1	Effects of Aortic Root Motion on Wall Stress in the Marfan Aorta Before and After
2	Personalised Aortic Root Support (PEARS) Surgery
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ABSTRACT

Aortic root motion was previously identified as a risk factor for aortic dissection due to increased longitudinal stresses in the ascending aorta. The aim of this study was to investigate the effects of aortic root motion on wall stress and strain in the ascending aorta and evaluate changes before and after implantation of personalised external aortic root support (PEARS).

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20 Finite element (FE) models of the aortic root and thoracic aorta were developed using 21 patient-specific geometries reconstructed from pre- and post-PEARS cardiovascular magnetic 22 resonance (CMR) images in three Marfan patients. The wall and PEARS materials were 23 assumed to be isotropic, incompressible and linearly elastic. A static load on the inner wall 24 corresponding to the patients' pulse pressure was applied. Cardiovascular MR cine images 25 were used to quantify aortic root motion, which was imposed at the aortic root boundary of 26 the FE model, with zero-displacement constraints at the distal ends of the aortic branches and 27 descending aorta.

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29 Measurements of the systolic downward motion of the aortic root revealed a significant 30 reduction in the axial displacement in all three patients post-PEARS compared with its pre-31 PEARS counterparts. Higher longitudinal stresses were observed in the ascending aorta when 32 compared with models without the root motion. Implantation of PEARS reduced the 33 longitudinal stresses in the ascending aorta by up to 52%. In contrast, the circumferential 34 stresses at the interface between the supported and unsupported aorta were increase by up to 82%. However, all peak stresses were less than half the known yield stress for the dilated 35 36 thoracic aorta.

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39 Introduction

40 Acute aortic dissection is the most prevalent cause of death in patients with Marfan 41 syndrome. Aortic wall abnormalities and aortic dilatation are known to influence mechanical 42 stresses in the aortic wall and are the most common risk factors for aortic dissection and rupture (Beller et al., 2004). It is well-known that in most acute dissections of the ascending 43 44 aorta there is a transverse intimal tear a few centimetres distal to the aorto-ventricular 45 junction (Hirst et al., 1958). More recent studies have suggested that aortic root motion may 46 be a factor for occurrence of dissection and the site of the intimal tear due to increased 47 longitudinal wall stresses (Beller et al., 2004, Beller et al., 2008b).

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49 Ventricular relaxation and contraction during every heartbeat provides a driving force for the 50 downward movement of the aortic annulus, which is then transmitted to the aortic root, 51 ascending aorta, transverse aortic arch and aortic branches. Beller et al. (2004) used 52 aortograms to analyse the extent of aortic root motion in 40 patients with coronary artery heart disease. It was found that the peak downward axial displacement of the aortic root 53 54 during a cardiac cycle ranged between 0% and 49% of the sinotubular junction (STJ) 55 diameter, with a median of 14% (IQR 7% to 22%). Other cardiac pathology also affected 56 aortic root movement, where patients with aortic insufficiency showed increased aortic root 57 motion because of increased left ventricular stroke volume while patients with left ventricular 58 systolic dysfunction displayed reduced aortic root motion because of reduced ventricular contraction. 59

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61 Stress analysis of the thoracic aorta was then carried out to investigate the influence of aortic 62 root motion on wall stress in the ascending aorta (Beller et al., 2004) and evaluate the risk of 63 aortic dissection (Beller et al., 2008b). A finite element (FE) model of an average adult 64 human aortic root (excluding the sinuses of Valsalva), aortic arch and aortic branches was 65 constructed using measurements obtained from a silicone mould of a normal human aorta while the arch spatial orientation was obtained from 3D reconstruction of MR images of a 66 67 healthy volunteer (Beller et al., 2008b). An 8.9 mm axial displacement was imposed at the aortic root base, followed by a 6° twist. These values were obtained from healthy volunteers 68 69 in studies by Kozerke et al. (1999) (for displacement) and Stuber et al. (1999) (for twist). Key 70 findings were that pressurisation alone did not appreciably deform the model, but including 71 the axial displacement caused significant deformation to the ascending aorta and brachiocephalic trunk. In the control model (without aortic root motion), high stress 72 73 concentrations were found at the ostia of the aortic arch branches. Upon addition of the aortic 74 root motion, there were no marked change in circumferential or longitudinal stresses between 75 these branches, but the longitudinal stress in the ascending aorta (approximately 2 cm above 76 the STJ) increased by 50%. Furthermore, including the twist did not result in any appreciable 77 changes in the deformation or longitudinal stresses.

