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In vitro Analysis of Localized Aneurysm Rupture

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Aneurysm, human aorta, inflation test, rupture, ultimate stress.

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31 **ABSTRACT**

32

33 In this study, bulge inflation tests were used to characterize the failure response of 15 layers of
34 human ascending thoracic aortic aneurysms (ATAA). Full field displacement data were collected
35 during each of the mechanical tests using a digital image stereo-correlation (DIS-C) system. Using the
36 collected displacement data, the local stress fields at burst were derived and the thickness evolution
37 was estimated during the inflation tests. It was shown that rupture of the ATAA does not
38 systematically occur at the location of maximum stress, but in a weakened zone of the tissue where
39 the measured fields show strain localization and localized thinning of the wall. Our results are the
40 first to show the existence of weakened zones in the aneurysmal tissue when rupture is imminent.
41 An understanding these local rupture mechanics is necessary to improve clinical assessments of
42 aneurysm rupture risk. Further studies must be performed to determine if these weakened zones can
43 be detected *in vivo* using non-invasive techniques.

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50 INTRODUCTION

51

52 Each year thoracic aneurysms are diagnosed in approximately 15,000 people in the United States and
53 more than 30,000 people in Europe (Clouse 1998). Of this number 50-60% are ascending thoracic
54 aortic aneurysms (ATAA) (Isselbacher 2005). However the rupture of the ATAA remains an almost
55 unexplored topic. ATAAs are caused by the remodeling of the arterial wall and they rupture when the
56 stress applied to the aortic wall locally exceeds its capacity to sustain stress (Vorp et al., 2003).

57

58 In an attempt to understand the mechanical behavior of the aortic tissue; different authors have
59 performed mechanical tests. Uniaxial tensile tests were performed by (Mohan and Melvin, 1982) on
60 healthy descending aortic specimens; they concluded that the most reasonable failure theory for
61 aortic tissue was the maximum tensile strain theory. (He and Roach, 1994) also performed uniaxial
62 tensile tests and showed that aneurysms were less distensible and stiffer than healthy tissues. Using
63 uniaxial tensile tests to compare healthy tissues with ATAA specimens (Garcia-Herrera et al., 2011)
64 concluded that the age, beyond the age of 35, was the cause of significant decrease of rupture load
65 and elongation at failure. They found no significant differences between the mechanical strength of
66 aneurysms and healthy tissues. In contrast, (Vorp et al., 2003) found a significant decrease in the
67 tensile strength of the ATAA specimens and concluded that its formation was associated with the
68 stiffening and weakening of the aortic wall. Providing data on the mechanical behavior in the
69 physiological range, (Duprey et al., 2010) found that the aortic wall was significantly anisotropic with
70 the circumferentially oriented samples being stiffer than the axial ones.

71

72 The biaxial mechanical behavior of the aortic tissue has been investigated with bulge inflation tests.
73 Dynamic and quasi-static bulge inflation tests (Mohan and Melvin, 1983) were performed on healthy
74 descending aortas. The failure of the aortic tissue always took place with a tear in the circumferential
75 direction. Similarly, (Marra et al., 2006) performed inflation tests using porcine healthy aortic tissues,

76 showing that the rupture occurs with a crack oriented in the circumferential direction of the artery.
77 More recently (Kim et al., 2012) performed inflation tests using ATAA specimens. Material
78 parameters were identified using the virtual fields method (Grédiac et al., 2006; Avril et al., 2010)
79 and the average Cauchy stress values at which the rupture occurred were derived for all the
80 specimens.

81

82 None of the studies mentioned above analyzed locally the rupture of the tissue from its first
83 initiation. Moreover, all these studies derived an average stress estimation across the specimens and
84 none were able to show if the rupture initiates at the location of maximum stress or if the rupture
85 was triggered by the existence of weakened parts within the tissue. Our objective was to address
86 this issue by carrying out full-field measurements in human ATAA specimens tested in a bulge
87 inflation test up to failure. In order to determine the cause and location of the rupture, thickness
88 evolution estimations and local stress distributions were calculated during the inflation of the
89 specimens.

90

91

92 **METHODS**

93

94 ***Sample Preparation and Experimental Protocol***

95 ATAA specimens were obtained from donor patients who underwent surgical replacement of their
96 ATAA with a synthetic graft. The collection of the aortic tissues was done in accordance with the
97 guidelines of the Institutional Review Board of the University Hospital Center of Saint-Etienne.
98 Specimens were kept at 4 °C in 0.9% physiological saline solution and testing was completed within
99 24 hours of tissue harvest (Adham et al. 1996). Table 1 lists the demographic information for the
100 collected ATAA specimens.

101

102 Each ATAA (Fig. 1-a) was cut into square specimen approximately 45 x 45 mm. Each specimen was
103 then separated into two layers: intima-media and adventitia (Fig. 1-b). The average thickness of each
104 layer was measured using digital calipers; the layer of interest was put between two plastic plates
105 and the thickness of the layer and the plates was measured. Then the thickness of the two plates was
106 subtracted from the measured value. The ATAA layer was clamped in the inflation device so that the
107 luminal side of the tissue faced outward and the circumferential direction of the artery coincided
108 with the horizontal axis of the clamp (Fig. 1-c). Finally a speckle pattern was applied to each sample
109 using black spray paint (Fig. 1-c). Note that the luminal side of each layer was chosen to face outward
110 since the adventitial surface was highly irregular making difficult for the speckle pattern to adhere to
111 the surface.

112

113 A hermetically sealed cavity was formed between the clamped ATAA layer and the inflation device.
114 During the inflation test, water was injected at a constant rate by pushing a piston pump at 15
115 mm/min until the tissue ruptured. Simultaneously, the pressure was measured with a digital
116 manometer (WIKA®, pressure gauge DG-10). Images were recorded using a commercial DIS-C system
117 (GOM®, ARAMIS 5M LT) at every 3 kPa, until the sample ruptured (Fig. 2). The DIS-C system was

118 composed of two 8-bit CCD cameras equipped with 50 mm lenses (resolution: 1624 x 1236 px). In
 119 this study, 15 ATAA layers were successfully tested until rupture. Only the specimens that ruptured in
 120 their central area (without touching the boundaries of the inflation device) were used.

121

122 **Data Analysis**

123 Once the experimental procedure was completed, image processing was performed using Aramis®
 124 software. In each of the acquired images (Fig. 2), the area of interest (AOI), which was a circle
 125 measuring 30 mm diameter, was identified. A facet size of 21 px and a facet step of 5 px were chosen
 126 based on the speckle pattern dot size, distribution, and contrast. The selected facet size and step
 127 yielded a resolution of 0.54 μm for in-plane displacements and 1.5 μm for the out-of-plane
 128 displacement.

129

130 To capture the kinematics of the membrane (Naghdi 1972; Green and Adkins 1970; Lu et al., 2008)
 131 we define the position vectors for a material point P in the initial and deformed configurations as
 132 $\mathbf{X}(P)$ and $\mathbf{x}(P)$, respectively (Fig. 4). The surface is parameterized using a pair of surface coordinates
 133 $\xi^\alpha(P) = \mathbf{X}(P) \cdot \mathbf{E}_\alpha$ where \mathbf{E}_α are the basis vectors of the global coordinate system GCS (Fig. 3) and
 134 $\alpha = 1, 2$. The local covariant basis vectors \mathbf{g}_α and \mathbf{G}_α for the deformed and initial configurations,
 135 respectively, are found using the following relationships:

136

$$\mathbf{g}_\alpha = \frac{\partial \mathbf{x}}{\partial \xi^\alpha} \qquad \mathbf{G}_\alpha = \frac{\partial \mathbf{X}}{\partial \xi^\alpha} \qquad (1)$$

137

138 The local contravariant basis vectors g^α and G^α are then defined as:

139

$$\mathbf{g}^\alpha = \frac{\partial \xi^\alpha}{\partial \mathbf{x}} \qquad \mathbf{G}^\alpha = \frac{\partial \xi^\alpha}{\partial \mathbf{X}} \qquad (2)$$

140

141 The two-dimensional deformation gradient, \mathbf{F} , is calculated from the current and initial basis vectors:

142

$$\mathbf{F} = \mathbf{g}_\alpha \otimes \mathbf{G}^\alpha \quad (3)$$

143

144 Then, at each material point, the two-dimensional Green-Lagrange strain, \mathbf{E} , is determined:

145

$$\mathbf{E} = \frac{1}{2}(\mathbf{F}^T \mathbf{F} - \mathbf{I}) \quad (4)$$

146

147 To define the three-dimensional deformation, we set $\lambda_3 = h/h_0$, where h and h_0 are the thicknesses
148 in the deformed and undeformed configurations, respectively, and required the transverse shear
149 strains to vanish. It follows that the three dimensional deformation gradient and Green-Lagrange
150 strain tensor are given by:

151

$$\mathbf{F} = \mathbf{g}_\alpha \otimes \mathbf{G}^\alpha + \lambda_3 \mathbf{n} \otimes \mathbf{N} \quad \mathbf{E} = \frac{1}{2}(\mathbf{g}_{\alpha\beta} \mathbf{G}^\alpha \otimes \mathbf{G}^\beta + \lambda_3^2 \mathbf{N} \otimes \mathbf{N} - \mathbf{I}) \quad (5)$$

152

153 where \mathbf{n} and \mathbf{N} are outward unit normals to the surface in the current and initial configurations,
154 respectively.

