SIMCor

In-Silico testing and validation of Cardiovascular Implantable devices

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Executive summary

This document was developed to provide two *standard operating procedures* (SOP) on flow field assessment of *transcatheter aortic valve implants* (TAVI) by means of numerical simulation applying *fluid structure interaction* (FSI) and particle image velocimetry measurements. The SOPs are designed for SIMCor partners as well as for the scientific community.

The SOP-D4.5.1 is about building a computational model and performing simulations in the field of FSI for TAVI. Where applicable, existing standards and guidance are referenced within this document. Additionally, specific exemplary applications of the general procedure and recommendations are given, using the TAVI use case, which represents a minimally invasive implantation of biological valve prostheses into the aortic root via catheterization.

The SOP-D4.5.2 provides recommendations and standardised procedures and workflows for performing flow field measurement in TAVI by means of *Particle Image Velocimetry* (PIV). The document describes working steps and gives general important information in preparation and performing PIV measurements in TAVI. Explanations and recommendations are provided throughout the protocol to extend the understanding of different components and working steps of a PIV system and the corresponding measurement method.

Standards, guidelines, and recommendations for flow field assessment in TAVI were applied. Confronting the current workflow with the evolving practice as the project continues may lead to updates, thus subsequent iterations of the SOP are foreseen.

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Introduction

The transcatheter aortic valve implantation (TAVI) is the treatment of choice for high-risk patients with severe aortic stenosis. It is a minimally invasive, catheter-based procedure to replace the aortic valve. The interaction of the TAVI device with the surrounding vessel and the blood flow leads to a complex situation for device development, testing, and validation.

In-silico methods represent a promising opportunity to improve the quality of safety, efficacy, and usability assessments of TAVI. In particular, *numerical modelling and simulation* (M&S) by means of *computational fluid dynamics* (CFD) and/or *fluid structure interaction* (FSI) can significantly extend the understanding of thrombus formation in TAVI devices. M&S is a cost-effective tool that enhances *in-vivo* and *in-vitro* findings. In particular, simulation can model flow parameters, such as wall shear stress or washout behaviour, that are difficult to measure in clinical settings or even under *in-vitro* conditions.

The complexity and speed of technological innovations in the field of M&S strongly demands the establishment of agreed standard operating procedures (SOPs) allowing for a standardised and reliable use of in-silico methodologies for development, testing and regulatory approval of medical devices.

The standard ISO 5840 “Cardiovascular implants - Cardiac valve prostheses” provides a guideline for a so-called *integrated approach* for assessing the thrombogenic or haemolytic potential of TAVI in which computational flow field assessment (e.g., FSI) and experimental flow field assessment (e.g., PIV) are key aspects besides *ex-vivo* flow testing.

SIMCor focuses on numerical simulations and corresponding validation. One aim of this project is to develop standard operating procedures (SOP) to increase the credibility and trustworthiness of simulations. Thus, this deliverable focuses on a key area of SIMCor.

In the context of TAVI, this deliverable will focus on two SOPs, one for performing FSI simulation (SOP D4.5.1), and the other for performing experimental measurements by means of *particle image velocimetry* (PIV) for model validation purposes (SOP D4.5.2).

The steps described in the following SOPs are meant to be generic, specific examples relative to the SIMCor projects will be highlighted in the main text of the document as follows:

Exemplary use case - specific processing step

This format is used to present practical applications of the general recommendations provided in this manuscript.

The funding received from the European Union’s Horizon 2020 research and innovation program under grant agreement No 101017578 is thankfully acknowledged. In particular, F. Borowski was given the opportunity to write her PhD thesis on the topic of *in-vitro* and *in-silico* methods to evaluate the thrombogenic potential of TAVI by using PIV measurements and FSI analysis [1], which was partially used for this deliverable.

Cover page of the SOP D4.5.1 - FSI

SIMCor responsible partner	IIB				
Short Title, ID	SOP-SIMCOR-D4.5.1	**Page**	1	of	X
Title	SOP for preparation, performing and post-processing of simulations of TAVI				
Version	1.0	**Created on**	31/12/2022		
Status	1st draft	**Related SOP**	SOP-D4.5.2, SOP-D4.3		

Purpose and field of application

Numerical simulations are used for *in-silico* modelling of implantable devices to accelerate certification and design improvement throughout medical device development and validation.
Simulation of the prosthetic heart valve is challenging due to the interaction between a highly deformable structure (TAVI leaflets) and the fluid flow. Therefore, structural mechanics of the valve and fluid mechanics of the blood flow should be simulated together, resulting in so-called *fluid structure interaction* (FSI). The various FSI models used for cardiovascular applications are very heterogeneous and not standardised.
This standard operating procedure (SOP) is about building a computational model and performing simulations in the field of FSI for TAVI. Where applicable, existing standards and guidance are referenced within this document. Additionally, specific exemplary applications of the general procedure and recommendations are given, using the TAVI use case, which represents a minimally invasive implantation of biological valve prosthesis into the aortic root via catheterization.

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V1.0		New version

Scope

In the context of the M&S lifecycle (see *Figure 1*), this procedure focuses on the "**Model Construction**" phase.

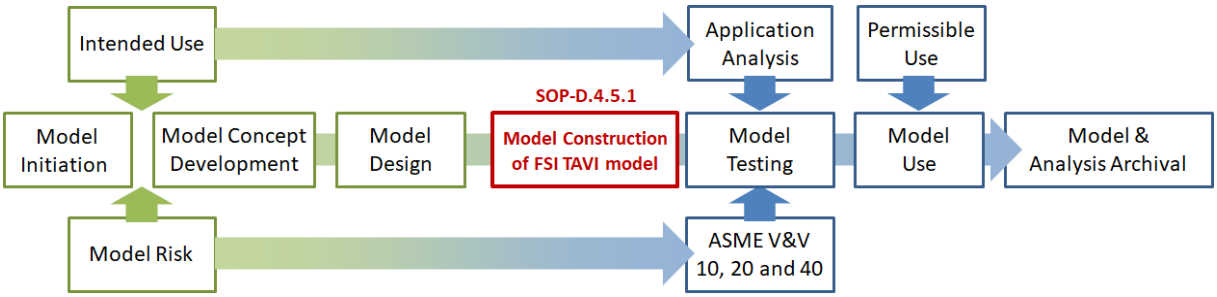

Figure 1: Schematic workflow of model development process involving model risk assessment and conceptual planning of validation and verification activities. Workflow was based on NASA-HDBK-7009A, ASME V&V 40-2018 and Pathmanathan et al. 2017. Figure is based on [2].

Descriptions of the workflow for "Model Initiation", "Model Concept Development" and "Model Design" are not part of this protocol. These steps were considered to be completed for the applicability of this SOP. For example, definition of the *context of use* (COU), simplifications of the real-world situation and selection of a certain numerical approach as well as software to be used must already have been made.

Furthermore, *validation and verification* (V&V) activities are not part of this SOP. Based on results obtained from V&V activities, one or even several steps of this protocol must be repeated to fulfil required accuracy criteria. However, before model construction, a plan for V&V activities should be conceived in order to address aspects of model risk assessment.

Both fluid mechanical tools - FSI and PIV - are complex methods which cannot be entirely standardised. In contrast, an interactive workflow is mandatory to obtain accurate flow fields in TAVI. Detailed knowledge in fundamental fluid mechanics and numerical as well as experimental fluid mechanics is required. As a consequence, the SOPs are not as user independent as usual. Therefore, both SOPs have additional characteristics of guidelines and depending on the specific situation; the user must adapt steps of the SOPs.

