

Silvia Bonardelli^{1*}, Amanda Inzoli^{1*}, Claudio Chiastra^{1,2}, Luke Boldock^{3,4}, Cecile M. Perrault^{3,4}, Andrew Narracott^{4,5}, Gabriele Dubini¹

1. Laboratory of Biological Structure Mechanics (LaBS), Department of Chemistry, Materials and Chemical Engineering "Giulio Natta", Politecnico di Milano, Italy
 2. Department of Biomedical Engineering, Thoraxcenter, Erasmus University Medical Center, Rotterdam, The Netherlands
 3. Department of Mechanical Engineering, University of Sheffield, Sheffield, UK
 4. INSIGNEO Institute for *In Silico* Medicine, University of Sheffield, UK
 5. Department of Cardiovascular Science, University of Sheffield, UK
- *Authors equally contributed

Contact address: gabriele.dubini@polimi.it

Introduction

According to recent studies, **in-stent restenosis (ISR)** is related to the effect of changes in flow patterns induced by the stent on **endothelial cells (EC)** physiological behaviour. In order to study this correlation, an experimental set-up reproducing **stented coronary artery** geometry and flow conditions (Fig. 1) was developed at the University of Sheffield. Since **computational fluid dynamics (CFD)** analysis allows study of wall shear stress (WSS) distributions at a level of detail that is not possible with experimental measurement alone, an **in silico replica** of the *in vitro* model starting from micro-computed tomography (μ CT) images was needed. The aim of our work was to assess the sensitivity of WSS distributions to different image processing parameters.

Materials and methods

The computational model construction was gained through four main steps (Fig. 2). (1) μ CT images of the stented sample were acquired, (2) an **image processing** was conducted to obtain μ CT slices and to reconstruct the stent geometry, (3) a **structural simulation** was performed to obtain the PDMS boundaries starting from the reconstructed stent geometry, and (4) **CFD analyses** were performed to assess the influence of image processing parameters on fluid dynamics quantities.

