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Aurélien Macron, Hélène Pillet, Jennifer Doridam, Isabelle Rivals, Mohammad Javad Sadeghinia, et al.. Is a simplified Finite Element model of the gluteus region able to capture the mechanical response of the internal soft tissues under compression?. *Clinical Biomechanics*, 2020, 71, pp.92-100. 10.1016/j.clinbiomech.2019.10.005 . hal-02332239

HAL Id: hal-02332239

<https://hal.science/hal-02332239>

Submitted on 24 Oct 2019

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1 **Is a simplified Finite Element model of the**
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4 **compression?**

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15

16

17 Keywords: Deep Tissue Injury; Pressure Ulcer; Subject specific; Buttock, Sitting, Finite Element Analysis

18

19 Word count: (Abstract: 210 words; Main text: 3856 words)

20 Original Article Submission (less than 4000 words), Word count (introduction through conclusion): 3827

21

22 **Abstract**

23 *Background:* Internal soft tissue strains have been shown to be one of the main factors responsible for the
24 onset of Pressure Ulcers and to be representative of its risk of development. However, the estimation of this
25 parameter using Finite Element (FE) analysis in clinical setups is currently hindered by costly acquisition,
26 reconstruction and computation times. Ultrasound (US) imaging is a promising candidate for the clinical
27 assessment of both morphological and material parameters.

28 *Method:* The aim of this study was to investigate the ability of a local FE model of the region beneath the
29 ischium with a limited number of parameters to capture the internal response of the gluteus region predicted
30 by a complete 3D FE model. 26 local FE models were developed, and their predictions were compared to those
31 of the patient-specific reference FE models in sitting position.

32 *Findings:* A high correlation was observed ($R= 0.90$, $p\text{-value} < 0.01$). A sensitivity analysis showed that the
33 most influent parameters were the mechanical behaviour of the muscle tissues, the ischium morphology and
34 the external mechanical loading.

35 *Interpretation:* Given the progress of US for capturing both morphological and material parameters, these
36 results are promising because they open up the possibility to use personalised simplified FE models for risk
37 estimation in daily clinical routine.

38

39

40 Introduction

41 Pressure Ulcers (PU) are painful, slow-healing wounds that develop during periods of prolonged
42 immobility, and that are likely to deteriorate the quality of life of people with poor mobility and sensitivity.
43 They can develop either superficially and progress inward or initiate at the deep tissues and progress outward
44 (called Deep Tissue Injury) depending on the nature of the surface loading (Bouten et al., 2003). The first type
45 is predominantly caused by shear stresses and is fairly easily detected and treated before it becomes
46 dangerous. The latter type, caused by sustained compression of the tissue, originates subcutaneously,
47 generally close to bony prominences (NPUAP/EPUAP, 2009). Although DTI represents a small proportion of
48 PUs (<10%) this latter type is considered especially harmful because layers of muscle, fascia, and
49 subcutaneous tissue may suffer substantial necrosis equivalent to a category III or IV PU with variable
50 prognosis.

51 Since the pioneer work of (Daniel et al., 1981; Kosiak, 1961; Reswick and Rogers, 1976) establishing
52 the dependence of PU development on both external pressure and time, interface pressure mapping has been
53 widely used in PU prevention. Although clinically useful, interface pressure monitoring is not predictive
54 enough of the risk of PU development. Indeed, it is now indisputable that there are at least two damage
55 mechanisms, which play an important role in PU development (Oomens et al., 2015): (i) mechanically induced
56 capillary occlusions that lead to low oxygen concentration in the tissue triggering a cascade of inflammatory
57 signals that culminate in ulceration (Gawlitza et al., 2007; Kosiak, 1959; Loerakker et al., 2011; Sree et al.,
58 2019a). This process can occur even for very small values of soft tissue strain and takes several hours before
59 the first signs of cell damage can be detected (Breuls et al., 2003; Loerakker et al., 2010; Stekelenburg et al.,
60 2007, 2006). (ii) "direct deformation damage" involving cells damage by direct (shear) deformation (Breuls et
61 al., 2003; Ceelen et al., 2008; Stekelenburg et al., 2006). This damage can be evident when the threshold for
62 deformation damage exceeds the normal physiological values experienced in daily life and can be detected in
63 a period of minutes (Ceelen et al., 2008; Loerakker et al., 2010). In addition, microclimate (skin surface
64 temperature and skin moisture) is also suspected to play a key role in PU causation (Gefen, 2011; Zeevi et al.,
65 2017) but the extent of the contribution and its interaction with sustained tissue deformations have yet to be
66 quantified.

67 Estimating the internal mechanical conditions within loaded soft tissues has the potential of
68 improving the management and prevention of PU and several Finite Element (FE) models have been
69 developed for more than 20 years to bridge the gap between external pressures and internal strains (Al-Dirini
70 et al., 2016; Linder-Ganz et al., 2009; Luboz et al., 2017; Moerman et al., 2017). Along these lines, we recently
71 proposed a new methodology to build a 3D patient-specific FE model based on the combination of ultrasound
72 (US), bi-planar x-ray radiographies and optical scanner (Macron et al., 2018) to estimate internal strains in
73 sitting position. However, the clinical use of such models is currently hindered by costly acquisition,
74 reconstruction and computation times. In contrast, there is a consensus in the results reported in the
75 literature that the clinically relevant mechanical response is localised under the ischium. This strongly
76 suggests that a local model of the soft tissue under the ischium could account for the major part of the
77 mechanisms. Recent evidence also suggest that response to damage, as observed by MRI, starts at some
78 distance from the deformation (Nelissen et al., 2018), highlighting the importance of evaluating the
79 mechanical response in 3 dimensions.