Definitions and abbreviations

ALE	Arbitrary Lagrangian Eulerian
CFD	Computational fluid dynamics
COU	Context of use
FSI	Fluid structure interaction
GOA	Geometric orifice area
ISO	International Organization for Standardization
M&S	Modelling and Simulation
PIV	Particle image velocimetry

SOP Standard operating procedure

TAVI Transcatheter aortic valve implants

UDF User defined function

V&V Validation and Verification

Procedure of FSI model construction

Note: In general, it is required to document the working steps in a detailed way.

Hardware specifications

Depending on the licence specification of the simulation software the hardware can be adapted. Software can feature certain *high performance* (HP) licences for parallelization of the numerical simulation which are hosted by one licence for each task. It should be noted that running a FSI simulation could require two licences utilising the structural and fluid mechanical solver.

As an example, if 16 HP(™) licences are available it is recommended to use a workstation or server solution with 18 cores (16+2 cores) to not entirely throttle the entire workstation while running the simulation. In addition to the limitations posed by the available software licences, parallelization of the software and the problem to be solved might vary. Thus, an individual analysis must be performed to find an optimum of hardware expenses, computation time, and software licence expenses.

1. Preparation for CFD / FSI simulation

Defining surrogate parameters for analysis

a) Surrogate parameters for decision making

Since simulations of TAVI are mostly integrated in a project with a certain research question, the surrogate parameters must be defined individually for the specific decision-making process.

Nonetheless, by solving the Navier-Stokes equation, the velocity and pressure distribution will be calculated. Based on the velocity field various surrogate parameters can be derived, such as shear rates and wall shear stresses.

b) Surrogate parameter for grid refinement study

It is recommended to evaluate the mesh accuracy on the same surrogate parameters which are further used for decision making. Furthermore, these surrogate parameters should be feasible for validation purposes and therefore the parameters must be measurable in-vitro. In our experience, the evaluation of the accuracy of a certain refinement level the flow velocity is feasible.

c) Surrogate parameter for V&V activities

Beside flow velocity and shear rate, the *geometric orifice area* (GOA) of the TAVI is found to be feasible for validation purposes. The GOA can be obtained without high effort in a numerical simulation as well as in an experimental measurement. For instance, GOA can be assessed experimentally by using a high-speed camera set up implemented in a pulse duplicator system.

SIMCor TAVI - Surrogate parameter for post-processing

Decision making can be supported by the velocity and shear rate distribution as well as the GOA. These surrogate parameters are found to be feasible for grid refinement and V&V activities. Furthermore, a passive transport equation for evaluation of the washout behaviour (evaluation of the washout behaviour is required by ISO 5840 but not defined in detail) can be used to support decision making. Therefore, a *user defined function* (UDF) must be implemented. The residence time of blood in a defined region can be calculated using a convection-diffusion equation [3, 4]:

$$dRT(\vec{x},t)dt + \nabla(\vec{u}(\vec{x},t) * RT(\vec{x},t)) = \nabla(DRT * \nabla RT(\vec{x},t)) + 1$$

The passive scalar was considered to be the residence time (RT), which increases by the defined time increment through the source term of one at each calculated time step.

Conceptual design of V&V activities

In existing regulatory documents, it is recommended to define a V&V plan before initiating any credibility activities. Here, we recommend starting the design of the V&V activities when constructing the model.

An FSI simulation of an artificial heart valve covers several structural and fluid mechanical aspects, which can be used for V&V purposes. Aspects such as the GOA or local velocity values should be identified according to the COU and according to possible V&V capabilities. Monitoring of selected hemodynamic parameters during simulation is recommended. Not only capabilities of future experiments (validation) should be evaluated but also options of post-processing routines of the simulation framework (e.g., ANSYS). In general, the design of the experimental and numerical domain should be as similar as possible, e.g., with respect to the length of the inflow and outflow section and measures of the mock vessel of the pulse duplicator system, to allow further validation.

SIMCor TAVI - Conceptual design of V&V activities

The following experimental setup was found to be feasible for validation purposes of TAVI FSI simulation (see also SOP 4.5.2 - PIV):

- Pulse duplicator system to model the left heart, equipped with flowmeter and pressure sensors (distal and proximal of the TAVI device), which are necessary for definition of FSI boundary conditions
- Silicone mock vessel of the aortic root to implant TAVI devices. Geometry of the vessel model can be used for designing of the computational domain.
- Mono-Particle Image Velocimetry system according to ISO 5840 (2021) requirements, which can be used for phase-resolved velocity measurements. Shear rate, Lagrangian particle tracking, etc. can be derived from the velocity field as post-processing routine
- High-speed camera system, which can be used for measurement of the GOA.

Defining the computational domain

The computational domain defines the section of the cardiovascular system which is planned to be analysed by means of CFD / FSI. In the field of TAVI simulation, the computational domain consists of the aortic root with the device implanted as well as an inflow and outflow section.

Due to the high computational cost by calculating a full 3D model, it is recommended to benefit from geometrical symmetry by considering only one third of the fluid domain. The applicability and limitations of this approach need to be explained and documented. If the asymmetry of the aortic root and the TAVI is substantial for the flow, a reduction of the domain is not valid. Therefore, knowledge of potential impacts of asymmetry of the hemodynamic is required and simplifications should be made carefully [5]. Wei et al. also provided several assumptions in order to simplify the computational domain by neglecting details of the TAVI device and anatomy, such as suturing or coronary arteries, respectively [5]. In general, the more aspects of patients-specific anatomy and haemodynamics are considered, the less valid assuming symmetry is.

The TAVI-stent could be neglected in order to reduce computational cost due to high grid refinement, which would be necessary by modelling the stent and resolving the flow around the stent struts. The outer skirt should be modelled due to the high impact of the flow. By assuming a rigid stent structure the commissural line remains static. In order to avoid the separation of the ventricular and aortic fluid domain, which could cause numerical problems, a gap of 1.0 mm between the closed leaflets is recommended. Even for simulations of only one of the three TAVI leaflets, using symmetry assumptions, a gap between leaflet and symmetry plane should be created (0.5 mm).

The native leaflet should be considered based on the huge impact on the flow (sinus and neo-sinus flow). See ISO 5840 for detailed description of the native leaflet design.

SIMCor TAVI – Defining the computational domain

For a generic aortic root model, the following assumption and simplification can be made:

- considering ⅓ of the vessel model and TAVI due to symmetry
- gap between symmetry plane and closed leaflet of 0.5 mm
- neglecting coronary arteries
- neglecting TAVI stent
- native leaflets can be modelled as cylinder with geometrical assumptions according to ISO 5840 (2021)
- cylindrical inlet and outlet (length should be selected to match experimental setup)
- closed TAVI configuration should be modelled initially.

Defining boundary conditions

It is possible to separate the FSI simulation in three different phases with specific boundary conditions: diastolic preload, systolic phase and diastolic phase.

Inlet and outlet conditions

In the first phase (**diastolic preload**), the diastolic pressure should be applied on the aortic side of the leaflet. As a result, the stresses and deformations of the leaflet can be simulated for a closed TAVI. The deformation and the normal and shear stresses in the leaflet were specified as initial conditions in the systolic phase. The velocities in the fluid domain were defined as zero. At the outlet the pressure needs to be set to zero.

Within the second phase (**systolic phase**), a flow rate needs to be specified at the inlet. A uniform velocity distribution can be defined at the inlet if a spatial velocity distribution is not available. Where a time varying velocity profile at the inlet is known, for example deduced from flow measurements at the patient, it can also be used. A static pressure of zero was used at the outlet. In the absence of reliable turbulence measurements, a uniform turbulence intensity of 5% can be specified at the inlet. Furthermore, a zero-gradient condition for the pressure can be used at the inlet. The systolic phase needs to be calculated utilising an FSI solver until the leaflets of the TAVI are closed again.

