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Biomechanical response of varicose veins to elastic compression: a numerical study

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Keywords: Varicose veins; trans-mural pressure; Finite Element Updating; Medical Compression Stockings

Word count (introduction through conclusion): 1 988

26 Abstract

27 A patient-specific Finite-Element (FE) model of the human leg is developed to model the stress
28 distribution in and around a vein wall in order to determine the biomechanical response of varicose veins
29 to compression treatment. The aim is to investigate the relationship between the local pressure on (the)
30 soft tissues induced by wearing the compression garment and the development and evolution of varicose
31 veins and various skin-related diseases such as varicose veins and ulcers. Because experimental data on
32 the mechanical properties of healthy superficial veins and varicose veins are scarce in literature,
33 ultrasound images of *in vivo* varicose veins are acquired and analysed to extract the material constants
34 using Finite Element Model Updating. The decrease in trans-mural pressure, which conditions the
35 effectiveness of compressive treatments, is computed from the simulation results. This constitutes the
36 original added value of the developed model as decreases in trans-mural pressures cannot be assessed
37 experimentally by any other means. Results show that external compression is effective in decreasing the
38 trans-mural pressure, thereby having a positive effect in the control and treatment of vein-related
39 diseases.

40

41 Introduction

42 Compression therapy by Medical Compression Stockings (MCS), which is considered as the “gold
43 standard” therapy for venous insufficiency, has been a topic of important research for 30 years. The
44 following effects or actions of MCS have gained a special interest:

45 - hemodynamic effects: (Mayberry et al., 1991), (Ibegbuna et al., 2003), (Guesdon et al., 2007), (Downie et
46 al., 2008) and (Wang et al., 2012), in continuation of pioneer studies on collapsible tubes: (Katz et al.,
47 1969), (Moreno et al., 1970) and (Kamm and Shapiro, 1979);

48 - clinical and post-surgery effects: (Nehler et al., 1992), (Nehler et al., 1993)(Kern et al., 2007),
49 (Villavicencio, 2009) and (Hamel-Desnos et al., 2010);

50 - skin and deep tissue compression: (Wildin et al., 1998), (Agu et al., 1999), (Best et al., 2000), , (Yeung et
51 al., 2004), (Liu et al., 2005), (Gaied et al., 2006), (Liu et al., 2006), (Dai et al., 2007), (Lee and Han, 2010),
52 (Martinez et al., 2010), (Avril et al., 2010) and (Dubuis et al., 2012).

53

54 However, some of the mechanisms by which MCS **act(s)** are still not clearly understood. The present study
55 aims at addressing the effect of MCS on varicose veins by adopting a finite-element modelling approach.

56

57 **Materials and methods**

58 **-1- Imaging methods**

59 Images are acquired on the calf of a 50 year old male patient with a varicose vein:

60 - Magnetic resonance imaging is applied with a two dimensional T1 TSE modality on a Siemens 1.5T
61 scanner using ()pixel resolution: $0.7813 \times 0.7813 \text{ mm}^2$, slice thickness: 3.9 mm ().

62 - Echography is applied for obtaining images with a better spatial resolution in the region of the varicose
63 vein. The ultrasound images are acquired with and without 15-20 mmHg MCS (AFNOR, 1986) both in the
64 standing and supine position (Fig 1).

65

66 **-2- Finite Element Model**

67 *Finite element mesh*

68 The geometry is reconstructed from both MRI (deep tissues) and ultrasound scans (vein). The meshing
69 tools available in ABAQUS® are used to generate the computational mesh of the reconstructed geometry
70 (Fig. 2). Continuum plane strain elements with a hybrid formulation are used for the muscle, fat and vein
71 wall. A 2-D model is used since (Avril et al., 2010) showed that the 2-D approach predicts a similar
72 pressure distribution in the calf tissues as a full 3-D model.

73 A hybrid formulation is preferred because the soft tissues are defined as quasi-incompressible (Poisson's
74 ratio > 0.475). Truss elements are used for the discretisation of the muscular aponeurosis, the skin and the
75 MCS. A relatively finer discretisation is used around the vein. The models contain about 13 600 elements
76 and 33 800 degrees of freedom (including the Lagrange multiplier variables). A mesh convergence study
77 was conducted showing that further mesh refinement produces a negligible change in the solution.

78

79 *Internal blood pressure in the vein*

80 The intravascular pressure is accounted for by a constant pressure applied on the inner surface of the vein
81 wall. The pressure imposed is 15mmHg in the supine position and 90mmHg in the standing position. This
82 pressure is responsible for an initial pre-stress of the vein wall before applying compression, which is
83 considered by applying an initial circumferential pre-stress on the vein wall to counterbalance this
84 pressure. The value of the circumferential pre-stress in each element of the vein wall is determined by

85 applying the Laplace law. A 1 kPa pre-stress is also defined on the skin in the circumferential direction
86 (Flynn et al., 2011).

87

88 *Boundary conditions*

89 The tibia and fibula are fixed in this model.

90

91 *Contact pressure on the skin.*

92 The interaction between the skin and the sock is enforced using the default ABAQUS® parameters in the
93 normal direction (Tab. 1) and using a penalty method in the tangential direction. A skin-to-textile friction
94 coefficient of 0.3 is used for the tangential direction, as reported in the literature (Gerhardt et al., 2009).

95

96 *Constitutive equations*

97 A summary is given in Tab 2. A linearized model is preferred for the vein because (i) the developed
98 biomechanical model is used to simulate the deformation of the leg between two states of loading
99 (compressed and uncompressed) which are very close one to the other, and (ii) we do not need to know
100 the stress-free state of our leg as (it) is the case with nonlinear material behaviour models. The Poisson's
101 ratio is fixed (to) at 0.49 (Wells and Liang, 2011) and two different stiffness values are identified, in supine
102 and standing positions respectively, as the diameter reduction of the vein lumen, due to a 15-20 mmHg
103 class compression sock, is (of) 10% in the supine and (of) 3% in the standing position.