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79 In spite of the high stress concentrations at the ostia of the aortic arch branches, mechanical 80 failures are not typically observed in these regions. However, increased longitudinal stress in 81 the ascending aorta may render this region at increased risk of degeneration of the aortic 82 media and intimal rupture (Beller et al., 2004, Beller et al., 2008b), especially in patients with a vulnerable aortic wall due to connective tissue disease. As an aortic aneurysm dilates, the 83 84 longitudinal stress in the dilated region also increases significantly, and may result in rupture 85 (Thubrikar et al., 1999). If located in the ascending aorta, aortic root motion may then result 86 in an additional increase in the longitudinal stress of the aneurysm, consequently enhancing 87 the risk of rupture of small aneurysms, which are not usually considered for surgery (Beller et 88 al., 2008b). Furthermore, aortic root motion may dislodge atherosclerotic debris from the 89 aortic wall, leading to stroke or other embolic events, or lead to accelerated degeneration of 90 homografts, autografts and bioprosthetic valves (Beller et al., 2008b). Changes in the 91 magnitude of aortic root motion before and after aortic valve replacement (AVR) was 92 evaluated in patients with aortic insufficiency, aortic stenosis and proximal aortic dissection 93 (Beller et al., 2008a). Postoperative aortic root motion was significantly reduced after AVR 94 in patients with initial aortic insufficiency, while it was appreciably increased in patients with initial aortic stenosis. However, based on their findings from the FE study (Beller et al., 2004, 95 96 Beller et al., 2008b), increased aortic root motion caused higher longitudinal wall stress, 97 which may in turn have harmful consequences in the context of a thinned, post-stenotic, 98 dilated aorta.

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100 These findings form the underlying interest in the effect of aortic root motion on mechanical 101 stresses in the Marfan aorta upon insertion of personalised external aortic root support 102 (PEARS; ExoVasc®, Exstent Ltd, Tewkesbury, UK) (Treasure et al., 2011). Follow-up 103 cardiovascular magnetic resonance (CMR) imaging studies of the aortic root upon insertion 104 of PEARS revealed that in addition to preventing further dilatation (Pepper et al., 2010a, 105 Pepper et al., 2010b), the stiffer PEARS also caused a reduction in the aortic root motion 106 (Izgi et al., 2015). In a previous study, FE models were developed to compare the stress and strain fields in Marfan aortas pre- and post-PEARS implantation, where one of the 107 108 assumptions made was zero-displacement at the aortic root (Singh et al., 2015). The present 109 study investigates the effects of aortic root motion on wall stress and strain in patient-specific 110 Marfan aortas before and after implantation of PEARS.

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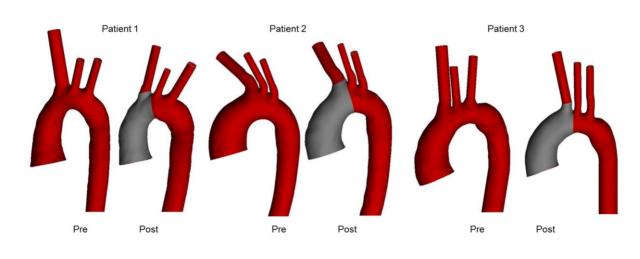
112 Methods

113 Patient-Specific Geometry

- MR images before and after implantation of PEARS were obtained (see Table 1 for imaging
 parameters). These were used to reconstruct patient-specific models of the aorta using
 Mimics (Materialise, Louvain, Belgium).

