1 **BM-D-16-00127 revision 1**

2 **Title: A validated methodology for patient specific computational modeling of self-expandable**
3 **transcatheter aortic valve implantation**

4 **Authors:**

5 Bart Bosmans^{1,2,3}, Nele Famaey¹, Eva Verhoelst², Johan Bosmans³, Jos Vander Sloten¹

6 **Affiliations:**

7 ¹ KULeuven, Faculty of Engineering Science, Celestijnenlaan 300C, 3001 Leuven, Belgium. Department
8 of Mechanical Engineering, Biomechanics Section

9 ² Materialise N.V., Technologielaan 15, 3001 Leuven, Belgium

10 ³ University of Antwerp, Faculty of Medicine and Health Sciences, Universiteitsplein 1, 2610 Antwerp,
11 Belgium. Department of Translational Pathophysiological Research, Cardiovascular diseases

12 Word count: 3499

13 **Corresponding author:**

14 Bart Bosmans

15 KULeuven – Departement of Mechanical Engineering, Biomechanics Section

16 Technologielaan 15,

17 3001, Leuven, Belgium.

18 Tel: +32 16 396 728

19 Fax: +32 16 396 606

20 Bart.Bosmans@kuleuven.be

21 **Abstract**

22 Leakage of blood alongside the implant is a relatively frequent and life-limiting complication after
23 transcatheter aortic valve implantation. The aim of this study is to develop and validate a workflow
24 to simulate the implantation prior to the intervention. Based on the simulation outcome, the amount
25 of leakage is estimated in order to evaluate the risk of a severe complication. A finite element model
26 of the stent implantation in 10 patients was created based on a pre-operative computed tomography
27 scan. All 10 patients also received a follow-up computed tomography scan, after the implantation.
28 This scan was used to extract the deformed geometry of the stent and the position of the
29 calcifications for validation of the simulation results. The maximal average perimeter difference
30 between the simulated stent and the post-operative stent is 2.9 ± 2.1 mm, and occurs at the bottom
31 of the device. The sensitivity of the simulation to the soft tissue material parameters and aortic root
32 wall thickness was tested. The maximal diameter deviation of 6% occurred when the thickness of the
33 aortic root was doubled. The result of the leakage analysis based on the distance between the
34 simulated stent and the surrounding aortic root corresponded well when no regurgitation was
35 observed. The developed tools have the potential to reduce the occurrence and severity of leakage
36 by providing the clinician with additional information prior to the intervention. The simulated
37 geometry and estimated leakage can help decide on the best implant type, size and position before
38 treatment.

39 **Introduction**

40 Aortic valve stenosis is the most commonly acquired valvular heart disease in the elderly. Despite
41 advances in cardiac surgery and low mortality rates after conventional surgical aortic valve
42 replacement, up to one third of patients with symptomatic aortic valve stenosis are not considered
43 for valve replacement, often due to age, frailty or co-morbidities [Bose et al., 2007; Thourani et al.,
44 2011]. Transcatheter aortic valve implantation (TAVI) has been proven to be a reasonable alternative
45 for the treatment of aortic valve stenosis in elderly (very) high-risk patients [Kodali et al., 2012].
46 However, aortic regurgitation (AR) after TAVI remains a frequent and life-limiting complication [Leon
47 et al., 2010; Linke et al., 2014]. Leakage alongside the implant, paravalvular AR, is hypothesized to
48 originate from the interaction between the implant and the calcified native aortic root.

49 Due to the complex physical interactions of the different materials and geometries, computational
50 modeling is the best approach to evaluate and predict the deployment process during a TAVI
51 intervention. With appropriate validation, these models could be used to aid the clinical decision and
52 planning process of the TAVI intervention. In recent literature, there are some studies which
53 investigate and report finite element simulation of this intervention [Auricchio et al., 2014; Bailey et
54 al., 2015; Capelli et al., 2012; de Jaegere et al., 2016; Morganti et al., 2014; Russ et al., 2013; Schultz
55 et al., 2016; Wang et al., 2012]. Only, Russ *et al.* (2013) and Schultz *et al.* (2016) compare their result
56 with a post-operative scan to verify the accuracy of their simulation result. However, the extensive
57 study of Schultz *et al.* (2016) does not contain the necessary details to recreate the simulations, try
58 them on other cases and advance the state of the art. Therefore, the goal of this paper is to develop
59 a simulation workflow based on pre-operative clinically available data, which allows to predict the
60 post-operative geometry and estimate the paravalvular AR, and validate it with post-operative scans
61 and aortic regurgitation evaluation of treated patients.