80 Only a few contributions have tried to explore this avenue in the literature. In 2011, Portnoy et al.
81 developed a simple 2D analytical model (Portnoy et al., 2011) based on the Hertz contact model. Promising
82 results have been reported regarding the comparison between the maximal Von Mises stress estimated by
83 their local model and that predicted by a full 3D FE model developed by Linder-Ganz (Linder-Ganz et al.,
84 2008a). In a sample of 11 healthy subjects, a Pearson correlation of 0.4 was obtained. However, the
85 consistency of the results can be expected to be improved by adding complementary parameters that have
86 been identified as predominant in the internal mechanical response of the ischial region, such as the radius of
87 the ischium (Agam and Gefen, 2007) and the mechanical behaviour of the soft tissue (Luboz et al., 2014).
88 Moreover, shear strains estimations also seem essential and were not reported in their work. Thus, there is a
89 need to extend this analytical approach to a more comprehensive model of the behaviour of the soft tissue in
90 the ischial region with the additional constraint that it should be based on parameters that can be routinely
91 obtained in a clinical environment.

92 At the same time, recent studies showed the potential of US imaging for the characterization of
93 morphological parameters. In a recent paper, Akins et al. reported that the measurement of the adipose and
94 muscle tissue thicknesses in the vicinity of the ischium using US was both reliable (ICC = 0.948) and highly

95 correlated with MRI assessment ($r = 0.988$ and 0.894 for the muscle and the adipose tissues
96 respectively)(Akins et al., 2016). On the contrary, the measurement of the radius of curvature of the ischium
97 was reported to have a poor inter operator reliability be it using US (ICC = -0.028) (Akins et al., 2016) or MRI
98 (ICC = 0.214) (Swaine et al., 2017). However, there is a high interest in the community for developing both the
99 US system (Bercoff et al., 2004; Gennisson et al., 2013, 2010) and clinical protocols that are suited to reliable
100 parameter assessment (Swaine et al., 2017). Similar efforts are also being made to characterize material
101 parameters (Makhsous et al., 2008). This makes US a promising candidate to substitute MR imaging for
102 clinically feasible assessment of both morphological and material parameters needed for the prevention of PU.

103 In this perspective, we propose here to evaluate the ability of a local model of the region beneath the
104 ischium to capture the maximum shear strain inside the muscle tissue. This evaluation will be made by
105 comparing the response provided by this model to the one predicted by a previously developed complete 3D
106 FE model of the buttock (Macron et al., 2018). In addition, the relative impact of the different parameters on
107 the local model response will be analysed.

108

109 **Methods**

110 For the sake of clarity, the experimental material and the construction of the reference FE model (Macron
111 et al., 2018) are briefly recalled hereunder in section 1.

112 **-1- Reference FE model**

113 13 subject-specific FE models (8 men and 5 women; age: 26 ± 5 yrs, weight: 70 ± 9 kg, BMI: 22.6 ± 3.4
114 kg/m^2) models (reference) were generated from previous experiments detailed in (Macron et al., 2018).

115 3D reconstruction of the pelvis was performed from biplanar X-rays in an unloaded sitting position. The
116 external envelope was reconstructed from the optical scan acquisition, and the adipose tissue thickness was
117 directly measured on the US image in the unloaded configuration.

118 The skin, fat and muscle tissues were each modelled with a first order Ogden hyperelastic material model
119 (Simo and Taylor, 1991). Material parameters for the skin were based on values reported in the literature
120 (Luboz et al., 2014). For the fat and the muscle, α was arbitrarily fixed to 5 (Oomens et al., 2016) and the shear
121 modulus μ was calibrated using Finite Element Updating to fit the experimental ischial tuberosity sagging
122 (Macron et al., 2018). The shear moduli of the adipose and muscle tissue will subsequently be referred to as
123 μF and μM .

124 For the boundary conditions, all the degrees of freedom (DOF) of the pelvis were fixed except the vertical
125 displacement. The experimental vertical force measured in the loaded sitting position was applied at the
126 centre of mass of the pelvis.

127 The nodes at the different interfaces (bone/muscle, muscle/fat, and fat/skin) of the model were tied. A
128 friction contact between the rigid plane and the skin surface was defined using a penalty algorithm. The
129 friction coefficient was set to 0.4 (Al-Dirini et al., 2016).

130 **-2- Local FE model**

131 **a. Extraction of model parameters**

132 The parameters necessary for the construction of the local FE model were quantified for the 13
133 subjects.

134 Two radii of curvature were calculated from the 3D pelvis reconstruction. For each side of the pelvis,
135 the extreme node of the surface mesh with the lowest vertical coordinate was identified. A region of interest
136 containing all the nodes at less than 8 mm of the extreme node was then defined. Several planes containing
137 the vertical direction were generated. The orientation of their normal vectors was distributed between 0 and
138 170 degrees by 10 degree increments. Each plane intersected the region of interest and allowed to define a set
139 of nodes which were used to extract a radius from a circular regression. The minimal radius obtained across
140 the planes is called ***R1***. The radius of curvature ***R2*** in the orthogonal plane was then extracted.