118	Table 1: Magnetic reso	nance imaging parame	eters for Patients 1, 2 and 3
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			Echo	Flip	Pixel	Slice	Interslice	Image
		Repetition	time	angle	size	thickness	distance	frequency
		time (ms)	(ms)	(°)	(mm)	(mm)	(mm)	(MHz)
Patient 1	Pre	292.10	1.22	80	1.328	6.0	3	63.67
	Post	296.38	1.07	70	0.594	1.5	var.	63.67
Patient 2	Pre	221.00	1.40	90	0.781	0.8	0.8	63.68
	Post	251.00	1.45	70	0.625	2.0	2.0	63.68
Patient 3	Pre	338.87	1.22	80	1.328	6.0	3.0	63.68
	Post	292.10	1.22	80	1.328	6.0	3.0	63.68



121 Figure 1: Reconstructed patient-specific geometries for Patients 1, 2 and 3 before and after implementation of PEARS

123 A uniform wall thickness was assumed for each aorta; the post-PEARS wall was thicker to account for the formation of a periarterial fibrotic sheet (Verbrugghe et al., 2013). The aortic 124 125 branches were assumed to have the same thickness as the aorta. ANSYS ICEM CFD 126 (ANSYS, Canonsburg, PA, USA) was used to discretise the resulting geometries using hexahedral elements. Mesh independence tests were performed using mesh sizes of 1.0×10^5 , 127 2.5×10^5 and 5.0×10^5 elements. The differences in terms of peak displacement, peak stress and 128 peak strain were less than 1.5% between the 1.0×10^5 element mesh and the 2.5×10^5 element 129 mesh and less than 1.0% between the 2.5×10^5 and 5.0×10^5 element mesh. Computational 130 time deficit was negligible in all cases, as each simulation was completed within 3 hours. 131 Consequently, the number of elements used was between 2.5×10^5 and 5.0×10^5 elements. 132

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134 Assessment of Aortic Root Motion

The aortic root motion was defined as the systolic downward motion of the aortic valve annulus. The left ventricular outflow tract cross-cut (LVOTxc) CMR cine images were used to identify the aortic valve annular plane in diastole and systole. These two planes were not parallel to each other due to the three-dimensional motion of the aortic root. Therefore, the systolic downward motion was measured as the length of the perpendicular line connecting the mid-point of the diastolic annulus plane and its intersection with the systolic annulus plane (see Figure 2) (Izgi 2015).

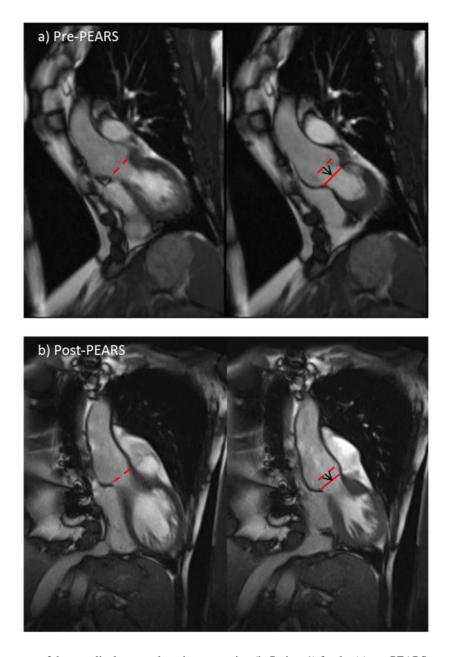


Figure 2: Measurement of the systolic downward aortic root motion (in Patient 1) for the (a) pre-PEARS aorta and (b) postPEARS aorta. The annular plane at end-diastole is illustrated by the dashed line, while the plane at end-systole is illustrated
by the solid line. The aortic root motion is quantified as the length of the perpendicular line connecting the mid-point of each
annular plane

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149 Material Properties

The aortic wall was modelled using a linear elastic constitutive equation, assuming it to be incompressible, homogenous and isotropic. It was assumed that the aortic branches had the same properties as the pre-PEARS aorta. The material properties are summarised in Table 2. 153 The justification for the choice of material properties for the post-PEARS material can be

154 found in our previous work (Singh et al., 2015).