For the third phase (**diastolic phase**) only a CFD simulation is performed. The velocity field needs to be transferred from the systolic phase as the initial condition of the diastolic phase. The flow rate at the inlet must be set to zero and at the outlet the pressure needs to be set to zero. This approach can be chosen to avoid numerical instabilities. After closure of the TAVI prosthesis, no significant deformations of its leaflets are expected and an interaction between fluid and structural domain can be assumed as unnecessary.

Rigid walls

At walls the no-slip condition must be defined by setting the velocity to 0 m/s and a zero-gradient condition for pressure is feasible.

Contact modules

Crucial for the convergence behaviour of the structural calculation is the contact simulation. Contact surfaces were defined to simulate the other leaflets and the stent frame of the TAVI. For this purpose, the contact situation must be defined, e.g., frictionless, frictional, rough. Depending on the contact situation, different algorithms can be applied to satisfy the contact conditions.

In the case of TAVI simulation, it is important that the penetration between the leaflet and the contact module is as low as possible, so that the fluid elements are neither highly skewed nor the fluid domain is separated. The reduction of the penetration can be achieved by increasing the contact stiffness, but this can lead to an oscillation of the reaction forces at the contact. This so-called chattering should be avoided by a suitable contact formulation and an adjustment of the contact stiffness.

SIMCor TAVI - Selection of boundary conditions

Boundary	diastolic preload	systolic phase	diastolic phase
inlet	zero pressure	flow rate V(t)	constant flow rate V = 0
outlet	zero pressure	zero pressure	zero pressure
wall	u = 0	u = 0	u = 0
leaflet	diastolic pressure (normal) + interaction surface	interaction surface	rigid

SIMCor TAVI - Selection of contact definitions

_Type	Frictional
Friction Coefficient	0,002
Behaviour	asymmetric
Formulation	Augmented Lagrange
Detection method	On Gauss Point

Defining material properties

Mechanical properties of the aortic root

The aortic root is extremely heterogeneous, consisting of different structures which include the sinuses, the aortic valve leaflets, the commissures and the inter-leaflet triangles. The aortic roots main structural components are elastin and collagen fibres, and a three-layered organisation typical for the healthy aortic wall can be found in the sinuses [6]. Differences in stiffness are found within the structures of the aortic root, with the annulus showing larger average stiffness compared to the sinuses, and also differences within the three different sinuses, with the non-coronary sinus being comparatively stiffer [7].

Despite the fact that the aortic root has complex biomechanical properties, a simplified assumption of the aortic root as a homogeneous body is currently employed by most of the research groups. Different tissue layers or components are neglected. This reduces the computational effort since an interaction between fluid and aortic root wall will not be modelled.

Mechanical properties of the TAVR leaflets

Although the prosthetic leaflets have complex biomechanical properties, a simplified material model can be initially implemented. It is proven to be feasible when the prosthetic leaflets are assumed to be linear elastic [7].

Fluid-mechanical properties of the fluid / blood

While blood is a multiphase suspension of plasma and several cells and proteins - most of them being erythrocytes - modelling these suspensions is not feasible for larger vessels as the cell count of erythrocytes per millilitre of blood is approximately $5*10^9$

The blood is often approximated as a homogeneous fluid with blood-like density (ρ = 1060 kg/m³) and viscosity. To consider the rheological characteristics of blood a non-Newtonian viscosity model is recommended. Several viscosity models are available in literature. The implementation of the Carreau model according to Cho and Kensey has proven to be feasible, see table below.

SIMCor TAVI - Selection of mechanical properties

isotropic, linear elastic material behaviour

Parameter	**formula character**	**value**
Density	rho_f	1100 kg/m^3
Young's modulus	E	1 MPa
Poisson's ratio	υ	0.45

SIMCor TAVI - Selection of fluid properties

homogeneous, incompressible, non-newtonian properties

Parameter	Formula character	Value
Density	rho_f	1060 kg/m^3
Lower viscosity threshold	eta_infty	0.000345 kg/ms
Upper viscosity threshold	eta_zero	0.0560 kg/ms
Exponent 1	p	2
Exponent 2	n	0.3568
Time variable	Lambda	3.313 s

Selection of numerical solver and turbulence model

Simulation of the heart valve is challenging due to the interaction between a highly deformable structure (TAVI leaflets) and the fluid flow. Therefore, structural mechanics of the valve and fluid mechanics of the blood flow should be simulated together, resulting in so-called FSI. The various FSI models used for cardiovascular applications are very heterogeneous, ranging from one-way FSI models to fully coupled two-way models. Both monolithic and partitioned approaches are used [9].

A two-way coupled partitioned FSI approach for the simulation of TAVI was found to be feasible, especially to calculate detailed flow conditions. With this approach, application-specific solvers can be used for the structural and fluid calculations. The coupling of the two domains is realised by transferring quantities (force and displacement) at the interaction surface.

The Navier-Stokes and continuity equation in ALE form can be solved using a pressure-based solver. Numerical methods in the form of a second-order spatial upwind method and a second-order temporal discretization should be feasible for the fluid solver. An implicit solver for the structural domain is viable.

SIMCor TAVI - Selection of numerical solver and turbulence model

Numerical aspect	Implementation
convection term	second order upwind
diffusion term	central difference scheme second order
time	implicit, second order
coupling	fully bidirectional coupling
turbulence	RANS; k-omega-SST

The k-omega-SST model is very commonly used for the simulation of flows in heart valves. Here, SST stands for shear stress transport. This model blends between the k-ϵ turbulence model, in free flows (e.g., jets), and the k-omega turbulence model for near-wall flows. Both models belong to the *Reynolds-averaged Navier-Stokes* (RANS) family, where turbulent properties are calculated using two transport equations. The k-omega (k-ω) turbulence model is one of the most commonly used models - even for industrial use - to capture the effect of turbulent flow conditions. It is particularly suitable for near-wall flows, especially for complex boundary layer flows and separation problems, as they are commonly found in simulation of heart valve prostheses. In contrast, the k-ϵ turbulence model is required to predict accurate flow velocities in free flows as well, which commonly occur in the ascending aorta. This combined approach also avoids the sensitivity of k-omega models to the turbulence characteristics of the inlet in free flow.

SIMCor TAVI - Selection of turbulence model parameter

Initially, the following k-omega-SST parameters can be used:

$\sigma k1 = 1.176$	$\sigma\omega2 = 1.168$	$\beta i2 = 0.0828$
$\sigma\omega1 = 2.0$	$\alpha1 = 0.31$	
$\sigma k2 = 1.0$	$\beta i1 = 0.075$	

Mesh generation

As the computational domain consists of two domains - fluid and structural domain - the mesh can be performed separately. Both domains can be discretized utilising an unstructured mesh with hexahedron and prismatic elements. Depending on the software used, different discretization schemes for the fluid and solid domain might be required.

For meshing the leaflets, the *sweep method* can be used to define two elements over the thickness of the leaflet. Using this approach, the surface mesh generated for one side of the leaflet is propagated towards the other, while generating the specified number of cells within the leaflet.

It is recommended to divide the fluid domain into three segments (Inflow region, the aortic root and the outflow region) which can be refined individually. Attention must be paid for the refinement of the walls, in particular of the leaflet. To minimise interpolation errors when transferring forces and displacements for FSI simulation, the refinement of the surface of the leaflets must be consistent for both domains.

The mesh deformation can be realised by using the **arbitrary Lagrangian-Eulerian method (ALE)**. In order to preserve the integrity of the mesh, which is required by the ALE method, a gap with an offset of 1.0 mm can be defined between the coapted leaflets [9].

Due to the fact that the leaflets move during the opening and closing process a specific meshing strategy must be applied. Several studies successfully used the ALE. This approach adapts the mesh according to the leaflet deformation. Due to large deformation of the leaflets, a re-meshing is recommended to prevent poor quality cells.