104

105 *Analysis procedure*

106 Simulation is divided into 3 steps as previously described:

107 *Step 1* Initial stress on vein wall and skin and blood pressure loading

108 *Step 2* Inflate sock and activate the contact conditions between the skin and the sock

109 *Step 3* Release the MCS and calculate the equilibrium position

110

111 The resolution is performed via an implicit scheme. The default convergence criteria in ABAQUS/Standard
112 are used (Tab. 1).

113

114 Results

115 -1- Mechanical properties of the vein wall and fat

116 The FE model is calibrated against the echographic images of compressed and uncompressed legs
117 acquired in the standing and supine positions. The identified Young's moduli for the vein wall are 100 kPa
118 in the supine position and 836 kPa in the standing position. The identified C_{10} constant for the fat,
119 characterizing the shear modulus in the Neo-Hookean strain energy function, is 5 kPa.

120

121 -2- Parametric study

122 Simulations are run corresponding to the supine and standing positions. Salient quantitative results of
123 each simulation are reported in the Appendix through Table A1 to A7, where the influence of the
124 following parameters is reported:

125 [a] Ratio of adipose tissue to leg size (Table A1);

126 [b] Position on the leg contour (Table A2);

127 [c] Vein lumen size (Table A3);

128 [d] Depth of vein in adipose tissue (Table A4);

129 [e] Effect of the applied external compression (Table A5);

130 [f] Influence of the "type" of fat (Table A6 for the influence of the stiffness and Table A7 for the
131 influence of the incompressibility parameter).

132

133 Based on the results, it can be summarized that the biomechanical response of veins is subject to three
134 main mechanical factors: the vein size, the local radius of curvature and the fat stiffness. This highlights
135 the strong patient-specific response of the leg to external compression.

136

137 Parametric studies were also (run about) carried out on the element types, the type of contact and the
138 type of material behaviour. Results (Tables A8 through A12) show that the modelling assumptions do not
139 affect the trends (about) of the three main mechanical factors.

140

141 Discussion

142 -1- Material properties

143 The stiffness properties of the fat and of the vessel wall are identified by Finite Element Model Updating.
144 The obtained values are consistent with values reported in the literature. In a study to determine the *in*
145 *vitro* elastic properties of human saphenous vein segments, (Wesly et al., 1975) reported that the *in vitro*
146 saphenous tangent modulus in the circumferential direction is considerably smaller at pressure ranges
147 corresponding to **the** supine position (30 kPa and 65 kPa at 10 mmHg and 25 mmHg of pressure
148 respectively) but is similar to carotid values at pressures similar to those encountered *in vivo* in the
149 standing position (990 kPa and 1.5 MPa at 75 mmHg and 100 mmHg of pressure respectively). This is
150 consistent with other studies, conducted both *in vivo* and *in vitro*, showing that veins exhibit a non-linear
151 mechanical behaviour and become stiffer as **(it) they deform(s)**(Buhs et al., 1999) (Zhao et al., 2007). More
152 recently, based on the material parameters reported by (Chuong and Fung, 1986), Han estimated the
153 Young's modulus of blood vessels to be 100 kPa (Han, 2011). Material parameters of the Fung exponential
154 strain energy function have also been reported for the human saphenous vein (Zhao et al., 2007) and for
155 porcine jugular veins (Lee and Han, 2010). They are all comparable with the elastic properties found in
156 our approach.

157
158 The material parameter identified for the fat lies within the range of values reported **(by)** in a study
159 involving six patients. (Dubuis et al., 2012)

160
161 The fact that the narrowing of the vein is less pronounced in the standing position, for a given level of
162 external compression, may also be due to the fact that the applied external pressure has to work against a
163 higher internal blood pressure (Partsch and Partsch, 2005), (Partsch, 2007).

164 165 -2- Main trends

166 The results obtained using the proposed model show that hydrostatic pressure in fat **is (i) (is)** effectively
167 increased and **(ii)** by an order of magnitude comparable to the mean contact pressure exerted by the MCS
168 on the skin.

169

170 The computed hydrostatic pressure in the fat is essential to understanding how the pressure is transmitted
171 through the superficial soft tissues. Moreover the increase in tissue pressure is regarded as a crucial
172 mechanism (to the) in compressive treatments (Bergan, 2007). Clearly, appreciating how geometric and
173 material parameters affect the transmission of pressure is an important step to understanding both the
174 modes of action of EC treatment and the rationales behind its efficacy.

175

176 Other research teams have reported satisfactory results for the measurement of vein deformation under
177 compression (Partsch et al., 2010) but have not used these results for quantifying the trans-mural
178 pressures. The results of our model indicate that 15-20 mmHg MCS are effective in decreasing the trans-
179 mural pressure on vein walls. The values predicted are twice as high in the standing position than in the
180 supine position. This trend corroborates that reported *in vitro* by (Gardon-Mollard and Ramel, 2008).

181

182 **-3- Clinical relevance**

183 From a clinical perspective, an increase of the trans-mural pressure on varicose vein walls exacerbates the
184 disease and the underlying Chronic Venous Insufficiency (CVI). The goal of compression therapy is to
185 restore a trans-mural pressure which is as normal as possible, by increasing the perivenous tissue
186 pressure (Gardon-Mollard and Ramel, 2008). The results reported here confirm the idea that MCS work
187 towards reducing the trans-mural pressure. In addition, trans-mural pressure is known to be related to
188 the tension of the vein wall according to the Laplace law (Gusic et al., 2005). Reduction of the tension
189 implies a smaller number of alterations in the vein wall associated with various pathologies. Another
190 consequence is a greater stability with respect to axial buckling and tortuosity development (Han,
191 2007)(Han, 2009)(Han, 2012).

192

193 The action of MCS may also affect the remodelling of the vein. (Travers et al., 1996) (have) observed that
194 varicose saphenous veins contained significantly higher amounts of collagen in all layers of the vein wall
195 and that these collagen fibres were seen to invade and break up regular muscle layers of the media in
196 varicosis. Reduction of the tension in the vein wall under the action of MCS is prone to hinder these
197 effects.

198

199 Another important clinical (important) aspect concerns the evolution of CVI more generally: because CVI
200 is both progressive and irreversible, clinical symptoms associated with venous insufficiency increase in
201 severity with time (Suzuki et al., 2009). Important efforts are still necessary to predict numerically the
202 long-term action of MCS in preventing the progression of venous stasis and the apparition of associated
203 symptoms such as oedema, pigmentation, and ulcers on the skin.