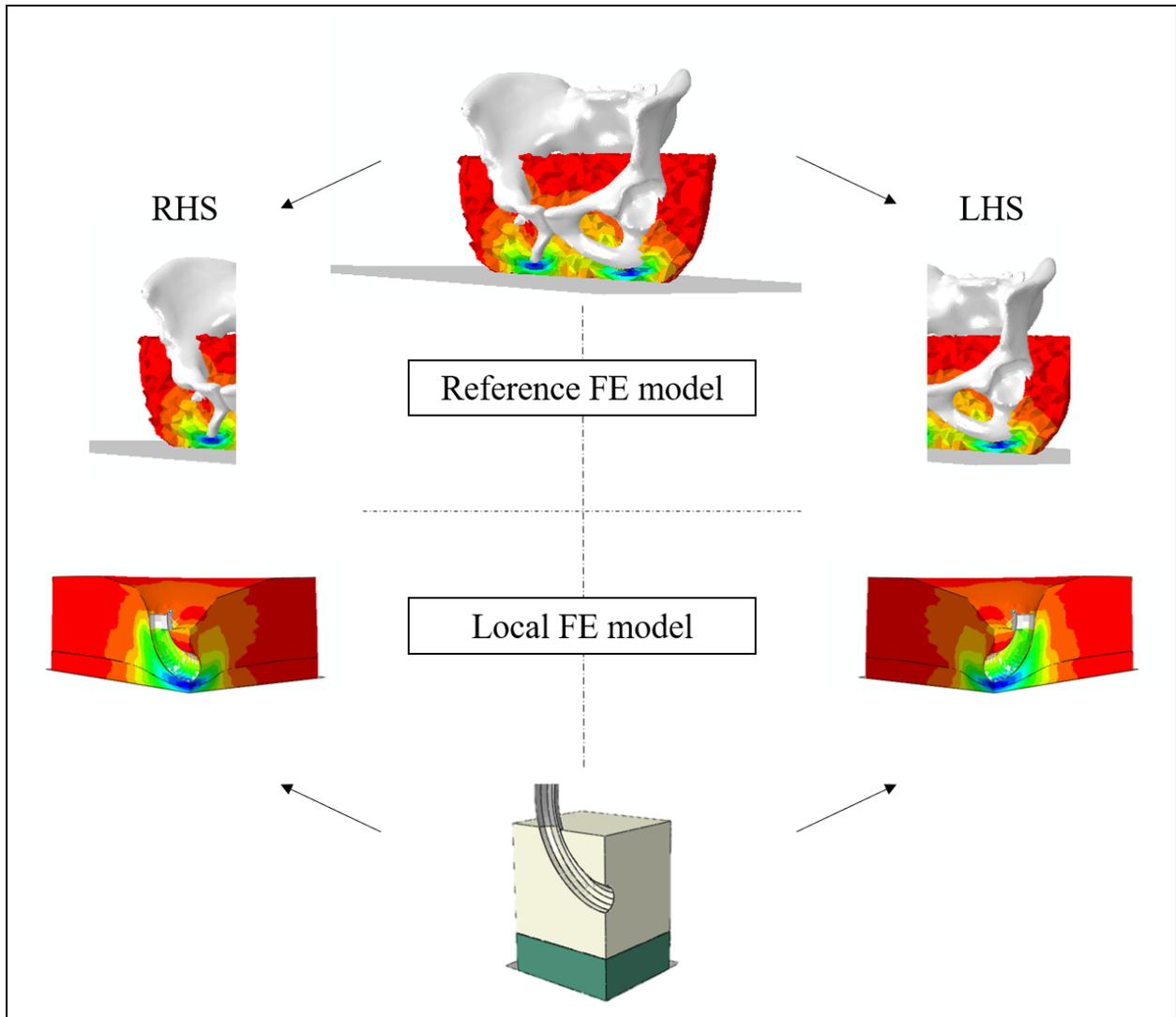
141 The fat thickness ***eF*** was extracted from the US image in the unloaded sitting position. The total
142 subdermal soft tissue thickness under the ischium was extracted from the sagittal x-ray image in the unloaded
143 sitting position, and the muscle thickness ***eM*** was calculated as the difference between the total thickness and
144 the fat thickness.

145 The static contact pressure distribution at the skin/seat interface computed by the reference FE
146 model in the loaded sitting position was used to extract the net reaction force. The pressure distribution was
147 first interpolated over a regular grid with 1 mm spatial resolution. The contact pressure of the nearest FE
148 surface node of the reference model was assigned to each point of the grid. The nodal vector force associated
149 to each grid node was then computed by multiplying the nodal pressure with the surface area (1 mm²). A net
150 reaction force ***F*** was calculated as the vector sum of the nodal forces on the left-hand side (LHS) and right-
151 hand side (RHS).

152 To summarize, seven parameters were considered: ***μF, μM, R1, R2, eF, eM, F***.

153 **b. Finite Element modelling**

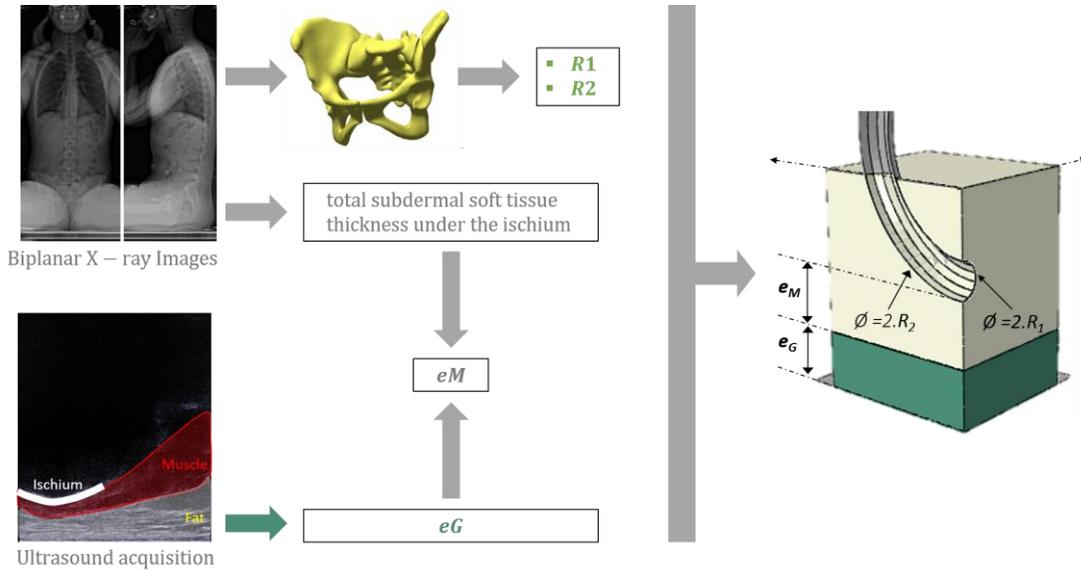
154 26 local FE models were developed to represent the mechanical response of the LHS and RHS of the
155 13 patient-specific reference FE models (Figure 1).



156

157 *Figure 1: Reference FE model (top) and associated LHS and RHS local FE models (bottom) for one subject.*

158 The local FE model geometry is presented in Figure 2. The ischial tuberosity is represented by a torus
 159 generated by the revolution of a parametric curve C containing a portion of a circle of radius $R2$ swept by a
 160 semi-disc of radius $R1$. A box of height h , length L and width L was defined to represent the whole subdermal
 161 soft tissue (fat + muscle). A convergence study showed that, above an L/h ratio of 2, the solution was not
 162 affected. A boolean operation was performed to subtract the ischium from the soft tissue volume. A skin layer
 163 of 1 mm thickness was defined. A rigid horizontal plane was created to model the seat support.