62 **Material and methods**

10 patients received a contrast enhanced, ECG-triggered, end diastolic computed tomography (CT) scan both before and at a follow-up after the TAVI procedure. The scans were performed on a 64-slice GE lightspeed (General Electric Company, Easton Turnpike, Fairfield, CT, USA) with a spatial resolution of 0.6 mm. All patients received an intravenous injection of 80ml of contrast agent at a flow rate of 4 ml/s, followed by 30 ml at 2.5 ml/s.

The average age of the patients was 74.2 years, three patients were female. All received a 29 mm CoreValve implant (Medtronic Inc., Minneapolis, MN, USA), prior to implantation the aortic valve was pre-dilated using a 20 mm or 22 mm balloon. The median volume of calcification in this patient group was 57 mm³ with a minimum of 17 mm³ and a maximum of 482 mm³. AR was graded at two separate points in time: (1) immediately after the implantation on the procedural angiography, as described by Seller *et al.* [Sellers et al., 1964], and (2) at hospital discharge or within 7 days after the implantation procedure using transthoracic echocardiography as described by Collas *et al.* (2015).

Image analysis

To extract the patient specific geometries, segmentation of the aortic root was performed on the pre-operative scans using Mimics 16.0 (Materialise N.V., Leuven, Belgium). The left ventricle and aorta were extracted from the CT images using a threshold on the contrast agent, as depicted in panel A of figure 1. The left ventricle and aorta were separated from connected structures and each other using a graph cut algorithm [Boykov and Kolmogorov, 2004]. 3-dimensional (3D) triangulated parts were created using a marching cubes triangulation (figure 1B). Smoothing was performed to remove noise and small substructures. Three leaflets were created starting from the left ventricle by smoothing and disconnecting the valve surface. Finally, the calcifications were extracted using a threshold above the intensity of the contrast agent and a region grow in the aortic root, followed by a marching cubes triangulation.

Based on the 3D triangulated surfaces, a finite element mesh was generated using 3-matic 8.0 (Materialise N.V., Leuven, Belgium). Triangular shell elements were used to model the aortic root and

the leaflets (figure 1C). Four node linear tetrahedral elements were used to model the calcifications. The calcifications were divided into separate volumes along the leaflet boundaries, as an approximation of the damage resulting from the balloon pre-dilation.

Constitutive material model

An isotropic neo-Hookean material model, in which the stiffness of the material increases at higher strain values was used to model the soft tissues (the aorta, the leaflets, the aortic annulus, the myocardium and the septum between the left ventricle and left atrium). The strain energy density function (ψ), relating stress (σ) to strain (ϵ) through $\sigma = \frac{\partial \psi}{\partial \epsilon}$, can be written as:

$$\psi = \frac{\mu}{2}(\bar{I}_1 - 3) + \frac{\kappa}{2}(J - 1)^2$$

where μ and κ are the shear modulus and bulk modulus associated with the deviatoric part and the volumetric part respectively of the strain energy density. $\bar{I}_1$ is the first invariant of the deviatoric part of the right Cauchy-Green tensor $\bar{C} = \bar{F}^T \bar{F}$: $\bar{I}_1 = J^{-2/3} I_1$, and J is the determinant of the deformation gradient or Jacobian $J = \det F$. The materials were considered to be nearly incompressible, κ was set to 10 MPa as a compromise between incompressibility and simulation stability [Famaey et al., 2012]. The initial value of μ was chosen based on previous experience in modeling cardiovascular tissue, and subsequently optimized to reach a good correspondence between the final simulation result and the stent extracted from the post-operative CT. Table 1 shows the values of the material parameters and the element thickness of the different soft tissues [Auricchio et al., 2014; Martin et al., 2011], the density was set to 1000 kg/m³. The calcifications were modelled using a linear-elastic material with Young's modulus, $E = 5$ MPa, Possion's coefficient, $\nu = 0.475$ and density, $\rho = 1200$ kg/m³, comparable values were found in literature [Holzapfel et al., 2004; Morganti et al., 2014].

Stent model

110 A μ CT scan of the stent in its unloaded state was made. The images were acquired on a Tomohawk
111 system (AEA Technology, Carlsbad, CA, USA) with a HOMX 161 x-ray source (Royal Philips,
112 Amsterdam, The Netherlands). The scans were conducted with a voltage of 80 KV and a current of
113 0.5 mA. The images had a spatial resolution of 59 μ m. The centerlines of the metal stent struts were
114 computed using Mimics 16.0 (Materialise N.V., Leuven, Belgium). A finite element model, consisting
115 of quadratic beam elements was created, based on the centerline curves. The beam elements had a
116 constant rectangular cross section (0.15 mm x 0.4 mm), measured using a Venier caliper and
117 confirmed on the μ CT. The stent was modelled with a super-elastic Nitinol material model, available
118 in Abaqus [Auricchio and Taylor, 1997; Auricchio et al., 1997]. The parameters for this model are
119 presented in table 2 [Simulia, 2010]. The density of Nitinol was set to 6450 kg/m³.