155

156 ***Determination of the Local Stress Fields***

157 The aneurysm wall is modeled as a nonlinear elastic membrane. A unique feature of modeling the
158 aneurysm wall as a nonlinear elastic membrane is that the tension in the vessel wall can be
159 determined *without* the use of a constitutive model to describe the elastic properties of the wall (Lu
160 et al., 2008). The local equilibrium equations for the elastostatic problem may be written as (Lu et
161 al., 2008; Zhao 2009):

162

$$\frac{1}{\sqrt{g}}(\sqrt{g}h\sigma^{\alpha\beta}\mathbf{g}_\alpha)_{,\beta} + p\mathbf{n} = \mathbf{0} \quad (6)$$

163
 164 where $g = \det(\mathbf{g}_\alpha \cdot \mathbf{g}_\beta)$ is the determinant of the metric tensor, h is the current thickness, p is the
 165 internal pressure applied for the inflation and $\sigma^{\alpha\beta}$ are the unknown components of the Cauchy
 166 stress tensor $\boldsymbol{\sigma}$ in the local covariant basis. Note that Eq. (6) is in tensorial form and the Einstein
 167 summation convention is used. Then, we approximate the spatial variations of all the quantities of
 168 Eq. (6) using linear shape functions of the surface coordinates which take on a null value at all nodes
 169 of the mesh except at node k where it is 1. The shape functions are defined on a triangular finite
 170 element mesh having N elements and K nodes (Fig. 5).

171

172 Using this approximation scheme, Eq. (6) is written at the centroid of each element, which yields:

173

$$\frac{1}{\frac{1}{3}\sum_{k=1}^3\sqrt{g(\mathbf{x}_k)}}\sum_{k=1}^3\left[\sqrt{g(\mathbf{x}_k)}h(\mathbf{x}_k)\sigma^{\alpha\beta}(\mathbf{x}_k)\mathbf{g}_\alpha(\mathbf{x}_k)\frac{d\varphi_k}{d\xi^\beta}\right] + p\frac{1}{3}\sum_{k=1}^3\mathbf{n}(\mathbf{x}_k) = \mathbf{0} \quad (7)$$

174

175 where $\frac{d\varphi_k}{d\xi^\beta}$ are the shape function derivatives at the centroid of the element and where the Einstein
 176 summation convention still applies for indexes α and β . Eq. (7) is then projected into the GCS and the
 177 procedure is repeated for each triangular element. A linear system of $3N$ equations is produced. It
 178 contains $3K$ unknowns which are the 3 components of the Cauchy stress tensor in the local covariant
 179 basis at the K nodes of the mesh. A convergence study showed that a mesh with $N=1203$ elements
 180 and $K=644$ nodes was a good compromise between precision and time of calculation.

181

182 The system was completed by a set of equations on the boundaries of the tested area, where it was
 183 assumed:

184

$$(\boldsymbol{\sigma} \cdot \boldsymbol{j}) \cdot \boldsymbol{n} = 0 \quad (8)$$

$$(\boldsymbol{\sigma} \cdot \boldsymbol{j}) \cdot \boldsymbol{i} = 0 \quad (9)$$

185

186 where $\boldsymbol{i}, \boldsymbol{j}, \boldsymbol{n}$ defines a local basis at the boundaries (Fig. 5-b) with \boldsymbol{i} is tangent to the boundary, \boldsymbol{n} is
 187 an outward unit normal vector to the surface and $\boldsymbol{j} = \boldsymbol{n} \otimes \boldsymbol{i}$ is chosen to make the local coordinate
 188 system right-handed. Along the boundaries, Eq. (8) sets the traction vector perpendicular to \boldsymbol{i} ,
 189 allowing in-plane tractions only and Eq. (9) sets the traction vector perpendicular to \boldsymbol{i} , allowing no
 190 shear on the boundary. The resultant boundary traction automatically balances the total pressure
 191 applied on the wall due to the local equilibrium equation (Eq. (6)) written for each element. The final
 192 over-determined linear system of equations was solved in the least-squares sense.

193

194 The calculated components of the stress tensor are finally projected in the orthonormal local
 195 coordinate system (LCS) ($\boldsymbol{e}_1, \boldsymbol{e}_2, \boldsymbol{e}_3$) defined such that:

196

$$\begin{aligned} \boldsymbol{e}_3 &= \boldsymbol{n} \\ \boldsymbol{e}_2 &= \frac{\boldsymbol{g}_2}{\|\boldsymbol{g}_2\|} \\ \boldsymbol{e}_1 &= \boldsymbol{e}_2 \otimes \boldsymbol{e}_3 \end{aligned} \quad (10)$$

197

198 where \boldsymbol{n} is again the outward unit normal to the surface.

199

200 The stress was analyzed at three locations:

201

- 202 • NodeMAX: node with the largest stress eigenvalue
- 203 • NodeTOP: node at the top of the inflated membrane
- 204 • NodeRUP: node where rupture initiates

205

206 At NodeMAX and NodeTOP locations, the largest eigenvalue of the Cauchy stress tensor (largest
207 principal stress) were found and denoted σ^{Max} and σ^{Top} , respectively. At NodeRUP, the stress in the
208 direction perpendicular to the crack that occurs at rupture was computed:

209

$$\sigma^{Rup} = (\boldsymbol{\sigma} \cdot \mathbf{q}_\theta) \cdot \mathbf{q}_\theta \quad (11)$$

210

211 where \mathbf{q}_θ is the unit vector perpendicular to the rupture (Fig. 8c). It is derived for each specimen
212 using the images obtained from the DIS-C system at the moment of the rupture. Using a custom
213 MatLab® code, a series of points were manually placed on an image of the ruptured edge. A linear
214 regression was then performed using those points and the angle between the fit line and the
215 horizontal axis was calculated.

216

217 ***Finite Element Validation Study***

218 Using a mesh size of $N=1203$ elements and $K=644$ nodes, a validation analysis was performed (see
219 Appendix A for details). The stress distributions obtained from a finite element analysis (FEA) were
220 defined as reference values and compared with the stress distributions obtained using the present
221 approach.

222

223 ***Thickness Evolution***

224 At every pressure step, the current thickness of each element was calculated. The aneurysmal tissue
225 was modeled as incompressible membrane therefore the following relationship holds between the
226 initial thickness, h_0 , and the current thickness, h .

227

$$h = \frac{h_0}{F_{11}F_{22} - F_{21}F_{12}} \quad (12)$$

228

229 We note that the *ex vivo* thickness, h_0 , was assumed to be initially homogeneous and that F_{11} , F_{22} ,
230 F_{21} and F_{12} are the components of the deformation gradient tensor (Eq. (3)).

231

232 **Laplace's Law**

233 Laplace's Law (Peterson et al., 1960; Humphrey 2002) was used to calculate a global estimate of the
234 ultimate stress for each ATAA layer by assuming the sample was a hemisphere

235

$$\sigma^{Lap} = \frac{pr}{2h} \quad (13)$$

236

237 where p was the inflation pressure, r was the radius of curvature estimated using a least-squares
238 surface fitting of the inflated shape, and h was the average current thickness of the elements in the
239 mesh.

240

241

242 **RESULTS**

243

244 The stress distributions obtained from the FEA simulation (Fig. 6-a) were compared with the stress
245 distributions obtained using the present approach (Fig. 6-b). The mean absolute error (Fig. 6-c) was
246 calculated revealing that the largest errors occurred at the boundaries. Ignoring the elements at the
247 boundaries, the average error was significantly reduced to 0.8%, 1.4%, and 0.8% for σ_{11} , σ_{22} , and
248 σ_{12} , respectively (Fig. 6-d). This showed that the stress estimates contain some errors along the
249 border due to the assumed boundary conditions but these errors vanish rapidly away from the
250 border. For this reason, only the tests where the rupture occurred at a distance of more than three

251 elements away from the border were included in this study.

252

253 Using the approach we have presented, the components of the Cauchy stress tensor were calculated
254 at every node for each 3 kPa pressure step until the sample ruptured (Fig. 7-a). The displacement
255 (Fig. 7-b) and strain fields (Fig. 7-c) used to calculate the stress and thickness evolution are also
256 shown.

257

258 In Table 2 we report the three components of the Cauchy stress tensor. Our results (mean \pm std) for
259 σ_{11} were 1.18 ± 0.64 MPa at NodeMAX, 1.12 ± 0.64 MPa at NodeTOP and 1.06 ± 0.59 MPa at
260 NodeRUP. The values for σ_{22} were 1.21 ± 0.80 MPa at NodeMAX, 1.17 ± 0.79 MPa at NodeTOP and
261 1.05 ± 0.71 MPa at NodeRUP.