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- 156

Table 2: Wall material properties used in the finite element models

	Pre-PEARS	Post-PEARS
Elastic modulus (kPa)	3000	6750
Poisson's ratio	0.49	0.45
Wall thickness (mm)	1.0	1.5
References	Nathan et al. (2011)	Verbrugghe et al. (2013)

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159 **Boundary Conditions**

A static load corresponding to the patients' pulse pressure (see Table 3) was applied perpendicular to the inner surface of the aorta. At the aortic root, an axial downward motion was specified based on the measurements obtained for each patient. Zero-displacement constraints were set at the distal ends of the brachiocephalic, left common carotid and left subclavian arteries, and in the mid-descending aorta.

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Table 3: Patient data used in this study

	Patient 1		Patient 2		Patient 3	
	Pre	Post	Pre	Post	Pre	Post
Blood Pressure (mmHg)						
Systolic	135	130	110	110	118	110
Diastolic	78	70	60	60	84	70
Pulse	57	60	50	50	34	40

ANSYS Mechanical (ANSYS, Canonsburg, PA, USA) was employed to obtain numerical solutions. Large-displacement (non-linear) static analyses were performed with the pressure and displacement loads ramped over several sub-steps. A preconditioned conjugate gradient (PCG) solver was selected and convergence was controlled by defining a square-root-sum-of-squares (SRSS) residual of 10⁻⁸, which was achieved within 6-12 iterations. Simulations were performed using a 16.0 GB RAM personal computer with Intel® Core™ i7-2600 3.40 GHz, running Windows 7 Enterprise.

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176 **Results**

177 Aortic Root Motion

The systolic downward motion of the aortic root in all three patients, pre- and post-PEARS implantation was measured and the results are given in Table 4. It shows clearly that PEARS implantation significantly reduced the axial root displacement in all three patients.

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Table 4: Downward systolic aortic root motion measurements

	Aortic Root Motion (mm)		
	Pre-PEARS	Post-PEARS	
Patient 1	15.5	8.3	
Patient 2	15.7	8.3	
Patient 3	10.5	7.0	

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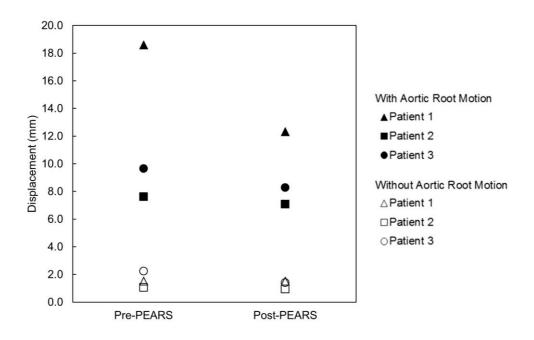
This is consistent with the study by Izgi et al. (2015) who examined a cohort of 24 patients (pre- and post-PEARS) and reported that the average systolic downward motion of the aortic root prior to implantation of PEARS was 12.6±3.6 mm while after implantation, it decreased to 7.9±2.9 mm.

189 **Deformation**

190 In all the models, introduction of the aortic root motion resulted in significantly greater 191 deformation of the aorta compared to pressurisation alone, as shown in Figure 3. Error! 192 Reference source not found. highlights the changes in spatial distributions of displacements 193 in each aorta. Without aortic root motion, peak displacements in the pre-PEARS and post-PEARS models were found at different locations: these were in the proximal ascending aorta 194 195 and around the aortic arch pre-PEARS, but in the descending aorta post-PEARS. Upon 196 introduction of root motion, peak displacements were shifted to the moving aortic root 197 boundary. The general trends can be summarised as follows:

Post-PEARS models showed a reduction in maximum displacement when compared with
 its pre-PEARS counterparts, with and without aortic root motion; and