120 ***Boundary conditions and simulation set-up***

121 The stent's axial position was based on the depth measured with respect to each of the three leaflets
122 on the post-operative CT scan (figure 1E). This allows for a fair comparison between the simulated
123 geometry and the post-operative geometry of the stent.

124 The displacement and rotation of the top and bottom nodes of the aortic root were set to zero. In a
125 separate simulation, the stent was pulled through a funnel onto a cylinder representing the catheter
126 and under another cylinder representing the cover sheet to reduce the stent diameter to 10 mm.
127 This procedure resulted in internal stresses in the stent struts which will push open the stent during
128 its placement. In the first step, a small pressure was applied to the tip of the leaflets to open the
129 valve, while holding the stent in place by preventing displacement of its nodes. In the second step,
130 general, frictionless contact was applied and the stent was allowed to expand gradually by controlling
131 the axial displacement of the top nodes. In this step, contact was made between the stent and the
132 calcified leaflets. In the final step, all boundary conditions on the stent were removed except the
133 axial displacement of the bottom nodes. This allowed for the stent and the aortic root to find an
134 equilibrium configuration.

The simulations for all ten cases were performed using Abaqus 6.13 explicit (SIMULIA, Providence, RI, USA). A mass-scaling of 5 was applied to increase the step time which was automatically optimized by the solver. A quasi-static solution was approached by setting the total step time to 0.55 seconds. Thereby, the resulting kinetic energy in the model was less than 5% of the internal energy.

Sensitivity to material model and wall thickness

Only the overall geometry of the aortic root could be derived from the CT scans. Therefore, there were no patient-specific values for the material parameters and the wall thickness. In order to test the sensitivity of the model to those parameters, the shear modulus of all soft tissue elements and the thickness of all shell elements except the leaflets were doubled and halved separately. In addition, all patients were simulated using an anisotropic linear-elastic material for the soft tissue elements. Table 3 contains the material parameters of this model. The circumferential stiffness was chosen to approximate the hyperelastic material properties. The longitudinal stiffness is half the circumferential stiffness.

Validation using a post-operative CT scan

The deformed stent geometry was extracted from the post-operative CT using Mimics 16.0 (Materialise N.V., Leuven, Belgium). The metal stent was segmented using a high threshold, 1000 Hounsfield units, and region grow of the connected voxels (figure 2L). To extract the calcifications from the post-op CT, a threshold of 600 Hounsfield units was used in combination with a region grow algorithm and marching cubes. The first surface only contains the stent, it was used to measure the diameter of the device at 4 cross sections, as depicted in figure 2R. The second surface contains the stent and the surrounding calcifications. Figure 3 depicts an overlay of this surface with the simulation results for comparison. At 4 axial cross sections (figure 2R), the center of the stent struts was used to fit a circle and calculate the perimeter of a curve connecting them, to quantify the stent dimensions.

Aortic regurgitation estimation

Considering the importance of AR, a method was developed to predict the amount of AR based on the simulation result. A shrink-wrap was performed on the simulated stent, to model the sealing skirt of the CoreValve device. The surface was triangulated with a minimum edge length of 0.25 mm, a maximum edge length of 0.5 mm and a minimum height-base ratio of 0.4 using 3-matic 10.0 (Materialise N.V., Belgium). From the nodes of this triangulated surface, the distance to the closest point of the aortic root was calculated (figure 4B). Then, a max-flow algorithm [Boykov and Kolmogorov, 2004] was used to calculate the flow paths from the top edge to the bottom edge of the sealing skirt. The max-flow algorithm takes a 1 dimensional connected graph, representing the flow network, as input. The edges of the triangulated surface, forming the sealing skirt, were used to construct this graph. Each edge forming a connection in the graph has a value representing its flow capacity. This was calculated as the average distance of the edge to the aortic root. Edges with an average distance smaller than 0.5 mm are considered to be in contact with the aortic root. Therefore, their capacity is set to zero.

Results

The simulations were performed on a computation node containing two 10-core Xeon E5-2680v2 CPUs (2.8 GHz) with 64 MB RAM, each simulation took between 18 and 26 hours. Table 4 contains the diameter measurements of the post-operative stent geometry derived from the post-operative CT scans. Comparing the diameter with the reference diameter of the unconstrained device, shows that the stents have on average the potential to expand another 15% at the bottom, 10% at the narrowest section and 30% at the top in order to reach the reference stent configuration. In addition, the root mean square (RMS) difference between 3 consecutive measurements on the stents are also presented in table 4. The metal stent has a high x-ray absorption compared to the surrounding tissue. Therefore, the stent model derived from the post-operative CT appeared thicker than it is in reality. Depending on which points of the struts were used to characterize the stent, the results varied. The RMS difference between the measurements gives an idea of the measurement error.