262

263 In Fig. 8-a, we show the thickness distribution (Eq. (12)) one pressure step before rupture for five
264 tests. For each of the samples thick (dark red) and thin (dark blue) regions can be identified. The
265 locations of NodeMAX, NodeTOP, and NodeRUP for these five tests are also shown in Fig. 8-b.
266 Contrary to the generally accepted theory that the rupture occurs at the location of the maximum
267 stress, the experimental results show that rupture often initiates at a different location (NodeRUP),
268 possibly due to the non-homogeneous strength of the tissue. An image of the ruptured layer is
269 shown in Fig. 8-c, where the magenta points and the blue regression line were used to determine the
270 rupture angle, θ .

271

272 Table 3 and Fig. 9 summarize the three ultimate stress values (σ^{Max} , σ^{Top} , and σ^{Rup}) calculated at
273 their corresponding locations (NodeMAX, NodeTOP and NodeRUP) compared with σ^{Lap} (Eq. (13)).
274 For the six adventitia layers, the average stress values (mean \pm std) were 1.49 ± 1.06 MPa, 1.76 ± 1.07
275 MPa, 1.69 ± 1.10 MPa, and 1.46 ± 1.03 MPa for σ^{Lap} , σ^{Max} , σ^{Top} , and σ^{Rup} , respectively. For the
276 remaining nine media layers, the average stress values were found to be 0.78 ± 0.26 MPa, 1.01 ± 0.36

277 MPa, 0.95 ± 0.31 MPa, and 0.78 ± 0.20 MPa for σ^{Lap} , σ^{Max} , σ^{Top} , and σ^{Rup} , respectively. The four
278 calculated ultimate stress values were higher for the adventitia layers, confirming its role of
279 structural support of the artery (Fung, 1993).

280

281

282 **DISCUSSION**

283

284 **Comparison with Existing Literature**

285 Other investigators performing inflation tests have reported rupture stresses between 0.751 and
286 1.75 MPa (Kim et al., 2012, Mohan and Melvin, 1983, Marra et al., 2006). In the present study the
287 rupture stress, σ^{Rup} , was on average 1.46 MPa for the adventitia layers and 0.72 MPa for the media
288 layers. The results obtained from our analysis were reasonable and lie within the range of reported
289 values in the literature. It must be noted that our results were twice as large of those of Kim et al.
290 (2012) who found 0.751 MPa for adventitia layers and 0.39 MPa for media layers. This can be
291 explained by the different methods used to calculate the rupture stress. While Kim et al. (2012)
292 assumed a constant thickness throughout the inflation, the present method was capable of
293 estimating the thickness evolution of the sample (Eq. (12)). Based on the large changes in thickness
294 observed in the samples (Fig. 10), it was expected that our values would be significantly larger than
295 those reported by Kim et al. (2012).

296

297 **Comparison of the Ultimate Stress at Different Locations**

298 The stress found using Laplace's Law, σ^{Lap} , in Eq. (13) was considered a global estimate of the
299 rupture stress, since it was computed using a global radius of curvature and the mean thickness of
300 the inflated ATAA layer. A comparison between this global stress value and the calculated local stress
301 values, σ^{Max} , σ^{Top} , and σ^{Rup} , was done as the majority of published studies have not calculated
302 local stress distributions. The stress calculated from Laplace's Law was frequently smaller than the

303 other local stress values. The difference can likely be explained by differences in the thickness
304 calculation. On the one hand Laplace's Law uses the average current thickness of the entire inflated
305 aortic layer while the three local stress values use the current local thickness of the element where
306 the node concerned was located.

307

308 **Detection of Weakened Zones in the Tissue**

309 In every test rupture was preceded by significant local deformation and reduction of the thickness.
310 This phenomenon was clearly illustrated in Fig. 8, where local thinning was observed at the rupture
311 location. Occasionally the maximum stress value was located in the weakened area, but more
312 frequently it was located elsewhere. This led us to hypothesize that the ATAA layers had weakened
313 regions that caused the localized thinning of the layer during the inflation test. When observing the
314 evolution of the ATAA layer thickness (Fig. 10), the region where the rupture was most likely to occur
315 could be observed many stages before the rupture. Moreover, the orientation of the rupture always
316 appeared in the same direction as the thickness heterogeneity in the inflated ATAA layer.

317

318 **Main Sources of Variability**

319 It was noticed that test number 2, an adventitia layer, had by far the highest ultimate stress values.
320 Possibly explained because this layer was the thinnest of all the tissue samples and the donor patient
321 was 36 years old, which made him by far the youngest patient donor (mean age: 66 years).

322

323 **Limitations**

324 *a) Comparison with healthy tissue*

325 Due to the difficulty of obtaining healthy ascending aortic specimens, there was no comparison
326 between healthy aorta and ATAA specimens. As many authors have noticed (Choudhury et al., 2008;
327 Cinthio et al., 2006; Prehn et al., 2009), this comparison can help understanding the causes of the
328 pathology.

329

330 *b) Initial thickness measurement*

331 The measurement of the *ex vivo* initial thickness h_0 of the ATAA tissue was an average estimate of
332 the thickness of the tissue. Measuring the thickness of the specimen at various locations in the tissue
333 was precluded as the sharp shape of the caliper can easily penetrate the soft tissue and damage the
334 tissue. The tests method could be further improved in the future by incorporating a technique
335 capable of capturing the location dependent thickness of the tissue. Other techniques such as, for
336 example, a PC-based video extensometer (Sommer et al., 2008) or a non-contact laser beam
337 micrometer (Iliopoulos et al., 2009) could be used to measure the thickness of the aortic tissue at
338 multiple locations.

339

340 *c) Effect of the loading conditions*

341 A finite element study was undertaken to show that the traction boundary conditions used in our
342 simulation (Eqs. 9-10) only minimally affected the stress calculations in the center region of the
343 specimen. Due to boundary effects, the present approach is limited to characterizing rupture
344 phenomenon occurring far from the boundaries. In the future it would be useful to improve the
345 precision by implementing an approach similar to Zhao (2009) who defined a boundary-effect-free
346 region where the calculated stress distribution remains invariant.

347

348 *d) Pure membrane assumption*

349 Using the present approach, the average stress across the thickness of the inflated ATAA layer was
350 calculated. The assumption of a pure membrane behavior is justified when the concerned tissue is
351 subjected to tensile extension, and is physically thin enough so the transverse shear and the across-
352 thickness stress variation are safely ignored (Horgan and Saccomandi 2003, Lu et al. 2008). Based on
353 the validation analysis (Appendix A), the stress distribution calculated using the present approach
354 was in very good agreement with the average stress distribution calculated between the outer and

355 inner surface using Abaqus® software. This indicates that the pure membrane assumption does not
356 affect the reconstruction of this average stress across the thickness.

357

358

359 **CONCLUSIONS**

360

361 In this manuscript, we have used a straight forward approach to investigate the *in vitro* rupture
362 behavior of ATAA layer during an inflation test. The main advantage of our approach was that local
363 stress field for the ATAA layer was obtained without requiring any material properties. Our results
364 showed that rupture in the ATAA inflated layers was more prone to occur in regions where the layer
365 was weakened. The majority of the time, rupture occurs where the thickness of the layer has been
366 reduced the most. Using maps of the local thickness as a function of pressure one can easily predict
367 the rupture location. Future studies must be conducted to determine if the localized thinning
368 observed in these experiments can also be observed *in vivo* using techniques such as magnetic
369 resonance imaging.

370

371

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373

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377

378

379 **CONFLICT OF INTEREST**

380

381 None

382

383

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- 3** Comparison between four different ultimate stress values calculated at different locations within the same tissue. Test No. 1 to 6 were adventitia layers and Test No. 7 to 15 were media layers.

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- 9 Four different ultimate stresses for each of the 15 ATAA samples where σ^{Lap} is the Laplace stress calculated from Eq. (13), σ^{Max} is the maximum principal stress, σ^{Top} is the maximum principal stress at the node of the top, and σ^{Rup} is the rupture stress calculated from Eq. (11).
- 10 Local thickness evolution (Eq. (12)) in mm. for one representative ATAA sample (Test No. 14). Top view from the initial stage (0.003 MPa) until the final stage (0.057 MPa) and the image captured by the DIS-C system at rupture are presented.

TABLE 1. Demographic information for the collected ATAA specimens.

Test No.	Layer Type	Sex/Age	Diameter before surgery (mm)	<i>Ex vivo</i> thickness (mm)
1	adventitia	M/67	50	1.18
2	adventitia	M/36	50	0.51
3	adventitia	M/55	53	0.79
4	adventitia	M/81	54	0.64
5	adventitia	M/76	52	0.62
6	adventitia	M/71	48	0.55
7	media	M/70	63	0.89
8	media	M/67	50	0.68
9	media	M/54	60	0.98
10	media	M/55	53	1.09
11	media	F/76	55	1.15
12	media	M/81	54	0.91
13	media	M/68	59	1.02
14	media	M/69	51	1.09
15	media	M/71	48	1.04

TABLE 2. Components of the Cauchy stress tensor reported at the NodeMAX, NodeTOP and NodeRUP locations (in MPa). Test No. 1 to 6 were adventitia layers and Test No. 7 to 15 were media layers.

