- Blood inside the LV is assumed to be at rest at end-systole.
- The mitral valve is assumed to remain closed (no inflow)
- The aortic valve (AV) will open during contraction (and may close again later)
- The outflow into the aorta requires the numerical model to comprise part of the aorta, and an outflow boundary at which a pressure has to be prescribed
- If the pressure in the aorta is not known but the flowrate is, the pressure may be obtained from a windkessel model

The simulations have been carried out with the existing Smoothed Particle Hydrodynamics (SPH) method within the VPS software from ESI-Group.

An important issue to be addressed is how to handle the aortic valve since the geometry (nor deformation) is available from the models obtained from MUG. This is due to the lack of (accurate) MRI information for the valve. For that reason a specific software tool to mimic the valve by a numerical model for the opening has been developed and employed for the patient specific model in this report.

Since the pressure in the aorta is not always available from clinical measurements, an alternative approach has been implemented by a windkessel model. In such a model the pressure may be obtained from the flow rate (which is more frequently available) assuming some parameter values for the resistances and capacities of the flow network representing the parts of the blood circuit not included in the model. This is an approach frequently adopted for cardiac flow [4].

**Summary of previously developed software tools required**

Since the blood flow as represented by the particles has to be driven by the motion of the boundaries of the LV and the aortic valve (and the aorta wall, if relevant), the initial geometry and the deformation of these structures has to be provided by a finite element (FE) mesh and the displacements of the FE nodes. This information has to be obtained from the tool to convert the FE model from MUG to the VPS input format as described in D5.1 [2] and D5.2 [3]. Since it would not be realistic to allow the blood to flow freely out of a section cut of the aorta, the previously developed pressure outflow boundary option for SPH (see D5.2) has to be applied at a more or less arbitrary location in the ascending aorta.

**Development of a numerical valve model**

Intracardiac flow is significantly influenced by the opening (and eventual closure) of the valves. Within CARDIOPROOF it is not feasible to include realistic models of the valves since:
- The MRI imaging data does not include the actual geometry of the valves
- Even if the (initial) geometry of the valves would be known, the material properties (elasticity) would still be unknown and generic properties would not be appropriate for a patient-specific approach
- In addition, finite element simulation of the passive opening of the aortic valve by pressure would require sufficiently fine elements and particles representing the blood, resulting in excessive CPU requirements for the flow simulations.

Hence, a numerical valve opening model has been developed. The valve model consists of three leaflets (represented by shell elements of dummy material) which will open in a symmetrical manner.

The information to be provided by the modeler is:

- A series of finite element node numbers that define the perimeter of the valve (subdivided into three leaflet edges)
- Flow area as function of time.

The algorithm will automatically generate the center of the valve and three C-nodes that define the leaflets, and triangular elements between the perimeter nodes and the C-nodes. The openings (blank in the figure 1) are also defined by elements each of which will have the shape of a kite which is very narrow at the start. Assuming symmetrical kites, the C-node position will be evaluated such that the open area equals the given flow surface area. Figure 1 displays the typical leaflet shape for an ideal case (circular geometry in-plane).

Since the valve opening is not instantaneous, a model (genvalve program) has been developed to define the leaflets of an idealized AV with a given function for the flow area. Although in many cases the actual flow area as a function of time may not be available, generic data may be used provided it has been tested that the sensitivity of the results for these assumptions remains limited.
Chain of Simulations

After the conversion of the FE mesh from the MUG model and subsequent closure of all opening, the initial distribution of the SPH particles representing the blood in the LV and the ascending aorta has to be generated. To avoid the tedious procedure of meshing the fluid domain and convert to spherical particles, the special EWVT filling algorithm as developed by ESI will be employed to obtain the optimal filling of the fluid domain with particles. It is currently foreseen to employ particles of equal size, although at some stage it could be decided to allow particles to differ in size in case it would be relevant to obtain a locally enhanced accuracy. One the filling has been completed and the numerical model of the AV opening has been incorporated, the model is ready for the actual flow simulation.

A sketch of the whole chain of simulations is presented in figure 2.

A detailed description of how to execute the chain of simulations as in the above sketch after the conversion of the FE model is available in a report from ESI [5].

The patient-specific model

The initial model of the LV and aorta of a specific patient (coded by B0305-28) was obtained from MUG by the end of March, 2015. The FE mesh and the nodal displacements were henceforth converted to the appropriate input for VPS. A global view of the complete model is shown in figure 3.
Note that the units of length have been converted to mm and that the correct units of time (in ms) and force (N) were used. This implies that pressure are in units of GPa. These are the units for the results, except when mentioned otherwise.