SIMCor TAVI - Mesh quality parameter

Using Ansys, the following mesh parameters were found to be feasible:

- unstructured mesh with hexahedron and prismatic elements
- two elements over the thickness of the leaflet
- skewness of the grid > $Q_{skew,max}$ = 0.9 used as re-meshing criteria during FSI simulation due to deformation of the leaflets

Conducting mesh convergence study

- **Selecting a test case for mesh convergence study**

  Mesh convergence study will only be performed on a representative test case. This test case could be a worst-case scenario in terms of mesh quality.

- **Selecting surrogate parameters on which different mesh resolution will be compared**

  It is suggested to compare different mesh resolutions by using surrogate parameters which will be already used for further analysis of the TAVR design, such as fluid velocity or shear rate.

- **Generation of different meshes**

  The generation of different mesh resolution should be conducted by using a certain refinement factor from low to high-resolved mesh.

- **Performing simulations for mesh convergence study**

SIMCor TAVI - Conducting mesh convergence study

For orientation, a mesh which features an element number of above 2.5 million cells reached converged results. To quantify the convergence the velocity magnitude during the systolic peak flow of the following positing can be captured and compared: jet flow, shear layer of the jet flow, within the recirculation zone of the sinus and near the vessel wall.

Monitoring and debugging

Reporting in the field of simulation is not limited to numerical results. Even residuals and other convergence criteria should be stated. Hence FSI simulations could last several days or weeks, it is therefore recommended to define hemodynamic parameters, as output parameters, which can be monitored during simulation. This helps to evaluate the plausibility of the simulation on the fly and could therefore save computational cost and time. Therefore, the following output parameters should be logged and evaluated during processing of the simulation.

SIMCor TAVI - Monitoring and debugging parameter

Logging Parameter:

- residuals
- mass conservation

Evaluation Parameter:

- maximum velocity values
- maximum deformation

2. Performing CFD / FSI simulation

A stepwise example workflow for FSI simulation of TAVI is given below:

1. Defining the computational domain
2. Mesh computational domain
3. First phase (diastolic preload)
   a. define boundary conditions
   b. definition of material properties
   c. solver selection (FEA)
   d. run and monitor structural simulation until convergence
   e. map deformation and normal and shear stresses on the leaflet to leaflets of step 3
4. second phase (systolic phase)
   a. define boundary conditions
   b. definition of material properties
   c. solver selection
   d. run and monitor FSI-simulation until the leaflets of the TAVI are closed again
   e. map closed geometry and velocities to step 4
5. third phase (diastolic phase)

a. define boundary conditions
b. definition of material properties
c. solver selection
d. run and monitor CFD-simulation until end time of the cardiac cycle

Contingencies

none

Attachments

none

Additional documents

NASA-HDBK-7009: NASA Handbook for Models and Simulations: An Implementation Guide for NASA-STD-7009.

ASME V&V 10: Guide for Verification and Validation in Computational Solid Mechanics. (2006). New York, NY: ASME.

ASME V&V 20: Standard for Verification and Validation in Computational Fluid Dynamics and Heat Transfer

Publication policy

To SIMCor partners, please mention the following statement in each of your publications: *"This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101017578"*.

Cover page of the SOP D4.5.2 - PIV

SIMCor responsible partner	Charité (CHA)				
Short Title, ID	SOP-SIMCOR-D4.5.2	**Page**	1	of	X
Title	SOP for preparation, performing and post-processing of particle image velocimetry measurement of the flow field in TAVI				
Version	1.0	**Created on**	31/12/2022		
Status	1st draft	**Related SOPs**	SOP-D4.5.1, SOP-D4.3		

Purpose and field of application

This document provides recommendations and standardised procedures and workflows for performing flow field measurement in TAVI by means of Particle Image Velocimetry (PIV).
Experimental measurements are essential for validation and verification (V&V) activities for *in-silico* models. Furthermore, performing PIV measurements can be used as a tool for developing new generations of implants by means of prototype testing. In addition, the PIV method is applicable to analyse implantation strategies of existing TAVI devices and, as mentioned before, can also be used for validation purposes of *in-silico* models.
PIV systems have a modular design and consist of various components, such as cameras with lenses and filters, laser sources, timing hardware, optical components, workstation, and software. Furthermore, a mock circulation loop (pulse duplicator systems) must be used for the measurement of heart valve prostheses. As a result, a large variety of custom-made test setups can be configured with complex and varying handling depending on the system to be used as well as the problem investigated.
This SOP for flow field assessment in TAVI by means of PIV describes working steps and gives general important information in preparation and performing PIV measurements in TAVI. Explanations and recommendations are provided throughout the protocol to extend the understanding of different components and working steps of a PIV system and the corresponding measurement method.

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Revision history:

Version	Amendment ID	Version summary
V1.0		New version

Scope

Experimental measurements are essential for validation of numerical models. Particle image velocimetry (PIV) is found to be a feasible tool for validation numerical flow simulation by comparing fluid velocity. Furthermore, surrogate parameters which can be derived from the velocity field, e.g., shear rate, can be used for validation purposes. If the context of use (COU) of the planned PIV campaign concerns validation, then the numerical and the experimental model should be aligned. This covers geometrical and fluid mechanical conditions as well as the desired hemodynamic metrics.

This SOP describes the preparation and conduction of particle image velocimetry measurements in order to assess the velocity field in transcatheter aortic valve prostheses. The SOP implements requirements of the ISO 5840 (2021). Furthermore, recommendations for best practices based on own expertise performed at IIB e.V.; published studies as well as guidelines, such as Raghav et al. 2018, were added.

Both fluid mechanical tools - CFD/FSI and PIV - are complex methods which cannot be applied in a linear way. In contrast, an interactive workflow is mandatory to obtain accurate flow fields in TAVI. A detailed knowledge in fundamental fluid mechanics and numerical as well as experimental fluid mechanics is required. As a consequence, this SOP is not as user independent as usual. Therefore, the SOP has additional characteristics of guidelines and depending on the specific situation, the user must adapt steps of the SOP.

Definitions and abbreviations

IA	Interrogation area
IFU	Instruction for use
Nd:YAG	neodymium-doped yttrium aluminium garnet
PIV	Particle Image Velocimetry
PMMA	polymethylmethacrylate
Re	Reynolds number
ROI	region of interest
SNR	signal-to-noise ratio
SOP	standard operating procedure
TAVI	Transcatheter aortic valve implant
Wo	Womersley number

Preliminary considerations, general requirements and components for particle image velocimetry measurements of TAVI

1. Principles of particle image velocimetry

The principle of *particle image velocity* (PIV) measurement is based on the definition of velocity as a travelled distance per time interval, see *Figure 2*. For this purpose, the fluid flow is seeded with particles, which follow the flow. The position of the particles following the fluid flow is detected by one or more PIV camera(s). According to the double frame approach, the PIV camera takes two images in a short sequence (Δt) and synchronously to emitted light pulses. Due to a sequentially taken picture series of double frames, the position of particle patterns can be tracked over time.