204

205 **Conclusion**

206 In this study, a FE model of a human leg with a varicose vein has been developed to compute the stress
207 distribution in and around the vein wall and analyse the biomechanical response of varicose veins to
208 external compression in terms of trans-mural pressures. Experimental data on the mechanical properties
209 of healthy superficial veins and varicose veins being scarce in literature, ultrasound images of *in vivo*
210 varicose veins have been acquired and analysed to extract the material constants of the vein wall and that
211 of the fat, using Finite Element Model Updating.

212

213 The model (brings)provides a new insight on MCS mechanical action and its possible benefits. The results
214 confirm the idea that MCS work towards reducing (the) trans-mural pressure and are effective in
215 narrowing leg veins, which is important for the clinical consequences.

216

217 Future developments include a validation of the proposed approach and of its medical outcomes using
218 clinical studies.

219

220 **Acknowledgement**

221 None

222 **Conflict of interest**

223 None

224

225 **References**

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| | |
|-----------|---|
| | results. |
| Table A10 | Influence of the contact formulation for the Fat/Vein interface (Fat/Vein). Two aspects of the contact specifications were considered: (i) normal and (ii) tangential behaviour of the contact interaction properties. Both “hard” and “soft” constraint methods were investigated for enforcing the contact pressure-overclosure relationship (normal direction). Furthermore, a tie constraint (each node on the slave surface is constrained to have the same motion as the point on the master surface to which it is closest) was also investigated in place of the contact interaction. Results show minor changes. |
| Table A11 | Influence of the contact formulation for the Fat/Muscle interface (Fat/Muscle). The same contact conditions were investigated. Very little change was observed. |
| Table A12 | Influence of the contact formulation for the Skin/MCS interface (Skin/MCS). Results show that the “softened” contact algorithms available in ABAQUS/Standard (and subsequently retained as a constraint method for enforcing the contact pressure-overclosure relationship) performed better than the “hard” contact algorithms. The main advantage of the “softened” contact algorithms is that clearance is calculated from surface to surface instead of from node to surface. As a consequence, the contact load is evenly distributed along the interacting surfaces. |

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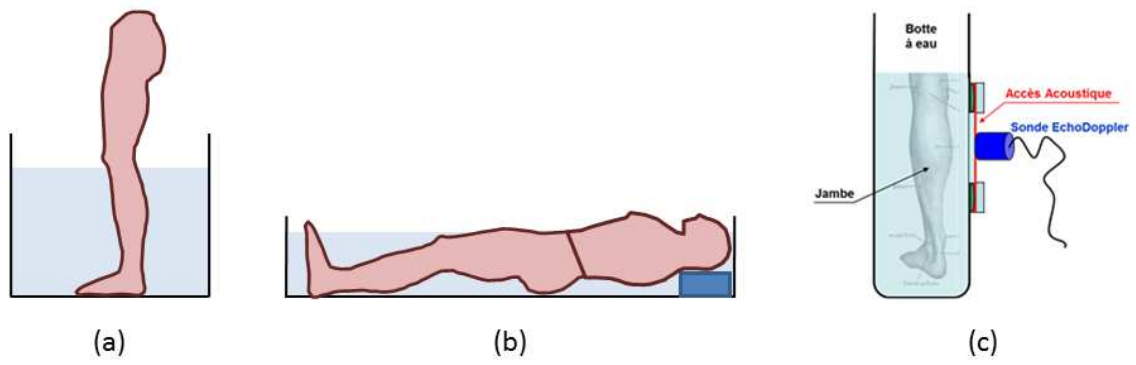


Figure 1. Acquisition of echographic images both in the standing and supine position (a and b). A special precaution was taken as illustrated in panel c.

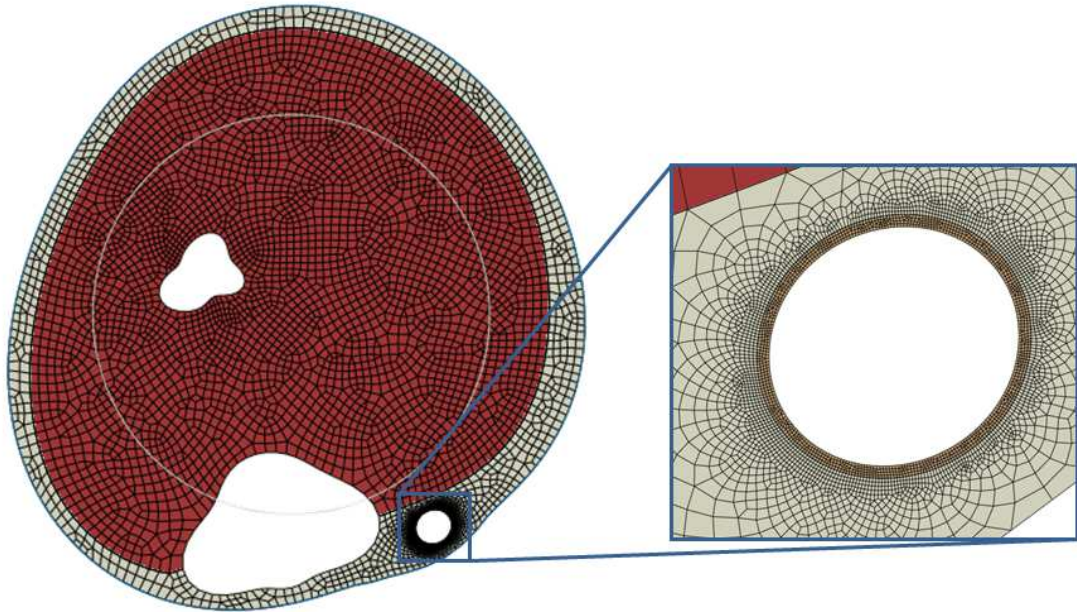



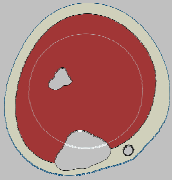
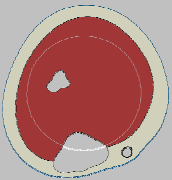
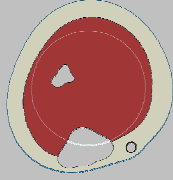
Figure 2: Finite element mesh of the 2D patient specific mesh. It consists of continuum plane strain elements for the muscle, fat and vein wall and truss elements for the muscular aponeurosis, skin and MCS. A relatively finer discretisation is used in the vicinity of the vein wall. The thickness-to-radius ratio of the vein is taken as 0.1, as reported in the literature.