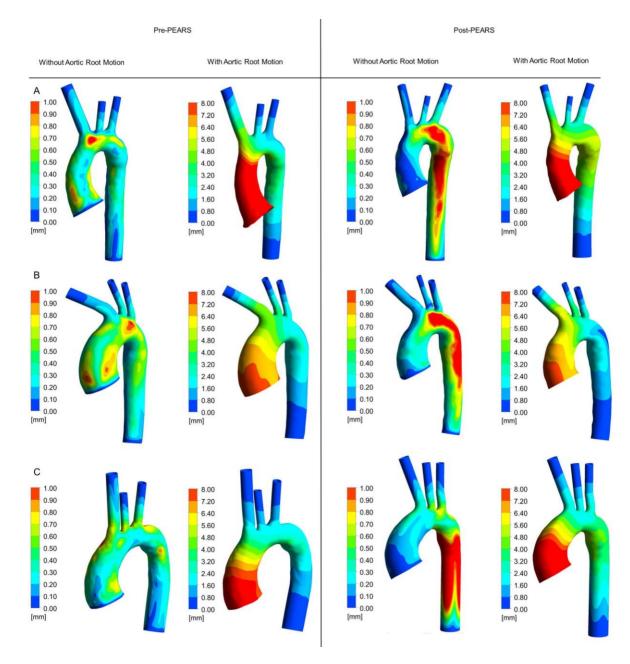
Including aortic root motion resulted in significant increases in peak displacement in all
 models.



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Figure 3: Peak displacement observed in the pre- and post-PEARS models with and without aortic root motion



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Figure 4: Displacement contours in the pre- and post-PEARS models with and without aortic root motion (A: Patient 1; B: Patient 2; C: Patient 3). Note the models with and without aortic root motion are displayed using different colour maps; the models without aortic root motion are illustrated with a maximum displacement (red) of 1 mm while the models with aortic root motion are illustrated with a maximum displacement (red) of 8 mm.

211 Stresses without Aortic Root Motion

212 Without aortic root motion, the pre-PEARS models displayed higher longitudinal and 213 circumferential stresses in the proximal ascending aorta compared with the post-PEARS models, as shown in Figure 5 and Figure 6. The high longitudinal and circumferential stress regions in the post-PEARS were located at the interface between the supported and unsupported aorta (between the BCA and the left common carotid artery (LCCA)) and regions distal to this interface.

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219 Stresses with Aortic Root Motion

220 It can immediately be recognised from Figure 5 that the aortic root motion resulted in higher 221 longitudinal stresses, particularly in the pre-PEARS models. The stiffer post-PEARS models, 222 on the other hand, experienced slightly more conservative increases. Additionally, elevated 223 longitudinal stress in the ascending aorta was located at the inner curvature and then extended 224 to the outer curvature proximal to the brachiocephalic trunk. Circumferential stress 225 distributions, shown in Figure 6, with and without aortic root motion, are quite similar. 226 Unlike the longitudinal stress patterns, high circumferential stress regions were found mostly 227 on the outer curvature of the ascending aorta. The absolute values of the changes in 228 circumferential and longitudinal stresses at two specific regions, with and without aortic root 229 motion, for all models are shown in Error! Reference source not found.. Since each model 230 was constructed using patient-specific geometries and loadings, the quantitative results were 231 different among the patients. However, the qualitative effects of aortic root motion are quite 232 similar and these are summarised as follows:

Circumferential stress between the BCA and LCCA: this was reduced in all models,
except for the pre-PEARS model of Patient 2 which showed an increase;

• Circumferential stress in the proximal ascending aorta: no change was observed in the pre-PEARS models of Patients 1 and 2, while Patient 3 showed a 25% decrease; in the post-PEARS, all models showed increased circumferential stress in this region;

238	•	Longitudinal stress between the BCA and LCCA: a significant increase was observed in
239		the pre- and post-PEARS models of Patient 2 and 3, while Patient 1 displayed a modest
240		increase;

Longitudinal stress in the proximal ascending aorta: again, all models showed significant
 increases.