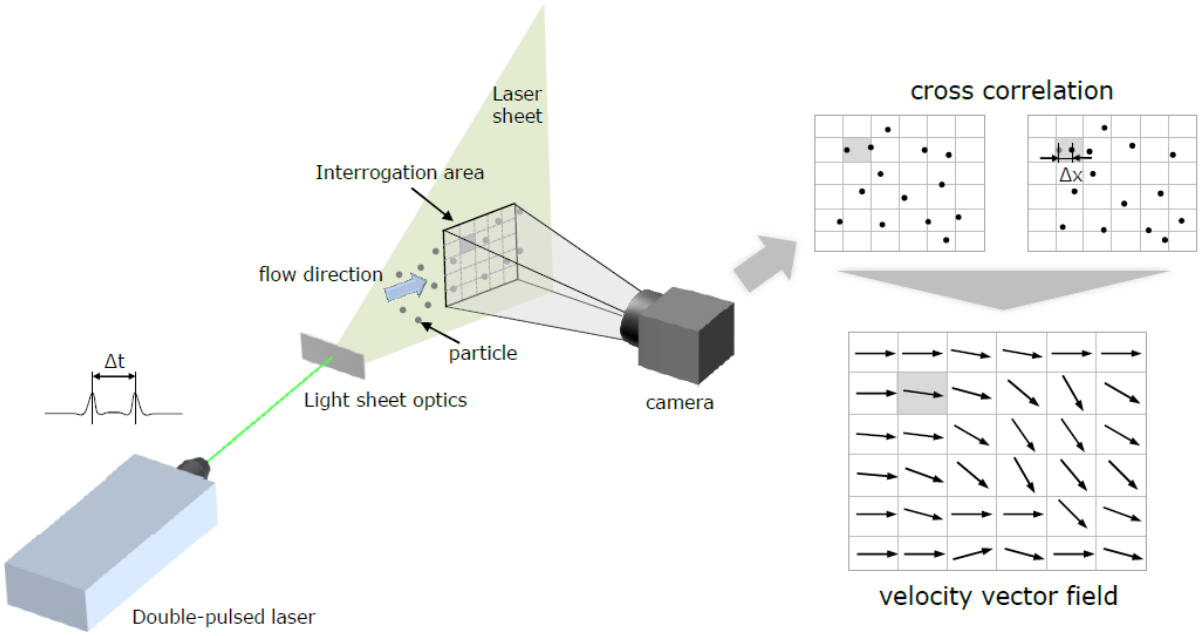

Figure 2: Schematic depiction of 2D2C-PIV measurement principle.

The flow velocity measurement is a result of the particle movement related to the time between each double frame, which was taken by the PIV camera. The movement of the particles is then analysed by means of a cross-correlation method in certain regions, the so-called *interrogation areas* (IA), as a post-processing routine. As a result, a stationary velocity field of the fluid flow is obtained. Further information can be found in Raffel et al. [11].

Due to the complexity of the test apparatus, composed of different components, a careful selection and a precise matching of the hardware components is essential. Usually a PIV-system can be purchased from different companies worldwide. These companies assemble a system depending on the user's needs and requirements.

The major requirement for the PIV measurement is the optical access to the test specimen, due to the optical measurement principle of the PIV method.

In general, the following components are necessary for the flow field assessment in TAVI:

- **PIV system**
  - light source and optical components
  - camera(s), lense(s) and filter(s)
  - synchronizer
  - traversing system
  - PIV-Workstation with software including acquisition, pre- and post-processing

- **pulse duplicator system**
  - pulsatile pump
  - compliance chambers (aortic, ventricular)
  - pressure and flow sensors with corresponding electronics
  - test chamber with optical access to the test specimen
  - heater and temperature control
  - target implantation geometry (model of the aortic root) with adequate optical characteristics to guarantee optical access to the test specimen

- **test fluid with adequate optical and rheological characteristics**
  - heated mixer
  - refractometer
  - rheometer

- **particles with matching optical characteristics to light source, camera(s) and filter(s)**

- **TAVI specimen**

2. Components of the PIV setup for flow characterization in TAVI

Light source

Typically, a pulsed laser of sufficient pulse power (10–130 mJ/pulse) should be selected for illumination. The most commonly used laser type for PIV measurements is the Nd:YAG laser with Nd3+ions as laser-active material embedded in an yttrium aluminium garnet crystal.

The laser should feature a light sheet optic to obtain a planar sheet of approx. 1 mm thickness in the area of the measurement plane. It is recommended to select a measuring range considerably smaller than the light-section height of the laser plane to achieve a light intensity as homogeneous as possible in the measuring range [11].

For performing phase resolved measurements, a low pulse rate (2 Hz - 15 Hz) is feasible. The wavelength of the laser light should match the fluorescent parameters of the particle used for the experiment. Fluorescent particles have a huge advantage, as they, after being excited by the laser light, emit light of a specific wavelength, which allows to filter scattered and background light, e.g., by reflections and absorption at walls.

Since the time between the laser pulses (Δt) is directly included in the calculation of the flow velocity from the movement of the particles, an arbitrarily adjustable Δt is often desired to resolve flow velocities of different magnitudes. For this reason, two lasers are often used (dual-cavity lasers), between which Δt can be set arbitrarily.

We have used the following settings for light source selection, which proved to be feasible for us. This does not exclude the existence of different light sources that are also suitable for this purpose.

SIMCor TAVI PIV - Light source

- double pulsed Nd:YAG dual-cavity laser (Litron Laser Ltd., Rugby, UK)
- wavelength: 532 nm
- max. laser energy: 145 mJ
- max. pulse rate: 15 Hz
- beam expansion: 1 mm wide laser-light plane using a light sheet optic

Camera equipment

The number of cameras depends on the number of desired velocity components (C) and spatial dimensionality (D) for the measurements. In general, the particles in the fluid flow move in three dimensions, with three components for the individual velocity vector of the particle. Therefore, 2D-2C, 2D-3C and 3D-3C PIV setups can be distinguished.

For a planar (2D) measurement of two velocity components (2C) only one camera is needed, so-called mono-PIV. In this case, a camera should be aligned orthogonally to the illuminated measuring plane (2D planar PIV).

If all three velocity components are required (3C), e.g., in complex flow geometries like the aortic root, a minimum of two cameras is necessary (stereo-PIV) and for three-dimensional measurements at least three cameras need to be integrated in the setup (tomo-PIV / volumetric-PIV, for example see additional documents Borowski et al. 2022.

According to the ISO 5840 (2021) standard, for approval relevant testing, only mono-PIV is required. With respect to measurement time and the efficient use of resources in a daily routine, this might be a feasible approach. Nevertheless, this has to be considered carefully because of the complex 3D-topology of the fluid flow in the aortic root which was verified in previous work [13].

The cameras should be provided with appropriate lenses to resolve desired spatial resolution (typically ca. 10 lm/pixel) and temporal scales of the velocity field should be used. In general, Charge-Coupled Device (CCD) cameras are used for low-repetition rate PIV and Complementary-Metal–Oxide–Semiconductor (CMOS) cameras for high-repetition rate PIV.

Furthermore, the lenses should be equipped with band-pass filters matching the wavelength of the fluorescent particles to minimise reflection and increase the signal-noise-ratio.

Additionally, Scheimpflug adapters should be used to guarantee parallelism of the image plane (camera sensor) and the lens plane (Scheimpflug condition).

We have used the following camera equipment, which proved to be feasible for us. This does not exclude the existence of other camera equipment and configurations that are also suitable for this purpose.

SIMCor TAVI PIV - Camera selection and configuration

- Configuration: 2D-2C
- CMOS cameras: EoSens 12CXP+ (Mikroton, Gilching, Germany)
- lenses: ZEISS Planar T* 1,4/50 (Carl Zeiss AG, Oberkochen, Germany)
- filters: 590 nm Edge Wavelength (AHF Analysetechnik, Tübingen, Deutschland)

Synchronizer

The synchronisation of the PIV components is necessary to fire the laser beam simultaneously to the camera shutter at a predefined time. In order to perform measurements at exact time points within the cardiac cycle, the synchronizer is triggered by an external trigger signal from the pulse duplicator.

With a user-defined delay between input trigger and output trigger a certain time interval for camera and laser can be defined. In this way, the optimal Q-switch delay was measured for this system (160 µs). To achieve the optimum laser power, this optimum Q-switch delay should be used.