| Simulation element | ABAQUS parameters used |
|---|--|
| Truss elements | Truss cross-sectional area = 1.0 mm ² |
| Contact pairs (for surfaces in contact) | <i>Contact algorithm: pure master-slave contact</i> |
| Contact between Skin and textile | <p>Tangential Behaviour: Friction formulation=PENALTY, Behaviour independent of slip rate, pressure and temperature, friction coefficient = 0.3</p> <p>Normal Behaviour : Contact pressure-overclosure relationship= EXPONENTIAL (SOFT), <i>This means that the contact pressure transmitted between the two interacting surfaces increases exponentially as the clearance between them, measured in the contact (normal) direction, diminishes (starting from a user-defined threshold value).</i> Separation of the surfaces is not allowed Constraint Enforcement Method= PENALTY</p> |
| Contact fat-muscle | <p>Tangential Behaviour : FRICTIONLESS</p> <p>Normal Behaviour: Contact pressure-overclosure relationship= EXPONENTIAL Separation of the surfaces is not allowed Constraint enforcement method= AUGMENTED_LAGRANGE</p> |
| Constraint between surfaces :- -1- Bone-Fat -2- Bone-Muscle -3- Fat-Vein -4- Aponeurosis-Muscle -5- Skin-Fat | <p>Type of constraint : TIE</p> <p><i>Tie constraint means that each node on the slave surface is constrained to have the same motion as the point on the master surface to which it is closest</i></p> <p>Slave surfaces are adjusted so that surfaces are in contact</p> <p>Rotational DOF are also tied</p> |
| Steps of the FE analysis (steps 1 to 3) | <p>Implicit resolution</p> <p>Maximum number of steps allowed = 100</p> <p>Initial increment time step size = 1.0s</p> <p>Minimum increment time step size = 1e-5s</p> <p>Maximum increment time step size = 1.0s</p> <p>Nlgeom=ON</p> <p>Solution technique = Full Newton</p> <p>Equation solver = Direct (<i>i.e. the solver finds the exact solution (up to machine precision) of the set of linear equations obtained at each iteration of the Newton method. It uses a sparse, direct, Gauss elimination method</i>)</p> |

Table 1: Default ABAQUS parameters used for the simulation (Hibbitt, 2009).

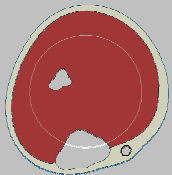
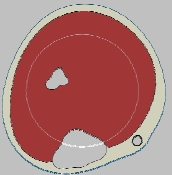
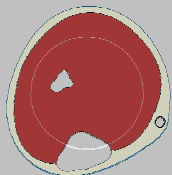
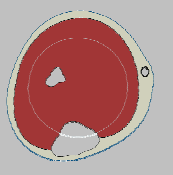
| Material | Model | Material parameters | Source |
|----------------------|---|---|---|
| Fat | Hyper-elastic Neo-Hookean | $C_{10} = 0.005 \text{ MPa}$ $D_1 = 0.14 \text{ MPa}^{-1}$ | Inverse identification (Dubuis et al., 2011) (Avril et al., 2010) |
| Muscle | Hyper-elastic Neo-Hookean | $C_{10} = 0.003 \text{ MPa}$ $D_1 = 0.14 \text{ MPa}^{-1}$ | (Dubuis et al., 2011) (Avril et al., 2010) |
| Skin | Hyper-elastic Neo-Hookean | $C_{10} = 0.1 \text{ MPa}$ $D_1 = 0.14 \text{ MPa}^{-1}$ | (Iivarinen et al., 2011) (Hendriks et al., 2006) |
| Muscular aponeurosis | Hyper-elastic Neo-Hookean | $C_{10} = 10 \text{ MPa}$ $D_1 = 80 \text{ MPa}^{-1}$ | (Wu, 2007) |
| Vein wall | Linearized (in standing and resting positions respectively) | $\nu = 0.49$ (fixed) | Inverse identification |
| MCS | Linear elastic | $E = 0.39$ $\nu = 0.49$ | SIGVARIS tensile test on 15-20 mmHg MCS and based on the French norm NF-G30-102 (AFNOR, 1986) |

Table 2: Material properties of the different constitutive parts of the model.

| Morphology of adipose tissue | | | | | | | | | | | | | | | | |
|---|---|------|----------|-------|---|------|----------|-------|---|------|----------|-------|---|------|----------|-------|
| |  | | | |  | | | |  | | | |  | | | |
| Note : all pressures given in mmHg | Reference configuration | | | | Geometry1 | | | | Geometry2 | | | | Geometry3 | | | |
| | Supine | | Standing | | Supine | | Standing | | Supine | | Standing | | Supine | | Standing | |
| Percentage circumferential reduction of the vein lumen | 10.0 | | 3.2 | | 10.1 | | 3.3 | | 10.2 | | 3.3 | | 10.3 | | 3.3 | |
| Average contact pressure at skin-sock interface | 17.3 | ±5.3 | 17.4 | ±5.8 | 17.3 | ±5.4 | 17.3 | ±6.0 | 17.4 | ±5.8 | 17.4 | ±6.1 | 17.4 | ±5.5 | 17.4 | ±6.0 |
| Mean trans-mural pressure in vein wall before EC | 11.0 | ±1.1 | 67.2 | ±5.4 | 11.0 | ±1.1 | 67.1 | ±5.5 | 11.0 | ±1.1 | 67.1 | ±5.7 | 11.0 | ±1.1 | 67.1 | ±6.0 |
| Mean decrease of trans-mural pressure in vein wall due to EC | 4.8 | ±2.5 | 12.3 | ±11.1 | 4.8 | ±2.7 | 12.2 | ±11.7 | 5.0 | ±2.5 | 12.6 | ±11.0 | 4.9 | ±2.6 | 12.5 | ±11.3 |
| Mean increase in hydrostatic pressure in fat due to EC | 19.8 | ±3.7 | 19.9 | ±6.6 | 19.7 | ±3.7 | 19.5 | ±6.4 | 19.6 | ±3.6 | 19.8 | ±5.8 | 19.2 | ±3.5 | 19.5 | ±5.7 |
| Maximum hydrostatic pressure in fat | 29.0 | | 39.3 | | 32.8 | | 44.0 | | 41.2 | | 43.8 | | 29.9 | | 39.3 | |