Excluding local deviations, at the bottom of the device, a good qualitative correspondence between the simulation results and the post-operative stent can be observed for all patients (Figure 3).

The mean ($\pm$ standard deviation) diameter of the simulated stent and the perimeter difference with the post-op stent are shown in table 4. There was a small underestimation of the perimeter at section A and a small overestimation at section C. The perimeter at section B and D was very close to the post-op perimeter.

Sensitivity analysis

Table 5 contains the average dimensions of the stent for all sensitivity experiments and the deviation from the first simulation. In addition, the perimeter difference with the post-op stent is shown. The largest difference was observed in the experiment where the thickness of the aortic root wall was doubled. The diameter decreased by 6% in section A and section B.

Aortic regurgitation estimation

The results of the leakage estimation are presented in table 6, together with both clinically observed AR grades. Patients 4, 8 and 10 which consistently had no AR in both clinical observations, also had very low max-flow values. Patient 7 had the highest max-flow value and also had the higher AR grade immediately after implantation. However, at the second evaluation using echocardiography, patient 9 had the highest AR grade, while the max-flow analysis of that patient resulted in the lowest value excluding the patients without AR.

Discussion

In this paper, a finite element based method was developed to simulate a transcatheter aortic valve implantation in a patient-specific geometry based on pre-operative CT scans. This method was validated using post-operative CT scans of the implanted device and the surrounding anatomy. The sensitivity to the material parameters and the aortic root thickness, which cannot be determined from the pre-operative CT scan, was tested. In addition, the leakage alongside the implant was

209 estimated based on the simulation result and compared with two clinical evaluations. The described
210 method could form the basis for a pre-interventional planning tool which would provide the clinician
211 with additional information about the best size, type and position of the device prior to the
212 implantation. This could help reduce the incidence of life-limiting post-interventional aortic
213 regurgitation.

214 In recent literature, several other patient specific finite element modeling strategies for TAVI have
215 been described. Schultz *et al.* (2016) performed an extensive study, simulating the implantation of a
216 CoreValve device in 33 patients and an Edwards Sapien XT in 6 patients and comparing them with
217 post-op CT results. They found a similar accuracy for the simulated perimeter and strong correlations
218 between the post-op result and the simulated stent. However, the essential details about the
219 simulation process and material properties were not published, which makes a comparison of the
220 methods impossible. In addition, their investigation did not contain a sensitivity analysis. de Jaegere
221 *et al.* (2016) started from these simulated implantations to model the blood flow during diastole with
222 computational fluid dynamics to assess aortic regurgitation. They found good correlation between
223 the estimated flow in 60 patients and the observed AR grade. The AR estimation method described in
224 this paper does not require a computational fluid simulation which makes it faster and easier to use.
225 However, further research and a validation including more patients is required to determine the
226 accuracy of the method.

227 When comparing the post-operative stents to the full size expanded device, it still has the potential
228 to expand at least 15%, this is probably a result of the oversizing of the device which is routinely
229 performed to reduce the occurrence and severity of paravalvular aortic regurgitation [Holmes et al.,
230 2012; Piazza et al., 2008].

231 The maximal deviation observed in the sensitivity analysis was -6%, occurring in the two bottom
232 sections after doubling the shell thickness. A shell of half the thickness only resulted in an additional
233 expansion of 3%, this difference shows the nonlinear behavior of the system. All other deviations

were around or below 4%, especially the top section showed little sensitivity to any of the parameters, considering its potential to expand further. Therefore, the shape of the aortic root, leaflets and calcifications appears to be the main influence of the shape of the device. This is beneficial for the usability of the method in clinical practice, since the shape of the aortic root and calcifications can be determined patient-specifically from the pre-operative CT scan. Further investigation into the contribution of the calcifications and leaflets is needed to support this observation.

To simulate the behavior of arterial tissue more accurately, an anisotropic hyperelastic representation, such as the Holzapfel-Gasser-Ogden model could have been used [Gasser et al., 2006; Holzapfel et al., 2000]. Wang *et al.* (2015, 2012) used this type of material model in their TAVI models. However, this material model required an estimation of the collagen fiber orientation and the pre-stress in the aortic root and leaflets. These parameters are hard to estimate with non-invasive measurements for each patient [Smoljkic et al., 2015]. In this study, the impact of anisotropy was tested using an anisotropic linear-elastic material model with a circumferential stiffness twice as large as the longitudinal stiffness. The sensitivity analysis showed the diameter of the simulated stent did not differ more than 4.2% on average.

A potential limitation of the model is the absence of a damage mechanism. Prior to the implantation of the device, a balloon expansion of the calcified valve was performed to facilitate the expansion of the actual implant. This was simulated in the model by splitting calcifications which cross leaflet boundaries. In addition, the myocardium was modelled as a passive structure, while in reality it is a muscle with an active component to its compliance.