The time between the laser pulses can be adjusted according to the velocity, which needs to be measured. If very low velocities need to be measured, a long-time delay between the pulses is suitable and vice versa.

If a measuring field is composed of very different velocity magnitudes, it is advisable to record the same time with different laser pulse delays.

We have used the following synchronizer, which proved to be feasible for us. This does not exclude the existence of other synchronizers and synchronising configurations that are also suitable for this purpose.

SIMCor TAVI PIV - Synchronizer

- Performance Synchronizer Dantec Dynamics (Dantec Dynamics, Skovlunde, Dänemark)

Test fluid

In order to create physiological conditions from the fluid mechanical point of view, the fluid properties of the test fluid should be analogous to those of blood. In accordance with ISO 5840, the kinematic viscosity of the test fluid should be adapted to the blood (v = 3.5 cSt). In addition, it is necessary to match the refractive index of the test fluid as well as of the aortic root model in order to avoid optical distortions and guarantee direct optical access for the PIV-measurement.

Several pure liquids and liquid solutions have already been used by researchers to define a blood substitute fluid, including a saline solution [14], a water (or saline)-glycerine mixture [15, 16], or other multi-component mixtures [17–19]. To define the ideal properties of the test fluid, the kinematic viscosity should be measured by means of a rheometer. The refractive index should be determined by using a refractometer. The measurement of the viscosity and the refractive index should be performed at 37°C. In order to adapt the mixture to the aortic root model, the refractive index of the aortic root model should also be determined.

Particles

The PIV measurement methodology does not directly measure the velocity of the fluid, but the movement of particles that are added to the fluid and should follow it without slip. For this reason, the interaction between fluid and particles in the flow is of immense importance for the exact measurement of flow velocity. A possible influencing factor on a velocity of the particles deviating from the fluid is the gravitational force. For selecting proper PIV particles, the velocity resulting from this force needs to be calculated. For example, the Stokes' equation can be used for this purpose:

$$u_g = \frac{{d_p}^2(\rho_p - \rho_f)}{18\,\mu} g$$

The diameter of the spherical particles is assumed to be dp, the density of the particles with ρp and the density of the fluid with ρf. The dynamic viscosity is given as μ and the gravitational force as g. The velocity component must be kept as low as possible in comparison to the main flow. This can be done by selecting the particle regarding a suitable density as well as diameter. If the difference of the densities is almost zero, a neutral buoyancy of the particles can be achieved. Furthermore, small particles lead to a reduced sink velocity. The adjustment of the fluid (viscosity) can also be done, but mostly the fluid mechanical aspects (Reynolds number *Re* or Womersley number *Wo*) define the fluid properties.

Furthermore, the following formula can be used to calculate the relaxation time t_{relax} of a particle [10].

$$t_{relax} = (d_p{}^2 * \rho_p)/(18\,\mu)$$

The relaxation time of a particle in an accelerated fluid provides an indication of how closely the particle flow matches the fluid flow. Again, the particle diameter and the particle density are the most important parameters in the selection of seeding particles.

A second important factor in selecting the right particles is their light scattering property. This property determines how intense the contrast on the captured image is between the particles and the background. For a spherical particle with a diameter larger than the illuminating wavelength λ, the Mie theorem can be used for the scattering of the light. The light scattering, according to the Mie theorem, is shown in Fig. 5 for 1 μm and 10 μm particles in planar view. In this case, the light radiates from the left and is scattered by the particles in all spatial directions, but most strongly at an angle of 180° to the light source (for 1 μm particles). In the case of larger particles (e.g., 10 μm), a large dose of the light is scattered in 90° direction. The illustrations show that a better contrast can be expected with larger particles. This contradicts the above-mentioned finding that the particles should be as small as possible to follow the flow. Accordingly, a compromise must be made with regard to particle size [11, 12].

Fluorescent particles can be used to reduce reflections and improve the signal-to-noise ratio. The particles must be selected with an appropriate filter. The filter is typically a high-pass filter that blocks the wavelength of the laser (and reflections) but allows the transmitting of the wavelength of the fluorescent particles.

Another factor to consider is the particle concentration. By the scattering of the particles, further particles can be stimulated, and thus the intensity of the scattered light of the particles increases. However, if there are too many particles in the fluid flow, the backlighting will also become more intense, resulting in a reduced contrast between the background and the particles.

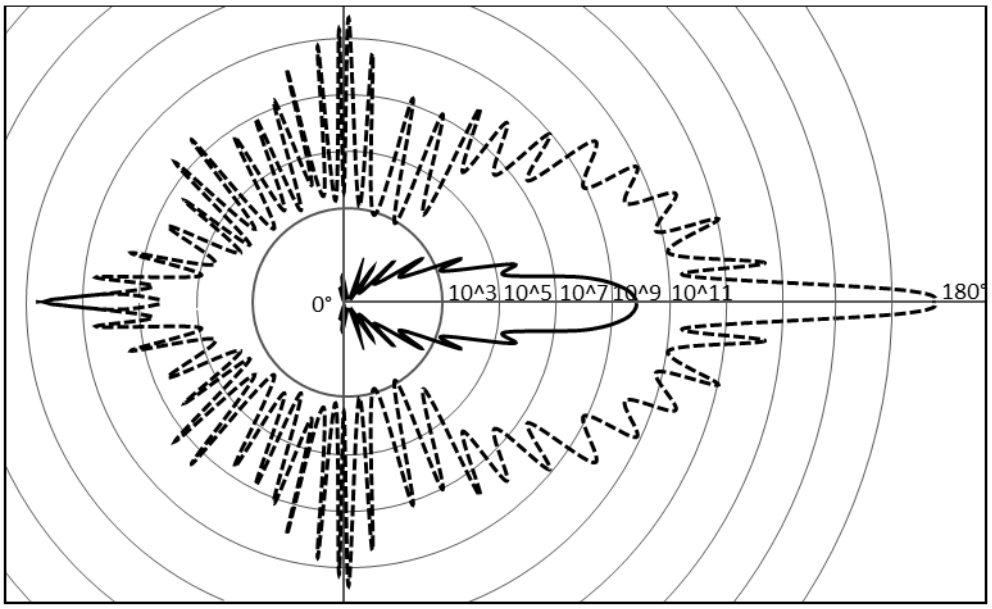

Figure 3: Schematic diagram of light scattering by particles with a diameter of 1µm (solid) and 10µm (dashed) according to the Mie theory adapted from [11].

Pulse duplicator system with PIV chamber

The pulse duplicator system offers the possibility to vary different hydrodynamic parameters concerning the flow through the TAVI. Using a piston pump, a membrane representing the left ventricle is compressed. The induced pressure increases, and ejection of the test fluid is transferred to the test chamber with the TAVI. The test chamber is in turn connected to the chamber representing the left atrium, creating a circuit.

The flow can be measured with a flow sensor and the pressure is detected in the atrium, on the ventricular side and on the aortic side of the TAVI. The compliance of the aorta is modelled by the Windkessel system. The configuration of the circulation model is controlled by software, which additionally allows a connection to the PIV system. In order to provide optical access for the laser plane and the camera, a test chamber consisting of *polymethylmethacrylate* (PMMA) can be constructed. In this chamber the aortic root model, where the aortic valve prosthesis is located inside, is fixed (*Figure 6*).