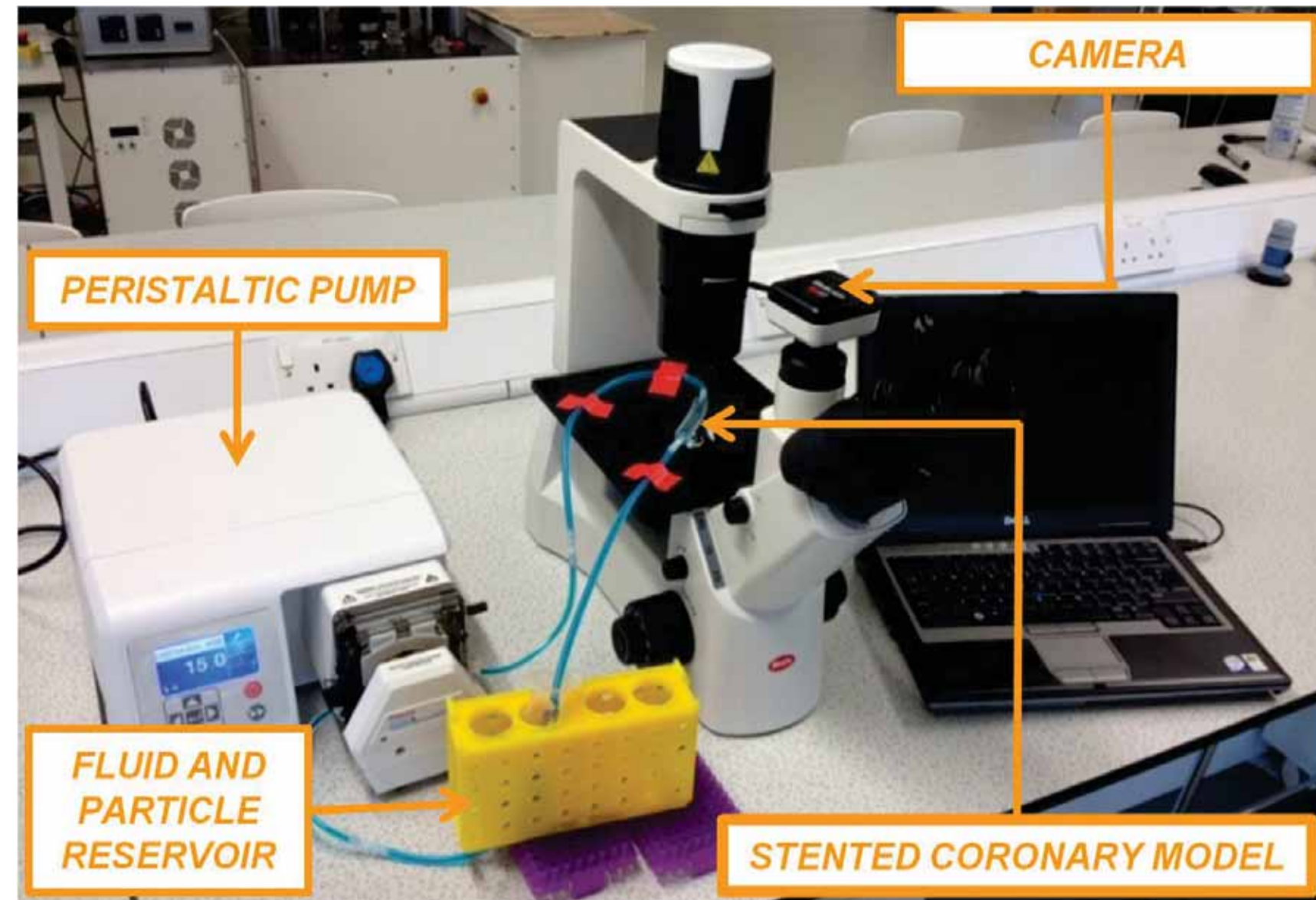


Fig. 1 Experimental set-up reproducing stented coronary artery geometry and flow conditions.

Image processing and stent reconstruction

The coronary artery model in PDMS was scanned and μ CT slices were obtained using different **image reconstructing parameters**. The most suitable ones were chosen by analysing the slices with an **algorithm** (Fig. 3) developed in **Matlab** (MathWorks Inc., Natick, MA, USA) that measured the strut radial thickness in each slice. The obtained mean value was compared with the stent manufacturer stated value ($65\mu\text{m}$). Set of slices obtained with three different reconstructing parameters were used to perform three 3D reconstructions of the same stent geometry using **Mimics** (Materialise, Belgium).