Test No.	NodeMAX			NodeTOP			NodeRUP		
	σ_{11}	σ_{22}	σ_{12}	σ_{11}	σ_{22}	σ_{12}	σ_{11}	σ_{22}	σ_{12}
1	1.124	1.091	-0.036	0.681	0.842	-0.098	1.128	1.062	-0.005
2	3.066	3.812	-0.065	3.035	3.778	-0.064	2.954	3.527	0.084
3	1.233	1.613	-0.011	1.246	1.554	0.023	0.977	0.949	0.189
4	0.938	0.853	0.001	0.922	0.863	-0.002	0.922	0.795	0.012
5	1.964	1.642	0.050	1.920	1.647	0.020	1.699	1.419	-0.042
6	1.035	1.019	-0.046	1.035	1.019	-0.046	0.920	0.933	-0.108
7	0.756	0.997	0.041	0.677	0.909	0.078	0.640	0.924	0.006
8	1.764	1.654	0.097	1.617	1.573	0.077	1.120	0.913	-0.051
9	1.042	1.064	-0.06	1.033	1.067	-0.05	0.903	1.049	-0.027
10	1.308	1.007	-0.012	1.042	1.038	-0.028	1.174	0.927	-0.042
11	0.627	0.622	-0.009	0.549	0.602	-0.03	0.552	0.605	-0.025
12	0.631	0.630	0.076	0.664	0.633	0.042	0.655	0.626	0.040
13	0.819	0.720	-0.055	0.805	0.714	-0.053	0.815	0.725	-0.051
14	0.728	0.866	-0.018	0.800	0.858	-0.016	0.791	0.805	0.0001
15	0.805	0.601	-0.037	0.79	0.588	-0.044	0.714	0.546	-0.041
Mean	1.18	1.21	-0.006	1.12	1.17	-0.013	1.06	1.05	-0.004
Std.	0.64	0.80	0.05	0.64	0.79	0.05	0.59	0.71	0.06

TABLE 3. Comparison between four different ultimate stress values calculated at different locations within the same tissue. Test No. 1 to 6 were adventitia layers and Test No. 7 to 15 were media layers.

Test No.	σ^{Lap} (MPa)	σ^{Max} (MPa)	σ^{Top} (MPa)	σ^{Rup} (MPa)
1	0.9695	1.1481	0.8889	1.0719
2	3.5825	3.8183	3.7841	3.5269
3	1.1725	1.6134	1.5558	0.9755
4	0.8116	0.9385	0.9222	0.8265
5	1.5928	1.9724	1.9221	1.4644
6	0.8414	1.0752	1.0752	0.9335
7	0.7275	1.0049	0.9337	0.6412
8	1.4016	1.8214	1.6756	1.0057
9	0.8503	1.1148	1.1036	0.9309
10	0.8215	1.3086	1.0692	1.1733
11	0.4863	0.6346	0.6169	0.6015
12	0.5559	0.7074	0.6936	0.6286
13	0.7283	0.8438	0.8302	0.7259
14	0.8244	0.8687	0.8623	0.8028
15	0.6386	0.8121	0.7994	0.5891
Mean	1.0669	1.3121	1.2488	1.0598
Std.	0.7573	0.7979	0.7933	0.7236

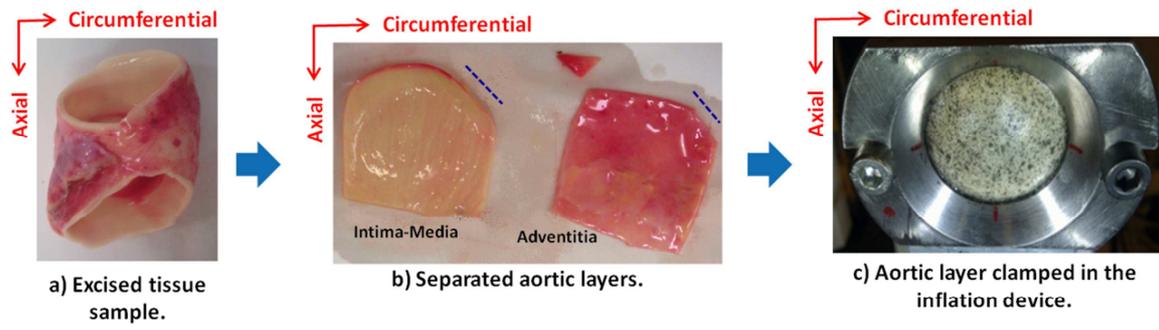


Fig. 1. ATAA specimen preparation for the inflation test.

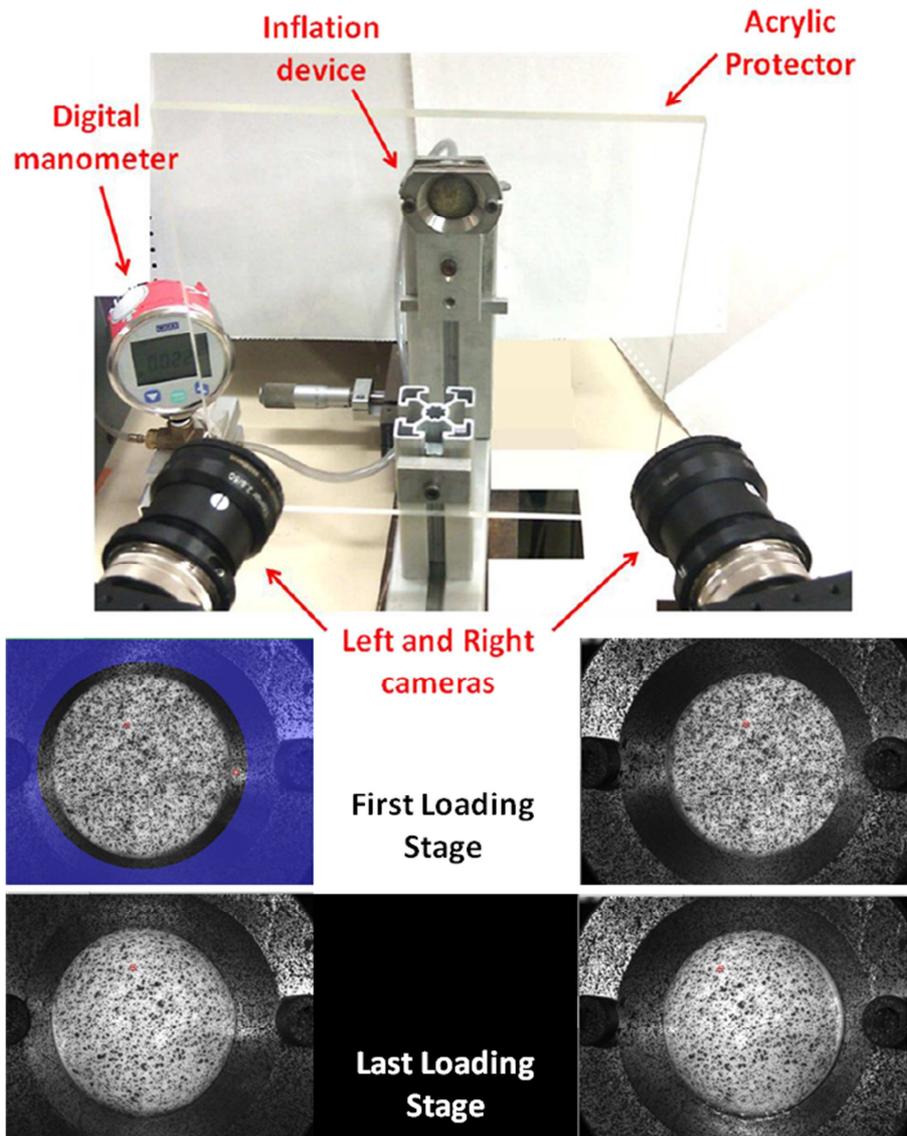


Fig. 2. View of the experimental set-up and the inflation of the ATAA layer through the left and right cameras of the DIS-C system. An image is recorded every loading stage defined at 3 kPa, for the duration of the test. Note that the acrylic protector is used to prevent water from reaching the cameras when the specimen bursts.