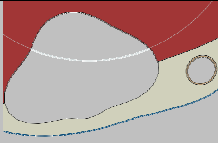
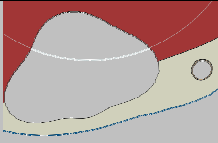
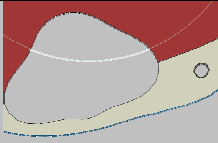
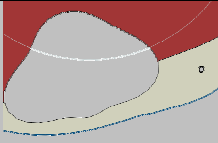
Note: average results given as *mean ± standard deviation*

Table A1: Ratio of adipose tissue to leg size

| Position of the vein on the leg contour |  | |  | |  | |  | | | | | | | | | |
|--|---|----------|---|----------|---|----------|---|----------|------|------|------|-------|------|------|------|-------|
| | Reference configuration | | Geometry1 | | Geometry2 | | Geometry3 | | | | | | | | | |
| Note : all pressures given in mmHg | Supine | Standing | Supine | Standing | Supine | Standing | Supine | Standing | | | | | | | | |
| Percentage circumferential reduction of the vein lumen | 10.0 | 3.2 | 11.0 | 3.5 | 12.3 | 4.0 | 10.7 | 4.0 | | | | | | | | |
| Average contact pressure at skin-sock interface | 17.3 | ±5.3 | 17.4 | ±5.8 | 17.3 | ±5.4 | 17.3 | ±6.0 | 17.4 | ±5.8 | 17.4 | ±6.1 | 17.5 | ±5.5 | 17.4 | ±6.1 |
| Mean trans-mural pressure in vein wall before EC | 11.0 | ±1.1 | 67.2 | ±5.4 | 11.0 | ±1.1 | 67.1 | ±5.4 | 11.0 | ±1.1 | 67.2 | ±5.6 | 11.0 | ±1.1 | 67.2 | ±5.6 |
| Mean decrease of trans-mural pressure in vein wall due to EC | 4.8 | ±2.5 | 12.3 | ±11.1 | 5.3 | ±2.1 | 13.2 | ±11.2 | 6.0 | ±3.5 | 14.9 | ±12.0 | 5.1 | ±2.9 | 14.9 | ±12.0 |
| Mean increase in hydrostatic pressure in fat due to EC | 19.8 | ±3.7 | 19.9 | ±6.6 | 21.4 | ±4.8 | 20.6 | ±7.0 | 23.1 | ±5.9 | 22.2 | ±7.1 | 21.1 | ±4.7 | 22.2 | ±7.1 |
| Maximum hydrostatic pressure in fat | 29.0 | | 39.3 | | 48.0 | | 48.0 | | 42.9 | | 54.9 | | 42.7 | | 54.9 | |

Note: average results given as *mean ± standard deviation*

Table A2: Position on the leg contour

| |  | |  | |  | |  | | | | | | | | | |
|---|---|------|--|-------|---|------|---|------|--------|------|----------|------|--------|------|----------|------|
| Initial vein c/s of vein lumen (in mm²) | 21.9 | | 11.2 | | 5.9 | | 1.0 | | | | | | | | | |
| Note : all pressures given in mmHg | Reference configuration | | Geometry1 | | Geometry2 | | Geometry3 | | | | | | | | | |
| | Supine | | Standing | | Supine | | Standing | | Supine | | Standing | | Supine | | Standing | |
| Percentage circumferential reduction of the vein lumen | 10.0 | | 3.2 | | 10.3 | | 3.4 | | 10.4 | | 3.5 | | 10.6 | | 3.6 | |
| Average contact pressure at skin-sock interface | 17.3 | ±5.3 | 17.4 | ±5.8 | 17.3 | ±5.5 | 17.4 | ±5.7 | 17.3 | ±5.6 | 17.3 | ±5.8 | 17.3 | ±5.7 | 17.3 | ±5.7 |
| Mean trans-mural pressure in vein wall before EC | 11.0 | ±1.1 | 67.2 | ±5.4 | 8.8 | ±0.7 | 63.5 | ±4.6 | 7.5 | ±0.6 | 61.2 | ±4.3 | 5.5 | ±0.4 | 57.6 | ±4.1 |
| Mean decrease of trans-mural pressure in vein wall due to EC | 4.8 | ±2.5 | 12.3 | ±11.1 | 5.3 | ±2.3 | 12.4 | ±9.7 | 5.6 | ±2.3 | 12.4 | ±8.9 | 5.9 | ±2.6 | 12.4 | ±8.5 |
| Mean increase in hydrostatic pressure in fat due to EC | 19.8 | ±3.7 | 19.9 | ±6.6 | 20.5 | ±3.7 | 20.5 | ±5.6 | 20.6 | ±3.8 | 20.9 | ±5.2 | 20.8 | ±3.5 | 21.1 | ±4.0 |
| Maximum hydrostatic pressure in fat | 29.0 | | 39.3 | | 29.7 | | 36.3 | | 33.4 | | 36.2 | | 33.6 | | 34.1 | |