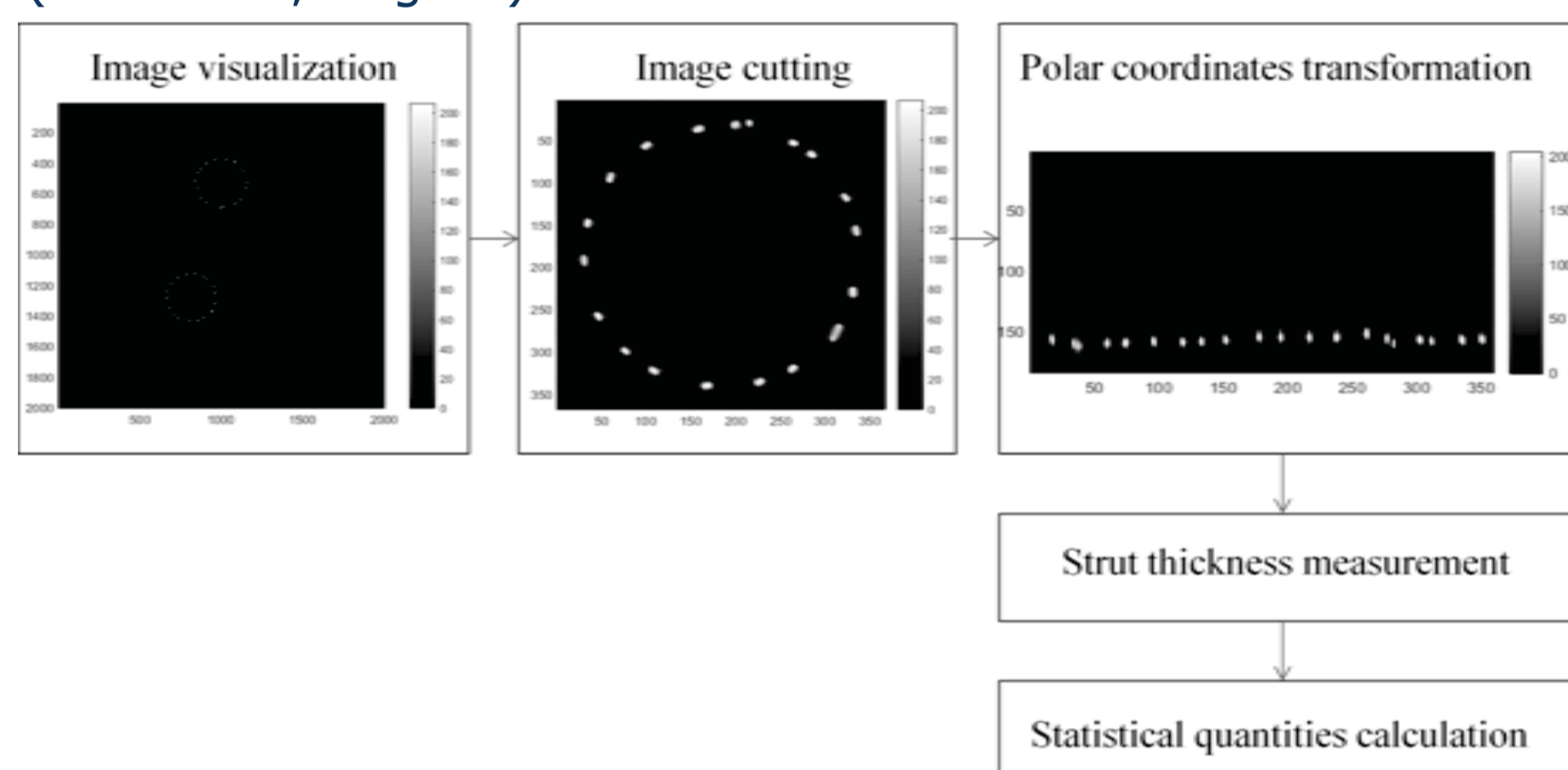


Fig. 3 Algorithm developed in Matlab to evaluate slice reconstructing parameters.

Results

Structural simulation: lumen prolapse verification

The best strut dimensions reached were 68.3 and $74.7\ \mu\text{m}$ whilst the worst one was $95.8\ \mu\text{m}$ (manufacturer value = $65\mu\text{m}$). The three different stent reconstructions starting from these slices were used in the structural analysis and in each case, at the end of the simulation, the PDMS internal mesh was smoothly deformed, thus resulting suitable for fluid domain mesh generation (Fig. 6). The measured lumen prolapse in the *in silico* model was of the same order of magnitude of the *in vitro* prolapse (Fig. 7).