164

165 *Figure 2: Local FE model geometry generated from the 4 geometric parameters $R1$, $R2$, eF , eM extracted from the ultrasound*
 166 *and bi-planar x-ray images. The ischial tuberosity is represented by a torus generated by the revolution of a circle of radius $R1$*
 167 *(minor radius of the torus) around a portion of a circle of radius $R2$ (major radius of the torus). eM and eF are used to define*
 168 *the muscle and fat thicknesses respectively.*

169 The soft tissues were meshed using linear tetrahedral elements with hybrid formulation (C3D4H) in
 170 ABAQUS Finite Element Analysis software (ABAQUS Inc., Providence, RI, USA). The pelvis was assumed to be
 171 rigid and meshed with triangular shell elements. The same constitutive laws and material parameters as those
 172 defined in section 1 for the reference FE model were used for each subject. Likewise, for the boundary
 173 conditions, all the DOF of the ischium were fixed except the vertical displacement. The force F was applied to
 174 the ischium. Only a quarter of the model was considered and the remainder was completed using the
 175 symmetry constraints (Figure 2).

176 c. Quantity of interest

177 The strains were post-processed from the principal stretches λ_i ($i = 1,2,3$). Based on these, the
 178 principal Green-Lagrange strains were calculated as: $E_i = \frac{(\lambda_i^2 - 1)}{2}$ and the principal shear strains were then
 179 computed as:

$$180 E_{shear} = \frac{1}{2} * \max(|E_1 - E_2|, |E_2 - E_3|, |E_3 - E_1|)$$

181 The third principal strain component E_3 corresponds to the principal compressive strain. This quantity
 182 will be referred to hereafter as E_{comp} .

183 In line with (Bucki et al., 2016; Luboz et al., 2017), a “cluster analysis” was performed to investigate
184 volumes of the model that are in given intervals of maximum shear strain. Clusters were defined as the union
185 of adjacent elements verifying the following criteria: (i) E_{shear} above 75% and (ii) E_{comp} above 45%. These
186 correspond to the damage thresholds reported by (Ceelen et al., 2008) for the muscle tissue. However, unlike
187 (Bucki et al., 2016) who investigated the response in both muscle and fat, only the muscle tissue was
188 investigated here.

189 To be able to compare our results with those of the literature, the **Engineering** strain was defined as
190 follows: $\varepsilon_i = \lambda_i - 1$. ~~The reason for using Cauchy's strain definition instead of the standard Green-Lagrange~~
191 ~~strain definition is that the latter poorly describes large compression (with a maximum compressive strain~~
192 ~~limit of 50%).~~ As previously, the principal shear strains were computed from the principal **Engineering**
193 strains:

$$194 \quad \varepsilon_{shear} = \frac{1}{2} * \max(|\varepsilon_1 - \varepsilon_2|, |\varepsilon_2 - \varepsilon_3|, |\varepsilon_3 - \varepsilon_1|)$$

195 For the reference FE model, the maximum principal shear strain $\varepsilon_{max} = \max(\varepsilon_{shear})$ in the cluster
196 with the largest volume inside the muscle tissue was extracted and analysed. For the local FE model, the
197 maximum principal shear strain $\varepsilon_{max} = \max(\varepsilon_{shear})$ was computed from the elements inside the muscle
198 tissue and on the axis of symmetry.

199 **-3- Correlation between the reference and the local model**

200 The correlation between the maximum principal shear strain predictions of the reference and local FE
201 models was quantified with Pearson's correlation coefficient on the 13 patients (left and right).

202 **-4- Sensitivity Analysis of the local model**

203 In order to investigate the impact of the input parameters (**$R1$, $R2$, eM , eF , μM , μF and F**) on the
204 maximum shear strain predicted by the local model, we chose to emulate the latter with a polynomial model.
205 using the same parameters. The ranges over which the $m = 7$ parameters were to be varied were defined
206 between their minimum and maximum value observed in the 13 subjects (LHS and RHS), see Table 1. After
207 normalization in $[-1; 1]$, experimental points were chosen according to a three-level full factorial design
208 resulting in 3^7 combinations (*i.e.* 2187 FE model simulations).

Table 1: Levels of the parameters used for the sensitivity analysis.

Parameter	Level of the parameter		
	Min Level (-1)	Mid-Level	Max Level (+1)
R1	5 (mm)	7 (mm)	9 (mm)
R2	15 (mm)	39 (mm)	63 (mm)
eM	19 (mm)	29 (mm)	39 (mm)
eG	9 (mm)	22 (mm)	35 (mm)
uM	1.0 (kPa)	4.5 (kPa)	8.0 (kPa)
uG	2.8 (kPa)	5.4 (kPa)	8.0 (kPa)
F	48 (N)	77.5 (N)	107 (N)

210

211 The output of the local FE model being noiseless, there is in principle no lower bound to the mean
 212 squared residuals of candidate models other than zero. In the following, the use of a polynomial model of
 213 degree at most equal to two will used:

$$214 \quad y(\theta) = \theta_0 + \sum_{i=1}^m \theta_i x_i + \sum_{i=1}^m \theta_{ii} (x_i)^2 + \sum_{i=1}^m \sum_{j>i} \theta_{ij} x_i x_j$$

215 The maximum value of two for the degree will be justified in section 2 of the results using the errors of the
 216 local FE model with respect to the reference FE model obtained on the 13 subjects (left and right).