Note: average results given as *mean ± standard deviation*

Table A3: Vein lumen size

| Distance to skin (mm) | 2.85 | | 1.96 | | 1.33 | | 0.39 | |
|---|-----------|------------|-------------------------|------------|-----------|------------|-----------|------------|
| Note : all pressures given in mmHg | Geometry1 | | Reference configuration | | Geometry2 | | Geometry3 | |
| | Supine | Standing | Supine | Standing | Supine | Standing | Supine | Standing |
| Percentage circumferential reduction of the vein lumen | 10.2 | 3.1 | 10.0 | 3.2 | 10.2 | 3.4 | 10.2 | 3.5 |
| Average contact pressure at skin-sock interface | 17.3 ±5.6 | 17.3 ±6.1 | 17.3 ±5.3 | 17.4 ±5.8 | 17.3 ±5.3 | 17.3 ±5.8 | 17.3 ±5.4 | 17.3 ±5.9 |
| Mean trans-mural pressure in vein wall before EC | 11.0 ±1.2 | 67.4 ±5.7 | 11.0 ±1.1 | 67.2 ±5.4 | 11.0 ±1.1 | 67.2 ±5.6 | 11.0 ±1.1 | 67.2 ±5.5 |
| Mean decrease of trans-mural pressure in vein wall due to EC | 4.8 ±2.9 | 11.9 ±11.6 | 4.8 ±2.5 | 12.3 ±11.1 | 4.9 ±2.5 | 12.8 ±11.5 | 4.9 ±3.3 | 13.4 ±12.5 |
| Mean increase in hydrostatic pressure in fat due to EC | 20.2 ±3.8 | 19.7 ±7.0 | 19.8 ±3.7 | 19.9 ±6.6 | 19.7 ±3.7 | 19.8 ±6.3 | 19.4 ±4.0 | 19.9 ±6.5 |
| Maximum hydrostatic pressure in fat | 32.9 | 44.4 | 29.0 | 39.3 | 29.4 | 41.8 | 32.7 | 66.2 |

Note: average results given as *mean ± standard deviation*

Table A4: Depth of vein in adipose tissue

| Mean external compression applied on skin (mmHg) | 17.4 | | 34.7 | | 52.0 | | 69.4 | | | | | | | | | |
|---|-------------------------|----------|-----------------|----------|-----------------|----------|-----------------|----------|------|-------|------|-------|-------|-------|-------|-------|
| Note : all pressures given in mmHg | Reference configuration | | Configuration 1 | | Configuration 2 | | Configuration 3 | | | | | | | | | |
| | Supine | Standing | Supine | Standing | Supine | Standing | Supine | Standing | | | | | | | | |
| Percentage circumferential reduction of the vein lumen | 10.0 | 3.2 | 16.8 | 5.7 | 22.4 | 7.9 | 27.4 | 10.0 | | | | | | | | |
| Average contact pressure at skin-sock interface | 17.3 | ±5.3 | 17.4 | ±5.8 | 34.7 | ±9.3 | 34.7 | ±9.8 | 52.0 | ±12.9 | 52.0 | ±13.4 | 69.3 | ±16.6 | 69.4 | ±17.2 |
| Mean trans-mural pressure in vein wall before EC | 11.0 | ±1.1 | 67.2 | ±5.4 | 11.0 | ±1.1 | 67.2 | ±5.4 | 11.0 | ±1.1 | 67.2 | ±5.4 | 11.0 | ±1.1 | 67.2 | ±5.4 |
| Mean decrease of trans-mural pressure in vein wall due to EC | 4.8 | ±2.5 | 12.3 | ±11.1 | 10.1 | ±4.5 | 23.7 | ±10.3 | 16.0 | ±8.3 | 34.8 | ±9.3 | 22.1 | ±14.4 | 45.8 | ±8.6 |
| Mean increase in hydrostatic pressure in fat due to EC | 19.8 | ±3.7 | 19.9 | ±6.6 | 37.2 | ±6.3 | 38.3 | ±7.7 | 54.3 | ±9.2 | 56.2 | ±8.6 | 71.2 | ±12.8 | 73.7 | ±9.7 |
| Maximum hydrostatic pressure in fat | 29.0 | | 39.3 | | 57.6 | | 59.8 | | 91.0 | | 91.1 | | 123.7 | | 119.9 | |

Note: average results given as *mean ± standard deviation*

Table A5: Effect of the applied external compression

| C₁₀ Fat (kPa) | 3 | | | | 5 | | | | 6 | | | | 7.5 | | | |
|---|-----------------|------|----------|-------|-------------------------|------|----------|-------|-----------------|------|----------|-------|-----------------|------|----------|-------|
| Note : all pressures given in mmHg | Configuration 1 | | | | Reference configuration | | | | Configuration 2 | | | | Configuration 3 | | | |
| | Supine | | Standing | | Supine | | Standing | | Supine | | Standing | | Supine | | Standing | |
| Percentage circumferential reduction of the vein lumen | 12.2 | | 3.3 | | 10.0 | | 3.2 | | 9.2 | | 3.1 | | 8.3 | | 3.0 | |
| Average contact pressure at skin-sock interface | 17.3 | ±4.9 | 28.7 | ±10.0 | 17.3 | ±5.3 | 17.4 | ±5.8 | 17.4 | ±5.5 | 17.4 | ±5.9 | 17.4 | ±5.7 | 17.3 | ±6.2 |
| Mean trans-mural pressure in vein wall before EC | 11.0 | ±1.1 | 67.3 | ±5.4 | 11.0 | ±1.1 | 67.2 | ±5.4 | 11.0 | ±1.1 | 67.2 | ±5.4 | 11.0 | ±1.1 | 67.2 | ±5.4 |
| Mean decrease of trans-mural pressure in vein wall due to EC | 6.4 | ±2.4 | 12.9 | ±10.9 | 4.8 | ±2.5 | 12.3 | ±11.1 | 4.3 | ±2.6 | 11.9 | ±11.1 | 3.7 | ±2.6 | 11.4 | ±11.2 |
| Mean increase in hydrostatic pressure in fat due to EC | 18.7 | ±3.0 | 19.1 | ±5.9 | 19.8 | ±3.7 | 19.9 | ±6.6 | 20.3 | ±4.1 | 20.2 | ±6.8 | 20.9 | ±4.7 | 20.5 | ±7.1 |
| Maximum hydrostatic pressure in fat | 27.6 | | 36.1 | | 29.0 | | 39.3 | | 29.9 | | 40.4 | | 32.1 | | 42.4 | |