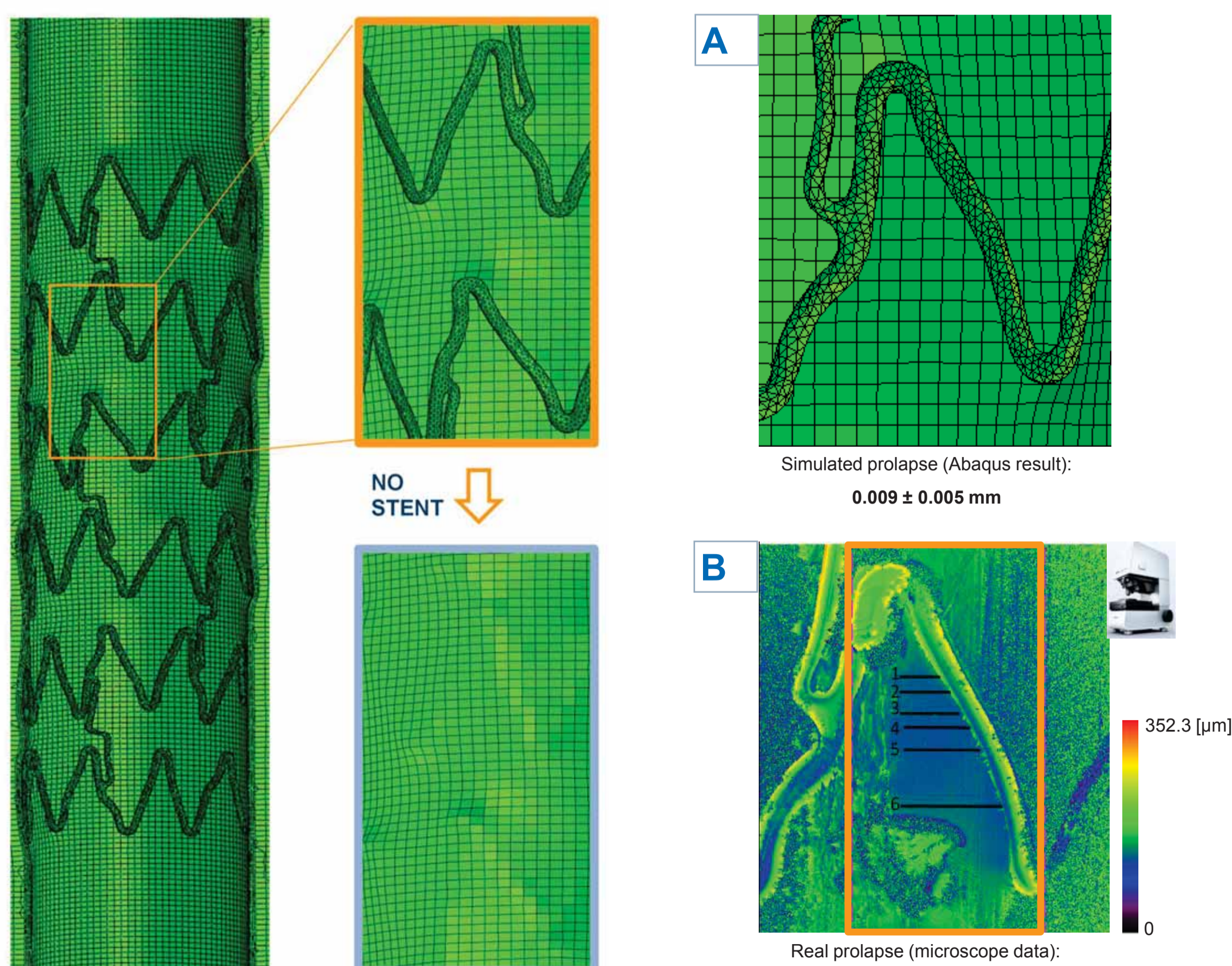


Fig. 6 Deformed PDMS configuration at the end of the structural simulation.

Fig. 7 Comparison between (A) *in silico* and (B) *in vitro* prolapses.

Conclusions

CFD analyses demonstrated that image processing has a noticeable influence on local fluid dynamic quantities. Hence, an analysis to evaluate the sensitivity of image processing parameters should be conducted every time a stented geometry is reproduced starting from μ CT images. Furthermore, our *in silico* model allows the study of a large range of flow conditions, e.g. different flow rate values and different fluid models. For every modeled flow condition, fluid dynamics parameters that are hard to measure experimentally but that are fundamental to understand cellular behavior and ISR can be calculated.