For the filling algorithm the entire boundary of the MUG model is closed by creating new dummy shell elements for any remaining opening. This has been done by connecting selected nodes along the edges of both valve openings with a (new) node in the middle of these openings. The position of the aortic valve was provided by MUG (plane in figure 4). The outflow opening was assumed to be located at a cut section of the ascending aorta (at some distance above the AV), and modeled with dummy shell elements as well.

The filling has been done with 64000 equal particles inside the LV and 4500 equal particles within the aortic root region intended to fill the part between the AV and the opening using the EWVT algorithm developed by ESI [6]. During the initial stage both sets of particles will expand until they fill the domain. Once the LV...
model (and a small part of the aortic root) has been filled with ‘growing’ particles, the particle number density (color) may be improved significantly by conducting an additional EWVT simulation with the **color gradient smoothing [7]**. The resulting particle distribution fills the entire fluid domain and displays a quite uniform particle number density (‘color’) indicating that the distribution is of high quality. During an initial flow simulation it was observed that the pressure inside the LV was not zero before the heart starts to contract and this will certainly affect the outflow which was indeed found to be very high. The possible reason for this problem is the non-equilibrium between the particle distribution and the contact with the walls. For that reason the initial particle distribution has to be redefined by an expansion simulation prior to the outflow. To obtain proper equilibrium of the particle distribution prior to the outflow simulation, the distribution obtained after step 2 of the EWVT filling was subjected to a dynamic flow simulation in which the walls remain fixed but an initial, positive pressure is defined for the fluid. In that case the fluid will expand and fit into the wall boundaries. This simulation does not require much CPU. Figure 8 shows the time history of the kinetic energy of the particles demonstrating that it is very close to zero after about 5 ms. The final position of the particles at that moment should be adequate to start the actual contraction and flow simulation.
Figure 6 Time history of the kinetic energy of the blood during the expansion simulation

To monitor the pressure during the flow simulations at a few locations, SPH Gauge particles have been defined [8]. At these locations the pressure is evaluated by a weighted average of the pressures of the nearby particles without contributing to the flow results.

For this case, these gauges are fixed in space; see figure 7.

Initial simulations with instantaneous valve opening

Before the special valve opening has been developed, flow simulations were conducted with model in which the AV opens (and closes) instantaneously at preset moments. Two simulations are reported below: for the first one, outflow2, the valve opens at 44 ms and closes at 244 ms; the outflow opening in the aorta
opens at 51.5 ms. For the outflow3 simulations, the valve times are 42 and 240 ms, respectively, whereas the outflow can start at 41.5 ms. Another relevant difference is that the assumed pressure in the aorta at the location of the outflow opening is given by a generic curve for outflow2, whereas that for outflow3 is a clinical pressure results provided by DHZB [ ] which is significantly higher.

Some results for the outflow2 simulation at 67.5 ms are shown in the partial views below. About 20 ms after AV opening, there are high flow velocities at the top of the AV and in the aorta. There is a pressure gradient from bottom to top in the LV.

The effect that the expansion simulation has on the pressures is shown in figure 9. The initial peak is a numerical effect and should be discarded. In contrast to the results for earlier simulations without a preceding expansion simulation, the pressure returns to zero after a few milliseconds demonstrating the efficacy to include the expansion in the simulation chain.
The pressure and velocity magnitude results for the outflow3 simulation at 60 ms are shown in the partial views below.

![Figure 10 Pressure distribution in a cut model of the LV for the outflow3 simulation at 60 ms.](image)

The velocity vectors in a partial section (slice) of the outflow3 simulation at 60 ms are shown in figure 12. Note that only the maximum pressures for the outflow3 simulation are in the physiological regime.

![Figure 11 Pressures (in mmHg) at one of the gauges in the aorta and the average fluid pressure for both simulations.](image)
Clinically relevant data are the flow rates and for the two simulations the results are displayed in figure 12. The outflow3 results appear to agree with a typical maximum flow rate of 250 ml/s. To provide some insight into the flow pattern inside the LV, the velocity vectors in a slice of the LV for outflow3 at a selected moment are shown in figure 13.

Figure 12 Computed flow rates in ml/s versus time (ms) through the aorta outflow surface for both simulations.

Figure 13 velocity vectors in a partial section (slice) of the outflow3 simulation at 60 ms
It may be concluded that the results (both in pressure and outflow) are very sensitive to the presumed time of opening for the valve (assumed to be instantaneous for the current simulations). Due to the (apparently) late opening of the AV for the outflow2 simulation, the pressures and flow rates are obviously too high.

Although the timing (and value?) of the opposing pressure in the aorta for outflow3 may not correct the resulting flow rates and pressures are not completely unrealistic.