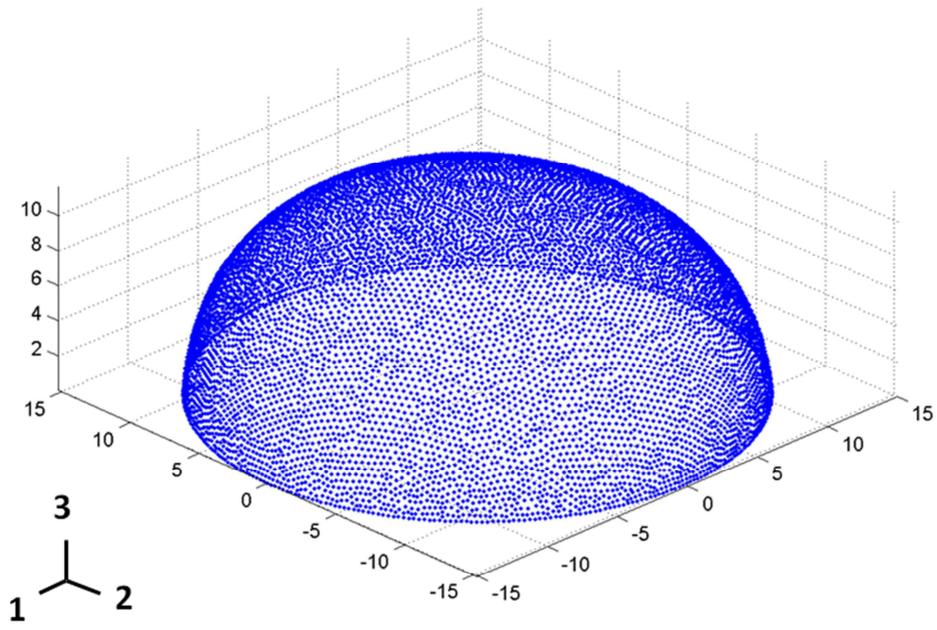


Fig. 3. Reconstructed shape of the ATAA layer at the final inflation stage. The 3D coordinates of each material point were used to reconstruct the shape.

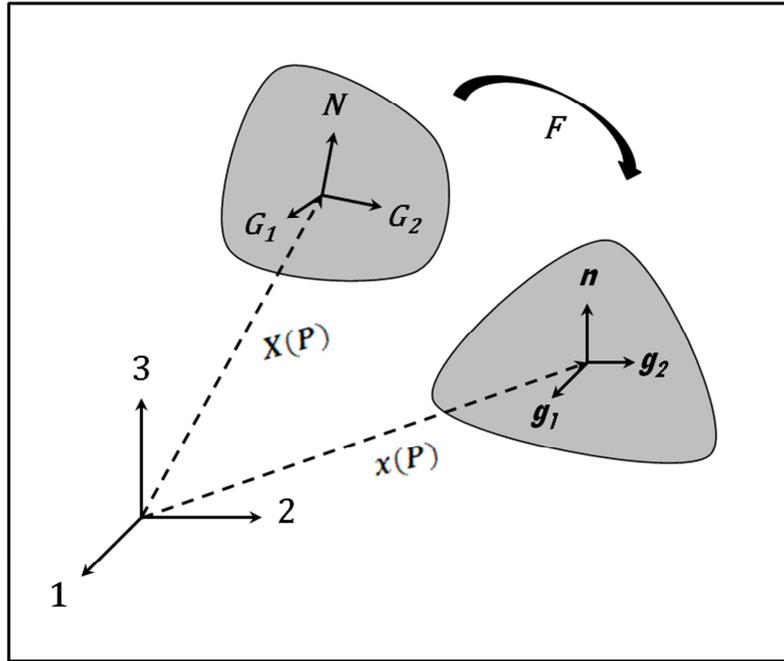


Fig. 4. Schematic of the kinematics and base vectors.

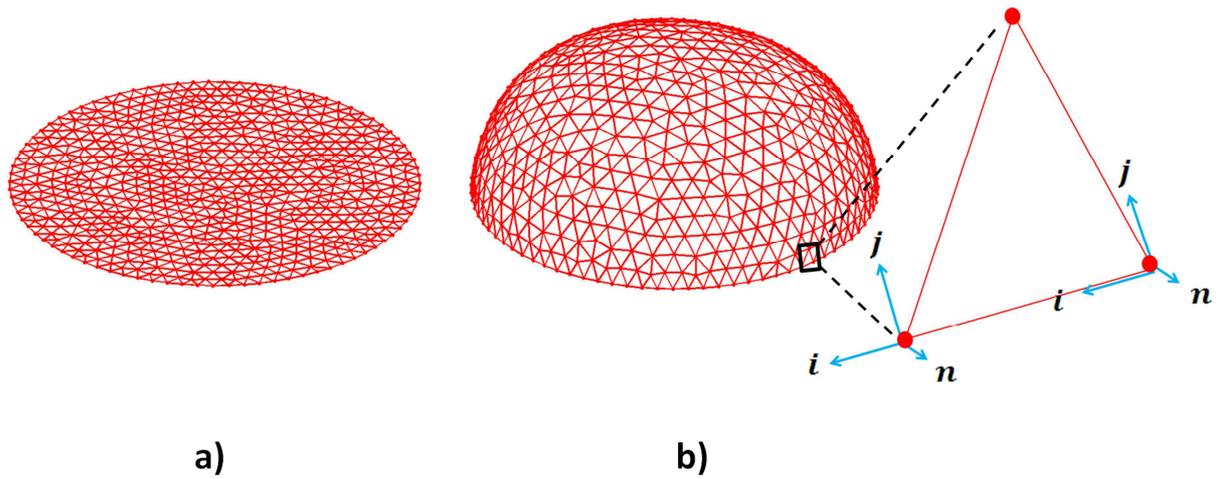


Fig. 5. Discretization of the surface. The unchanged mesh is deformed from a) the initial to b) the current configuration. For one boundary element the local (i, j, n) Cartesian frame used to define the boundary conditions is shown.

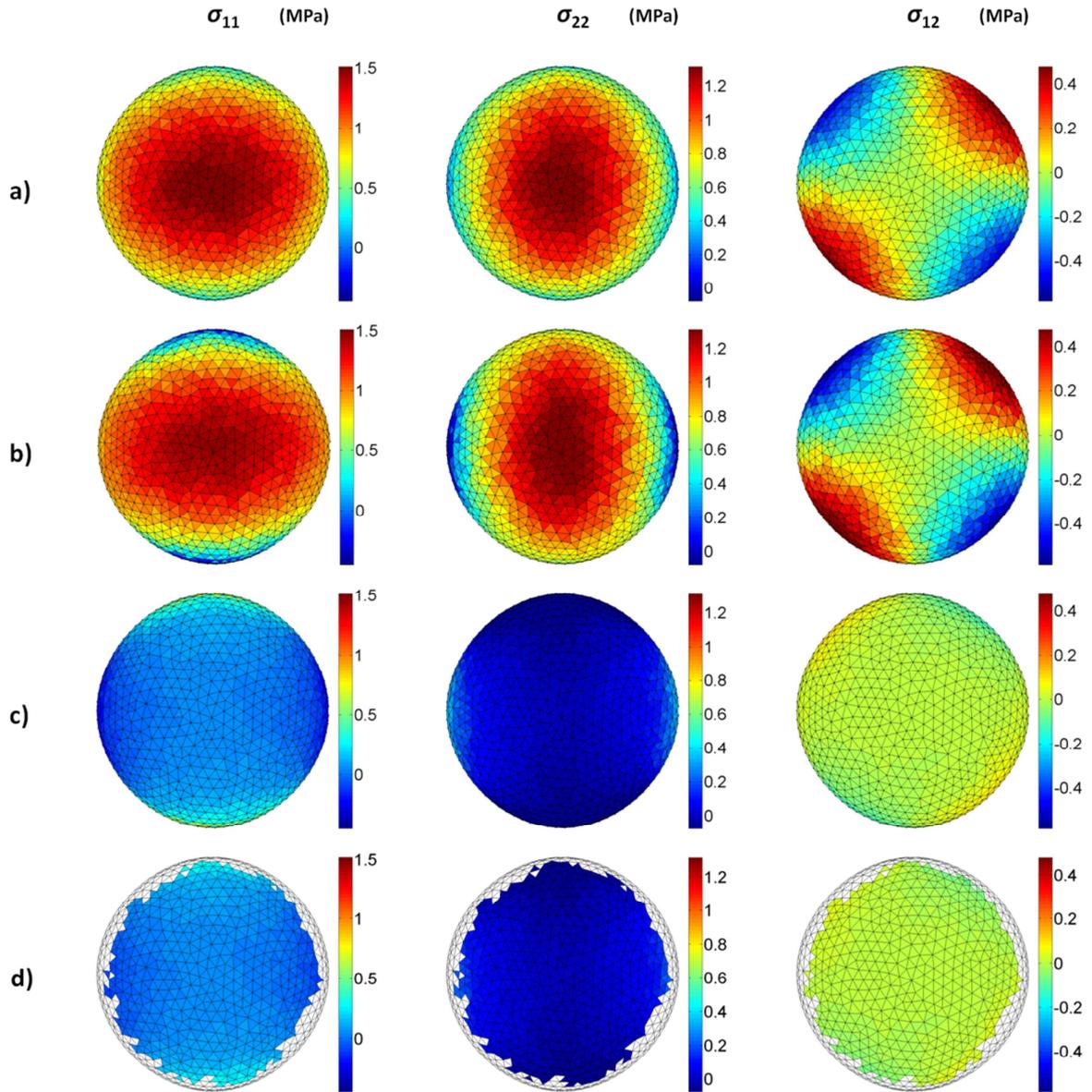


Fig. 6. Top view of the element by element comparison between stress fields calculated by a) the FEA simulation (reference) and b) our approach. The absolute error (in MPa) between a) and b) is presented in c) and in d) where the boundary elements are neglected.