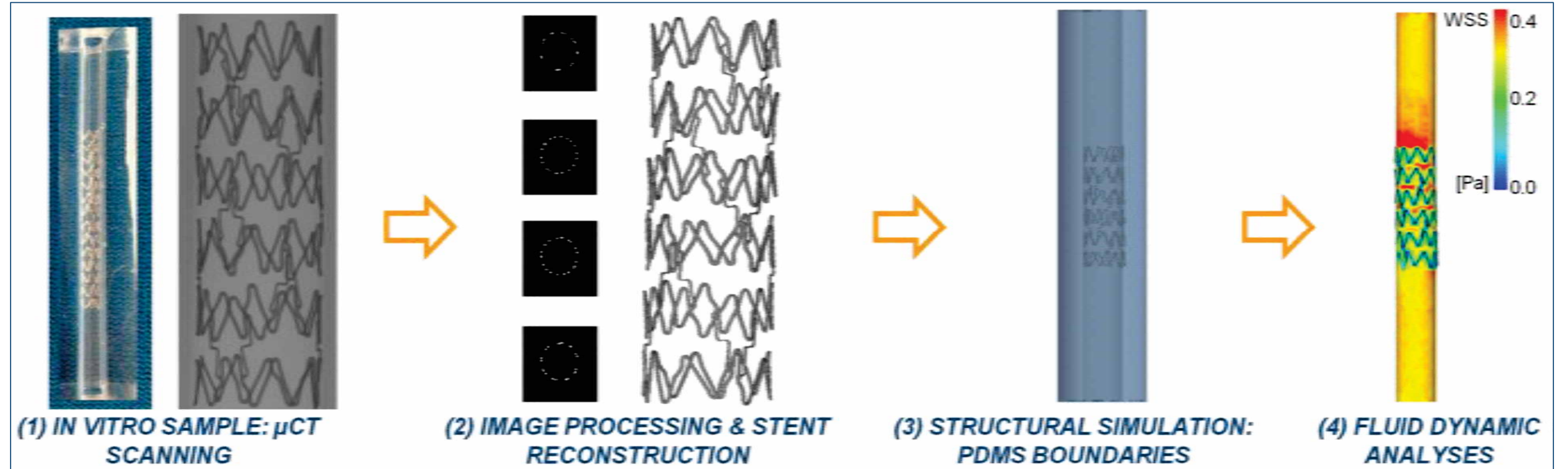


Fig. 2 General workflow to reconstruct the *in silico* model starting from μ CT images. The PDMS wall could not be directly reconstructed from μ CT acquisitions because of artefacts and a structural simulation was required.

Structural simulation to reconstruct PDMS walls

The PDMS structure was modeled through a quasi-static finite element analysis implemented in **ABAQUS/Explicit** (Dassault Systems Simulia Corp., RI, USA). The simulation considered the **deployed stent geometry** in its final configuration as a **scaffolding structure** on which a simulated model of the channel structure retracted after being initially expanded (Fig. 4). The obtained position of the deformed channel with respect to the stent was compared with real lumen prolapse data measured with a **scanning laser microscope** to verify the obtained PDMS configuration.