**Additional simulations with the new valve model**

With the computational model from the previous section new simulations have been done with the gradual opening of the artic valve. To that purpose, the time history for the open flow area had to be provided. Unfortunately, no information for this specific patient was available, so generic data had to be used which was provided by DHZB. The flow area in mm$^2$ versus time in ms are defined in the table below:

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<th>Time (ms)</th>
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<tr>
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<tr>
<td>13.7</td>
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<tr>
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<tr>
<td>65.1</td>
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<td>151.0</td>
<td>261.0</td>
</tr>
<tr>
<td>194.0</td>
<td>266.0</td>
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<tr>
<td>228.0</td>
<td>219.0</td>
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<tr>
<td>250.0</td>
<td>1.0</td>
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With the list of node numbers along the perimeter of the AV, divided into three leaflet sections, the additional elements for the leaflets and their displacement functions were generated using the genvalve program and appended to the numerical model of the LV and aorta.

For the first new simulation, poutvalve2, the same simple pressure at the outflow opening was used as for the outflow2 simulation. Figure 14 shows the finite elements as generated by genvalve. The open area in between the three leaflets is available for the flow through the AV. Due to the opening being partial at 60 milliseconds, there is a pressure drop across the AV as shown in figure 15.

The second new simulation, poutvalve3, has as goal to demonstrate that the windkessel model as referred to above is consistent. To that purpose, the flow rate obtained from the poutvalve2 simulation is used as input for the new simulation. Depending on the values for the windkessel parameters, the results for the poutvalve3 simulation should be similar to those of poutvalve2. Figure 16 shows that the flow rates of both simulations are indeed quite similar, indicating that the approach for the windkessel model for the outflow is working correctly. Figure 17 shows some pressure results and it may be observed that the difference between the two simulation results remains limited.
From the results of the previous section it could be observed that the initial particle distribution that is in equilibrium with the boundary conditions due to the walls (see figure 6) can be obtained in a period of time that is shorter than the time at which the LV starts to contract. This suggests that it might be possible to avoid the separate expansion simulation and combine the expansion with the initial part of the flow simulation. This has been done for the poutvalve4 simulation which differs from poutvalve3 by using the initial particle distribution from the step before the expansion case and the same initial fluid pressure and damping as used for the expansion simulation.
Figure 16 Flowrate for the poutvalve2 and poutvalve3 simulations.

Figure 17 Time histories of the average fluid pressure and the pressure at gauge 5 for the poutvalve2 and poutvalve3 simulations. The vertical scale is pressure in mmHg units.

Figure 18 shows the contact forces between the fluid and the walls of the LV and aorta (CONTACT-1), and between the fluid and the three leaflets of the AV (CONTACT-2). It may be observed that the general characteristics of the curves is similar, but that the results for the poutvalve4 simulations have reduced maximum values.
Figure 18 Time histories of the contact forces between the fluid and the walls of the LV and aorta (CONTACT-1), and between the fluid and the three leaflets of the AV (CONTACT-2).

Figure 19 Time histories of the massflux for the poutvalve3 and poutvalve4 simulations.
Selected conclusions

1. To avoid that the blood inside the ventricle is pressurized prior to the contraction it is recommended to perform an expansion simulation in which the fluid attains equilibrium with the contact surfaces, or to start the flow simulations with an initial pressure and temporary damping before the contraction starts.

2. The algorithm to semi-automatically define the (aortic) valve and its opening appears to function, including the closure at the later stage. This is important since the time required to open the AV does influence the flow results and the geometry (and deformation) of the actual AV leaflets is not available with the clinical information obtained within CARDIOPROOF. Even if the open surface area of the AV as function of time would not be available, an assumed (generic) flow area curve is assumed to be better than an instantaneous opening.

3. The results of the simulation with the valve opening appear to be more realistic although for most results such as the flow rate the differences are not very great.

4. The results for the simulation with the windkessel model appear to be consistent with the results for a simulation with a corresponding outlet pressure, indicating that such a model is working correctly. This is important since in many cases the aortic pressure cannot be provided for a specific patient but when the mass flow through the aorta is known and windkesselmodel parameters may be assumed, this can be applied as outflow condition inside the aorta.
5. With the models and software discussed in this report it is possible to conduct SPH simulations for patient specific models.

References
[2] CARDIOPROOF Deliverable 5.1, Implementation of software tools for the integration of the computational models of the morphology and the 4D VEC MRI information, June 30th, 2014
[4] N. Stergiopulos, B. E. Westerhof and N. Westerhof, Total arterial inertance as the fourth element of the windkessel model, 1999 paper 0363-6135/99 from the American Physiological Society