In all simulations, the diameter at the narrowest cross section of the stent was larger than the post-operative result. The cause of this systematic error is currently unknown to us. Therefore, further investigation into the stent model and material parameters is needed.

The simulations required a considerable amount of time on a powerful computation node. The small elements in the stent and calcifications resulted in a small time step, while a sufficiently long simulation time was needed for the soft tissue to reach a quasi-static solution. Further research is needed to reduce the computational cost in order to make the technology clinically applicable. One possibility could be the use of GPU-based FE implementations, as proposed e.g. in Strbac et al. (2015).

Comparing the output of the regurgitation estimation, the results were mixed. When both the grades immediately after implantation and at hospital discharge were zero, the results of the analysis corresponded well. However, the patient with problematic AR (grade ≥ 2) is different in the two evaluations. The patient with the highest regurgitation estimate also had the highest grade in the angiographic evaluation immediately after implantation. However, the echocardiographic evaluation at hospital discharge has been proven to be a better predictor of increased mortality [Collas et al., 2015]. The difference between both AR evaluations could be due to the difference in time, the imaging technique or the grading system. True AR volume quantification would be best to evaluate and validate the regurgitation estimation. However, such a measurement was not available for the patients in this study.

In summary, the results of the simulation showed good correspondence with the post-operative outcome of the transcatheter aortic valve implantation, both visually and quantitatively. We believe that the main elements to explain a good correspondence are the accurate geometrical model of the aortic root and the limited sensitivity of the simulation to the material parameters which, at this point, cannot be determined patient-specifically from pre-operative available data. However, a systematic overestimation of the perimeter at the narrowest section of the stent and an underestimation at the bottom could still be observed, both in the order of 3 mm. In addition, the model was not very sensitivity to the non-patient-specific parameters, wall thickness and material properties. The estimation of leakage based on the distance between the sealing skirt of the

simulated device and the surrounding aortic root, showed promise, especially in the detection of very good implantations. Further research in both the simulation and regurgitation estimation is needed, including more cases, to confirm these results and improve the accuracy. To conclude, with access to sufficient computational resources, these tools have the potential to help reduce the occurrence of aortic regurgitation in the patient population by providing information on optimal position, type and size of the device for a patient prior to the operation, by virtually testing these different options and evaluating the risk of leakage.

Acknowledgements

This work was supported in part by a PhD grant from the *agency for innovation through science and technology (IWT)* of the Flemish government and in part by the Research Foundation Flanders (FWO).

Conflicts of interest statement

Prof. Dr. Johan Bosmans is part-time clinical proctor for Medtronic. Prof. Dr. ir. Jos Vander Sloten is a member of the Board of Directors of Materialise NV and a shareholder. The remaining authors have no conflicts of interest to declare.

297 **References**

- 298 Auricchio, F., Conti, M., Morganti, S., Reali, a, 2014. Simulation of transcatheter aortic valve
299 implantation: a patient-specific finite element approach. *Comput. Methods Biomech. Biomed.*
300 *Engin.* 17, 1347–57.
- 301 Auricchio, F., Taylor, R.L., 1997. Shape-memory alloys : modelling and numerical simulations the
302 finite-strain superelastic behavior. *Comput. Methods Appl. Mech. Eng.* 7825, 175–194.
- 303 Auricchio, F., Taylor, R.L., Lubliner, J., 1997. Shape-memory alloys : macromodelling and numerical
304 simulations of the superelastic behavior. *Comput. Methods Appl. Mech. Eng.* 7825.
- 305 Bailey, J., Curzen, N., Bressloff, N.W., 2015. Assessing the impact of including leaflets in the
306 simulation of TAVI deployment into a patient-specific aortic root. *Comput. Methods Biomech.*
307 *Biomed. Engin.* 5842, 1–12.
- 308 Bose, A.K., Aitchison, J.D., Dark, J.H., 2007. Aortic valve replacement in octogenarians. *J.*
309 *Cardiothorac. Surg.* 2, 33–5.
- 310 Boykov, Y., Kolmogorov, V., 2004. An experimental comparison of min-cut/max-flow algorithms for
311 energy minimization in vision. *IEEE Trans. Pattern Anal. Mach. Intell.* 26, 1124–37.
- 312 Capelli, C., Bosi, G.M., Cerri, E., Nordmeyer, J., Odenwald, T., Bonhoeffer, P., Migliavacca, F., Taylor,
313 A.M., Schievano, S., 2012. Patient-specific simulations of transcatheter aortic valve stent
314 implantation. *Med. Biol. Eng. Comput.* 50, 183–92.
- 315 Collas, V.M., Paelinck, B.P., Rodrigus, I.E., Vrints, C.J., Bosmans, J.M., 2015. Aortic regurgitation after
316 transcatheter aortic valve implantation (TAVI) — Angiographic, echocardiographic and
317 hemodynamic assessment in relation to one year outcome. *Int. J. Cardiol.* 194, 13–20.
- 318 de Jaegere, P., De Santis, G., Rodriguez-olivares, R., Bosmans, J., Bruining, N., Dezutter, T., Rahhab, Z.,
319 El Faquir, N., Collas, V., Bosmans, B., Verhegghe, B., Ren, C., Geleinese, M., Schultz, C., van