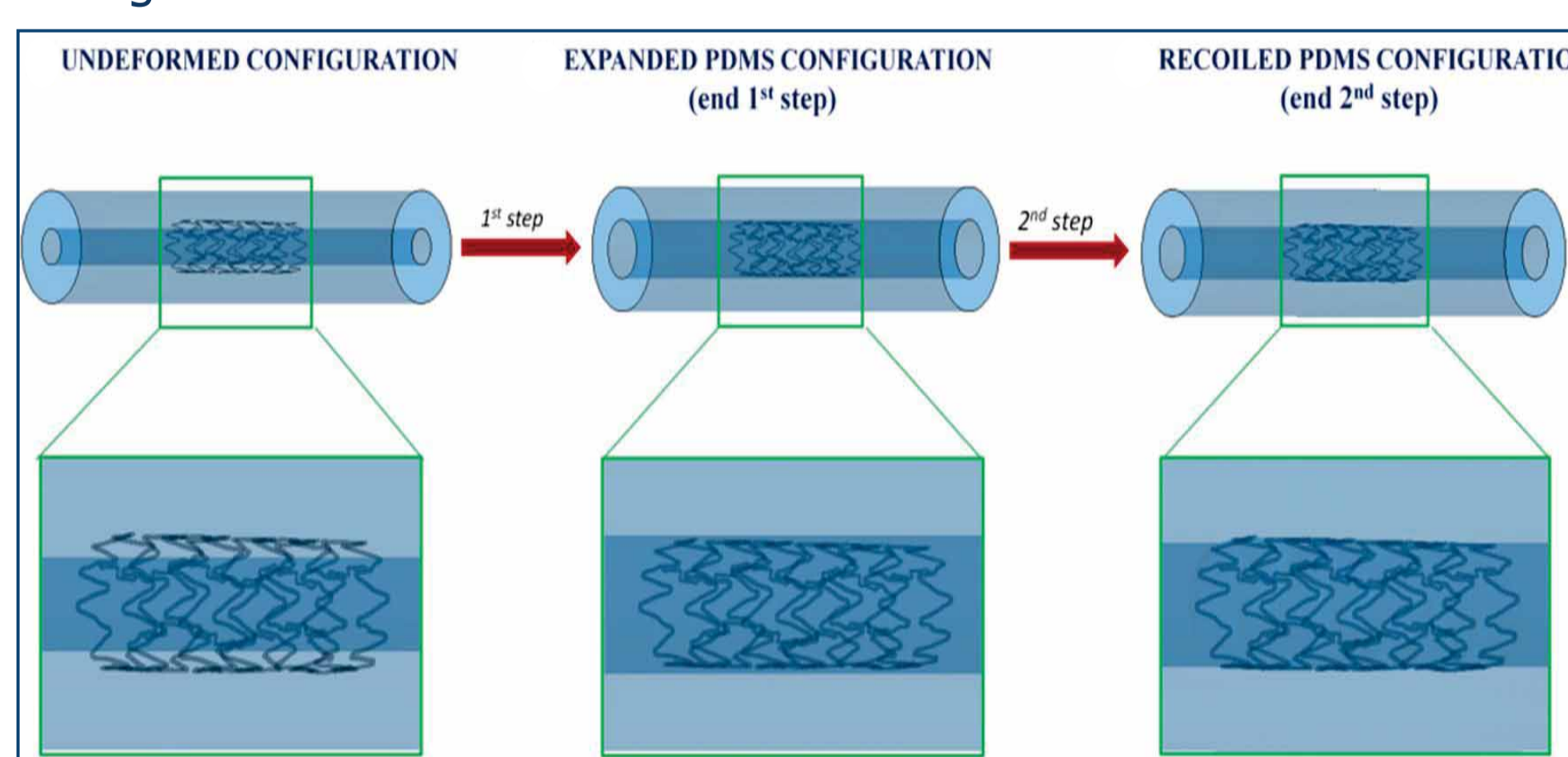


Fig. 4 A) Unexpanded PDMS and stent positions. B) PDMS expansion below the stent diameter. C) Final deformed configuration of the PDMS.

Fluid dynamic simulation

The obtained geometry was imported into **ANSYS ICEM CFD** (Ansys Inc. - Canonsburg, PA, USA) where the fluid domain was discretized with a tetrahedral mesh (Fig. 5). **Steady-state simulations** were performed using **ANSYS Fluent** (Ansys Inc.) imposing a paraboloid-shaped velocity profile at the inlet and a reference pressure of $0\ \text{Pa}$ at the outlet. Analyses to **reproduce current experiments in Sheffield** (fluid = water) and **assess stent image processing sensitivity** (fluid = water or blood modelled as Newtonian fluids, same Reynolds number imposed) were conducted.