217 The sensitivity of the model to each input (linear term, square, order-two interaction) can be simply
 218 defined as the percentage of variance due to this input. Assuming the parameters (**R1**, **R2**, **eM**, **eF**, **uM**, **uF** and
 219 **F**) independent and uniformly distributed in [-1, 1] (i.e. with second and fourth order moments of respectively
 220 1/3 and 4/45), we have:

$$221 \quad \begin{cases} s_i = \text{var}(q_i x_i) = q_i^2 \text{var}(x_i) = q_i^2 \times \frac{1}{3} \\ s_{ii} = \text{var}(q_{ii} x_i^2) = q_{ii}^2 \text{var}(x_i^2) = q_{ii}^2 \times \frac{4}{45} \\ s_{ij} = \text{var}(q_{ij} x_i x_j) = q_{ij}^2 \text{var}(x_i) \text{var}(x_j) = q_{ij}^2 \times \frac{1}{9} \\ \text{var}(y) = \sum_{i=1}^m s_i + \sum_{i=1}^m s_{ii} + \sum_{i=1}^m \sum_{j>i} s_{ij} \end{cases}$$

222 For the degree 1 model, the sensitivity to the i-th parameter is hence given by the following percentage:

223

$$S_i = \frac{s_i}{\text{var}(y)} = \frac{q_i^2}{\hat{\sigma}^2 q_i^2}$$

224 For the degree 2 model, the sensitivities to the i-th parameter and to its interaction with parameter j are given

225 by the percentages:

226

$$S_i = \frac{s_i + s_{ij}}{\text{var}(y)}, S_{ji} = \frac{s_{ij}}{\text{var}(y)}$$

227

Results

229 -1- Subjects and parameters

230 The values of the parameters for the 13 modelled subjects are reported in Table 2 below for each side.

231 The simulation of the local FE model corresponding to the LHS of subject #8 did not converge.

232 *Table 2: Characteristics of subjects for each side (right and left). The LHS of subject #8 is indicated in a different color because*
 233 *the simulation of the local FE model did not converge.*

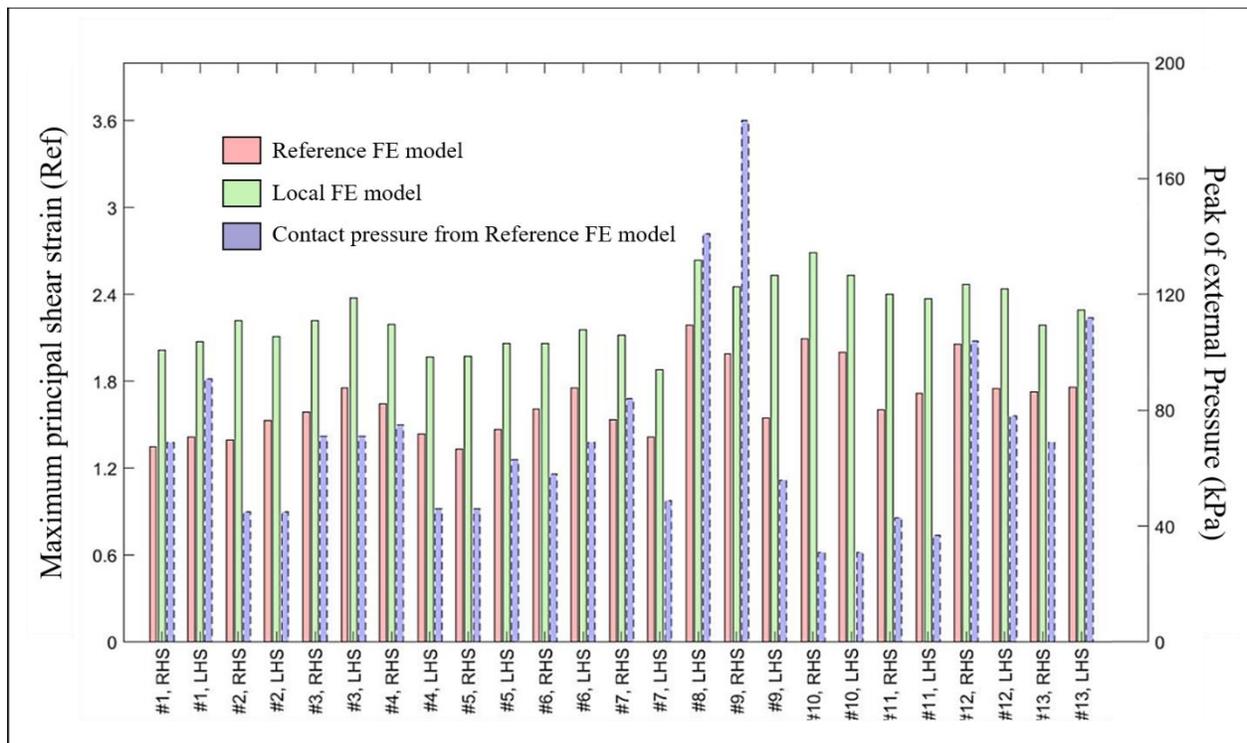
Subject	Side	R1 (mm)	R2 (mm)	eM (mm)	eF (mm)	μM (kPa)	μF (kPa)	F (N)
#1	R	6.9	19.7	28	10	8.00	5.00	196
	L	7.1	22.8	31	10	8.00	5.00	258
#2	R	6.9	20.3	26	33	4.80	3.75	251
	L	6.9	20.8	27	33	4.80	3.75	251
#3	R	8.5	18.9	31	19	6.25	3.75	324
	L	7.2	19.1	26	19	6.25	3.75	378
#4	R	7.0	24.8	26	14	8.00	6.25	329
	L	7.3	28.8	25	14	8.00	6.25	237
#5	R	6.7	20.3	21	11	8.00	2.75	194
	L	6.8	22.2	21	11	8.00	2.75	218
#6	R	6.9	22.8	21	25	8.00	8.00	244
	L	7.0	21.5	24	25	8.00	8.00	334
#7	R	7.0	29.9	28	9	8.00	2.75	302
	L	8.9	15.2	33	9	8.00	2.75	211
#8	R	6.7	18.1	29	22	1.00	4.50	246
	L	7.2	21.3	29	22	1.00	4.50	288
#9	R	7.3	30.3	19	35	4.50	2.75	429
	L	6.5	63.3	29	35	4.50	2.75	232
#10	R	5.5	52.1	36	23	2.75	4.50	268
	L	7.1	21.0	39	23	2.75	4.50	211
#11	R	7.0	24.0	38	30	6.25	6.25	296

	L	7.8	21.0	38	30	6.25	6.25	387
#12	R	4.8	30.2	22	16	4.50	2.75	305
	L	5.3	34.9	24	16	4.50	2.75	251
#13	R	7.3	27.1	22	12	6.25	4.50	223
	L	7.4	33.0	22	12	6.25	4.50	242

234

235 **-2- Maximum shear strains and external pressures**

236 The bar plot below (Figure 3) summarizes the maximum principal shear strains estimated by the
 237 reference FE model and the local FE model for each subject and for each side (right and left). In addition, the
 238 external pressure is also plotted with a secondary axis.