320 Miegheem, N., De Beule, M., Mortier, P., 2016. Patient-specific computer modeling to predict
321 aortic regurgitation after Transcatheter Aortic Valve Replacement. *JACC. Cardiovasc. Interv.* 9,
322 508–512.

323 Famaey, N., Sommer, G., Vander Sloten, J., Holzapfel, G. a, 2012. Arterial clamping: finite element
324 simulation and in vivo validation. *J. Mech. Behav. Biomed. Mater.* 12, 107–18.

325 Gasser, T.C., Ogden, R.W., Holzapfel, G. a., 2006. Hyperelastic modelling of arterial layers with
326 distributed collagen fibre orientations. *J. R. Soc. Interface* 3, 15–35.

327 Holmes, D.R., Mack, M.J., Kaul, S., Agnihotri, A., Alexander, K.P., Bailey, S.R., Calhoon, J.H., Carabello,
328 B.A., Desai, M.Y., Edwards, F.H., Francis, G.S., Gardner, T.J., Kappetein, A.P., Linderbaum, J.A.,
329 Mukherjee, C., Mukherjee, D., Otto, C.M., Ruiz, C.E., Sacco, R.L., Smith, D., Thomas, J.D., 2012.
330 2012 ACCF/AATS/SCAI/STS Expert Consensus Document on Transcatheter Aortic Valve
331 Replacement. *J. Am. Coll. Cardiol.* 59, 1200–1254.

332 Holzapfel, G. a., Sommer, G., Regitnig, P., 2004. Anisotropic Mechanical Properties of Tissue
333 Components in Human Atherosclerotic Plaques. *J. Biomech. Eng.* 126, 657.

334 Holzapfel, G.A., Gasser, T.C., Ogden, R.W., 2000. A new constitutive framework for arterial wall
335 mechanics and a comparative study of material models. *J. Elast.* 61, 1–48.

336 Kodali, S.K., Williams, M.R., Smith, C.R., Svensson, L.G., Webb, J.G., Makkar, R.R., Fontana, G.P.,
337 Dewey, T.M., Thourani, V.H., Pichard, A.D., Fischbein, M., Szeto, W.Y., Lim, S., Greason, K.L.,
338 Teirstein, P.S., Malaisrie, S.C., Douglas, P.S., Hahn, R.T., Whisenant, B., Zajarias, A., Wang, D.,
339 Akin, J.J., Anderson, W.N., Leon, M.B., 2012. Two-year outcomes after transcatheter or surgical
340 aortic-valve replacement. *N. Engl. J. Med.* 366, 1686–95.

341 Leon, M.B., Smith, C.R., Mack, M., Mille, C.D., Moses, J.W., Svensson, L.G., Tuzcu, E.M., Webb, J.G.,
342 Fontana, G.P., Makkar, R.R., Brown, D.L., Block, P.C., Guyton, R.A., Pichard, A.D., Bavaria, J.E.,
343 Herrmann, H.C., Douglas, P.S., Petersen, J.L., Akin, J.J., Anderson, W.N., Wang, D., Pocock, S.,

344 2010. Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot
 345 Undergo Surgery. *N. Engl. J. Med.* 363, 1597–1607.

346 Linke, A., Wenaweser, P., Gerckens, U., Tamburino, C., Bosmans, J., Bleiziffer, S., Blackman, D.,
 347 Schafer, U., Muller, R., Sievert, H., Sondergaard, L., Klugmann, S., Hoffmann, R., Tchetché, D.,
 348 Colombo, A., Legrand, V.M., Bedogni, F., lePrince, P., Schuler, G., Mazzitelli, D., Eftychiou, C.,
 349 Frerker, C., Boekstegers, P., Windecker, S., Mohr, F.-W., Woitek, F., Lange, R., Bauernschmitt, R.,
 350 Brecker, S., 2014. Treatment of aortic stenosis with a self-expanding transcatheter valve: the
 351 International Multi-centre ADVANCE Study. *Eur. Heart J.* 35, 2672–2684.

352 Martin, C., Pham, T., Sun, W., 2011. Significant differences in the Material Properties between Aged
 353 Human and Porcine Aortic Tissues. *Eur. J. Cardiothorac. Surg.* 40, 28–34.