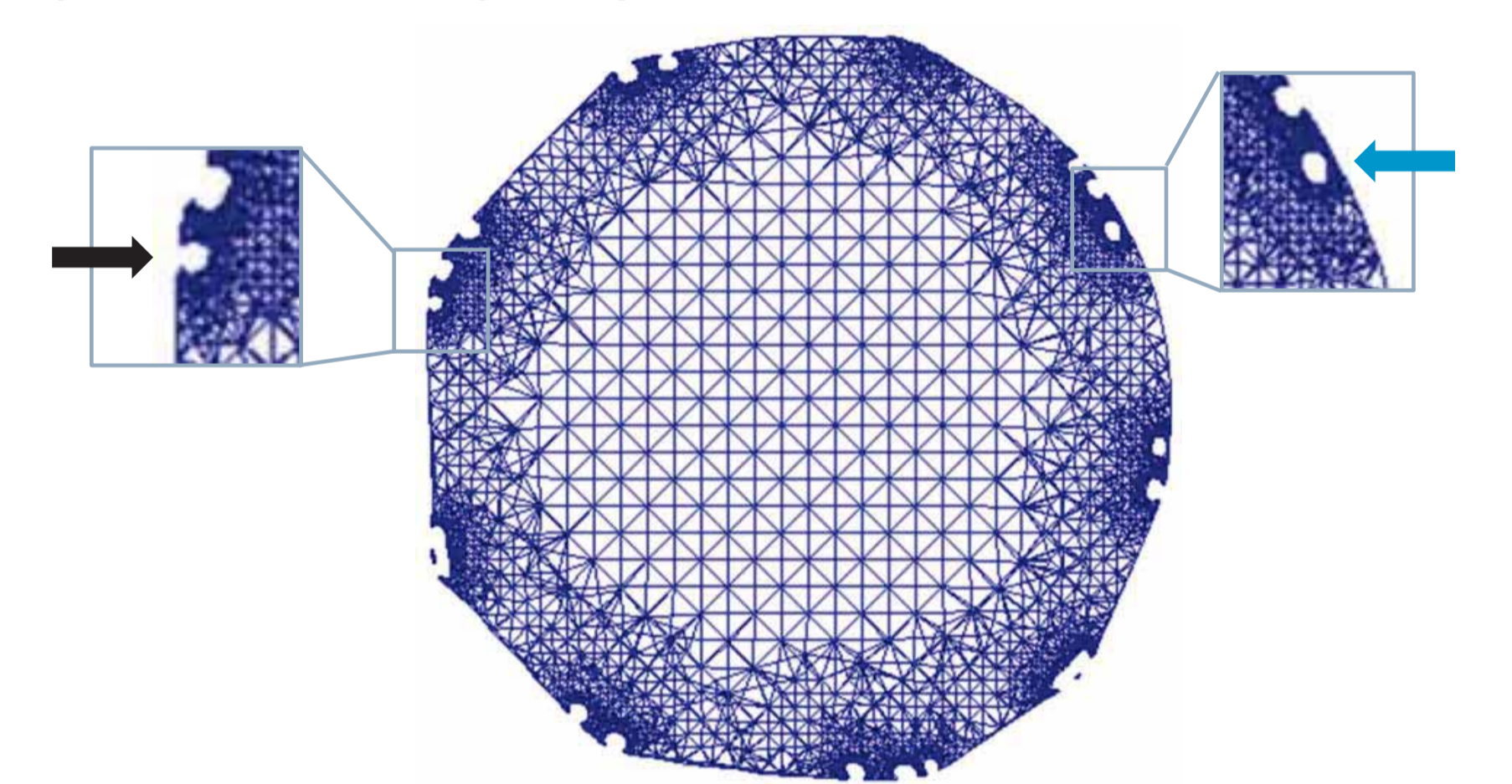


Fig. 5 Section of the CFD mesh. The asymmetric geometry is well defined and both malapposed (blue arrow) and well-apposed struts (black arrow) are described.

Fluid dynamic simulation: sensitivity of image processing parameters

Fig. 8 shows the WSS along a reference line, normalized to the maximum WSS analytical value calculated at the inlet, either for water or blood whilst Fig. 9 shows WSS contour plots for water and blood at the same *Re*. In both cases, the difference in WSS obtained using different image processing parameters was noticeable. The highest difference in WSS magnitude was seen at the inlet of the stented region and at the first stent ring (region where the flow perturbation induced by the variation in diameter was confined). In detail, the areas with a WSS lower than the thresholding restenosis risk value (i.e. $0.4\ \text{Pa}$) showed changes of 1.5% and 2% with respect to the case with strut thickness of $68.3\mu\text{m}$ because of changes in strut dimension. The differences in area-weighted averaged WSS and in the maximum WSS were up to 17% with respect to the case with strut thickness of $68.3\mu\text{m}$.