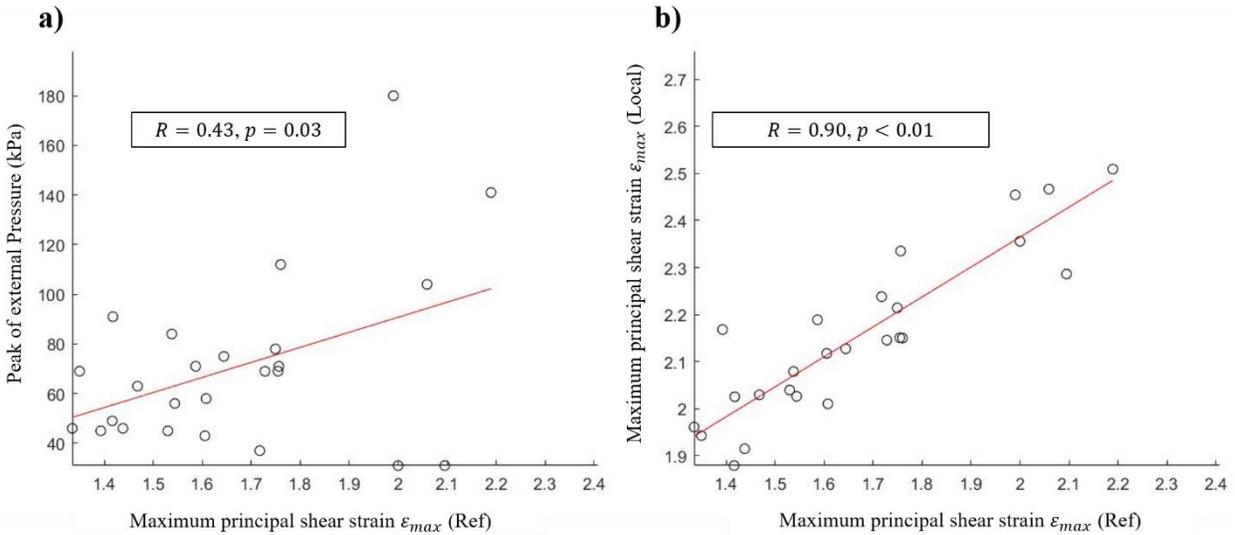


239

240 *Figure 3: Bar plots representing the maximum shear strains estimated by the local FE model (green) and the reference FE*
 241 *model (red), and the external pressure (blue).*

242 As shown on figure 3, the external pressure is poorly correlated to the maximum principal shear
 243 strain estimated by the two FE models. For example, subject #10 endures a low pressure on both sides, but
 244 suffers high internal strains. On the contrary, subject #1's left side shows a high pressure associated to a small
 245 internal strain.

246 Pearson's correlation coefficient between ϵ_{max} estimated by the reference and local FE models was
 247 0.90 ($p < 0.01$). In contrast, Pearson's correlation coefficient between ϵ_{max} estimated by the reference model
 248 and the external pressure was 0.43 ($p = 0.03$).



249
 250 *Figure 4: (a) maximum principal shear strains estimated by the reference FE model versus external pressure for the thirteen*
 251 *subjects, (b) maximum principal shear strains estimated by the reference FE model versus the predictions of the local FE*
 252 *model.*

253 The results depicted in figure 4(b) show a high linear correlation between the local FE model and the
 254 reference FE model, but a poor agreement: the mean squared error between reference and local model
 255 predictions equals 0.25. *Note that for the sensitivity analysis using a polynomial model emulating the local FE*
 256 *models, since their outputs are noiseless, we need a lower limit for the mean square error between local model*
 257 *and polynomial outputs for the choice of the adequate polynomial complexity. Since even a constant model has*
 258 *smaller mean squared residuals (0.075) than the local FE models, their mean square error of 0.25 cannot be used*
 259 *to select the degree of the polynomial model emulating the local model.*

260 However, considering the good linear correlation between the local and the reference model, we can
 261 compute the mean squared error obtained after regressing the reference model on the local one, which
 262 represents the error achieved by the local model if it were in agreement with the reference model. Thus, it
 263 provides a lower limit for the mean squared residuals of candidate polynomial models for the emulation of the
 264 local FE model. Numerically, this corrected mean squared error equals $5.7 \cdot 10^{-3}$.

265 **-3- Sensitivity analysis**

266 Out of the 2187 simulations, 239 did not converge (11%). A possible reason may be the chosen values for
 267 the minimum and maximum parameter values, the minimum muscle shear modulus value in particular.
 268 Indeed, a single experimental measure was used to calibrate the material properties of both muscle and
 269 adipose tissues by an inverse method. Using the remaining simulations, the coefficients of the degree 1 and
 270 degree 2 models were estimated with ordinary least squares. The first order sensitivities to the 7 parameters
 271 obtained with the linear model are given in Table 3, in decreasing order of sensitivity.