354 Morganti, S., Conti, M., Aiello, M., Valentini, a, Mazzola, a, Reali, a, Auricchio, F., 2014. Simulation
 355 of transcatheter aortic valve implantation through patient-specific finite element analysis: Two
 356 clinical cases. *J. Biomech.* 47, 2547–2555.

357 Piazza, N., de Jaegere, P., Schultz, C., Becker, A.E., Serruys, P.W., Anderson, R.H., 2008. Anatomy of
 358 the Aortic Valvar Complex and Its Implications for Transcatheter Implantation of the Aortic
 359 Valve. *Circ. Cardiovasc. Interv.* 1, 74–81.

360 Russ, C., Hopf, R., Hirsch, S., Sundermann, S., Falk, V., Szekely, G., Gessat, M., 2013. Simulation of
 361 transcatheter aortic valve implantation under consideration of leaflet calcification. *Conf. Proc.*
 362 *IEEE Eng. Med. Biol. Soc.* 711–4.

363 Schultz, C., Rodriguez-olivares, R., Bosmans, J., Lefèvre, T., De Santis, G., Bruining, N., Collas, V.,
 364 Dezutter, T., Bosmans, B., Rahhab, Z., El Faquir, N., Watanabe, Y., Segers, P., Verheghe, B.,
 365 Chevalier, B., van Mieghem, N., De Beule, M., Mortier, P., de Jaegere, P., 2016. Patient-specific
 366 image-based computer simulation for the prediction of valve morphology and calcium
 367 displacement after TAVI with the Medtronic CoreValve and the Edwards SAPIEN valve.

368 EuroIntervention 11, 1044–1052.

369 Sellers, R.D., Levy, M.J., Amplatz, K., Lillehei, C.W., 1964. Left retrograde cardioangiography in
370 acquired cardiac disease: Technique, indications and interpretations in 700 Cases. Am. J.
371 Cardiol. 14, 437–447.

372 Simulia, 2010. Abaqus Technology Brief: Simulation of Implantable Nitinol Stents.

373 Smoljkic, M., Vander Sloten, J., Segers, P., Famaey, N., 2015. Non-Invasive, enery-based assessment
374 of patient-specific material properties of arterial tissue. Biomech. Model. Mechanobiol. 14,
375 1045–56.

376 Strbac, V., Vander Sloten, J., Famaey, N., 2015. Analyzing the potential of GPGPUs for real-time
377 explicit finite element analysis of soft tissue deformation using CUDA. Finite Elements in
378 Analysis and Design, 105, 79-89.

379 Thourani, V.H., Ailawadi, G., Szeto, W.Y., Dewey, T.M., Guyton, R. a, Mack, M.J., Kron, I.L., Kilgo, P.,
380 Bavaria, J.E., 2011. Outcomes of surgical aortic valve replacement in high-risk patients: a
381 multiinstitutional study. Ann. Thorac. Surg. 91, 49–55; discussion 55–6.

382 Wang, Q., Sirois, E., Sun, W., 2012. Patient-specific modeling of biomechanical interaction in
383 transcatheter aortic valve deployment. J. Biomech. 45, 1965–71.

384

Figure captions

Figure 1: (A) Coronal view of the computed tomography scan of patient 5 with the left chambers and aorta blood pool colored yellow. (B) Three dimensional reconstruction of the relevant geometry. (C) The resulting aortic root model used for finite element simulation. (D) The beam element model of the 29mm CoreValve stent. (E) Positioning of the crimped stent in the calcified aortic root at the start of the simulation

Figure 2: (L) A coronal view of the post-operative computed tomography scan of patient 5 with the segmented stent. (R) An overview of the locations of the cross section diameter measurements

Figure 3: Overview of the simulated deployed stent (black) and calcifications (blue) on top of the post-operative stent and calcifications (white) segmented from the post-operative computed tomography scans

Figure 4: (A) The simulated stent deployed in the calcified aortic root of patient 5. (B) A color map of the closest point distance of the sealing zone to the calcified aortic root

Figure 1
[Click here to download high resolution image](#)

Figure 2

[Click here to download high resolution image](#)

Figure 3
[Click here to download high resolution image](#)

A

B

Table 1

Table 1: The shear modulus (μ) and thickness (t) of the aorta, annulus, leaflets, septum and myocardium used in the baseline simulation

	μ [KPa]	t [mm]
Aorta	500	1.5
Annulus	200	1
Leaflets	1000	0.5
Septum	100	1
Myocardium	500	5

Table 2: The material parameters of the nitinol stent, for the Abaqus super-elastic nitinol material model [Simulia, 2010]

	E_a [GPa]	ν_a	E_m [GPa]	ν_m	ε^l	$\left(\frac{\delta\sigma}{\delta T}\right)_l$	σ_L^S [MPa]	σ_L^E [MPa]	T_0	$\left(\frac{\delta\sigma}{\delta T}\right)_u$	σ_U^S [MPa]	σ_U^E [MPa]	σ_{CL}^S [MPa]	ε_V^l
Stent	50	0.33	25	0.33	0.07	6.7	380	400	37	6.7	250	220	900	0.07

Table 3

Table 3: The circumferential (E_c), axial (E_a) and radial (E_r) Young's modulus of the aorta, annulus, septum and myocardium, for the simulation with an anisotropic linear-elastic material model. In addition, the shear modulus (μ) and Poisson's coefficient (ν) are also shown.