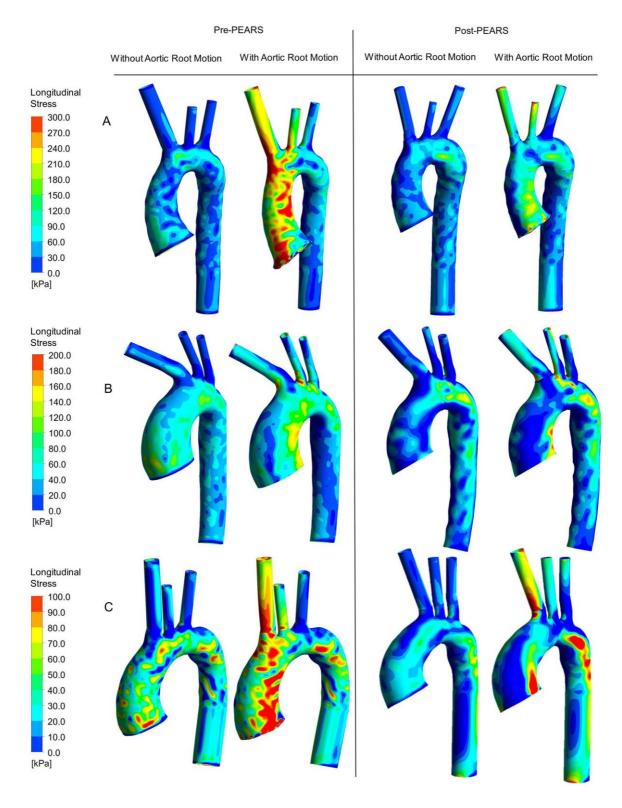


Figure 5: Longitudinal stress contour plots for the pre- and post-PEARS models of Patients 1, 2 and 3 (labelled A, B and C, respectively), with and without aortic root motion. Note that each patient is illustrated using a different contour colour map scale owing to differences in biomechanical properties

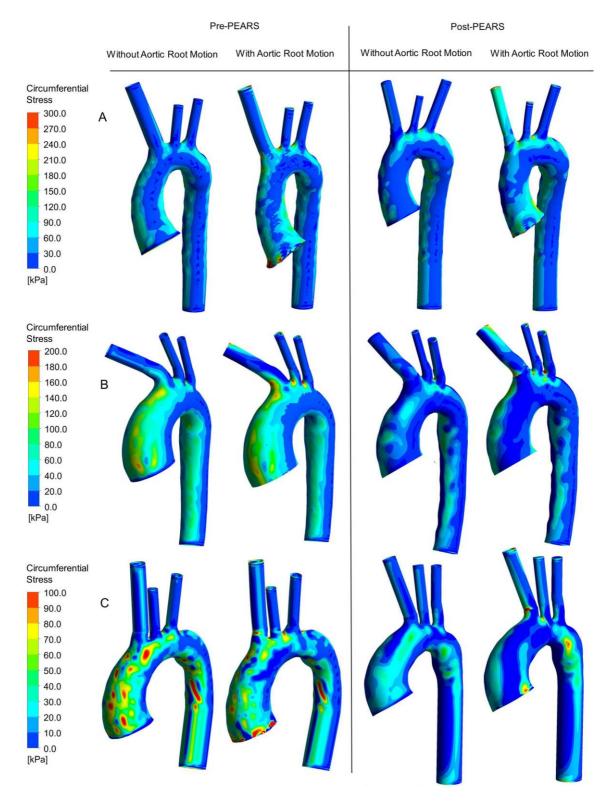
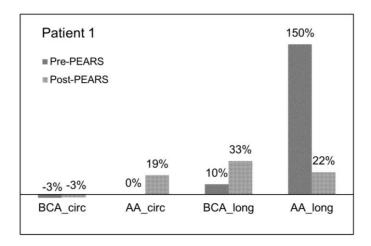
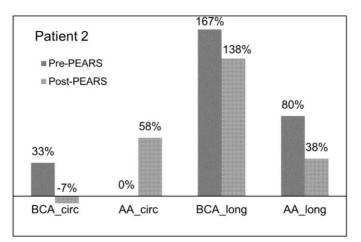
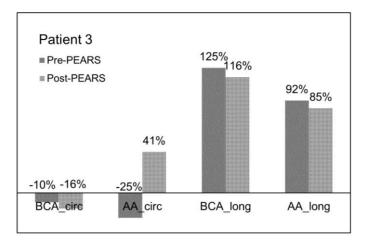