272

273

274

Table 3 First order sensitivities to the 7 parameters in decreasing order of magnitude.

parameters	coefficient θ_i	Si (%)
μM	-0.1770	38
$RCCI2$	-0.1604	31
F	+0.1226	18
$RCCI1$	-0.1092	10
eM	+0.0213	0.55
eF	+0.0184	0.41
μG	-0.0178	0.39

275

276 The mean squared residuals of the linear model ($2.0 \cdot 10^{-2}$) largely exceeded the corrected mean squared error
 277 of $5.7 \cdot 10^{-3}$ obtained with the comparison to the reference model, so that first order sensitivities might not
 278 capture the complexity of the local FE model. Thus, we computed the sensitivities obtained with the second-
 279 degree model, see Table 4. Since its mean squared residuals ($3.9 \cdot 10^{-3}$) are close to the corrected mean
 280 squared error, this model is neither too simple, nor excessively complex. Note that, due to the missing data
 281 corresponding to the simulations that did not converge, the experiment matrix is not strictly orthogonal,
 282 hence the slight modification of the linear coefficients θ_i when adding the interactions and the squared terms.

283

Table 4 Second-order sensitivities (> 1%) in decreasing order of magnitude.

parameters	coefficients θ_1, θ_{ii} or θ_{ij}	S_i (%)
μM	-0.1662, -0.0547	33
$RCCI2$	-0.1632, +0.0985	29
F	+0.1068, -0.0425	16
$RCCI1$	-0.0817, + 0.0223	8.9
$\mu M * eM$	-0.1153	4.5
$\mu M * F$	+0.1080	3.7
$\mu M * eF$	-0.0607	1.3

284

285

286 Discussion

287 The aim of this study was to investigate the ability of a local model of the region beneath the ischium
288 to capture the internal response of the buttock soft tissues predicted by a complete 3D FE model from a
289 limited number of parameters. Our long term ambition is to take advantage of the potential of basic US for the
290 measurement of both morphological and material parameters in daily clinical routine. To this end, we also
291 investigated the relative impact of the main parameters reported in the literature to drive the internal
292 response of the soft tissues.

293 The analysis of the results obtained in this contribution shows the biomechanical response of the
294 internal soft tissues predicted by a local FE model in 13 subjects is similar to the one predicted by the
295 complete and complex reference 3D FE model (Pearson coefficient of 0.90 and p-value < 0.01). Previous
296 attempts to develop and evaluate simplified models built from a limited number of parameters have been
297 reported in the literature (Agam and Gefen, 2007; Oomens et al., 2003; Portnoy et al., 2011). Some of these
298 models focused on analytical solutions of the Hertz contact problem to predict both the peak interface contact
299 pressure at the bone/muscle interface (Agam and Gefen, 2007) and the internal von Mises soft tissue stresses
300 (Portnoy et al., 2011), and displayed a relatively good agreement with patient-specific FE von Mises stresses
301 published by Linder-Ganz et al. on the same 11 patients ($R = 0.4$) with a relatively low computation time
302 facilitating real-time operation and portability. However, they rely on important assumptions: elasticity of the
303 two contacting bodies, relatively small area of contact in comparison to the size of the geometry modelled.
304 These assumptions particularly hinder models ability to estimate shear strain in the soft tissue, identified as
305 the primary cause of soft tissue breakdown in both animal models and tissue engineered constructs at the cell
306 level. The high correlation obtained in our contribution between the local FE model and the reference FE
307 model for the estimation of the principal shear strain is very promising because, for the first time , it allows to
308 consider the use of such personalised simplified models in daily clinical setup. Moreover, the results obtained
309 in this study confirmed previous observations reported in the literature that external contact pressures are
310 poorly correlated ($R=0.43$, $p=0.3$) to the internal local strains endured by soft tissues (Bouten et al., 2003;
311 Chow and Odell, 1978; Dabnichki et al., 1994; Luboz et al., 2014).

312 The sensitivity analysis establishes that the most influential parameter is the mechanical behaviour of
313 the muscle soft tissue, which is in agreement with the conclusion of (Luboz et al., 2014). In particular, the
314 authors observed that a variation of Young's modulus of the muscle between 40kPa and 160 kPa resulted in a
315 variation of the maximum Von Mises strain of 38.5%. In our study, the shear modulus of the muscle explained
316 33 % of the internal soft tissue response variance. We also observed that changing the mechanical properties
317 of the underlying adipose tissue did not influence the mechanical response of the muscle tissue. This had
318 already been reported by (Oomens et al., 2003). **From a clinical perspective, this result supports recent**
319 **findings that SCI patients with fat infiltration, scarring or spasms puts them at a higher risk for DTI because of**
320 **increased internal loads in the gluteus muscles in the vicinity of the ischial tuberosities during sitting (Sopher**
321 **et al., 2011).** The maximum shear strain in the muscle tissue is also very sensitive (29%) to the radius of
322 curvature (R2) in the plane perpendicular to the shortest radius of curvature (R1) referred to as radius of
323 curvature in the long axis by (Swaine et al., 2017). This result could be expected because in indentation-like
324 configurations, the geometry of the indenter is known to have a paramount importance. This observation
325 could explain the increasing enthusiasm of the community for the measurement of this anatomical feature-
326 related risk factor using medical imaging (Akins et al., 2016; Linder-Ganz et al., 2008a; Swaine et al., 2017). In
327 the literature however, only (Swaine et al., 2017) represented the ischium using two radii of curvature. Our
328 results confirm that this is essential to consider the variability along both axes in order to properly capture
329 the mechanical response of the soft tissue. The external force explains 16% of the variability of the response.
330 Unlike the other parameters, its measurement is relatively easy even in clinical routine. A particular attention
331 should be paid to the extraction of the force that is transferred to the ischium from the global measurement
332 base on pressure mattresses. Adding the smallest radius of curvature to the above list of parameters allows to
333 explain 82% of the total variability of the mechanical response.

334 The remaining 18% are mainly explained by the interaction between muscle mechanical behavior
335 and (1) muscle thickness (4.5%), (2) external force (3.7%), and (3) fat thickness (1.3%). Thus, considering a
336 fixed muscle mechanical behavior, an increase of the maximum shear strain will result from an increase in the
337 external force and/or a decrease in the muscle and fat thicknesses. This is consistent with the results reported
338 by (Oomens et al., 2003; Portnoy et al., 2011).