	E_c [KPa]	E_a [KPa]	E_r [KPa]	μ [KPa]	ν
Aorta	850	425	200	200	0.475
Annulus	340	170	85	85	0.475
Septum	170	85	42.5	42.5	0.475
Myocardium	850	425	200	200	0.475

Table 1: The average cross sectional diameter of the post-operative stents, an estimation of the measurement variability and the dimensions of the simulated stent

	Section A	Section B	Section C	Section D
Average post-op diameter [mm] (% from full expansion)	25.1 ± 0.9 (15.6%)	24.7 ± 0.6 (17.8%)	21.5 ± 0.6 (11.7%)	31.2 ± 1.5 (38.3%)
RMS difference on post-op diameter measurement [mm]	0.45	0.25	0.21	0.30
Simulation average diameter [mm] (% from post-op)	23.9 ± 0.8 (-5%)	24.3 ± 0.7 (-1.4%)	22.6 ± 0.4 (5.1%)	31.3 ± 1.5 (0.3%)
Perimeter difference (simulation – post-op) [mm]	-2.9 ± 2.1	-0.2 ± 2.3	2.6 ± 2.3	-0.4 ± 4.5
RMS = root mean square				

Table 5

Table 5: Sensitivity of the stent frame dimensions to changes in the aortic root model

		Section A	Section B	Section C	Section D
2*shear modulus simulation	average diameter [mm] (%) difference)	23 ± 1.2 (-3.7%)	23.4 ± 1.0 (-3.9%)	22 ± 0.7 (-2.8%)	30.8 ± 1.6 (-1.7%)
	Perimeter difference (simulation – post-op) [mm]	-5.0 ± 2.9	-2.5 ± 2.4	0.9 ± 3.4	-1.9 ± 4.3
½*shear modulus simulation	average diameter [mm] (%) difference)	24.4 ± 0.7 (2.3%)	24.9 ± 0.6 (2.5%)	23.1 ± 0.4 (2.7%)	31.8 ± 1.7 (1.6%)
	Perimeter difference (simulation – post-op) [mm]	-1.5 ± 2.6	1.4 ± 2.7	4.3 ± 2.6	1.1 ± 5.2
Anisotropic simulation	average diameter [mm] (%) difference)	24.8 ± 0.7 (4.0%)	25.3 ± 0.6 (4.2%)	23.4 ± 0.3 (3.5%)	32.0 ± 1.6 (2.9%)
	Perimeter difference (simulation – post-op) [mm]	-0.5 ± 1.4	2.8 ± 2.0	4.9 ± 1.8	2.2 ± 4.4
2*Wall thickness simulation	average diameter [mm] (%) difference)	22.4 ± 1.3 (-6.3%)	22.9 ± 1.1 (-5.9%)	22.2 ± 0.6 (-2.1%)	30.7 ± 1.7 (-1.8%)
	Perimeter difference (simulation – post-op) [mm]	-6.8 ± 2.7	-4.0 ± 2.5	1.4 ± 2.8	-2.1 ± 4.6
½* Wall thickness simulation	average diameter [mm] (%) difference)	24.7 ± 0.7 (3.4%)	25.1 ± 0.6 (3.4%)	23.2 ± 0.4 (2.7%)	32.3 ± 1.6 (3.1%)
	Perimeter difference (simulation – post-op) [mm]	1.0 ± 1.5	2.0 ± 1.9	4.4 ± 2.0	2.5 ± 4.4

Table 6

Table 6: The max-flow analysis on the closest point distance maps of the sealing zone of the simulated stent, in combination with two post-operative aortic regurgitation evaluations

	Max-flow [mm]	Post-op Angiographic AR grade [0 – 4]	7 days post-op Echocardiographic AR grade [0 – 4]
Patient 1	72	0	1
Patient 2	30.3	1	1
Patient 3	56.4	0	1
Patient 4	0	0	0
Patient 5	75.4	1	1
Patient 6	36.1	1	1
Patient 7	138.6	2	1
Patient 8	1.6	0	0
Patient 9	22.5	1	3
Patient 10	7.3	0	0

AR = Aortic Regurgitation