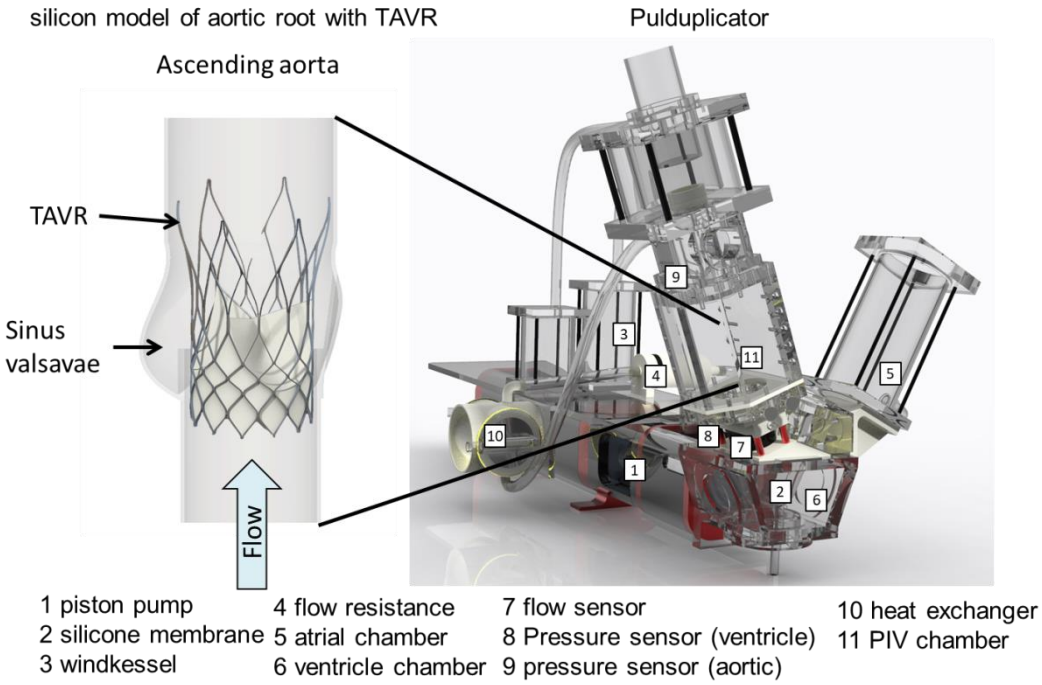

Figure 4: Pulse duplicator system (Vivitro Labs Inc., Victoria, BC, Canada) with custom made PIV chamber and TAVI device within an aortic root model (detailed view) [13].

For the presented test setup the following pulse duplicator system was used:

SIMCor TAVI PIV - Pulse duplicator and aortic root model

- ViVitro pulse duplicator system (Vivitro Labs Inc., Victoria, BC, Canada) with custom made PIV chamber
- aortic root model of transparent silicone Sylgard 184 (The Dow Chemical Company, Midland, USA) with refractive index of n = 1.41 at 37°C.

Procedure

1. Preparation

Selecting particles

As described, a PIV measurement does not directly measure the velocity of the fluid, but the movement of particles that are added to the fluid. Therefore, the identification selection of the right particles is crucial for a resilient PIV-measurement result.

The main particle selection criteria are

- particle density
- particle size
- particle light scattering
- particle concentration in the test fluid

Finding the right particle concentration is an iterative process. Therefore, initially only a small number of particles should be added to the test fluid mixture. Test pictures should be taken and analysed regarding the detected number of particles per interrogation area.

SIMCor TAVI PIV - Seeding Particle

Fluorescent polystyrene particles with diameter 10 µm and density of 1,05 g/cm3 (micro particles GmbH, Berlin, Germany) were proven to be feasible.
The concentration of particles should be high enough to achieve a sufficient number of particles within a small interrogation area for evaluation (N > 10), but also low enough to allow clear identification of individual particles. In accordance with the camera used, the particles should have a size between 2 and 5 pixels on the double image.

Mixing the fluid

A mixture of glycerine and water is recommended as test fluid. The mixing must be carried out very accurately to obtain a homogeneous mixture. From this batch, several samples need to be taken for viscosity and refractive measurements. The total volume of the mixture depends on the pulse duplicator system to be used.

To define the ideal volume fraction, analyse the mixture with regard to kinematic viscosity and refractive index, see *Figure 5*. For measuring the viscosity of water-glycerol mixtures, a plate-cone rheometer can be used. At least three samples of each mixture should be examined. Since most rheometers capture the dynamic viscosity, the kinematic viscosity needs to be calculated by dividing the dynamic viscosity by the density of the mixture. It must be pointed out that all measurements should be performed at 37°C.

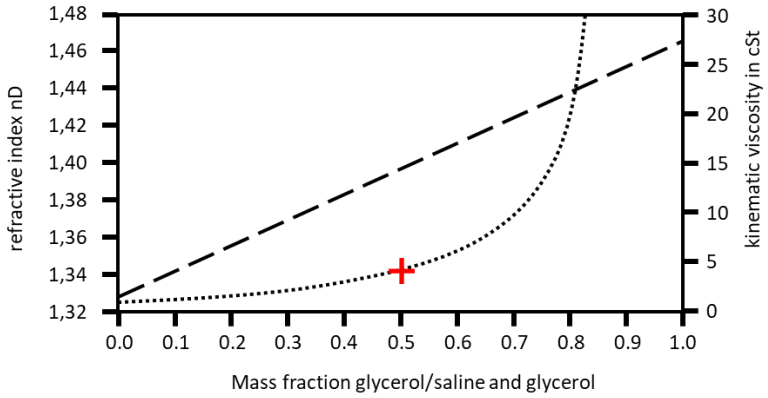

Figure 5: the refractive index and the kinematic viscosity were determined for nine different mixing ratios with a refractometer (ABBE refractometer AR4, A. KRÜSS Optronic GmbH, DE) and a rheometer (HAAKE RheoStress 1, Thermo Fisher Scientific GmbH, DE).

The refractive index of the mixture can be determined on the basis of the angle of total reflection at the medium boundary by means of a refractometer. The measurement of the refractive index needs to be carried out at 37°C. At least three samples of each mixture must be examined.

If a long PIV campaign needs to be carried out, the viscosity should be measured at least every day due to evaporation of the water.

We have used the following test fluid and measurement equipment, which proved to be feasible for us. This does not exclude the existence of other mixtures of test fluid that are also suitable for this purpose.

SIMCor TAVI PIV - Selection of test fluid and measurement equipment

water glycerine solution	$m_{glycerine}/m_{water}$ = 0.506
Rheometer	HAAKE RheoStress 1 (Thermo Fisher Scientific GmbH, Germany)
Kinematic viscosity	v = 3.5 cSt
Refractometer	ABBE AR4 (A. KRÜSS Optronic GmbH, Germany)
Refractive index	1.401

Adjustment of the laser light

Safety advice: Handling with high energy laser light could cause burns and blindness. The person operating the laser equipment is responsible for compliance with the safety measures.

In most PIV measurement setups, the creation of a laser light sheet is done by a cylindrical lens. The laser light sheet thickness can then be adjusted using a spherical lens. It should be noted that the light intensity within the light section plane depends on the location, as shown in *Figure 6*.

It is recommended to select a measuring range considerably smaller than the light-section height of the laser plane, in order to achieve a light intensity as homogeneous as possible in the measuring range [11, 12]. To do so, the light sheet height needs to be measured in the area of the fluid domain to be measured.