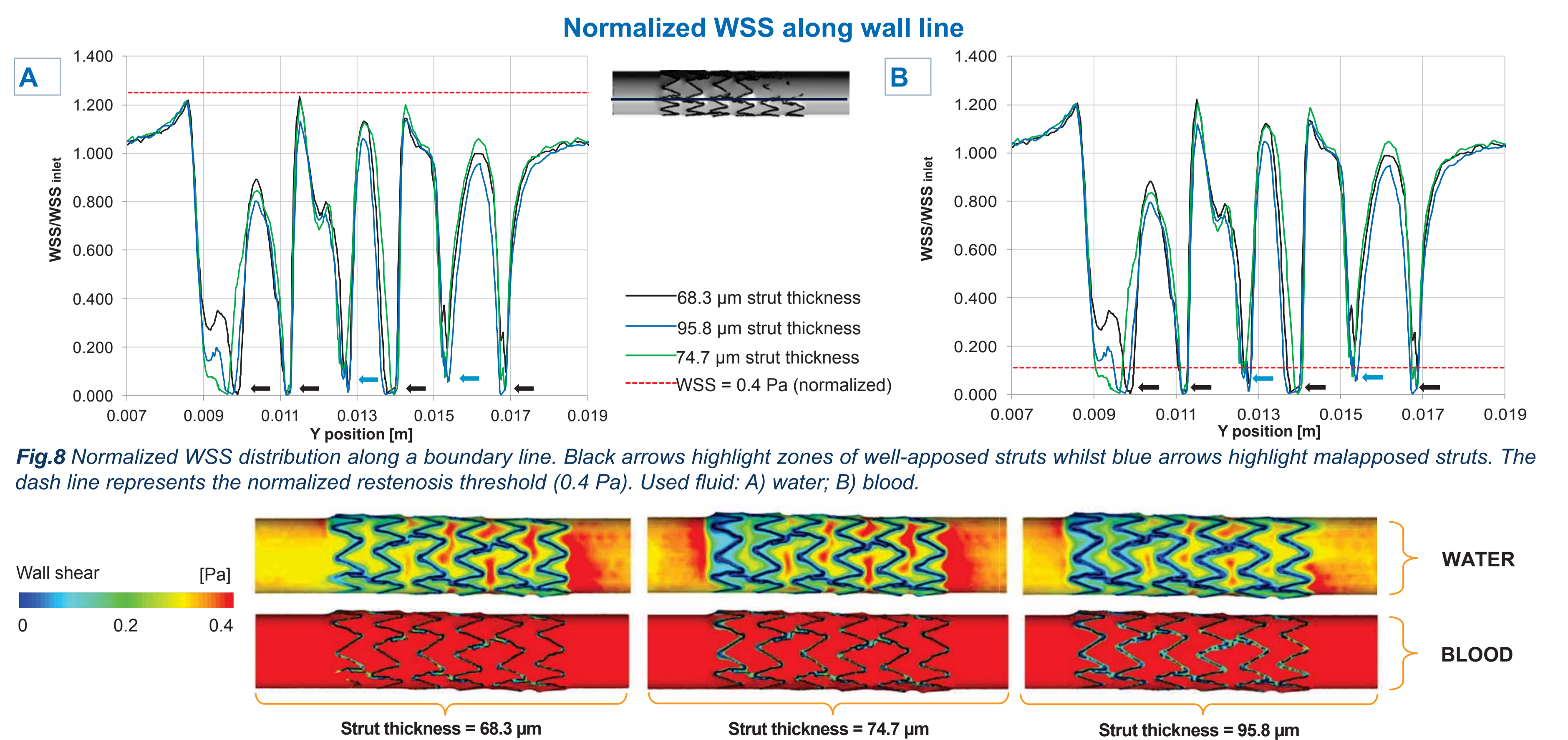


Fig. 9 Qualitative comparison between WSS contours maps obtained with different geometries using water and blood as fluid at the same *Re*.