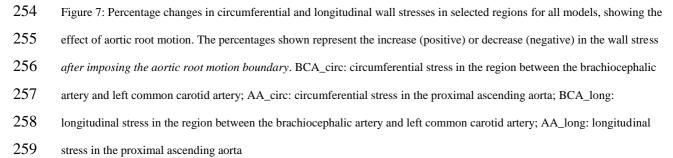


Figure 6: Circumferential stress contour plots for the pre- and post-PEARS models of Patients 1, 2 and 3 (labelled A, B and C, respectively), with and without aortic root motion. Note that each patient is illustrated using a different contour colour map scale owing to differences in biomechanical properties









261 **Pre-PEARS vs Post-PEARS**

Figure 8 shows changes in circumferential and longitudinal stresses in regions between the BCA and LCCA and the proximal ascending aorta upon addition of the PEARS, with and without aortic root motion. Like the data analysed from Figure 7, the quantitative differences arise due to variations in patient-specific geometries and applied loading. Regardless of the effect of aortic root motion, the post-PEARS models showed qualitatively similar trends when compared to their pre-PEARS counterparts:

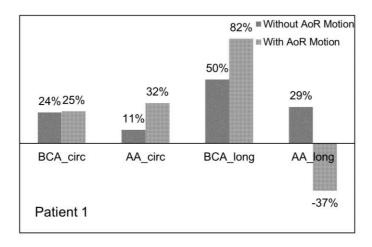
Circumferential stress between the BCA and LCCA: this was increased in all patients, for
 models with and without aortic root motion;

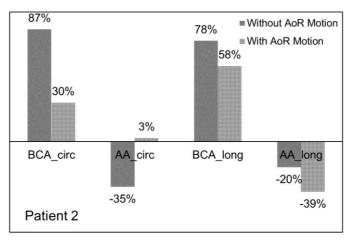
Circumferential stress in the proximal ascending aorta: there was a significant increase in
 Patient 2 and 3 when the root was fixed, but no appreciable changes were found when the
 root motion was included; Patient 1 displayed an increase in circumferential stress both
 with and without the aortic root motion;

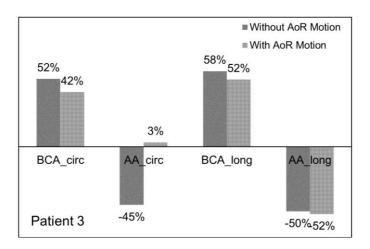
• Longitudinal stress between the BCA and LCCA: In all models, this stress was increased;

• Longitudinal stress in the proximal ascending aorta: Patients 2 and 3 showed reductions in this stress both with and without the aortic root motion; Patient 1 however had an increase when the root was fixed but a reduction upon addition of the root motion.

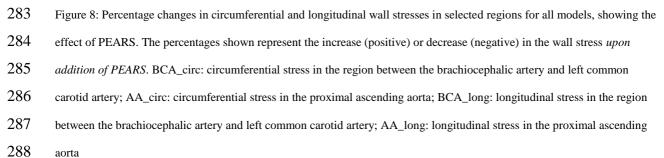
The latter finding is of particular interest because it shows the post-PEARS models had reduced longitudinal stress in the proximal ascending aorta when compared to the pre-PEARS models.











290 Discussion

291 In a previous FE study (Singh et al., 2015), the overall stress distributions in the pre- and 292 post-PEARS models were investigated under the assumption that the aortic root was fixed. It 293 was observed that in the pre-PEARS models, the ascending aorta and aortic arch had higher 294 von Mises stresses than regions distal to the aortic arch. Upon integration of PEARS into the 295 aortic wall, the high stress regions shifted to the unsupported aortic wall, with peak stresses 296 located at the interface between the supported and unsupported aorta. This study extends the 297 analysis by removing the fixed root assumption and further examining the circumferential 298 and longitudinal stresses separately.