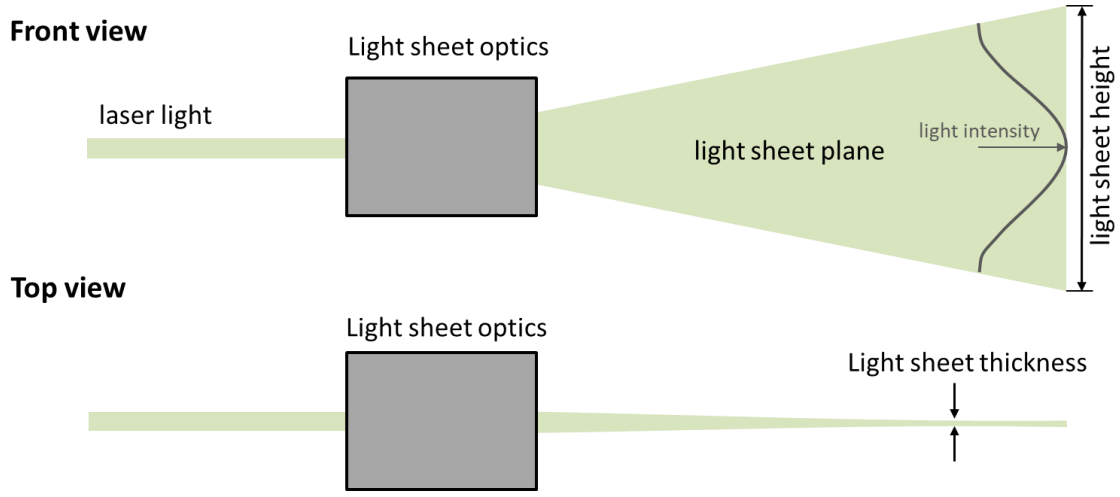

Figure 6: *Widening of the laser beam by means of a cylindrical lens and adjustment of the light section thickness by a spherical lens as a possible combination of lenses to form a light section plane for PIV measurement.*

Implanting the TAVI

The TAVI specimen must be implanted in the silicon mock vessel according to the instruction for use (IFU).

Camera adjustment and calibration

In case of mono-planar 2D-2C PIV, a camera should be aligned orthogonally to the illuminated measuring plane. The camera should be mounted to reduce vibration and maintain the correlation between the laser and the camera during the measurement. The Cameras should be focused on the plane to which the light sheet is adjusted and the illuminated region of interest. It is recommended to align the camera orthogonally to the light section, as well as to all media interfaces (air, test chamber, test liquid) to minimise distortions. If distortions are unavoidable, they should be compensated using appropriate methods. For example, this can be done during calibration by de-wrap distortions on images that do occur, e.g., by using polynomials to convert measured spatial information into real spatial information. If no distortions are given, or if it has been proven that appearing distortions are negligibly small, the calibration procedure is confined to the determination of a scaling factor between image dimensions and real dimensions. For this purpose, a calibration target should be used. The target is positioned in the actual measurement region and contains information about the real spatial dimensions in the measurement plane. If fluorescent particles are used, a feasible filter should be mounted on the camera.

Define measurement scheme for temporal resolution

The preliminary considerations for the temporal measurement principle are decisive for the further procedure and should therefore be carried out at this point. In this context, there are two approaches, based on the intended information that is to be derived from the velocity fields. These two approaches are, namely, time-resolved and non-time-resolved measurements. Furthermore, a distinction can be made between phase-averaged and instantaneous measurements. If we are interested in measuring certain time points in the cardiac cycle, such as the peak systolic flow, it is necessary to know these time points in advance. In phase-triggered measurement, in order to capture temporal fluctuations in the flow case, the instantaneous velocity field is recorded with the PIV system several times at the same instants within the cycle. The actual number of images to be acquired should be determined by convergence measurements. The acquisition of 100-200 measurements per time point in the cycle were found to be feasible. In all measurement configurations, the conditions of the incoming trigger pulse received from the pump generating the

pulsatile heartbeat needs to be known. Another approach is to measure time-resolved velocity fields, either by high-speed measurements or by phase-averaged measurements. The former is mainly limited by the hardware available. Phase-resolved measurements are the most common. In phase-resolved measurements, in each cardiac cycle, an instantaneous velocity field can be measured. However, it is possible to conceive more complex trigger schemes to shorten the measurement time by performing multiple measurements in one cycle, limited only by the maximum pulse frequency of the laser and the recording capacity of the camera. To fully investigate time-dependent phase-averaged flow phenomena, an appropriate time step size should be chosen, especially in the systolic phase.

SIMCor TAVI PIV - Define measurement scheme for temporal resolution

- time-resolved PIV measurement by utilising a trigger signal from the pump of the pulse duplicator system
- acquisition of 100-200 measurements per time point in the cycle for statistical valid velocity field
- In order to resolve various levels of velocity scales, an adaptive adjustment of the delay between the laser pulses is necessary. Therefore, measurements should be repeated with 3 different laser pulse delays (100, 500 and 2000 µs)

Predefine PIV parameter

The measurement of the velocity implies the determination of the displacement of the particles during a certain interval of time. Respectively, the expected spatial displacements in different time intervals have to be considered in advance. Depending on the expected velocities, mainly the laser pulse delay and the size of the IA must be taken into account. Since also the optimal settings for particle density and laser pulse delay depend on the desired size of the interrogation area, this should be considered in advance.

SIMCor TAVI PIV - PIV measurement parameter

For classical cross-correlation evaluations, there should be a particle density of about 10 particles per IA. The particles should have a size of 3-5 pixels. Furthermore, the particles should have a displacement smaller than the IA size, and should be approximately ¼ of the IA. Nevertheless, the aimed spatial resolution is important for determining the IA size. After pre-defining an IA size, one can further begin the actual PIV measurement process. We found an IA between 32 to 64 to be feasible.

2. Performing PIV measurements

Baseline workflow

- Mount the silicon mock vessel with implanted TAVI specimen inside pulsatile flow loop system
- Run pulsatile flow loop system
- Warm up of test fluid with temperature check
- Acquire test images without particle
- Insert particle
- Acquire test image with particle
- Determine particle density in IA, if particle density < 10: begin from 4.
- Define laser pulse delay
- Acquire test image with particle
- Check actually measured displacement of particle in IA in ROI, begin at step 7 until displacement > ¼ IA length but < IA length
- Check particle intensity on images from both cameras, if different: Adjust exposure time of cameras or adjust pulse intensity of lasers
- Acquire double frame images, do a plausibility quick check of velocity measurements using post processing routine
- Set up trigger/measurement scheme
- During PIV-Measurements observe the flow loop system is working as intended

3. Analyzing PIV measurements

1. Use methods to enhance SNR like background subtraction with mean images from same trigger time
2. Mask out reflections or region of no interest
3. If possible, define regions where walls are, to correct for false velocities in wall intersecting IAs.
4. Perform cross correlation with pre-defined IA. Recommended with adaptive IA (32-64) and allowed overlapping of approximately 50%.
5. Post-process the vector field (outlier detection/removing/replacement, average sliding window etc.), smooth vector field, mask out region of no interest
6. Compute statistics of phase-averaged measurements
7. Export the results in a file format suitable for further processing
8. Compute hemodynamic parameter (e.g., shear stress) as intended

Documentation

Every step of preparation, performing and post-processing of particle image velocimetry measurements needs to be documented. Furthermore, rationale, assumptions and limitations must be discussed. See also Raghav et al. 2020 [20].

Additional documents

- ISO 5840-1:2021
- ISO 5840-2:2021
- ISO 5840-3:2021
- Manufacturers instruction for use (IFU) of TAVI
- Handbook pulse duplicator system
- Handbook refractometer
- Handbook rheometer
- Handbook PIV system
- Guideline for documentation D4.2
- F. Borowski, S. Kaule, J. Oldenburg, K.-P. Schmitz, A. Öner und M. Stiehm, „Particle-Image-Velocimetry zur strömungsmechanischen Analyse des thrombogenen Potentials von Transkatheter-Aortenklappenprothesen“, *tm - Technisches Messen*, Jg. 89, Nr. 3, S. 189–200, 2022, doi: 10.1515/teme-2021-0124.

Contingencies

none

Attachments

none

Publication policy

To SIMCor partners, please mention the following statement in each of your publications: *“This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 101017578”*.

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