339 Limitations and perspectives of this work are detailed herein. **First**, the fact that local shear strains
340 predicted by the local FE model are all higher than those predicted by the reference FE model strains points at
341 a systematic error. This may be partly due to the fact that approximating the ischial tuberosity by a torus is
342 too gross and leads to biases in the mechanical response. Examination of the ischial tuberosities on the US
343 images revealed that some subjects roughly had a triangular bore rather than a circular bore in shape. As
344 discussed above, in indentation-like configurations, the geometry of the indenter is known to have a
345 paramount importance. As far as the authors are aware of, analysis of the inter-individual variations of the
346 morphological cross section of the ischial tuberosity has never been investigated before and further work is
347 required to improve the geometric approximation of the ischial tuberosity from US images. The systematic
348 error also suggests that, in addition to the choice of the geometric approximation of the ischial tuberosity,
349 other factors involved in the definition and measurement of the principal shear strain in the local FE model
350 might be lacking, their identification requiring further work. **Second**, the extraction of the material properties
351 using an inverse identification method (for which the optimal parameters are obtained by minimizing the
352 distance between experimental measures and numerical results), although popular for lower limb soft tissues
353 (Affagard et al., 2015; Frauziols et al., 2016; Macron et al., 2018; Rohan et al., 2014; Sadler et al., 2018), is not
354 compatible with clinical implementation because of lengthy solver times for the models and the need for a
355 trained user to develop and interpret the FE model. Ultrasound Elastography, and, in particular, Supersonic
356 Shear Imaging (SSI) technique, is emerging as an innovative tool that could provide a quantitative evaluation
357 of biomechanical properties of soft tissues (Eby et al., 2013; Gennisson et al., 2010; Haen et al., 2017; Vergari
358 et al., 2014). However, to our knowledge and to date, no correlation has been done between shear moduli
359 obtained by Shear Wave Elastography and mechanical properties from classic ex vivo mechanical testing
360 methods. The development of surrogate models that allow equivalent predictions to single FEA solutions,
361 across a broad population with sufficiently reduced computational expense for clinical use (Steer et al., 2019)
362 is a promising alternative that will be explored in future work. **Third**, the strain damage thresholds (above
363 75% and above 45%) reported in the literature for tissue injury (motivated by the work of (Ceelen et al.,
364 2008; Loerakker et al., 2011) come from animal models and should be *considered* with some caution since
365 they might not be relevant for humans. Very recently, in an attempt to elucidate the soft tissue injuries leading
366 from pressure-driven ischemia, a computational model linking microvascular collapse to tissue hypoxia in a

367 multiscale model of pressure ulcer initiation has been proposed (Sree et al., 2019a, 2019b) in the context of
368 pressure ulcer formation. These types of models, coupled with recent improvements in ultrasound imaging
369 technologies that allow to measure tissue perfusion in clinical routine, constitute opportunities for elucidating
370 some of the scientific challenges associated with the *customization* of the injury thresholds.

371 In the present contribution, the authors have used a multimodal approach based on B-mode
372 ultrasound images and low-dose biplanar X-ray images in a non-weight-bearing sitting posture for the fast
373 generation of patient-specific FE models of the buttock. Compared to previously conducted, MRI-based
374 computational models (Al-Dirini et al., 2016; Levy et al., 2017; Levy and Gefen, 2017; Linder-Ganz et al.,
375 2007a, 2008b, 2009; Moerman et al., 2017; Sopher et al., 2010; Zeevi et al., 2017), our protocol suffers from a
376 number of limitations including the poor visibility of B-mode ultrasound for viewing the organization and
377 composition of the buttock soft tissues (muscle groups, tendon, fat pads and ligament borders) and the limited
378 field of view of B-mode ultrasound. However, most MRI-based computational models in the literature model
379 these as a single homogenous material to allow for convergence of tissue geometry and, therefore, clearly fail
380 to take advantage of the capacity of MRI to differentiate between the individual soft tissue structures.
381 Moreover, long acquisition times of MR imaging prevent the representation of a realistic unloaded sitting
382 position without resorting to devices such as: rubber tires (Linder-Ganz et al. 2007), inclined plane (Al-Dirini
383 et al. 2016) and thigh and arms supports (Call et al., 2017). On the contrary, the proposed protocol allows to
384 reproduce the unloaded sitting position easily. Finally, acknowledging the fact that mechanical strains are
385 responsible for deformation-induced damage involved in the initiation of Deep Tissue Injury (DTI), a better
386 assessment of the internal behavior could enable to enhance the modeling of the transmission of loads into
387 the different structures composing the buttock. If MRI is a potential tool for the quantitative evaluation of
388 subdermal soft tissue strains, it has important drawbacks including long acquisition time, examination cost
389 and confined environment. A contrario, in a recent publication (Doridam et al., 2018), we showed the
390 feasibility of using B-mode ultrasound imaging for the quantification of internal soft-tissue strains of buttock
391 tissues in two perpendicular planes during sitting. Further research is currently under progress to develop
392 and validate computational modeling based on ultrasound data alone. This would make additional DTI
393 research more accessible and attainable, and would allow for translational development of future patient-
394 specific risk assessment tools.

395 This work proposed a promising new step towards estimating internal mechanical conditions within
396 loaded soft tissues from data potentially compatible with daily clinical routine. While additional experimental
397 validation is required for the design of appropriate protocols for the robust extraction of both the
398 morphological parameters of interest and the characterization of the mechanical behavior of the soft tissue of
399 interest, this work opens a way to overcome the barriers to clinical implementation of biomechanical metrics
400 as surrogates for improving the management and prevention of PU including difficulty in obtaining imaging
401 data.

402

403 **Author contributions statement**

404 AM, HP and PYR contributed to the conception and design of the study; JD, MJS and AM performed experiment
405 and data collection; IR performed the statistics. All the authors contributed to data interpretation and
406 preparation of the manuscript. All authors approved the final version of the manuscript.

407

408 **Conflict of interest statement**

409 The authors certify that no conflict of interest is raised by this work.

410 **Acknowledgments**

411 This work was supported by the Fondation de l'Avenir (grant number AP-RM-2016-030), by la Fondation des
412 Arts et Métiers and the Fonds de dotation Clinatéc. The authors are also grateful to the ParisTech BiomecAM
413 chair program on subject-specific musculoskeletal modelling.

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