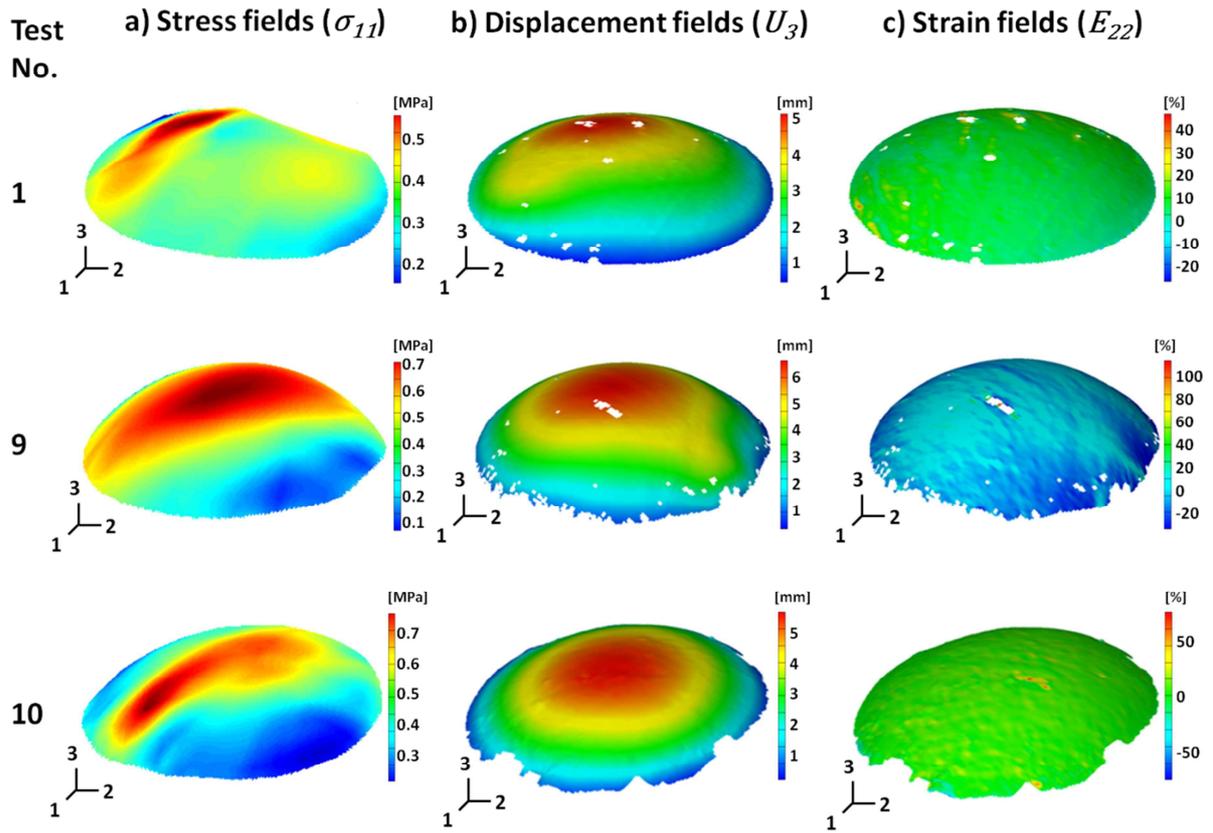


Fig. 7. The a) stress field (σ_{11}), b) displacement field (U_3) and c) strain field (E_{22}) for three ATAA specimens all at a pressure of 0.027 MPa.

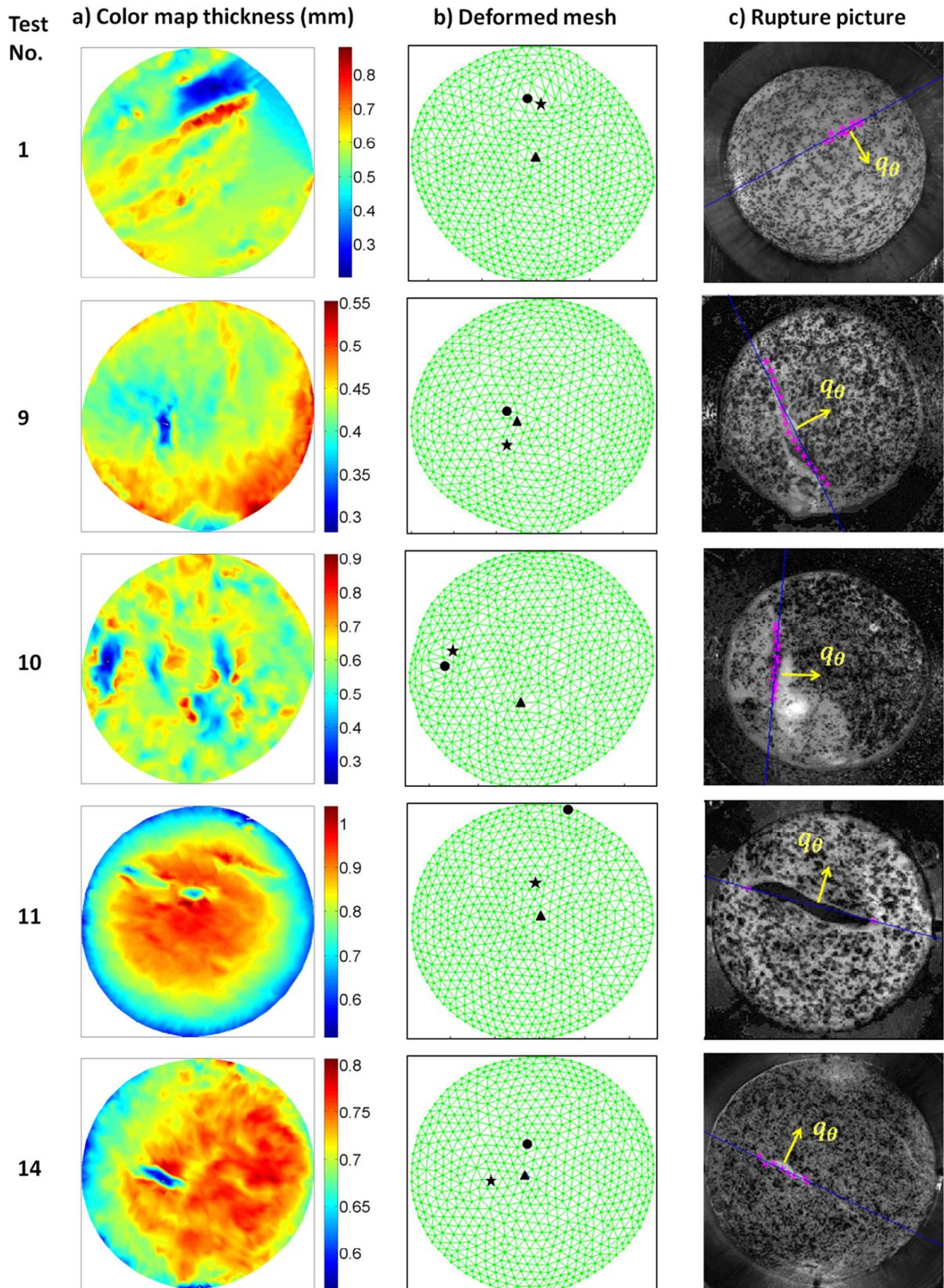


Fig. 8. ATAA rupture. For each test, a) the color map of the thickness measurement, b) the deformed mesh (● = NodeMAX, ▲ = NodeTOP, ★ = NodeRUP) and c) the rupture picture where q_θ is the unit vector perpendicular to the rupture.

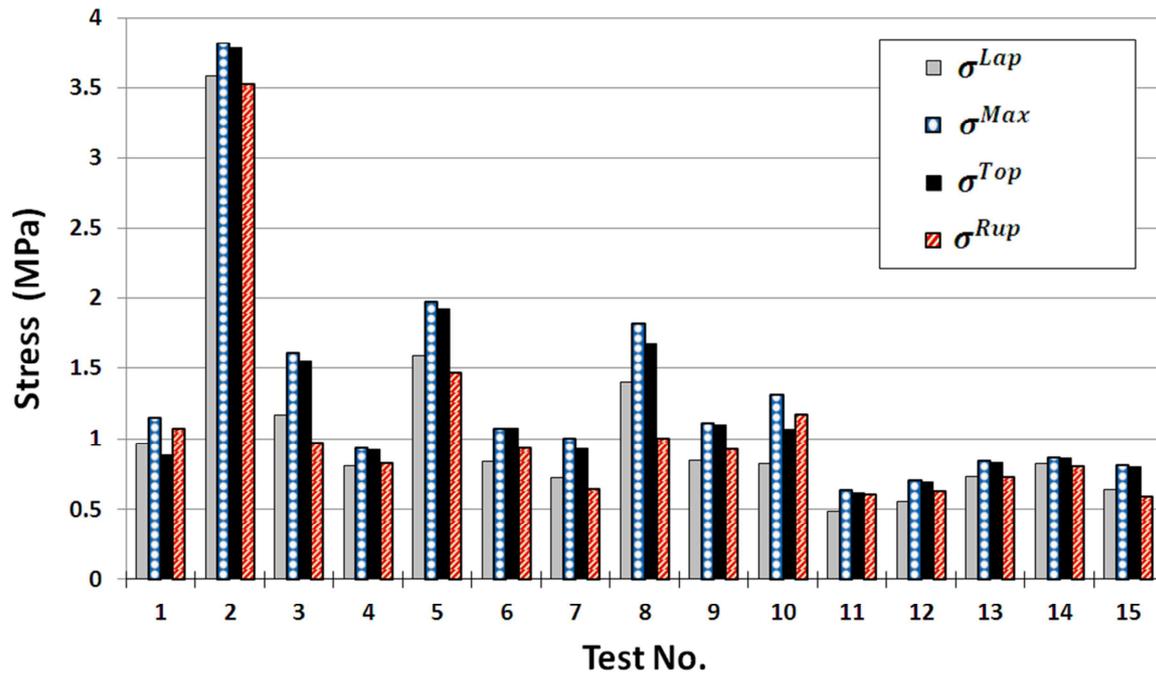


Fig. 9. Four different ultimate stresses for each of the 15 ATAA samples where σ^{Lap} is the Laplace stress calculated from Eq. (12), σ^{Max} is the maximum principal stress, σ^{Top} is the maximum principal stress at the node of the top, and σ^{Rup} is the rupture stress calculated from Eq. (10).