299

300 The first major finding was the increase in aortic wall deformation upon introduction of 301 aortic root motion. In cardiac patients, the aortic root was found to experience a downward 302 movement ranging from 0 to 22 mm (Beller et al., 2008a). The values measured from MR 303 images of the patients included in this study were well within this range, 13.1±5.5mm (pre-304 PEARS) and 10.3±2.0mm (post-PEARS). As expected, the post-PEARS aortas had reduced 305 displacements at the aortic root and ascending aorta due to its stiffer mechanical properties. 306 Stress analyses revealed that there were significant changes in the peak stress values when 307 aortic root motion was included in the models. At the junction between the BCA and LCCA, 308 there was a modest increase in the longitudinal stress for Patient 1, with a 10% increased pre-309 PEARS and 33% increased post-PEARS. Patients 2 and 3, however, displayed increases of 310 167% and 125% respectively in their pre-PEARS models and 138% and 116% respectively in 311 their post-PEARS models. Similarly, in the ascending aorta, the longitudinal stresses increased by 150%, 80% and 92% in the pre-PEARS models of patients 1, 2 and 3, 312

respectively, and 22%, 38% and 85% in the corresponding post-PEARS models. The effects
of aortic root motion on circumferential stresses were more modest.

315

316 It has been reported that about 65 to 87% of aortic dissections occur in the ascending aorta 317 (Hirst et al., 1958, Thubrikar et al., 1999). This, along with observations of increasing 318 longitudinal stresses in aortic aneurysm growth, has led to the postulate that intimal tears in 319 the circumferential direction could be explained on the basis that the tear is caused by rapidly 320 increasing longitudinal stress on the inner surface of the aneurysm. Since aortic root motion 321 has been directly related to increased longitudinal stress, it has been identified as an 322 additional risk factor for aortic dissection (Beller et al., 2008b). Wrapping of the Marfan aorta 323 with the much stiffer PEARS has an obvious additional advantage in reducing aortic root 324 motion and ascending aorta deformation. As expected, the decreased aortic motion then 325 resulted in reduction of longitudinal wall stress in the post-PEARS aortas (by 37-52%) when compared with their pre-PEARS counterparts. However, it also caused an increase in 326 327 circumferential stress. In a multi-layer analysis of the aortic wall, Gao et al. (2006) suggested 328 that high stress regions were typically found in the stiffer aortic layers. One of the concerns 329 of PEARS is that the aortic wall distal to the support is unprotected and therefore susceptible 330 to abnormal stress patterns and consequently dissection. It was shown that upon addition of 331 PEARS, the circumferential and longitudinal stresses between the BCA and LCCA were 332 increased by 25 to 42% and 52 to 82%, respectively. Nevertheless all peak stresses were 333 below the known yield stress of the dilated thoracic aorta (1.18±0.12 MPa in circumferential and 1.21±0.09 MPa in longitudinal directions) (Vorp et al., 2003), with the maximum 334 335 longitudinal stress predicted by the models reaching just less than half this value, and 336 therefore did not present an imminent risk.

In addition to the limitations presented in Singh et al. (2015), this study included two additional assumptions: exclusion of the sinuses of Valsalva and simplification of the aortic root motion by neglecting its twisting. Previous studies revealed that most acute dissections of the ascending aorta were distal within the first few centimetres of the ascending aorta, and so for simplicity, the sinuses of Valsalva were neglected. Additionally, Beller et al. (2004) found that twisting of the aortic root did not appreciably change the wall stresses obtained, and was therefore neglected in these models.

345

346 Conclusions

347 After PEARS implantation, the axial downward motion of the aortic root was significantly 348 reduced. Aortic root motion was previously identified as a risk factor for aortic dissection due 349 to the corresponding increase in longitudinal stress in the ascending aorta. In this manuscript, 350 the impact of aortic root motion on stress distribution in the Marfan aorta, pre- and post-351 PEARS implantation, was investigated. While the qualitative changes in stress were similar 352 with and without aortic root motion, models incorporating aortic root motion were a step 353 closer to a realistic description of the biomechanical environment of the aorta. It was 354 confirmed that with the root motion, there was indeed a concentration of longitudinal wall 355 stress in the ascending aorta of the pre-PEARS models. However, implantation of PEARS 356 reduced this stress by up to 52% in the three patients examined in this study.

357

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