Note: average results given as *mean ± standard deviation*

Table A6: Influence of the “type” of fat for the stiffness

| D₁ Fat (MPa⁻¹) | 0.005 | | | | 0.14 | | | | 1 | | | | 10 | | | |
|---|-----------------|------|----------|-------|-------------------------|------|----------|-------|-----------------|------|----------|-------|-----------------|------|----------|-------|
| Note : all pressures given in mmHg | Configuration 1 | | | | Reference configuration | | | | Configuration 2 | | | | Configuration 3 | | | |
| | Supine | | Standing | | Supine | | Standing | | Supine | | Standing | | Supine | | Standing | |
| Percentage circumferential reduction of the vein lumen | 10.0 | | 3.2 | | 10.0 | | 3.2 | | 10.0 | | 3.2 | | 10.0 | | 3.2 | |
| Average contact pressure at skin-sock interface | 17.4 | ±5.4 | 17.4 | ±5.9 | 17.3 | ±5.3 | 17.4 | ±5.8 | 17.4 | ±5.4 | 17.3 | ±5.8 | 17.3 | ±5.3 | 17.3 | ±5.4 |
| Mean trans-mural pressure in vein wall before EC | 11.0 | ±1.1 | 67.4 | ±5.4 | 11.0 | ±1.1 | 67.2 | ±5.4 | 11.0 | ±1.1 | 67.2 | ±5.4 | 11.0 | ±1.1 | 67.2 | ±5.4 |
| Mean decrease of trans-mural pressure in vein wall due to EC | 4.8 | ±2.5 | 12.2 | ±11.1 | 4.8 | ±2.5 | 12.3 | ±11.1 | 4.8 | ±2.5 | 12.3 | ±11.1 | 4.7 | ±2.7 | 12.0 | ±11.2 |
| Mean increase in hydrostatic pressure in fat due to EC | 19.8 | ±3.8 | 19.9 | ±6.6 | 19.8 | ±3.7 | 19.9 | ±6.6 | 19.6 | ±3.7 | 19.8 | ±6.6 | 18.4 | ±3.6 | 18.4 | ±6.1 |
| Maximum hydrostatic pressure in fat | 29.1 | | 39.1 | | 29.0 | | 39.3 | | 28.5 | | 38.9 | | 26.4 | | 36.1 | |

Note: average results given as *mean ± standard deviation*

Table A7: Influence of the “type” of fat for the incompressibility parameter

| Constitutive behaviour law for the vein wall | Bi-linear elastic model | | | | Neo-Hookean material behaviour law | | | |
|---|-------------------------|------|----------|-------|------------------------------------|------|----------|-------|
| Note : all pressures given in mmHg | Reference configuration | | | | | | | |
| | Supine | | Standing | | Supine | | Standing | |
| Percentage circumferential reduction of the vein lumen | 10.0 | | 3.2 | | 9.8 | | 3.2 | |
| Average contact pressure at skin-sock interface | 17.3 | ±5.3 | 17.4 | ±5.8 | 17.3 | ±5.3 | 17.3 | ±5.8 |
| Mean trans-mural pressure in vein wall before EC | 11.0 | ±1.1 | 67.2 | ±5.4 | 11.0 | ±1.3 | 67.1 | ±6.6 |
| Mean decrease of trans-mural pressure in vein wall due to EC | 4.8 | ±2.5 | 12.3 | ±11.1 | 5.3 | ±2.7 | 12.2 | ±12.4 |
| Mean increase in hydrostatic pressure in fat due to EC | 19.8 | ±3.7 | 19.9 | ±6.6 | 19.8 | ±3.7 | 19.9 | ±6.5 |
| Maximum hydrostatic pressure in fat | 29.0 | | 39.3 | | 29.0 | | 39.2 | |

Note: average results given as *mean ± standard deviation*

Table 8A:

| Element type used for the FE mesh | Normal formulation (CPE4, CPE3, T2D2) | | | | Reduced integration (CPE4R, CPE3, T2D2) | | | | Hybrid formulation and reduced integration (CPE4RH, CPE3H, T2D2H) | | | | Geometric order: Quadratic elements used instead of linear elements (CPE8, CPE6, T2D3) | | | |
|---|---------------------------------------|------|----------|-------|---|------|----------|-------|---|------|----------|-------|--|-------|----------|-------|
| | Supine | | Standing | | Supine | | Standing | | Supine | | Standing | | Supine | | Standing | |
| Percentage circumferential reduction of the vein lumen | 10.0 | | 3.2 | | 10.0 | | 3.2 | | 10.0 | | 3.2 | | 10.0 | | 3.2 | |
| Average contact pressure at skin-sock interface | 17.3 | ±5.3 | 17.3 | ±5.8 | 17.3 | ±5.3 | 17.3 | ±5.8 | 17.3 | ±5.3 | 17.4 | ±5.8 | 17.6 | ±6.0 | 17.6 | ±6.4 |
| Mean trans-mural pressure in vein wall before EC | 10.9 | ±1.1 | 67.1 | ±5.8 | 11.0 | ±1.1 | 67.2 | ±5.4 | 11.0 | ±1.1 | 67.2 | ±5.4 | 14.5 | ±1.2 | 88.3 | ±6.7 |
| Mean decrease of trans-mural pressure in vein wall due to EC | 5.9 | ±2.7 | 14.8 | ±13.1 | 4.8 | ±2.5 | 12.3 | ±11.1 | 4.8 | ±2.5 | 12.3 | ±11.1 | 6.3 | ±3.1 | 16.1 | ±13.0 |
| Mean increase in hydrostatic pressure in fat due to EC | 19.8 | ±3.8 | 19.9 | ±6.6 | 19.8 | ±3.7 | 19.9 | ±6.6 | 19.8 | ±3.7 | 19.9 | ±6.6 | 20.6 | ±16.6 | 20.4 | ±17.6 |
| Maximum hydrostatic pressure in fat | 29.2 | | 39.6 | | 29.1 | | 39.2 | | 29.0 | | 39.3 | | 286.0 | | 285.7 | |