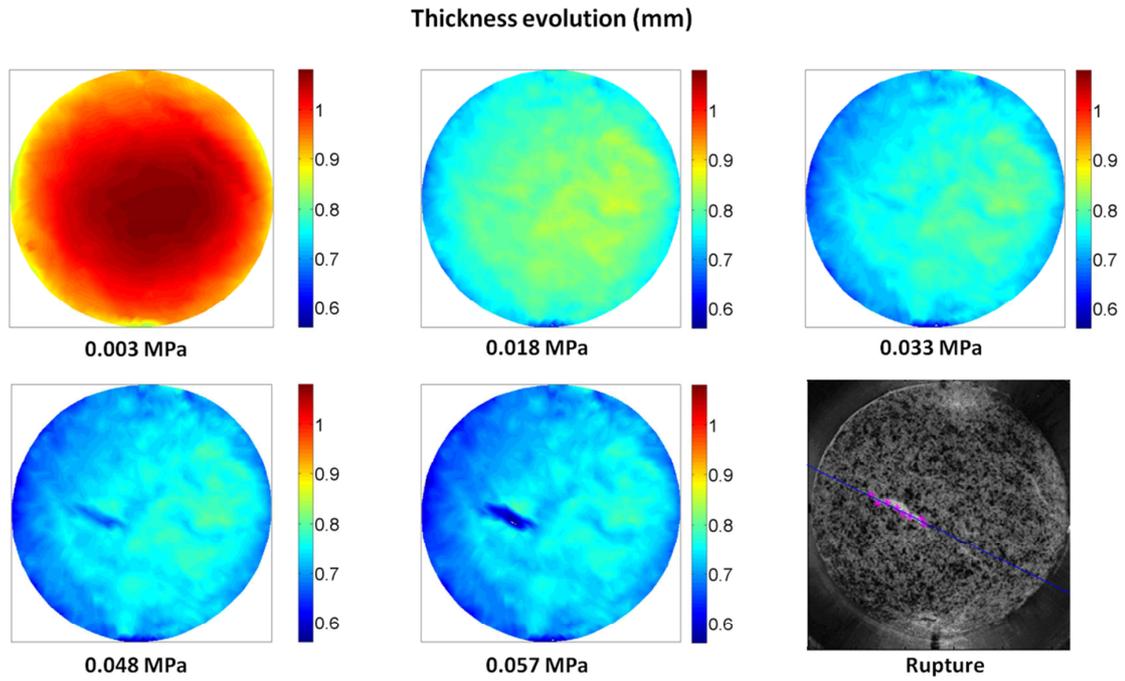


Fig. 10. Local thickness evolution (Eq. (11)) in mm. for one representative ATAA sample (Test No. 14). Top view from the initial stage (0.003 MPa) until the final stage (0.057 MPa) and the image captured by the DIS-C system at rupture are presented.

1 APPENDIX A

2 To validate the membrane assumption the stress fields calculated by our approach on a pre-defined
3 geometry were compared to reference stresses provided by a finite element analysis (FEA) on the
4 same reference geometry. In order to compare exactly the data at the same points, we used the
5 same nodal arrangement for both methods, which means that we had to interpolate the reference
6 FEA results into our own predefined mesh used in our approach (644 nodes and 1203 elements).

7

8

9 **Validation Process**

10

11 A FEA simulation of the inflation process was performed with the aim to numerically reproduce an
12 experimental dataset. Using the Abaqus® software we created a 0.85 mm thick circular patch of 30
13 mm of diameter, corresponding to the area of interest (AOI) for an inflated of the experimental aortic
14 layers. In order to perform the numerical simulation it was necessary to define the material
15 properties of the circular patch, which were based on the anisotropic hyperelastic Holzapfel-Gasser-
16 Ogden (HGO) model (Holzapfel et al. 2000). The material properties defined for the FEA simulation
17 were obtained from the literature: $density= 5.0e-4$, $C_{10}= 0.0764$ MPa, $D= 1.e-8$, $k_1= 0.0839611$ MPa,
18 $k_2= 1.2644611$, $\kappa= 0$ and $\beta= 41^\circ$.

19

20 The nodes on the boundary of the circular patch were pinned allowing their rotation. The applied
21 load was defined as a uniform pressure of 0.06 MPa, applied to the inner surface of the circular patch
22 (Fig. A1). Finally the mesh size of the simulation was defined by 10119 nodes and 19887 shell
23 elements.

24

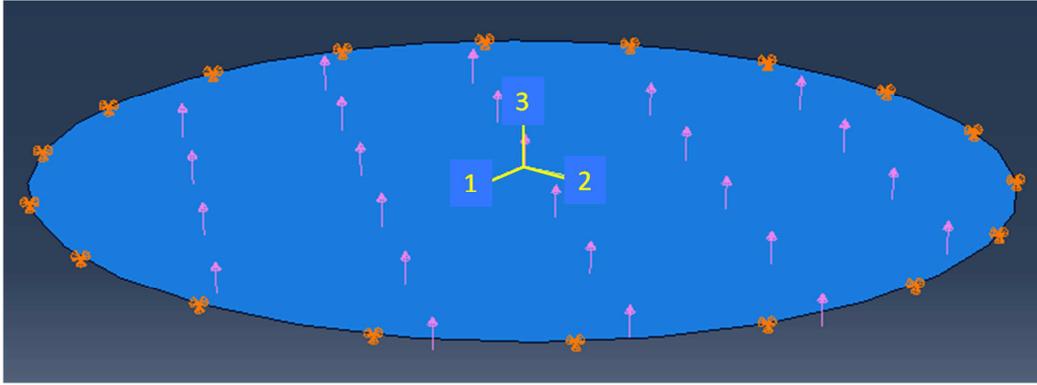


Fig. A1. Lateral view of the circular patch created in Abaqus® software. Boundary conditions allow the rotation. A uniform pressure is applied to the inner surface of the patch.

25

26 The FEA simulation provided the displacement and stress distributions at the end of the inflation. The
27 stress fields provided by this FEA simulation were then used as a reference for the validation of our
28 approach and the final geometry provided by this FEA was also used as the reference geometry for
29 validating our approach.

30

31 For our simulation, we used shell elements which yielded two sets of stress fields in the results, one
32 located at the inner surface (Fig. A2-a) and another located at the outer surface (Fig. A2-b) of the
33 inflated membrane. The stress at the inner surface was slightly lower than the stress at mid-thickness
34 and the stress at the outer surface was slightly higher than the stress at mid-thickness. For a 0.85 mm
35 thick sheet, it was estimated that the mean absolute difference between the stress at the inner and
36 outer surface was 0.32 MPa for σ_{11} , 0.26 MPa for σ_{22} and 0.0013 MPa for σ_{12} . In contrast, our
37 approach provides directly the stress field at mid-thickness. Knowing this, the two stress fields, outer
38 and inner, obtained from the FEA simulation were averaged to provide an accurate comparison with
39 our approach.