Note : all pressures given in mmHg

Reference configuration

Note: average results given as *mean ± standard deviation*

Table A9

| Contact formulation for the interface Fat/Vein | Tie constraint | | | | Frictionless | | | | Friction - "Hard" contact contact pressure-overclosure relationship | | | | Friction - Exponential ("Soft") contact pressure-overclosure relationship | | | |
|---|-------------------------|------|----------|-------|--------------|------|----------|-------|---|------|----------|-------|---|------|----------|-------|
| | Reference configuration | | | | | | | | | | | | | | | |
| | Supine | | Standing | | Supine | | Standing | | Supine | | Standing | | Supine | | Standing | |
| Percentage circumferential reduction of the vein lumen | 9.9 | | 3.1 | | 10.1 | | 3.2 | | 10.1 | | 3.1 | | 10.1 | | 3.2 | |
| Average contact pressure at skin-sock interface | 17.3 | ±5.3 | 17.4 | ±5.8 | 17.3 | ±5.3 | 17.4 | ±5.8 | 17.3 | ±5.3 | 17.4 | ±5.8 | 17.3 | ±5.3 | 17.4 | ±5.8 |
| Mean trans-mural pressure in vein wall before EC | 11.0 | ±1.1 | 67.2 | ±5.4 | 10.8 | ±1.1 | 67.2 | ±5.4 | 10.9 | ±1.1 | 67.2 | ±5.4 | 9.8 | ±0.9 | 64.6 | ±5.1 |
| Mean decrease of trans-mural pressure in vein wall due to EC | 4.7 | ±2.5 | 12.0 | ±11.0 | 5.2 | ±2.3 | 12.8 | ±12.0 | 5.1 | ±1.9 | 12.4 | ±11.3 | 5.6 | ±1.6 | 12.7 | ±10.6 |
| Mean increase in hydrostatic pressure in fat due to EC | 19.5 | ±3.7 | 19.7 | ±6.5 | 19.9 | ±4.8 | 20.0 | ±4.9 | 19.8 | ±4.5 | 19.8 | ±5.5 | 20.0 | ±4.6 | 20.1 | ±5.6 |
| Maximum hydrostatic pressure in fat | 36.5 | | 39.4 | | 35.2 | | 35.6 | | 34.9 | | 37.0 | | 29.8 | | 38.0 | |

Note: average results given as *mean ± standard deviation*

Table A10

| Contact formulation for the interface Fat/Muscle | Tie constraint | | | | Frictionless | | | | Friction - "Hard" contact contact pressure-overclosure relationship | | | | Friction - Exponential ("Soft") contact pressure-overclosure relationship | | | |
|---|----------------|------|----------|-------|--------------|------|----------|-------|---|------|----------|-------|---|------|----------|-------|
| | Supine | | Standing | | Supine | | Standing | | Supine | | Standing | | Supine | | Standing | |
| Note : all pressures given in mmHg | | | | | | | | | | | | | Reference configuration | | | |
| Percentage circumferential reduction of the vein lumen | 9.9 | | 3.2 | | 10.0 | | 3.0 | | 9.9 | | 3.1 | | 10.0 | | 3.2 | |
| Average contact pressure at skin-sock interface | 17.3 | ±5.3 | 17.4 | ±5.8 | 17.3 | ±5.3 | 17.4 | ±5.8 | 17.3 | ±5.3 | 17.4 | ±5.8 | 17.3 | ±5.3 | 17.4 | ±5.8 |
| Mean trans-mural pressure in vein wall before EC | 11.0 | ±1.1 | 67.3 | ±5.4 | 11.0 | ±1.1 | 67.2 | ±5.4 | 11.0 | ±1.1 | 67.2 | ±5.4 | 11.0 | ±1.1 | 67.2 | ±5.4 |
| Mean decrease of trans-mural pressure in vein wall due to EC | 4.8 | ±2.5 | 12.3 | ±11.1 | 4.6 | ±2.6 | 11.1 | ±11.2 | 4.7 | ±2.5 | 12.0 | ±11.0 | 4.8 | ±2.5 | 12.3 | ±11.1 |
| Mean increase in hydrostatic pressure in fat due to EC | 19.6 | ±4.3 | 20.0 | ±7.0 | 19.4 | ±3.6 | 18.7 | ±6.4 | 19.5 | ±3.7 | 19.7 | ±6.5 | 19.8 | ±3.7 | 19.9 | ±6.6 |
| Maximum hydrostatic pressure in fat | 39.7 | | 39.5 | | 31.8 | | 38.8 | | 36.5 | | 39.4 | | 29.0 | | 39.3 | |

Note: average results given as *mean ± standard deviation*

Table A11

| Contact formulation for the interface Skin/MCS | Tie constraint | | Frictionless | | Friction - "Hard" contact contact pressure-overclosure relationship | | | | Friction - Exponential ("Soft") contact pressure-overclosure relationship | | | | |
|---|--|----------|--------------|------------|---|------------|-----------|------------|---|-------------------------|--|--|--|
| | Supine | Standing | Supine | Standing | Supine | Standing | Supine | Standing | Supine | Standing | | | |
| Note : all pressures given in mmHg | | | | | | | | | | Reference configuration | | | |
| Percentage circumferential reduction of the vein lumen | | | 10.0 | 3.0 | 9.9 | 3.1 | 10.0 | 3.2 | | | | | |
| Average contact pressure at skin-sock interface | | | 17.3 ±5.3 | 17.4 ±5.8 | 18.8 ±23.3 | 18.8 ±23.5 | 17.3 ±5.3 | 17.4 ±5.8 | | | | | |
| Mean trans-mural pressure in vein wall before EC | Not relevant because loading of the leg is done by simulating the contact between the MCS and the skin | | 11.0 ±1.1 | 67.2 ±5.4 | 11.0 ±1.1 | 67.2 ±5.4 | 11.0 ±1.1 | 67.2 ±5.4 | | | | | |
| Mean decrease of trans-mural pressure in vein wall due to EC | | | 4.6 ±2.6 | 11.1 ±11.2 | 4.7 ±2.5 | 12.0 ±11.0 | 4.8 ±2.5 | 12.3 ±11.1 | | | | | |
| Mean increase in hydrostatic pressure in fat due to EC | | | 19.4 ±3.6 | 18.7 ±6.4 | 19.5 ±3.7 | 19.7 ±6.5 | 19.8 ±3.7 | 19.9 ±6.6 | | | | | |
| Maximum hydrostatic pressure in fat | | | 31.8 | 38.8 | 36.5 | 39.4 | 29.0 | 39.3 | | | | | |

Note: average results given as *mean ± standard deviation*

Table A12