40

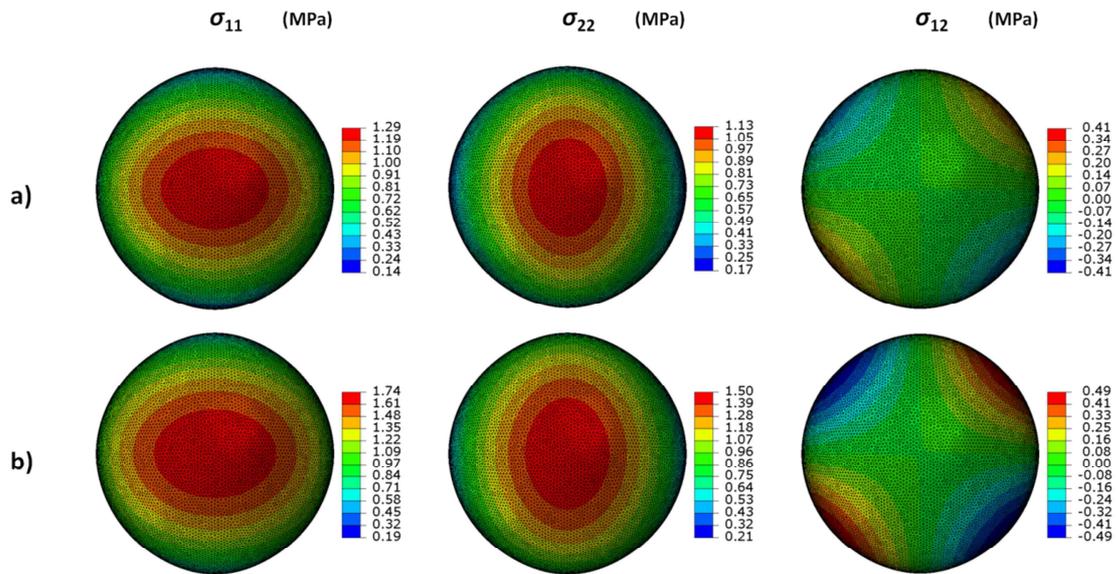


Fig. A2. FEA computation (Abaqus® software top view) provided stress fields located at a) the inner surface and b) the outer surface of the inflated membrane.

41

42 After extracting the nodal displacements, we interpolated the values across a grid of pixels in order
 43 to create a dataset with the same spatial resolution as the experimental data (Fig. A3). Then we
 44 applied our approach to these experimental-like data in order to reconstruct the maps of the Cauchy
 45 stress tensor. Using the Abaqus® output file, we interpolated the stress values at the same nodes
 46 that we reconstructed them. Afterwards our Cauchy stress estimates, from applying our approach to
 47 the experiment-like data, were compared to the Cauchy stress values provided by the FEA
 48 computation.

49

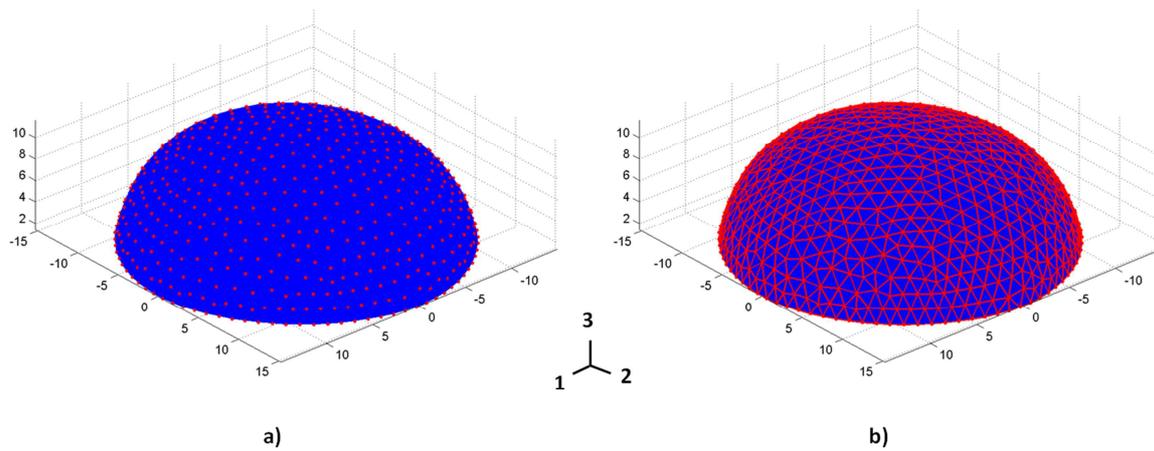


Fig. A3. The 3D deformed geometry (surface) obtained with the FEA simulation (blue) was imported into Matlab®

- a) Nodes where the Cauchy stress will be estimated are defined (red dots) across this surface**
- b) The surface is meshed using the Delaunay triangulation.**

50

51 Therefore, we were able to compare, element by element, the results of our approach and those of a
 52 reference FEA simulation. In Figure A4-a the reference stress distribution from the FEA simulation is
 53 shown and in Figure A4-b the stress distribution from our approach is displayed. The difference
 54 between both was calculated at each element and is presented in Figure A4-c. Mean absolute errors
 55 of 0.031 MPa for σ_{11} , 0.002 MPa for σ_{22} , and 0.005 MPa for σ_{12} . were calculated between our
 56 approach and the FEA simulation. These mean absolute errors are equivalent to mean relative errors
 57 of 3.5% for σ_{11} , 0.3% for σ_{22} and 0.5% for σ_{12} .

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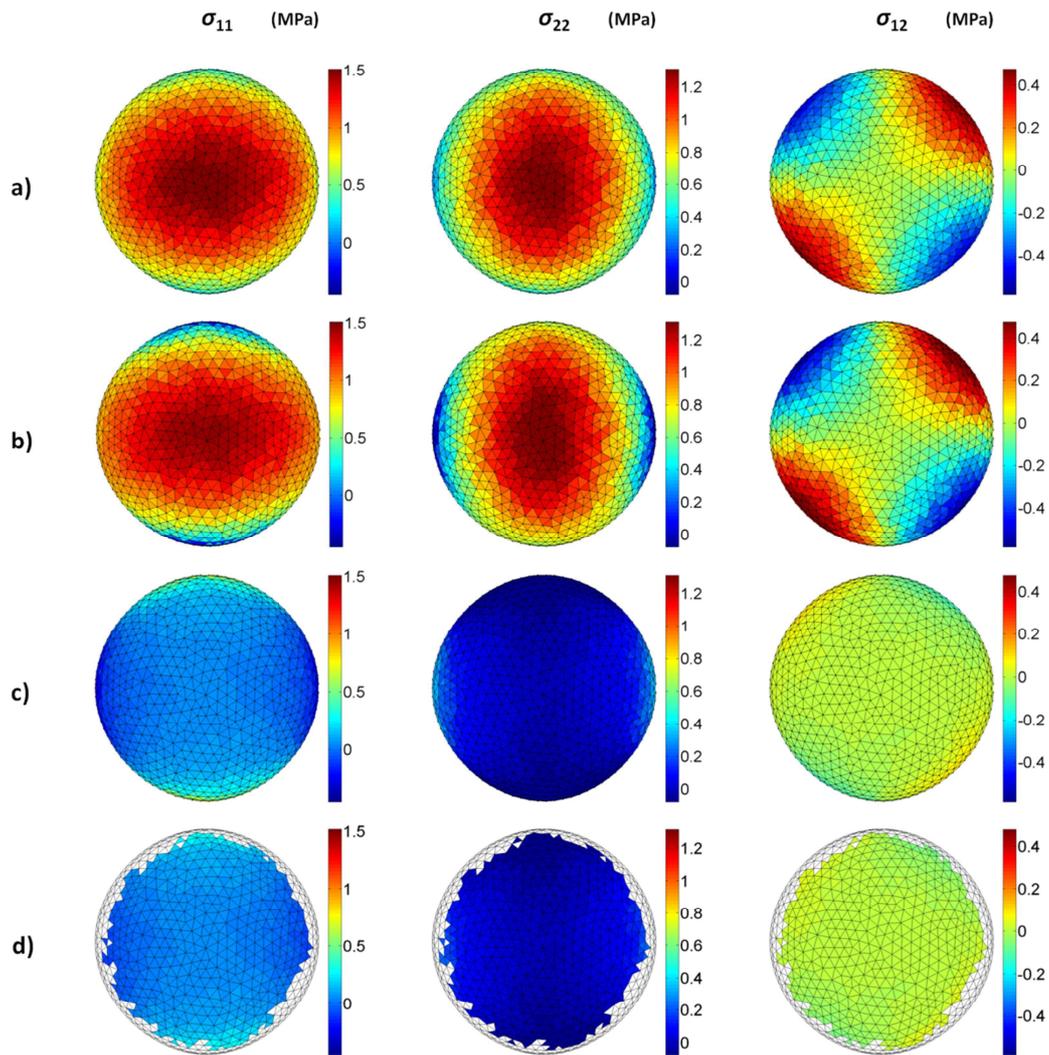


Fig. A4. Top view of the element by element comparison between stress fields calculated by a) the FEA simulation (reference) and b) our approach. The absolute error (in MPa) between a) and b) is presented in c) and in d) where the boundary elements are neglected.

59

60 The differences in the results are due to the different boundary conditions used for each method (i.e.

61 pinned for the FEA approach and traction boundary conditions for our approach). An interesting

62 result was that the boundary conditions only affected the estimated stress near the border. After

63 removing the three first stripes of triangles adjacent to the border (Fig. A4-d), the mean absolute

64 errors were reduced to 0.008 MPa for σ_{11} , 0.013 MPa for σ_{22} , and 0.008 MPa for σ_{12} . These mean

65 absolute errors are equivalent mean relative values of 0.8% for σ_{11} , 1.4% for σ_{22} and 0.8% for σ_{12} ,

66 indicating that the stress estimates contain some errors along the border due to the assumed

67 boundary conditions but these errors vanish rapidly away from the border.